October 28, 2019

DiaSorin Inc.
Sandra Zimniewicz
Senior Regulatory Affairs Specialist
1951 Northwestern Avenue
Stillwater, Minnesota 55082-0285

Re: K192046
Trade/Device Name: LIAISON XL Zika Capture IgM II and
LIAISON XL Zika Capture IgM II Control Set
Regulation Number: 21 CFR 866.3935
Regulation Name: Zika Virus Serological Reagent
Regulatory Class: Class II
Product Code: QFO, QCH
Dated: July 30, 2019
Received: July 31, 2019

Dear Sandra Zimniewicz:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's

requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Uwe Scherf, M.Sc., Ph.D.
Director
Division of Microbiology Devices
OHT7: Office of In Vitro Diagnostics
and Radiological Health
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

510(k) SUMMARY

1. DATE PREPARED: July 30, 2019

2. APPLICANT INFORMATION:

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3. REGULATORY INFORMATION:

Trade Name:	LIAISON® XL Zika Capture IgM II
Common Names/Descriptions:	Zika virus assay
Classification Names:	Zika Virus Serological Reagents: Class II, 21 CFR 866.3935; Microbiology (83) Assayed quality control material for clinical microbiology assays: Class II, 21CFR 866.3920; Microbiology (83)
Product Code:	QFO - Zika Virus Serological Reagents QCH - Assayed quality control material for clinical microbiology assays

4. PREDICATE DEVICE: InBios ZIKV *Detect*™ 2.0 IgM Capture ELISA (DEN180069)

5. INTENDED USE / INDICATIONS FOR USE

LIAISON® XL Zika Capture IgM II

The DiaSorin LIAISON® XL Zika Capture IgM II assay is intended for the presumptive qualitative detection of Zika virus IgM antibodies in human sera collected from individuals meeting 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 must be collected not earlier than day 8 after the onset of symptoms or risk of exposure, respectively. 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 combination with clinical observations, patient history, epidemiological information, and other laboratory evidences. Zika IgM levels over the course of illness are not well characterized. IgM levels are variable, 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.

This LIAISON® XL Zika Capture IgM II assay is not indicated for testing blood or plasma donors.

The test has to be performed on the LIAISON® XL Analyzer.

LIAISON® XL Zika Capture IgM II Control Set

The DiaSorin LIAISON® XL Zika Capture IgM II Control Set is intended for use as assayed quality control samples to monitor the performance of the LIAISON® XL Zika Capture IgM II assay. The performance characteristics of the LIAISON® XL Zika Capture IgM II controls have not been established for any other assay or instrument platforms different from the LIAISON® XL.

6. DEVICE DESCRIPTION

The LIAISON® XL Zika Capture IgM II assay is an automated immunoassay utilizing chemiluminescent (CLIA) detection technology for the detection of human IgM antibodies against Zika Virus in patient sera.

The LIAISON® XL Zika Capture IgM II assay consists of the components described in the following tables.

ZIKV-M Reagent Integral Composition

Magnetic Particles (2.4 mL)	Magnetic particles coated with a mouse monoclonal antibody to human IgM diluted in phosphate buffer containing BSA, surfactant, and <0.1% sodium azide.
Specimen Diluent (28.0 mL)	Buffer containing BSA, surfactant, 0.2% ProClin® 300, and an inert yellow dye.
Assay Buffer (28.0 mL)	Buffer containing BSA, surfactant, and 0.2% ProClin® 300
Number of tests	100

Additional components provided not on the ZIKV-M Reagent Integral

Calibrator 1 Lyophilized 2 vials	Human serum/defibrinated plasma containing Zika virus IgM, phosphate buffer, BSA, surfactant, 0.18% ProClin® 300, and <0.1% sodium azide. Reconstitute with 2.0 mL of distilled or deionized water.
Calibrator 2 Lyophilized 2 vials	Human serum/defibrinated plasma containing Zika virus IgM, phosphate buffer, BSA, surfactant, 0.18% ProClin® 300, and <0.1% sodium azide. Reconstitute with 2.0 mL of distilled or deionized water.
ZIKV-M Conjugate Lyophilized 1 vial	Recombinant Zika virus NS1 antigen conjugated to an isoluminol derivative diluted in buffer containing BSA, surfactant, and 0.2% ProClin® 300. Reconstitute with 5.0 mL of distilled or deionized water.

