510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:

K170509

B. Purpose for Submission:

New Device

C. Measurand:

IgM antibodies to *Toxoplasma gondii* (*T. gondii*), Rubella virus and Cytomegalovirus (CMV)

D. Type of Test:

Multiplexed Microparticle Immunoassay (multiplexed fluoromagnetic bead assay)

E. Applicant:

Bio-Rad Laboratories

F. Proprietary and Established Names:
BioPlex 2200 ToRC IgM
BioPlex 2200 ToRC IgM Calibrator Set
BioPlex 2200 ToRC IgM Control Set

G. Regulatory Information:

Product code	Classification	Regulation section	Panel
PUQ: Multiplex flow immunoassay, *T. gondii*, Rubella, CMV IgM	Class II	866.3510 - Rubella Virus Serological Reagents	Microbiology
JIX: Calibrator, multi- analyte mixture	Class II	862.1150 - Calibrator	Clinical Chemistry
JJX: Single (specified) analyte controls (assayed and unassayed)	Class I	862.1660 - Quality Control Material (assayed and unassayed)	Clinical Chemistry

Note: The BioPlex™ 2200 ToRC IgM Kit is a multiplex immunoassay for the detection of IgM antibodies to *T. gondii*, Rubella virus and CMV. This device is classified as Class II as described above and a new product code is assigned for this device as the primary product code, listed under the regulation section for Rubella reagents. The following are the additional regulation sections and product codes that are applicable to the other analytes detected by the subject device of this submission.

866.3175 - Cytomegalovirus serological reagents. Class II (Microbiology). Antibody IgM, IF, cytomegalovirus virus (LKQ) and Enzyme Linked Immunosorbent Assay, Cytomegalovirus (LFZ)

866.3780 – *Toxoplasma gondii* Serological Agents. Class II (Microbiology). Enzyme Linked Immunosorbent Assay, *Toxoplasma gondii* (LGD)

H. Intended Use:

1. Intended use(s):

BioPlex 2200 ToRC IgM kit
The BioPlex 2200 ToRC IgM kit is a multiplex flow immunoassay intended for the qualitative detection of IgM antibodies to *Toxoplasma gondii* (*T. gondii*), Rubella and Cytomegalovirus (CMV) in human serum and plasma (K3 EDTA, lithium heparin, or sodium heparin).

The BioPlex 2200 ToRC IgM kit is intended for use with the Bio-Rad BioPlex 2200 System.

This kit is intended as an aid in the diagnosis of a current or recent *T. gondii*, Rubella and/or CMV infection, in individuals suspected of having one of the respective disease states including women of child bearing age.

This assay is not FDA cleared or approved for use in testing (screening) blood or plasma donors.

Performance characteristics for the ToRC IgM assays have not been evaluated in immunosuppressed or organ transplant individuals. Performance characteristics of this kit have not been established for use in neonatal screening or for use at point of care facilities.

BioPlex 2200 ToRC IgM Calibrator Set
The BioPlex 2200 ToRC IgM Calibrator Set is intended for the calibration of the BioPlex 2200 ToRC IgM Reagent Pack.

BioPlex 2200 ToRC IgM Control Set
The BioPlex 2200 ToRC IgM Control Set is intended for use as an assayed quality control to monitor the overall performance of the BioPlex 2200 Instrument and BioPlex 2200 ToRC IgM Reagent Pack in the clinical laboratory.

2. Indication(s) for use:

   Same as Intended Use

3. Special conditions for use statement(s):

   For Prescription use only

4. Special instrument requirements:

   Bio-Rad BioPlex 2200 System

I. Device Description:

BioPlex ToRC IgM Reagent Pack:

The BioPlex ToRC IgM Reagent Pack includes the following components:

- One (1) 10 mL vial, containing dyed beads coated with lysates of *T. gondii*, Rubella virus and CMV plus an Internal Standard bead (ISB) and a Serum Verification bead (SVB) in buffer with Glycerol and protein stabilizers (bovine and caprine). ProClin 300 (≤ 0.3%), sodium benzoate (≤ 0.1%) and sodium azide (< 0.1%) as preservatives.
- One (1) 5 mL vial, containing phycoerythrin-conjugated murine monoclonal anti-human IgM antibody and phycoerythrin-conjugated murine monoclonal anti-human FXIII antibody, in buffer with protein stabilizers (bovine and murine). ProClin 300 (≤ 0.3%), sodium benzoate (≤ 0.1%) and sodium azide (< 0.1%) as preservatives.
- One (1) 10 mL vial, containing goat anti-human IgG antibody and protein stabilizers (bovine and murine) in buffer. ProClin 300 (≤ 0.3%), sodium benzoate (≤ 0.1%) and sodium azide (< 0.1%) as preservatives.

BioPlex 2200 ToRC IgM Calibrator:
The BioPlex 2200 ToRC IgM Calibrator set contains two (2) 0.5 mL vials. The calibrators are provided in a human serum matrix made from defibrinated plasma with added known analyte concentrations consisting of HuCAL recombinant IgM antibodies against Rubella virus and human disease state plasma derived antibodies against T. gondii and CMV. All calibrators contain ProClin 300 (≤ 0.3%), sodium benzoate (≤ 0.1%) and sodium azide (< 0.1%) as preservatives.

BioPlex 2200 ToRC IgM Control:
The BioPlex 2200 ToRC IgM Control set contains two (2) 1.5 mL Positive Control serum vials, containing human disease state plasma derived IgM antibodies against T. gondii and CMV, and HuCAL® recombinant IgM antibodies against Rubella virus in a human serum matrix made from defibrinated plasma; and two (2) 1.5 mL Negative Control serum vials, in a human serum matrix made from defibrinated plasma. All controls contain Amikacin (0.003%), Cycloheximide ($C_{15}H_{23}NO_4$) (0.009%), Amphotericin B (0.002%), Cefotaxime Sodium (0.002%), Ciprofloxacin (0.005%), ProClin 300 (≤ 0.3%), sodium benzoate (≤ 0.1%) and sodium azide (< 0.1%).

