K093784

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Zeus Scientific Inc. 510K Summary:

AtheNA Multi-Lyte® ToRCH IgG Plus Test System

Administrative Information

1. 510(k): number: k093784
2. Submission Purpose: Intent to market referenced device for the simultaneous qualitative detection and differentiation of specific human IgG class antibodies to Toxoplasma gondii (Toxo), Rubella, Cytomegalovirus (CMV) and Herpes Simplex 1 (HSV-1) and Herpes Simplex 2 (HSV-2).
3. Measurand: Toxoplasma, Rubella, CMV, HSV 1 and HSV 2 IgG antibodies.
4. Type of Test: Multiplex microparticle immunoassay.
5. Applicant: Zeus Scientific, Inc. (Zeus), PO Box 38, Raritan, NJ 08869 (908)526-3744
6. Proprietary Name: AtheNA Multi-Lyte® ToRCH IgG Plus Test System.
7. Established name: Toxoplasma, Rubella, Cytomegalovirus, Herpes Simplex 1 and Herpes Simplex 2 serological reagents

Regulatory Information

Toxo

Device Classification: Enzyme Linked Immunoabsorbent Assay
Regulation Description: Toxoplasma gondii serological reagents
Class: Class 2
Product Code: LGD
Panel: Microbiology
Regulation Number: 866.3780

Rubella

Device Classification: Enzyme Linked Immunoabsorbent Assay
Regulation Description: Rubella virus serological reagents
Class: Class 2
Product Code: LFX
Panel: Microbiology
Regulation Number: 866.3510

CMV

Device Classification: Enzyme Linked Immunoabsorbent Assay
Regulation Description: Cytomegalovirus serological reagents
Class: Class 2
Product Code: LFZ
Panel: Microbiology
Regulation Number: 866.3175

HSV-1

Device Classification: Enzyme Linked Immunoabsorbent Assay
Regulation Description: Herpes Simplex virus serological reagents
Class: Class 2
Product Code: MXJ
Panel: Microbiology
Regulation Number: 866.3305

HSV-2
Device Classification: Enzyme Linked Immunoabsorbent Assay
Regulation Description: Herpes Simplex 2 serological reagents
Class: Class 2
Product Code: MYF
Panel: Microbiology
Regulation Number: 866.3305

Intended Use

The Zeus Scientific, Inc. **AtheNA Multi-Lyte®** ToRCH IgG Plus Test System is intended for the qualitative detection of specific human IgG class antibodies to Toxoplasma gondii (*T.gondii*), Rubella, Cytomegalovirus (CMV) and HSV 1 & 2 in human serum. The results of this assay are intended to be used as an aid in the assessment of serological status to Toxoplasma gondii, Rubella and CMV. For HSV 1 and HSV 2, the test is indicated for sexually active adults and expectant mothers, as an aid for presumptively diagnosing Herpes Simplex 1 and Herpes Simplex 2.

The test is not intended for use in screening blood or plasma donors.

The performance of this assay has not been established for use in a pediatric population, neonatal screening, immunocompromised or immunosuppressed patients or for use at point of care facilities.

Device Description

The Zeus Scientific, Inc. AtheNA Multi-Lyte® ToRCH IgG Plus Test System is a multiplex immunoassay intended for the simultaneous qualitative detection and differentiation of specific human IgG class antibodies to Toxoplasma gondii, Rubella, Cytomegalovirus (CMV), Herpes Simplex 1 (HSV-1) and Herpes Simplex 2 (HSV-2) in human serum. The results of this assay are intended to be used as an aid in the assessment of a patient's serological status to infection with Toxoplasma gondii, Rubella, CMV, HSV 1 and HSV 2 and in the determination of immune status of individuals including pregnant women. The test system is comprised of the AtheNA Multi-Lyte test kit, software and the Luminex Corp instrument.

The AtheNA Multi-Lyte ToRCH IgG Plus Test System provides the following components:

Reactive Reagents:

All reactive reagents contain sodium azide as a preservative at a concentration of 0.1% (w/v).

1. Multiplexed bead suspension 1. Ready to use, 5.5 mL bottle. The suspension contains separate distinguishable 5.6 micron polystyrene beads that are conjugated with:
    - Toxo grade 2 antigen

- Rubella K2S grade antigen
- CMV grade 2
- HSV-1 type-specific recombinant gG-1 protein antigen
- HSV-2 gG-2 type-specific recombinant gG-2 protein antigen

The bead mix also contains one bead set designed to detect non-specific antibodies in the patient sample (if present) and four separate bead sets used for assay calibration.

2. Conjugate: Phycoerythrin conjugated goat anti-human IgG (γ chain specific). Ready to use, 15 mL amber bottle.
3. Human positive serum control 1. One, 0.2 mL vial.
4. Human positive serum control 2. One, 0.2 mL vial.
5. Human negative serum control. One, 0.2 mL vial.
6. SAVe Diluent®. One 50 mL bottle containing phosphate-buffered-saline. Ready to use. NOTE, the sample diluent will change color in the presence of serum.
7. Wash Buffer Concentrate: dilute 1 part concentrate + 9 parts deionized or distilled water. One bottle containing 10 X concentrate of phosphate buffered saline.

