Food and Drug Administration
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Silver Spring, MD 20993-0002
www.fda.gov

510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT

I Background Information:

A 510(k) Number

K200506

B Applicant

Chembio Diagnostic Systems

C Proprietary and Established Names

DPP Zika IgM System, DPP Zika IgM System Control Pack, and DPP Micro Reader

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
QFO	Class II	21 CFR 866.3935 - Zika Virus Serological Reagents	MI - Microbiology
QCH	Class II	21 CFR 866.3920 - Assayed quality control material for clinical microbiology assays	MI - Microbiology
JJQ	Class I	21 CFR 862.2300 - Colorimeter, photometer, or spectrophotometer for clinical use	CH - Clinical Chemistry

II Submission/Device Overview:

A Purpose for Submission:

The purpose of this premarket notification is to submit a new device (DPP Zika IgM System) to the FDA for consideration for clearance.

B Measurand:

Human IgM antibodies against Zika virus.

C Type of Test:

The Chembio DPP Zika IgM System is a qualitative immunochromatographic assay for the presumptive detection of IgM antibodies to Zika virus.

III Intended Use/Indications for Use:

A Intended Use(s):
See Indications for Use below.

B Indication(s) for Use:

DPP Zika IgM System

The DPP Zika IgM System is intended for the presumptive qualitative detection of Zika virus IgM antibodies in human serum (plain or separation gel), potassium-EDTA plasma, potassium-EDTA venous whole blood, or fingerstick whole blood specimens, collected from individuals meeting the CDC Zika virus clinical criteria (e.g., a history of clinical signs and symptoms associated with Zika virus infection) and/or CDC Zika virus epidemiological criteria (e.g., history of residence in or travel to a geographic region with active Zika transmission at the time of travel, or other epidemiological criteria for which Zika virus testing may be indicated). Specimens from symptomatic patients or returning travelers from endemic areas should not be collected prior to 8 days after symptom onset or after potential exposure as a sample collected earlier may return a negative result. If testing is needed after day 4 but before day 8 and results are negative, testing must be repeated one week later. Positive results must be confirmed by following the latest CDC guidelines for the diagnosis of Zika virus infection.

Results of this test are intended to be used in conjunction with clinical observations, patient history, epidemiological information, and other laboratory results. Zika IgM levels over the course of illness are not well characterized. Zika IgM levels are variable during the course of infection and may be detectable near day 4 post-onset of symptoms and persist up to approximately 12 weeks following initial infection.

Negative results may be seen in specimens collected before day four post-onset of symptoms or after the window of detectable IgM closes and therefore do not preclude the possibility of Zika virus infection, past or present.

The Chembio DPP Zika IgM System is not indicated for testing blood or plasma donors.

The test cannot be visually interpreted by the operator and must be read on the DPP Micro Reader.

DPP Zika IgM System Control Pack

The Chembio DPP Zika IgM System Control Pack is an external quality control kit for use with the DPP Zika IgM System only. The performance characteristics of the DPP Zika IgM System Control Pack have not been established for any other assay or instrument different from the DPP Micro Reader.

DPP MicroReader

The DPP Micro Reader is a reflectance reader used to obtain test results from DPP Zika IgM System. The DPP Micro Reader is necessary to minimize errors from direct visual interpretation; therefore, the results of DPP Zika IgM System cartridges must be read exclusively with the DPP Micro Reader.

C Special Conditions for Use Statement(s):
Rx - For Prescription Use Only

D Special Instrument Requirements:
Chembio DPP Micro Reader

IV Device/System Characteristics:

A Device Description:

The Chembio DPP Zika IgM System is a qualitative immunochromatographic assay for the presumptive detection of IgM antibodies to Zika virus. The Chembio DPP Zika IgM System includes the DPP Zika Test Device and the DPP Micro Reader.

MATERIALS PROVIDED
Each kit contains the reagents and tools to perform 20 tests:
20 individually pouched DPP Zika IgM Test Devices, each containing:

- 1 DPP Zika Test Device (membrane strip with immobilized recombinant Zika NS-1 antigen in the TEST (T) area and Protein A in the CONTROL (C) area.
- 1 Desiccant Pouch

20 Disposable 10 µL Microsafe Tubes
20 Sample vials
20 Transfer Pipets (100 µl)
1 DPP Zika IgM Buffer– YELLOW Cap

- 7.5 mL contains sodium phosphate, sodium chloride, EDTA, NP-40, Tween 20, Urea, chicken serum, gentamicin, streptomycin, and sodium azide as preservative.

1 Product Insert for the DPP Zika IgM System
1 Quick Reference Guide for the DPP Zika IgM System

MATERIALS REQUIRED BUT NOT PROVIDED (SYSTEM RELATED)

- Chembio DPP Micro Reader.
  Each kit contains:
  - DPP Micro Reader with Zika IgM RFID sticker

    - 3 Lithium-ion, type CR2032 (3 V/230 mAh), coin cell batteries (installed)
  - Custom power adapter cable (USB to 2.0 mm jack)
  - Power plug adaptor
  - DPP Cartridge Holder
  - Microfiber cloth
  - User Manual

ADDITIONAL REQUIRED MATERIALS (ASSAY RELATED)

- Chembio DPP Zika IgM System Control Pack
  - 1 DPP Zika Reactive Control (volume of 300 µL; enough to perform 15 tests): undiluted, naturally occurring Zika IgM positive plasma sample.
  - 1 DPP Non-Reactive Control (volume of 300 µL; enough to perform 15 tests): undiluted, naturally occurring Zika IgM negative plasma sample.
  - 1 DPP Zika Diluent (300 µL; enough to perform 15 tests): undiluted, naturally occurring Zika IgM negative plasma samples.
  - 1 Product Insert

  All reagents are supplied ready to use.
- Clock, watch, or other timing device
- Pipettor capable of delivering 10-100 µL of sample may be used in lieu of the disposable 10 µL MicroSafe Tube and 100 µL Transfer Pipets supplied with the kit (for serum, potassium-EDTA plasma, and potassium-EDTA venous whole blood specimens or with the Chembio DPP Zika IgM System Control Pack)
- Microcentrifuge Tubes
- Disposable gloves
- Antiseptic wipes
- Biohazard disposal container
- For fingerstick whole blood specimens:
  - Sterile gauze
  - Sterile Safety Lancets for fingerstick whole blood specimens
- For venous whole blood or serum/plasma specimens:
  - Collection devices

For a fingerstick whole blood sample, sample collection uses a 10 µl Microsafe Tube. For human serum (plain or separation gel), potassium-EDTA plasma, potassium-EDTA venous whole blood specimens, 10 µl of sample is collected using a calibrated laboratory pipet. Once the sample and buffer combination are added to the DPP Zika IgM Test Device, results are read by using the Chembio DPP Micro Reader, a portable, maintenance-free, battery-powered instrument that is operated by a single, multi-function button. The results of the DPP Zika IgM Test Device cannot be visually interpreted by the operator. Controls are kit lot specific and must not be interchanged between different DPP Zika IgM System lots.

