510(k) Summary

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirement of SMDA 1990 and 21 CFR 807.92.

The assigned 510(k) number is: K072732

APR 15 2008

1 Submitter Name, Address, and Contact

Ortho-Clinical Diagnostics, Inc.
1001 US Highway 202
Raritan, NJ 08869-0606

Contact Person: Laura C. Vellucci
(908) 218-8532

2 Preparation Date

Date 510(k) prepared: September 20, 2007

3 Device Name

Trypanosoma cruzi (*T. cruzi*) Whole Cell Lysate Antigen,
ORTHO® *T. cruzi* ELISA Test System

Common Name: *Trypanosoma cruzi (T. cruzi)* Whole Cell Lysate Antigen

Trade Name: ORTHO® *T. cruzi* ELISA Test System

Classification Name: *Trypanosoma* spp. Serological reagents (21 CFR 866.3870)

Assay Class: I (general controls)

4 Predicate Device

The ORTHO *T. cruzi* ELISA Test System is substantially equivalent to K930272 Hemagen Chagas' Kit (EIA Method) - Hemagen Diagnostics, Inc., and/or K023889 Enzyme Linked Immunosorbent Assay, *T. cruzi* - Wiener Laboratories and the *T. cruzi* indirect immunofluorescence assay, IFA, performed by Focus Diagnostics, Cypress, CA is the comparator method.

5 Device Description

The ORTHO *T. cruzi* ELISA Test System is an enzyme-linked immunosorbent assay (ELISA). ELISA technology utilizes the principle that antigens or antibodies bound to the solid phase can be detected by complementary antibodies or antigens labeled with an enzyme capable of acting on a chromogenic substrate. When substrate is applied, the presence of antigens or antibodies can be detected by development of a colored end product. The optical densities are read spectrophotometrically.

This ELISA was developed to detect human antibodies to *T. cruzi* in serum and plasma. The assay utilizes microwells coated with a whole-cell lysate containing *T. cruzi* antigens as the solid phase. The assay procedure is a three-stage test carried out in a microwell coated with lysate (antigens) prepared from *T. cruzi*. In the first stage, test specimen, Negative Control, and Positive Calibrator are diluted directly in the test well containing Specimen Diluent, and incubated for a specified length of time. If antibodies to *T. cruzi* are present, antigen-antibody complexes will form on the microwell surface. If antibodies to *T. cruzi* are absent, complexes will not form. Unbound antibodies in the sample will be removed during the subsequent wash step.

In the second stage, murine monoclonal antibody conjugated with Horseradish Peroxidase (Conjugate) is added to the test well. The Conjugate binds specifically to the antibody portion of the antigen-antibody complex. If complexes are not present, the unbound Conjugate is removed by the subsequent wash step.

In the third stage, an enzyme detection system composed of *o*-phenylenediamine (OPD) and hydrogen peroxide is added to the test well. If bound Conjugate is present, the OPD will be oxidized, resulting in a colored end product. Sulfuric acid is then added to stop the reaction. The color intensity depends on the amount of bound Conjugate and, therefore, is a function of the concentration of antibodies to *T. cruzi* present in the specimen. The intensity of color in the substrate solution is then determined with a microwell reader (spectrophotometer) designed to measure light absorbance in a microwell.

Special Instrumentation Requirements

There are no special ELISA instrument requirements for the device. All 510(k) performance testing was conducted using semi-automated instrumentation defined as:

- Ortho Summit Sample Handling System or
- Fixed or Adjustable Single-Channel Micropipette
- AutoWash 96 (multichannel aspirator-washer device)
- AutoReader IV (dual wavelength microwell reader)
- Model 120 Incubator
- Ortho Assay Software (OAS)
  (instrumentation process and data management software)
- Ortho *T. cruzi* CT (Clinical Trial) OAPD (Ortho Assay Protocol Disk)

The instructions for use call for:

- Adjustable multichannel micropipettes, or equivalent reagent dispenser capable of delivering 50 µL and 200 µL with at least ± 5% accuracy
- Fixed or adjustable single channel micropipettes or equivalent pipetter-dilutor capable of delivering 20 µL and 200 µL with at least ± 5% accuracy
- 50 µL to 300 µL disposable pipette tips or equivalent
- 20 µL disposable pipette tips or equivalent
- Appropriately sized serological pipette or graduated cylinder

