

Recommendations for Screening, Testing and Management of Blood Donors and Blood and Blood Components Based on Screening Tests for Syphilis

Guidance for Industry

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**U.S. Department of Health and Human Services
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Center for Biologics Evaluation and Research
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Recommendations for Screening, Testing and Management of Blood Donors and Blood and Blood Components Based on Screening Tests for Syphilis

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Note: Changes have been made to update the guidance of the same title dated September 2014, including:

- Revised the recommended deferral period following treatment for syphilis or gonorrhea to 3 months;
- Added a recommendation for reentry of donors with false positive screening test results who are subsequently determined to have never had a diagnosis of syphilis;
- Removed the recommendation for donors to provide written evidence of completion of syphilis treatment prior to reentry;
- Updated Code of Federal Regulation citations to reflect current requirements; and
- Made editorial or formatting changes.

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This guidance represents 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

We, FDA, are providing you, blood establishments that collect Whole Blood or blood components, including Source Plasma, with recommendations for screening and testing of donors and management of donations based on screening tests for syphilis. Syphilis is a relevant transfusion-transmitted infection (Title 21 Code of Federal Regulations (CFR) 630.3 (h)(1)(v)). Licensed blood establishments must report the implementation of the recommendations contained in this guidance in accordance with 21 CFR 601.12.¹

This guidance updates the guidance of the same title dated September 2014. The September 2014 guidance finalized the draft guidance of the same title dated March 2013, and superseded the memorandum dated December 12, 1991, entitled “Clarification of FDA Recommendations for Donor Deferral and Product Distribution Based on the Results of Syphilis Testing.”

In general, FDA’s guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe 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.

¹ Licensed blood establishments that implement the revised recommendations for donor deferral and reentry provided in this updated guidance document, dated December 2020, must report the changes to FDA in an annual report under 21 CFR 601.12(d), noting the date the process was implemented.

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II. BACKGROUND

A. Transfusion-Transmission of Syphilis

Syphilis, caused by the spirochete *Treponema pallidum* (*T. pallidum*), is most often acquired after sexual contact with an infected individual. Syphilis can also be transmitted from mother to child or, rarely, transmitted by transfusion of blood or blood components from donors with active syphilis (Ref. 1). The last reported case of transfusion-transmitted syphilis in the United States (U.S.) occurred in 1966 (Ref. 2). Universal testing of blood donors may have played a role in the disappearance of transfusion-transmitted syphilis. Other possible explanations for the decline in transfusion-transmitted syphilis include: that direct donor-to-recipient transfusions no longer take place; inactivation of *T. pallidum* (a cold-sensitive microorganism) in refrigerated blood components; the decline in rates of syphilis in the general population, which in turn is reflected in the donor population; self-deferral of blood donors who are ill during spirochetemia (presence of spirochetes—the causative agent of syphilis infection—in the circulating blood); screening and deferral of potential donors who report high risk behavior for acquiring syphilis infection (e.g., persons who received money, drugs, or other payment for sex); wide use of antibiotics among transfusion recipients; and difficulties in diagnosing transfusion-transmitted syphilis in recipients (Ref. 3). However, none of these explanations has been quantified or adequately validated.

Information from the American Red Cross on serological testing of donors revealed that there were 324 cases of syphilis infections among American Red Cross repeat allogeneic donors in 2007-2008, a figure several times higher than the numbers of repeat allogeneic donors identified with human immunodeficiency virus (HIV), hepatitis B virus (HBV), hepatitis C virus (HCV), and human T-cell lymphotropic virus (HTLV) infections, which were 92, 47, 127 and 9, respectively, during the same time period (Ref. 4). Several published studies (Refs. 5 through 9) that investigated the presence or absence of *T. pallidum* nucleic acid in blood samples from individuals with confirmed or possible syphilis detected spirochete nucleic acid in blood samples from persons with syphilis, some of whom had a latent infection with no symptoms. Another study failed to confirm that finding (Ref. 10). This suggests that some asymptomatic blood donors might have spirochetemia. Donations from such blood donors might have the potential to transmit syphilis to recipients. Although syphilis testing has a low sensitivity and positive predictive value as a surrogate marker for detecting known transfusion-transmitted viruses, in 2009, the American Red Cross published data (Ref. 11) indicating that there were significantly higher rates of HIV-, HCV-, HBV-, HBsAg (hepatitis B surface antigen)-, and HTLV-positive donations among donors with positive syphilis test results compared to donors with negative syphilis test results.