Non-Reactive Reagents

1. One, 96-well filtration plate for rinsing the microspheres
2. Data Labels: One label is adhered to the inside lid of the kit box and a second label is inside the kit box.
3. Package Insert providing instructions for use
4. Calibration CD: a compact disc that includes all lot-specific kit calibration values required for specimen analysis and assay quality control

Substantial Equivalence

Examination of enclosed data indicates that the Zeus Scientific, Inc AtheNA Multi-Lyte ToRCH IgG Plus Test System for the simultaneous detection and differentiation of IgG class antibodies to Toxo, Rubella, CMV, HSV-1 and HSV-2 is substantially equivalent to commercially marketed test systems which have been previously cleared by the FDA for *in vitro diagnostic use.*

The comparator information for both cleared and investigational analytes are listed:

Toxoplasma

1. Name of Predicate Device: Toxo IgG ELISA Test System
2. Manufacturer of Predicate Device: Zeus Scientific, Inc.
3. 510(k)891781

Rubella

1. Name of Predicate Device: Rubella IgG ELISA Test System
2. Manufacturer of Predicate Device: Zeus Scientific, Inc.
3. 510(k)891783

CMV

1. Name of Predicate Device: CMV IgG ELISA Test System
2. Manufacturer of Predicate Device: Zeus Scientific, Inc.

3. 510(k)924096

HSV-1

1. Name of Predicate Device: HerpeSelect 1 and 2 Immunoblot IgG
2. Manufacturer of Predicate Device: Focus Diagnostics
3. 510(k)000238

HSV-2

1. Name of Predicate Device: HerpeSelect 1 and 2 Immunoblot IgG
2. Manufacturer of Predicate Device: Focus Diagnostics
3. 510(k)000238

Test Principle

The Zeus Scientific, Inc. **AtheNA Multi-Lyte** ToRCH IgG Plus Test System is designed to detect IgG class antibodies in human sera to Toxo, Rubella, CMV, HSV-1 and HSV-2. The test procedure involves four incubation steps:

1. Patient sera are diluted and the diluted test sera are incubated in a vessel containing a multiplexed mixture of the bead suspension. The multiplexed bead suspension contains a mixture of distinguishable sets of polystyrene microspheres; each set conjugated with Toxoplasma, Rubella, CMV, HSV-1 and HSV-2 antigens. The bead mix also contains one bead set designed to detect non-specific antibodies in the patient sample (if present) and four separate bead sets used for assay calibration. If present in patient sera, the individual antibodies will bind to the corresponding immobilized antigen bead set. The microspheres are rinsed to remove non-reactive serum proteins.
2. Phycoerythrin-conjugated goat anti-human IgG is added to the vessel and the plate is incubated. The conjugate will react with IgG antibody immobilized on the beads in step 1. The bead suspension is then analyzed by the **AtheNA Multi-Lyte®** instrument. The bead set(s) are sorted (identified) and the amount of reporter molecule (PE conjugate) is determined for each bead set. Using the *Intra-Well Calibration Technology®*, internal calibration bead sets are used to to convert raw fluorescence into outcome (units).

Analytical Specificity

Interfering Substances

The effect of potential interfering substances on sample results generated using the AtheNA Multi-Lyte test system was evaluated with the following possible interfering substances based on the guidelines established in CLSI EP7-A2: albumin, bilirubin, cholesterol, hemoglobin, triglycerides and intralipids.

The quantity of analyte in each interfering substance is as follows and is based on CLSI EP7-A2:

Bilirubin: 1mg/dL (low), 15 mg/dL (high)

Albumin: 3.5 g/dL (low), 5 g/dL (high)
Cholesterol: 150 mg/dL (low), 250 mg/dL (high)
Triglycerides: 150 mg/dL (low), 500 mg/dL (high)
Hemoglobin: 20 g/dL (low), 20 g/dL (high)
Intralipid: 300 mg/dL (low), 750 mg/dL (high)

Three samples each for Toxo, Rubella, CMV, HSV 1 and 2 IgG were chosen based on their performance on the AtheNA Multi-Lyte test system: positive, borderline and negative. The samples were exposed to the possible interfering substance and tested. All samples showed less than a 20% change in signal with the following exceptions:

	Potential Interfering Substance Spikes Exhibiting Change in Signal Greater than 20%											
	Bilirubin		Albumin		Cholesterol		Triglycerides		Hemoglobin		Intralipid	
Analyte/Level of Sample	High	Low	High	Low	High	Low	High	Low	High	Low	High	Low
Toxoplasma Positive	<20%	<20%	<20%	<20%	<20%	<20%	<20%	<20%	<20%	22%	<20%	<20%
Toxoplasma Borderline	<20%	<20%	-33%	-30%	<20%	<20%	<20%	<20%	<20%	<20%	<20%	<20%
Toxoplasma Negative	<20%	<20%	78%	89%	31%	<20%	<20%	<20%	<20%	22%	78%	<20%
Rubella Positive	<20%	<20%	<20%	<20%	<20%	<20%	<20%	<20%	<20%	24%	<20%	<20%
Rubella Borderline	<20%	<20%	<20%	<20%	-27%	<20%	<20%	<20%	<20%	-31%	<20%	<20%
Rubella Negative	50%	50%	<20%	-33%	<20%	-33%	-33%	-33%	<20%	-33%	<20%	<20%
CMV Positive	<20%	<20%	-27%	-25%	-32%	-31%	<20%	<20%	-33%	-35%	<20%	<20%
CMV Borderline	<20%	<20%	<20%	<20%	<20%	<20%	<20%	<20%	<20%	31%	24%	<20%
CMV Negative	<20%	25%	<20%	32%	<20%	<20%	<20%	<20%	<20%	25%	<20%	25%
HSV 1 Postive	<20%	<20%	<20%	<20%	<20%	<20%	<20%	<20%	27%	22%	<20%	<20%
HSV 1 Borderline	<20%	<20%	<20%	<20%	<20%	<20%	<20%	<20%	<20%	<20%	<20%	<20%
HSV 1 Negative	<20%	<20%	41%	36%	<20%	<20%	<20%	20%	56%	26%	<20%	<20%
HSV 2 Positive	<20%	<20%	<20%	<20%	27%	<20%	24%	21%	<20%	23%	<20%	<20%
HSV 2 Borderline	<20%	<20%	<20%	<20%	<20%	<20%	<20%	<20%	<20%	<20%	<20%	<20%
HSV 2 Negative	50%	41%	<20%	<20%	<20%	<20%	<20%	<20%	32%	35%	<20%	<20%

