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SUMMARY OF SAFETY AND EFFECTIVENESS

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SUBMITTED BY:

Judith J. Smith
Sienna Biotech, Inc.
9115 Guilford Rd. Suite 180
Columbia, MD 21046

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NAME OF DEVICES:

Trade Name:

Copalis One Immunoassay System; Copalis TORC Total Antibody Assay; Copalis *Toxoplasma gondii* Total Antibody Assay; Copalis Rubella Total Antibody Assay Copalis CMV Total Antibody Assay

Common Names/Descriptions:

Immunoassay Analyzer; Immunoassay for the Detection of Total Antibodies to *Toxoplasma gondii*, Rubella and Cytomegalovirus

Classification Names:

Nephelometer for clinical use; Toxoplasma gondii serological reagents; Rubella virus serological reagents; Cytomegalovirus serological reagents

PREDICATE DEVICES:

BioWhittaker Toxostat; Becton Dickinson And Co. Rubascan and CMVscan; Abbott IMx

DEVICE DESCRIPTION:

INTENDED USE: The Copalis™ TORC, Toxo, Rubella, and CMV Total Antibody Assays use Coupled Particle Light Scattering (Copalis) technology in microparticle agglutination-based immunoassays for the qualitative detection of total antibodies (IgG and IgM) to *Toxoplasma gondii*, rubella and/or cytomegalovirus (CMV) in human serum using the Copalis™ I Immunoassay System. The presence of antibodies is indicative of current or prior infection with the suspected organism. The results of these assays on a single serum specimen are used to determine the patient's immune status for rubella and to determine the patient's immunological experience for *Toxoplasma gondii* and CMV. When evaluating properly paired sera, the results of these assays are used to demonstrate seroconversion as evidence of recent infection. Both specimens should be tested simultaneously (see Interpretation of Results).

These assays has not been FDA cleared or approved for the screening of blood or plasma donors.

The assay will also be offered as separate microparticle immunoassays for the qualitative detection of total antibodies (IgG and IgM) to *Toxoplasma gondii*, rubella and cytomegalovirus (CMV) in human serum using the Copalis™ One Immunoassay System. The intended use of the individual assays will be specific to the individual antibodies detected but, other than that, will remain the same as the combination assay.

KIT DESCRIPTION: Coupled Particle Light Scattering (Copalis) technology provides a rapid method for the measurement of antibodies to specific viral or protozoal pathogens.

The Copalis™ TORC, Toxo, Rubella, and CMV Total Antibody Assays are based on the principle of antibody-dependent particle aggregation as detected by measurement of changes in light scattering. Due to the unique measuring system, a sample can be tested for antibodies to *Toxoplasma gondii*, rubella and CMV using a single TORC reagent and obtain results for the individual antibodies. Sized latex microparticles coated with inactivated *Toxoplasma gondii*, rubella and CMV antigens aggregate in the presence of antibodies to these infectious agents. After 10 minutes of agitation, the levels of aggregation are determined by discrimination of particle sizes (for the TORC assay) and measurement of the number of reacted and unreacted particles as they flow past a detector. Reactivity is assessed by the level of aggregation per particle size relative to a cutoff value. The Copalis TORC and individual Total Antibody Assays detect the presence of both IgM and IgG antibodies. Two levels of controls are used to monitor system performance.

PERFORMANCE DATA:

Comparison: A comparison study was performed of patient specimens and controls using the Copalis TORC Total Antibody Assay and the Copalis individual assays. Analyses of the data by One Way Analysis of Variance showed that the differences in mean values between the component of the TORC assay and the corresponding individual assay are not great enough to exclude the possibility that the difference is due to random sampling variability; there is not a statistically significant difference ($p = 0.849$).

In addition, a reproducibility study was conducted to compare the components of the Copalis TORC Total Antibody Assay and the Copalis individual assays. The difference in mean CTRs and %CVs of the component of the TORC assay and the individual assay were not clinically significant. Therefore, it can be concluded that the clinical performance of the TORC and individual assays are equivalent.

Clinical trials were conducted at 3 sites (2 clinical laboratories and Sienna Biotech laboratory) to evaluate the performance of the Copalis TORC, Toxo,

Rubella, and CMV Total Antibody Assays in detecting antibodies to *Toxoplasma gondii*, rubella and CMV on the modified Copalis One Immunoassay System. The assay performance was compared to the BioWhittaker ToxoStat (ToxoStat) and the Becton Dickinson and Co. Rubascan (Rubascan) and CMVscan (CMVscan) assays.

A total of 769 serum samples were tested, 20% of which were fresh samples. Combined site testing results for each component of the assay are presented in Table A.