ZIKV-C Reagent Integral Composition

Magnetic Particles (2.4 mL)	Magnetic particles coated with a mouse monoclonal antibody to human IgG diluted in phosphate buffer containing BSA, surfactant, and <0.1% sodium azide.
Specimen Diluent (2 X 28.0 mL)	Buffer containing BSA, surfactant, 0.2% ProClin® 300, and an inert yellow dye.
Assay Buffer (28.0 mL)	Buffer containing BSA, surfactant, and 0.2% ProClin® 300
Number of tests	100

Additional components provided, not on the ZIKV-C Reagent Integral

Calibrator 1 1 vial x 0.9 mL	Human serum/defibrinated plasma containing Zika virus IgG, < 0.3% ProClin® 300, and < 0.1% sodium azide.
Calibrator 2 1 vial x 0.9 mL	Human serum/defibrinated plasma containing Zika virus IgG, < 0.3% ProClin® 300, and < 0.1% sodium azide.
ZIKV-C Conjugate Lyophilized 1 vial	Recombinant Zika virus NS1 antigen conjugated to an isoluminol derivative diluted in buffer containing BSA, surfactant, and 0.2% ProClin® 300. Reconstitute with 5.0 mL of distilled or deionized water.

ProClin® is a trademark of the Dow Chemical Company (Dow) or an affiliated company of Dow.

Materials required but not provided (system related)

LIAISON® XL Analyzer
LIAISON® Wash/System Liquid (REF 319100)
LIAISON® XL Waste Bags (REF X0025)
LIAISON® XL Cuvettes (REF X0016)
LIAISON® XL Starter Kit (REF 319200)
LIAISON® XL Disposable Tips (REF X0015)
LIAISON® XL Zika Capture IgM II Control Set (REF 317151)

Additional required materials (assay related)
LIAISON® XL Zika Capture IgM II Control Set (REF 317151)

7. PURPOSE OF THE SUBMISSION
The purpose of this premarket notification was to submit a new device (LIAISON® XL Zika Capture IgM II) to FDA for clearance as a 510(k).

8. COMPARISON TO FDA CLEARED METHOD

Table 1:Table of Similarities

Characteristic	Candidate Device LIAISON® XL Zika Capture IgM II	Predicate Device InBios ZIKV *Detect*™ 2.0 IgM Capture ELISA DEN180069
Intended Use	Qualitative detection of Zika virus IgM antibodies in human serum	Qualitative detection of Zika virus IgM antibodies in human serum
Sample Matrix	Serum	Same
Reagent Storage	2-8°C, On-board or in Refrigerator	2-8°C, Refrigerator only

Table 2: Table of Differences

Characteristic	Candidate Device LIAISON® XL Zika Capture IgM II	Predicate Device InBios ZIKV *Detect*™ 2.0 IgM Capture ELISA DEN180069
Type of Assay	Chemiluminescent Immunoassay	Enzyme Immunoassay
Sample Handling/Processing	Automated	Manual
Interpretation of Results	• Presumptive Zika IgM Positive • Presumptive Recent Zika Positive • Presumptive Recent Zika Negative • Negative	• Reactive for Zika IgM Antibodies • Reactive for Other Flavivirus IgM Antibodies • Negative
Calibrators	Two	Three (Antigen reagents)
Detector	Zika virus NS1 antigen conjugated to an Isoluminol derivative	Horseradish peroxidase-labeled anti-mouse antibody
Capture Reagent	ZIKV-M: Magnetic particles coated with mouse monoclonal to human IgM ZIKV-C: Magnetic particles coated with mouse monoclonal to human IgG	Microwells coated with polyclonal antibodies to human IgM
Sample Volume	25 µL w/o dead volume	50 µL

