

Our STN: BL 125653/0

**BLA FILING NOTIFICATION**

Roche Molecular Systems, Inc.  
Attention: Julie Tai, PhD  
4300 Hacienda Drive  
Pleasanton, CA 94588-2722

Dear Dr. Tai:

This letter is in regard to your biologics license application (BLA) submitted under section 351 of the Public Health Service Act.

We have completed an initial review of your application dated April 7, 2017 for cobas® Zika to determine its acceptability for filing. Under 21 CFR 601.2(a), we have filed your application today. The review goal date is October 6, 2017. This acknowledgment of filing does not mean that we have issued a license nor does it represent any evaluation of the adequacy of the data submitted.

While conducting our filing review, we identified the following potential review issues:

- 1) Please verify that there was no impact to the facility and/or equipment (i.e. facility changes, new equipment, etc.) in order to establish the Zika Test Kit manufacturing at the (b) (4) facility.
- 2) The submission is missing information regarding test specifications and validation records for some cobas Zika-specific assay components, including:
  - a. Test specifications for:
    - i. Zika primers and probe, both individually and as components of the oligo pool
    - ii. Zika positive control, both in bulk and labeled containers
    - iii. MMX-R2 reagent, both as bulk and labeled vessels
    - iv. cobas® Zika test kit
    - v. cobas® Zika control kit
  - b. Validation records for processes pertaining to:
    - i. Zika primers and probe
    - ii. MMX-R2
    - iii. Zika positive control
    - iv. cobas® Zika test as a whole

Please provide the missing test specifications and validation records. Additionally, you indicated in the May 19, 2017 IR Response that process validation for the cobas® Zika Test Kit (480T) (7972466190) and the cobas® Zika Control Kit (8129690190) was previously submitted in the BLA; please clarify the location of your process validation information.

- 3) You have provided test specifications and process validation information regarding the cobas omni Reagent and Common Components which are shared with other assays used on the cobas 6800/8800 system. In order to complete the review, we need to confirm that the omni Reagents and Common Components have continued to meet specifications since the validations were originally performed. Please provide a description and the results of the process verification activities to include manufacturing process specific to the cobas® omni Reagent and Common Component Manufacturing which verify critical parameters to be used as in-process control to ensure the continued success of routine production.
- 4) Please provide microbial testing results to include bioburden, (b) (4) specific to the cobas® Zika Test Kit (480T) (7972466190) and Master Mix R2 (7972555001) to ensure lack of sample inhibition.
- 5) You indicated under the addendums titled Test Method Validation Equivalency Final Report Addendum for Additional Materials that identical formulations of test materials can be incorporated into previous test method validations by an addendum without additional validation tests. Please provide a list of identically formulated test materials along with the documented history of revision and history of the performance of the cobas® Zika Test Kit.
- 6) Please provide documentation to illustrate that a risk analysis was performed for the revised formulation for the cobas® Zika Positive Control and the cobas® Zika Negative Control.
- 7) In regards to purchasing controls, please describe the controls and measures in place to ensure that the supplier(s) meet the specified requirements.

We are providing the above comments to give you preliminary notice of potential review issues. Our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our complete review. Issues may be added, deleted, expanded upon, or modified as we review the application. If you respond to these issues during this review cycle, we may not consider your response before we take an action on your application. Following a review of the application, we shall advise you in writing of any action we have taken and request additional information if needed.

If you have any questions, please contact the Regulatory Project Manager, Dr. Vasantha Kumar at (240) 402-8413 or [Vasantha.Kumar@fda.hhs.gov](mailto:Vasantha.Kumar@fda.hhs.gov).

Sincerely,

Iliana Valencia, MS  
Chief, Regulatory Project Management Staff  
Office of Blood Research and Review  
Center for Biologics Evaluation and Research

**Concurrence Page**

Application Number: BL 125653/0  
Letter Type: Filing Notification (FL) –Deficiencies (DI)  
cc: EDR

History:  
Drafted Vasantha Kumar/June 2, 2017  
QC Iliana Valencia/June 2, 5, 2017  
Review: Caren Chancey/June 2, 2017 and June 5, 2017  
Cecily Jones/June 2, 2017  
Carolyn Renshaw/June 5, 2017  
Sanjai Kumar/June 2, 2017  
Sayah Nedjar/June 5, 2017  
J. Peyton Hobson/June 5, 2017

**Concurrence:**

OBRR/IO  
Vasantha Kumar

OBRR/DETTD/LEP  
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Iliana Valencia

**Template Approval Date: February 1, 2008**

Last Modified: September 14, 2016

Note: Modified to include new FDA Visual Identity Letterhead effective September 6, 2016.

Effective Date: February 1, 2008