B Principle of Operation:

The Chembio DPP Zika IgM System is a qualitative immunochromatographic assay for the presumptive detection of IgM antibodies to Zika virus. The device employs Chembio's DPP (Dual Path Platform) technology that differs from traditional lateral flow technology by

delivering the sample directly onto the capture zone, followed by delivery of the colored conjugate. To initiate the test, a 10 µL specimen is collected, diluted with kit buffer and applied to the SAMPLE+BUFFER Well#1 of the DPP Zika Test Device. The specimen migrates along the sample path membrane and is delivered to the TEST (T) area of the reagent strip, where Zika NS1 antigens are immobilized. Zika-specific antibodies, if present in the sample, bind to the immobilized NS1 antigens in the T area, while non-specific antibodies bind to the Protein A in the CONTROL (C) area. Successful sample application is indicated by the disappearance of soluble dye lines in the T and C areas. Five minutes after adding the sample, buffer is added into the BUFFER Well #2. The buffer hydrates the dried IgM antibody-binding colored conjugate, which migrates to the T area. Interpretation of reactions is performed by using the Chembio DPP Micro Reader an instrument that uses assay-specific algorithms to verify the presence of the C line and measure color intensity at the T line position.

The DPP Micro Reader interprets the result using assay-specific cut-off values, and reports a REACTIVE, NON-REACTIVE or INVALID result along with a numerical intensity value for the IgM test line after approximately 3 seconds. The results are presented through a 14-segment liquid crystal display (LCD) on the top of the instrument and displays the test results to the operator.

Patient results should be interpreted as follows:

READER DISPLAY	Result	Interpretation	Follow-Up
<20	NON-REACTIVE	Zika IgM antibodies were not detected in the specimen.	Pregnant women and sexually active men not practicing birth control should be re-tested with a later bleed taken at least **7 days** from the first specimen. In the case of pregnant women please follow the latest CDC *Interim Guidance for Health Care Providers Caring for Pregnant Women with Possible Zika Virus* regarding clinical management of negative results (https://www.cdc.gov/zika/hc-providers/index.html).
≥ 20	REACTIVE	IgM antibodies to Zika virus detected in the specimen.	The result should be confirmed by the latest CDC testing algorithms. For information regarding Zika testing algorithm, please refer to CDC guidance for state and local public health laboratories: https//:www.cdc.gov/zika/laboratories/index.html.
INV	INVALID	The test results cannot be interpreted	It is recommended that the INVALID test be repeated with a new device.

Note: The magnitude of the reported Index value is not indicative of the amount of Zika virus immunoglobulin present in the patient sample.

Results should be read 15 minutes after addition of the Buffer into Well #2.

Negative results with specimens collected before 8 days after onset of symptoms must be repeated with a later bleed taken at least **7 days** from the first specimen.

The DPP Micro Reader is necessary to minimize errors from direct visual interpretation; therefore, results of DPP Zika IgM System must be read exclusively with the DPP Micro Reader.

The DPP Micro Reader is not configurable by the user. The DPP Micro Reader has been individually adapted for specific use with the DPP Zika IgM System through a product-specific configuration file stored on a dedicated, irremovable, Radio Frequency Identifier (RFID) sticker affixed to the Micro Reader. The RFID must be used to operate the reader. The configuration file on the RFID sticker carries the parameters specific to the detection and quantitation of the "TEST" and "CONTROL" lines and the algorithm used by the reader to qualify and display test line results as reactive, non-reactive or indeterminate. The configuration file is uploaded onto the reader each time a measurement is made by the user.

C Instrument Description Information:

Modes of Operation	Yes	No
Does the applicant's device contain the ability to transmit data to a computer, webserver, or mobile device?	☐	☒
Does the applicant's device transmit data to a computer, webserver, or mobile device using wireless transmission?	☐	☒
Software		
FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types.	☒	☐

1. Instrument Name:

   DPP Micro Reader

2. Specimen Identification:

   Sample identification is manually captured in a paper record.

3. Specimen Sampling and Handling:

   Managed by a trained technician.

4. Calibration:

   Not applicable

5. Quality Control:

   The Chembio DPP Zika IgM System Control Pack is an external quality control kit for use with the DPP Zika IgM System only. The performance characteristics of the DPP Zika IgM

System Control Pack have not been established for any other assay or instrument different from the DPP Micro Reader.

Chembio DPP Zika IgM System Control Pack Reactive/Non-Reactive Controls are human, plasma-based reagents. The controls are specifically formulated and manufactured to ensure performance of the test and are used to verify the user's ability to properly perform the test and interpret the results. Use of control reagents manufactured by another source may not produce the required results, and therefore, may not meet the requirements for an adequate quality assurance program for the DPP Zika IgM System.

If control values lie outside the expected ranges, the test is invalid and patient results cannot be reported. It is the responsibility of each site using the DPP Zika IgM System to establish an adequate quality assurance program to ensure the performance of the device under its specific locations and conditions of use. Quality control requirements should be followed in conformance with local, state, and federal regulations or accreditation requirements and the site's standard quality control procedures.

V Substantial Equivalence Information:

A Predicate Device Name(s):
ZIKV Detect 2.0 IgM Capture ELISA

B Predicate 510(k) Number(s):
DEN180069

C Comparison with Predicate(s):

Device & Predicate Device(s):	K200506	DEN180069
Device Trade Name	Chembio DPP Zika IgM System	Inbios ZIKV Detect 2.0 IgM Capture ELISA
General Device Characteristic Similarities		
Analyte	Human Zika virus IgM antibodies	Same

