

## Valencia, Iliana

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**From:** Valencia, Iliana  
**Sent:** Friday, November 11, 2016 1:44 PM  
**To:** 'Jan Pullen'  
**Cc:** Wolfgang Pieken  
**Subject:** STN 125588 Babesia microti Nuclei Acid Test (NAT)- interactive review responses

Dear Dr. Pullen,

Via this email, FDA is addressing your responses to questions 1-7 to the FDA's complete response letter (dated Sep 29, 2015) for the purpose of interactive review for STN 125588 Babesia microti Nuclei Acid Test (NAT).

We have the following comments and request for additional information regarding the following items contained in your responses submitted for interactive review on August 25, 2016.

1. Your responses to FDA questions #2a, b, and c on protocol deviations for 18S internal control testing and re-evaluation of the data is acceptable.
2. In your response to FDA questions #3a and b, you have clarified that Clinical Study 1 was exploratory and no data from that study were intended to be used to establish clinical sensitivity for the final assays. Further you have clarified that the cut-off of (b) (4) was consistently used to determine positivity in Clinical Studies 2, 3a, 3b, and 4; therefore no re-analysis was needed. Your response is acceptable.
3. In your response to FDA question #4, you have clarified that that for 707 samples where line item data for the *Babesia* 18S Ct and the Hu18S Ct value columns were blank; these values were excluded from the MSTDONOR.xlsx due to a transcription error and not to a protocol deviation. You have reexamined the records and have provided an updated MSTDONOR.xlsx spreadsheet containing the corrected data. Your response is acceptable.
4. In your response to FDA questions #5 a and b on use of NAT assay different from the investigational NAT, you have clarified that Clinical Study 1 was exploratory and no data from that study were intended to be used to establish clinical sensitivity for the final assays. Your response is acceptable.
5. In your response to FDA question #7, you have provided the summary of the data supporting sensitivity and specificity of the clinical studies in 2/1, 2/2 or 2/3 table format, as appropriate. Your response is acceptable, but the final tables may change with resolution of some discrepancies listed below in question 8.
6. In your response to FDA question # 1 regarding clinical sensitivity, you have provided the summary of the data generated to demonstrate the clinical sensitivity of your NAT assay. Please provide the line data for the 72 samples tested under clinical sensitivity and include results with details of other tests conducted on these clinical samples.
7. In your response to FDA question # 6 regarding the lots of *Babesia* NAT manufactured by IMUGEN that were used in the clinical studies, you have provided documentation for lots of the NAT assay components used for clinical studies. We defer the response to this question until we have the information on how the lots are defined for your *Babesia* NAT.

8. The following comments apply to the data contained in the document MSTDONOR\_  
PROSPECTIVE, Attachment-6\_BCR-PCR-ATT-6"

- a. The line data for samples (b) (6) have only (b) (4) PCR repeat testing result instead of (b) (4) results. Please clarify this deviation.
- b. The line data for two samples (b) (6) have similar initial and repeat PCR test results; but their final interpretations are different: one is inconclusive and the other one was negative (see the table below). Please clarify.

DONOR_ID	Bab_Ct	Bab_Ct_rep_1	Bab_Ct_rep_2	Bab_Ct_rep_3	PCR_RESULT
(b) (6)	(b) (4)	Undet	Undet	Undet	Inconclusive
		Undet	Undet	Undet	Negative

- c. The line data for two samples (b) (6) has the initial Hu18S Ct result as "Undet," but the SOP for retesting was not followed. Please clarify this deviation.
- d. There is data entry errors observed regarding the PCR repeat testing results for the two samples (b) (6) Please update the data sheet.

Sincerely,

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