Recommendations for Reducing the Risk of Transfusion-Transmitted Babesiosis

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Guidance for Industry

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U.S. Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research
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Contains Nonbinding Recommendations

Recommendations for Reducing the Risk of Transfusion-Transmitted Babesiosis

Guidance for Industry

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I. INTRODUCTION

We, the Food and Drug Administration (FDA), are notifying you, blood establishments that collect blood and blood components, that we have determined babesiosis to be a relevant transfusion-transmitted infection (RTTI) under 21 CFR 630.3(h)(2).[1] Accordingly, we are providing recommendations for donor screening, donation testing, donor deferral and product management to reduce the risk of transfusion-transmitted babesiosis (TTB). The recommendations contained in this guidance apply to the collection of blood and blood components, except Source Plasma.[2]

This guidance finalizes the draft guidance of the same title dated July 2018.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidance documents describe the Agency'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 Agency guidance means that something is suggested or recommended, but not required.

II. BACKGROUND

Human babesiosis is a tick-borne zoonosis caused by infections of humans with intra-erythrocytic protozoa of the genus *Babesia*. Babesiosis can also be transmitted by transfusion of blood and blood components (Refs. 1, 2) and by transplantation of solid organs (Ref. 3) collected

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

[2] Source Plasma is used for further manufacture of plasma-derived products. Pathogen inactivation and removal methods that are currently used in the manufacturing process for plasma-derived products are sufficient to reduce the risk of *Babesia* transmission.

from an infected donor. Babesiosis is transmitted in many parts of the world but the highest prevalence is reported in the United States (U.S.). The first documented human case of babesiosis in the U.S. was identified in 1968 (Ref. 4). The vast majority of U.S. babesiosis cases are caused by *B. microti*, the species that is prevalent in the Northeast and upper Midwest (Ref. 5). Less commonly, other *Babesia* species such as *B. duncani* (Refs. 6, 7) and related organisms are implicated in transmission of *Babesia* in several western U.S. states, while transmission of *Babesia* by "*B. divergens*-like" agents (Ref. 8) have been reported in multiple U.S. states.

Most cases of *B. microti* infections are asymptomatic and never diagnosed (Ref. 9). While the duration of *B. microti* infections in healthy adults is not precisely known, in limited studies, the parasitemic period is reported to last from 2 to 7 months (Ref. 10), but parasitemia may persist for more than 2 years (Ref. 11). In a study of asymptomatic blood donors who were reactive for *B. microti* using investigational nucleic acid tests (NAT) and antibody tests, follow-up testing demonstrated DNA clearance in 86% (48 of 56 donors) after 1 year, and 95% (53 of 56 donors) after 2 years (Ref. 10). *Babesia* transmission is generally seasonal and coincides with tick activity (traditionally May-September) in affected states, but tick-borne (Refs. 12-17) and transfusion-transmitted infections are reported throughout the year (Ref. 9). Transfusion of blood and blood components collected from asymptomatic infected donors may result in TTB, leading to potentially fatal clinical illness in blood transfusion recipients.

III. DISCUSSION

FDA has determined, as discussed below, that babesiosis is a transfusion-transmitted infection (TTI) under 21 CFR 630.3(l) and an RTTI under 21 CFR 630.3(h)(2). This determination is based on the severity of the disease, confirmed transfusion-transmission by blood and blood components, the availability of appropriate screening measures and donor screening tests and significant incidence and prevalence affecting the potential donor population.

A. Transfusion-Transmitted Infection

A transfusion-transmitted infection (21 CFR 630.3(l)) means a disease or agent:

(1) That could be fatal or life-threatening, could result in permanent impairment of a body function or permanent damage to a body structure, or could necessitate medical or surgical intervention to preclude permanent impairment of body function or permanent damage to a body structure; and

(2) For which there may be a risk of transmission by blood or blood components, or by a blood derivative product manufactured from blood or blood components, because the disease or disease agent is potentially transmissible by that blood, blood component, or blood derivative product.