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B. Testing of Blood and Blood Components for Syphilis

Current testing requirements for syphilis are found in 21 CFR 610.40(a)(2). Individuals who test reactive² with a screening test for syphilis must be deferred (21 CFR 610.41(a)) and notified of their deferral (21 CFR 630.40). You must further test each donation found to be reactive by a donor screening test, except you are not required to perform further testing of a donation found to be reactive by a treponemal screening test for syphilis (21 CFR 610.40 (e)). Additional testing to requalify the donor in accordance with (21 CFR 610.41(b)) is recommended in sections IV.B and C of this document. In accordance with (21 CFR 610.40(h)(2)(vi)), FDA allows use of blood and blood components, excluding Source Plasma, that test reactive by a screening test for syphilis, if the donation is further tested by an adequate and appropriate test which demonstrates that the reactive screening test is a biological false-positive and the blood or blood component is labeled with both test results. Under 21 CFR 610.40(h)(2)(vii), you may use Source Plasma from a donor who tests reactive by a screening test for syphilis, if the donor meets the requirements of 21 CFR 640.65(b)(2).

FDA requirements regarding syphilis testing specific to Source Plasma are as follows:

1. Current collection, testing and labeling requirements related to results of serologic tests are found in 21 CFR 640.65 (b) and 606.121.
2. A sample of blood must be drawn from Source Plasma donors on the day of the first medical examination or plasmapheresis, whichever comes first, and at least every 4 months thereafter, and these samples must be tested for syphilis (21 CFR 640.65(b)(1)(i)).
3. A donor with a reactive test result for syphilis must not be plasmapheresed again until the donor tests nonreactive, except as stated in points 4 and 5, below (21 CFR 640.65(b)(2)(ii)).
4. A donor with a reactive biologic false-positive syphilis test result may be plasmapheresed, provided that the donor's file: (a) identifies the reactive serologic test and the results used to confirm the biologic false-positive results; and (b) indicates that the physician on the premises has determined the false-positive reaction is not the result of an underlying disorder that would disqualify the donor from participating in the plasmapheresis program (21 CFR 640.65(b)(2)(iii)).
5. A donor with a reactive syphilis test result may be plasmapheresed only to obtain plasma to be used for further manufacturing into control serum for the serologic test for syphilis, provided that: (a) the physician on the premises

² The term "reactive" includes "repeatedly reactive" results. You should follow the instructions in the package insert of the assay you are using.

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approves the donation; and (b) the donor's file contains a signed statement from a physician or clinic establishing that treatment for syphilis has commenced and that continuance in the plasmapheresis program will not interfere with or jeopardize the syphilitic donor's treatment (21 CFR 640.65(b)(2)(iv)).

6. Plasma collected from a donor with a reactive test result for syphilis must be appropriately labeled, as stated in 21 CFR 606.121(e)(5)(iv).

III. CHARACTERISTICS OF SEROLOGIC ASSAYS FOR SYPHILIS

There are two different types of serologic assays for syphilis: (A) nontreponemal assays; and (B) treponemal assays.

(A) *Nontreponemal assays*, such as the rapid plasma reagin (RPR) test, the venereal disease research laboratory (VDRL) test, and the automated reagin test (ART), are non-specific tests that detect "reagin" antibodies directed against an antigen called cardiolipin that is present in a variety of tissues. Antibodies to cardiolipin appear in the serum of persons with active syphilis or with other medical conditions. However, some individuals who were previously infected with syphilis but successfully treated maintain low levels of antibody to cardiolipin for a long time.