Table 2 cont.: Table of Differences		
Measurement System	Photomultiplier (flash chemiluminescence reader)	ELISA Spectrophotometer
Total Incubation	37 minutes	3.3 hours (201 minutes)
Controls	Provided Separately	Included

9. PERFORMANCE STANDARDS

The following recognized standards from Clinical Laboratory Standards Institute (CLSI) and special controls were used as a basis of the study procedures described in this submission:

- Interference Testing in Clinical Chemistry, Approved Guideline. CLSI EP07-A2 Second Edition; November 2005 (Recognition no. 7-127)
- User Verification of Precision and Estimation of Bias, Approved Guideline. CLSI EP15-A3 Third Edition; September 2014 (Recognition no. 7-253)
- Supplemental Tables for Interference Testing in Clinical Chemistry. 1st Edition (CLSI EP37, 2018; Recognition No. 7-284)
- Special controls under 21CFR 866.3935, Zika virus serological reagents, Code of Federal Regulation, 2019

10. PERFORMANCE CHARACTERISTICS

10.1 CLINICAL STUDIES

Specimens from patients infected with Zika virus and uninfected individuals were prospectively collected from endemic and non-endemic regions for Zika virus and include pregnant women. Testing was performed at three (3) sites with samples distributed across sites. Samples were tested with the LIAISON® XL Zika Capture IgM II assay and a comercially available Zika IgM assay.

COMPARATIVE AGREEMENT STUDIES

Positive Agreement

Positive agreement was evaluated using 211 serial serum samples prospectively collected from 46 symptomatic subjects. All subjects were confirmed positive for Zika virus by nucleic acid testing and were positive for Zika antibodies in at least one of the serial bleeds by the comparator assay. The analysis also includes 33 single bleeds. Four (4) of them, within the 0-7 day time frame, were only positive by nucleic acid testing. The rest of the 29 single bleeds were positive by the comparator assay and most of them also by nucleic acid testing. The positive population therefore consisted of 244 specimens from 79 subjects from the Dominican Republic, including 22 pregnant women.

The results were calculated to generate positive percent agreement with the comparator assay in the following table.

Days post onset of symptoms	Comparator Assay: Zika IgM Reactive[#]		Comparator Assay: Zika IgM Non-Reactive[##]		Total (n)
	LIAISON® XL Zika Capture IgM II Assay Positive (P)[&]	LIAISON® XL Zika Capture IgM II Assay Negative (N)[&&]	LIAISON® XL Zika Capture IgM II Assay Positive (P)[&]	LIAISON® XL Zika Capture IgM II Assay Negative (N)[&&]	
0-7*	6	11	1	32**	50
8-14	53	3	0	0	56
15-28	62	0	2	0	64
29-42	33	0	3	0	36
43-56	14	3	4	1	22
57-70	7	2	2	0	11
71-84	5	0	0	0	5
Total	180	19	12	33	244

*This time frame is outside the claimed window of detection.
**Four (4) single bleeds were positive only by nucleic acid testing.
[#]Comparator assay positive samples include Possible and Presumptive Zika Positive specimens.
[##]Comparator assay negative samples include Negative and Presumptive Other Flavivirus Positive specimens.
[&]Positive samples include presumptive recent Zika positive and presumptive Zika IgM positive specimens based on a similar required clinical follow-up.
[&&]Negative samples include presumptive recent Zika negative and negative specimens as presumptive samples are considered negative until re-testing results are obtained.

Days post onset of symptoms	Comparator Assay: Zika IgM Reactive	Comparator Assay: Zika IgM Nonreactive
	Positive Percent Agreement	Negative Percent Agreement
0-7*	6/17=35.3%*	32/33=97.0%
8-14	53/56=94.6%	N/A
15-28	62/62=100%	0/2=0%
29-42	33/33=100%	0/3=0%
43-56	14/17=82.4%	1/5=20%
57-70	7/9=77.8%	0/2=0%
71-84	5/5=100%	N/A
Total (Day 8-84)	**174/182=95.6% (%CI 91.6-97.8%)**	**1/12=8.3%**

*This time frame is outside the claimed window of detection.
N/A: Not Applicable dvision by 0.