- Multichannel micropipette reservoirs or equivalent containers
- OCD microwell plate or strip washer or equivalent multichannel microwell aspirator-washer device capable of at least 5 cycles of wash by dispensing and aspirating at least 700 µL of fluid per well and leaving a full well of fluid to soak at least 20 seconds.
- OCD microwell plate or strip reader or equivalent dual wavelength microwell reader capable of reading at 490 or 492 nm with a reference filter of 620 or 630 nm. A 610 nm filter is required for performing Sample Omission Monitoring (SOM) reads. Linearity of the microwell reader must range from at least 0 to 2.5 absorbance units.
- 37°C ± 1°C microwell incubator (dry)

Users are instructed, when using semi-automated and automated instruments, to follow the procedures that are contained in the operator's manual provided by the device manufacturer. Laboratories must follow their approved validation procedures to demonstrate compatibility of this product on semi-automated and automated systems.

6 Device Intended Use

ORTHO *T. cruzi* ELISA Test System is an enzyme-linked immunosorbent assay for the *in vitro* qualitative detection of antibodies (Immunoglobulin G) to *Trypanosoma cruzi (T. cruzi)* in human adult serum (glass, plastic, or serum separator tubes) and plasma (EDTA, lithium heparin or citrate) using whole-cell lysate antigens. Reactive assay results are presumptive evidence of past infection, and in conjunction with other serological and clinical information, may be used for the laboratory diagnosis of individuals with Chagas' disease.

Definitive diagnosis of an acute phase of infection (including acute congenital infection) must be made by alternate methods, e.g., hemoculture, blood smear.

This test is not intended for use on samples of cord blood or screening blood or plasma donors.

7 Comparison to Predicate Device

The ORTHO *T. cruzi* ELISA Test System is substantially equivalent to K930272 Hemagen Chagas' Kit (EIA Method) – Hemagen Diagnostics, Inc., and/or K023889 Enzyme Linked Immunosorbent Assay, *T. cruzi* – Wiener Laboratories and the *T. cruzi* indirect immunofluorescence assay, IFA, performed by Focus Diagnostics, Cypress, CA is the comparator method.

Comparison of the ORTHO *T. cruzi* ELISA Test System to the K930272 Hemagen Chagas' Kit (EIA Method) – Hemagen Diagnostics, Inc., and K023889 Enzyme Linked Immunosorbent Assay, *T. cruzi* – Wiener Laboratories

	New Device	Predicate Device	Predicate Device
Device Characteristic	ORTHO T. cruzi ELISA Test System	K930272 Hemagen Chagas' Kit (EIA Method) – Hemagen Diagnostics, Inc.	K023889 Enzyme Linked Immunosorbent Assay, *T. cruzi* – Wiener Laboratories
Intended Use	... for the *in vitro* qualitative detection of antibodies ((Immunoglobulin G) to *Trypanosoma cruzi (T. cruzi)*	... for the detection of circulating antibodies to *Trypanosoma cruzi*, the causative agent of Chagas' disease	Qualitative detection of antibody to *Trypanosoma cruzi*, the causative agent for Chagas' disease in human serum or plasma.
Indications for Use	Reactive assay results are presumptive evidence of past infection, and in conjunction with other serological and clinical information, may be used for the laboratory diagnosis of individuals with Chagas' disease.	When used according to instructions, the kit is useful in exhibiting prior exposure to T. cruzi and as an aid in the diagnosis of Chagas' disease.	When using according to instructions, the kit is useful in establishing prior exposure to *T. cruzi* and as an aid in the diagnosis of Chagas' disease.
Basic Principle	Enzyme-linked immunosorbent assay, ELISA	Enzyme-linked immunosorbent assay, ELISA	Enzyme-linked immunosorbent assay, ELISA
Where used	CLIA Certified Clinical Laboratory	CLIA Certified Clinical Laboratory	CLIA Certified Clinical Laboratory
Sample Type	Serum or Plasma (EDTA, lithium heparin or citrate)	Serum	Serum or Plasma (heparin, EDTA, and citrate based anticoagulants)
Antigen	Trypanosoma spp. (*T. cruzi* Tulahuen)	Trypanosoma spp.	Recombinant *T. cruzi* antigens from the trypomastigote parasite stage: #1, #2, #13, #30, and #36)
Antigen Prep	Whole cell lysate coated onto plastic microwells	Purified antigens from cultured *T. cruzi* organisms	Recombinant technology
Sample Volume	20 µL	10 µL	10 µL
Procedure	Diluted sample is incubated with the antigen prep. After an appropriate time the serum dilution in removed, and the antigen prep is washed. The antigen prep is overlaid with	Diluted sample is incubated with the antigen prep. After an appropriate time the serum dilution in removed, and the antigen prep is washed. The antigen prep is overlaid with	Diluted sample is incubated with the antigen prep. After an appropriate time the serum dilution in removed, and the antigen prep is washed. The antigen prep is overlaid with