Cross Reactivity

Studies were performed at the manufacturing facility to assess cross reactivity with the Athena Multi-Lyte ToRCH IgG Plus test system using samples that were sero-positive to Measles, Mumps, Rubella, VZV, EBV VCA IgG, EBNA-1, HSV-1, HSV-2, CMV, Syphilis, Toxoplasma and ANA and Rf IgM. Micro-particle and ELISA immunoassay test systems manufactured for commercial distribution were used to determine the sero-positivity of the samples. Ten samples minimally for each possible cross-reactant were tested. The results presented were obtained by testing the analytes against high concentrations of possible cross reactants.

	AtheNA Multi-Lyte ToRCH IgG Plus Cross Reactivity Summary				
Analyte	Toxoplasma	Rubella	CMV	HSV 1	HSV 2
Measles	0/10	0/20	0/10	0/10	0/10
Mumps	0/10	0/20	0/10	0/10	0/10
Rubella	0/10	N/A	0/10	0/10	0/10
VZV	0/10	0/20	0/10	0/10	0/10
VCA IgG	0/10	0/20	0/10	0/10	0/10
EBNA IgG	0/10	0/20	0/10	0/10	0/10
HSV 1	0/10	0/20	0/10	N/A	0/10
HSV 2	0/10	0/20	0/10	0/10	N/A
ANA	0/10	0/4	0/10	0/10	0/10
RF	0/10	0/10	0/10	0/10	0/10
CMV	0/10	0/20	N/A	0/10	0/10
Syphilis	0/10	0/10	0/10	0/10	0/10
Toxoplasma	NA	0/20	0/10	0/10	0/10

Clinical Performance

Clinical Data Generated for Submission

1. **Comparative testing of the Intended Use Populations:** AtheNA Multi-Lyte ToRCH IgG Plus versus predicate assays. 851 unselected samples submitted for ToRCH testing were obtained from various serum vendors. The samples were submitted for ToRCH antibody testing, sequentially numbered, de-identified and archived and made available for purchase. After procurement, 300 samples were tested at a hospital laboratory located in the Mid-Atlantic region; 351 samples were tested at a hospital laboratory located in the Northeast. 200 samples were from Expectant Mothers and were tested at the manufacturing site's laboratory. All results are from data generated concurrently using the AtheNA Multi-Lyte ToRCH IgG Plus test system.
2. **Comparative testing in Populations other than those for Intended Use:** Additional clinical performance was assessed in special populations other than the intended use populations. Performance data was gathered on HSV-1 and HSV-2 low prevalence populations and the relative specificity of Rubella was assessed internally at Zeus using pre-selected banked samples of sera which previously tested negative for Rubella antibody by the predicate device
3. **Clinical performance with International Standards and CDC Reference Panels:** Performance of the AtheNA Multi-Lyte ToRCH IgG Plus was assessed using the CDC Reference Panels. Traceability and linearity was demonstrated for Rubella using the WHO standard. The performance of Rubella IgG was demonstrated using the CDC low titer standard.
4. **Precision and Reproducibility:** Precision of the device was assessed using nine samples. These repeatability studies were performed internally at the manufacturing site's laboratory. Reproducibility was assessed using six samples tested at three sites, two external and one internal.

Expected Results

Observed prevalence was evaluated at three sites in a prospective study including individuals and pregnant women undergoing ToRCH testing.

1. 651 masked samples prospectively collected from individuals between the ages of <1 and 89 were tested at two external sites. 300 samples were submitted for ToRCH antibody assessment. 351 samples were submitted for testing of one or more of the anlytes in the ToRCH panel. Testng was performed on all five markers on all samples. Results from a subset of 596/651 individuals between the ages of 17 and 69 were used to calculate HSV 1 and HSV 2 prevalence. Site 1, a hospital laboratory located in the Mid-Atlantic region tested 300 samples. Site 2, a hospital laboratory in the Northeast tested 351 samples.
2. 200 masked samples prospectively collected from pregnant women for ToRCH antibody assessment were obtained from two serum vendors. The women ranged in age from 15 to 46.The samples were tested internally at the manufacturer site for all five analytes.