Among the 174 LIAISON® positive samples, there were 136 (78.2%) that were presumptive Zika IgM positive (PIgM-pos) and 38 (21.8%) that were presumptive recent Zika positive (PR-pos).

Among the 8 LIAISON® negative samples, there were 4 (50%) that were negative (neg) and 4 (50%) that were presumptive recent Zika negative (PR-neg).

Negative Agreement
Negative percent agreement testing included 500 serum samples confirmed negative for Zika IgM by a comparator assay. These specimens consisted of 250 subjects from an

area non-endemic for Zika virus (continental United States) and 250 subjects from an area endemic for Zika virus (Dominican Republic). Of the 250 subjects from the Dominican Republic, 37 were pregnant women. Pregnancy status for the U.S. subjects is unknown. The results are shown in the following table.

	LIAISON® XL Zika Capture IgM II Assay				
Population	Negative#	Positive##	Total	Negative Agreement	95% Confidence Intervals
Non-endemic (U.S)^	249	1*	250	99.6%	97.8 – 99.9%
Endemic (Dominican Republic)^^	244	6*	250	97.6%	94.9 – 98.9%
Total	**493**	**7**	**500**	**98.6%**	**97.1% - 99.3%**

#Negative samples include presumptive recent Zika negative and negative specimens as presumptive samples are considered negative until re-testing results are obtained.
##Positive samples include presumptive recent Zika positive and presumptive Zika IgM positive specimens based on a similar required clinical follow up.
*Samples were negative for Zika IgM by the comparator assay.
^Includes samples from Texas (83) and Florida (87). These samples were collected in June 2017 when very few cases of locally acquired Zika were reported.
^^37 pregnant subjects were included in the normal subject population and were negative.

Among 493 LIAISON® negative samples, there were 436 (87.2%) that were negative (neg) and 57 (11.4%) that were presumptive recent Zika negative (PR-neg).

Among 7 LIAISON® positive samples, there were 2 (0.4%) that were presumptive Zika IgM positive (PIgM-pos) and 5 (1%) that were presumptive recent Zika positive (PR-pos).

10.2 PRECISION/REPRODUCIBILITY

A within-laboratory precision study was performed consulting CLSI document EP15-A3 in the preparation of the testing protocol. Four samples with negative, high negative, low positive and moderate positive levels of Zika IgG and IgM antibodies and kit controls (negative and positive) were assayed with their respective reagent packs (ZIKV-C and ZIKV-M). Each sample was tested in triplicate, in 2 runs per day over 5 operating days with multiple technicians. The following within-laboratory precision results were obtained from samples tested internally at DiaSorin Inc. using 3 kit lots.

ZIKV-C

Sample ID N=90	Mean Index	Within Run		Between-Run		Between-Day		Between-Lot/Instrument		Total*	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Neg Ctrl	0.392	0.009	2.2	0.005	1.4	0.031	7.9	0.073	18.5	0.080	20.3
Pos Ctrl	9.71	0.135	1.4	0.082	0.8	0.375	3.9	0.435	4.5	0.596	6.1
Sample #1	0.775	0.013	1.6	0.000	0.0	0.037	4.8	0.156	20.1	0.160	20.7
Sample #2	3.19	0.034	1.1	0.042	1.3	0.120	3.8	0.157	4.9	0.205	6.4
Sample #3	5.68	0.073	1.3	0.020	0.3	0.212	3.7	0.501	8.8	0.549	9.7
Sample #4	11.1	0.181	1.6	0.067	0.6	0.399	3.6	0.793	7.2	0.909	8.2

