

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
DEVICE ONLY TEMPLATE**

A. 510(k) Number:

K031834

B. Analyte:

Giardia and Cryptosporidium antigens

C. Type of Test:

Chromatographic immunoassay

D. Applicant:

Remel Inc.

E. Proprietary and Established Names:

Xpect™ Giardia/Cryptosporidium Lateral Flow Assay

F. Regulatory Information:

1. Regulation section:
21 CFR Part 866.3220 Entamoeba histolytica serological reagents
2. Classification:
Class II
3. Product Code:
MHI – Giardia spp.
MHJ – Cryptosporidium spp.
4. Panel:
83 (Microbiology)

G. Intended Use:

1. Intended use(s):
Xpect Giardia/Cryptosporidium kit is an *in vitro* qualitative immunoassay for the detection of Giardia and Cryptosporidium antigens in preserved and unpreserved fecal specimens. This test is intended as an aid in the laboratory diagnosis of suspected Giardia and Cryptosporidium infections.
2. Indication(s) for use:
Xpect Giardia/Cryptosporidium kit is an *in vitro* qualitative immunoassay for the detection of Giardia and Cryptosporidium antigens in preserved and unpreserved fecal specimens. This test is intended as an aid in the laboratory diagnosis of suspected Giardia and Cryptosporidium infection
3. Special condition for use statement(s):
Not applicable
4. Special instrument Requirements:
Not applicable

H. Device Description:

The kit contains 20 test devices consisting of a membrane striped with rabbit anti-Giardia, rabbit anti-Cryptosporidium, and goat anti-mouse IgG; conjugate consisting of dark-blue microparticles coated with anti-Giardia MAb, red microparticles coated with anti-Cryptosporidium MAb and dark blue microparticles coated with mouse

IgG; specimen dilution buffer; a procedure card; disposable transfer pipettes, dilution tubes and instructions for use.

I. Substantial Equivalence Information:

1. Predicate device name(s):
BD ColorPAC Giardia/Crypto Rapid Assay
2. Predicate K number(s):
K 983399
3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	Detection of Giardia and Cryptosporidium antigens in fecal specimens	Detection of Giardia and Cryptosporidium antigens in fecal specimens
Technology	Qualitative immunochromatographic assay	Qualitative immunochromatographic assay
Antibodies:conjugate	Monoclonal anti-Giardia and Cryptosporidium	Rabbit anti-Giardia, monoclonal anti-giardia and Cryptosporidium
Specimen type	Human stool preserved in 10% formalin, SAF, MIF or Cary Blair	Human stool preserved in 10% formalin, SAF, MIF, or Cary Blair
Differences		
Item	Device	Predicate
Capture antibodies or molecules	Rabbit anti-Giardia, rabbit anti-Cryptosporidium, goat anti-mouse IgG	Mouse anti-Cryptosporidium, goat anti-mouse IgG, avidin derivative
Material: membrane	Mylar-backed nitrocellulose	Nitrocellulose
Material: conjugate	Anti-Giardia, anti-mouse and anti-Cryptosporidium colored polystyrene particles diluted in buffer	Colloidal dye labeled monoclonal antibodies to Giardia and Cryptosporidium
Sample volume	100µl	50µl

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

Not applicable

K. Test Principle:

The Xpect™ Giardia/Cryptosporidium Lateral Flow Assay is a chromatographic immunoassay that detects the presence of *Giardia* and *Cryptosporidium* antigens. The test utilizes sample wicking to capture *Giardia* and *Cryptosporidium* antigens on discrete test lines containing antigen-specific antibodies for each organism. A specimen is added to a dilution tube containing a buffered solution. A conjugate

containing colored micro-particles linked to monoclonal antibodies specific for *Giardia* and *Cryptosporidium* is added. The mixture is dispensed into the sample well of the device and wicks across a membrane containing capture antibody strips. The *Giardia/Cryptosporidium* immune complexes if present react with anti-*Giardia* antibody and/or anti-*Cryptosporidium* antibody at the test line. Conjugates not bound at the test lines are later captured at the control line containing anti-mouse antibody. A blue line will appear at the *Giardia* test position if *Giardia* antigen is present and a pink line will appear at the *Cryptosporidium* test position if *Cryptosporidium* antigen is present. A line in the Control position indicates that the test is working properly.

L. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Reproducibility testing was conducted at seven sites, including one in-house site, on three separate days with ten blinded samples of varying activity. All samples tested for *Cryptosporidium* and *Giardia* produced the expected result.

b. Linearity/assay reportable range:

Not applicable

c. Traceability (controls, calibrators, or method):

Not applicable

d. Detection limit:

For *Giardia*, detection limit was 1 organism per 0.1 ml. of specimen
For *Cryptosporidium*, detection limit was 6 organisms per 0.1 ml. of specimen

e. Analytical specificity:

Cross-reactivity:

No cross-reactivity was observed using samples containing the following organisms: *Ascaris lumbricoides*, *Blastocystis hominis*, *Campylobacter coli*, *Campylobacter jejuni*, *Candida albicans*, *Chilomastix mesnili*, *Cyclospora cayetanensis*, *Dientamoeba fragilis*, *Endolimax nana*, *Entamoeba coli*, *Entamoeba hartmanni*, *Entamoeba histolytica*, *Enterobius vermicularis*, *Escherichia coli*, hookworm, *Hymenolepis nana*, *Iodamoeba bütschlii*, *Isospora* sp., *Microsporidia*, Rotavirus, *Salmonella choleraesuis* subsp. *choleraesuis* serotype *Typhimurium*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Strongyloides stercoralis*, *Taenia* sp., and *Trichuris trichiura*. There was no cross-reactivity of *Giardia lamblia* in the *Cryptosporidium* test area or of *Cryptosporidium parvum* in the *Giardia* test area. Cross-reactivity to Astrovirus and Caliciviruses has not been established.

Interfering Substances:

Prior to testing, positive and negative samples were spiked (20% v/v) with blood, mucin, fecal fat or the following over-the-counter anti-diarrheal products: Pepto-Bismol[®], Imodium[®] A-D, and Kaopectate[®] (active ingredients: bismuth subsalicylate, loperamide HCl, and attapugite respectively). Testing indicated

that none of these substances interfered with the expected result except for Imodium[®] A-D. Imodium[®] A-D at 20% (v/v) in stool interfered with the detection of low levels of Cryptosporidium antigen

f. Assay cut-off:

The assay can detect 1 Giardia organism per 0.1ml of specimen and 6 Cryptosporidium organisms per 0.1 ml of specimen. Clinically relevant detection limits were determined using true clinical specimens diluted to an end point titration with the Xpect Giardia Cryptosporidium test. Sequential serial dilutions were tested until an endpoint dilution was reached. The endpoint dilution was defined as one dilution above where the sample became negative. The quantity of organisms detected at the titration endpoint in each specimen was calculated from the numbers seen microscopically in a 10 µl sample using DFA.

2. Comparison studies:

a. Method comparison with predicate device:

Percent Agreement: Xpect™ & Predicate Device vs. Microscopy:

The Xpect™ Giardia/Cryptosporidium and a commercially available lateral flow test (the “Predicate Device”) were compared side-by-side to microscopy. The Percent Agreement of each assay versus microscopy was as follows:

<i>Giardia</i>		Microscopy		
		+	-	
<u>Xpect™</u>	+	19	5	Agreement
	-	2	120	
Total		21	125	95.2% (139/146)

<u>Predicate</u>		+	-	Agreement
		19	7	
2	118			
Total		21	125	93.8% (137/146)

<i>Cryptosporidium</i>		Microscopy		
		+	-	
<u>Xpect™</u>	+	28	5	Agreement
	-	2	111	
Total		30	116	95.2% (139/146)

<u>Predicate</u>	+	29	21	Agreement
	-	1	95	
Total		30	116	84.9% (124/146)

b. *Matrix comparison:*

Not applicable

3. Clinical studies:

a. *Clinical sensitivity:*

Sensitivity and Specificity Compared to Microscopy:

The performance of the Xpect™ Giardia/Cryptosporidium was evaluated at six geographically diverse laboratories. The overall sensitivity and specificity of the test was compared to microscopy using 577 specimens. Samples tested were samples routinely submitted for microscopic exam. Performance relative to patients' clinical status has not been established. Data is listed below.

		Microscopy	
		+	-
Xpect™	+	92	7
	-	4	474
Total		96	481

Sensitivity: 95.8% (92/96); 95% CI = 89.8-98.4%

Specificity: 98.5% (474/481); 95% CI = 97.0-99.3%

		Microscopy	
		+	-
Xpect™	+	108	7
	-	4	458
Total		112	465

Sensitivity: 96.4% (108/112); 95% CI = 91.2-98.6%

Specificity: 98.5% (458/465); 95% CI = 96.9-99.3%

b. Clinical specificity:

Refer to (a) above

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

Not applicable

4. Clinical cut-off:

See assay cut off above

5. Expected values/Reference range:

Expected values were established from literature. Worldwide, Giardia is the most commonly identified parasite in stool specimens with a prevalence rate of 2-5%. Incidence of giardiasis is higher in children than in adults. In the USA, the asymptomatic carriage rate of Giardia is estimated to be 3-7%. Rates tend to be higher in southern USA regions and in children younger than 36 months who attend daycare centers.

Prevalence rates for Cryptosporidium range from 1-3% in North America and Europe to 7-9% in less developed countries. Rates tend to be higher in children under 2 years and in persons with weakened immune systems.

M. Conclusion:

In clinical settings, the Xpect™ Giardia/Cryptosporidium Lateral Flow Assay is substantially equivalent in performance to the predicate device and to microscopic examination for the identification of Giardia or Cryptosporidium in fecal specimens.