J. Substantial Equivalence Information:

1. Predicate device name(s):
   BioPlex 2200 Rubella and CMV IgM Kit
   bioMeriéux, Inc. VIDAS® TOXO IgM

2. Predicate 510(k) number(s):
   K092587
   K923166

3. Comparison with predicate:

BioPlex 2200 **Rubella** and CMV IgM Kit

Similarities		
Item	Device BioPlex 2200 ToRC IgM	Predicate BioPlex 2200 Rubella and CMV IgM Kit K092587)
Intended use	Qualitative detection of **IgM antibodies to** *Toxoplasma gondii* (*T. gondii*), **Rubella and Cytomegalovirus (CMV) To be used as an aid in the diagnosis of a current or recent** *T. gondii*, **Rubella and/or CMV infection**	Qualitative detection of **IgM antibodies to Rubella and Cytomegalovirus (CMV) To be used as an aid in the diagnosis of a current or recent**, **Rubella and/or CMV infection**
Technology	Automated multiplex flow immunoassay	same

Differences		
Item	Device BioPlex 2200 ToRC IgM	Predicate BioPlex 2200 Rubella and CMV IgM Kit K092587)
Matrix	Serum and Plasma (K3 EDTA and Lithium or Sodium Heparin)	Serum, potassium EDTA or Sodium Heparin plasma

VIDAS® TOXO IgM

Similarities		
Item	Device BioPlex 2200 ToRC IgM	Predicate bioMeriéux, Inc., VIDAS® TOXO IgM K923166
Intended use	Qualitative detection of IgM antibodies to ***Toxoplasma gondii* (*T. gondii*)**, Rubella	Qualitative detection of anti-*Toxoplasma gondii* antibodies

Similarities		
Item	Device BioPlex 2200 ToRC IgM	Predicate bioMeriéux, Inc., VIDAS® TOXO IgM K923166
	and Cytomegalovirus (CMV) **To be used as an aid in the diagnosis of a current or recent *T. gondii***, Rubella and/or CMV infection	To be used as an aid in the diagnosis of acute, recent, or reactivated *Toxoplasma gondii* infection

Differences		
Item	Device BioPlex 2200 ToRC IgM	Predicate bioMeriéux, Inc., VIDAS® TOXO IgM K923166
Technology	Automated multiplex flow immunoassay	Manual enzyme linked fluorescent immunoassay (ELFA)
Matrix	Serum and Plasma (K3 EDTA and Lithium or Sodium Heparin)	Serum

K. Standard/Guidance Document Referenced (if applicable):

EP05-A3, Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline, Third Edition (Vol. 34 No.13)
EP07-A2, Interference Testing in Clinical Chemistry, Approved Guideline, Second Edition (Vol. 25 No.27)
EP09-A3, Measurement Procedure Comparison and Bias Estimation Using Patient Samples, Approved Guideline- Third Edition (Vol. 33, No. 11)
EP12-A2, User Protocol for Evaluation of Qualitative Test Performance; Approved Guideline-Second Edition (Vol. 28, No. 3)
EP15-A3, User Verification of Precision and Estimation of Bias; Approved Guideline - Third Edition (Vol. 34, No. 12)
EP25-A, Evaluation of Stability of In Vitro Diagnostic Reagents; Approved Guideline (Vol. 29, No. 20)

L. Test Principle:

The BioPlex 2200 ToRC IgM kit employs a panel of three antigen-coated fluoromagnetic beads with unique fluorescent signatures to identify the presence of IgM class antibodies to *T. gondii*, Rubella virus, and CMV antigens in a two-step assay format. In the first step, the system combines an aliquot of patient sample with sample diluent and bead reagent and then agitates the mixture at 37°C. In the second step, immobilized IgM is identified indirectly using a fluorescent

anti-human IgM reporter conjugate in a manner similar to antibody detection using an enzyme-linked reporter in an EIA. The assay is calibrated using a set of two distinct calibrator vials, supplied separately by Bio-Rad Laboratories. One vial containing negative sample, one vial containing *T. gondii* IgM, Rubella IgM, and CMV IgM are used for qualitative calibration of the assays.Two control beads are used. One is used to normalize assay output for fluctuations in detector function (internal standard bead, ISB) and the other control bead is used to verify that the sample is serum or plasma (serum verification bead, SVB). The fluorescent properties of the beads allow multi-analyte data to be acquired simultaneously from a single sample and segregated based upon the fluorescent codes embedded in the antigen-coated and control beads. The magnetic properties of the beads allow rapid washing to remove unbound molecules in between assay steps. Bead classification and reporter data are acquired as the beads flow through the reader which uses a dual laser detector employing the same principles utilized by fluorescence activated cell sorters. Raw data are reported as relative fluorescent intensity (RFI).

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. Precision/Reproducibility:

   Precision:
   Precision testing of the BioPlex 2200 ToRC IgM kit on the BioPlex 2200 instrument was performed in accordance with the CLSI EP5-A3 guideline. Samples were tested in duplicate, two (2) runs per day, over 20 days (2 replicates per run x 2 runs per day x 20 days (N= 80 data points per panel member) using one reagent lot, calibrator set and control set. The data were analyzed for within-run (repeatability), between-run, between-day, and total reproducibility and the mean (AI), standard deviation (AI) and percent coefficient of variation (%CV) are summarized in the tables below.

