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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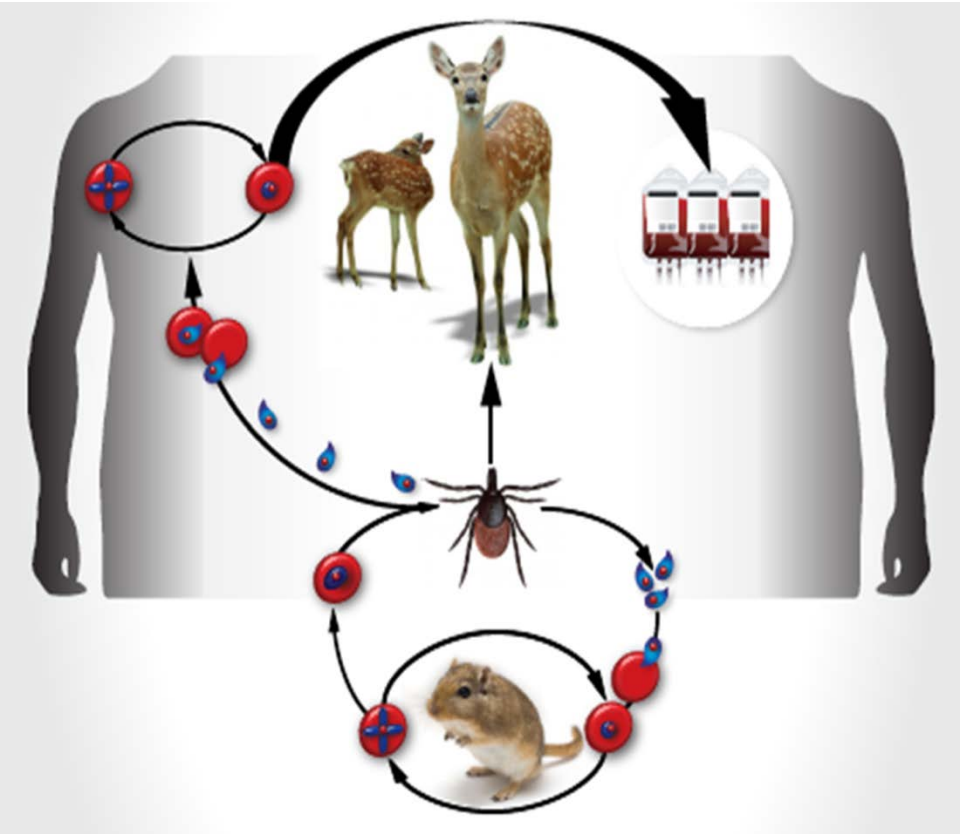
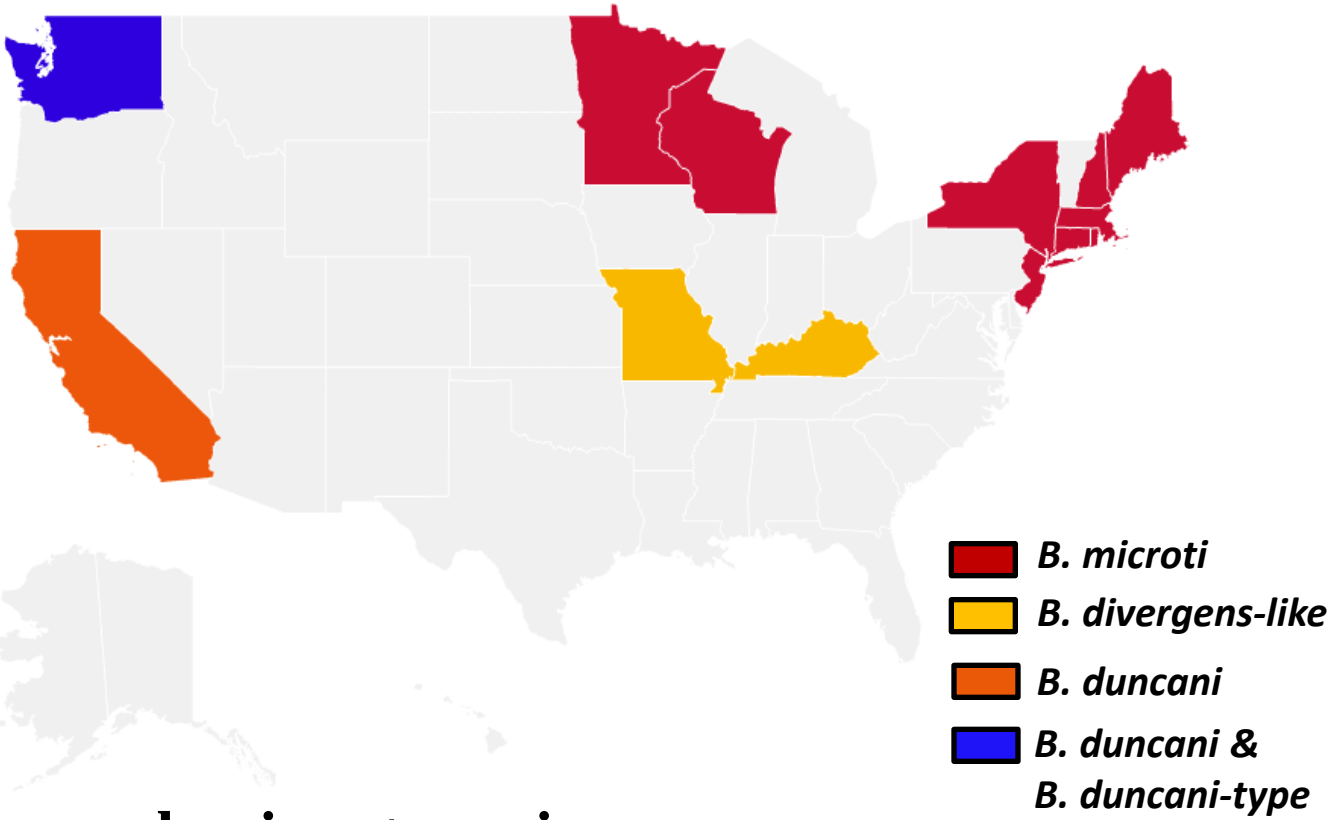
Life Cycle of *B. microti*



