K980185

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May 12, 1998

SUMMARY OF SAFETY AND EFFECTIVENESS

SUBMITTED BY:

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Becton Dickinson Microbiology Systems
7 Loveton Circle
Sparks, MD 21152

NAME OF DEVICE:

Trade Name: ColorPAC™ Toxin A
Common Name/Description: Reagents, *Clostridium difficile* Toxin

PREDICATE DEVICE: Cytotoxin B

DEVICE DESCRIPTION:

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 the 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.

KIT CONTENTS:

The following components are included in the **ColorPAC™ Toxin A** Test kit.

Reagent 1	(30 ml)	Sample Buffer: Buffered saline with a mucolytic agent, 1% detergent.
Reagent W	(2.3 ml)	Wash Reagent: Buffered saline solution with bovine protein stabilizer, 0.1 % detergent.
Reagent 2	(1.5 ml)	Detector A: Rabbit *C. difficile* toxin A antibody coated liposomes.
Reagent 3	(1.5 ml)	Detector B: Rabbit antibody coated liposomes specific for Detector Reagent A.

Control +	(1.0 ml)	Positive Control: Buffered saline solution with bovine protein stabilizer, inactivated *C. difficile* toxin A.
Control -	(1.0 ml)	Negative Control: Buffered saline solution with bovine protein stabilizer.
		Reagents and controls each contain 0.2% sodium azide (preservative)
30 Test Devices		Each containing a test strip coated with monoclonal *C. difficile* toxin A antibody and *C. difficile* toxin A.

30 SQ-EASY™ Tubes and Filter Tips, 30 Applicator Sticks, 30 Transfer Pipets, 1 Dropper Rod

PRINCIPLE OF PROCEDURE: The **ColorPAC Toxin A** test is comprised of a capture line consisting of *C. difficile* toxin A antibody immobilized on a chromatographic test strip which is contained within a test device. A specimen (stool, colonies, or BHI broth) is diluted with sample buffer and added to the sample well of the test device. The diluted sample wicks up the test strip by capillary action. Toxin A, if present, binds to the capture antibody at the test line as the specimen migrates across the test strip. The wash and remaining reagents are added to the reagent well of the test device.

Upon addition of Detector A, toxin A antibody coated liposomes containing a pink dye migrate across the test strip and attach to the *C. difficile* toxin A antigen that was bound to the test strip in the previous step. Color formation is enhanced upon addition of a second liposome reagent, Detector B, that binds to the complex formed between Detector A and sample antigen at the test line. Following the final wash, the reactions are read visually. If toxin A antigen is detected in the patient specimen, a pink test line and a pink control line will appear, indicating a positive result. In the absence of toxin A, only the pink control line will appear, indicating a negative result. The result is uninterpretable if there is no pink control line or if the background obscures reading of the control line.

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PERFORMANCE DATA:

ANALYTICAL STUDIES:

1. Cross-Reactivity

The **ColorPAC™ Toxin A** test was evaluated for cross reactivity by seeding microorganisms (i.e. bacteria, yeast, viruses and parasites) into toxin A positive and toxin A negative stool specimens to a final concentration of 10^7-10^8 CFU/ml for bacteria and yeast, $10^{3.2}$ - $10^{6.2}$ $TCID_{50}$/ml for viruses and 10^6 parasites/ml. The only organism shown to cross-react was a highly toxigenic isolate of *Clostridium sordellii* (VPI 9048). The *Staphylococcus aureus* Cowan strain ATCC 12598, which produces protein A, did not show cross reactivity. In addition, *Escherichia coli* ATCC 43889, 43894, and 43895 which produce Shiga-like toxins, did not show any cross reactivity.

2. Limit of Detection

The analytical sensitivity of the **ColorPAC Toxin A** test was performed by seeding known concentrations of toxin A into 5 specimens each of liquid, semi-solid, and solid stools. Seeded specimens were tested in triplicate. The limit of detection range for liquid, semi-solid, and solid stool specimens was 1.4-5.2, 1.6-18.7, 3.2-22.6 ng/ml, respectively.

3. Interfering Substances

The evaluation of interfering substances was performed by seeding substances that may be present in stool specimens from patients suspected of having *C. difficile*-associated disease. **ColorPAC Toxin A** test results are not affected by ampicillin, cephalexin, metronidazole, vancomycin, barium sulfate, laxatives, blood, and antidiarrheal medications.

4. Stability of Stool Specimens with Known Amounts of Toxin A

Multiple freeze thaw cycles (up to three) had no significant effect on the assay. A subset of clinical trial samples that were tested at one site demonstrated that specimens can be stored up to 72 hours at 2-8°C . If specimens are to be tested after 72 hours, they should be frozen at -70°C immediately upon receipt in the laboratory. Specimens may be frozen up to 2 months.