In this regard, FDA examined:

Severity of Disease

Clinical symptoms of babesiosis, caused by *B. microti*, range from asymptomatic or mild to severe, and can result in death, particularly in certain high-risk populations. In the majority of individuals who develop illness, clinical symptoms appear 1 to 4 weeks after an infectious tick bite (Ref. 5). Common symptoms include fever, chills, body aches, weakness, malaise and fatigue (Refs. 5, 9, 18, 19). Severe disease caused by *B. microti* infection requiring hospitalization is generally seen in neonates, the elderly, asplenic patients, and those receiving immunosuppressive drugs for cancer therapy (Refs. 5, 19, 20). The most common severe clinical manifestations include acute respiratory distress syndrome and disseminated intravascular coagulopathy. Congestive heart failure, coma, liver failure and renal failure are also reported (Refs. 5, 19, 20). In tick-borne cases, fatality rates range from 6 to 9% among hospitalized patients and up to 21% in immunosuppressed patients (Refs. 19, 20). In TTB cases, a fatality rate of about 20% has been reported in the literature (Ref. 21).

Transfusion Transmission

Babesiosis can be transmitted by transfusion of blood and blood components, with the first U.S. case of TTB reported in 1980 (Refs. 1, 2). Since then, more than 200 TTB cases have been documented (Refs. 2, 22). While *B. microti* remains the major causative agent, three TTB cases have been attributed to *B. duncani (*Ref. 2) and one possible case to *B. divergens* in the U.S. (Ref. 23). Following transfusion of blood components collected from an infected donor, symptoms in transfusion recipients have been observed anywhere from 1 week to 9 weeks, and as long as 6 months after transfusion (Ref. 2).

In conclusion, FDA has determined that babesiosis is a TTI because it is a disease agent that can be fatal or life-threatening and is transmissible by blood or blood components.

B. Relevant Transfusion-Transmitted Infection

Having determined that babesiosis is a TTI, we outline, below, the criteria establishing babesiosis as an RTTI under 21 CFR 630.3(h)(2)(i) and (ii).

An RTTI is a transfusion-transmitted infection not listed in 21 CFR 630.3(h)(1) when the following conditions are met:

(1) Appropriate screening measures for the transfusion-transmitted infection have been developed and/or an appropriate screening test has been licensed, approved, or cleared for such use by the FDA and is available; and

(2) The disease or disease agent: (A) May have significant incidence and/or prevalence to affect the potential donor population; or (B) May have been

released accidentally or intentionally in a manner that could place potential donors at risk of infection.

Availability of Appropriate Screening Measures or Screening Tests

Licensed Screening Tests: On March 6, 2018, FDA licensed two independent assays for screening donors for *B. microti:* the Imugen *Babesia microti* Arrayed Fluorescent Immunoassay (AFIA) for the detection of *B. microti*-specific antibodies and the Imugen *Babesia microti* Nucleic Acid Test (NAT) for the detection of DNA of *B. microti*. However, the manufacturer notified FDA of the permanent discontinuance of both donor screening tests in November 2018. On January 24, 2019, FDA licensed the Grifols Procleix Babesia Assay for the detection of RNA from *Babesia* species (*B. microti*, *B. duncani*, *B. divergens*, and *B. venatorum*) in whole blood specimens for use in screening donors of whole blood and blood components.

Pathogen Reduction: FDA has approved pathogen reduction devices that report effective reduction of *B. microti* for indicated plasma or platelet components in the instructions for use, which can be used as an alternative to testing or donor questions.

Donor History Questionnaire (DHQ): Upon implementing the recommendations in this guidance, we do not find it necessary for blood establishments to continue to ask about a history of babesiosis using the current question on the DHQ. Donors implicated in TTB cases have been unaware of their infection status and hence have not reported a history of babesiosis before donation (Ref. 24). When testing for *Babesia* begins according to the recommendations in this guidance, we expect that some asymptomatic blood donors will learn about their infection status when they are deferred. However, these donors might still present to donate in a state where testing or pathogen reduction is not performed. Accordingly, we are recommending a question on the DHQ, as follows:

- If donations are not tested or pathogen reduced, we are recommending a question to assess donors for a history of ever having a positive test result for *Babesia*, obtained either from a medical diagnosis or reactive donor screening test. Such donors are not eligible for donation, unless they are requalified by the recommendations in this guidance.

- If donations are tested, or if blood components from the donation are pathogen reduced using an FDA-approved device effective against *Babesia* according to the instructions for use, we are not recommending any *Babesia*-related questions. However, if establishments choose to continue to ask a *Babesia*-related question, donors with risk should be deferred according to the recommendations in this guidance.