BioPlex 2200 Toxo IgM				Within-Run		Between-Run		Between-Day		Total	
Sample Type	*T. gondii* IgM Panel Members	N	Mean (AI)	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Serum	Negative	80	0.5	0.039	7.9%	0.000	0.0%	0.007	1.3%	0.039	8.0%
	High Negative	80	0.7	0.034	4.8%	0.011	1.6%	0.012	1.7%	0.037	5.3%
	Cut-Off	80	0.9	0.050	5.5%	0.000	0.0%	0.031	3.4%	0.059	6.5%
	Cut-Off	80	1.0	0.064	6.3%	0.000	0.0%	0.030	2.9%	0.071	6.9%
	Low Positive	80	1.3	0.057	4.3%	0.042	3.2%	0.039	2.9%	0.081	6.1%
	Positive	80	2.3	0.113	5.0%	0.000	0.0%	0.034	1.5%	0.118	5.2%
	Positive	80	3.3	0.164	4.9%	0.034	1.0%	0.053	1.6%	0.175	5.3%
Potassium EDTA	Negative	80	0.5	0.019	3.9%	0.000	0.0%	0.002	0.4%	0.019	3.9%
	High Negative	80	0.7	0.046	6.2%	0.000	0.0%	0.027	3.7%	0.053	7.2%
	Cut-Off	80	0.9	0.056	6.3%	0.000	0.0%	0.017	1.9%	0.059	6.6%
	Low Positive	80	1.2	0.073	6.0%	0.000	0.0%	0.049	4.0%	0.088	7.3%
	Positive	80	2.0	0.089	4.4%	0.037	1.8%	0.062	3.1%	0.114	5.7%
	Positive	80	3.2	0.167	5.3%	0.059	1.9%	0.098	3.1%	0.203	6.4%
Sodium Heparin	Negative	80	0.4	0.045	10.3%	0.000	0.0%	0.018	4.1%	0.048	11.1%
	High Negative	80	0.7	0.032	4.3%	0.030	4.0%	0.025	3.4%	0.050	6.8%
	Cut-Off	80	0.9	0.058	6.2%	0.025	2.7%	0.022	2.4%	0.067	7.2%
	Low Positive	80	1.3	0.068	5.3%	0.000	0.0%	0.035	2.7%	0.076	5.9%
	Positive	80	2.1	0.109	5.3%	0.000	0.0%	0.060	2.9%	0.124	6.0%
	Positive	80	3.1	0.117	3.8%	0.000	0.0%	0.049	1.6%	0.127	4.1%
Lithium Heparin	Negative	80	0.5	0.050	10.9%	0.011	2.4%	0.010	2.3%	0.052	11.4%
	High Negative	80	0.7	0.042	6.0%	0.000	0.0%	0.017	2.4%	0.045	6.4%
	Cut-Off	80	0.9	0.061	6.7%	0.000	0.0%	0.018	2.0%	0.064	7.0%
	Low Positive	80	1.3	0.063	5.0%	0.050	4.0%	0.019	1.5%	0.083	6.6%
	Positive	80	2.0	0.108	5.4%	0.045	2.2%	0.031	1.6%	0.121	6.1%
	Positive	80	3.1	0.145	4.7%	0.000	0.0%	0.064	2.1%	0.159	5.1%

BioPlex 2200 Rubella IgM				Within-Run		Between-Run		Between-Day		Total	
Sample Type	Rubella IgM Panel Members	N	Mean (AI)	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Serum	Negative	80	0.3	0.011	3.7%	0.000	0.0%	0.000	0.0%	0.011	3.7%
	High Negative	80	0.6	0.040	6.6%	0.000	0.0%	0.016	2.6%	0.043	7.1%
	Cut-Off	80	0.8	0.049	5.9%	0.000	0.0%	0.014	1.6%	0.051	6.1%
	Cut-Off	80	1.1	0.066	5.8%	0.000	0.0%	0.031	2.7%	0.073	6.4%
	Low Positive	80	1.2	0.063	5.4%	0.027	2.3%	0.027	2.2%	0.074	6.3%
	Positive	80	1.5	0.085	5.7%	0.039	2.6%	0.000	0.0%	0.094	6.2%
	Positive	80	2.7	0.146	5.5%	0.000	0.0%	0.000	0.0%	0.146	5.5%
	Positive	80	3.0	0.157	5.3%	0.035	1.2%	0.091	3.0%	0.185	6.2%
Potassium EDTA	Negative	80	0.3	0.011	3.7%	0.000	0.0%	0.000	0.0%	0.011	3.7%
	High Negative	80	0.6	0.045	7.0%	0.000	0.0%	0.029	4.6%	0.053	8.4%
	Cut-Off	80	1.0	0.055	5.6%	0.016	1.6%	0.026	2.7%	0.063	6.5%
	Low Positive	80	1.1	0.064	5.7%	0.016	1.4%	0.016	1.4%	0.068	6.1%
	Positive	80	1.6	0.084	5.4%	0.000	0.0%	0.057	3.7%	0.101	6.5%
	Positive	80	2.4	0.118	4.9%	0.000	0.0%	0.084	3.5%	0.145	6.0%
	Positive	80	3.0	0.168	5.6%	0.000	0.0%	0.103	3.4%	0.198	6.5%
Sodium Heparin	Negative	80	0.3	0.045	13.3%	0.011	3.3%	0.014	4.1%	0.048	14.4%
	High Negative	80	0.6	0.042	6.8%	0.011	1.8%	0.023	3.7%	0.049	8.0%
	Cut-Off	80	1.0	0.045	4.6%	0.034	3.4%	0.029	2.9%	0.063	6.4%
	Low Positive	80	1.1	0.066	5.8%	0.016	1.4%	0.018	1.6%	0.070	6.2%
	Positive	80	1.6	0.092	5.7%	0.000	0.0%	0.044	2.7%	0.102	6.3%
	Positive	80	2.5	0.123	4.9%	0.039	1.5%	0.036	1.4%	0.134	5.3%
	Positive	80	3.2	0.155	4.9%	0.019	0.6%	0.029	0.9%	0.159	5.0%
Lithium Heparin	Negative	80	0.3	0.019	6.5%	0.000	0.0%	0.000	0.0%	0.019	6.5%
	High Negative	80	0.6	0.047	8.3%	0.000	0.0%	0.023	4.1%	0.053	9.2%
	Cut-Off	80	1.0	0.063	6.6%	0.000	0.0%	0.032	3.3%	0.071	7.4%
	Low Positive	80	1.2	0.079	6.6%	0.000	0.0%	0.027	2.2%	0.083	7.0%
	Positive	80	1.5	0.089	5.9%	0.047	3.1%	0.026	1.7%	0.105	6.8%
	Positive	80	2.6	0.158	6.1%	0.000	0.0%	0.000	0.0%	0.158	6.1%
	Positive	80	3.1	0.150	4.8%	0.070	2.2%	0.039	1.3%	0.170	5.5%

