



FINAL REVIEW MEMORANDUM

STN: 125588/0

Date: December 5, 2017

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Products: *Babesia microti* Nucleic Acid Test

Sponsor: Oxford Immunotec, Inc.
700 Nickerson Road, Suite 200
Marlborough, MA 01752

Subject: Biological License Application (BLA) Final Review

Disciplines Reviewed: Pre-clinical studies
Chemistry, Manufacturing and Controls

Recommendation: Approval

Description of the test:

The *Babesia microti* Nucleic Acid Test (NAT) is a blood screening (b) (4) test for the detection of specific DNA to *Babesia microti* in whole blood samples collected using EDTA collection tubes.

The test is based on (b) (4). Sample's DNA is purified using the (b) (4) automated nucleic acid purification instrument and then amplified using the (b) (4). The assay employs the following controls:



- Internal endogenous control (Human 18S rRNA)
- *Babesia microti*-specific controls (high and low positive controls), consisting of *Babesia microti* infected (b) (4) whole blood diluted in negative human whole blood.
- Negative control, that consists of *Babesia microti* negative human whole blood.
- No-template control.

The assay allows the analysis of blood specimens collected in EDTA collection tubes and can be used as a stand-alone blood screening application for testing of blood donors and blood donations for evidence of *Babesia microti* infection.

Since there is currently no FDA licensed test for the diagnosis of babesiosis, this BLA qualified to be as Priority Review.

Intended Use:

The *Babesia microti* NAT is intended for use as a donor screening test to detect *Babesia microti* DNA in whole blood samples from individual human donors, including volunteer donors of whole blood and blood components, as well as other living donors. It is also intended to screen organ and tissue donors when specimens are obtained while the donor's heart is still beating.

This test is not intended for use on specimens from cadaveric (non-heart beating) donors or on cord blood samples

Review Summary:

This submission was received on May 12, 2015 and was granted priority review status. FDA issued a Complete Response Letter on September 29, 2015. Responses to FDA's letter were received on December 14, 2016 Amendment 13). My review focused on the evaluation of the sponsor's responses to Questions 8-16 (Pre-clinical studies) and Questions 18-26 (Chemistry, Manufacturing and Controls). My comments to Oxford Immunotec, Inc.'s responses are included in a review memo dated June 1, 2017 (attached).

After review of Amendment 13, FDA issued a new information request on February 17, 2017. I reviewed sponsor's responses to Question 3-12 (Pre-clinical studies) and Questions 13 (Chemistry, Manufacturing and Controls). My comments to Oxford Immunotec, Inc.'s responses are also included in my review memo dated June 1, 2017 (attached). I found most of the sponsor's responses to be acceptable.

However, I recommended the inclusion of *Leishnmania sp.* infected blood or the use of spiked samples (commercially available *Leishnmania sp.* DNA spiked into normal human blood) to complete the specificity studies.



On June 13, 2017 FDA sent a new Complete Response Letter to Oxford Immunotec, Inc. that did not include my recommendation for specificity testing using *Leishnmania sp.* infected blood or spiked samples.

This decision was made by DETTD management based on the sponsor's response dated December 14, 2016, which showed data from NCBI primer-BLAST searches against sequences within GenBank, summarized in the following tables and figures:

1. Table 24.1, page 49: Analysis of the specificity of IMUGEN *B. microti* primers for *B. microti*, related species and *Apicomplexan* species known to infect humans.
2. Figure 24.1, page 51: Screen shot of the alignment of IMUGEN primers and probe to closely related species and other *Apicomplexan* species known to infect humans.
3. Figure 24.3, page 53: Results from a Primer-BLAST against sequences within GenBank.

The data shows no cross reactivity with relevant organisms that could be found in donor blood.

In addition, I performed a BLAST search of the primers and probe sequences and no *Leishnmania sp.* genomes appeared in the first 101 hits rendered. I also performed sequence alignments of the primers and probe sequences and found only a 1% identity with *Leishnmania* 18s rDNA.

Recommendation

Based on my review and revision of the data submitted by Oxford Immunotec, Inc. on December 14, 2016, I recommend the approval of this BLA.