510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT COMBINATION TEMPLATE

A. 510(k) Number:

K172412

B. Purpose for Submission:

To obtain a substantial equivalence determination for the BacterioScan 216Dx System for qualitative determination of the presence or absence of viable bacteria in urine specimen.

C. Measurand:

Viable bacteria in urine specimen

D. Type of Test:

Qualitative determination of presence or absence of viable bacteria based on a predetermined density cut-off

E. Applicant:

BacterioScan, Ltd

F. Proprietary and Established Names:

BacterioScan 216Dx System

G. Regulatory Information:

1. Regulation section:

   21CFR 866.2560 Microbial growth monitor

2. Classification:

   Class I

3. Product code:

   QBQ

4. Panel:

   83- Microbiology

H. Intended Use:

1. Intended use(s):

   The BacterioScan 216Dx System is a semi-automated, *in vitro* diagnostic system (consisting of an instrument, software, and disposable Multicuvettes) that analyzes light scattering to measure any bacterial growth directly from urine sample incubated in trypticase soy broth. The BacterioScan 216Dx is for qualitative determination (presumptive positive or presumptive negative) of bacteriuria at a density of $\geq 5x10^4$ CFU/mL. The BacterioScan 216Dx results are intended for use in conjunction with other clinical and laboratory findings to aid in the diagnosis of Urinary Tract Infections (UTIs).

   The 216Dx System is not intended to provide bacteriuria levels, bacterial identification or differentiation. The system does not distinguish between growth of infecting, colonizing or contaminating bacteria, or if mixed urogenital flora are present. Presumptive positive urine samples must be cultured. Presumptive negative urine samples must be cultured if a low level of bacteriuria is suspected and is clinically relevant. The system also does not detect anaerobic bacteria, fungi/yeasts, fastidious organisms or those associated with sterile pyuria.

2. Indication(s) for use:

   Same as Intended Use

3. Special conditions for use statement(s):

   - For prescription use only
   - BacterioScan 216Dx Multicuvettes must be used only with the BacterioScan 216Dx System.
   - The BacterioScan 216Dx System is a qualitative test based on a defined cut-off and is not designed to provide bacteria quantitative information.
   - Failure to follow the BacterioScan 216Dx System procedures can result in assay failure or false results. Additionally, improper handling, loading, or contamination of the Multicuvette can generate false results.
   - During the clinical studies, the negative control (i.e. commercially available TSB) failure rate was 7.5%. One positive control and one negative control should be included in each instrument run.
   - The limit of detection for *Pseudomonas aeruginosa*, *Staphylococcus saprophyticus*, *Streptococcus agalactiae*, *Corynebacterium urealyticum* and *Aerococcus* spp. was above the defined cut-off ($5x10^4$ CFU/mL) and therefore may not be detected unless present in a sample at higher density levels.
   - The following substances in high concentration could interfere with performance:

Phenazopyridine (>200 µg/mL), Mucin (>0.039%, v/v), Bilirubin (>20 µg/mL), Leukocytes (>10^3 cells/mL), and blood (>0.0156%).

- Urine samples that are highly turbid, opaque, with intense coloration (e.g., dark yellow, orange) or visibly contaminated with blood should not be tested on the BacterioScan 216Dx System.
- In analytical interference studies, talcum powder (0.4% w/v) and *Haemophilus parainfluenzae* ($1.1x10^5$ CFU/mL) demonstrated interference (i.e., false positivity); acidic urine (pH 6.0) may interfere with the positivity of *Enterobacter cloacae* at density levels of $\leq 5x10^4$ CFU/mL.
- In the analytical studies, there were instances where *S. aureus* did not give positive results at the Limit of Detection (LoD) density level.
- In analytical inclusivity studies, consistent positive results with *Enterococcus faecium* at the defined cut-off were not observed.
- Laser warning statement (User Manual):
  Laser Radiation Class 1 Laser Product
  Avoid direct exposure to eyes. Do not manually open the instrument door unless instructed by BacterioScan

4. Special instrument requirements:

- BacterioScan 216Dx Instrument, handheld barcode scanner, a network appliance computer with pre-loaded software
- Disposable BacterioScan Multicuvettes

I. Device Description:

The BacterioScan 216Dx System consists of a self-contained benchtop 216Dx Instrument with a handheld barcode scanner, a network appliance computer with pre-loaded software, and required power and interconnecting Ethernet cable(s). One network appliance can support up to ten BacterioScan instruments.