Significant Incidence and Prevalence

In 2011, babesiosis became a nationally notifiable disease. Between 2011 and 2017, an average of 1,628 (range 937-2,100) babesiosis cases per year was observed in 26 states,

excluding several *Babesia*-risk states because disease reporting was not required in those states (Refs. 12-17). According to data from the Centers for Medicare and Medicaid Services (CMS), babesiosis cases were reported among elderly Medicare beneficiaries in all states and Washington, D.C., except for Wyoming (Refs. 25, 26). In aggregate, more than 200 cases of TTB have been documented (Refs. 2, 22, 27). About 99% of the clinical babesiosis cases reported and 95% of TTB cases reported are from Connecticut, Massachusetts, Rhode Island, New York, New Jersey, Minnesota, Wisconsin, New Hampshire, Maine, Maryland, Virginia, Vermont, Pennsylvania, Delaware, and Washington, D.C. (Refs. 12-17, 25, 26).

TTB risk in other states is mostly attributed to infected donors who had lived or traveled in *Babesia*-risk states or to distribution of blood components collected in areas affected by *Babesia* to other states.

In summary, we have determined that babesiosis meets the criteria in 21 CFR 630.3(h)(2) for an RTTI because of the availability of appropriate screening measures and screening tests, and because of the sufficient incidence and prevalence of *Babesia* to affect the potential donor population in the U.S.

IV. PUBLIC WORKSHOP AND ADVISORY COMMITTEE MEETINGS ON RISK MITIGATION FOR TTB

FDA solicited public input on how best to mitigate the risk of TTB in the U.S. and support the development of donor screening tests for *Babesia*. On September 12, 2008, FDA convened a public workshop entitled "Approaches to Reduce the Risk of Transfusion-Transmitted Babesiosis in the United States" (Refs. 28, 29). The focus of this workshop was to discuss various aspects of TTB in the U.S. including the status of detection technologies and possible strategies to identify and defer blood donors who might have been exposed to *Babesia* parasites. Experts emphasized the need for better understanding of the epidemiology of babesiosis in the U.S. and efforts to develop highly sensitive and specific laboratory tests to identify *Babesia*-infected blood donors, especially tests to distinguish between current infections and resolved infections. Discussions also focused on the biology, pathogenesis and epidemiology of babesiosis. A detailed summary of this workshop has been published in *Transfusion* and the meeting transcript is available on the FDA website (Refs. 28, 29).

On July 26, 2010, FDA discussed "Risk of *Babesia* Infection by Blood Transfusion and Potential Strategies for Donor Testing" at a Blood Products Advisory Committee (BPAC or Committee) meeting (Ref. 30). Based on the information available at that time, the Committee recommended regional testing of blood donors for *Babesia*. The Committee did not provide advice on the question of the most suitable technologies for donor screening for *Babesia*, noting that additional information on the performance of different testing technologies was needed. A transcript of the meeting and the presentations delivered at this BPAC meeting are available on the FDA website (Refs. 30-34).

On May 13, 2015, FDA again sought advice from the BPAC on strategies to test blood donors for evidence of *B. microti* infection using licensed tests, when such tests become available (Ref. 25). In recent years, limited testing of blood donations using the available investigational tests has provided additional information on the magnitude of *B. microti* prevalence in endemic areas and on the relative value of NAT and antibody-based tests in identifying *Babesia*-exposed donors with resolved infections as opposed to parasitemic donors. The sponsors of the investigational *B. microti* tests presented the results of their clinical studies (Refs. 35, 36). The Committee advised that the scientific data and FDA analysis support the concept of nationwide, year-round testing of blood donations for *Babesia* risk by an antibody-based test. The Committee also recommended unanimously that NAT-based testing should be performed on blood donations in certain high-risk states, and the majority supported NAT testing in the nine states considered endemic at that time (i.e., Connecticut, Maine, Massachusetts, Minnesota, New Hampshire, New Jersey, New York, Rhode Island, and Wisconsin). The Committee recommended including the bordering state of Pennsylvania in the year-round NAT-based testing program. Additionally, the Committee supported a deferral period of at least 2 years for donors with reactive test results, after which time, donor eligibility would be assessed based on testing by both antibody and NAT-based testing. Since the meeting, Pennsylvania has been identified as a *B. microti* endemic state.