- **Enzootic transmission**
- **Sylvatic reservoir**
- **Human is incidental host**
- **Chronically infected asymptomatic individuals cause TTB**

Babesia Species Prevalent in United States



- ***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

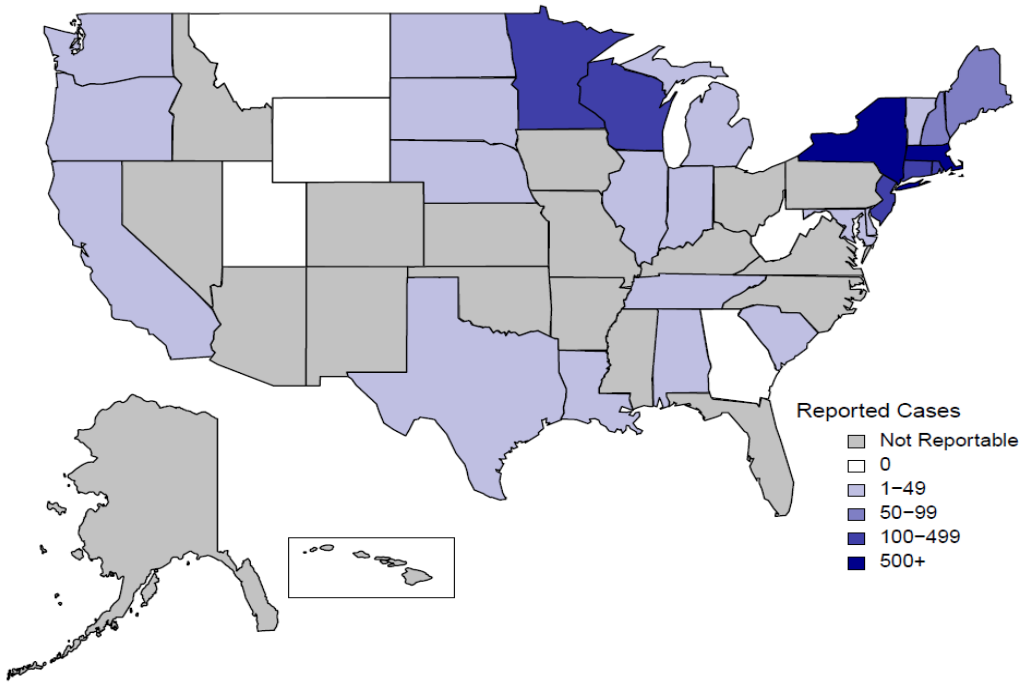
- **TTB risk is nationwide, because**
  - **Donors from non-endemic areas travel to endemic areas and acquire infection**
  - **Donors who normally reside in endemic areas may donate elsewhere**
  - **Blood products are often shipped between widely separated regions across the U.S.**