BioPlex 2200 CMV IgM				Within Run		Between-Run		Between-Day		Total	
Sample Type	CMV IgM Panel Members	N	Mean (AI)	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Serum	Negative	80	0.4	0.039	10.3%	0.019	5.2%	0.005	1.5%	0.044	11.6%
	High Negative	80	0.8	0.060	7.5%	0.000	0.0%	0.017	2.2%	0.063	7.8%
	Cut-Off	80	1.1	0.065	6.1%	0.030	2.8%	0.032	3.0%	0.078	7.4%
	Cut-Off	80	1.2	0.152	12.2%	0.000	0.0%	0.000	0.0%	0.152	12.2%
	Low Positive	80	1.2	0.089	7.2%	0.000	0.0%	0.000	0.0%	0.089	7.2%
	Positive	80	1.7	0.122	7.0%	0.000	0.0%	0.000	0.0%	0.122	7.0%
	Positive	80	3.0	0.196	6.6%	0.000	0.0%	0.030	1.0%	0.198	6.7%
	Positive	80	3.1	0.214	7.0%	0.000	0.0%	0.077	2.5%	0.227	7.4%
Potassium EDTA	Negative	80	0.3	0.047	13.8%	0.000	0.0%	0.022	6.5%	0.052	15.3%
	High Negative	80	0.8	0.047	6.2%	0.030	3.9%	0.015	1.9%	0.058	7.5%
	Cut-Off	80	1.1	0.070	6.5%	0.000	0.0%	0.028	2.6%	0.075	7.0%
	Low Positive	80	1.3	0.089	6.7%	0.000	0.0%	0.000	0.0%	0.089	6.7%
	Positive	80	1.9	0.128	6.8%	0.000	0.0%	0.078	4.1%	0.150	8.0%
	Positive	80	3.1	0.185	6.0%	0.000	0.0%	0.088	2.9%	0.205	6.7%
	Positive	80	2.9	0.196	6.7%	0.000	0.0%	0.122	4.2%	0.231	7.9%
Sodium Heparin	Negative	80	0.3	0.022	7.5%	0.000	0.0%	0.000	0.0%	0.022	7.5%
	High Negative	80	0.8	0.065	7.8%	0.000	0.0%	0.000	0.0%	0.065	7.8%
	Cut-Off	80	0.8	0.047	6.3%	0.022	3.0%	0.017	2.3%	0.055	7.3%
	Low Positive	80	1.3	0.083	6.2%	0.019	1.4%	0.000	0.0%	0.085	6.3%
	Positive	80	2.0	0.121	6.0%	0.000	0.0%	0.048	2.4%	0.130	6.5%
	Positive	80	3.1	0.193	6.2%	0.000	0.0%	0.064	2.1%	0.203	6.5%
	Positive	80	3.1	0.167	5.4%	0.000	0.0%	0.076	2.5%	0.184	6.0%
Lithium Heparin	Negative	80	0.3	0.040	14.2%	0.000	0.0%	0.000	0.0%	0.040	14.2%
	High Negative	80	0.7	0.060	8.8%	0.000	0.0%	0.022	3.3%	0.064	9.4%
	Cut-Off	80	1.0	0.085	8.7%	0.000	0.0%	0.037	3.7%	0.093	9.5%
	Low Positive	80	1.4	0.104	7.5%	0.000	0.0%	0.055	4.0%	0.118	8.5%
	Positive	80	1.9	0.133	7.1%	0.019	1.0%	0.042	2.2%	0.140	7.6%
	Positive	80	3.0	0.222	7.5%	0.096	3.2%	0.000	0.0%	0.242	8.1%
	Positive	80	2.7	0.153	5.7%	0.030	1.1%	0.000	0.0%	0.156	5.8%

Reproducibility:

A reproducibility panel, consisting of six (6) panel members made using serum matrix and BioPlex ToRC IgM QC controls was prepared by Bio-Rad Laboratories. The serum sample panel included one (1) low negative, one (1) high negative, one (1) low positive near cut-off, one (1) medium positive, and one (1) high positive sample, and one (1) positive control for all three (3) analytes. Reproducibility testing was performed at three (3) US testing facilities using one (1) lot of the BioPlex 2200 ToRC IgM Pack, one (1) lot of BioPlex 2200 ToRC IgM Calibrator Set and one (1) lot of BioPlex 2200 ToRC IgM Control Set. The panels were provided to each of the testing sites. Each of the panel members and control sets were tested in replicates of four (4) on two runs per day over five (5) days at three (3) sites (4 replicates x 2 runs

x 5 days x 3 Sites = 120 replicates per panel member). The data were analyzed for within-run (repeatability), between-run, between-day, between-site and total precision according to the principles described in Clinical Laboratory Standards Institute (CLSI) EP15-A3. The grand mean, standard deviation (SD) and percent coefficient of variation (% CV) were calculated.

BioPlex 2200 Toxo IgM

T. gondii IgM Panel Member	Mean (AI)	Within Run		Between Run		Between Day		Between Site		Total	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Positive Control	2.0	0.092	4.7%	0.103	5.2%	0.000	0.0%	0.178	9.0%	0.225	11.4%
Low Negative	0.2	0.029	13.8%	0.016	7.6%	0.000	0.0%	0.010	4.7%	0.035	16.5%
High Negative	0.8	0.040	4.8%	0.012	1.5%	0.028	3.3%	0.100	12.0%	0.112	13.4%
Low Positive	1.3	0.051	4.0%	0.032	2.5%	0.023	1.8%	0.148	11.6%	0.162	12.7%
Mid Positive	2.2	0.081	3.7%	0.058	2.6%	0.032	1.5%	0.257	11.7%	0.278	12.7%
High Positive	3.2	0.172	5.3%	0.093	2.9%	0.043	1.3%	0.280	8.7%	0.344	10.7%

