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8.0 510(k) SUMMARY (page 1 of 4)

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: K991829

A. Safety and effectiveness information required per [§807.92(a)(1)]:

- **SUBMITTER'S NAME**: BioStar, Inc.
- **ADDRESS**: 6655 Lookout Rd. Boulder, CO 80301
- **TELEPHONE**: (303) 530-3888 ext. 659
- **FAX**: (303) 530-6601
- **CONTACT PERSON**: Curtis A. Carlson
- **DATE 510(k) SUMMARY PREPARED**: May 28, 1999; revised October 27, 1999.

B. Safety and effectiveness information required per [§807.92(a)(2)]:

- **TRADE OR PROPRIETARY NAME**: CdTOX A OIA®
- **COMMON NAME**: *C. difficile* Toxin A Assay
- **CLASSIFICATION NAME**: Direct Antigen Detection Assay, *Clostridium difficile*

C. Identification of legally marketed device to which we are claiming equivalence [§807.92(a)(3)]:

- **TRADE OR PROPRIETARY NAME**: PREMIER™ *C. difficile* Toxin A
- **REGULATORY CLASS**: Class I
- **PRODUCT CODE**: 83LLH
- **MANUFACTURER**: Meridian Diagnostics, Inc.
- **510(k) NUMBER**: K903456

Note: Performance of the CdTOX A OIA product was also established versus cytotoxicity assay.

D. Description of device [§807.92(a)(4)]:

Principle of the Test:

The CdTOX A OIA test involves the qualitative detection of the enterotoxin (Toxin A) produced by *Clostridium difficile*. The Optical ImmunoAssay technology enables the direct visual detection of a physical change in the optical thickness of molecular thin films. This change is a result of antigen-antibody binding on an optical surface (silicon wafer). When a sample containing Toxin A (antigen) from *Clostridium difficile* is placed directly on the optical surface, the immobilized specific antibody captures the antigen. After washing, the substrate is added, increasing the thickness (Mass Enhancement) of the molecular thin film. This change in thickness alters the reflected light path and is visually perceived as a color change. Slight changes in optical thickness produce a distinct, visible color change. A positive result appears as a purple spot on the predominant gold background. When antigen is not present in the specimen, no binding takes place. Therefore, the optical thickness remains unchanged and the surface retains the original gold color indicating a negative result.

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Device Components:

The CdTOX A OIA test kit contains the following:

Reaction Tubes
Reagent 1: Conjugate
Wash Solution
Substrate
Test Devices
Positive Control
Negative Control
Transfer Pipettes
Sampling Brushes

E. Intended use of device [§807.92(a)(5)]:

The BioStar® CdTOX A OIA assay is an Optical ImmunoAssay test for the rapid qualitative detection of *Clostridium difficile* Toxin A in human fecal samples from patients suspected of having *Clostridium difficile* associated disease (CDAD). This test is intended for *in vitro* diagnostic use as an aid in the diagnosis of CDAD.

F. Technological characteristics [§807.92(a)(6)]:

Technological Characteristic	Predicate Device (Premier™ Toxin A)	Our Device (CdTOX A OIA)
Intended Use	The Premier™ *C. difficile* Toxin A assay is an Enzyme ImmunoAssay for the Detection of *C. difficile* Toxin A in Stool Specimen.	The BioStar® CdTOX A OIA assay is an Optical ImmunoAssay test for the rapid qualitative detection of *Clostridium difficile* Toxin A in human fecal samples from patients suspected of having *Clostridium difficile* associated disease (CDAD). This test is intended for *in vitro* diagnostic use as an aid in the diagnosis of CDAD.
Detection	Detects *C. difficile* Toxin A	Detects *C. difficile* Toxin A
Technology	Enzyme Immunoassay (EIA) Microwell	Optical Immunoassay (OIA)
Specimens Evaluated	Stool	Stool

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G. Summary of nonclinical testing [§807.92(b)(1)]:

Analytical Sensitivity:

The analytical sensitivity was determined by adding known concentrations of Toxin A to five specimens each of liquid, semi-solid, and solid stools. Seeded specimens were tested in duplicate by the CdTOX A OIA test. Results are summarized in the table below.

Limit of Detection by Stool Type

Toxin A Seeded Matrix	Limit of Detection (ng/g)
Buffer Control	3
Liquid Stool	3-8
Semi-Solid Stool	4-8
Formed Stool	3-5

Analytical Specificity (Cross Reactivity):

To determine the analytical specificity of the CdTOX A OIA test, microorganisms were grown on the appropriate media and suspended to a concentration of approximately 1.0 X 10^9 cfu/mL or greater and tested in the absence and presence of Toxin A near the lower limit of detection of the assay. . *Cryptosporidium parvum* and *Giardia lamblia* were tested at 1.25 X 10^6 cysts/mL. No cross reactivity or interference was observed.

