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(c).

The assigned 510(k) number is: K061889

A. Information required per [§807.92(a)(1)]:

DEC 1 2 2006

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Date 510(k) Summary Prepared: December 6, 2006

B. Information required per [§807.92(a)(2)]:

Name of the Device:	BioStar® OIA® SHIGATOX
Common Name:	Direct Antigen Detection, Shiga Toxins, *Escherichia coli,* other enterohemorrhagic organisms
Product Code:	GNA -- Antisera, all types, *Escherichia coli* GMZ – Antigens, all types, *Escherichia coli*
Regulation Section:	21 CFR Part 866.3255 *Escherichia coli* Serological Reagents
Classification:	Class I
Panel:	83 Microbiology

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

Predicate Device Name(s); K Numbers; Manufacturers

i. Premier EHEC; K953362; Meridian Diagnostics, Inc.
ii. ProSpecT® Shiga Toxin Microplate Assay; K980507; Alexon – Trend, Inc.

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

a. Summary and Explanation

Shiga toxin-producing *Escherichia coli* (STEC) strains are an important cause of epidemic and endemic diarrhea, hemorrhagic colitis, and hemolytic uremic syndrome (HUS). The most commonly reported serotype associated with outbreaks in the United States has been O157:H7. However, as many as 50 other serotypes of *E. coli* have also been shown to produce Shiga toxins and have been reported to be associated with outbreaks and sporadic disease both within and outside the United States[1]. Due to the morbidity and mortality associated with outbreaks and sporadic cases of STEC diseases, these pathogens are now considered major public health problems of worldwide importance. STEC strains share the potential to produce a variety of virulence factors, including two Shiga toxins (Stx 1 and Stx 2). Human STEC strains can produce Stx 1 or Stx 2 alone or in combination[2].

The ability to control the spread of outbreaks associated with STEC depends upon the rapid detection of these pathogens. Laboratory diagnosis of diarrhea has been recommended as it may alert public health officials to a common source of illness in a community. For the affected patient, laboratory confirmation of STEC may preclude costly additional tests, allow earlier implementation of supportive treatment in impending HUS, and, while controversial, exclude administration of potentially harmful antimicrobial agents[3]. The method used in most clinical microbiology laboratories is based on sorbitol MacConkey agar culture (SMAC), coupled with specific detection of the O157 antigen. This approach neglects other STEC serotypes and also other Shiga toxin-producing bacteria[2]. The cytotoxin assay described by Karmali is used to screen stool samples for evidence of STEC infections. However, this test is slow, labor-intensive, difficult to standardize, and it requires cell culture facilities, making it impractical for routine diagnostic laboratories[4].

b. Principle of the Test

The OIA SHIGATOX test involves the qualitative detection of Shiga toxins 1 and 2 (Stx1 and Stx 2) produced by certain strains of *Escherichia coli* and other organisms. The Optical ImmunoAssay technology enables the direct visual detection of a physical change in the optical thickness of molecular thin films. This change is the result of antigen – antibody binding on an optical surface (silicon wafer). After a specimen potentially containing Shiga toxin is mixed with conjugates and placed directly on the optical surface, the immobilized surface antibodies capture the antigen/conjugate complex. 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 this alteration is visually perceived as a color change. Slight changes in the optical thickness produce a distinct visible color change. A positive result appears as a purple spot on the 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.

More specifically, the BioStar OIA SHIGATOX device is based on a novel thin film optical detection technology that relies on the interaction of white light with thin films to create a destructive interference phenomenon. Characteristic of this phenomenon is the generation of a reflective surface that changes color as a function of the change in optical thickness (refractive index x thickness) of the films on the surface of the device. To take advantage of this phenomenon for monitoring biological binding events, the optical surface with a special background color is coated with a capture reagent specific to the analyte of interest. In the OIA SHIGATOX device, the biological capture film is a combination of affinity-purified polyclonal antibodies to Shiga toxins 1 and 2 (Stx 1 and Stx 2). Samples suspected of containing either or both of the toxins are mixed with cocktail containing polyclonal antibodies to Stx 1 and Stx 2 that have been covalently conjugated to horseradish peroxidase (HRP). Once a sample containing toxins or either toxin is applied to the surface, the immune complex of toxin(s) and the anti-toxin-HRP conjugate(s) are bound to the surface antibodies. Following a wash step, a precipitating substrate for HRP is added, and a thin film generated by the immobilized immune complex is enhanced by the precipitation of the HRP product. Once washed and dried, a simple color change relative to the gold background color is observed as an indication of the presence of Stx 1 or Stx 2 in the original specimen.