- **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**

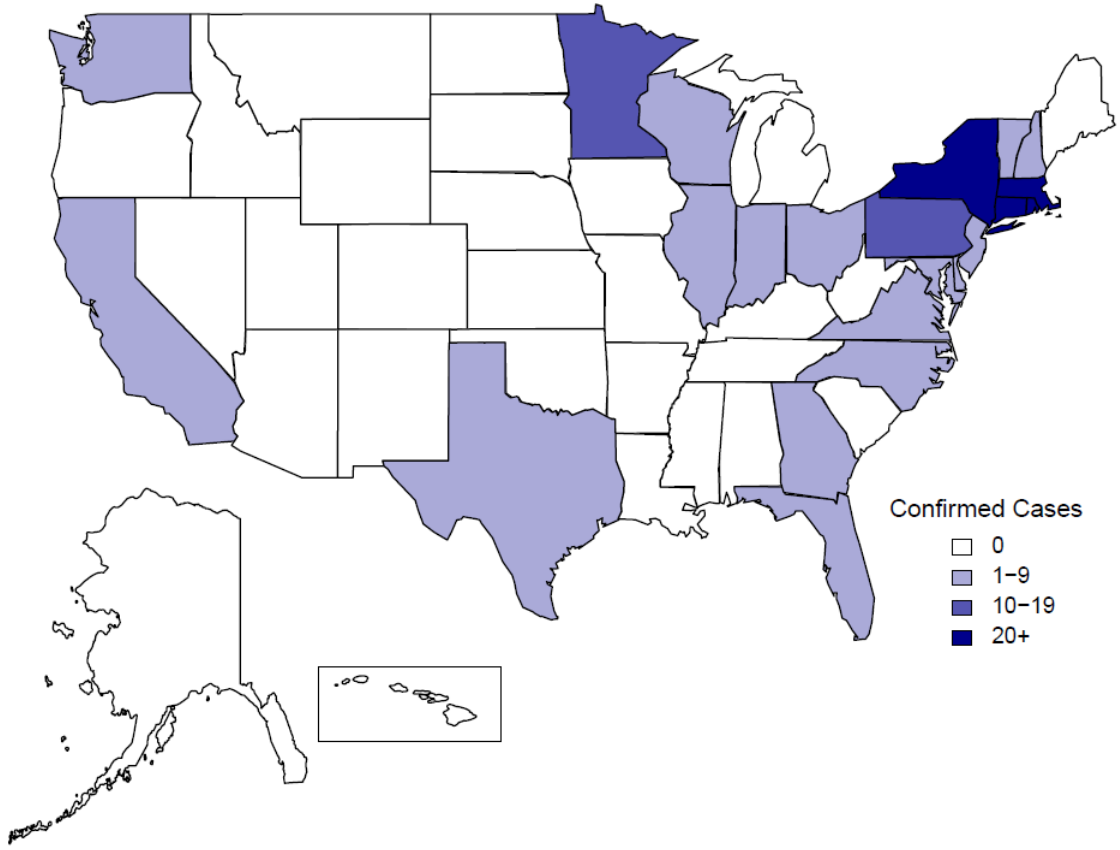
Clinical Babesiosis Cases by State*



- **Notifiable disease since of 2011. Cases observed in 26 states**
- **<u>2013</u>**
  - **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**