FDA considered this BPAC recommendation for testing donations year-round by universal antibody testing and regional NAT in states with the highest *Babesia* risk. Subsequently, we performed an independent risk assessment that determined year-round antibody and NAT testing in *Babesia*-risk states only is a preferred strategy that balances risk reduction with the scope of testing. However, at the time of this writing, a licensed *Babesia* antibody test is not available for blood donor screening. Consequently, we are recommending regional, year-round testing using a licensed NAT for *Babesia*, or use of an FDA approved pathogen reduction device, in the highest risk states. Consistent with BPAC's advice, and based on the available published data on *Babesia* DNA persistence in some screened blood donors beyond one year (Ref. 10), we are recommending a 2-year deferral following a reactive donor NAT.

V. RECOMMENDATIONS

A. Donation Testing, Donor History Questionnaire, Donor Deferral and Requalification

The recommendations in this guidance for regional testing for *Babesia* or pathogen reduction of indicated blood components are based on the current epidemiological data on *Babesia* and the risk of TTB, and the availability of FDA-licensed and approved devices. FDA may modify these recommendations in the future based on scientific evidence as it becomes available, for example, if we determine that regional NAT testing alone does not adequately reduce the risk of TTB or if there is a need to expand the recommendations to include additional *Babesia*-risk states as they are identified. In addition, we may modify the recommendations in the future based on the availability of licensed serology tests and approved pathogen reduction devices.

1. We recommend that you update your donor history questionnaire, including full-length and abbreviated donor history questionnaires, and accompanying materials as necessary to incorporate the recommendations provided in this document. You must update your standard operating procedures to reflect any such changes (21 CFR 606.100(b)).

2. To comply with the requirements in 21 CFR 610.40(a)(3), you must test donations as described in section V.A.3. of this document or implement pathogen reduction technology for platelets and plasma using an FDA-approved pathogen reduction device effective against *Babesia*, according to the manufacturer's instructions for use. If an FDA-approved pathogen reduction device becomes available for Whole Blood or red blood cells that effectively inactivates *Babesia*, you may implement pathogen reduction technology for such blood components.

3. You must test each donation for evidence of *Babesia* using a licensed NAT[3] when collected in Connecticut, Delaware, Maine, Maryland, Massachusetts, Minnesota, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, Vermont, Virginia, Wisconsin and Washington, D.C. (21 CFR 610.40(a)(3) and 610.40(b)). Testing must be performed year-round and in accordance with the instructions for use of the device (21CFR 610.40 (a)(3) and 606.65(e)).

    a. You must defer donors with a reactive NAT result for *Babesia* for at least 2 years from the date of the reactive donation (21 CFR 610.41(a) and 21 CFR 630.35(a)). You must make reasonable attempts to notify any donor whose blood tests reactive for *Babesia* of their deferral and of their test results, within 8 weeks after determining that the donor is deferred (21 CFR 630.40). Deferred donors must be counseled about the possible medical significance of the results (21 CFR 630.40(b)).

    b. When testing or pathogen reduction is performed, you may discontinue asking donors questions about a history of babesiosis.[4] If you choose

[3] Blood establishments that are participating in a clinical trial and testing for *Babesia* using an unlicensed NAT may continue in the clinical trial but must implement the regulatory requirement to use a licensed donor screening test for *Babesia* nucleic acid by 12 months of this guidance issuance date (21 CFR 610.40(b)).

[4] To provide for appropriate donor screening and testing for this RTTI, the Director of the Center for Biologics Evaluation and Research is providing an alternative procedure (testing, as described in section V. of this document) under 21 CFR 640.120(b) to the provisions in 21 CFR 630.10 that require blood establishments to assess donors for risk factors for babesiosis before collecting blood or blood components. Specifically, FDA is not recommending assessing donors for risk factors for babesiosis, in particular, travel to or residence in an area endemic or at risk for babesiosis. Assessing donors for travel to or residence within the United States and deferring donors for time spent in areas endemic or at risk for babesiosis is not feasible because of the anticipated detrimental effect on the blood supply. Approximately one-quarter of the U.S. population resides in the states identified at risk for babesiosis in this guidance, and a large number of prospective blood donors may travel to the at-risk states.

to ask a donor question about *Babesia*, you should follow the recommendations in section V.A.4. of this document.

c. When testing or pathogen reduction is performed, donors who were previously deferred for a history of babesiosis based on their responses on the donor history questionnaire may be eligible to donate provided they have not had a positive test result for *Babesia* in the last 2 years obtained from either a medical diagnosis or a positive donor screening test result and they meet all other donor eligibility criteria (21 CFR 630.35(b)).

