NOV 15 2004

K041951

510(k) SUMMARY

Contact Information: **Mary Ann Silvius**
Director, Business & Product Development
Remel Inc.
12076 Santa Fe Drive
Lenexa, KS 66215
Phone: (913) 895-4054
Fax: (913) 895-4054
email: msilvius@remel.com

Date Prepared: July 16, 2004

Device Trade Name: Xpect™ Clostridium difficile Toxin A/B

Predicate Device: BD ColorPAC™ Toxin A

Device Classification: 21 CFR 866.2660; Microorganism differentiation and identification device; reagents, *Clostridium difficile* toxin.

Intended Use: REMEL's Xpect™ Clostridium difficile Toxin A/B is a rapid *in vitro* immunochromatographic test for the direct, qualitative detection of *Clostridium difficile* Toxin A and/or B in human fecal specimens from patients suspected of having *Clostridium difficile*-associated disease (CDAD). The test is intended for use as an aid in diagnosis of CDAD. The test can also be used for confirmation of toxigenic *Clostridium difficile* from Brain Heart Infusion (BHI) broth culture.

Device Description: The Xpect™ Clostridium difficile Toxin A/B test is a qualitative immunochromatographic assay that detects *C. difficile* Toxin A and Toxin B in stool specimens or cultures of toxigenic *C. difficile*. In performing the test, a specimen is first diluted with Specimen Diluent to help solubilize the toxins. A portion of the diluted sample is then mixed with a volume of Conjugate 1 containing antibodies to Toxin A and Toxin B coupled to colored microparticles, plus a volume of Conjugate 2 containing biotinylated antibodies to Toxin A and Toxin B. A volume of this mixture is transferred to a test device having immobilized streptavidin as a test line and goat anti-immunoglobulin antibody as a control line. Immunocomplexes of toxin and conjugated antibodies form a visible band as they flow across the test line. Excess colored particle conjugates form a visible band at the control line to document that the test is functioning properly.

Device Comparison:

Characteristic	ColorPAC™ Toxin A	Xpect™ C. difficile Toxin A/B
Intended Use	ColorPAC™ Toxin A is a rapid chromatographic assay for the qualitative detection of *Clostridium difficile* Toxin A (enterotoxin) in stool specimens from patients suspected of having *C. difficile*-associated disease. The test can also be used for confirmation of suspect colonies of toxigenic *C. difficile* from agar plates or BHI Broth. This assay is intended for use as an aid in the diagnosis of *C. difficile*-associated disease.	REMEL's Xpect™ Clostridium difficile A/B test kit is a rapid *in vitro* immunochromatographic test for the direct, qualitative detection of Clostridium difficile Toxin A and/or B in human fecal specimens from patients suspected of having *Clostridium difficile*-associated disease (CDAD). The test is intended for use as an aid in diagnosis of CDAD. The test can also be used for confirmation of toxigenic *Clostridium difficile* from Brain Heart Infusion (BHI) broth culture.
Detection	Qualitative; Toxin A only detected.	Qualitative; Toxin A and Toxin B detected.
Technology	Chromatographic membrane assay	Immunochromatographic membrane assay
Specimen Type	Fecal specimens, colonies, BHI Broth	Fecal specimens, BHI Broth

Summary of Performance Data:

Clinical Accuracy:

The performance of the Xpect™ Clostridium difficile Toxin A/B was evaluated at four geographically diverse regions of the United States. A total of eight hundred fifteen specimens were tested with the Xpect™ Clostridium difficile Toxin A/B test and compared to results obtained from the cytotoxin assay (CTA).

Overall		CTA Results +	CTA Results -
Xpect™ Results	+	132	25
	-	21	637
	TOTAL	153	662

Sensitivity: 86.3% (95% CI = 79.8-91.3%)
Specificity: 96.2% (95% CI = 94.5-97.5%)
Positive Predictive Value: 84.1% (95% CI = 77.4-89.4%)
Negative Predictive Value: 96.8% (95% CI = 95.2=98.0%)
% Correlation: 94.4% (95% CI = 92.5-95.8%)

Note : CI = Confidence Interval

Discordant results were further investigated by toxigenic culture and microwell enzyme immunoassay that detects both Toxin A and B. Four of 25 specimens that were cytotoxin negative and Xpect™ Clostridium difficile Toxin A/B positive on initial testing were positive by toxigenic culture and enzyme immunoassay. Ten of 21 (47.6%) specimens that were CTA positive and Xpect™ Clostridium difficile Toxin A/B negative on initial testing were negative by toxigenic culture and microwell enzyme immunoassay.

Performance Compared to Commercially Available Devices:
The Xpect™ C. difficile Toxin A/B test was also compared to two commercially available products. Each of the four clinical trial sites tested a chromatographic membrane assay that detects Toxin A only (Predicate Device), the Xpect™ C. difficile Toxin A/B test, and cytotoxin assay (CTA) for each sample. In addition, one clinical trial site tested a microwell enzyme immunoassay for the detection of both Toxin A and B for each sample. The results presented below are calculated using CTA as the reference.

	n = 815		n = 267	
	Xpect™ C. difficile Toxin A/B	Predicate Device	Xpect™ C. difficile Toxin A/B	EIA
Sensitivity	86.3%	62.7%	91.0%	80.6%
Specificity	96.2%	98.8%	98.0%	97.5%
Agreement	94.4%	92.0%	96.3%	93.3%

BHI Broth Culture Performance:
An in-house study was conducted using twenty-one known reference strains and thirty-six suspect *Clostridium difficile* isolates from stool specimens. BHI broth cultures were tested with the Xpect™ Clostridium difficile Toxin A/B test following 72-hours incubation. Under these conditions, the BHI broth culture of *Clostridium sordellii* ATCC® 9714 produced a positive reaction. There was 94.7% (54/57) agreement with expected values.