BioPlex 2200 Rubella IgM

Rubella IgM Panel Member	Mean (AI)	Within Run		Between Run		Between Day		Between Site		Total	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Positive Control	1.9	0.086	4.5%	0.053	2.8%	0.043	2.3%	0.198	10.5%	0.227	12.0%
Low Negative	0.3	0.026	9.3%	0.013	4.7%	0.000	0.0%	0.042	15.3%	0.051	18.5%
High Negative	0.8	0.048	6.2%	0.000	0.0%	0.026	3.3%	0.097	12.4%	0.111	14.2%
Low Positive	1.2	0.056	4.8%	0.019	1.7%	0.000	0.0%	0.143	12.3%	0.155	13.3%
Mid Positive	1.5	0.051	3.5%	0.014	1.0%	0.027	1.8%	0.197	13.6%	0.206	14.2%
High Positive	2.8	0.139	4.9%	0.015	0.5%	0.030	1.1%	0.328	11.6%	0.358	12.6%

BioPlex 2200 CMV IgM

CMV IgM Panel Member	Mean (AI)	Within Run		Between Run		Between Day		Between Site		Total	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Positive Control	2.3	0.098	4.3%	0.053	2.4%	0.058	2.6%	0.145	6.4%	0.192	8.5%
Low Negative	0.3	0.032	9.1%	0.000	0.0%	0.013	3.8%	0.052	15.1%	0.063	18.1%
High Negative	0.7	0.048	7.0%	0.011	1.6%	0.009	1.3%	0.062	9.0%	0.080	11.6%
Low Positive	1.2	0.071	6.2%	0.029	2.5%	0.000	0.0%	0.096	8.3%	0.123	10.6%
Mid Positive	1.7	0.081	4.7%	0.021	1.3%	0.038	2.3%	0.208	12.2%	0.227	13.4%
High Positive	2.9	0.146	5.1%	0.026	0.9%	0.065	2.3%	0.257	9.0%	0.304	10.6%

b. Linearity/assay reportable range:

Not Applicable

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*

Calibrator Traceability

The BioPlex ToRC IgM calibrators are traceable against frozen internal standards which are anchored to a quantitation panel. The quantitation panel consists of patient samples whose analyte values span the assay range.

The BioPlex 2200 ToRC IgM Reagent Kit is calibrated using a set of two distinct serum based calibrators. A negative calibrator and a multianalyte *T. gondii*, Rubella CMV IgM calibrator are used to calibrate the *T. gondii*, Rubella and CMV IgM assays. The cut-off value and assignment of the calibrators were determined by determining the 98-99th percentile on normal samples and performing concordance and Receiver Operator Characteristic (ROC) analysis during feasibility and development.

The manufacturing target ranges of the Calibrator Set are listed below.

Calibrator Set	Range (AI)
Calibrator Level 1	0.0 – 0.2
Calibrator Level 2	1.1 – 2.0

Controls

The control set includes two vials each of a negative control and a multianalyte positive control that contains *T. gondi*i, Rubella and CMV IgM. The positive control contains known concentrations of human *T. gondii*, Rubella and CMV IgM, and is prepared by blending human disease state serum (*T. gondii* and CMV) and human recombinant Rubella IgM (huCal) with ToRC IgM negative serum matrix.

The assignment for the BioPlex 2200 ToRC IgM Control Set is performed using a minimum of two reagent lots along with matched calibrators with a target of three reagent lots with matched calibrators. For each control lot, three vials per control level are tested in replicates of five on all reagent lots for a total of fifteen replicates per reagent lot. This testing is performed on three analyzers yielding a total of forty-five replicates per reagent lot. The total number of replicates for each control level is 90 when two reagent lots are used and 135 when three reagent lots are used.

The manufacturing target ranges of the Control Set are listed below.

Control Set	Range (AI)
Negative Control	0.0 – 0.5
Positive Control	2.0 – 2.6

Kit Stability
BioPlex 2200 ToRC IgM Kit: Real Time (unopened) Kit Stability, 12 months or until the date of expiration when stored unopened on the instrument or at 2 to 8°C; the open kit claim is 60 days.

Calibrator and Control Stability
BioPlex 2200 ToRC IgM Control and Calibrator Sets:
Calibrator Open Vial Stability (2 to 8°C), 60 days from first opening;
Control Open Vial Stability (2 to 8°C), 60 days from first opening;
Onboard Calibration Curve Stability, 30 days;
Real Time Stability of calibrators and controls (2 to 8°C), 12 months; labeled as until expiration date;
Calibrators and Controls Accelerated Stability (2 to 8°C), 18 months predicted;
Calibrators and Controls Freeze-thaw (-20ºC or -70ºC), 5 freeze thaw cycles.

Sample Stability
Serum or plasma (K3 EDTA, lithium heparin, or sodium heparin) samples may be stored at room temperature (18 – 30°C) for up to 3 days and under refrigeration (2 – 8°C) for up to 7 days. For longer storage of samples, keep at -20°C or colder. Up to 5-freeze thaw cycles at -20ºC and -70ºC is acceptable.

d. Detection limit:

Not Applicable

e. Analytical specificity:

Cross Reactivity:
The study was conducted to determine if samples from various disease states interfere with test results when tested with the BioPlex 2200 ToRC IgM kit. A panel of at least ten (10) specimens that are positive for each cross reactant were evaluated for possible cross reactivity with the BioPlex 2200 ToRC IgM kit for each of the three antibody assays. The potentially cross reactive samples were tested in commercially available predicate kits in order to confirm their negative status for the target analyte.

Cross reactivity, expressed as percent negative agreement is calculated by the ratio of the number of negative results to the total number of samples assayed for each cross reactant set of samples The results of each potential cross reactant are listed below.