BacterioScan provides Multicuvettes for use in the system, along with a calibrated pipettor for sample processing. The Multicuvettes are single-use disposable cartridges. One Multicuvette contains four cartridge wells and can be used to test up to four samples; up to four Multicuvettes may be processed by the 216Dx in a single run (16 samples total).

Using aseptic technique, 2.5 mL of sterile trypticase soy broth (TSB) and 360 µL of urine sample are added to each Multicuvette well. Inoculated Multicuvette can be placed in any available test position. Alternatively, remove any Multicuvettes that have completed testing to allow this position to be used for an untested, inoculated Multicuvette.

The 216Dx examines changes in optical signals over a 3-hour period. Optical signal changes represent bacterial growth in the urine samples. Testing can be interrupted periodically while loading or unloading Multicuvettes from the instrument. It is recommended that pausing the instrument be limited to removing used Multicuvettes, and/or to load a new Multicuvette. Pauses longer than 15 minutes or frequent pauses in operation will create data analysis gaps

that might adversely impact results. Once the testing of the Multicuvettes is finished, the sample analysis is available.

Interpretation

A "Presumptive Positive" result indicates that bacteriuria may be present in the sample at a density of $\geq 5x10^4$ CFU/mL. Samples reported as Presumptive Positive must be cultured for bacteriuria levels, mixed flora evaluation, organism isolation/identification, and antimicrobial susceptibility testing.

A "Presumptive Negative" result may indicate either one of the following:

a. No bacteriuria
b. Bacteriuria at densities below the defined cut-off ($5x10^4$ CFU/mL), or
c. Mixed urogenital flora contaminants (or other organisms not commonly associated with UTI) may be present in the sample, but not detected by the BacterioScan 216Dx.

Samples classified as Presumptive Negative by the 216Dx must be cultured if bacteriuria is suspected and considered clinically relevant. Other laboratory information and clinical symptoms must be considered for final determination of bacteriuria.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   BACTEC 9240 System

2. Predicate 510(k) number(s):

   K915796

3. Comparison with predicate:

Table 1: Comparison with the Predicate Device

Similarities		
Item	**Device** **BacterioScan 216Dx System** **(K172412)**	**Predicate** **BACTEC 9240 System** **(K915796)**
Intended Use	The BacterioScan 216Dx System is a semi-automated, *in vitro* diagnostic system (consisting of an instrument, software, and disposable Multicuvettes) that analyzes light scattering to measure any bacterial growth directly from urine sample incubated in trypticase soy broth. The BacterioScan 216Dx is for qualitative determination (presumptive positive or presumptive negative) of bacteriuria at a density of $\geq 5x10^4$ CFU/mL. The BacterioScan 216Dx results are intended for use in conjunction with other clinical and laboratory findings to aid in the diagnosis of Urinary Tract Infections (UTIs). The 216Dx System is not intended to provide bacteriuria levels, bacterial identification or differentiation. The system does not distinguish between growth of infecting, colonizing or contaminating bacteria, or if mixed urogenital flora are present. Presumptive positive urine samples must be cultured. Presumptive negative urine samples must be cultured if a low level of bacteriuria is suspected and is clinically relevant. The system also does not detect anaerobic bacteria, fungi/yeasts, fastidious organisms or those associated with sterile pyuria.	The BACTEC 9240 System (Instrument, Aerobic and Anaerobic F Culture Vials) is intended for the detection of aerobic and anaerobic microorganisms (bacteria and fungi) in clinical cultures of blood using a fluorescence - based detection system
Sample	Direct	Same
Growth media	Liquid	Same
Incubation	Required	Same
Technology	Continuous monitoring bacterial growth over a period of time in liquid medium during incubation	Same
Qualitative output	Presumptive positive/presumptive negative	Same

Differences		
Item	Device	Predicate
Sample type	Urine	Blood
Detection Technology	Laser light scattering analysis	Fluorescence analysis
Sample processing	360 µL urine and 2.5 mL trypticase soy broth (TSB) contained in one multicuvette well	5 – 7 mL blood and 40 mL enriched soybean-casein digest broth with CO_2 contained in one culture vial
Incubation time	Approximately 3 hours	Up to 5 – 7 days for negatives; positive ring/signal at any time