4 In states that do not test donations for *Babesia* or pathogen reduce blood components we recommend the following:

a. Revise your donor history questionnaire to ask prospective donors if they have ever had a positive test result for *Babesia*, obtained from either a medical diagnosis or a reactive donor screening test.

b. You must defer donors who report a history of a positive test result for *Babesia*, obtained from either a medical diagnosis or a reactive donor screening test result (21 CFR 630.10(h)). Such donors should be indefinitely deferred or deferred for at least 2 years from the date of the positive test and evaluated for requalification as described below in section V.A.4.c. of this document.

c. A donor who was previously deferred for a history of babesiosis or is deferred for a history of a positive test result for *Babesia* may be eligible to donate under 21 CFR 630.35(b) provided the following conditions are met:

i. On the day of donation, the donor has not had a positive test result for *Babesia* in the last 2 years and they meet all other eligibility criteria.

ii. The donation must be tested for *Babesia* by a licensed NAT and found to be nonreactive at the time of blood collection (21 CFR 610.40(a)(3)(ii)(A).

If the donor meets the criteria for requalification in section V.A.4.c.i and ii., subsequent donations do not need to be tested for *Babesia* provided the donor is assessed by the DHQ and has not had a positive test for *Babesia* since the date of the last negative test result that was the basis for requalification.

5. For donor counseling purposes, the responsible physician may perform additional testing such as alternative *Babesia* NAT and/or diagnostic antibody

tests that are not indicated for use in donor screening. The results of such testing cannot be used to requalify a deferred donor with a reactive screening test by a licensed NAT.

B. Product Management, Retrieval and Quarantine, Notification of Consignees of Blood and Blood Components

1. You may release donations that are nonreactive for *Babesia* by a licensed donor screening test provided all other donation suitability requirements are met (21 CFR 630.30).

2. You must not ship or use a donation that is reactive for *Babesia*, unless an exception for shipment or use is applicable (21 CFR 610.40(h) and 21 CFR 630.30(b)(1)).

3. We recommend that you take the following actions when a donation tests reactive for *Babesia* by a licensed donor NAT:

    a. Identify all cellular blood components previously collected from that donor in the 12 months prior to the date of the reactive index donation. The responsible physician may also consider the disposition of in-date cellular components (e.g., frozen RBC components) collected more than 12 months prior to the reactive index donation, especially those that were not tested; and

    b. Quarantine the identified in-date cellular components held at your establishment; and

    c. Notify consignees of all identified cellular blood components collected from the donor in the 12 months prior to the date of the reactive index donation that have been distributed, and:

        1. Retrieve the identified in-date cellular blood components.
        2. If components were transfused, encourage consignees to have a discussion with the recipient's physician of record about a possible risk of TTB, particularly if the involved component(s) had not been tested or pathogen reduced.

    The recommendation for consignee notification and retrieval does not apply to previously distributed cellular blood components that were pathogen reduced using an FDA-approved device according to its instructions for use.

4. We recommend that you take the following actions when a donor later reports a history of a positive test result for *Babesia* and should have been deferred according to the recommendations in section V.A.4.b.

a. Identify all cellular blood components previously collected from that donor going back 12 months prior to the reported date of the positive test result for *Babesia*; and

b. Quarantine the identified in-date cellular components held at your establishment; and

c. Notify consignees of all identified cellular blood components collected from the donor in the 12 months prior to the reported date of the positive test for *Babesia* and retrieve the identified in-date cellular blood components. This recommendation does not apply to previously distributed cellular blood components that were pathogen reduced using an FDA-approved device according to its instructions for use.

5. If you previously collected acellular blood components (i.e., frozen plasma products) intended for transfusion or for further manufacturing from a donor that tests reactive for *Babesia* by a licensed donor NAT or from a donor who later reports a history of a positive test result for *Babesia* and should have been deferred according to the recommendations in section V.A.4.b, quarantine any in-date acellular blood components held at your establishment collected from the donor in the 12 months prior to the date of the reactive index donation or reported date of a positive test for *Babesia*.

Note: Based on the very low risk of TTB associated with frozen acellular blood components, we are not recommending notification of consignees or product retrieval if you distributed such products.