Intended Use/Indications For Use	The DPP Zika IgM System is intended for the presumptive qualitative detection of Zika virus IgM antibodies in human serum (plain or separation gel), potassium-EDTA plasma, potassium-EDTA venous whole blood, or fingerstick whole blood specimens, collected from individuals meeting the CDC Zika virus clinical criteria (e.g., a history of clinical signs and symptoms associated with Zika virus infection) and/or CDC Zika virus epidemiological criteria (e.g., history of residence in or travel to a geographic region with active Zika transmission at the time of travel, or other epidemiological criteria for which Zika virus testing may be indicated). Specimens from symptomatic patients or returning travelers from endemic areas should not be collected prior to 8 days after symptom onset or after potential exposure as a sample collected earlier may return a negative result. If testing is needed after day 4 but before day 8 and results are negative, testing must be repeated one week later. Positive results must be confirmed by following the latest CDC guidelines for the diagnosis of Zika virus infection. Results of this test are intended to be used in conjunction with clinical observations, patient history, epidemiological information, and other laboratory results. Zika IgM levels over the course of illness are not well characterized. Zika IgM levels are variable during the course of infection and may be detectable near day 4 post-onset of symptoms and persist up to approximately 12 weeks following initial infection. Negative results may be seen in specimens collected before day four post-onset of symptoms or after the window of detectable IgM closes and therefore do not preclude the possibility of Zika virus infection, past or present. The Chembio DPP Zika IgM System is not indicated for testing blood or plasma donors. The test cannot be visually interpreted by the operator and must be read on the DPP Micro Reader.	The ZIKV Detect 2.0 IgM Capture ELISA is intended for the qualitative detection of Zika virus IgM antibodies in human sera for the presumptive clinical laboratory diagnosis of Zika virus infection. The assay is intended for use only in patients with clinical signs and symptoms consistent with Zika virus infection, and/or CDC Zika virus epidemiological criteria (e.g., history of residence in or travel to a geographic region with active Zika transmission at the time of travel, or other epidemiological criteria for which Zika virus testing may be indicated). Assay results are for the presumptive detection of IgM antibodies to Zika virus (ZIKV). Positive results must be confirmed by following the latest CDC guidelines for the diagnosis of Zika virus infection. Results of this test are intended to be used in conjunction with clinical observations, patient history, epidemiological information, and other laboratory evidence to make patient management decisions. Zika IgM levels are variable over the course of the infection and may be detectable near day four post onset of symptoms and persist up to approximately 12 weeks following initial infection. Negative results may be seen in specimens collected before day four post onset of symptoms or after the window of detectable IgM closes, and therefore do not preclude the possibility of Zika virus infection, past or present. This assay is not indicated for testing blood or plasma donors.
General Device Characteristic Differences		

Sample Type	Human serum (plain or separation gel), potassium-EDTA plasma, potassium-EDTA venous whole blood, or fingerstick whole blood specimens	Human serum
Sample Size	Minimum of 10 µL before dilution	Minimum of 4 µL before dilution
Antibody target	NS-1 protein	Zika envelope glycoproteins
Type of Test	Lateral cross-flow dual path platform (DPP) immunochromatographic assay	IgM Capture enzyme-linked immunosorbent assay (ELISA)
Quality Control	Provided Separately	Included
Interpretation of Results	<20 NON-REACTIVE ≥20 REACTIVE INVALID Result is displayed through use of the DPP Microreader. No calculations are required by the user.	Zika Ag OD450 ≥ Threshold Zika Ag OD450 AND Zika ISR value > 1.90: Presumptive Zika Positive Initial: Zika Ag OD450 ≥ Threshold Zika Ag OD450 AND 1.50 ≤ Zika ISR ≤ 1.90: Retest in duplicate Retest: Zika Ag OD450 ≥ Threshold Zika Ag OD450 AND Zika ISR value ≥ 1.70 **Presumptive Zika Positive** Not Presumptive Zika Positive & CCA / NCA ratio ≥ 5.00: **Presumptive Other Flavivirus Positive** Not Presumptive Zika Positive & CCA / NCA ratio < 5.00: **Negative** Interpretation requires calculations performed by the user prior to reporting the result
Time to Result	Time to result is 15 minutes after addition of Buffer into Well#2.	Time to result is approximately 3.5 hrs.
Reagent Storage	2-8°C Refrigerator or up to 23°C	2-8°C Refrigerator only

VI Standards/Guidance Documents Referenced:

Standard Title	*Document Number*	*Publication Date*	*Recognition Number*
Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline – Third Edition	CLSI EP05-A3	2014	7-251
Interference Testing in Clinical Chemistry. Third edition	CLSI EP07-3rd Ed.	2018	7-275
User Protocol for Evaluation of Qualitative Test Performance Approved Guideline – Second Edition	CLSI EP12-A2	2008	7-152
User of Performance for Precision and Trueness, Approved Guideline— Third edition	CLSI EP15-A3	2014	7-253
Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline - Second Edition	CLSI EP17-A2	2012	7-233
Evaluation of Stability of *In Vitro* Diagnostic Reagents; Approved Guideline.	CLSI EP25-A	2009	7-235
Supplemental Tables For Interference Testing In Clinical Chemistry	CLSI EP37	2018	7-284
EMC-the International Electrotechnical Commission (IEC)	(IEC) 60601-1-2 Edition 4.0 2014-02	2014	19-8
Quality System Regulation	21CFR 820		N/A
Labeling for *in vitro* diagnostic products	21CFR 809.10		N/A
Colorimeter, photometer, or spectrophotometer for clinical use	21 CFR §862.2300		N/A
Special controls under, Zika virus serological reagents	21 CFR §866.3935	2019	N/A

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

a. DPP Zika IgM System

Multi-site precision of the DPP Zika IgM System was evaluated at three US sites. A four-member panel (negative, high negative, low positive and high positive) plasma samples were measured using three (3) lots of the DPP Zika IgM System. Testing was performed over five days, with two runs per day. Each run was performed by one operator at each site, for a total of 6 operators and instruments (operator is confounded with the run and instrument). Each panel member was tested by only one operator in triplicates for each of the 3 assay lots (5 x 3 x 3 x 2 x 3 design; n = 270 for each sample).

Precision estimates were derived for reproducibility.

Reproducibility Results for the DPP Zika IgM System

			Within-Run		Between-Operator/ Instrument		Between-Day		Between-Lot		Between-Site		Total*	
Sample ID	Mean Reader Value	N	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Moderate Positive	110.0	270	13.4	12.2	2.8	2.5	0.0	0.0	6.3	5.8	0.0	0.0	15.1	13.7
Low Positive	36.5	270	5.5	15.0	2.4	6.7	0.0	0.0	3.6	1.0	0.0	0.0	7.0	19.0
High Negative	15.1	270	3.3	21.5	1.5	9.8	0.0	0.0	1.0	6.6	0.0	0.0	3.7	24.5
Negative	1.7	270	1.3	n/a	0.0	n/a	0.0	n/a	0.0	n/a	1.3	n/a	1.8	n/a

%CV coefficient of variation expressed as a percentage; SD standard deviation.

