510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:

K120001

B. Purpose for Submission:

To obtain a substantial equivalence determination for a new device

C. Measurand:

Giardia lamblia antigens

D. Type of Test:

Lateral flow immunoassay

E. Applicant:

Trinity Biotech

F. Proprietary and Established Names:

UniGold™ Giardia

G. Regulatory Information:

1. Regulation section:

   21 CFR 866.3220 *Entamoeba histolytica* serological reagents

2. Classification:

   Class II

3. Product code:

   MHI - *Giardia spp.*

4. Panel:

   83 Microbiology

H. Intended Use:

1. Intended use(s):

   Trinity Biotech Uni-Gold™ Giardia is a single use rapid immunoassay for the qualitative detection of *Giardia lamblia (G. lamblia)* antigens in human stool specimens. This test is intended for use with patients with gastrointestinal symptoms as an aid in the diagnosis of suspected *Giardia* gastrointestinal infections. As with other *Giardia* tests, results should be considered in conjunction with the clinical evaluation and medical history. For In-Vitro Diagnostic use.

2. Indication(s) for use:

   Trinity Biotech Uni-Gold™ Giardia is a single use rapid immunoassay for the qualitative detection of *Giardia lamblia (G. lamblia)* antigens in human stool specimens. This test is intended for use with patients with gastrointestinal symptoms as an aid in the diagnosis of suspected *Giardia* gastrointestinal infections. As with other *Giardia* tests, results should be considered in conjunction with the clinical evaluation and medical history. For In-Vitro Diagnostic use.

3. Special conditions for use statement(s):

   For prescription use only

4. Special instrument requirements:

   Not applicable

I. Device Description:

The Trinity Biotech Uni-Gold™ Giardia test strip (5mm x 60mm) combines a nitrocellulose membrane with designated fiber pads (conjugate, sample and absorbent). The test strip is placed into a plastic housing and is sealed constituting the Test Device. The test strip consists of A) Mouse anti-*Giardia lamblia* antibody coated onto the Test Line region, B) Rabbit anti-goat IgG antibody coated onto the Control Line region, C) Goat anti-*Giardia lamblia* antibodies and Goat IgG antibodies conjugated to red latex particles and dried onto the inert glass fiber conjugate pad which is positioned on the test strip below the nitrocellulose zone. The housing contains a window where the diluted stool sample is added (Sample Well) and a window above where the results are read in 15 minutes.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Remel Xpect® Giardia Lateral Flow Assay

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

K031942

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
	Trinity Biotech UniGold™ Giardia	Remel Xpect™ Giardia Lateral Flow Assay
Intended Use	Detection of *Giardia lamblia* antigens in human stool specimens	Detection of *Giardia* antigens in preserved and unpreserved fecal specimens
Technology	Qualitative immunochromatographic assay	Qualitative immunochromatographic assay
Specimen Type	Human stool samples, unpreserved: fresh/frozen, preserved: 10% formalin, SAF, or Cary-Blair Transport Medium	Human stool samples, unpreserved: fresh/frozen, preserved: 10% formalin, SAF, or Cary-Blair Transport Medium
Reading Method	Visual	Visual
Test time	15 minutes	15 minutes

Differences		
Item	Device	Predicate
	Trinity Biotech UniGold™ Giardia	Remel Xpect™ Giardia Lateral Flow Assay
Conjugate antibodies	Goat anti-Giardia, Goat IgG antibodies	Mouse anti-Giardia monoclonal, Normal Mouse IgG antibodies
Conjugate material	Red latex conjugated antibodies dried on a conjugate pad.	Dark blue polystyrene microparticles coated with antibodies and diluted in buffer.
Capture antibodies on membrane	Mouse anti-Giardia lamblia "Test Line"; Rabbit anti-Goat IgG "Control Line"	Rabbit anti-Giardia antibody "Test Line"; Goat anti-mouse IgG "Control Line"
Membrane material	Nitrocellulose	Mylar-backed nitrocellulose

Differences		
Item	Device	Predicate
Sample volume	100 µL	2 drops ~ 40-60 µL

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

CLSI M28-A2 Procedures for the Recovery and Identification of Parasites from the Intestinal Tract

L. Test Principle:

A buffered solution is added to a dilution tube followed by the addition of two drops of the stool specimen via a disposable pipette. This mixture is then dispensed in total into the sample well of the lateral flow cartridge device with a dropper pipette. The mixture migrates through a pad containing red latex microspheres that have been coated with an antibody specific for the Giardia antigen.

When Giardia antigens are present in the sample they combine with the antibody/red latex conjugate. As this complex migrates it binds to the antibodies in the test region of the device forming a visible pink/red band.

Excess red latex conjugate forms a second pink/red band in the control region of the device. The control line should always appear as a visible pink/red band in the control region of the device to indicate that the test device is functioning correctly.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Reproducibility was assessed at three sites using a blind coded sample panel with varying amounts of *Giardia* cysts spiked into negative human stool matrix. The panel consisted of two low positive, two high positive, and two negative samples. The panels were tested in two runs at each site by two operators each day for five days. Each site ran positive and negative controls for each day of testing. Reproducibility was 100%.