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	New Device	Predicate Device	Predicate Device
	antibody labeled with an chromogenic substrate	antibody labeled with an chromogenic substrate	antibody labeled with an chromogenic substrate
Conjugate Antibody	Anti-human IgG	Anti-human IgG	Anti-human IgG
Tracer	Horseradish peroxidase with a Substrate Solution made from Substrate Buffer and OPD Tablets	Horseradish peroxidase with substrate 3, 3', 5, 5' – tetramethylbenzidine (TMB)	Horseradish peroxidase with substrate 3, 3', 5, 5' – tetramethylbenzidine (TMB)
Antibodies Detection	The antibody-HRP bound to the whole cell lysate-antibody complex reacts with the OPD producing a colored end product. The OD is read spectrophotometrically	The antibody-HRP bound to the whole cell lysate-antibody complex reacts with the TMB producing a colored end product. The OD is read spectrophotometrically	The antibody-HRP bound to the recombinant antigens-antibody complex reacts with the TMB producing a colored end product. The OD is read spectrophotometrically

Performance

ORTHO *T. cruzi* ELISA and *T. cruzi* IFA Results among High Risk and Low Risk Subjects

Specimens from 1074 subjects at high or low risk for *T. cruzi* infection were tested with a comparator *T. cruzi* IFA and with the ORTHO *T. cruzi* ELISA Test System. The results are presented in the following table.

ORTHO *T. cruzi* ELISA vs. *T. cruzi* IFA Results (N=1074)			
ORTHO *T. cruzi* ELISA Result	***T. cruzi* IFA Result**		**Total**
	Positive	**Negative**	
Repeatedly Reactive	82	16 [2]	98
Nonreactive	3 [1]	973	976
Total	85	989	1074

[1] These three specimens were also negative with the *T. cruzi* RIPA.
[2] Ten of these 16 specimens were also positive with the *T. cruzi* RIPA.

Percent Agreement

The table below summarizes the percent agreement between the ORTHO *T. cruzi* ELISA and the *T. cruzi* IFA. Data are listed by population and overall, with positive and negative percent agreement and 95% exact confidence intervals (CI).

Positive and Negative Percent Agreement of the ORTHO *T. cruzi* ELISA with the *T. cruzi* IFA by Study Population (N=1074)

Population	Positive Percent Agreement	95% Exact Confidence Interval	Negative Percent Agreement	95% Exact Confidence Interval
High Risk	96.47% (82/85)	90.03% - 99.27%	96.93% (474/489)	94.99% - 98.27%
Low Risk			100% (300/300)	98.78% - 100%
Pregnancy Low Risk			99.50% (199/200)	97.25% - 99.99%
Total	96.47% (82/85)	90.03% - 99.27%	98.38% (973/989)	97.39% - 99.07%

ORTHO *T. cruzi* ELISA Results and Most Probable *T. cruzi* Antibody Status among High Risk and Low Risk Subjects

Because the *T. cruzi* IFA is a non-reference standard for detection of antibodies to *T. cruzi*, the most probable *T. cruzi* antibody status of the high and low risk study subjects was determined by ORTHO *T. cruzi* ELISA Test System, comparator *T. cruzi* IFA and supplemental *T. cruzi* RIPA testing according to a pre-specified testing algorithm. Specimens not tested with RIPA that were negative with both the ORTHO *T. cruzi* ELISA and the *T. cruzi* IFA were assigned a most probable *T. cruzi* antibody status of negative. Specimens tested with the RIPA were assigned a most probable *T. cruzi* antibody status of positive, negative or indeterminate based on the RIPA results.

A comparison of the ORTHO *T. cruzi* ELISA results to most probable *T. cruzi* antibody status is presented in the following table.