CLINICAL STUDIES:

1. ColorPAC Toxin A vs. Cytotoxin B

The performance of the **ColorPAC™ Toxin A** test was determined in evaluations conducted at four major independent medical centers. The sites were located in geographically diverse areas of the United States. A total of 598 fresh and 162 frozen stool specimens from patients with suspected *C. difficile* associated disease were tested. Each site compared its routine cytotoxin B assay to **ColorPAC Toxin A.** Results of this initial comparison at each individual site are summarized below.

			Cytotoxin B Result			
Site	No.	**ColorPAC Toxin A**	Positive	Negative		95% Confidence Intervals
1	240	Positive	28	6	Sensitivity 82%	(65.5%,93.2%)
		Negative	6	200	Specificity 97%	(93.8%,98.9%)
2	135	Positive	18	1	Sensitivity 90%	(68.3%,98.8%)
		Negative	2	114	Specificity 99%	(95.3%,99.9%)
3	207	Positive	21	11	Sensitivity 81%	(60.7%,93.5%)
		Negative	5	170	Specificity 94%	(89.4%,96.9%)
4	178	Positive	29	1	Sensitivity 74%	(57.9%,87.0%)
		Negative	10	138	Specificity 99%	(96.1%,100%)
Combined	760	Positive	96	19	Sensitivity 81%	(72.4%,87.3%)
		Negative	23	622	Specificity 97%	(95.4%,98.2%)

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2. Reproducibility:

Reproducibility of the **ColorPAC Toxin A** test was evaluated by testing stool panels consisting of three levels of toxin A and a toxin A negative antigen control. Blinded specimens were tested in triplicate on each of three days at each of four different clinical trial sites. **ColorPAC Toxin A** demonstrated 100% intra and inter assay reproducibility.

3. Colony Confirmation:

A study was conducted to evaluate the **ColorPAC™ Toxin A** test performance for providing culture confirmation from suspected colony growth for toxin producing strains of *C. difficile* using selective agar, anaerobic blood agar, and Brain Heart Infusion (BHI) broth. A total of 111 clinical isolates that met morphological characteristics of *C. difficile* were tested from each medium using the **ColorPAC Toxin A** test. After identification of the colonies by biochemical methods, toxigenic status was determined by a cytotoxin B assay. Results from this initial comparison for each medium are summarized below:

Media Type	**No. Specimens**	**Sensitivity 95% Confidence Intervals**	**Specificity 95% Confidence Intervals**
BHI Broth	111	95% (84.9%,98.8%)	93% (82.7%,98.0%)
Selective Agar	111	95% (84.9%, 98.8%)	93% (82.7%,98.0%)
Anaerobic Blood Agar	111	89% (77.7%,95.9%)	95% (85.1%,98.9%)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

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Becton Dickinson Microbiology Systems
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Re: K980185
Trade Name: ColorPAC™ Toxin A
Regulatory Class: I
Product Code: LLH
Dated: May 13, 1998
Received: May 14, 1998

Dear Ms. Rohrbeck:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we 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). 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 (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially equivalent determination assumes compliance with the Current Good Manufacturing Practice requirements, as set forth in the Quality System Regulation (QS) for Medical Devices: General regulation (21 CFR Part 820) and that, through periodic QS inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal laws or regulations.

Under the Clinical Laboratory Improvement Amendments of 1988 (CLIA-88), this device may require a CLIA complexity categorization. To determine if it does, you should contact the Centers for Disease Control and Prevention (CDC) at (770)488-7655.

This letter will allow you to begin marketing your device as described in your 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 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll free number (800) 638-2041 or at (301) 443-6597 or at its internet address "http://www.fda.gov/cdrh/dsmamain.html"

Sincerely yours,

Steven Gutman

Steven I. Gutman, M.D., M.B.A.
Director
Division of Clinical Laboratory Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure

510(k) Number (if known): K980185

Device Name: ColorPAC™ Toxin A

Indications for Use:

The ColorPAC™ Toxin A test is indicated 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 the confirmation of suspect colonies of toxigenic *C. difficile* from agar plates or BHI broth. The assay is intended for use as an aid in the diagnosis of *C. difficile* associated disease. The test is not indicated for asymptomatic adults or children. This device is not intended for use in a point of care setting.

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

Concurrence of CDRH, Office of Device Evaluation (ODE)

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K980185

Prescriptive Use X OR Over-the-Counter-Use ___
(Per 21CFR 801.109)