AtheNA Multi-Lyte ToRCH IgG Plus Observed Prevalence in Intended Use Populations

Observed Prevalence in Individuals Undergoing ToRCH Antibody Assessment

Prevalence of Analytes in Prospective Samples							
		Toxoplasma		Rubella		CMV	
Age	Gender	Pos/Total	% Prevalence	Pos/Total	% Prevalence	Pos/Total	% Prevalence
0-9	Male	0/2	0.0%	1/2	50.0%	1/2	50.0%
	Female	1/2	50.0%	1/2	50.0%	1/2	50.0%
10-19	Male	1/3	33.3%	3/3	100.0%	2/3	66.7%
	Female	5/55	9.1%	50/55	90.9%	38/55	69.1%
20-29	Male	2/24	8.3%	23/24	95.8%	9/24	37.5%
	Female	58/257	22.6%	232/257	90.3%	184/257	71.6%
30-39	Male	3/16	18.8%	12/16	75.0%	8/16	50.0%
	Female	57/189	30.2%	170/189	89.9%	145/189	76.7%
40-49	Male	6/11	54.5%	11/11	100.0%	8/11	72.7%
	Female	14/44	31.8%	39/44	88.6%	30/44	68.2%
50-59	Male	1/10	10.0%	9/10	90.0%	5/10	50.0%
	Female	3/11	27.3%	10/11	90.9%	10/11	90.9%
60-69	Male	3/6	50.0%	6/6	100.0%	4/6	66.7%
	Female	3/4	75.0%	4/4	100.0%	3/4	75.0%
70+	Male	0/0	0.0%	0/0	0.0%	0/0	0.0%
	Female	1/1	100.0%	1/1	100.0%	1/1	100.0%
Unkown Age	Male	0/0	0.0%	0/0	0.0%	0/0	0.0%
	Female	2/13	15.4%	9/13	69.2%	10/13	76.9%

Unknown Gender/Age	0/3	0.0%	1/3	33.3%	3/3	100.0%
Total	160/651	24.6%	582/651	89.4%	459	71.0%

Observed Prevalence in Pregnant Women

Prevalence of Analytes in Pregnant Women										
	Toxoplasma		Rubella		CMV		HSV 1		HSV 2	
Age	Pos/Total	% Prevalence	Pos/Total	% Prevalence	Pos/Total	% Prevalence	Pos/Total	% Prevalence	Pos/Total	% Prevalence
16-19	2/23	9.2%	23/23	100.0%	16/23	69.6%	15/23	65.2%	3/23	13.0%
20-29	12/131	27.0%	35/39	89.7%	104/131	79.4%	92/124	74.2%	51/124	41.1%
30-39	10/37	55.6%	127/129	28.4%	26/37	70.3%	30/36	83.3%	14/36	38.9%
40-49	5/9	8.3%	9/9	100.0%	5/9	55.6%	8/9	88.9%	7/9	77.8%
Total	29/200	14.50%	194/200	97.90%	151/200	75.50%	160/200	80.00%	75/200	37.50%

Observed Prevalence in Sexually Active Adults

		HSV 1		HSV 2	
Age	Gender	Pos/Total	% Prevalence	Pos/Total	% Prevalence
17-19	Male	0/0	0.0%	0/0	0.0%
	Female	27/38	71.1%	6/38	15.8%
20-29	Male	6/23	26.1%	1/23	4.3%
	Female	180/246	73.2%	57/245	23.3%
30-39	Male	10/16	62.5%	3/15	20.0%
	Female	165/187	88.2%	52/187	27.8%
40-49	Male	10/11	90.9%	3/11	27.3%
	Female	31/44	70.5%	16/44	36.4%
50-59	Male	5/10	50.0%	5/10	50.0%
	Female	8/11	72.7%	6/11	54.5%
60-69	Male	4/6	66.7%	2/6	33.3%
	Female	4/4	100.0%	2/4	50.0%
Total		450/596	75.5%	153/594	25.8%

HSV Hypothetical Predictive Values by Prevalence

Sexually Active Adults	
HSV-1	HSV-2

Expectant Mothers	
HSV-1	HSV-2

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Prevalence	PPV	NPV	PPV	NPV	PPV	NPV	PPV	NPV
50.0%	94.8%	98.5%	93.7%	96.8%	87.0%	99.2%	92.9%	97.0%
40.0%	92.4%	99.0%	90.9%	97.8%	81.7%	99.5%	89.7%	98.0%
30.0%	88.7%	99.4%	86.5%	98.6%	74.2%	99.6%	84.9%	98.7%
25.0%	85.9%	99.5%	83.2%	98.9%	69.1%	99.7%	81.4%	99.0%
20.0%	82.0%	99.6%	78.8%	99.2%	62.6%	99.8%	76.6%	99.2%
15.0%	76.3%	99.7%	72.5%	99.4%	54.2%	99.9%	69.8%	99.5%
10.0%	67.0%	99.8%	62.4%	99.6%	42.7%	99.9%	59.3%	99.7%
5.0%	49.0%	99.9%	44.0%	99.8%	26.1%	100.0%	40.8%	99.8%

Performance in Prospectively Collected Intended Use Populations

The performance of the ToRCH panel was evaluated using prospectively collected frozen remnant serum samples from a total of 651 individuals for which ToRCH IgG panel or testing for each of the individual analytes was ordered. Outside investigators tested 300 and 351 samples respectively.