* Total = Within-Run + Between-Operator/Instrument + Between-Day + Between-Lot + Between-Site

b. DPP Zika IgM System Control Pack

The precision of the controls was assayed separately using a single lot of controls and reagents. Testing was performed at a single site, over five days, with two operators per day, two instruments per operator, two runs per instrument, and two replicates per run (5 x 2 x 2 x 2 x 2 design; n = 80 for each sample). The data were analyzed for the Within-Run, Between-Run, Between-Instrument, Between-Operator, Between-Day and Total/Within-Lab.

5-day Precision Results for DPP Zika IgM System Control Pack

			Within-Run		Between-Run		Between-Instrument		Between-Operator		Between-Day		Total*	
Sample ID	**Mean Reader Value**	**N**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
Moderate Positive Control	54.1	80	8.5	15.7	0.0	0.0	4.7	8.6	0.0	0.0	0.0	0.0	9.7	17.9
Low Positive Control	31.9	80	5.6	17.5	0.9	3.0	1.8	5.6	4.2	13.0	0.0	0.0	7.2	22.7
Negative Control	3.4	80	1.3	n/a	0.3	n/a	0.6	n/a	0.0	n/a	0.3	n/a	1.5	n/a

* Total = Within-Run + Between-Run + Between-Instrument + Between-Operator + Between-Day

2. Linearity:

Not applicable

3. Analytical Specificity/Interference:

a. *Cross-Reactivity*:

The performance of the DPP Zika IgM System was evaluated for the potential interference caused by autoantibodies, and antibodies against other closely related viruses as well as pathogens where infection produces symptoms similar to those observed during Zika virus infection, and potentially naturally occurring cross-reactive samples, previously characterized as positive per the supplier's Certificate of Analysis for various disease states using FDA cleared/ approved devices when possible. Except for specimens with HCV, HBV, Leptospira, ANA, Rheumatoid Factor, HAMA, Malaria, and Yellow Fever Virus Post-Immunization, only specimens confirmed positive for IgM of the respective disease state were included in the analysis.

One Dengue IgM sample (1/48) and two Cytomegalovirus IgM samples (2/38) were cross-reactive using the DPP Zika IgM System. Babesia cross-reactivity was not evaluated.

Summary of DPP Zika IgM System Cross-Reactivity

			DPP Zika IgM System		
	Organism/Condition	**# of Specimens**	**# Zika Negative**	**# Zika Positive**	**% Cross-reactivity**
Flavivirus	Anti-Chikungunya virus IgM	26	26	0	0%
	Anti-Dengue Virus IgM	48	47	1*	2%
	Anti-West Nile Vile IgM	28	28	0	0%
	Yellow fever virus post-immunization[1]	32	32	0	0%
Other Viruses/diseases	Anti- Malaria/anti-*plasmodium falciparum*[2]	20	20	0	0%
	Anti-*Borrelia sp*. (Lyme Disease) IgM	10	10	0	0%
	Anti-Cytomegalovirus (CMV) IgM	38	36	2**	5.3%
	Anti-Epstein Barr Virus (EBV) IgM	10	10	0	0%

	Anti-Hepatitis (B) virus (Total)	13	13	0	0%
	Anti-Hepatitis (C) virus (Total)	10	10	0	0%
	Anti-Herpes simplex virus 1 and 2 (HSV-1, HSV-2) IgM	23	23	0	0%
	Anti-Leptospira (Leptospirosis) IgM[3]	16	16	0	0%
	Anti-nuclear Antibodies (ANA)	11	11	0	0%
	Anti-Parvovirus B19 IgM	7	7	0	0%
	Anti-Rubella virus IgM	12	12	0	0%
	Rheumatoid Factor	12	12	0	0%
	Anti-Varicella zoster virus IgM	3	3	0	0%
	Human Anti-mouse Antibody (HAMA)	10	10	0	0%
	Total	329	326	3	

* Negative by an FDA cleared Zika Assay; West Nile equivocal.
** Negative by an FDA cleared Zika Assay.
[1] IgM levels could not be established.
[2] Specimens were confirmed positive for Malaria infection by Giemsa and Microscopy but serological status is not known.
[3] Pretreated with rheumatoid factor-absorbent prior to IgM detection.

b. *Endogenous Interference*:

The DPP Zika IgM System was evaluated for potential interference with endogenous substances. These interfering substances were spiked into low reactive and normal human plasma samples to evaluate their impact on assay performance. In addition, to assure that the negative plasma itself had no effects on the test result, it was tested alone on the assay giving negative results. To further corroborate that the positive Zika IgM spike was appropriate, it was also tested alone on the assay showing positive results near cut-off. Each sample was tested in triplicate by one operator.

None of the tested endogenous substances cause a change in clinical interpretation for the DPP Zika IgM System.

Summary DPP Zika IgM System Endogenous Interference

		DPP Zika IgM system (#reactive/ #tested)	
		Negative diluent	Zika IgM Spike
Interfering substances	**Concentration**	**(Non-Reactive)**	**(Reactive)**
Hemoglobin	10 mg/mL	0/3	3/3
Bilirubin, Conjugated	0.4 mg/mL	0/3	3/3
Bilirubin, Un-Conjugated	0.4 mg/mL	0/3	3/3
Serum Proteins	60 mg/mL	0/3	3/3
HAMA	732 ng/mL	0/3	3/3
Cholesterol	4 mg/mL	0/3	3/3
Rheumatoid Factor	2000 IU/mL	0/3	3/3
Triglycerides	15 mg/mL	0/3	3/3

4. Assay Reportable Range:

Not applicable

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

a. *Traceability/Analytical Sensitivity*:

The analytical sensitivity at the cut-off values for the DPP Zika IgM System was established using WHO 1st International standard for anti-Asian lineage Zika virus antibody (human) (NIBSC 16/352). This preparation contains antibodies reactive to Dengue virus. The standard was used to prepare a dilution series. The concentration of the reference reagent that corresponds to average reader values just above the cut-off of 20 (average values of <30 when analyzed by the DPP Micro Reader) and where at least 95% of all replicates tested reactive was 650 IU/mL in serum, 700 IU/mL in potassium-EDTA plasma, and 725 IU/mL in potassium-EDTA venous whole blood.

Results obtained with other NS1 assays suggest the standard has low concentration for the IgM isotype against this analyte, while the response is stronger for envelope-based assays.

b. *Stability*:

Sample Stability:
The study data supports specimen stability at the following storage temperatures and storage times:

- Potassium-EDTA venous whole blood and fingerstick whole blood immediate use
- Stored at 2–8°C separated serum and potassium-EDTA plasma samples for up to 3 days*
- No more than 2 freeze-thaw cycles for separated serum samples and 5 freeze-thaw cycles for potassium-EDTA plasma

Summary of Stability Claims for the DPP Zika IgM System Reagents	
Stability Type	**Claim**
DPP Zika IgM System Reagent Shelf-Life Stability (up to 23 °C)	6 months
DPP Zika IgM System Reagent Shelf-Life Stability (2-8 °C)	12 months
DPP Zika IgM System Reagent In Use (up to 23 °C)	1 month when used within the expiration date

The user must not open the pouch until ready to perform a test.