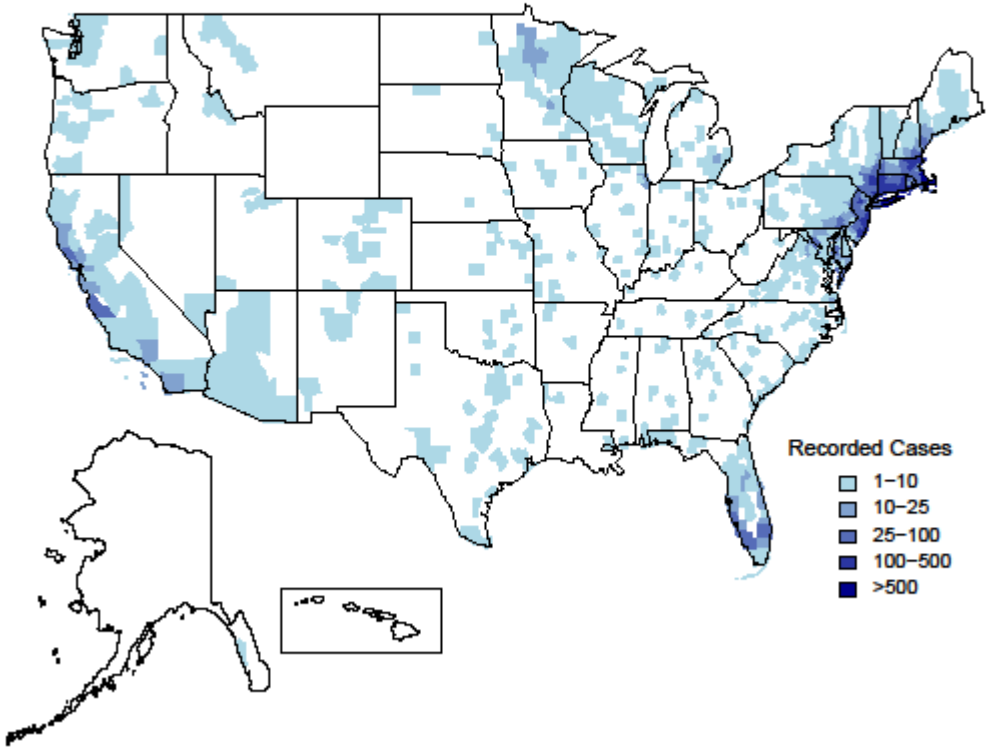
Distribution of TTB by State



- **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**

Testing Scenario	Percent TTB Risk Reduction	Positive Predictive Value	Units From Positive Donors Interdicted	False Positive Donor Test Results
No Donor Testing	**0**	0	0	0
5 States CT, MA, RI, NY, NJ	**73.7**	58.3	752	315
9 States CT, MA, RI, NY, NJ, WI, MN, NH, ME,	**77.1**	52.2	787	424
13 States + DC CT, MA, RI, NY, NJ, MD, NH, ME, DC, MN, VT, PA, DE, WI	**82.9**	45.8	847	589
14 States + DC CT, MA, RI, NY, NJ, MD, NH, ME, DC, VA, MN, VT, PA, DE, WI	**84.9**	43.9	868	652
15 States + DC CT, MA, RI, NY, NJ, MD, NH, ME, DC, VA, MN, VT, PA, DE, WI, FL	**88.3**	39.7	902	804
50 States + DC	**96.0**	19.3	985	2422

Summary of Benefits and Risks under Selected TTB Testing Scenarios

	S: 5	S+N: 5	S: 9	S+N: 9	S: 15 + DC	S: 15 + DC, N: 5	S+N: 15 + DC	S: 50+DC	S: 50 +DC, N: 5	S: 50 +DC, N: 9	S: 50 +DC, N: 15+ DC	S: 50 +DC
TTB Risk Reduction (%)	70	74	73	77	84	87	88	91	95	95	96	96
Positive Units Interdicted	716	752	748	787	858	894	902	939	975	978	983	985
Positive Predictive Value	57	58	51	52	39	39	40	19	19	19	19	19
Donors with False Positive Results	315	315	424	424	804	804	804	2,422	2,422	2,422	2,422	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:

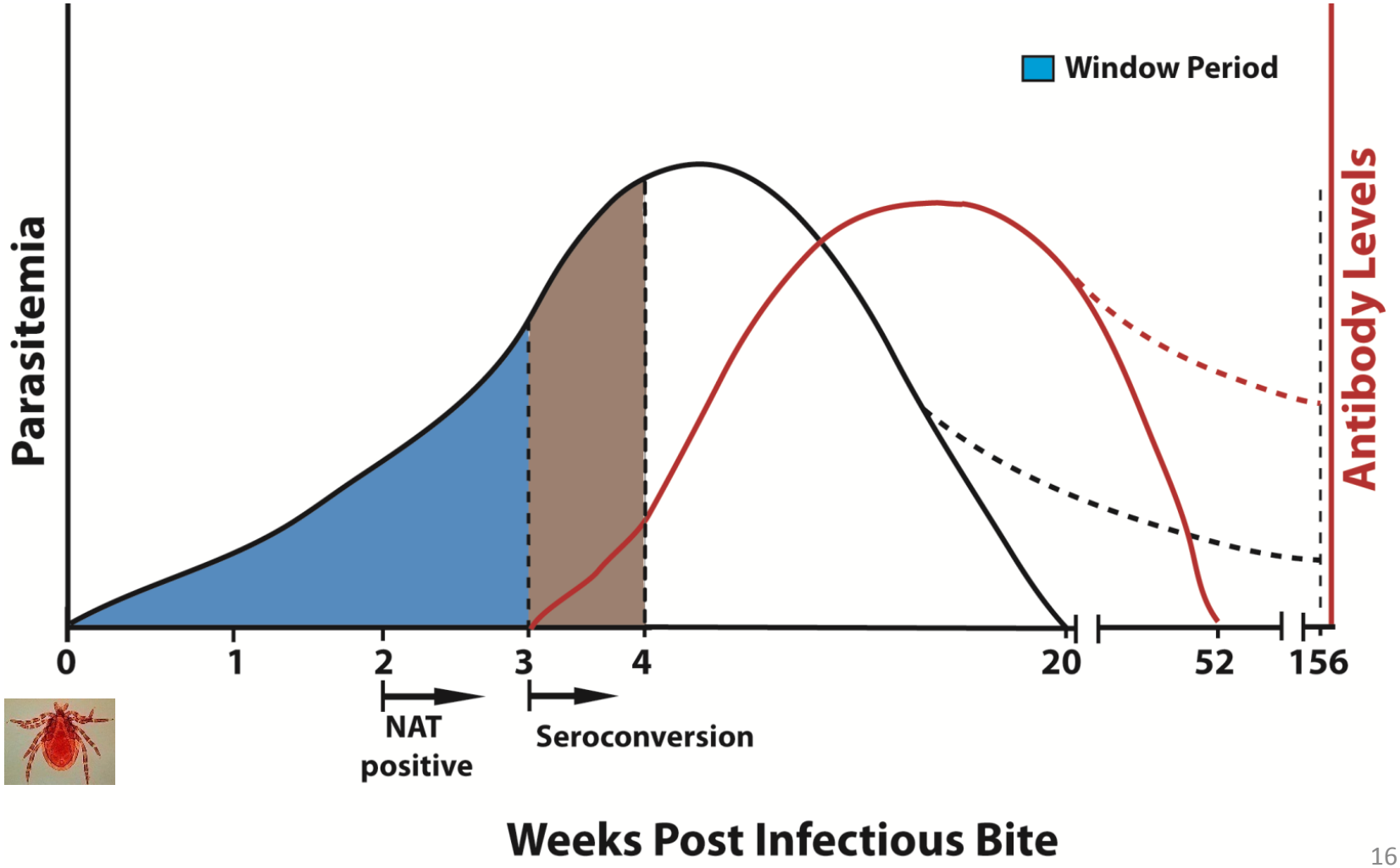
i) 5 states (highest endemic): CT, MA, RI, NY and NJ

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.

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