Additional in-house studies were conducted to demonstrate performance near the assay cutoff and to demonstrate repeatability across lots. A panel of low positive, moderate positive, and high negative samples were tested in quadruplicate in two runs by two operators each day for five days. Repeatability in this study was 100%. Lot-to-lot repeatability across three lots was evaluated with a panel of ten positive and ten negative samples, and also with a panel of five positive and two negative samples run in triplicate. Lot-to-lot repeatability was 100%. The reproducibility and repeatability study

results are acceptable.

b. *Linearity/assay reportable range:*

Not applicable

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

Controls:
Good Laboratory Practice recommends the use of control specimens to ensure proper device performance at least once daily. Uni-Gold™ Giardia Controls are available separately for use only with Uni-Gold™ Giardia. These controls are used to verify correct device performance, operator procedure and result interpretation. The positive control will produce a reactive test result and the negative control will produce a non-reactive test result as described in the package insert.

It is recommended that positive and negative controls are run

- By all new operators performing testing on patient specimens
- With each new kit lot and whenever a new shipment of test kits is received
- At periodic intervals as specified in the laboratory Quality Assurance program

Uni-Gold™ Giardia Controls must give the expected reactive or non-reactive results; otherwise the test results are not valid and the test must be repeated.

Sample stability:
Giardia cysts were spiked into human stool samples in the following fixative and transport medium types: 10% formalin, SAF, Cary Blair, C&S, or fresh (unpreserved). Negative samples were also prepared in each medium type. The samples were stored under different temperature conditions as described below and tested at various time points during storage. All samples produced the expected positive or negative results. The data supports the following sample storage parameters:

Fresh stool	48 hours at 2-8°C
Frozen Stool	2 months at -20°C
Cary Blair or C&S transport media	7 days at 2-8°C
Cary Blair or C&S transport media	2 months at -20°C
10% formalin or SAF fixed stool	2 months at 2-30°C

A multiple freeze/thaw study was also conducted with negative and positive spiked fresh stool samples. All samples produced the expected results in the study. Multiple freeze/thaw cycles should be avoided.

High-dose hook effect:

High levels of *Giardia* cysts were spiked into negative human stool matrix, serially diluted, and then tested. High cyst concentrations produced the expected positive results in the Uni-Gold Giardia and did not produce a high-dose hook effect.

d. Detection limit:

The limit of detection was determined by spiking purified *Giardia* cysts quantified by DFA microscopy into negative human stool samples. The samples were serially diluted and three replicates from each dilution were tested with the Uni-Gold Giardia to determine the concentration that produced a positive result 95% of the time. A limit of detection concentration of 254 cysts/mL was confirmed by testing an additional 20 replicates.

e. Analytical specificity:

Cross reactivity:
No cross reactivity was observed with samples containing the following microorganisms:

Adenovirus serotype 3	Coronavirus OC43	*Iodamoeba butschlii*
Adenovirus serotype 5	Coxsackievirus	*Isospora sp.*
Adenovirus serotype 7	*Cryptosporidium parvum*	*Klebsiella pneumoniae*
Adenovirus serotype 41	*Cyclspora cayetanensis*	*Microsporidia*
Adenovirus serotype 40	*Cytomegalovirus (CMV)*	*Salmonella typhimurium*
Aeromonas hydrophila	*Dientamoeba fragilis*	*Shigella dysenteriae*
Ascaris lumbricoides	*Diphyllobothrium latum*	*Shigella flexneri*
Bacteroides fragilis	Echovirus 20	*Shigella sonnei*
Bacillus cereus	*Endolimax nana*	*Staphylococcus aureus*
Bacillus subtilis	*Entamoeba coli*	*S. aureus (Cowan's)*
Blastocystis hominis	*Entamoeba hartmanni*	*Staphylococcus epidermidis*
Campylobacter coli	*Entamoeba histolytica*	*Strongyloides stercoralis*
Campylobacter fetus	*Enterobius vermincularis*	*Taenia sp.*
Campylobacter jejuni	*Enterococcus faecalis*	*Trichurius trichiura*
Candida albicans	*Escherichia coli*	*Vibrio parahaemolyticus*
Chilomastix mesnili	*Escherichia coli 0157H7*	*Yersinia enterocolitica*
Clostridium difficile	*Hookworm*	
C. biffermentans	*Hymenolepis nana*	

Cross reactivity to *E. dispar* was not evaluated.

Cross reactivity study results are acceptable.