The OIA SHIGATOX device produces a qualitative result for the presence or absence of Shiga toxin as the device output. Input to the device is the simple addition of an aliquot of fecal material or broth culture to the reagents contained in the kit. Fecal samples are routinely collected, and no special collection requirements exist beyond the elimination of the use of fecal transport media. Test devices within the kit are single use devices, and disposal instructions are provided in the Package Insert. The kit contains all components necessary for analysis of the direct stool sample with the exception of a timer.

c. Device Description

Reagent 1 - Conjugate 1: Contains anti-Shiga Toxin 1 antibodies (rabbit) conjugated to Horseradish Peroxidase (HRP) in a buffered protein solution, preserved with 0.5% ProClin® 300 preservative.

Reagent 2 - Conjugate 2: Contains anti-Shiga Toxin 2 antibodies (rabbit) conjugated to Horseradish Peroxidase (HRP) in a buffered protein solution, preserved with 0.5% ProClin 300 preservative.

Wash - Contains buffered saline solution preserved with 0.1% ProClin 300 preservative.

Substrate - Tetramethylbenzidine (TMB) and hydrogen peroxide (H_2O_2).

Test Devices - Surfaces coated with anti-Stx 1 and anti-Stx-2 affinity purified rabbit polyclonal antibodies and containing an internal procedural control spot composed of Shiga toxin 1 toxoid in the center of the test device.

Positive Control - Inactivated Purified Shiga toxin preserved with 0.01% Microcide II and 0.005% gentamycin preservative in a buffered protein solution.

Diluent / Negative Control - Buffered protein solution preserved with 0.01% Microcide II and 0.005% gentamycin.