BioPlex 2200 ToRC IgM Cross Reactivity

Potential Cross Reactant	*T. gondii* IgM			Rubella IgM			CMV IgM		
	N	Neg	Pos	N	Neg	Pos	N	Neg	Pos
ANA Screen	19	19	0	19	19	0	19	19	0
CMV IgM	10	10	0	10	10	0	N/A	N/A	0
EBV IgM	11	11	0	11	11	0	11	11	0
HAMA	15	15	0	15	15	0	15	15	0
hCG	12	12	0	12	12	0	12	12	0
HIV	10	10	0	10	10	0	10	10	0
HSV-1/2 IgM	13	13	0	13	13	0	13	13	0
Hypergamma-globulinemia IgM	21	21	0	21	20	1	21	21	0
Influenza	18	17	1	18	18	0	18	18	0
Measles IgM	16	16	0	16	16	0	16	16	0
Mumps IgM	13	12	1	13	13	0	13	13	0
Multiple Myeloma	17	17	0	17	17	0	17	17	0
Parvovirus B 19 IgM	14	14	0	14	13	1	14	14	0
Rheumatoid Factor	11	11	0	11	11	0	11	11	0
Rubella IgM	16	16	0	N/A	N/A	0	16	16	0
Toxo IgM	N/A	N/A	0	10	10	0	10	10	0
VZV IgM	13	12	1	13	13	0	13	12	1

Interfering Substances:

An interfering substances study was conducted to evaluate the potential interference of specific endogenous and exogenous substances with the BioPlex 2200 ToRC IgM assay according to the CLSI EP7-A2 guideline.

No significant interference was observed with any of the substances tested.
The substances and the maximum levels tested are shown in the table below.

Substance	Concentration
Hemoglobin	≤ 500 mg/dL
Bilirubin (unconjugated)	≤ 20 mg/dL
Bilirubin (conjugated)	≤ 30 mg/dL
Cholesterol	≤ 500 mg/dL
Red Blood Cells	≤ 0.4% (v/v)
Gamma Globulin	≤ 6 g/dL

Substance	Concentration
Triglycerides	≤ 3300 mg/dL
Beta Carotene	≤ 0.6 mg/dL
Protein (total)	≤ 12 g/dL
Ascorbic Acid	≤ 6 mg/dL
Sodium Heparin	≤ 8000 units/dL
Lithium Heparin	≤ 8000 units/dL
EDTA (K2 and K3)	≤ 800 mg/dL

f. Assay cut-off:

A final cut-off of 1.0 AI was established for the BioPlex 2200 ToRC IgM assay based on an evaluation of 401, 454 and 511 test-ordered and retrospective positive samples for *T. gondii*, Rubella and CMV IgM, respectively, for which the serological status was determined from the predicate *T. gondii*, Rubella and CMV IgM assays. The assay employs an equivocal zone that brackets the cut-off, which results in samples > 1.1 AI being positive and < 0.9 AI being negative. This analysis was used to optimize sensitivity and specificity for the BioPlex 2200 ToRC IgM assay.

2. Comparison studies:

a. Method comparison with predicate device:

Not Applicable

b. Matrix comparison:

Matched serum and plasma (EDTA and heparin sodium) samples drawn from the same donor were acquired from an outside reference lab. For each assay in the panel, a minimum of 40 sets of paired serum and plasma samples were prepared and values within the measurement range of the assay were analyzed in accordance with CLSI EP09-A3. Samples were assayed in replicates of two (2) with the second replicate run in reverse order. Mean plasma AI values were compared to matched mean serum AI values. Linear regression analysis was used to determine the presence of a matrix effect when compared to serum. The regression correlation parameters for slope, intercept and correlation coefficient (r) are shown below.

Matrix Comparison	N	BioPlex ToRC IgM Assay	Slope (95% CI)	Intercept (95% CI)	Correlation (r)
K3 EDTA vs. Serum	54	*T. gondii* IgM	1.02 (0.99 to 1.06)	-0.05 (-0.12 to 0.02)	0.994
	53	Rubella IgM	1.03 (1.00 to 1.06)	-0.02 (-0.08 to 0.05)	0.994
	60	CMV IgM	1.01 (0.97 to 1.05)	-0.02 (-0.10 to 0.05)	0.989
Lithium Heparin vs. Serum	54	*T. gondii* IgM	1.02 (0.98 to 1.06)	-0.04 (-0.12 to 0.04)	0.992
	51	Rubella IgM	1.03 (1.00 to 1.06)	-0.02 (-0.08 to 0.04)	0.995
	60	CMV IgM	0.98 (0.93 to 1.02)	0.00 (-0.09 to 0.09)	0.985
Sodium Heparin vs. Serum	54	*T. gondii* IgM	1.03 (0.99 to 1.06)	-0.05 (-0.12 to 0.02)	0.994
	51	Rubella IgM	1.01 (0.97 to 1.05)	-0.01 (-0.09 to 0.06)	0.993
	59	CMV IgM	0.99 (0.96 to 1.03)	-0.04 (-0.11 to 0.04)	0.991

3. Clinical studies:

   a. Clinical Sensitivity:

   Not Applicable

   b. Clinical specificity:

   Not Applicable

   c. Other clinical supportive data (when a. and b. are not applicable):

   Prospective Study:
   The performance of the BioPlex 2200 ToRC IgM kit was tested against corresponding commercially available predicate *T. gondii*, Rubella and CMV IgM assays. A total of 2,129 prospective samples (approximately 700 samples per analyte) submitted for *T. gondii*, Rubella, or CMV testing were tested at 3 U.S. clinical testing sites. Of the approximate 700 samples per analyte, 200 were from pregnant women for each analyte.

   Results from all sites are shown and summarized in the table below.

BioPlex 2200 ToRC IgM vs Commercially Available Immunoassay (Prospective Study)

Test Ordered				BioPlex 2200 ToRC IgM Assay					
				Pos (+)	Eqv	Neg (-)	Total	Pos (+) % Agreement 95% CI	Neg (-) % Agreement 95% CI
Commercially Available Immunoassay	*T. gondii* IgM	Pregnant Women	Pos (+)	0	0	0	0	N/A	98.0% (196/200) 95.0 to 99.2%
			Eqv	0	0	0	0		
			Neg (-)	3	1	196	200		
			Total	3	1	196	200		
		Test Ordered	Pos (+)	0	0	0	0	N/A	97.4% (481/494) 95.6 to 98.5%
			Eqv	1	0	0	1		
			Neg (-)	9	3	481	493		
			Total	10	3	481	494		
	Rubella IgM	Pregnant Women	Pos (+)	0	0	0	0	N/A	100.0% (198/198) 98.1 to 100.0%
			Eqv	0	0	2	2		
			Neg (-)	0	0	198	198		
			Total	0	0	200	200		
		Test Ordered	Pos (+)	4	1	2	7	40.0% (4/10)* 16.8 to 68.7%	99.6% (498/500) 98.6 to 99.9%
			Eqv	0	2	3	5		
			Neg (-)	1	1	498	500		
			Total	5	4	503	512		
	CMV IgM	Pregnant Women	Pos (+)	8	2	4	14	50.0% (8/16)** 28.0 to 72.0%	100.0% (183/183) 97.9 to 100.0%
			Eqv	0	1	2	3		
			Neg (-)	0	0	183	183		
			Total	8	3	189	200		
		Test Ordered	Pos (+)	20	1	11	32	55.6% (20/36)*** 39.6 to 70.5%	98.6% (480/487) 97.1 to 99.3%
			Eqv	0	0	4	4		
			Neg (-)	3	4	480	487		
			Total	23	5	495	523		