Table A
Comparison of the Copalis™ TORC Total Antibody Assay with Commercially Available Assays - Combined Site Results

	Toxoplasma gondii Antibody	Rubella Antibody	CMV Antibody
Relative Sensitivity (95% Confidence Interval)	95.4%	95.0%	93.0%
	(92.0 - 97.6%)	(92.9 - 96.5%)	(90.3 - 95.2%)
Relative Specificity (95% Confidence Interval)	93.9%	91.7%	97.1%
	(91.5 - 95.8%)	(87.6 - 94.8%)	(94.6 - 98.6%)
Initial Agreement	94.3%	93.9%	94.7%
Agreement Following Resolution of Discordants	97.9%	97.8%	99.7%

Reproducibility:

Reproducibility studies were performed at the 3 sites using one lot of TORC tests. Assay component reproducibility was determined by testing 4 samples - 1 negative, 1 low positive (near the components' cutoffs) and 2 high positive (near the upper limit of the components' ranges). Samples were tested in triplicate twice a day for 5 days. The results are summarized in Table B.

Table B
Reproducibility Results For Copalis Torc Total Antibody Assay - Combined Sites

SAMPLE	ANTIBODY TO *TOXOPLASMA GONDII*			ANTIBODY TO RUBELLA			ANTIBODY TO CMV		
	MEAN CTR	WITHIN RUN %CV	TOTAL %CV	MEAN CTR	WITHIN RUN %CV	TOTAL %CV	MEAN CTR	WITHIN RUN %CV	TOTAL %CV
RP1 (n = 89)	103	1.8	2.0	105	1.9	2.0	102	2.1	2.8
RP2 (n = 86)	129	3.0	4.4	116	2.1	2.7	132	3.9	4.6
RP3 (n = 86)	157	4.1	5.9	128	3.0	5.2	166	4.5	5.8
RP4 (n = 85)	177	4.7	7.3	150	3.6	7.3	207	4.8	7.7

During the clinical trials, the Negative and Low Positive Controls were assayed each day of use at each site for the length of the trial. Results are summarized in Table C.

Table C
Controls Total Precision

Control		Component		
		Toxoplasma gondii	Rubella	CMV
Negative	Mean	102	102	101
	% CV	2.6	3.1	2.8
	n	36	36	35
Low Positive	Mean	124	120	124
	% CV	4.5	4.5	4.1
	n	95	95	95

Lot-to-lot reproducibility was established using 3 test cup lots of Copalis Rubella Total Antibody Assay. A summary of the data is presented in Table D.

Table D
Lot-to-Lot Reproducibility - Antibody to Rubella

Level		Lot #1	Lot #2	Lot #3
Negative	Mean	100	100	102
	% CV	1.3	3.0	1.5
Low Positive	Mean	131	125	128
	% CV	4.7	2.9	2.4
Mid Positive	Mean	162	150	156
	% CV	7.6	6.7	4.8
High Positive	Mean	204	187	197
	% CV	5.1	2.9	7.1

CDC SERUM PANELS: The following information is from Rubella and CMV Serum Panels obtained from the CDC and tested by Sienna Biotech, Inc. The results are presented as a means to convey further information of the performance of this assay with masked, characterized serum panels. This does not imply an endorsement of the assay by the CDC.

The Rubella Serum Panel consists of 82% positive and 18% negative samples. The Copalis TORC Total Antibody Assay demonstrated 100% total agreement with the CDC rubella antibody results.

The CMV Serum Panel consists of 66% positive and 34% negative samples. The Copalis TORC Total Antibody Assay demonstrated 100% total agreement with the CDC CMV antibody results.

WHO AND CDC REFERENCE STANDARD TESTING: The WHO 3rd International Standards for *Toxoplasma gondii* (1000 IU/mL) and rubella (1700 IU/mL) and the CDC Rubella Standard (21 IU/mL) were tested on the Copalis TORC Total Antibody Assay. Each was diluted and tested in replicates of 5 to

establish the quantitative sensitivity of the assay components' cutoffs and the reproducibility at those cutoffs. Results are summarized in Table E.

Table E
WHO and CDC Reference Standard Testing Results

	WHO 3rd I.S. *Toxoplasma gondii* (1000 IU/mL) 25 IU/mL Dilution	WHO 3rd I.S. Rubella (1700 IU/mL) 10 IU/mL Dilution	CDC Rubella (21 IU/mL) 10 IU/mL Dilution
Mean (CTR)	116	117	116
%CV	0.9%	2.1%	1.3%
Range (CTR)	115 - 118	114 - 120	115 - 118