Sera and plasma from individuals previously infected with syphilis who were successfully treated do not generally remain reactive in nontreponemal tests for more than one to two years after successful treatment. Therefore, persons with active or recently treated syphilis infections generally have reactive results with nontreponemal tests, while uninfected persons or persons successfully treated years earlier usually have nonreactive nontreponemal test results. Nontreponemal assays are useful in identifying recent syphilis infection, and to monitor the progression of syphilis and response to antibiotic therapy.

(B) *Treponemal assays* include enzyme immunoassays (EIA), fluorescent treponemal antibody "absorbed" assays (FTA-ABS), *Treponema pallidum* microhemagglutination assays (MHA-TPA) and *Treponema pallidum* particle agglutination assays (TP-PA). Treponemal assays test for antibodies to antigens that are specific to treponemes. Treponemal assays are most useful in identifying recent and past syphilis infections. They are not generally useful in monitoring the response to antibiotic therapy. With some exceptions, positive results of tests for specific treponemal antibodies remain positive throughout an individual's life regardless of whether the individual is currently infected or has been cured following successful treatment (Ref. 12). Retesting sera that are reactive in nontreponemal assays using a specific treponemal test is valuable in distinguishing true-positive results that indicate active syphilis infection from biological false-positive results due to other conditions.

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Since both the nontreponemal and treponemal assays detect antibodies rather than the infectious treponemes themselves, neither assay reliably identifies patients in the “window period” of very early syphilis, after infection has been acquired but before antibodies to either treponemal antigens or to cardiolipin have appeared.

Many blood establishments use automated treponemal assays with high throughput that have been cleared by FDA for purposes of screening donors for syphilis, such as the treponemal assays EIA, MHA-TPA and TP-PA (Ref. 13). However, some blood establishments might be using a nontreponemal assay as a screening test for syphilis. Therefore, we are providing recommendations for management of donors and blood and blood components for situations in which a blood establishment would use either a nontreponemal screening test or a treponemal screening test.

To distinguish the results of screening tests for syphilis from the results of additional syphilis tests, we use the terms “reactive” and “nonreactive” for results of screening tests (both nontreponemal and treponemal) and reserve the terms “positive” and “negative” for results of further testing using treponemal tests (used for donor counseling and requalification) on samples of the same blood specimen previously used for screening. A test result that is read as “indeterminate,” “questionable,” or equivocal” according to the package insert should be considered as equivalent to a reactive test result (for screening tests) or positive test result (for subsequent treponemal tests) for purposes of this guidance document.

Establishments that screen donors using a nontreponemal assay as the test of record may use a treponemal diagnostic test for the purposes of further testing under 21 CFR 610.40(e), donor reentry under 21 CFR 610.41(b), and also for demonstrating that a reactive screening test result is a biological false-positive (21 CFR 610.40(h)(2)(vi)).

IV. RECOMMENDATIONS FOR DONOR TESTING AND MANAGEMENT AND PRODUCT DISPOSITION WHEN USING TESTS FOR SYPHILIS

A. Identification of Donors with a History of Syphilis

1. To assess the eligibility of the donor as required in 21 CFR 630.10(e), we recommend that you assess donors for a history of syphilis or gonorrhea or treatment for syphilis or gonorrhea in the past 3 months.
2. We recommend that you defer for 3 months after completion of treatment, an individual with a history of syphilis or gonorrhea or treatment for syphilis or gonorrhea in the past 3 months. After this 3 -month period, the individual may be eligible to donate provided the individual meets all donor eligibility criteria.