K. Standard/Guidance Document Referenced (if applicable):

Not applicable

L. Test Principle:

The BacterioScan 216Dx System uses laser light scattering to measure turbidity (particle density) of a prepared urine-broth sample during a period of incubation. The system is designed to kinetically capture digital measurements of sample turbidity at very low particle densities. Classification software analyzes these optical signal measurements, and interprets increasing turbidity as bacterial growth. Samples with robust growth during the second half of the test cycle, and/or high turbidity, are reported as "Presumptive Positive". Low turbidity samples that do not exhibit growth are classified as "Presumptive Negative." Results are available in approximately three hours.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

A reproducibility panel consists of *E. coli* and *E. faecalis* at high, moderate, and low density levels was tested at three sites, by two operators in quadruplicate for six non-consecutive days. All samples were blinded and randomized to the operator. For simplicity, results are presented for all levels and for high and moderate density levels combined (i.e. at or above the defined cut-off). Results stratified by operators, sites, and days are shown in Tables 2.1, 2.3, and 2.5 respectively.

Unspiked human urine (i.e. <50 CFU/mL) was used as a "negative" sample and the performance stratified by operators, sites, and days is shown in Tables 2.2, 2.4, and 2.6 respectively.

Table 2.1: Reproducibility Performance by Operator

Isolate	Density Level (CFU/mL)	# of Positive (% of total)						Total Pos/Total Tested	% Positive (95% CI)
		Site 1		Site 2		Site 3			
		Operator 1	Operator 2	Operator 1	Operator 2	Operator 1	Operator 2		
E. coli	All Levels ($1.87x10^3$-$5.03x10^5$)	68 (94.4)	67 (93.1)	72 (100)	72 (100)	66 (91.7)	63 (87.5)	408/432	94.4% (91.9%, 96.3%)
	High+ Moderate only ($1.20x10^4$-$5.03x10^5$)	48 (100)	48 (100)	48 (100)	48 (100)	47 (97.9)	44 (91.7)	283/288	98.3% (96.0%, 99.3%)
E. faecalis	All Levels ($2.37x10^3$ -$3.37x10^5$)	53 (73.6)	52 (72.2)	58 (80.6)	60 (83.3)	54 (75.0)	51 (70.8)	328/432	75.9% (71.7%, 79.7%)
	High+ Moderate only ($2.27x10^4$-$3.37x10^5$)	48 (100)	48 (100)	48 (100)	48 (100)	48 (100)	44 (91.7)	284/288	98.6% (96.5%, 99.5%)

Table 2.2: Negative Control Reproducibility Performance by Operator

Isolate	Density Level (CFU/mL)	# of Positive						Total Neg/ Total Tested	% Negative (95% CI)
		Site 1		Site 2		Site 3			
		Operator 1	Operator 2	Operator 1	Operator 2	Operator 1	Operator 2		
Unspiked Urine	<50	0	0	2	3	0	0	139/144	96.5% (92.1%, 99.5%)

Table 2.3: Reproducibility Performance by Site

Isolate	Density Level (CFU/mL)	# of Positive (% of total)			Total Pos/Total Tested	% Positive (95% CI)
		Site 1	Site 2	Site 3		
E. coli	All Levels ($1.87x10^3$-$5.03x10^5$)	135 (93.8)	144 (100)	129 (89.6)	408/432	94.4% (81.9%, 96.2%)
	High+ Moderate only ($1.20x10^4$-$5.03x10^5$)	96 (100)	96 (100)	91 (94.8)	283/288	98.3% (96.0%, 99.3%)
E. faecalis	All Levels ($2.37x10^3$ -$3.37x10^5$)	105 (72.9)	118 (81.9)	105 (72.9)	328/432	75.9% (71.7%, 79.7%)
	High+ Moderate only ($2.27x10^4$-$3.37x10^5$)	96 (100)	96 (100)	92 (95.8)	284/288	98.6% (96.5%, 99.5%)

Table 2.4: Negative Control Reproducibility Performance by Site

Isolate	Density Level (CFU/mL)	# of Positive (% of total)			Total Neg/Total Tested	% Negative (95% CI)
		Site 1	Site 2	Site 3		
Unspiked Urine	<50	0	5	0	139/144	96.5% (92.1%, 99.5%)