Interference study:
The following substances did not interfere with positive or negative results when tested in spiked human stool samples at the following concentrations:

Human blood (20% v/v), Mucin (10% w/v), Stool fat (Triglycerides 0.14mg/ml or Stearic Acid 20% v/v), Pepto-Bismol (Bismuth) (20% v/v), Imodium A-D (Loperamide HCl) (20% v/v), Kaopectate (Attapugite) (20%

v/v), Vancomycin (0.6mg/ml), K-Y jelly (0.289mg/ml), Vasoline (0.22mg/ml), Condom lubricant (1.716mg/ml), Maalox (magnesium hydroxide, calcium carbonate) (20% v/v), Tagamet (Cimetidine) ($2.0x10^{-2}$ mg/ml), Pepsid (Famotidine) ($6.0x10^{-4}$ mg/ml), Zantac (Ranitidine) ($6.0x10^{-3}$ mg/ml), Prilosec (Omeprazole) ($6.0x10^{-3}$ mg/ml), Nitrazoxanide ($6.96x10^{-3}$ mg/ml), Atovaquone (0.031mg/ml), Azithromycin ($1.2x10^{-2}$ mg/ml), Metronidazole (0.12mg/ml), Paromomycin (0.42mg/ml), Trimethoprim-sulfamethoxazole (TRM 0.04mg/ml & Sulf 0.4mg/ml).

Interference study results are acceptable.

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

The Uni-Gold Giardia was compared to a commercially available lateral flow test on 267 retrospective stool samples in the following stool matrix types: unpreserved frozen (42), C&S (15), SAF (139), and formalin (71). The percent agreement of the Uni-Gold Giardia versus the comparator device was as follows:

Site 1		Comparator Device	
		+	-
Uni-Gold Giardia	+	26	3*
	-	0	48

PPA: 100% (26/26)
NPA: 94.1% (48/51)

Site 2		Comparator Device	
		+	-
Uni-Gold Giardia	+	51	0
	-	0	49

PPA: 100% (51/51)
NPA: 100% (49/49)

Site 3		Comparator Device	
		+	-

Uni-Gold Giardia	+	54	6**
	-	0	30

PPA: 100% (54/54)
NPA: 83.3% (30/36)

*At Site 1, the three samples that tested positive on Uni-Gold Giardia and negative on the comparator device were positive by DFA microscopy in agreement with the Uni-Gold Giardia result.
**At Site 3, the six samples that tested positive on Uni-Gold Giardia and negative on the comparator device were positive by Iron Hematoxylin stain microscopy in agreement with the Uni-Gold Giardia result.

b. Matrix comparison:

See sample stability results in section M1c above.

3. Clinical studies:

The clinical performance of the Uni-Gold Giardia was evaluated on 567 retrospective stool samples at three external laboratories and on 378 prospective stool samples at a fourth external laboratory.

a. Clinical Sensitivity:

Retrospective study:
The sensitivity and specificity of the test was compared to DFA microscopy with retrospective samples at sites 1 and 2 as shown in the following tables:

Site 1		DFA Microscopy	
		+	-
Uni-Gold Giardia	+	37	0
	-	0	117

Site 2		DFA Microscopy	
		+	-
Uni-Gold Giardia	+	54	0
	-	0	33

Total		DFA Microscopy	
		+	-
Uni-Gold Giardia	+	91	0
	-	0	150

Sensitivity: 100% (91/91), 95% CI 95 – 100%
Specificity: 100% (150/150), 95% CI 97 – 100%

The positive samples were tested in the following matrix types: formalin (48), SAF (13), unpreserved frozen (17), Cary Blair (3), and C&S (10). The negative samples were tested in the following matrix types: formalin (42), SAF (70), unpreserved frozen (25), Cary Blair (3), and C&S (10)

Additional retrospective studies
Performance of the test was compared to non-fluorescent microscopy (staining) at two external laboratories. At site 2, 67 retrospective samples were evaluated and demonstrated a Positive Percent Agreement (PPA) of 100% (22/22) and a Negative Percent Agreement (NPA) of 100% (45/45) versus Wheatley's Stain. At site 3, 259 retrospective samples were evaluated and demonstrated a PPA of 100% (60/60) and a NPA of 100% (199/199) versus Iron Hematoxylin Stain.

Prospective study
Test performance was compared against DFA microscopy at site 4 with 378 prospective samples in the following stool sample types: fresh (153), frozen (45), 10% formalin (45), SAF (45), C&S (45), and Cary Blair (45). Due to infection prevalence, no positive samples were encountered during this study.

Site 4		DFA Microscopy	
		+	-
Uni-Gold Giardia	+	0	0
	-	0	378

Specificity: 100% (378/378) 95% CI 99 – 100%

b. Clinical specificity:

See section M3a.

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

Not applicable

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

The performance of the Uni-Gold Giardia Test Kit was evaluated at four external

laboratories. Samples were collected from Hospitals throughout the US and Canada and consisted of both male and female patients, of all ages from pediatric to adult, who presented with gastrointestinal symptoms. The retrospective study included 173 positive samples and 394 negative samples confirmed by microscopy. The prospective study included 378 samples which were subsequently confirmed negative by microscopy. There were no differences observed in clinical performance between males or females, or between pediatric or adult populations.

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.