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

ZIKV-M

Sample ID N=90	Mean Index	Within Run		Between-Run		Between-Day		Between-Lot/Instrument		Total*	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Neg Ctrl	0.523	0.032	6.1	0.022	4.2	0.045	8.7	0.051	9.7	0.078	15.0
Pos Ctrl	5.82	0.124	2.1	0.111	1.9	0.236	4.1	0.118	2.0	0.312	5.4
Sample #1	0.578	0.053	9.2	0.035	6.1	0.062	10.7	0.012	2.1	0.090	15.5
Sample #2	0.841	0.048	5.8	0.057	6.8	0.067	7.9	0.000	0.0	0.100	11.9
Sample #3	2.69	0.078	2.9	0.090	3.3	0.16	5.9	0.204	7.6	0.285	10.6
Sample #4	6.25	0.172	2.8	0.224	3.6	0.326	5.2	0.412	6.6	0.596	9.5

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

A reproducibility/precision study was performed at 2 US external sites and internally at DiaSorin Inc. consulting CLSI document EP15-A3 in the preparation of the testing protocol. Four samples with negative, high negative, low positive and moderate positive levels of Zika IgG and IgM antibodies and kit controls (negative and positive) were assayed with their respective reagent packs (ZIKV-C and ZIKV-M). Each sample was tested in triplicate, in 2 runs per day over 5 operating days with multiple technicians. The following reproducibility/precision results were obtained from samples tested at the 3 sites with 1 kit lot.

ZIKV-C

Sample ID N=90	Mean Index Value	Within Run		Between-Run		Between-Day		Between-Site		Total*	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Neg Ctrl	0.409	0.015	3.6	0.013	3.1	0.018	4.5	0.028	6.9	0.039	9.5
Pos Ctrl	10.1	0.181	1.8	0.418	4.1	0.422	4.2	0.519	5.1	0.809	8.0
Sample #1	0.656	0.019	2.9	0.022	3.4	0.032	4.9	0.064	9.8	0.077	11.8
Sample #2	3.27	0.082	2.5	0.137	4.2	0.115	3.5	0.071	2.2	0.209	6.4
Sample #3	5.54	0.091	1.6	0.229	4.1	0.239	4.3	0.033	0.6	0.345	6.2
Sample #4	12.2	0.215	1.8	0.580	4.8	0.656	5.4	0.356	2.9	0.969	8.0

*Total = Within-Run + Between-Run + Between-Day + Between-Site

ZIKV-M

Sample ID N=90	Mean Index Value	Within Run		Between-Run		Between-Day		Between-Site		Total*	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Neg Ctrl	0.496	0.027	5.4	0.023	4.6	0.042	8.4	0.042	8.4	0.069	13.8
Pos Ctrl	5.48	0.160	2.9	0.072	1.3	0.323	5.9	0.388	7.1	0.534	9.7
Sample #1	0.624	0.049	7.9	0.011	1.7	0.061	9.8	0.053	8.5	0.095	15.3
Sample #2	0.881	0.048	5.4	0.042	4.8	0.074	8.4	0.000	0.0	0.098	11.1
Sample #3	2.87	0.117	4.1	0.082	2.8	0.141	4.9	0.000	0.0	0.200	7.0
Sample #4	6.48	0.306	4.7	0.203	3.1	0.398	6.1	0.000	0.0	0.542	8.4

*Total = Within-Run + Between-Run + Between-Day + Between-Site

10.3 ASSAY REPORTABLE RANGE

The ZIKV-M reagent pack measures between 0.1 and 29 Index value. The lowest reportable value is 0.1 Index. Values below 0.1 Index should be reported as < 0.1 Index. Values above 29 Index should be reported as > 29 Index.

The ZIKV-C reagent pack measures between 0.01 and 35 Index value. The lowest reportable value is 0.01 Index. Values below 0.01 Index should be reported as < 0.01 Index. Values above 35 Index should be reported as > 35 Index.

10.4 DETECTION LIMITS

Detection Limits (Limit of Blank, Limit of Detection, Limit of Quantitation) are not applicable to the LIAISON® XL Zika Capture IgM II assay.