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B. Donor Testing and Management When Using a Nontreponemal Screening Test as the Test of Record for the Detection of Syphilis (See Figure 1)

You must test each donation of blood and blood components for syphilis using a serological test (21 CFR 610.40 (a)(2)). You must test a donor of Source Plasma for syphilis at least every 4 months (21 CFR 640.65(b)(1)(i)). You must use a serological screening test for syphilis cleared by FDA for such use (21 CFR 640.10(b)).

1. If the nontreponemal screening test is nonreactive, the donor is considered to be negative for syphilis infection. You may release the donation, provided it meets all donation suitability requirements, and retain the donor.
2. If the nontreponemal screening test is reactive, you must defer the donor indefinitely (21 CFR 610.41(a)), unless evaluated for reentry, following the method described below. However, Source Plasma donors may be allowed to donate plasma for further manufacture into noninjectable products (21 CFR 640.65(b)(2)(ii) through (iv)).

You must perform further testing as required in 21 CFR 640.10(e) to provide additional information concerning the reactive donor's infection status.

You must not ship or use the donation, unless an exception for shipment or use is applicable (21 CFR 610.40(h)). As provided in 21 CFR 610.40 (h)(2)(vi) and (vii), you may use the donation when a negative treponemal test result is obtained using the method described below.

Product Management and Reentry under 21 CFR 610.41(b) of Deferred Donors

3. If the nontreponemal test is reactive, you may perform a treponemal test³ using either a sample from the index donation or a follow-up sample from the donor collected at a later date.
 - a. If the treponemal test result is negative (suggesting that the reactive nontreponemal test result is a biological false-positive result), you may reenter the donor under 21 CFR 610.41(b).

If the sample tested was from the index donation, the donation, excluding Source Plasma, may be released (21 CFR 610.40(h)(2)(vi)), provided the donation meets all other suitability requirements, and must be appropriately labeled under 21 CFR 610.40(h)(2)(vi) and 21 CFR 606.121. Under 21 CFR 610.40(h)(2)(vii), you may use Source Plasma from a

³ Establishments may use a treponemal diagnostic test for further testing (21 CFR 610.40(e)), donor reentry (21 CFR 610.41(b)) or for demonstrating that the reactive screening test is a biological false-positive (21 CFR 610.40(h)(2)(vi)).

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donor who tests reactive by a screening test for syphilis, if the donor meets the requirements of 21 CFR 640.65(b)(2)(ii)-(iv).

You may consider counseling the donor about the potential medical significance of a biological false-positive screening test.

- b. If the treponemal test result is positive, you must continue to defer the donor indefinitely (21 CFR 610.41(a)) unless evaluated for reentry.

You must discard the donation unless an exception for shipment or use is applicable (21 CFR 610.40(h)).

You may reenter the donor under 21 CFR 610.41(b) if the donor subsequently reports being treated for syphilis, provided that the treatment was successful and completed at least 3 months before the next donation; and the donor meets all donor eligibility criteria.