Summary of Performance Characteristics In Individuals Undergoing ToRCH Antibody Assessment

		Predicate					
		Positive	Equivocal	Negative	Site Total	PPA NPA	95% CI
AtheNA Multi-Lyte IgG Plus	Toxoplasma						
	Positive	136	3	16	155	99.3% (136/137)	96.0% - 100%
	Equivocal	0	0	3	3		
	Negative	0	1	490	491	95.7% (450/514)	98.0% - 99.9%
	Invalid	0	0	2	2		
	Site Total	136	4	511	651		
	Rubella						
	Positive	533	4	4	541	98.5% (533/541)	97.1% - 99.4%
	Equivocal	3	1	1	5		
	Negative	2	3	60	65	'87% (60/69)	76.7% - 93.9%
	Invalid	0	0	0	0		
	Site Total	538	8	65	611		
	CMV						
	Positive	450	6	6	462	99.6% (450/452)	98.4% - 100%

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	Equivocal	1	2	4	7		
	Negative	1	0	181	182	91.3% (181/197)	87.2% - 95.3%
	Invalid	0	0	0	0		
	Site Total	452	8	191	651		

*4/4 discrepant Rubella samples which tested positive by AtheNA and negative by ELISA had low positive values for AtheNA and high negative values for ELISA. 4/4 discrepant Rubella samples which tested positive by AtheNA and equivocal by ELISA had low positive values for AtheNA and high equivocal values for ELISA.

HSV1 and HSV2 Performance in Sexually Active Adults

The performance of the HSV1 and HSV2 was evaluated in prospectively collected samples using results from 596/651 individuals between the ages of 17 and 69.

Summary of Performance Characteristics in Sexually Active Adults

		Predicate					
		Positive	Equivocal	Negative	Site Total	Sensitivity Specificity	95% CI
AtheNA Multi-Lyte IgG Plus	HSV 1						
	Positive	418	0	8	426	98.6% (418/424)	97.0% - 99.5%
	Equivocal	4	0	1	5		
	Negative	2	0	163	165	94.6% (163/172	90.3% - 97.6%
	Invalid	0	0	0	0		
	Site Total	424	0	172	596		
	HSV 2						
	Positive	127	0	27	154	96.9% (127/131)	92.4% - 98.8%
	Equivocal	1	0	3	4		
	Negative	3	0	433	436	93.5% (433/463)	90.9% - 95.6%
	Invalid	0	0	0	0		
	Site Total	131	0	463	594*		

Performance in Pregnant Women Population

Zeus Scientific internally evaluated 200 frozen remnant serum samples collected from pregnant women between the ages of 15 and 46 for which ToRCH antibody testing was requested.

Summary of Performance Characteristics in a Population of Pregnant Women:

		Predicate					
		Positive	Equivocal	Negative	Site Total	PPA NPA	95% CI
AtheNA Multi-Lyte IgG Plus : Toxoplasma	Toxoplasma						
	Positive	22	1	6	29	100.0% (22/22)	87.3% - 100%

	Equivocal	0	0	1	1		
	Negative	0	0	170	170	95.3% (170/178)	91.3% - 98.0%
	Invalid	0	0	0	0		
	Site Total	22	1	177	200		
	Rubella						
	Positive	194	0	0	194	99.0% (194/196)	96.4% - 99.9%
	Indeterminate	1	0	0	1		
	Negative	0	1	4	5	100.0% (4/4)	47.3% - 100%
	Invalid	0	0	0	0		
	Site Total	195	1	4	200		
	CMV						
	Positive	151	0	0	151	98.1% (151/154)	94.4% - 99.6%
	Equivocal	0	0	0	0		
	Negative	0	3	46	49	100.0% (46/46)	93.7% - 100%
	Invalid	0	0	0	0		
	Site Total	151	3	46	200		
	HSV 1						
	Positive	137	0	8	145	99.3% (137/138)	96.1% - 100%
	Equivocal	0	0	0	0		
	Negative	1	0	46	47	85.2% (46/54)	72.3% - 93.4%
	Invalid	0	0	0	0		
	Site Total	138	0	54	192		
	HSV 2						
	Positive	68	0	7	75	97.1% (68/70)	90.1% - 99.7%
	Equivocal	0	0	2	2		
	Negative	2	0	113	115	92.6% (113/122	86.5% - 96.6%
	Invalid	0	0	0	0		
	Site Total	70	0	122	192		

Agreement with CDC Panel

The performance of the AtheNA Multi-Lyte ToRCH IgG Plus test system was assessed using masked, well characterized serum panel from the CDC. The panels consist of:

1. 70% Toxo positive and 30% Toxo negative samples.

2. 80% Rubella positive and 20% Rubella negative samples.
3. 54% CMV positive and 46% CMV negative samples.
4. 24% HSV1 and HSV2 dual-positive samples, 50% HSV1 positive and 50% HSV1 negative samples and 48% HSV2 positive and 52% HSV2 negative samples.

The results are presented to convey further information on the performance of the test kit and do not imply endorsement of the assay by the CDC.

Agreement with CDC Characterized Serum Panels

		CDC Result				
		Positive	Negative	Site Total	PPA NPA	95% CI
AtheNA Multi-Lyte ToRCH IgG Plus	**Toxoplasma**					
	Positive	70	0	70	100.0% (70/70)	95.8% - 100.0%
	Equivocal	0	0	0		
	Negative	0	30	30	100.0% (30/30)	90.5% - 100.0%
	Invalid	0	0	0		
	Site Total	70	30	100		
	Rubella					
	Positive	80	0	80	100.0% (80/80)	96.3% - 100.0%
	Equivocal	0	0	0		
	Negative	0	20	20	100.0% (20/20)	86.1% - 100.0%
	Invalid	0	0	0		
	Site Total	80	20	100		
	CMV					
	Positive	52	2	54	100.0% (52/52)	94.4% - 100.0%
	Equivocal	0	0	0		
	Negative	0	46	46	95.8% (46/48)	90.2% - 100.0%
	Invalid	0	0	0		
	Site Total	52	48	100		
	HSV 1					
	Positive	50	0	50	100.0% (50/50)	94.2% - 100.0%
	Equivocal	0	0	0		
	Negative	0	50	50	100.0% (50/50)	94.2% - 100.0%