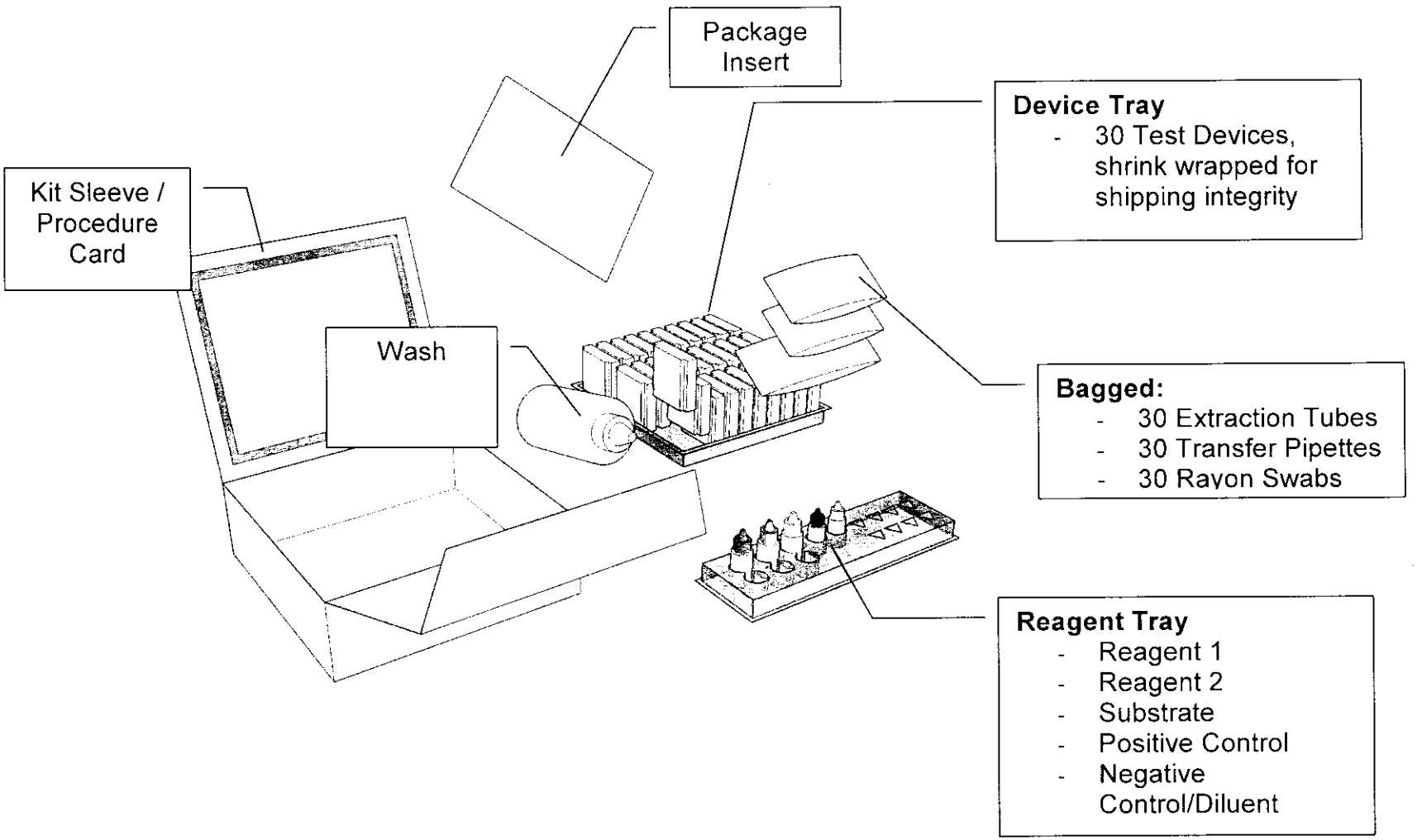
Reaction Tubes

Transfer Pipettes

Rayon Swabs

Materials Required But Not Provided – timer

Below is a diagrammatic representation of the kit and the kit components:



Assay Protocol

- **Liquid Specimens:** The Transfer Pipette provided should be used for liquid fecal specimens.
- **Semi-Solid Specimens:** Dip the swab into the specimen, rotating gently to absorb sample. Rotate the swab gently against the wall of the sample container to remove excess fecal material. Add 2 drops of Diluent / Negative Control to the reaction tube.

Remove reagents from refrigerated storage and allow to warm to room temperature (15° to 30°C). Store Wash Solution at room temperature (15° to 30°C) after opening. If stored refrigerated, Wash Solution will take up to 2 hours to warm to room temperature.

Remove one Reaction Tube for each specimen to be tested and place it upright in a rack or holder. Label Reaction Tubes and Test Devices with appropriate patient information. Place Test Devices on a level surface while the assay is being performed. **Mix all fecal specimens thoroughly before sampling.**

1. Add 3 drops of Reagent 1 to the Reaction Tube.

2. Add 3 drops of Reagent 2 to the Reaction Tube.

   Note: The combined Reagents 1 and 2 in the Reaction Tube should have a blue color.

3. Thoroughly mix the fecal specimen with the Transfer Pipette. Add 2 drops of the specimen to the Reaction Tube and mix by squeezing the sides of the tube. For semi-solid specimens, an enclosed swab may be used to add specimen into the tube. Refer to "Semi-Solid Specimens" under the Test Procedure for additional information.

4. Within 1 minute of mixing, use the Transfer Pipette to place 1 to 2 drops (to cover the surface) of the sample mixture directly onto the center of the test surface. Wait 10 minutes.

5. Wash the surface vigorously with a hard squirt of Wash Solution, taking care not to exceed the capacity of the absorbent material surrounding the test surface.

   Note: Vigorous washing will aid in obtaining a clean test surface. Insufficient washing of the test surface may leave debris that may result in the appearance of a ring or spots surrounding the positive Internal Control dot. These effects should not be interpreted as a positive result due to the lack of color shading within the ring area.

6. Confirm that the blotter in the Test Device lid is in Position I. Close the Test Device at the corners. Leave closed for 10 seconds to remove residual moisture from the test surface.

7. Open the lid, change the blotter to Position II, and apply 1 drop of Substrate directly to the center of each Test Device. Wait 5 minutes.

   Note: Do not cover the entire surface of the Test Device with Substrate. The gold, unreacted areas surrounding the reaction circle serves as a negative Internal Control and reference for comparing signal intensity.

8. Repeat Step 5, washing the test surface vigorously with Wash Solution. Close the Test Device at the corners. Leave closed for 10 seconds. Open and examine the test surfaces for color changes (See Interpretation of Test Results).

