510(k) Summary

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

The assigned 510(k) number is: **K033479**.

A. Contact:

David Teicher
Remel Inc. Ramsey Operations
14000 Unity Street NW
Ramsey, MN
Phone: (763) 712-2367
Fax: (763) 323-7858
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B. Date of Preparation: January 19, 2004

C. Name of Device and Classification

Name: ProSpecT® Clostridium difficile Toxin A/B Microplate Assay
Classification: 866.2660 Reagents, Clostridium difficile toxin, Class I, LLH

D. Predicate Devices

Meridian Premier Toxins A&B:	510(k) K993914
Wampole *C. difficile* TOX A/B II:	510(k) K003306/K971182

E. Device Description

The ProSpecT® Clostridium difficile Toxin A/B test detects the presence of Toxin A and Toxin B in clinical stool specimens through the use of specific antibodies. Microwell strips are coated with mouse monoclonal anti-Toxin A and rabbit anti-Toxin B antibodies. A stool specimen is diluted in Sample Diluent or used directly if pre-diluted in modified Cary-Blair medium. The sample is added to a microwell allowing the toxins, if present, to bind to the immobilized antibodies. After washing to remove unbound components, a conjugate reagent containing goat anti-Toxin A-HRP and rabbit anti-Toxin B-HRP is added to each well. Unbound conjugate is removed by washing and a chromagenic substrate solution is added to detect the presence of bound toxin. A stop reagent is added and the test results are read visually or spectrophotometrically. The presence of a yellow color indicates the presence of toxin.

F. Intended Use Statement

Remel's ProSpecT® Clostridium difficile Toxin A/B Microplate Assay is a qualitative enzyme immunoassay (EIA) for the detection of *C. difficile* Toxin A and B in human fecal specimens from patients suspected of having *Clostridium difficile* disease. The test is intended for use as an aid in diagnosis of *Clostridium difficile*-associated disease (CDAD).

G. Device Comparison

Product Feature	ProSpect®	Wampole	Merdian
Intended Use	Detection of *C. difficile* Toxins A and B in fecal specimens	Detection of *C. difficile* Toxins A and B in fecal specimens	Detection of *C. difficile* Toxins A and B in fecal specimens
Technology	Enzyme Immunoassay	Enzyme Immunoassay	Enzyme Immunoassay
Capture Antibodies or Molecules: Device	Mouse monoclonal anti-Toxin A and rabbit anti-Toxin B	Polyclonal goat antibody against Toxins A and B	Mouse monoclonal anti-Toxin A and polyclonal goat anti-Toxin B
Antibodies: Conjugate	Goat anti-Toxin A and rabbit anti-Toxin B	Toxin A monoclonal mouse antibody and Toxin B polyclonal goat antibody	Polyclonal goat anti-Toxin A and anti-Toxin B
Material: Device	Microwell	Microwell	Microwell
Material: Conjugate	Horseradish peroxidase conjugated to anti-toxins	Horseradish peroxidase conjugated to anti-toxins	Horseradish peroxidase conjugated to anti-toxins
Specimen Type	Fresh human stool specimens or specimens in modified Cary-Blair	Fresh human stool specimens	Fresh human stool specimens
Sample volume	200 µl	50 µl	50 µl

H. Summary of Performance Data

The performance of the ProSpecT® Clostridium difficile Toxin A/B Microplate Assay was evaluated in a clinical trial at three sites in the USA. The kit and predicate devices were compared to the cellular cytotoxicity assay (CTA).

Overall Performance:

Dual Wavelength (450/620-650 nm) Results:
Sensitivity: (149/165) x 100 = 90.3%; 95% CI = 84.7% - 94.4%
Specificity: (576/599) x 100 = 96.2%; 95% CI = 94.3% - 97.5%

		CTA Results	
		+	-
ProSpecT® EIA Results (Dual)	+	149	23
	-	16	576
Total		**165**	**599**

Visual Interpretation of Test:
Sensitivity: (85/100) x 100 = 85.0%; 95% CI = 76.5% - 91.4%
Specificity: (464/486) x 100 = 95.5%; 95% CI = 93.2% - 97.1%

		CTA Results	
		+	-
ProSpecT® EIA Visual Results	+	85	22
	-	15	464
Total		100	486

Percent Agreement: (580/586) x 100 = 99.0%

		ProSpecT® EIA Results OD 450/620-650	
		+	-
ProSpecT® EIA Visual Results	+	104	3
	-	3	476
Total		**107**	**479**

Comparison to Predicate Devices:

EIA	Performance versus CTA			
	Sensitivity		Specificity	
	#	%	#	%
ProSpecT®*	33/40	82.5	263/268	98.1
Predicate 1	33/40	82.5	260/268	97.0
ProSpecT®	115/124	92.7	302/320	94.3
Predicate 2	98/124	79.0	309/320	96.5

I. Reproducibility

Reproducibility testing was conducted at three sites on three separate days with four blinded samples. Each site tested eight replicate wells of each specimen on each day of testing (n=288). The specimens included one negative specimen and three positive specimens with varying levels of reactivity. The average intra-assay coefficient of variation (CV) for a mid-range sample was 7.7%. The average inter-assay CV for a mid-range sample was 18.9%.

