



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

MEMORANDUM

To: STN 125653

From: Kori Francis, Team Leader, LACBRP, DBSQC, OCBQ
Ishrat Sultana, PhD, DBSQC, OCBQ

Through: Lokesh Bhattacharyya, PhD, Chief, LACBRP, DBSQC, OCBQ
James Kenney, PhD, Acting Director, DBSQC, OCBQ

Sponsor: Roche Molecular Systems, Inc. (RMS)

Product: The cobas® Zika Nucleic Acid Test Kit for use on the cobas® 6800/8800 Systems

Subject: Results of in-support testing of the Roche Molecular Systems, Inc. (RMS) cobas® Zika test kit.

CC: Caren Chancey, PhD, DETTD, OBRR
Pradip Akolkar, PhD, DETTD, OBRR
Maria Rios, PhD, DETTD, OBRR

Recommendation: Approval

Summary of Review:

This document constitutes the Review Memo of the in vitro nucleic acid screening test for the direct detection of Zika virus RNA in human plasma and serum on the cobas® 6800/8800 systems submitted by the Roche Molecular Systems, Inc. (RMS) for cobas® Zika IVD (STN 125653/0) on April 7, 2017. This reviewer recommends approval of the cobas® Zika test on the cobas® 6800/8800 systems based on the review of the decoded results of the Zika panel members for 3 kit lots and comparison against the corresponding FDA/CBER Lot Release Panel Expected Reactivity specifications as agreed to by RMS and FDA during the BLA review.

Background:

The cobas® Zika for use on the cobas® 6800/8800 Systems, is a qualitative in vitro nucleic acid screening test for the direct detection of Zika RNA in human plasma. This test is intended for use to screen donor samples for Zika RNA in plasma samples from individual human donors, including donors of whole blood and blood components, as well as other living donors. This test is also intended for use to screen organ and tissue donors when donor samples are obtained while the donor's heart is still beating. Plasma from all donors should be screened as individual samples. This test is not intended for use as an aid in diagnosis of Zika virus infection.

This test is not intended for use on samples of cord blood or other body fluids.

The cobas® Zika test consists of the cobas® Zika Test Kit, cobas® Zika Control Kit and the cobas® NHP Negative Control Kit. Additionally, the individual cobas omni reagents (MGP Reagent, Specimen Diluent, Lysis Reagent and Wash Reagent) are required for sample preparation. These four reagents are external to the cobas® Zika Test Kit and are required for assay performance.

The Office of Blood Research and Review/Division of Emerging and Transfusion Transmitted Diseases (OBRR/DETTD) and the Office of Compliance and Biologics Quality/ Division of Biological Standards and Quality Control (OCBQ/DBSQC) agreed that due to the large footprint of the cobas® 6800/8800 instrument and the excessive resources required to maintain the instrument, coded panels would be used for lot release testing at RMS. The results of the coded samples will be forwarded to DBSQC through the Center for Biological Evaluation and Review (CBER) Sample Custodian. DBSQC will decode the results using the key provided by DETTD and evaluate the results against the established expected reactivity for each lot release panel.

Information Reviewed - 125653/0/12 Received 06-Sep-2017:

- Lot Submission Protocol for Kit Cobas 6800/8800 Zika 480T IVD, Batch Y12974
- Lot Submission Protocol for Kit Cobas 6800/8800 Zika 480T IVD, Batch YD2970
- Lot Submission Protocol for Kit Cobas 6800/8800 Zika 480T IVD, Batch YD2971

Results:

The sponsor provided coded test results from 3 master lots (Y12974, YD2970 and YD2971) of the cobas® 6800/8800 Zika kit.

The results of the 3 master lots of RMS cobas® 6800/8800 Zika kit submitted to CBER were decoded and compared to the established Expected Reactivity of the FDA/CBER

Zika RNA Lot Release Panel #29 (Table 1). The established expected reactivity for the lot release panel is stored in the (b) (2), (b) (4) folder. Each lot release panel member is characterized for the presence or absence of Zika RNA and is designed to provide a release criterion for each lot of product. The CBER Zika RNA Lot Release Panel is comprised of 7 panel members. Six of them are composed of human plasma spiked with different concentrations of Zika virus and one member is composed of human plasma without spiking with Zika viral stock. CBER provided RMS with three sets of (10) blinded vials of the FDA/CBER Zika lot release panel. Three of the panel members were duplicated in each set and each vial was assigned a unique identification number by DETTD using the EXCEL random number generator function. Since three panel members are duplicated in this scheme, a total of 10 results were produced for each master kit lot tested by RMS. See Table 1 below. The key to the coded sample was provided to DBSQC and is stored in the (b) (2), (b) (4) folder.

The results presented in Table 1 show that each of the 3 master lots (Y12974, YD2970 and YD2971) of the cobas® Zika test was able to detect Zika RNA panel members correctly. That is, each of the 10 blinded (coded vials) was decoded and the Expected Reactivity matched the determination produced by each of the three master kit lots. The three duplicated panel members also matched the correct Expected Reactivity. For kit lot YD2970, panel member 2905 produced a Reactive on one and Non-reactive on the duplicate coded sample. See Table 1 column 4 below. This determination is expected since the panel member contains a very low level of Zika which is under the predicted level of detection (LOD) of the kit. All panel members whose expected reactivity's (acceptance criteria) were Reactive (R) tested reactive, all panel members whose expected reactivity's were Non-reactive (NR) tested non-reactive. Lots Y12974, YD2970 and YD2971 met the FDA/CBER established lot release criteria (Expected Reactivity). All 3 lots "Passed" lot release evaluation.

A summary of the decoded results of the FDA/CBER Zika virus RNA Lot Release Panel #29 and the Expected Reactivity of each panel member is presented in Table 1 below. The Pass/Fail determination of the lot release panel and each cobas® Zika kit is presented in Table 2 below.

Table 1: Decoded RMS cobas® Zika RNA Test Kit Lot Release Results

FDA/CBER Panel ID	Expected Reactivity	Y12974	YD2970	YD2971
		FDA/CBER Zika virus RNA Lot Release Panel #29		
2901	R	R	R	R
2902	R	R	R	R
2903	R	R	R	R
		R	R	R
2904	R	R	R	R
		R	R	R
2905	R/NR	R	R	R
		R	NR	
2906	NR	NR	NR	NR
2907	R/NR	R	NR	NR
				NR

R - Reactive NR - Non-Reactive

Table 2: Pass/Fail Determination of Lot Release Panels and cobas® Zika Kit Lots

Batch ID	Expiration Date	Zika Panel #29 Pass/Fail	Kit Lot Pass/Fail
Y12974	07/2018	Pass	Pass
YD2970	08/2018	Pass	Pass
YD2971	08/2018	Pass	Pass

Conclusions:

The results presented in the lot release protocols of the 3 master lots (Y12974, YD2970 & YD2971) submitted in support of licensure and summarized above demonstrate that the cobas® Zika Virus Nucleic acid test for use on the cobas® 6800/8800 Systems using the designated FDA/CBER Zika virus RNA Lot Release Panel #29 were able to correctly detect the presence or absence of Zika RNA. All the known reactive Zika panel members were reactive and known nonreactive members were nonreactive.

Based on a review of the Zika panel members results presented in the Lot Submission Protocols for the three lots noted above, this reviewer recommends approval of the cobas® Zika virus Nucleic acid test for use on the cobas® 6800/8800 Systems.