E. Intended Use [§807.92(a)(5)]:

The Inverness Medical, BioStar OIA SHIGATOX assay is an Optical Immunoassay (OIA) test for the qualitative, rapid detection of the presence of Shiga toxins in human diarrheal fecal specimens, broth cultures, and swab sampling of colonies from a culture plate. This test is intended for *in vitro* diagnostic use as an aid in the diagnosis of infection by Shiga toxin-producing *Escherichia coli* (STEC) both O157 and all non – O157 Shiga toxin producing strains.

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

See Table 1 below.

G. Summary of non - clinical testing [§807.92(b)(1)]

a. Analytical Sensitivity

To determine the analytical sensitivity, two-fold serial dilutions of purified Stx 1 or Stx 2 toxin were prepared. These dilutions were then spiked into buffer and the spiked samples were tested in triplicate. The Limit of Detection (LOD) was defined as the lowest toxin concentration producing at least two positive results of the three tests or at least 50% of the total number of samples tested. In an antigen diluent formulation, the limits of detection were 1 ng/mL and 0.5 ng/mL for Stx 1 and Stx 2, respectively. The same tests were repeated in a liquid stool matrix and the LOD for each toxin was determined to be 1 ng/mL. Five samples at each concentration were analyzed on 2 lots of devices. While lower levels of toxin were detected in some lots of product the LOD was set at the lowest concentration routinely observed in multiple product lots.

b. Analytical Strain Recognition

Toxigenic Strain Testing

To establish that the OIA SHIGATOX assay detects all Shiga toxin-producing strains and organisms, the following studies were conducted. Clinical isolates, previously analyzed for the presence of Shiga toxin genes and serotyped, were obtained from a Department of Public Health (49 isolate strains) and a university laboratory (21 isolate strains) or other commercial source. Lists of the isolates from each source are presented in the tables. Tubes of MacConkey broth were inoculated with each isolate and cultured overnight at 37° C under aerobic conditions. A 60-µL sample of the broth was then tested in the OIA SHIGATOX assay without further processing using the same protocol as was used with clinical samples after broth enrichment.

Department of Public Health Isolate List

		Number of strains		
Somatic Antigen	Flagellar Antigen	Stx-1 only	Stx-2 only	Stx-1 + Stx-2
O26	H11	9		3
O28	H25		1	
O76	H19	1		
O103	H2	1		
	H25	1		
O111	Non-motile	4	1	
O121	H19		2	
	Non-motile		1	
O145	Non-motile	3	1	
O146	H21		1	
O157	H7		3	14
O165	Non-motile			1
Undetermined	H34	1		
	Non-motile	1		

University Laboratory Isolate List

		Number of strains		
Somatic Antigen	Flagellar Antigen	Stx-1 only	Stx-2 only	Stx-1 + Stx-2
O26	Not Available	5		
O103	Not Available	5		
O128	Not Available	2		1
O157	H7	5	3	

In addition, *Shigella dysenteriae* (ATCC 13313) was tested and produced a positive result as expected. All 70 clinical isolates produced the expected positive assay result. The OIA SHIGATOX assay detects the Shiga toxin from a wide range of toxin-producing *E. coli*. Similar results were observed with multiple lots of material throughout the development process.

c. Analytical Specificity (Cross Reactivity)

Bacteria were grown on appropriate media and suspended in Antigen Diluent, a buffered protein solution, to stock concentrations of 1×10^7 organisms/mL or higher. The organisms were tested with and without spiking with 2.5 ng/mL Stx 1 and 2.5 ng/mL Stx 2. The exceptions were that *Cryptosporidium* and *Giardia* were tested at 1×10^6 cysts/mL, and *Candida albicans* was tested at 9.3×10^7 cells/mL. All members of the cross reactivity panel produced the expected negative result without the toxin spike and the expected positive result with the toxin spike.

Aeromonas hydrophila
Bacillus cereus
Bacillus subtilis
Bacteroides fragilis
Bifidobacterium adolescentis
Campylobacter fetus
Campylobacter jejuni
Candida albicans
Citrobacter freundii
Clostridium botulinum Type A
Clostridium butyricum
Clostridium histolyticum
Clostridium innocuum
Clostridium novyi
Clostridium perfringens
Clostridium septicum
Clostridium sordellii
Clostridium subterminale
Clostridium tetani
Cryptosporidium parvum
Enterobacter aerogenes
Enterobacter cloacae
Enterococcus faecalis
Escherichia coli (non-STEC)
Giardia lamblia
Klebsiella pneumoniae
Peptostreptococcus anaerobius
Porphyromonas asaccharolytica
Proteus vulgaris
Providencia rettgeri
Pseudomonas aeruginosa
Salmonella diarizonae
Salmonella enteriditis
Salmonella typhi
Salmonella typhimurium
Serratia liquefaciens
Serratia marcescens
Shigella flexneri Serotype 1A
Shigella sonnei
Staphylococcus aureus
Staphylococcus aureus Cowan I
Staphylococcus epidermidis
Staphylococcus saprophyticus
Veillonella parvula
Vibrio cholerae
Vibrio parahaemolyticus
Yersinia enterocolitica