10.5 ANALYTICAL SENSITIVITY/ ASSAY CUT-OFFs

Analytical sensitivity was evaluated using the WHO 1st International Standard for anti-Asian lineage Zika virus antibody (human) (NIBSC 16/352). This preparation is composed of pooled serum obtained from six individuals who tested positive for Zika infection. The undiluted standard (1000 IU/mL) returned a positive result in the LIAISON® XL Zika Capture IgM II assay with Index values just above the ZIKV-M and ZIKV-C cut-off values of 1 and 4, respectively. The standard tested at a 1:3 dilution returned a negative result in the assay.

10.6 ANALYTICAL SPECIFICITY/CROSS-REACTIVITY and INTERFERENCE

The cross reactivity study for the LIAISON® XL Zika Capture IgM II assay was designed to evaluate potential interference from antibodies against other closely related viruses as well as organisms whose infection produces symptoms similar to those observed during Zika virus infection. Samples containing IgM and IgG antibodies against other flavivirus specimens and disease state specimens were used to test for potentially cross-reactive antibodies.

One Dengue IgM sample (1/43) was reactive in the LIAISON® XL Zika Capture IgM II assay although this sample was also reactive with the comparator method. Additionally, one Parvovirus B19 IgM (1/14) and one rheumatoid factor (1/16) samples were reactive in the LIAISON® XL Zika Capture IgM II assay. There is a possibility of cross-reactivity to Chikungunya IgM in the assay as a sample cross-reactive in the first version of the assay was not available for repeat measurements with the LIAISON® XL Zika Capture IgM II assay.

Organism/Condition	Samples tested	Number Reactive with LIAISON® XL Zika Capture IgM II Assay	% Reactive
Anti-Chikungunya virus (IgM)	17	0	0
Anti-Chikungunya virus (IgG)	14	0	0
Anti-Cytomegalovirus (IgM)	11	0	0
Anti-Cytomegalovirus (IgG)	11	0	0

Anti-Dengue virus (IgM)	43	1^	2.33%
Anti-Dengue virus (IgG)	53	0	0
Anti-Epstein Barr Virus (IgM)	11	0	0
Anti-Epstein Barr Virus (IgG)	10	0	0
Anti-Parvovirus B19 (IgM)	14	1&	7.14%
Anti-Parvovirus B19 (IgG)	13	0	0
Anti-Varicella zoster virus (IgM)	11	0	0
Anti-Varicella zoster virus (IgG)	14	0	0
Yellow fever virus post-immunization	17	0	0
Anti-West Nile Virus (IgM)	15	0	0
Anti-West Nile Virus (IgG)	19	0	0
Anti- Malaria/anti-*plasmodium falciparum**	10	0	0
Adenovirus**	10	0	0
Enterovirus***	10	0	0
Anti-Hepatitis (C) virus (Total IgG)	10	0	0
Anti-Hepatitis (B) virus (IgM)	10	0	0
Anti-Hepatitis (B) virus (Total Antibodies)	10	0	0
Anti-Herpes simplex virus 1 (HSV-1) (IgM)	10	0	0
Anti-Herpes simplex virus 1 (HSV-1) (IgG)	10	0	0
Anti-Herpes simplex virus 2 (HSV-2) (IgM)	10	0	0
Anti-Herpes simplex virus 2 (HSV-2) (IgG)	10	0	0
Anti-Rubella virus (IgM)	10	0	0
Anti-Rubella virus (IgG)	10	0	0
Anti-*Borrelia sp*.(Lyme Disease) (IgM)	10	0	0
Anti-*Borrelia sp*.(Lyme Disease) (Total Ig)	12	0	0
Anti-*Treponema pallidum*.(Syphilis) (Total Antibodies)	20	0	0
Human Anti-mouse Antibody (HAMA)	11	0	0
Anti-nuclear antibodies (ANA)	29	0	0
Rheumatoid Factor	16	1&	6.25%

*Specimens were confirmed positive for Malaria infection, but serological status is not known.
**Presence of antibodies was assumed from the results of culture and complement fixation in 3/10 samples; 4/10 showed IgA and IgG presence by ELISA; 3/10 were not characterized.
***Presence of antibodies was assumed from the results of culture and complement fixation.
^This sample was Zika IgM positive by a comparator assay.
&This sample was Zika IgM negative by a comparator assay.