	Invalid	0	0	0		
	Site Total	50	50	100		
	HSV 2					
	Positive	48	1	49	100.0% (48/48)	94.0% - 100.0%
	Equivocal	0	0	0		
	Negative	0	51	51	98.1% (51/52)	94.3% - 100.0%
	Invalid	0	0	0		
	Site Total	48	52	100		

HSV 1 & 2 Performance in a Low Prevalence Population

The relative specificity of HSV 1 & 2 was assessed internally using sera from a low prevalence population. The low prevalence population was comprised of serum samples from 18 and 19 year old subjects previously tested for infections considered non-sexual in nature.

HSV-1 Reactivity: The predicate immunoblot device was positive for 7 samples and negative for 60 samples. The AtheNA Multi-Lyte HSV 1& 2 IgG test system agreed with 85.7% (6/7) of immunoblot positives and 98.3% (59/60) of immunoblot negatives.

HSV-2 Reactivity: The predicate immunoblot device was positive for 0 samples and negative for 67 samples. The AtheNA Multi-Lyte HSV 1& 2 IgG test system agreed with 100% (0/0) of immunoblot positives and 100% (67/67) of immunoblot negatives.

Performance in Low Prevalence Population

		Predicate					
		Positive	Equivocal	Negative	Site Total	PPA NPA	95% CI
AtheNA Multi-Lyte IgG Plus	HSV 1						
	Positive	8	0	2	10	100.0% (8/8)	68.8% - 100%
	Equivocal	0	0	0	0		
	Negative	0	0	56	56	96.6% (56/58)	88.1% - 99.6%
	Invalid	0	0	0	0		
	Site Total	8	0	58	66		
	HSV 2						
	Positive	3	0	1	4	100.0% (3/3)	36.8% - 100%
	Equivocal	0	0	0	0		
	Negative	0	0	62	62	98.4% (62/63)	91.5% - 100%
	Invalid	0	0	0	0		

	Site Total	3	0	63	66		

Rubella Retrospective Negative Sample Study

The relative specificity of Rubella was assessed internally at Zeus using pre-selected banked samples of sera which previously tested negative for Rubella antibody by the predicate device.

Rubella Reactivity: The predicate ELISA device was positive for 0 samples and negative for 100 samples. The Rubella analyte in the AtheNA Multi-Lyte ToRCH IgG Plus test system agreed with 100% (0/0) of ELISA positives and 100% (100/100) of ELISA negatives.

Rubella Retrospective Negative Sample Study

		Predicate					
		Positive	Equivocal	Negative	Site Total	PPA NPA	95% CI
AtheNA Multi-Lyte IgG Plus	Rubella						
	Positive	0	0	0	0	N/A	N/A
	Indeterminate	0	0	0	0		
	Negative	0	0	100	100	100.0% 100/100)	97.1% - 100%
	Invalid	0	0	0	0		
	Site Total	0	0	100	100		

Clinical performance with International Standards

Performance of the AtheNA Multi-Lyte ToRCH IgG Plus was assessed using the CDC Reference Panels. Traceability and linearity was demonstrated for Rubella using the WHO standard. The performance of Rubella IgG was demonstrated using the CDC low titer standard.

Rubella Traceability to WHO Standard

Traceability was investigated internally to assess the device's correlation to the WHO Standard at the cut-off. The Standard was diluted and tested in duplicate with the device on two lot numbers and the Percent Recovery calculated. At the WHO Standard dilution of 10.63, the mean of the results on Lot 1 was 9.1 with a recovery of 96%. The mean of results for Lot 2 was 10 with a recovery of 102%.

Rubella Traceability Study

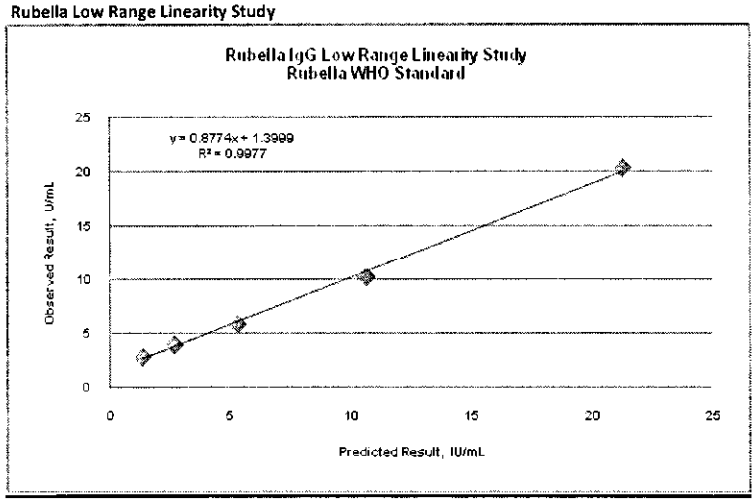
Expected	AtheNA Multi-Lyte lot 1				AtheNA Multi-Lyte lot 2			
Result	Measured Mean		Mean % Recovery		Measured Mean		Mean % Recovery	
IU/mL	Result	IU/mL	Result	IU/mL	Result	IU/mL	Result	IU/mL
1.33	3	2.7	210	205	3	2.7	231	205
2.66	4	3.6	148	137	4	3.6	146	137
5.31	6	5.5	110	103	6	5.5	105	103

10.63	10	9.1	96	86	11	10	102	94
21.25	20	18.2	96	86	20	18.2	92	86

Rubella Low Range Study

A Rubella IgG low range linearity study was performed to demonstrate linearity across the lower range of the assay using the WHO Standard. The Standard was diluted in duplicate, the means established and the percent recovery of the expected results calculated.