Table 2.5: Reproducibility Performance by Day

Isolate	Density Level (CFU/mL)	# of Positive (% of total)						Total Pos/Total Tested	% Positive (95% CI)
		Day 1	Day 2	Day 3	Day 4	Day 5	Day 6		
E. coli	All Levels ($1.87x10^3$-$5.03x10^5$)	65 (90.3)	71 (98.6)	71 (98.6)	69 (98.6)	65 (90.3)	67 (93.1)	408/432	94.4% (91.9%, 96.3%)
	High+ Moderate only ($1.20x10^4$-$5.03x10^5$)	44 (91.7)	48 (100)	48 (100)	48 (100)	47 (97.9)	48 (100)	283/288	98.3% (96.0%, 99.3%)
E. faecalis	All Levels ($2.37x10^3$ -$3.37x10^5$)	48 (66.7)	53 (73.6)	60 (91.7)	55 (76.4)	61 (84.7)	51 (70.8)	328/432	75.9% (71.7%, 79.7%)
	High+ Moderate only ($2.27x10^4$-$3.37x10^5$)	44 (91.7)	48 (100)	48 (100)	48 (100)	48 (100)	48 (100)	284/288	98.6% (96.5%, 99.5%)

Table 2.6: Negative Control Reproducibility Performance by Day

Isolate	Density Level (CFU/mL)	# of Positive (% of total)						Total Neg/Total Tested	% Negative (95% CI)
		Day 1	Day 2	Day 3	Day 4	Day 5	Day 6		
Unspiked Urine	<50	0	2	0	1	0	2	139/144	96.5% (92.1%, 99.5%)

The study demonstrated reproducible results across operators, sites and days for density level of $\geq 10^4$ CFU/mL. Results were acceptable at >95% (positivity: >98%; negativity: 96.5%).

b. *Linearity/assay reportable range:*

The linearity/dynamic range study was conducted to validate the accuracy of the 216Dx algorithm for extrapolation of the growth curve to determine the starting organism concentration and to assess the dynamic range of the assay for different bacterial species. The study included a panel consisting of three gram negative and three gram positive common UTI pathogens which were spiked into negative human urine and serially diluted to approximate clinical cut-off. Each inoculum concentration of each organism was tested in quadruplicates. The following organisms were evaluated and the density level in CFU/mL at which 100% (4/4) samples were positive is indicated in parenthesis: *E. coli* ($2.37x10^3$), *K. pneumoniae* ($1.70x10^3$), *E. faecalis* ($7.33x10^3$), *S. aureus* ($2.1x10^3$), *P. mirabilis* ($3.6x10^4$), and *E. faecium* ($4.03x10^5$).

Unspiked urine samples were used as negative control and were 100% negative (4/4)

Results demonstrated that the dynamic ranges of detection for each gram-negative and gram-positive organism are within the range of detection and the algorithm for reporting "Presumptive Negative" or "Presumptive Positive" are within the tested range of the dynamic range.

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*

A single positive and negative control were run on each instrument each day of testing at the clinical site during the comparative studies.

Positive Control

The positive control isolates are *E. coli* ATCC 25922, *K. pneumoniae* ATCC 700603, *E. faecalis* ATCC 29212, and *S. aureus* ATCC 29213 and they were tested at a rotating basis. The positive control rate was 99.6% (238/239) due to one *E. faecalis* QC failure.

Negative Control

Commercially available TSB (2.5 mL) pipetted into a multicuvette well is used as a negative control. The negative control rate was 92.5% (221/239). Due to the failure rate of 7.5% with the negative control, one positive and one negative control should be included in each instrument run. It is noted in the QC and the limitation sections of the package insert.

Recommendation added in the package insert is:

- Positive and negative controls in each instrument run
- Specify aseptic technique for negative control
- The run is invalid if negative control fails
- Negative control should be repeated as noted in Table 3 below.