Controlled studies of potentially interfering substances performed on 3 negative and 3 positive serum samples near the clinical decision points showed only interference in the LIAISON® XL Zika Capture IgM II assay for hemoglobin. The positive interference for hemoglobin at 10 mg/mL was significant while at 2 mg/mL interference was minimal with no change in the final call. The testing was based on CLSI-EP7-A2.

Endogenous Substance	Concentration Tested
Hemoglobin	10 mg/mL and 2 mg/mL
Bilirubin (conjugated)	0.4 mg/mL

Bilirubin (unconjugated)	0.4 mg/mL
Triglycerides	30 mg/mL
Cholesterol	5 mg/mL
Albumin	60 mg/mL
HAMA	800-1380 ng/mL
Rheumatoid Factor	3500-17800 IU/mL

10.7 CLASS SPECIFICITY

Antibody class specificity was evaluated on each of the ZIKV-M (anti-IgM antibody) and ZIKC-C (anti-IgG antibody) reagent packs. Six (6) specimens containing various levels of Zika virus IgM antibodies and high levels of Zika virus IgG antibodies were used for this testing. DTT was used to specifically inactivate IgM antibodies without affecting IgG antibodies.

Class specificity for the LIAISON® XL Zika Capture IgM II assay was demostrated as all IgM positive samples dropped below the assay cut-off value after treatment with DTT while the IgG positive samples demonstrated ≤ 10% change in Index value.

10.8 CARRY-OVER

Sample carry-over testing was performed independently for the ZIKV-M and ZIKV-C reagent packs on the LIAISON® XL to determine if there is potential instrument carry-over. The study was designed to demonstrate that a sample containing a high level of analyte which preceded a sample containing no analyte will not cause an inappropriate elevation of the subsequent negative sample signal. Carry-over was not observed in either the ZIKV-M or the ZIKV-C reagent pack under the specific testing conditions. For each run, the average of the negative sample replicates following the high sample showed ≤ 10% difference from the average of the negative sample replicates which were tested prior to the high sample. Additionally, the percent of negative results of the negative sample following the high sample was 100% for each reagent pack.

11.0 STABILITY

LIAISON® XL Zika Capture IgM II Reagents	
Study	Stability
Kit Shelf-Life at 2-8 °C	9 months
ZIKV-M Reagent Integral Shelf-Life at 2-8 °C	9 months
ZIKV-C Reagent Integral Shelf-Life at 2-8 °C	18 months
Calibration Curve	14 days
Reagent Integrals Open Use Storage On-board Analyzer at 11-15 °C	14 days
Reagent Integrals Open Use Storage at 2-8 °C	14 days
Reconstituted Conjugates Open Use Storage at 2-8 °C	14 days
ZIKV-M Reconstituted Calibrator Open Use at Room Temperature (18-25°C)	6 hours
ZIKV-M Reconstituted Calibrator Open Use at 2-8 °C	24 hours
ZIKV-C Calibrator Open Use at 2-8 °C	14 days

LIAISON® XL Zika Capture IgM II Control Set	
Study	Stability
ZIKV-M Controls Shelf-Life at 2-8 °C	10 months
ZIKV-C Controls Shelf-Life at 2-8 °C	10 months
Control Open Use Storage On-board Analyzer at 18-25 °C	24 hours
Control Open Use Storage at 2-8°C	56 days

SPECIMEN STABILITY

Studies were performed to determine the stability of human serum samples at storage temperatures of 2-8°C, and 18-25°C. A multiple freeze/thaw (F/T) study was also performed. Testing was performed with both the ZIKV-M and ZIKV-C reagent packs using a minimum of five (5) serum samples having index values below, near and above the respective reagent pack cut-off values. Stability of human serum samples was determined to be 7 days at 2- 8 °C and 24 hours at room temperature (18 – 25 °C). Serum samples are stable through 3 freeze/thaw cycles.

12. CONCLUSION:

The material submitted in this premarket notification is complete and supports a substantial equivalence decision. The labelling is sufficient and it satisfies the requirements of 21CFR 809.10.