Rubella Low Range Linearity Study



Rubella Performance with CDC Low Titer Standard

Rubella performance was assessed with the CDC low titer sample (21 IU/mL). The sample was aliquoted, diluted in duplicate and tested by three technicians. Percent recovery was calculated for both neat and diluted samples

Rubella Performance With CDC Low Titer Sample

	CDC Low Titer Rubella Standard: 21 IU/mL					
Tech	Neat	Interpretation	% Recovery	1:2 Dilution	Interpretation	% Recovery
1	22	Positive	102%	11	Positive	102%
1	20	Positive	93%	10	Positive	99%
2	22	Positive	103%	11	Positive	109%
2	22	Positive	105%	11	Positive	104%
3	20	Positive	95%	11	Positive	101%
3	21	Positive	100%	12	Positive	111%

Precision and Reproducibility

Assay precision and reproducibility was evaluated internally and at two external clinical sites. The study was conducted as follows: A panel of six samples was identified and/or prepared (by Zeus Scientific, Inc.) for use in the study based upon their activity on the **AtheNA Multi-Lyte** assay. Two samples of the panel

were negative, two were high positives and the other two samples were near the assay cut off for each specific target. To assess reproducibility, each sample was aliquoted twice and each aliquot was run in triplicate, each day. This resulted in six results per day. This was repeated for three days at each site and the resulting data used to assess precision at each facility

I	Sample	Mean	Within-Run		Between-Day		Between-Run		Between-Site		Total	
Member	N	AU/mL	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Toxo IgG Positive 1	54	747.2	52.1	7.3	61.6	8.5	34.5	4.7	71.5	8.7	157.2	8.0
Toxo IgG Positive 2	54	770.3	50.8	6.8	63.1	8.3	39.2	4.9	78.7	8.5	170.3	8.6
Toxo IgG Positive 1 (near Cut-off)	54	158.8	158.8	9.3	18.2	11.3	12.6	8.0	18.8	12.1	29.5	11.9
Toxo IgG Positive 2 (near Cut-off)	54	140.2	140.2	8.4	16.8	11.3	13.0	8.3	20.2	12.1	33.2	12.9
Toxo IgG Negative 1	54	10.5	10.5	40.9	3.8	39.7	1.3	15.0	4.3	38.4	5.0	40.7
Toxo IgG Negative 2	54	9.1	9.1	45.4	4.1	47.4	2.4	22.6	4.7	48.0	5.6	49.8
Rubella IgG Positive 1	54	1296.9	50.1	3.9	68.4	5.0	54.5	3.7	95.4	5.3	301.3	5.7
Rubella IgG Positivetive 2	54	1102.6	58.2	5.4	63.6	5.8	37.3	3.4	99.5	6.5	173.1	7.0
Rubella IgG Positive 1 (near Cut-off)	54	242.8	13.3	5.4	15.6	6.5	10.2	4.4	25.6	6.2	51.9	6.4
Rubella IgG Positive 2 (near Cut-off)	54	189.9	10.1	5.2	15.5	9.5	11.5	5.7	28.3	10.1	37.9	10.4
Rubella IgG Negative 1	54	27.9	4.8	20.5	16.1	21.9	1.8	8.3	4.2	21.3	19.4	19.3
Rubella IgG Negative 2	54	47.4	4.0	10.3	6.5	9.8	3.7	9.4	8.8	10.9	23.8	11.0
CMV IgG Positive 1	54	996.5	88.2	8.5	99.2	9.7	58.5	5.9	108.2	10.1	167.2	10.0
CMV IgG Positive 2	54	756.9	54.5	7.0	66.7	8.7	46.8	6.3	73.3	8.8	1.6.3	8.7
CMV IgG Positive 1 (near Cut-off)	54	119.2	10.1	8.2	13.2	11.1	9.6	8.3	14.9	10.9	18.3	10.1
CMV IgG Positive 2 (near Cut-off)	54	135.3	13.6	9.9	16.4	12.1	12.6	9.4	19.5	10.7	21.2	10.8
CMV IgG Negative 1	54	17.9	5.6	29.8	6.1	32.7	3.4	19.5	6.3	28.2	7.4	27.1
CMV IgG Negative 2	54	16.4	5.5	35.5	5.9	37.1	3.6	23.4	6.3	35.4	7.3	35.4