Summary of Stability Claims for the DPP Zika IgM System Control Pack	
Stability Type	**Claim**
DPP Zika IgM System Control Shelf-Life Stability (-20 °C)	6 months
DPP Zika IgM System Control In Use Stability (-20 °C)	N/A**

DPP Zika IgM System Control Freeze-Thaw Cycles	3

* Based on two instead of three studies.

** It is recommended that the end user divide the controls into smaller aliquots that are then frozen back. The end user dilutes the controls only before use, and immediately discards any remaining material after use. Frozen aliquots are acceptable if they are both within the freeze-thaw cycles and the shelf life claimed above.

6. Detection Limit:

   See Section 5.a, *Traceability/Analytical Sensitivity*.

7. Assay Cut-Off:

   The assay cut-off value was determined using the Limit of the Blank (LoB) approach and through the testing of 569 natural serum samples sourced from United States and Mexico, both non-endemic populations; 184 natural plasma samples sourced from a non-endemic population from the United States (n=95) and an endemic population from Peru (n= 89); 215 natural venous whole blood samples sourced from a non-endemic population from the United States; and 102 natural capillary whole blood samples sourced from a non-endemic population from the United States.

   The cut-off value was set at 20 when analyzed by the DPP Micro Reader: a reader value of < 20 is considered non-reactive and a value ≥ 20 is considered reactive. The value was corroborated by the clinical studies.

8. Prozone/ Hook Effect:

   A high dose hook effect is not expected to occur due to the separation between the capture step and the conjugate addition step in the DPP Zika IgM System. On the primary flow path of DPP devices, the sample migrates towards the immobilized immunoreagents on the horizontal strip, that capture the analyte of interest, if present. Following a brief incubation to maximize binding efficiency, the detector nanoparticles are released from the conjugate pad via the secondary flow path. In addition, the conjugate buffer, devoid of any analyte, “cleans” the test membrane by “pushing” any remaining free analyte along the test strip. This sequential approach resembles the traditional ELISA assay process and minimizes the potential of the prozone (or hook) effect. Formal Hook Effect testing was not performed.

9. Class Specificity:

   Antibody class specificity was evaluated on the DPP Zika IgM System. The reducing agent dithiothreitol (DTT) was used to specifically inactivate IgM antibodies. In this study, tests with sample buffer containing 10 mM DTT were run and compared to tests with the standard Zika IgM sample buffer formulation on three clinical Zika IgM positive samples. Sample buffer with 10 mM DTT resulted in non-reactive DPP Zika IgM System results in all the samples, suggesting that the IgM antibody reactivity was abolished. In contrast, standard Zika IgM sample buffer formulation resulted in the expected reactive DPP Zika IgM System results when tested with the same three clinical Zika IgM positive samples.

DTT Effect on IgM Measurements for the DPP Zika IgM System

	Specimens		
	A EDTA PLASMA IgM+/IgG+	**B (neat) EDTA PLASMA IgM/IgG+**	**B (1:64) EDTA PLASMA IGM+/ IgG+**
	DPP Zika IgM System Results		
Standard Sample buffer	140 (R)	320 (R)	330 (R)
Sample buffer with 10 mM DTT	9 (NR)	3 (NR)	1 (NR)

* This study was performed with an older version of the device that was determined equivalent to the one under clearance. The devices differ in that the cleared device 1) replaces the liquid form of the goat anti-human IgG antibodies and heterophilic antibody (HA) interference blocker for treatment of the specimen with the dehydrated form of the reagents placed in the DPP Zika IgM System device, and 2) replaces the DPP Zika IgM Sample Buffer and DPP Zika IgM Running Buffer vials by a single vial that is labeled DPP Zika IgM Buffer. Class specificity should not be affected by the changes, as the DTT treatment is added to the sample.

The results of these studies demonstrate IgM class specificity for the DPP Zika IgM System.

10. Carry-Over:

Not applicable as a single sample is run per device.

B Comparison Studies:

1. Method Comparison with Predicate Device:

See section "C" below.

2. Matrix Comparison:

The performance of the DPP Zika IgM System was evaluated using different matrices. Potassium-EDTA plasma is considered the reference matrix for the DPP Zika IgM System as it is the matrix presented for the main clinical study involving serial bleeds. Equivalency to potassium-EDTA plasma was evaluated using:

a. 11 positive and negative natural matched frozen potassium-EDTA whole blood, potassium-EDTA plasma, and serum samples
b. 49 plasma-replaced venous whole blood. For plasma replacement, negative whole blood specimens from 49 individuals obtained from a U.S blood bank were centrifuged, the plasma portion was removed, and the pellet was carefully suspended in an equal volume of Zika IgM antibody positive potassium-EDTA plasma from the 49 Zika positive plasma samples.
c. 30 samples for each serum and potassium-EDTA plasma prepared from 5 individual negative sera and plasma sources respectively, spiked with up to a 10% volume of positive potassium-EDTA plasma specimens to obtain high negative, low positive, and 4 values across the dynamic range of the DPP assay and tested in duplicates

d. 50 matched negative sample sets for serum and potassium-EDTA plasma samples sources and spiked with up to 10% volume of positive potassium-EDTA plasma specimens to obtain high negative, low positive, moderate positive, and high positive specimens tested in duplicates. Un-spiked negative samples were also included.

In conclusion, the results for four studies for the Matrix Equivalency are summarized below.

Summary Table for Matrix Equivalency of the DPP Zika IgM System with Known Positive and Negative Zika Specimens

	Potassium-EDTA Whole Blood	**Serum^**
Potassium-EDTA Plasma	100% (60/60) (%CI 94.0 – 100%)	97.3% (88.5*/91) (%CI 91.5-99.2%)

^ Average of mean agreement values obtained for each experiment. Some studies have 1 while others 2 replicates per sample. When one replicate agreed and one disagreed, it was counted as 0.5 sample agreement.
* Discordant results were only found in high negative samples prepared by spiking. Above the cut-off of the assay, agreement was 100%.

C Clinical Studies:

1. Positive Predictive Agreement:

Serum

One-hundred and forty-two (142) serum samples were collected from patients residing in flavivirus endemic regions in the Dominican Republic (11), Peru (99), and Brazil (32 samples from 26 individuals bled a first time and 6 repeated a second time). Six out of eleven (6/11) samples from Dominican Republic, all the samples from Peru, and the twenty-six (26) individual donors for the Brazilian samples were positive for Zika virus by rtPCR. One sample from Peru did not have sufficient volume to be tested by the comparator and was excluded. From the 141 samples available for comparator testing, 41 samples were positive by the comparator assay.