C. Product Disposition and Labeling

1. We recommend that you destroy or relabel blood and blood components that were collected from a donor who should have been deferred based on their responses to the DHQ according to the recommendations in section V.A.4. of this document. If you relabel the blood and blood components, they may be released for research if labeled appropriately as described below.

   You must label the unit as required under 21 CFR 606.121. You must use the following statements to prominently relabel the blood and blood components (21 CFR 606.121(c)):

   a. "NOT FOR TRANSFUSION: Collected from a Donor with a History of a Positive Test Result for *Babesia*"

   AND

   b. "Caution: For Laboratory Research Only"

2. We recommend that you destroy or relabel blood and blood components that test reactive for *Babesia* by a licensed donor NAT. If you relabel the blood and blood components, they may be released for research or for further manufacture into non-injectable products or in vitro diagnostic reagents when no other suitable sources are available, when written approval by FDA is obtained and if labeled appropriately as described below. (see 21 CFR 610.40(h)(2)(ii))

   You must label the reactive unit as required under 21 CFR 606.121 and with the "BIOHAZARD" legend (21 CFR 610.40(h)(2)(ii)(B)). You must use the following statements to prominently relabel the blood components (21 CFR 606.121(c)):

   a. "NOT FOR TRANSFUSION: Collected from a Donor Determined to be Reactive for *Babesia*"

   AND

   b. "Caution: For Laboratory Research Only"

   OR

   "Caution: For Further Manufacturing into In Vitro Diagnostic Reagents for Which There Are No Alternative Sources"

   OR

   "Caution: For Further Manufacturing Use as a Component of a Medical Device for Which There Are No Alternative Sources"

D. Circular of Information

Under 21 CFR 606.122(h), the circular of information must include the names and results of all tests performed when necessary for safe and effective use.

1. When testing is performed, you must update your circular of information (21 CFR 606.122(h)). We recommend the following statement:

"A licensed NAT for *Babesia* has been performed and found to be nonreactive."

2. If a blood system distributes components from both tested and untested donations, we recommend the following statement:

"A licensed NAT for *Babesia* has been performed and found to be nonreactive for blood collected in states where testing is required by FDA."

VI. IMPLEMENTATION AND REPORTING CHANGES UNDER 21 CFR 601.12

You may implement the recommendations as soon as feasible. FDA intends to begin requiring compliance with the underlying regulatory requirements regarding relevant transfusion-transmitted infection screening, testing, and product management 12 months after the guidance issuance date. Licensed blood establishments must report changes under 21 CFR 601.12, as follows:

A. Donor History Questionnaire

Licensed blood establishments that modify the donor history questionnaire (DHQ) must report the change under 21 CFR 601.12 as follows:

1. If you implement testing of each donation for *Babesia* or pathogen reduction consistent with the recommendations in section V.A.3. of this document, you may remove the current question regarding a history of babesiosis from your DHQ. Report this change in your next annual report, noting the date the change was made (21 CFR 601.12(d)).

2. If you do not implement testing for *Babesia* or pathogen reduction, you should revise your current DHQ consistent with the recommendations in section V.A.4. of this document. Revising the existing question on babesiosis or using a revised DHQ found acceptable to FDA is considered a minor change and must be reported in your next annual report, noting the date that the change was made (21 CFR 601.12(d)).

3. You must submit a Prior Approval Supplement if you wish to revise your DHQ other than as recommended in section V.A.4. of this document, as this constitutes a major change (21 CFR 601.12(b)(1)).

B. Testing

Licensed blood establishments that implement testing for Babesia must report the change under 21 CFR 601.12 as follows:

1. If you implement testing consistent with the recommendations in section V.A.3. of this document, submit the change in an annual report under 21 CFR 601.12 (d),[5] noting the date that the testing was implemented.

2. You must submit a Prior Approval Supplement if you wish to implement a testing strategy other than as recommended in section V.A.3. of this document (21 CFR 601.12(b)(1)).

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

Note: If you wish to implement a testing strategy that is more restrictive (e.g., testing in other states in addition to those required or nationwide testing) than recommended in this document, you may submit the change as an annual report under 21 CFR 601.12.

C. Circular of Information

Licensed blood establishments that update their circular of information to include a test statement recommended in this document must report this change under 21 CFR 601.12. You may include this change in your supplement reporting implementation of testing or you may include it in your next annual report.

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