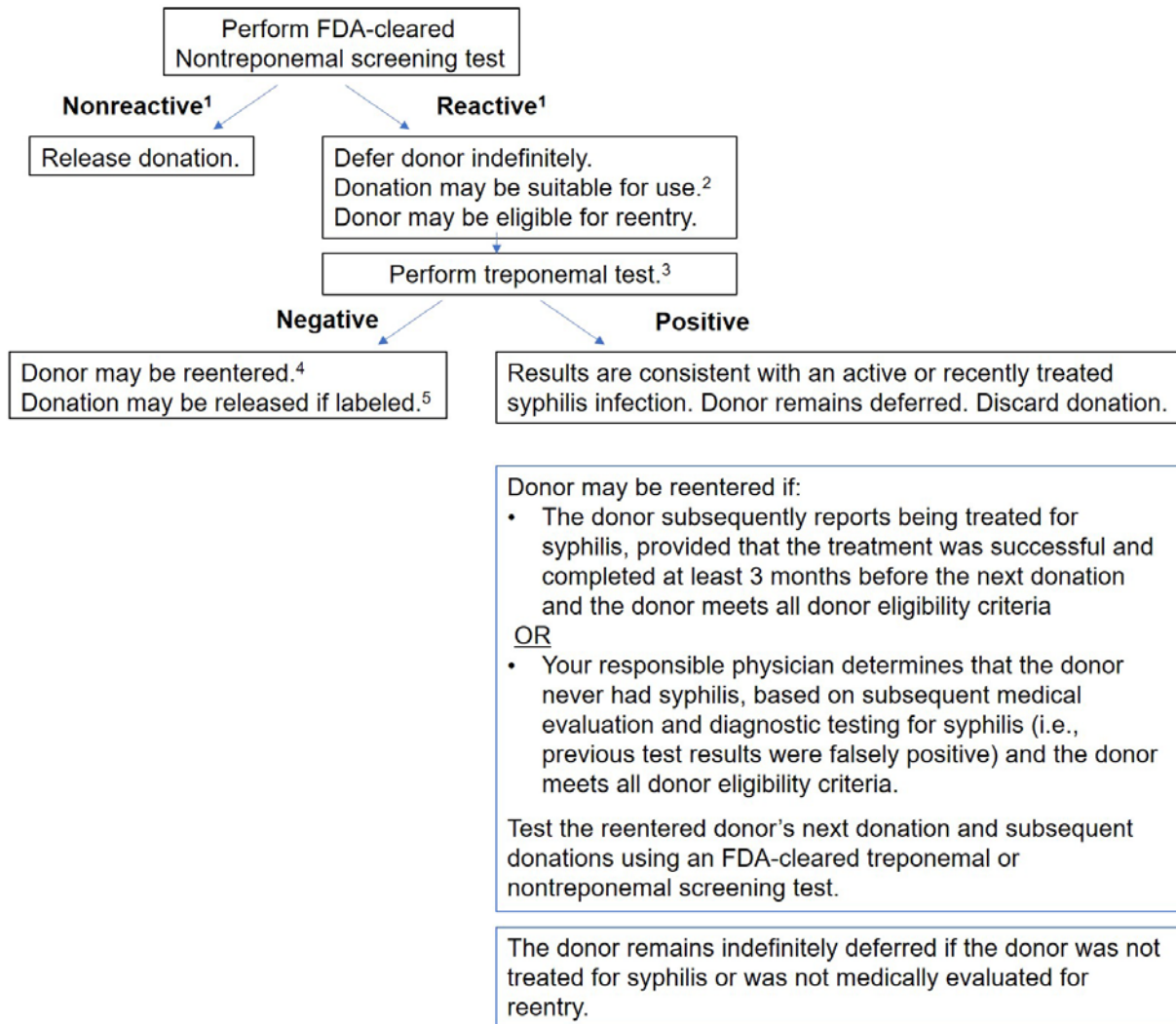
Alternatively, the donor may be reentered without treatment if your responsible physician determines that the donor never had syphilis based on subsequent medical evaluation and diagnostic testing for syphilis (i.e., the screening results were falsely positive), and the donor meets all donor eligibility criteria.

You may use either an FDA-cleared nontreponemal screening test or an FDA-cleared treponemal screening test to test the reentered donor's subsequent donations.

The donor remains indefinitely deferred if the donor was not treated for syphilis or was not medically evaluated for reentry.

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Figure 1: Donor Testing and Management When Using a Nontreponemal Screening Test as the Test of Record for the Detection of Syphilis



¹The term “reactive” includes “repeatedly reactive” results. You should follow the instructions in the package insert of the assay you are using.

²Source Plasma donations with these test results may be used under some circumstances, but the donor must be deferred unless certain conditions apply (21 CFR 610.40(h)(2)(vii)) and 21 CFR 640.65(b)(2)(ii) through (iv)). Other donations must not be used unless a negative treponemal test result is obtained or another exemption under (21 CFR 610.40(h)(2)) applies.