In addition, one clinical trial site tested three stools in the OIA SHIGATOX assay that were positive in a commercial lateral flow, EIA assay for Rotavirus. All 3 samples were negative in the OIA SHIGATOX assay as expected.

d. Interfering Substances

The OIA SHIGATOX assay was tested with whole blood, mucin, liquid Imodium AD, Pepto Bismol, Kaopectate, and Barium Sulfate for the potential of these materials to interfere with assay results. Clinical trial lots of product were tested, and the conjugate and test surface were specific to each lot. To test for potential nonspecific signal generation, a 30 µL aliquot of each potential interferent stock was mixed with 30 µL of Antigen Diluent or a liquid or semi – solid stool specimen and run as the sample with the standard assay protocol. To test for potential interference with the positive signal, the 30 µL aliquot was mixed with 30 µL Antigen Diluent or a liquid or semi – solid stool specimen containing 5 ng/mL of each toxin (final concentrations of Stx 1 and Stx 2 were 2.5 ng/mL). Each sample was tested in duplicate.

Interferents diluted into antigen diluent

Test Material	Stock Concentration (used 1:1 in the sample)	Interferent + Negative Sample		Interferent + Positive Sample	
		Lot 1	Lot 2	Lot 1	Lot 2
Barium Sulfate	58% (Neat)	-,-	-,-	+,+	+,+
Bovine Mucin	25 mg/g	-,-	-,-	+,+	+,+
Kaopectate®	Neat	-,-	-,-	+,+	+,+
Pepto Bismol®	Neat	-,-	-,-	+,+	+,+
Imodium®	Liquid (Neat)	-,-	-,-	+,+	+,+
Whole Blood	Neat	-,-	-,-	+,+	+,+

None of the substances, tested at the stated concentration, caused a false positive or false negative result in the assay. Therefore, the OIA SHIGATOX assay is tolerant to:

29% Barium sulfate
12.5 mg/g mucin
50% Kaopectate
50% Pepto Bismol
50% Liquid Imodium
50% Whole blood

Interferents tested in liquid and semi – solid stool

Test Material	Stock Concentration (used 1:1 in the sample)	Interferent + Negative Sample		Interferent + Positive Sample	
		Liquid Stool	Semi - Solid	Liquid Stool	Semi - Solid
Barium Sulfate	58% (Neat)	-,-	-,-	+,+	+,+
Bovine Mucin	25 mg/g	-,-	-,-	+,+	+,+
Kaopectate®	Neat	-,-	-,-	+,+	+,+
Pepto Bismol®	Neat	-,-	-,-	+,+	+,+
Imodium®	Liquid (Neat)	-,-	-,-	+,+	+,+
Whole Blood	Neat	-,-	-,-	+,+	+,+

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

Reproducibility

Reproducibility studies were performed using a blinded method at each of the three Clinical Trial sites and 3 operators at 2 Point of Care sites. Standard OIA product training was provided to all sites prior to the initiation of the reproducibility study. A panel of twenty-seven fecal specimens containing no Shiga toxin or spiked with low or moderate levels of Stx 1 and/or Stx 2 were placed in a random order and given code numbers. These specimens were tested on three successive days with the order being changed for each day. The specimens produced the expected results in 100% of the tests.

Clinical Sensitivity and Specificity

Swab Sampling of Colonies from a Culture Plate (Colony Sweep Method)

One clinical site evaluated twenty two frozen fecal specimens in a colony sweep procedure. These samples were previously found to contain Shiga toxin producing *E. coli.* All samples were streaked onto XLD (xylose lysine deoxycholate) plates and incubated overnight at 37°C. One sample failed to produce any growth. A sterile rayon swab was used to sweep the first and second quadrants of the growth area and was then immersed into a reaction tube containing 3 drops each of Reagents 1 and 2 and the standard assay protocol followed. The OIA SHIGATOX assay detected 21/21 of the colony sweeps that produced growth for 100% agreement with the previous specimen result.