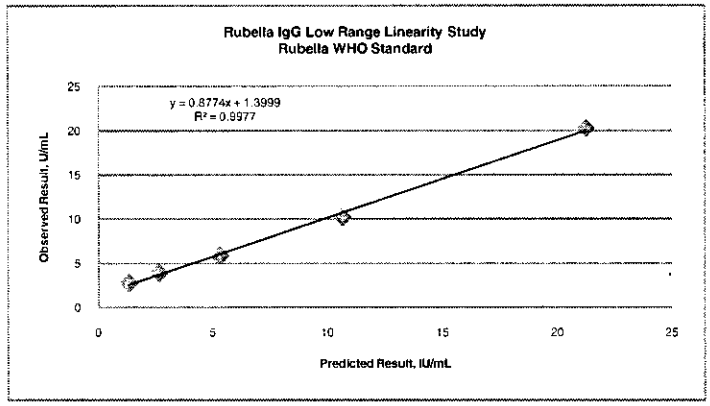
HSV 1 IgG Positive 1	54	310.1	24.2	7.9	24.8	8.1	10	3.3	31	8.9	32.3	10.1
HSV 1 IgG Positive 2	54	392.7	31.5	8.0	32.3	8.2	15.6	3.8	48.1	8.7	50.8	8.4
HSV 1 IgG Positive 1 (near Cut-off)	54	144.6	15.4	10.7	17.2	12.0	8.9	6.0	22.3	12.4	23.0	12.4
HSV 1 IgG Positive 2 (near Cut-off)	54	191.7	17.6	9.1	19.7	10.2	9.6	5.1	24.5	9.9	27.4	10.6
HSV 1 IgG Negative 1	54	26.4	3.9	15.5	3.9	15.5	1.4	5.2	4.8	16.2	6.1	16.8
HSV 1 IgG Negative 2	54	8.2	2.3	30.7	2.5	34.1	1.3	17.0	2.7	36.9	3.5	39.4
HSV 2 IgG Positive 1	54	445.7	26.9	6.1	40.1	8.9	33.8	7.4	53.4	9.2	58.1	9.1
HSV 2 IgG Positive 2	54	355.6	27.0	7.4	30.5	8.4	18.8	5.2	51.5	8	57.2	8.6
HSV 2 IgG Positive 1 (near Cut-off)	54	152.2	14.9	9.9	16.0	10.6	7.6	5.2	25.3	10.0	31.6	11.2
HSV 2 IgG Positive 2 (near Cut-off)	54	114.1	11.4	9.8	12.5	10.9	6.3	5.7	15.4	10.8	20.4	10.8
HSV 2 IgG Negative 1	54	16.9	4.0	29.7	4.3	31.3	2.0	12.1	4.3	35.8	7.0	41.0
HSV 1 IgG Negative 2	54	21.2	5.9	27.5	6.5	30.6	3.1	15.2	6.8	26.6	8.9	27.6

Linearity Study **lot 09046891**

AtheNA Multi-Lyte Torch IgG Plus lot#09046891								
WHO Value	Rubella IgG							
	AU	U/mL	converted IU/mL	AU	U/mL	converted IU/mL	Mean(U/mL)	converted IU/mL
21.25	198	18	17	245	22	20	20	18
10.63	122	11	10	101	9	8	10	9
5.31	57	5	5	71	7	6	6	5
2.66	45	4	4	41	4	3	4	4
1.33	25	2	2	36	3	3	3	3

WHO Value IU	Means U/mL
21.25	20
10.63	10
5.31	6
2.66	4
1.33	3

WHO Value IU	Converted Means IU/mL
21.25	18
10.63	9
5.31	5
2.66	4
1.33	3



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
10903 New Hampshire Avenue
Document Mail Center – WO66-0609
Silver Spring, MD 20993-0002

Zeus Scientific Inc.
c/o Ms. Ewa Nadolczak
Manager Clinical Affairs
200 Evans Way
Branchburg, NJ 08876

JUL 16 2010

Re: K093784
Trade/Device Name: AtheNA Multi-Lyte® ToRCH IgG Plus Test System
Regulation Number: 21 CFR 866.3510
Regulation Name: Rubella Virus Serological Reagents.
Regulatory Class: Class II
Product Code: OPM, LGD, LFZ, MXJ, MYF
Dated: July 12, 2010
Received: July 13, 2010

Dear Ms. Nadolczak:

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. 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.

If your device is classified (see above) into class II (Special Controls), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. 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 Parts 801 and 809); medical device reporting (reporting of

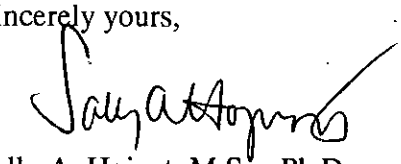
medical device-related adverse events) (21 CFR 803); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Parts 801 and 809), please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety at (301) 796-5450. 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 http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,



Sally A. Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of *In Vitro* Device Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number: k093784

Device Name: AtheNA Multi-Lyte® ToRCH IgG Plus Test System

Indications for Use:

The Zeus Scientific, Inc. **AtheNA Multi-Lyte®** ToRCH IgG Plus Test System is intended for the qualitative detection of specific human IgG class antibodies to Toxoplasma gondii (*T.gondii*), Rubella, Cytomegalovirus (CMV) and HSV 1 & 2 in human serum. The results of this assay are intended to be used as an aid in the assessment of serological status to Toxoplasma gondii, Rubella and CMV. For HSV 1 and HSV 2, the test is indicated for sexually active adults and expectant mothers, as an aid for presumptively diagnosing Herpes Simplex 1 and Herpes Simplex 2.
The test is not intended for use in screening blood or plasma donors.
The performance of this assay has not been established for use in a pediatric population, neonatal screening, immunocompromised or immunosuppressed patients or for use at point of care facilities.

Prescription Use __X__ AND/OR Over-The-Counter Use _____
(Part 21 CFR 801 Subpart D) (21 CFR 807 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Devices (OIVD)

Division Sign-Off

Office of In Vitro Diagnostic Device Evaluation and Safety

510(k) k093784