Analytical Sensitivity:
The analytical sensitivity was evaluated using purified *C. difficile* Toxin A and Toxin B. Xpect™ C. difficile Toxin A/B assay detects Toxin A at levels of $\geq$ 6.25 ng/ml (0.12 ng/test device) and Toxin B at levels of $\geq$ 40.0 ng/ml (0.76 ng/test device).

Cross-Reactivity:
Fifty-four microorganisms were evaluated with the Xpect™ C. difficile Toxin A/B test. No cross-reactivity was observed. Bacteria and yeast isolates were tested at 10^8 colony-forming units per ml concentration. Viral isolates were tested at concentrations of 10^4 to 10^5 $TCID_{50}$ (tissue culture infectious dose) per ml concentration. The following organisms were tested in the Xpect™ C. difficile Toxin A/B test.

Aeromonas hydrophila
Bacillus cereus
Bacillus subtilis
Bacteroides fragilis
Campylobacter coli
Campylobacter fetus subsp. *fetus*
Campylobacter jejuni subsp. *jejuni*
Campylobacter lari
Candida albicans
Clostridium botulinum (toxin 20 µg/ml)
Clostridium beijerinickii
Clostridium difficile (non-toxigenic)
Proteus mirabilis
Proteus vulgaris
Pseudomonas aeruginosa
Salmonella Typhimurium
Serratia liquefaciens
Shigella boydii
Shigella dysenteriae
Shigella flexneri
Shigella sonnei
Staphylococcus aureus (Cowan)
Staphylococcus epidermidis

Clostridium haemolyticum
Clostridium histolyticum
Clostridium innocuum
Clostridium novyi
Clostridium perfringens
Clostridium septicum
Clostridium sordellii
Clostridium sporogenes
Clostridium subterminale
Clostridium tetani
Enterobacter aerogenes
Enterobacter cloacae
Enterococcus faecalis
Enterococcus faecium
Escherichia coli
Klebsiella pneumoniae
Peptostreptococcus anaerobius
Porphyromonas asaccharolytica
Vibrio cholerae
Vibrio parahaemolyticus
Yersinia enterocolitica
Giardia intestinalis
Entamoeba histolytica
Adenovirus type 2
Adenovirus type 40
Adenovirus type 41
Coxsackievirus B4
Cytomegalovirus
Echovirus (type 22)
Enterovirus (type 69)
Rotavirus

Interfering Substances:
The following substances were tested with the Xpect™ C. difficile Toxin A/B test and no interference was observed in the assay for any substance tested at the indicated levels: blood, mucous, fecal fat, Pepto-Bismol® (10%v/v), Imodium® AD (10%v/v), Kaopectate® (10%v/v), Castoria® (10%v/v), vancomycin (12.5 mg/ml), metronidazole (12.5 mg/ml), and barium sulfate (12.5 mg/ml).

Reproducibility:
Reproducibility testing was conducted at three sites, including one in-house site, on four separate days with six blinded samples. The samples consisted of known positive and negative stool specimens. The samples produced the expected result with the Xpect™ C. difficile Toxin A/B test 98.6% (71/72) of the time.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

NOV 15 2004

Ms. Mary Ann Silvius
Director. Business and Product Development
Remel Inc.
12076 Santa Fe Drive
Lenexa, KS 66215

Re: k041951
Trade/Device Name: Xpect™ Clostridium difficile Toxin A/B
Regulation Number: 21 CFR 866.2660
Regulation Name: Microorganism Differentiation and Identification Device
Regulatory Class: Class I
Product Code: LLH
Dated: October 19, 2004
Received: October 22, 2004

Dear Ms. Silvius:

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.

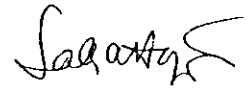
If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish 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 information about the application of labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety at (301) 594-3084. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). 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) 443-6597 or at its Internet address http://www.fda.gov/cdrh/dsma/dsmamain.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

INDICATIONS FOR USE

510(k) Number (if known): K041951

Device Name: Xpect™ Clostridium difficile Toxin A/B

Indications For Use: REMEL's Xpect™ Clostridium difficile Toxin A/B is a rapid *in vitro* immunochromatographic test for the direct, qualitative detection of *Clostridium difficile* Toxin A and/or B in human fecal specimens from patients suspected of having *Clostridium difficile*-associated disease (CDAD). The test is intended for use as an aid in diagnosis of CDAD. The test can also be used for confirmation of toxigenic *Clostridium difficile* from Brain Heart Infusion (BHI) broth culture.

Prescription Use X **AND/OR** **Over-The-Counter Use**
(Part 21 CFR 801 Subpart D) **(Part 21 CFR 801 Subpart C)**

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

Concurrence of CDRH, Office of Device Evaluation (ODE)

Freddie T. Poole

Division Sign-Off

Office of In Vitro Diagnostic Device Evaluation and Safety

510(k) K041951