Direct Stool

A prospective study was conducted at three clinical trial sites in the Eastern, Southern and Western regions of the United States to compare the performance of the BioStar OIA SHIGATOX to a commercial EIA test. Sites analyzed the stool specimens collected for direct testing from the stool sample by both assays and then placed an aliquot of the stool in MacConkey broth within 48 hours of specimen collection. Broth cultures were incubated for 20 – 30 hours and then tested by both immunoassays. A SMAC culture (Sorbitol MacConkey plates) was also plated within 48 hours of the specimen collection for the determination of *E. coli* O157. All positive results from either immunoassay method were confirmed by cytotoxicity testing, CTA.

A total of 272 prospective specimens from diarrheal patients were tested in the OIA SHIGATOX and the EIA method.

Comparison of OIA SHIGATOX to EIA for Direct Stool Samples

		EIA +	EIA -
OIA SHIGATOX	+	12	5
	-	0	255

Positive Agreement: 100% (95%CI: 73.5 –100%)
Negative Agreement: 98.1% (95%CI: 95.6 – 99.4%)
Overall Percent Agreement: 98.2% (95% CI: 95.8 – 99.4%)

Of the five OIA+/EIA - specimens, one was positive by CTA. One of the samples that was negative by direct stool testing in both the EIA and the OIA methods was positive in the OIA broth culture sample and by CTA from the direct stool.

Two of the clinical sites also performed a study in which sixty-two additional frozen specimens were prospectively tested by OIA SHIGATOX and EIA without the operator's knowledge of the original Shiga toxin result.

Comparison of OIA SHIGATOX to EIA for Frozen Direct Stools

		EIA +	EIA -
OIA SHIGATOX	+	21	1
	-	3	37

Positive Agreement: 87.5% (95% CI: 67.6 – 97.3%)
Negative Agreement: 97.4% (95% CI: 86.2 – 99.9%)
Overall Percent Agreement: 93.6% (95% CI: 84.3 – 98.2%)

Broth Culture

A total of 269 prospective specimens from diarrheal patients were tested by OIA SHIGATOX and the EIA method from the broth culture. Three fecal specimens failed to produce any growth upon broth culture.

Comparison of OIA SHIGATOX to EIA for Broth Enriched Culture from Fresh Stools

		EIA +	EIA -
OIA SHIGATOX	+	12	1
	-	0	256

Positive Agreement: 100% (95% CI: 73.5 -100%)
Negative Agreement: 99.6% (95% CI: 97.9 - 100%),
Overall Percent Agreement: 99.6% (95% CI: 98.0 – 100%)

The single OIA SHIGATOX +/EIA – result was confirmed to be a true positive by the CTA analysis of the direct stool.

In the prospective frozen sample study, ten of the frozen specimens were not tested in overnight Sorbitol MacConkey broth culture. Two of the remaining specimens failed to exhibit growth after overnight Sorbitol MacConkey broth culture. The percent positive agreement was 100% and the percent negative agreement was 96.4%. The overall percent agreement in the study was 98%.

Comparison of OIA SHIGATOX to EIA for Broth Enriched Culture from Frozen Stools

		EIA +	EIA -
OIA SHIGATOX	+	22	1
	-	0	27

Positive Agreement: 100% (95% CI: 84.6 -100%)
Negative Agreement: 95.6% (95% CI: 81.7 - 99.9%)
Overall Percent Agreement: 98% (95% CI: 89.4 – 100%)

SMAC Culture

Two hundred and sixty nine (269) of the direct stool samples were analyzed by SMAC culture. The OIA SHIGATOX and EIA assays were compared to the SMAC culture results. Interpretation of the comparison between the OIA SHIGATOX or the EIA test and SMAC is confounded by the fact that, as a metabolic test, SMAC is specific for *E. coli* O157:H7, while OIA SHIGATOX reacts with all Shiga toxin-producing *E. coli* (STEC). Also, SMAC requires the presence of live cells in the sample, while the OIA SHIGATOX test does not have that limitation. Based on these differences, it was anticipated that a number of samples could be SMAC-negative and OIA SHIGATOX positive.