³You may use a treponemal diagnostic test for further testing (21 CFR 610.40(e)), donor reentry (21 CFR 610.41(b)) and for demonstrating that the reactive screening test is a biological false-positive (21 CFR 610.40(h)(2)(vi)).

⁴Consider counseling the donor about the possible medical significance of a biological false-positive result.

⁵Sample tested must be from the index donation. Excluding Source Plasma, you must label such donations as reactive by a screening test for syphilis and negative by a treponemal test (21 CFR 610.40(h)(2)(vi)). Under 21 CFR 610.40(h)(2)(vii), you may use Source Plasma from a donor who tests reactive by a screening test for syphilis, if the donor meets the requirements of 21 CFR 640.65(b)(2)(ii)-(iv).

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C. Donor Testing and Management When Using a Treponemal Screening Test as the Test of Record for the Detection of Syphilis (See Figure 2)

You must test each donation of blood and blood components for syphilis using a serological test (21 CFR 610.40(a)(2)). You must test a donor of Source Plasma for syphilis at least every 4 months (21 CFR 640.65(b)(1)(i)). You must use a serological screening test for syphilis cleared by FDA for such use (21 CFR 640.10(b)).

1. If the treponemal screening test is nonreactive, the donor is considered to be negative for syphilis infection. You may release the donation, provided it meets all donation suitability requirements, and retain the donor.
2. If the treponemal screening test is reactive, further testing is not required, and you must defer the donor indefinitely (21 CFR 610.41(a)) unless evaluated for reentry following the method described below. However, Source Plasma donors may be allowed to donate plasma for manufacture into non-injectable products (21 CFR 640.65(b)(2)(iv)).

In addition, you must not ship or use the donation, unless an exception for shipment or use is applicable (21 CFR 610.40(h)).

Reentry under 21 CFR 610.41(b) of Deferred Donors

3. Because the possibility exists that a treponemal test might be false-positive for reasons unrelated to the analyte (e.g., failure to remove excess conjugate during the performance of the test), the donor may be eligible for reentry. You may perform another treponemal screening test that is different from the initial treponemal screening test used as the test of record, using either a sample from the index donation or a follow-up sample from the donor collected at a later date.⁴
 - a. If the additional treponemal screening test result is negative, you may reenter the donor.
 - b. If the additional treponemal screening test result is positive, the donor remains deferred indefinitely (21 CFR 610.41(a)) unless evaluated for reentry, as described below.

⁴ When treponemal screening test results are reactive, we do not consider negative results on an additional treponemal test to be indicative of biological false-positives on the screening test under 21 CFR 610.40(h)(2)(vi). Regardless of the result from the additional treponemal screening test, you must not release the index donation unless an exception applies (21 CFR 610.40(h)). Source Plasma donations with these test results may be used under some circumstances, provided that the requirements under 21 CFR 610.40(h)(2)(vii) and 21 CFR 640.65(b)(2)(ii) through (iv) are met.

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For reentry purposes, you may test the sample from the donor which was positive on the additional treponemal screening test using a nontreponemal screening test to assess whether the donor has an active infection.⁵ If the nontreponemal screening test result is negative, the results are consistent with recovery or cure from a previous syphilis infection. If the nontreponemal screening test is positive, the results are consistent with an active or recently treated syphilis infection.

In either case, you may reenter the donor under 21 CFR 610.41(b) if the donor subsequently reports being treated for syphilis, provided the treatment was successful and completed at least 3 months before the next donation; and the donor meets all donor eligibility criteria.

Alternatively, the donor may be reentered if your responsible physician determines that the donor never had syphilis based on subsequent medical evaluation and diagnostic testing for syphilis (i.e., previous test results were falsely positive), and the donor meets all donor eligibility criteria.

