Strategies for Implementation of Antibody and Nucleic Acid-based Testing for Babesia microti in Blood Donations: Summary of May 13th 2015 Blood Product Advisory Committee Meeting

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Life Cycle of *B. microti*

- Enzootic transmission
- Sylvatic reservoir
- Human is incidental host
- Chronically infected asymptomatic individuals cause TTB
- *B. microti* – predominant species
- *B. duncani* and *B. duncani*-type
- *B. divergens*-like

Assays designed for *B. microti* may fail to detect the other *Babesia* species prevalent in U.S.
Epidemiology of Babesiosis

• Endemic transmission is reported mostly in Northeastern, Mid-Atlantic and Upper Midwestern states

• Area of endemic transmission is reported to be expanding, particularly into the states adjoining the endemic states

• Several other states without recognized endemic areas also report babesiosis cases due to infections acquired during travel to endemic areas
Babesia Transmission is Regional While TTB Risk is Systemic

- TTB risk is nationwide, because
  - Donors from non-endemic areas travel to endemic areas and acquire infection
  - Donors who normally reside in endemic areas may donate elsewhere
  - Blood products are often shipped between widely separated regions across the U.S.

- Therefore, screening is needed where blood is collected
Assessment of Babesiosis Risk in the United States based on the following data sets

- National Babesiosis Surveillance Program, CDC 2011-2013
- Transfusion-Transmitted Babesiosis Cases 1979-2009 (CDC)
- Center for Medicare & Medicaid Services (CMS) health records for beneficiary claims for diagnosis of babesiosis in persons 65 and older 2006-2013
Clinical Babesiosis Cases by State*

- Notifiable disease since 2011. Cases observed in 26 states
- 2013
  - 22 states, 1,792 cases
- 98.5% of all cases in 9 endemic states

*Likely underreported due to nondiagnosis or misdiagnosis of clinical and asymptomatic infections
Since 1979, 205 cases, for whom state of donation was known, were reported from 22 states – About 87% of cases in 9 endemic states
Nationwide Prevalence of Babesiosis (CMS)

- 2006-2013
  - 10,301 unique diagnoses of babesiosis
- Cases reported from all states and Washington D.C., except Wyoming
Issue for BPAC Discussion

Sought advice on donor testing strategies for evidence of *Babesia microti* infection

a. Should antibody testing be nationwide and year round

b. Should NAT be limited to certain high risk states

c. Should alternative approaches be considered based on geographic and seasonal risk

d. What should be the appropriate donor deferral time?
FDA Benefit-Risk Model for *B. microti* Testing of Blood Donations

FDA model using the CMS dataset to estimate:

- Potential risk of babesiosis in U.S. blood donors

- Potential reduction in TTB risk under various testing strategies
  - Antibody-only testing in selected states or nationwide
  - Testing with both antibody and NAT in selected states or nationwide

- Potential blood unit loss due to false positive test results

- Positive predictive value of testing for markers of infection
<table>
<thead>
<tr>
<th>Testing Scenario</th>
<th>Percent TTB Risk Reduction</th>
<th>Positive Predictive Value</th>
<th>Units From Positive Donors Interdicted</th>
<th>False Positive Donor Test Results</th>
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<td>No Donor Testing</td>
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<td>9 States</td>
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<td>13 States + DC</td>
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<td>45.8</td>
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<tr>
<td>50 States + DC</td>
<td>96.0</td>
<td>19.3</td>
<td>985</td>
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</table>
Summary of Benefits and Risks under Selected TTB Testing Scenarios

TTB Risk Reduction (%)

- S: 5
  - 70%
- S+N: 5
  - 74%
- S: 9
  - 73%
- S+N: 9
  - 77%
- S: 15 + DC
  - 84%
- S+N: 15 + DC
  - 87%
- S: 50 + DC
  - 88%
- S+N: 50 + DC, N: 5
  - 91%
- S: 50 + DC, N: 9
  - 95%
- S+N: 50 + DC, N: 15 + DC
  - 95%
- S: 50 + DC
  - 96%

Positive Units Interdicted

- S: 5
  - 716
- S+N: 5
  - 752
- S: 9
  - 748
- S+N: 9
  - 787
- S: 15 + DC
  - 858
- S+N: 15 + DC
  - 894
- S: 50 + DC
  - 902
- S+N: 50 + DC, N: 5
  - 939
- S: 50 + DC, N: 9
  - 975
- S+N: 50 + DC, N: 15 + DC
  - 978
- S: 50 + DC
  - 983
- S+N: 50 + DC
  - 985

Positive Predictive Value

- S: 5
  - 57%
- S+N: 5
  - 58%
- S: 9
  - 51%
- S+N: 9
  - 52%
- S: 15 + DC
  - 39%
- S+N: 15 + DC
  - 39%
- S: 50 + DC
  - 40%
- S+N: 50 + DC, N: 5
  - 19%
- S: 50 + DC, N: 9
  - 19%
- S+N: 50 + DC, N: 15 + DC
  - 19%
- S: 50 + DC
  - 19%

Donors with False Positive Results

- S: 5
  - 315
- S+N: 5
  - 315
- S: 9
  - 424
- S+N: 9
  - 424
- S: 15 + DC
  - 804
- S+N: 15 + DC
  - 804
- S: 50 + DC
  - 804
- S+N: 50 + DC, N: 5
  - 2,422
- S: 50 + DC, N: 9
  - 2,422
- S+N: 50 + DC, N: 15 + DC
  - 2,422
- S: 50 + DC
  - 2,422
- S+N: 50 + DC
  - 2,422

Blood Products Advisory Committee Meeting, May 13, 2015
Questions for the Committee (I)

1. Do the available scientific data and FDA analysis support the concept of nationwide, year round testing of blood donations for Babesia-risk by an antibody-based test?

1a. If not, please comment on alternative options that FDA should consider, including limitation of antibody testing to specific states.

The committee agreed that the scientific data and FDA analysis support the concept of nation-wide, year round testing of blood donations for Babesia-risk by an antibody-based test. 11 yes votes. 3 no votes, 0 abstained.
Questions for the Committee (II)

2. Does the Committee agree that NAT-based testing should be performed in blood donations in certain high-risk states?

The Committee voted unanimously for NAT-based testing in blood donations in certain high-risk states. (Vote 14 yes, 0 no).

a. If so, please advise whether year round NAT testing should be considered in the following:

   i) 5 states (highest endemic): CT, MA, RI, NY and NJ

   ii) 9 states (all known endemic): CT, MA, RI, NY, NJ, MN, WI, NH and ME

   iii) 15 States plus DC (largest risk capture with the smallest number of states): CT, MA, RI, NY, NJ, MN, WI, NH, ME, MD, DC, VA, VT, PA, DE and FL

The majority of the Committee voted in favor of the 9 states testing option (8 votes). The remaining Committee members (6 votes) supported the 15 states, plus D.C. testing option. Some members commented that PA should be added to the 9 states option.
Window Period, Seroconversion, Duration of Parasitemia and Antibody Response: Implications for NAT and Antibody Testing for *B. microti*
Questions for the Committee (III)

3. Please comment whether it would be appropriate to apply a time-based deferral for those donors who have *B. microti*-positive test result(s)?

3a. If so, please advise on a suitable deferral period for donors who had *B. microti*-positive test results?

Members supported a deferral period of at least two years and that a reentry algorithm should include antibody and NAT testing.
Acknowledgements

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