ORTHO *T. cruzi* ELISA Results and Most Probable *T. cruzi* Antibody Status in the High Risk and Low Risk Populations (N=1074)

ORTHO *T. cruzi* ELISA Results	Most Probable *T. cruzi* Antibody Status			
	Positive	Negative	Indeterminate[1]	TOTAL
Repeatedly Reactive	92	6	0	98
Nonreactive	1	975	0	976
TOTAL	93	981	0	1074

[1] There were no *T. cruzi* RIPA indeterminate results and therefore no specimens with a most probable *T. cruzi* antibody status of indeterminate among the high and low risk specimens.

Percent Agreement

The table below summarizes the percent agreement between the ORTHO *T. cruzi* ELISA and most probable *T. cruzi* antibody status. Data are listed by population and overall, with positive and negative percent agreement and 95% exact confidence intervals.

Positive and Negative Percent Agreement of the ORTHO *T. cruzi* ELISA with Most Probable *T. cruzi* Antibody Status by High Risk and Low Risk Study Population (N=1074)				
Population	**Positive Percent Agreement**	**95% Exact Confidence Interval**	**Negative Percent Agreement**	**95% Exact Confidence Interval**
High Risk	98.92% (92/93)	94.15% - 99.97%	98.96% (476/481)	97.59% - 99.66%
Low Risk			100% (300/300)	98.78% - 100%
Pregnancy Low Risk			99.50% (199/200)	97.25% - 99.99%
Total	98.92% (92/93)	94.15% - 99.97%	99.39% (975/981)	98.67% - 99.78%

Specimens Presumed Positive for Antibodies to *T. cruzi* by Serological Methods
ORTHO *T. cruzi* ELISA versus *T. cruzi* IFA

A total of 810 specimens were included in the *T. cruzi* serological presumed positive population based upon two positive serological tests for *T. cruzi* antibodies in use in the countries of origin (i.e., ELISA, IFA, hemagglutination, or complement fixation). The comparator *T. cruzi* IFA was not used to admit specimens to the study. The specimens were obtained from the endemic countries of Bolivia (17.8%), Brazil (24.7%), Chile (10.6%), Guatemala (2.2%), Mexico (32.5%) and Nicaragua (12.2%). ORTHO *T. cruzi* ELISA testing was performed at two testing sites in Camp Hill, PA and Newark, NJ. Direct comparison of the ORTHO *T. cruzi* ELISA with the *T. cruzi* IFA is presented in the following table.

ORTHO *T. cruzi* ELISA vs. *T. cruzi* IFA Results in Specimens Presumed Positive by Serologic Methods (N=810)			
ORTHO *T. cruzi* ELISA Result	***T. cruzi* IFA Result**		**Total**
	Positive	**Negative**	
Repeatedly Reactive	565	99 [2]	664
Nonreactive	5 [1]	141 [3]	146
Total	570	240	810

[1] These five specimens were also negative with the *T. cruzi* RIPA.
[2] Ninety-seven of these 99 specimens were also positive with the *T. cruzi* RIPA.
[3] All 141 specimens were negative with the *T. cruzi* RIPA.

Percent Agreement

Positive, negative and overall percent agreement of the ORTHO *T. cruzi* ELISA with the *T. cruzi* IFA and 95% exact confidence intervals are shown in the following table.

Positive, Negative and Overall Percent Agreement of the ORTHO *T. cruzi* ELISA with the *T. cruzi* IFA in the Serological Presumed Positive Population (N=810)

Population	Positive Percent Agreement	95% Exact Confidence Interval	Negative Percent Agreement	95% Exact Confidence Interval	Overall Percent Agreement	95% Exact Confidence Interval
Serological Presumed Positive	99.13% (565/570)	97.96% - 99.71%	58.75% (141/240)	52.24% - 65.04%	87.16% (706/810)	84.66% - 89.39%

ORTHO *T. cruzi* ELISA versus Most Probable *T. cruzi* Antibody Status

Because the *T. cruzi* IFA is a non-reference standard for detection of antibodies to *T. cruzi*, the most probable *T. cruzi* antibody status of the study subjects presumed positive by serologic methods was determined by ORTHO *T. cruzi* ELISA Test System, comparator *T. cruzi* IFA and supplemental *T. cruzi* RIPA testing according to a pre-specified testing and interpretation algorithm. Specimens that were ORTHO *T. cruzi* ELISA repeatedly reactive and positive with the *T. cruzi* IFA were assigned a most probable *T. cruzi* antibody status of positive and were not tested with the *T. cruzi* RIPA. All specimens negative with both assays or with discordant results between the two assays were tested with the *T. cruzi* RIPA and assigned a most probable *T. cruzi* antibody status based upon the RIPA results. A comparison of ORTHO *T. cruzi* ELISA results and most probable *T. cruzi* antibody status is presented in the following table