A high percentage of false positive results was observed against the comparator, largely contributed to by the source of the samples.

Positive Percent Agreement with the Comparator Assay on Serum from Endemic Areas - Internal site Overall Serum Agreement

Collection Site	**Total (n)**	**Comparator[1] Zika IgM Reactive**			**Comparator[1] Zika IgM Non-Reactive**		
		DPP Zika IgM System Reactive (R)[2]	DPP Zika IgM System Non-Reactive (NR)[2]	**Positive Percent Agreement (95% CI)**	DPP Zika IgM System Reactive (R)[2]	DPP Zika IgM System Non-Reactive (NR)[2]	Negative Percent Agreement
Dominican Republic	11	8	2[3]	**80% (8/10)**	1[4]	0	0% (0/1)
Peru	98	23	0	**100% (23/23)[5]**	68	7	9.3% (7/75[5, 6])
Brazil	32	8[7]	0	**100% (8/8)**	4	20	83.3% (20/24)

Total	141	39	2	**95.1% (39/41)[8] (83.9-98.7%)**	73	27	27% (27/100)

[1] EUA comparator assay reactive samples include Possible and Presumptive Zika Positive Specimens. EUA comparator assay non-reactive samples include Negative and Presumptive Other Flavivirus Positive specimens.
[2] This study was performed with an older version of the DPP Zika IgM System that was determined equivalent to the one under clearance.
[3] Negative for Zika IgM antibody by both the DPP Zika IgM System and a second authorized Zika IgM assay, while positive by an EUA Zika virus rtPCR assay and the EUA test used as a comparator.
[4] Negative for Zika IgM antibody by both the EUA test used as a comparator and a second authorized Zika IgM assay, while positive by an EUA Zika virus rtPCR assay.
[5] All samples tested positive by a rtPCR assay for Zika virus.
[6] All samples were ≤7 days post onset of symptoms. Even when positive by PCR, depending on the sensitivity of the assay, the level of antibodies may be low for detection.
[7] There were 8 positive samples in total in the 32. Two out of eight (2/8) samples were a single sample picked in both the first and second blood draw; 1/8 was only picked on the first blood draw; 5/8 were picked only on the second blood draw.
[8] Two of the eight (2/8) Brazilian positive samples were a single sample picked in both the first and second blood draw and counted twice for final performance calculations. Without double counting the specimen, the total PPA would be 95.0% (83.5-98.6%).

Potassium-EDTA Plasma

Internal Site

Positive percent agreement (PPA) for potassium-EDTA plasma was evaluated using archived samples consisting of eight serial samples collected from 50 symptomatic subjects from the Dominican Republic. Of these subjects confirmed positive for Zika virus by nucleic acid testing, only forty-eight (48) tested also positive for Zika antibodies in at least one of the serial bleeds by a Zika IgM comparator assay and were included in the analysis, for a total of 299 samples. The 48 subjects included 12 pregnant women. All samples were tested at an internal site and results are presented below.

Positive Percent Agreement with the Comparator Assay on Potassium-EDTA Plasma, Stratified by Number of Days Post-Onset of Symptoms - Internal site

Days Post Onset of Symptoms	**Total (n)**	**Comparator[1] Zika IgM Reactive[2]**			**Comparator[1] Zika IgM Non-Reactive[3]**		
		DPP Zika IgM System Reactive (R)	DPP Zika IgM System Non-Reactive (NR)	Positive Percent Agreement[4] (95% CI)	DPP Zika IgM System Reactive (R)	DPP Zika IgM System Non-Reactive (NR)	Negative Percent Agreement
0-7*	51	6	5	54.6% (6/11)	11	29	72.5% (29/40)
8-14	39	39	0	100.0% (39/39)	NT	NT	NT
15-28	86	82	0	100.0% (82/82)	4	0	0% (0/4)
29-42	86	79	0	100.0% (79/79)	7	0	0% (0/7)
43-56	82	61	0	100.0% (61/61)	21	0	0% (0/21)
57-70	29	19	0	100.0% (19/19)	9	1	10% (1/10)
71-84	11	8	0	100.0% (8/8)	3	0	0% (0/3)
Total	384	294	5	**100% (288/288) (95% CI 98.7-100.0%)**	55	30	2.2% (1/45)

* Data from Days 0 – 7 is not included in the calculation of total PPA because obtaining samples prior to 8 days after symptom onset or exposure is not recommended and false negative results are anticipated.
[1] EUA comparator assay
[2] Comparator reactive samples include Possible and Presumptive Zika Positive Specimens.
[3] Comparator non-reactive samples include Negative and Presumptive Other Flavivirus Positive specimens.
[4] Calculated using the score method.
NT: Not tested.

External Sites

Of the total of 299 positive samples from the Zika IgM endemic region mentioned in the study above, a subset of 171 bleeds from 39 positive individuals, including 11 samples from pregnant women, were divided and distributed among two external clinical sites (82 and 89 samples respectively). Forty-nine (49) prospectively collected plasma samples from asymptomatic pregnant women living in the continental United States known to be negative for Zika IgM antibodies by the comparator were interspersed for blinding (24 and 25 samples per site respectively). The combined data are summarized in the following table:

Positive Percent Agreement with the Comparator Assay on Potassium-EDTA Plasma, Stratified by Number of Days Post-Onset of Symptoms - External Sites

Days Post Onset of Symptoms	**Comparator[1] Zika IgM Reactive**		**Comparator[2] Zika IgM Non-Reactive**
	Positive Percent Agreement[3]	95% Confidence Interval	Negative Percent Agreement[3] (95% CI)
Asymptomatic	N/A	N/A	98.0% (48[4]/49) (95% CI 89.3-99.6%)
8-14	100.0% (29/29)	88.3-100.0%	NT
15-28	100.0% (48/48)	92.6-100.0%	NT
29-42	100.0% (46/46)	92.3-100.0%	NT
43-56	100.0% (29/29)	88.3-100.0%	NT
57-70	100.0% (12/12)	75.8-100.0%	NT
71-84	100.0% (7/7)	64.6-100.0%	NT
Total	**171/171=100.0% (95%CI 97.8-100.0%)**		

[1] EUA comparator assay reactive samples include Possible and Presumptive Zika Positive Specimens.
[2] Cleared comparator assay non-reactive samples include Negative and Presumptive Other Flavivirus Positive (non-Zika) specimens.
[3] Calculated using the score method.
[4] For one sample, the microreader value indicated a negative result, but the end-user recorded an interpretation of "R" for Reactive.
NT: Not Tested and not included in the calculations.