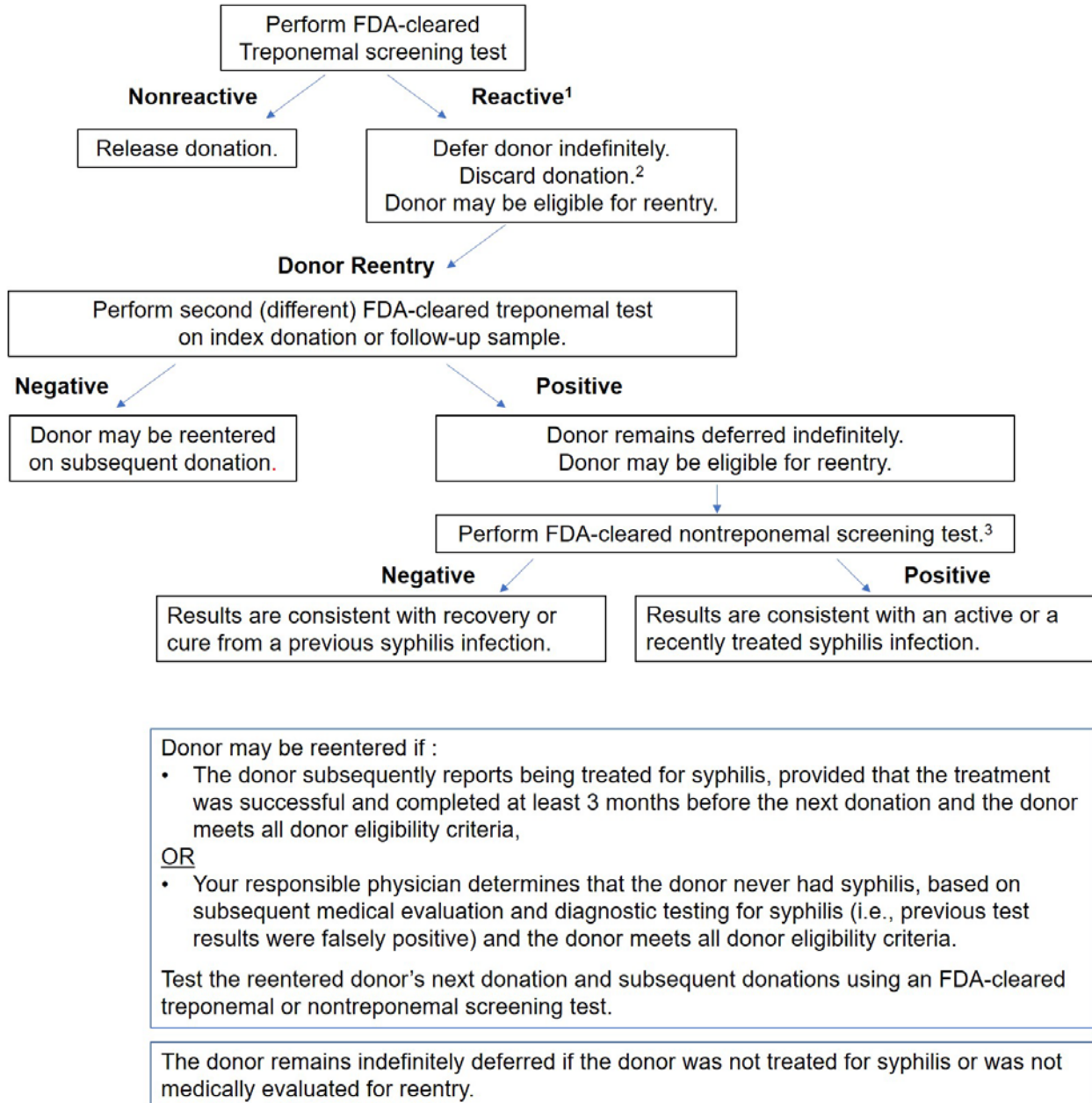
You may use either a nontreponemal screening test or a treponemal screening test that has been cleared by FDA for such intended use to test the reentered donor's subsequent donations.