J. Analytical Sensitivity

The ProSpecT® Clostridium difficile Toxin A/B Microplate Assay detects Toxin A at levels of $\geq$0.20 ng/ml and Toxin B at levels of $\geq$0.61 ng/ml.

K. Cross-Reactivity

Forty (40) microorganisms were evaluated with the ProSpecT® Clostridium difficile Toxin A/B Microplate Assay. Bacteria and yeast isolates were tested at $\geq 10^8$ colony-forming units per ml (cfu/ml). Viral isolates were tested at concentrations of 10^4 $TCID_{50}$/ml (tissue culture infectious dose per milliliter). No cross-reactivity was observed. There was no cross-reactivity observed with *Clostridium sordellii* ATCC® 9714. However, published literature indicates that certain strains of *C. sordellii* can produce toxins which may be cross-reactive with antibodies to *C. difficile* Toxins A and B. The following organisms were tested in the ProSpecT® Clostridium difficile Toxin A/B Microplate Assay.

Organism	ATCC® designation
Aeromonas hydrophila	35654
Bacillus cereus	11778
Bacillus subtilis	6633
Bacteriodes fragilis	25285
Campylobacter coli	33559
Campylobacter jejuni	33291
Candida albicans	10231

Organism	ATCC® designation
Clostridium beijerinckii (butyricum)	8260
Clostridium difficile (non-toxigenic)	700057
Clostridium haemolyticum	9650
Clostridium histolyticum	19401
Clostridium novyi (toxin A)	19402
Clostridium perfringens (Type A)	13124
Clostridium septicum	12464
Clostridium sordellii	9714
Clostridium sporogenes	19404
Clostridium tetani	19406
Enterobacter aerogenes	35028
Enterobacter cloacae	13047
Enterococcus faecalis	19433
Escherichia coli	11229
Klebsiella pneumoniae	13882
Peptostreptococcus anaerobius	27337
Porphyromonas asaccharolytica	25260
Proteus vulgaris	49132
Pseudomonas aeruginosa	27853
Salmonella choleraesuis (typhimurium)	23852
Serratia liquefaciens	27592
Shigella dysenteriae	11835
Shigella flexneri	12022
Shigella sonnei	25931
Staphylococcus aureus	25923
Staphylococcus aureus (Cowan)	12598
Staphylococcus epidermidis	12228
Vibrio cholerae	9459
Vibrio parahaemolyticus	17802
Yersinia enterocolitica	23715
Adenovirus type 40	VR-930
Adenovirus type 41	VR-931
Rotavirus (Complement fixation antigen)	

L. Interfering Substances

The following substances were tested with the ProSpecT® Clostridium difficile Toxin A/B Microplate Assay: Vancomycin (12.5 mg/ml), Metronidazole (12.5 mg/ml), blood, mucous, fecal fat, and the following over-the-counter anti-diarrheal products: Pepto-Bismol®, Imodium® A-D, and Kaopectate® (active ingredients: bismuth subsalicylate, loperamide HCl, and attapugite respectively). No interference with positive or negative specimens was observed.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

FEB 26 2004

Mr. David Teicher
Manager Quality Systems and Regulatory Affairs
Remel Inc.
Ramsey Operation
14000 Unity Street NW
Ramsey, MN 55303

Re: k033479
Trade/Device Name: ProSpecT® *C. difficile* Toxin A/B Microplate Assay
Regulation Number: 21 CFR 866.2660
Regulation Name: Microorganism differentiation and identification device
Regulatory Class: Class I
Product Code: LLH
Dated: January 19, 2004
Received: January 20, 2004

Dear Mr. Teicher:

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.

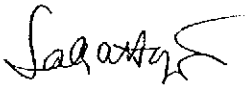
If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish 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): K033479

Device Name: ProSpecT® *C. difficile* Toxin A/B Microplate Assay

Indications For Use:

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For *In vitro* Diagnostic Use.

Prescription Use ___X___ AND/OR Over-The-Counter Use _____
(Part 21 CFR 801 Subpart D) (21 CFR 807 Subpart C)

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

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

Freddie Te Paole

Division Sign-Off

Office of In Vitro Diagnostic Device Evaluation and Safety

510(k) K033479