Potassium-EDTA Venous Whole blood

The PPA of the DPP Zika IgM System for potassium-EDTA venous whole blood was evaluated by two studies. For the first study, samples were tested at either an internal site or at external sites:

Internal Site

The positive percent agreement of the assay in potassium-EDTA venous whole blood was evaluated at an internal site using 10 frozen natural potassium-EDTA whole blood from the Dominican Republic that tested positive by the comparator assay, in addition to 42 contrived samples due to the low prevalence of Zika virus during the time of the study.

The contrived samples were prepared by plasma replacement, using serial bleeds from 6 individuals residing in the Dominican Republic. All subjects from this endemic area confirmed positive for Zika virus by nucleic acid testing were also positive for Zika antibodies in at least one of the serial bleeds by the comparator assay. Potassium-EDTA negative whole blood specimens from 42 individuals obtained from a U.S blood bank were replaced with potassium-EDTA serial plasma from the six Zika immune individuals. Results for all 42 plasma-replaced whole blood samples were reactive for Zika IgM antibodies on the DPP Zika IgM System, with 41 agreeing with the EUA comparator assay.

External Sites
For the external sites, the same subset of 171 antibody positive plasma specimens plus the 49-antibody negative potassium-EDTA plasma specimen from asymptomatic pregnant women from the US as described in the plasma study above, was used in a plasma replacement study. Results were confirmed by the comparator assay. The one-hundred and seventy-one (171) plasma replaced venous whole blood positive specimens were distributed among two clinical sites (82 and 89 samples per site) combined with 24 or 25 known negative plasma samples respectively.

The summary of the results obtained with potassium-EDTA natural and potassium-EDTA plasma reconstituted venous whole blood across the sites mentioned above is shown below:

Positive Percent Agreement with the Comparator Assay on Natural and Potassium-EDTA Plasma Replaced Venous Whole Blood, Stratified by Number of Days Post-Onset of Symptoms Across Internal and Clinical SitesDays Post onset of Symptoms	**Comparator[1] Zika IgM Reactive**		**Comparator Zika IgM Non-Reactive**
	Positive Percent Agreement[2]	95% confidence interval	Negative Percent Agreement[2]
Negative[3]	N/A	N/A	98% (48[4]/49)
0-7*	83.3% (10/12)	55.2-95.3%	NT
8-14	97.1% (33[5]/34)	85.1-99.5%	NT
15-28	94.7% (54/57)	85.6-98.2%	NT
29-42	96.4% (53/55)	87.7-99.0%	NT
43-56	84.2% (32/38)	69.6-92.6%	NT
57-70	80.0% (12/15)	54.8-93.0%	0/1[1,6]
71-84	90.9% (10/11)	62.3-98.4%	NT
Total			96.0% (48/50) (95% CI 86.5-98.9%)
Total	**92.4% (194/210) (95%CI 88.0-95.3)**		

* Data from Days 0 – 7 is not included in the calculation of total PPA because obtaining samples prior to 8 days after symptom onset or exposure is not recommended and false negative results are anticipated.
[1] EUA comparator assay reactive samples include Possible and Presumptive Zika Positive Specimens.
[2] Calculated using the score method.
[3] Cleared comparator assay non-reactive samples include Negative and Presumptive Other Flavivirus Positive (non-Zika) specimens.
[4] For one sample, the microreader value indicated a negative result, but the end-user recorded an interpretation of "R" for Reactive.
[5] For one sample, the microreader value indicated a reactive result, but the end-user recorded an interpretation of "NR" for Non-Reactive.
[6] Negative by a second authorized Zika IgM serology assay.
NT: Not Tested and not included in the calculations.

The second study was conducted at 3 clinics in the US using prospectively-collected potassium-EDTA venous whole blood from subjects enrolled in an "all comers" fashion. One of the 300 subjects was excluded because their naïve whole blood tested reactive in the DPP Zika IgM System without being spiked, leaving 299 subjects for analysis. In order to assess positive agreement, samples were contrived by potassium-EDTA plasma replacement into venous whole blood samples to yield negative, low positive, and moderate positive specimens. The contrived samples were tested in a blinded fashion across three sites. Results were compared against the expected results based on the spiking level for each sample.

Agreement with Expected Reactivity of Potassium-EDTA Plasma Replaced Venous Whole Blood Across Three Sites

Zika IgM Target Level	Agreement to Expected Reactivity by Levels[1]	Combined Agreement
Negative	100% (120/120) (95%CI 96.9-100.0%)	NPA 100% (120/120) (95%CI 96.9-100.0%)
Low reactive (<3xLoD)	99.1% (115/116) (95%CI 95.3-99.9%)	PPA 99.4% (178/179) (95%CI 96.9-99.9%)
Moderate reactive (≥3xLoD)	100.0% (63/63) (95%CI 94.3-100.0%)	

[1] Calculated using the score method.

Capillary Whole Blood

The performance of the assay with capillary whole blood was evaluated in a total of 375 adult subjects across four near-patient sites in the US enrolled on an "all comers" basis. Due to the low prevalence of Zika virus during the time of the study, the evaluation of the performance of the assay with fingerstick was performed using contrived samples. After exclusion of a sample detected as reactive before spiking, the remaining 374 fingerstick samples prospectively collected were immediately placed into pre-labeled samples vials spiked with negative, low or moderate levels of anti-Zika IgM. Presence or absence of Zika IgM antibodies in the spiking material was corroborated by comparator testing. The vials were coded so that study staff and the two trained operators at the clinical laboratory were not aware of the predetermined reactivity of the spiked sample vials. Two samples were later eliminated from the analysis due to deviations in data transcription. In total, there were 372 vials (135 negative, 149 low and 88 moderate levels of Zika antibodies) that were tested with the DPP Zika IgM System. All testing was performed in near-patient settings.

Agreement with Expected Reactivity of Capillary Whole Blood

Zika IgM Target Level	Agreement to Expected Reactivity by Level[1]	Combined Agreement
Negative	97.8% (132/135) (95%CI 93.7-99.2%)	NPA 97.8% (132/135) (95%CI 93.7-99.2%)
Low reactive (2.5x - <3x Cut-Off)	98.0% (146/149) (95%CI 92.3-99.3%)	PPA 98.7% (234/237) (95%CI 96.4-99.6%)
Moderate reactive (≥3x - 5x Cut-Off)	100.0% (88/88) (95%CI 95.8-100%)	

[1] Calculated using the score method.