Interfering Substances:

Interference testing was performed to determine the effect of substances which might be encountered in the collection of specimens. Whole blood, Red Blood Cells (RBC), White Blood Cells (WBC), mucous (25mg/g), and barium sulfate (58% w/w suspension) were tested and did not interfere with the CdTOX A OIA test. All assays were run per the procedure described in the package insert.

Sample/Toxin Stability

Toxin stability in liquid, semi-solid, and formed stool was judged by spiking Toxin A (Lee Laboratories) at levels near the analytical sensitivity of the assay and testing at the specified times. Spiked samples were initially held at room temperature for 2 hours then transferred to 2-8°C storage. These results show that over the sample consistency types tested, the toxin is sufficiently stable to allow detection in samples handled as recommended in the package insert.

Stool Consistency Reactivity:

The reactivity of stools with liquid, semi-solid, or formed consistency was evaluated using the CdTOX A OIA test and microwell EIA test. The positivity rates were similar for the two assays across all three types of stool specimens. All of the specimens in the clinical performance evaluation of the CdTOX A OIA test were submitted for *C. difficile* testing on the basis of clinical history of the patient, not the consistency of the specimen. Test results are illustrated in the table below.

Reactivity Data From Four Clinical Sites

	Stool Consistency		
	Liquid (445)	Semi-solid (298)	Formed (80)
CdTOX A OIA +	42 (9 %)	54 (18 %)	21 (26 %)
EIA +	51 (11 %)	50 (17 %)	19 (24%)

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H. Summary of clinical testing [§807.92(b)(2)]:

Reproducibility

Reproducibility testing was conducted using a stool matrix at three hospital laboratories. Ten blinded samples were tested at each site at three separate times. Samples consisted of negative, low, and moderate levels of *C. difficile* Toxin A. The concentration of toxin in the low samples was less than 2-fold over the minimum detectable limit.. The overall reproducibility was 94.4% (85/90). An additional study was done using artificial stool matrix. Comparable samples were prepared and tested at four hospital laboratories and three physician office laboratories (POLs). Overall reproducibility in this study was 97.6% (205/210); at the hospitals, 97.5% (117/120) at the POLs, 97.8% (88/90).

Clincal Sensitivity and Specificity

A study comparing the CdTOX A OIA test and a commercial microwell immunoassay, the Premier EIA, to cytotoxicity assay (CTA) was performed at a central hospital lab. The sensitivity, specificity, and concordance of the CdTOX A OIA test was 77.3%, 93.8%, and 91.0% respectively. The sensitivity, specificity, and concordance of the Premier EIA test was 81.8%, 92.0%, and 90.3% respectively.

The CdTOX A OIA test was evaluated versus the Premier EIA at four clinical trial sites (central hospital labs) located in the Southwest, Midwest, Mid-Atlantic and East Coast regions of the United States. A total of 874 specimens from patients suspected of having or with a history of CDAD were evaluated by the CdTOX A OIA test and the Premier EIA. Of these, 823 gave unequivocal results using the EIA method. Concordance between the Cd TOX A OIA test and the Premier EIA test was 95.0% (98+/+, 684 -/-); discordance was 5.0% (19 +/-, 22 -/+).

I. Conclusions from nonclinical / clinical testing [§807.92(b)(3)]:

The results of the above described internal and external studies demonstrate that the CdTOX A OIA test is as safe and effective as the cleared predicate device.

J. Additional information [§807.92(d)]:

No additional information has been requested by FDA at this time.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

NOV - 2 1999

Curtis A. Carlson, Ph.D.
Director, Regulatory Affairs
BioStar, Inc.
6655 Lookout Road
Boulder, Colorado 80301

Re: K991829
Trade Name: CdTOX A OIA® Test Kit
Regulatory Class: I
Product Code: LLH
Dated: October 7, 1999
Received: October 8, 1999

Dear Dr. Carlson:

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

INDICATIONS FOR USE STATEMENT

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510(k) Number (if known): K991829

Device Name: CdTOX A OIA®

Indications For Use:

The BioStar® CdTOX A OIA assay is an Optical ImmunoAssay test for the rapid qualitative detection of *Clostridium difficile* Toxin A in human fecal samples from patients suspected of having *Clostridium difficile* associated disease (CDAD). This test is intended for ***in vitro*** diagnostic use as an aid in the diagnosis of CDAD.

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

Concurrence of CDRH, Office of Device Evaluation (ODE)

Woody Dubois

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K991829

Prescription Use (Per 21 CFR 801.109) OR Over-The-Counter Use

(Optional Format 1-2-96)