OIA SHIGATOX Direct Fresh Stool Results compared to SMAC Culture of Direct Stools

		SMAC +	SMAC -
OIA SHIGATOX	+	9	8
	-	1	251

Positive Agreement: 90% (95% CI: 55.5 – 99.8%)
Negative Agreement: 96.9% (95% CI: 94.0 – 98.7%)
Overall Percent Agreement: 96.7% (95% CI: 93.7 – 98.5%)

EIA Direct Fresh Stool Results compared to SMAC Culture of Direct Stools

		SMAC +	SMAC -
EIA	+	8	4
	-	2	255

Positive Agreement: 80% (95% CI: 44.4 - 97.5%)
Negative Agreement: 98.5% (95% CI: 96.1 – 99.6%)
Overall Percent Agreement: 97.8% (95% CI: 95.2 – 99.2%)

The one apparent OIA false negative result compared to the SMAC result was not confirmed by CTA and was not positive by EIA. Of the 8 apparent false positives by the OIA method, 4 of the samples were positive by CTA. The second EIA false negative result was positive by CTA and the OIA method. One of the OIA +/SMAC + samples was negative by CTA. The 2 EIA -/SMAC + samples were negative by CTA and one of the samples was negative by the OIA method as well. Three of the EIA +/SMAC – samples were positive by CTA and the OIA method. The remaining EIA +/SMAC – sample was negative by CTA but positive by the OIA method.

In addition, two of the clinical sites conducted a prospective comparison of the OIA method to SMAC culture using frozen samples. Thawed aliquots of all samples were tested in the OIA and SMAC methods for this comparison.

Frozen Stool samples comparing OIA SHIGATOX to SMAC

		SMAC +	SMAC -
OIA SHIGATOX	+	9	13
	-	0	40

Positive Agreement: 100% (95%CI: 66.4 - 100%)
Negative Agreement: 75.5% (95%CI: 61.7 – 86.2%)
Overall Percent Agreement: 79% (95%CI: 66.8 – 88.3%)

All thirteen of the OIA+/SMAC- samples were positive for STEC in previous testing.

CTA

In the clinical study there were 19 specimens positive by OIA, EIA, or both methods. An aliquot of the stool specimen for each of these 19 specimens was submitted for CTA along with an aliquot of the broth culture media. One sample produced an inconclusive result and was excluded from this analysis. Thirteen of the samples were positive by CTA. The OIA SHIGATOX detected 12 of these 13 samples while the EIA method detected 11. Twelve of the broth aliquots were positive by CTA. The OIA SHIGATOX assay detected all 12 of these samples as did the EIA method. Of the 13 CTA positives, SMAC was positive for only 8 samples.

Comparison of OIA SHIGATOX, EIA, and SMAC to CTA for Direct Stool and Broth Culture Samples

	CTA Direct Stool	CTA Broth Culture
OIA SHIGATOX	12/13	12/12
EIA	11/13	12/12
SMAC	8/13	N/A

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

The results of the above described internal and external studies demonstrate that the BioStar OIA SHIGATOX is as safe and effective as the cleared predicate devices.

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

No at this time.

TABLE 1: Substantial Equivalence Summary

BioStar® OIA® SHIGATOX Test versus the legally marketed predicate devices, the Premier EHEC and ProSpecT® Shiga Toxin Microplate Assay.