2. Negative Predictive Agreement:

Negative percent agreement was evaluated using a total of 500 prospectively collected specimens tested at seven (7) near-patient sites, including four (4) sites in areas endemic for mosquito-borne flaviviruses (250 samples) and three (3) sites in non-endemic areas (250 samples). Potassium-EDTA venous and fingerstick whole blood were tested at near-patient settings. Paired serum, potassium-EDTA plasma and urine were sent to a reference laboratory where they were tested for Zika virus antibodies with the DPP Zika IgM System and the comparator method (data not shown).

Samples were expected to be negative for Zika IgM antibodies due to the low prevalence of Zika virus during the study. For those samples found positive, results were expressed as a percentage of positive results in the total population under study. Samples were tested by the DPP Zika IgM System, the cleared comparator assay, and an additional serology EUA test. Results are summarized in the following tables. The different rate of positive results may be partially explained by the differential target of the detected antibodies and an increased false positive rate for each assay in endemic populations due to the low prevalence of the virus at the moment of collection.

Endemic Area

	NPA[#] of ***DPP Zika IgM System*** by Comparison with Samples Negative By				Percent of Positive Results in Population		
	FDA Cleared Comparator[1]	Additional EUA Test[2]	Both FDA Cleared and EUA tests		***DPP Zika IgM System***[3]	FDA Cleared Comparator[1]	Additional EUA Test[2]
Serum	94.3% (213/226) 95%CI 90.4-98.6	94.8% (218/230) 95%CI 91.1-97.0	95.7% (202/211) 95%CI 92.1-97.7		8.0% (20[a]/250)	9.6% (24/250)	7.6% (19/250)
Potassium-EDTA Plasma	93.4% (211/226) 95%CI 89.3-95.9	93.0% (214/230) 95%CI 89.0-95.7	93.8% (198/211) 95%CI 89.8-96.4		8.8% (22[b]/250)	9.6% (24/250)	7.6% (19/250)
Potassium-EDTA Venous Whole Blood	93.8% (212/226) 95%CI 89.9-96.3	94.4% (217/230) 95%CI 90.6-96.7	94.8% (200/211) 95%CI 90.9-97.1		7.6% (19[c]/250)	9.6% (24/250)	7.6% (19/250)
Capillary Whole Blood	96.0% (217/226) 95%CI 92.6-97.9	96.5% (222/230) 95%CI 93.3-98.2	97.2% (205/211) 95%CI 93.9-98.7		5.6% (14[d]/250)	9.6% (24/250)	7.6% (19/250)

[#] Calculated using the score method.
[1] Detects IgM antibodies against envelope
[2] Detects IgM and IgG antibodies anti NS-1
[3] Detects IgM antibodies anti NS-1.
[a] 15 agree in 3 or all matrices, the remaining in 2 or less
[b] 14 agree in 3 or all matrices, the remaining in 2 or less
[c] 14 agree in 3 or all matrices, the remaining in 2 or less
[d] 11 agree in 3 or all matrices, the remaining in 2 or less

Non-Endemic Area

	NPA[#] of ***DPP Zika IgM System*** by Comparison with Samples Negative By				Percent of Positive Results in Population		
	FDA Cleared Comparator[1]	Additional EUA Test[2]	Both FDA Cleared and EUA tests		***DPP Zika IgM System***[3]	FDA Cleared Comparator[1]	Additional EUA Test[2]
Serum	98.0% (239/244) 95%CI 95.3-99.1	98.3% (225/229) 95%CI 95.6-99.3	98.2% (220/224) 95%CI 95.5-99.3		2.0% (5[a]/250)	2.4% (6/250)	8.4% (21/250)
Potassium-EDTA Plasma	96.7% (236/244) 95%CI 93.7-98.3	97.8% (224/229) 95%CI 95.0-99.1	97.8% (219/224) 95%CI 94.9-99.0		3.2% (8[b]/250)	2.4% (6/250)	8.4% (21/250)

Potassium-EDTA Venous Whole Blood	97.1% (237/244) 95%CI 94.2-98.6	97.4% (223/229) 95%CI 94.4-98.8	97.3% (218/224) 95%CI 94.3-98.8		2.8% (7[c]/250)	2.4% (6/250)	8.4% (21/250)
Capillary Whole Blood	98.4% (239/243)[4] 95%CI 95.9-99.4%)	98.7% (226/229) 95%CI 96.2-99.6	98.7% (221/224) 95%CI 96.1-99.5		1.6% (4[d]/250)	2.4% (6/250)	8.4% (21/250)

[#] Calculated using the score method.
[1] Detects IgM antibodies against envelope;
[2] Detects IgM and IgG antibodies anti NS-1;
[3] Detects IgM antibodies anti NS-1.
[4] FS result from one subject excluded due to protocol deviation (Test read < 15-minutes)
[a] 4 agree in 3 or all matrices, the remaining in 2 or less;
[b] 4 agree in 3 or all matrices, the remaining in 2 or less;
[c] 4 agree in 3 or all matrices, the remaining in 2 or less;
[d] 3 agree in 3 or all matrices, the remaining in 2 or less

3. Performance Against the FDA Plasma Zika Panel:

Performance of the DPP Zika IgM System was evaluated by testing a panel of samples provided to the sponsor by FDA. The panel consists of plasma samples from individuals infected with Zika, West Nile, or Dengue viruses. Samples were collected at different time points from Zika infection documented by PCR; samples taken early or late after infection may be anticipated to be antibody negative. Samples were randomized and blinded for testing. Results were as follows:

		DPP Zika IgM System	
		Presumptive Zika Positive	**Negative**
Zika IgM Consensus	**Positive (n=24)**	23	1
	Negative (n=12)	1	11

PPA= 23/24, 95.8%

NPA= 11/12, 91.7%

		DPP Zika IgM System	
		Presumptive Zika Positive (False Positives)	**Negative**
Cross-reactivity Evaluation	**West Nile* (n=10)**	1	9
	Dengue* (n=10)	0	10

* Samples were antibody positive for West Nile or Dengue viruses, and negative for Zika virus.

This evaluation was performed using samples provided by Blood Systems Research Institute (BSRI, now Vitalant Research Institute) from a study supported by Contract No. HHSN268201100001I from the National Heart, Lung, and Blood Institute (NHLBI), National Institutes of Health. The panel composition and consensus results are the responsibility of the FDA and do not necessarily represent the official views of BSRI, the NHLBI, or the National Institutes of Health.

4. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

Not applicable

D Clinical Cut-Off:

Not applicable

E Expected Values/Reference Range:

Not applicable

F Other Supportive Instrument Performance Characteristics Data:

Not applicable

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.