* Three samples were predicate equivocal and BioPlex Rubella IgM negative, two samples were predicate positive and BioPlex Rubella IgM negative and one sample was predicate positive and BioPlex Rubella IgM equivocal.

** Of the sixteen samples, Six samples were negative and three were equivocal by BioPlex CMV IgM. Eight samples were negative and one equivocal by another FDA cleared device.

*** Eleven positive and four equivocal results for the predicate were all negative by BioPlex CMV IgM. One positive result for the predicate was equivocal by BioPlex CMV IgM. All but three were confirmed negative by another FDA cleared device.

Retrospective Study:

Performance of the BioPlex 2200 ToRC IgM kit was also evaluated against corresponding commercially available *T. gondii*, Rubella, and CMV IgM immunoassays using presumptive positive samples. Three clinical sites tested 210 *T. gondii* (134 female, 76 male), 101 Rubella (44 female, 57 male) and 213 CMV (119 female, 94 male) IgM presumptive positive samples. Presumed positive banked samples for ToRC IgM were further selected by the respective predicate device use for the comparative analysis. The characteristics of samples with presumptive positive status are shown below.

BioPlex 2200 ToRC IgM vs Commercially Available Immunoassay (Retrospective Study)

Presumptive Positive for *T. gondii*, Rubella or CMV IgM			**BioPlex 2200 ToRC IgM Agreement**				
			Pos (+)	**Eqv**	**Neg (-)**	**Total**	**Pos (+) % Agreement 95% CI**
Commercially Available Immunoassay	***T.gondii* IgM**	**Pos (+)**	203	3	3	209	97.1% (203/209) 93.9 to 98.7%
		Eqv	1	0	0	1	
		Neg (-)	0	0	0	0	
		Total	204	3	3	210	
	Rubella IgM	**Pos (+)**	96	1	1	98	98.0% (96/98) 92.9 to 99.4%
		Eqv	1	0	0	1	
		Neg (-)	1	0	1	2	
		Total	98	1	2	101	
	CMV IgM	**Pos (+)**	198	2	1	201	98.5% (198/201) 95.7 to 99.5%
		Eqv	4	1	0	5	
		Neg (-)	4	0	3	7	
		Total	206	3	4	213	

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Correlation with CDC Evaluation Panels:

A correlation study was performed to evaluate the characteristics of the BioPlex 2200 ToRC IgM kit with serum panels provided by the Centers for Disease Control and Prevention (CDC) for *T. gondii* IgM. The results are presented as a means to convey further information on the performance. This does not imply an endorsement of the BioPlex 2200 ToRC IgM kit by the CDC. Results are presented in the table below.

Results From Testing of CDC *T. gondii* Reference Sera (N=97)

CDC Panel *T. gondii* IgM	BioPlex *T. gondii* IgM					
	Pos(+)	Eq	Neg(-)	Total	Positive Agreement	Negative Agreement
Pos (+)	32	0	0	32	100.0% 89.3 to 100.0	100.0% 94.4 to 100.0
Neg (-)	0	0	65	65		
Total	32	0	65	97		

Seroconversion Testing:

Commercially available seroconversion panels for *T. gondii*, Rubella and CMV IgM were tested with the BioPlex 2200 ToRC IgM kit and compared with the predicate commercial method.

BioPlex 2200 ToRC IgM Kit, Comparison to Commercial Method – *T. gondii* IgM

Panel	Day	*T. gondii* IgM	
		VIDAS Toxo IgM	BioPlex ToRC IgM
		Index	Antibody Index (AI)
Antibody Systems	0	0.24(Neg)	<0.2(Neg)
	7	1.62(Pos)	2.1(Pos)
	9	3.24(Pos)	3.3(Pos)
	14	5.78(Pos)	>4.0(Pos)
	16	5.80(Pos)	>4.0(Pos)
	23	5.38(Pos)	>4.0(Pos)
	27	5.24(Pos)	>4.0(Pos)
	30	5.04(Pos)	>4.0(Pos)
	49	4.59(Pos)	>4.0(Pos)
	53	4.35(Pos)	>4.0(Pos)
	86	3.30(Pos)	>4.0(Pos)
	88	2.94(Pos)	3.6(Pos)
	93	2.67(Pos)	3.1(Pos)
	95	2.62(Pos)	2.7(Pos)
	100	2.58(Pos)	2.8(Pos)
	104	2.34(Pos)	2.6(Pos)
	107	2.36(Pos)	2.2(Pos)
	112	2.28(Pos)	2.4(Pos)
	114	2.21(Pos)	2.3(Pos)
	119	2.29(Pos)	2.1(Pos)