Parameter	OIA SHIGATOX Test	Premier EHEC K953362	ProSpecT Shiga Toxin K980507
INTENDED USE	The BioStar® OIA® SHIGATOX assay is an Optical Immunoassay (OIA) test for the qualitative, rapid detection of the presence of Shiga Toxins in human diarrheal fecal specimens, broth cultures, and a swab sampling of colonies on a culture plate. This test is intended for *in vitro* diagnostic use as an aid in the diagnosis of infection by Shiga Toxin-producing *Escherichia coli* (STEC) both O157 and all non – O157 Shiga toxin producing strains.	Same	Same (Minus the colony sweep)
ANALYTE	Undifferentiated detection of Shiga toxins 1 and 2	Same	Same
TECHNOLOGY	Optical Immunoassay	Enzyme Immunoassay (microplate)	Enzyme Immunoassay (microplate)
SPECIMEN TYPE	Liquid or semi – solid fecal or broth culture or swab sampling from colonies	Same plus stools in transport medium or agar plate colonies	Same plus stools in transport medium
ANALYTICAL SENSITIVITY	Shiga Toxin 1 ---- 1 ng/mL Shiga Toxin 2 ---- 1 ng/mL	Shiga Toxin 1 ---- 7 pg/well Shiga Toxin 2 ---- 15 pg/well	Shiga Toxin 1 ---- 52 pg/mL Shiga Toxin 2 ---- 126 pg/mL
ANALYTICAL SPECIFICITY	Does not cross-react with the 49 bacteria ($\geq 10^7$ organisms/ml) evaluated.	Does not cross-react with the 42 bacteria (2.4×10^8 cfu/mL) evaluated.	Does not cross-react with the 20 bacteria ($> 1 \times 10^7$ cfu/mL) evaluated.
INTERFERING SUBSTANCES	The 49 bacteria tested do not interfere with the generation of a positive signal in the presence of toxins. No non – specific binding nor interference with a positive result was observed in the presence of 29% barium sulfate, 25 mg/g mucin, 50% Kaopectate, 25% PeptoBismol, 50% liquid Imodium, or 50% whole blood.	None of the bacteria tested interfered with the generation of a positive signal. No additional interference testing data is available.	None of the bacteria tested interfered with the generation of a positive signal. No additional interference testing data is available.
REPRODUCIBILITY	Six individual operators tested 27 samples on three consecutive days; 100% reproducibility for the qualitative OIA method.	Intra – assay variability ranged from 3.1 to 4.9% with an average of 3.9% Inter – assay variability ranged from 8.1 to 18.9% with an average of 9.5%	Intra – assay variability ranged from 4.0 to 15.6% with a mean of 8.7% Inter – assay variability ranged from 2.7 to 8.0% with a mean of 4.6%
Positive Agreement	Direct Stool – 100% (95% CI: 73.5 - 100%) vs. EHEC Broth Culture – 100% (95%CI: 73.5 - 100%) vs. EHEC	Direct Stool – 78.9% (95% CI: 56.6-91.5%) vs. culture Broth Culture – 100% (95%CI: 85.1 – 100%)	Direct Stool – 87.0% (95% CI: 66.4-97.2%) vs. culture Broth Culture – 95.5% (95%CI: 87.3 – 99.1%)
Negative Agreement	Direct Stool – 98% (95% CI: 95.6 – 99.4%) vs. EHEC Broth Culture – 99.6% (95%CI: 97.9 – 99.9%) vs. EHEC	Direct Stool – 95.8% (95% CI: 93.4 – 97.4%) vs. culture Broth Culture – 97.9% (95%CI: 95.2 – 99.1%) vs. culture	Direct Stool – 98.6% (95% CI: 96.7 – 99.5%) vs. culture Broth Culture – 98.7% (95%CI: 97.6 – 99.4%) vs. culture
PRIMARY COMPARISON METHOD	Premier EHEC	Cytotoxicity	Cytotoxicity

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Robin C. Hart, Ph. D.
Vice President of Regulatory and Quality Systems
Inverness Medical – BioStar Inc.
331 South 104th St.
Louisville, CO 80027

DEC 12 2006

Re: k061889
Trade/Device Name: BioStar® OIA® SHIGATOX
Regulation Number: 21 CFR 866.3255
Regulation Name: Escherichia coli serological reagents
Regulatory Class: Class I
Product Code: GMZ
Dated: September 20, 2006
Received: September 22, 2006

Dear Dr. Hart:

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.

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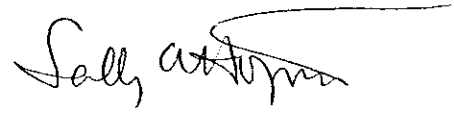
If you desire specific information about the application of labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at (240)276-0450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). Other general information on your responsibilities under the Act may be obtained 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): K061889

Device Name: BioStar® OIA® SHIGATOX

Indications For Use:

The BioStar® OIA® SHIGATOX assay is an Optical Immunoassay (OIA) test for the qualitative, rapid detection of the presence of Shiga Toxins in human diarrheal fecal specimens, broth cultures, and swab sampling of colonies from a culture plate. This test is intended for *in vitro* diagnostic use as an aid in the diagnosis of infection by Shiga Toxin-producing *Escherichia coli* (STEC), both O157 and all non – O157 Shiga toxin producing strains.

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

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

Concurrence of CDRH, Office of Device Evaluation (ODE)

Freddie W. Poole

Division Sign-Off

Office of In Vitro Diagnostic Device Evaluation and Safety

K061889