The donor remains indefinitely deferred if the donor was not treated for syphilis or was not medically evaluated for reentry.

⁵ Further testing under 21 CFR 610.40(e) is not required; however, performing a nontreponemal test after positive treponemal test results are obtained can assist in determining a donor's status in regard to syphilis infection and in determining eligibility of the donor.

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Figure 2: Donor Testing and Management When Using a Treponemal Screening Test as the Test of Record for the Detection of Syphilis



¹The term “reactive” includes “repeatedly reactive” results. You should follow the instructions in the package insert of the assay you are using.

²Source Plasma donations with reactive test results for syphilis may be used under some circumstances, but the donor must be deferred, unless certain conditions apply (21 CFR 610.40(h)(2)(vii) and 21 CFR 640.65(b)(2)(ii) through (iv)). Other donations must not be used unless another exemption under 21 CFR 610.40(h)(2) applies.

³Further testing is not required; however, performing a nontreponemal test after positive treponemal test results are obtained can assist in determining a donor’s status in regard to syphilis infection and in determining future eligibility of the donor.

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V. REFERENCES

1. Turner TB and Diseker TH. Duration of infectivity of *Treponema pallidum* in citrated blood stored under conditions obtaining in blood banks. *Bull Johns Hopkins Hosp* 1941; 68:269-279.
2. Chambers, RW, Foley, HT, Schmidt, PJ. Transmission of syphilis by fresh blood components. *Transfusion* 1969; 9:32-34.
3. Katz, LM. A test that won't die: the serological test for syphilis. *Transfusion* 2009; 49:617-619.
4. Zou, S, Stramer, SL, Dodd, RY. Donor testing and Risk: current prevalence, incidence, and residual risk of transfusion-transmitted agents in US allogeneic donations. *Transfusion Medicine Reviews* 2012; 26(2):119-128.
5. Marfin, AA, et al. Amplification of DNA polymerase I gene of *Treponema pallidum* from whole blood of persons with syphilis. *Diagnostic Microbiology and Infectious Disease* 2001; 40:163-166.
6. Kouznetzov, AV, et al. Detection of the 47-kilodalton membrane immunogen gene of *Treponema pallidum* in various tissue sources of patients with syphilis. *Diagnostic Microbiology and Infectious Disease* 2005; 51:143-145.
7. Castro, R, et al. Detection of *Treponema pallidum* sp *pallidum* DNA in latent syphilis. *International Journal of STD & AIDS* 2007; 18:842-845.
8. Flasarova, M, et al. (Abstract) Molecular detection and subtyping of *Treponema pallidum* subsp. *Pallidum* in clinical specimens. *Epidemiol. Mikrobiol. Immunol.* 2006; 3:105-111.
9. Rodionova, EN, et al. Detection of *Treponema pallidum* DNA and RNA in clinical material from patients with syphilis at different stages. *Zh. Mikrobiol Epidemiol. Immunobiol.* 2003; 3:43-50.
10. Orton, SL, et al. Prevalence of *Treponema pallidum* DNA and RNA in blood donors with confirmed-positive syphilis tests. *Transfusion* 2002; 42:94-99.
11. Zou, S, Notari, EP, Fang, CT, Stramer, SL, Dodd, RK. Current value of serologic test for syphilis as a surrogate marker for blood-borne viral infections among blood donors in the United States. *Transfusion* 2009; 49:655-661.
12. Centers for Disease Control and Prevention. Discordant results from reverse sequence syphilis screening. *MMWR* 2011 (February); 60(5):133-137.
13. Aberle-Grasse J, Orton SL, Notari E IV, Layug LP, Cable RG, Badon S, Popovsky MA, Grindon AJ, Lenes BA, Williams AE. Predictive value of past and current screening tests for syphilis in blood donors: changing from a rapid plasma reagin test to an automated specific treponemal test for screening. *Transfusion* 1999 (February); 39(2):206-211.