BioPlex 2200 ToRC IgM Kit, Comparison to Commercial Method – Rubella IgM

Panel	Day	Rubella IgM	
		BioPlex RC IgM	BioPlex ToRC IgM
		Antibody Index (AI)	Antibody Index (AI)
Liquicheck - RP011	0	<0.2 (Neg)	<0.2 (Neg)
	3	<0.2 (Neg)	<0.2 (Neg)
	9	<0.2 (Neg)	<0.2 (Neg)
	12	<0.2 (Neg)	<0.2 (Neg)
	16	1.3 (Pos)	1.0 (Eq)
	19	>4.0 (Pos)	>4.0 (Pos)
	24	>4.0 (Pos)	>4.0 (Pos)
	27	>4.0 (Pos)	>4.0 (Pos)
	31	3.6 (Pos)	3.4 (Pos)
	36	2.1 (Pos)	2.0 (Pos)
	39	1.5 (Pos)	1.4 (Pos)
	43	1.0 (Eq)	1.0 (Eq)
	46	0.7 (Neg)	0.6 (Neg)
	50	0.6 (Neg)	0.5 (Neg)
	53	0.3 (Neg)	0.4 (Neg)
	57	0.3 (Neg)	0.4 (Neg)
	60	0.3 (Neg)	0.3 (Neg)
	64	0.2 (Neg)	0.2 (Neg)
	67	0.2 (Neg)	0.2 (Neg)
	71	0.2 (Neg)	0.2 (Neg)

BioPlex 2200 ToRC IgM Kit, Comparison to Commercial Method – CMV IgM

Panel	Day	CMV IgM	
		BioPlex RC IgM	BioPlex ToRC IgM
		Antibody Index (AI)	Antibody Index (AI)
Liquicheck - RP003	1	>4.0 (Pos)	2.8 (Pos)
	4	>4.0 (Pos)	>4.0 (Pos)
	8	>4.0 (Pos)	>4.0 (Pos)
	51	1.9 (Pos)	2.3 (Pos)
	55	1.8 (Pos)	2.1 (Pos)
	59	1.2 (Pos)	1.8 (Pos)
	65	1.3 (Pos)	1.5 (Pos)
	67	1.4 (Pos)	1.5 (Pos)
	72	1.3 (Pos)	1.1 (Pos)
	74	1.1 (Pos)	1.0 (Eq)
	79	1.6 (Pos)	1.2 (Pos)
	84	1.4 (Pos)	1.3 (Pos)
	88	1.3 (Pos)	1.4 (Pos)
	95	1.3 (Pos)	1.1 (Pos)
	99	1.4 (Pos)	1.0 (Eq)

IgM Specificity:

Samples positive for *T. gondii*, Rubella and CMV IgM and IgG were treated with dithiothreitol (DTT) to inactivate IgM activity. The samples were assayed neat and diluted into assay range in replicates of two. IgM was measured using the BioPlex 2200 ToRC IgM kit.

BioPlex ToRC IgM - *T. gondii* IgM Specificity

Sample ID	***T. gondii* IgM (AI) Before DTT**	**DTT Treatment AI (% recovery)**
Sample 1	9.5	0.1 (1.05%)
Sample 2	9.5	0.1 (1.05%)
Sample 3	18.0	0.3 (1.67%)
Sample 4	15.5	0.5 (3.23%)
Sample 5	9.0	0.1 (1.11%)
Sample 6	14.0	0.2 (1.43%)
Sample 7	14.0	0.1 (0.71%)
Sample 8	15.0	0.1 (0.67%)
Sample 9	15.0	0.1 (0.67%)
Sample 10	16.5	0.1 (0.61%)

BioPlex ToRC IgM – Rubella IgM Specificity

Sample ID	Rubella IgM (AI) Before DTT	DTT Treatment AI (% recovery)
Sample 1	8.0	0.1 (1.25%)
Sample 2	9.0	0.0 (0.00%)
Sample 3	8.5	0.0 (0.00%)
Sample 4	5.0	0.1 (2.00%)
Sample 5	9.0	0.1 (1.11%)
Sample 6	7.0	0.1 (1.43%)
Sample 7	4.0	0.0 (0.00%)
Sample 8	5.0	0.0 (0.00%)
Sample 9	9.0	0.2 (2.22%)
Sample 10	6.0	0.1 (1.67%)

BioPlex ToRC IgM – CMV IgM Specificity

Sample ID	CMV IgM (AI) Before DTT	DTT Treatment AI (% recovery)
Sample 1	25.0	0.1 (0.40%)
Sample 2	11.0	0.2 (1.82%)
Sample 3	8.5	0.1 (1.18%)
Sample 4	20.0	0.5 (2.50%)
Sample 5	15.5	0.2 (1.29%)
Sample 6	18.5	0.2 (1.08%)
Sample 7	21.0	0.2 (0.95%)
Sample 8	6.0	0.0 (0.00%)
Sample 9	16.5	1.2 (7.27%)
Sample 10	31.5	0.7 (2.22%)

4. Clinical cut-off**:**

   Not Applicable

5. Expected values/Reference range:
   Expected values for the BioPlex 2200 ToRC IgM kit are presented by age and gender in the following tables for samples from pregnant women and patients sent to the lab for *T. gondii*, Rubella or CMV IgM testing. A total of two hundred (200) each of pregnant women samples sent to the lab for *T. gondii*, Rubella or CMV IgM testing and approximately five hundred (500) each of samples sent to the lab for *T. gondii*, Rubella or CMV IgM testing were tested.

BioPlex 2200 ToRC IgM Prevalence Results by Age and Gender: Samples from Pregnant Women Who Were Sent for *T.gondii*, Rubella, or CMV IgM Testing by Age Group

Age	*T. gondii* IgM		Rubella IgM		CMV IgM	
	Pos/Total	% Prevalence	Pos/Total	% Prevalence	Pos/Total	% Prevalence
15-25	1/81	1.2%	0/86	0.0%	4/85	4.7%
26-35	2/98	2.0%	0/93	0.0%	4/100	4.0%
36-43	0/21	0.0%	0/21	0.0%	0/15	0.0%
Total	3/200	1.5%	0/200	0.0%	8/200	4.0%

BioPlex 2200 ToRC IgM Prevalence Results by Age and Gender: Samples from Patients Who Were Sent for *T.gondii*, Rubella, or CMV IgM Testing

Age	Gender	T. gondii IgM		Rubella IgM		CMV IgM	
		Pos/Total	% Prevalence	Pos/Total	% Prevalence	Pos/Total	% Prevalence
<1-90	F	5/357	1.4%	3/357	0.8%	14/325	4.3%
	M	5/137	3.6%	2/155	1.3%	9/198	4.5%
Total		10/494	2.0%	5/512	1.0%	23/523	4.4%

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

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