ORTHO *T. cruzi* ELISA Results and Most Probable *T. cruzi* Antibody Status in the Serological Presumed Positive Population (N=810)

ORTHO *T. cruzi* ELISA Results	Most Probable *T. cruzi* Antibody Status			TOTAL
	Positive	Negative	Indeterminate[1]	
Repeatedly Reactive	662	2	0	**664**
Nonreactive	0	146	0	**146**
TOTAL	**662**	**148**	**0**	**810**

[1] There were no *T. cruzi* RIPA indeterminate results and therefore no specimens with a most probable *T. cruzi* antibody status of indeterminate among the serological presumed positive specimens tested with RIPA.

Percent Agreement

Positive, negative and overall percent agreement of the ORTHO *T. cruzi* ELISA with most probable *T. cruzi* antibody status and 95% exact confidence intervals are shown in the following table.

Positive, Negative and Overall Percent Agreement of the ORTHO *T. cruzi* ELISA with Most Probable *T. cruzi* Antibody Status for the Serological Presumed Positive Population (N=810)

Population	Positive Percent Agreement	95% Exact Confidence Interval	Negative Percent Agreement	95% Exact Confidence Interval	Overall Percent Agreement	95% Exact Confidence Interval
Serological Presumed Positive	100% (662/662)	99.44% - 100%	98.65% (146/148)	95.20% - 99.84%	99.75% (808/810)	99.11% - 99.97%

8 Conclusions

The ORTHO *T. cruzi* ELISA Test System is substantially equivalent to K930272 Hemagen Chagas' Kit (EIA Method) - Hemagen Diagnostics, Inc., and/or K023889 Enzyme Linked Immunosorbent Assay, *T. cruzi* - Wiener Laboratories

The data presented in the Premarket notification provide a reasonable assurance the ORTHO *T. cruzi* ELISA Test System is safe and effective for the stated intended use and is substantially equivalent to the predicate device.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

Ortho-Clinical Diagnostics, Inc.
Laura C. Vellucci
1001 US Highway 202
Raritan, NJ 08869-0606

APR 15 2009

Re: k072732
Trade/Device Name: ORTHO® *T. cruzi* ELISA Test System
Regulation Number: 21 CFR 866.3870
Regulation Name: *Trypanosomma* spp. Serological reagents
Regulatory Class: Class I
Product Code: MIU
Dated: September 29, 2008
Received: October 1, 2008

Dear Ms. Vellucci:

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 either class II (Special Controls) or class III (PMA), 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); 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 Part 801), please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at 240-276-0450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding postmarket surveillance, please contact CDRH's Office of Surveillance and Biometric's (OSB's) Division of Postmarket Surveillance at 240-276-3474. For questions regarding the reporting of device adverse events (Medical Device Reporting (MDR)), please contact the Division of Surveillance Systems at 240-276-3464. 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 (240) 276-3150 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* Diagnostic Device
Evaluation and Safety
Center for Devices and
Radiological Health

Enclosure

510(k) Number (if known): K072732

Device Name: Trypanosoma cruzi (*T. cruzi*) Whole Cell Lysate Antigen, ORTHO® *T. cruzi* ELISA Test System

Indications for Use:

ORTHO *T. cruzi* ELISA Test System is an enzyme-linked immunosorbent assay for the *in vitro* qualitative detection of antibodies (Immunoglobulin G) to *Trypanosoma cruzi (T. cruzi)* in human adult serum (glass, plastic, or serum separator tubes) and plasma (EDTA, lithium heparin or citrate) using whole-cell lysate antigens. Reactive assay results are presumptive evidence of past infection, and in conjunction with other serological and clinical information, may be used for the laboratory diagnosis of individuals with Chagas' disease.

Definitive diagnosis of an acute phase of infection (including acute congenital infection) must be made by alternate methods, e.g., hemoculture, blood smear.

This test is not intended for use on samples of cord blood or screening blood or plasma donors.

Prescription Use ___x_____ AND/OR Over -The-Counter Use _____
(Per 21 CFR 801 Subpart D) (21 CFR 801 Subpart C)

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

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

Division Sign-Off

Office of In Vitro Diagnostic
Device Evaluation and Safety
April 9, 2009

510(k) K072732