Table 3: Invalid Calls and Recourse

Call	*Reason*	*Recourse*
Negative Control that is read as positive	Possible: TSB contamination Particle interference	Repeat negative control. If negative control repeat fails, notify technical support (See Troubleshooting Section)

The overall QC rate was 96.0% (459/478).

d. Detection limit:

A limit of detection (LoD) study was conducted to determine the estimated analytical sensitivity (the lowest organism density level detected with an approximate accuracy of ≥95%). Ten common and seven rare uropathogens were tested in the study. For initial LoD estimation, each strain was spiked into fresh, culture-negative human urine, serially dilution to four density levels at clinical cut-off and tested in quadruplicate to determine the approximate LoD.

Each strain was then tested in replicates of twenty at the approximated density. LoD was confirmed when density level performance demonstrated ≥95% or ≥19/20 (Presumptive Positive). The LoD (CFU/mL) was confirmed by 100% (20/20) positivity for the following UTI pathogens with LoD in parenthesis.

The organisms commonly recognized as UTI pathogens that were found to be approximately equivalent to the defined cut-off (10^4 CFU/mL) are noted below:

E. coli ($4.40x10^3$), *Proteus mirabilis* ($8.70x10^3$), *Enterobacter cloacae* ($6.67x10^3$), *Staphylococcus aureus* ($1.11x10^3$), *Klebsiella pneumoniae* ($1.37x10^4$), *Enterococcus faecalis* ($2.33x10^4$), and *Enterococcus faecium* ($4.37x10^4$). The rare UTI pathogens were: *Acinetobacter baumannii* ($1.60x10^4$), *Citrobacter freundii/koseri* ($2.80x10^4$), *Morganella morganii* ($4.23x10^4$), *Actinobaculum schaalii* ($2.80x10^4$), and *Corynebacterium striatum* ($4.03x10^4$).

The organisms commonly recognized as UTI pathogens that were found to have LoD higher than defined cut-off are:

Pseudomonas aeruginosa ($4.87x10^5$), *Staphylococcus saprophyticus* ($2.20x10^5$), *Streptococcus agalactiae* ($1.42x10^5$), *Aerococcus* spp. ($1.77x10^5$), and *Corynebacterium urealyticum* ($2.63x10^5$).

Information regarding these organisms was included in the Limitations section of the package insert.

Analytical Inclusivity

To demonstrate analytical inclusivity, multiple strains of each common and rare UTI pathogen were tested on the 216Dx System. All strains were spiked into fresh, culture-negative human urine, serially diluted to a bacteriuria density of approximately 2-3x LoD for each individual organism to be tested. All samples were

evaluated in quadruplicate. There were ten common and seven rare uropathogens comprising of 85 and 18 strains respectively.

The uropathogens tested were *Escherichia coli* (10)*, Klebsiella pneumoniae* (9)*, Enterobacter* spp. (8), *Pseudomonas aeruginosa* (9)*, Proteus mirabilis* (9)*, Enterococcus faecalis* (8)*, Enterococcus faecium* (5)*, Staphylococcus aureus* (9)*, Staphylococcus saprophyticus* (9)*,* and *Streptococcus agalactiae* (9)*;* the positivity rate was 98.8% (336/340).

When stratified, the positivity rate was 85% (17/20) at density level range of $3.20x10^4$ to $1.03x10^5$ CFU/mL for *E. faecium*, and 97.2% (35/36 due to one failure at $4.90x10^3$) or density level range of $4.90x10^3$ to $5.57x10^4$ CFU/mL for *S. aureus.* Because of the 85% positive rate, a limitation for *E. faecium* was added in the package insert:

"*In analytical inclusivity studies, consistent positive results with Enterococcus faecium at the defined cut-off were not observed."*

The rare uropathogens tested were *Acinetobacter baumannii* (3)*, Actinobaculum schaalii* (1)*, Aerococcus* spp. (3), *Citrobacter* spp. (5), *Corynebacterium striatum* (1)*, Corynebacterium urealyticum* (1)*,* and *Morganella morganii* (4)*;* the positivity rate was 100% (72/72).

Unspiked urine samples were 100% negative (8/8).

e. Analytical specificity:

Endogenous or Exogenous Substances/Microbial Interference

This study was conducted to evaluate the 216Dx performance in the presence of endogenous or exogenous substances that may be found in urine, or various organisms present in urine that are not expected to grow under the standard conditions in the BacterioScan system. Representative strains of four gram-negative (*E. coli, K. pneumoniae, P. mirabilis,* and *E. cloacae*) and three gram-positive (*E. faecalis, E. faecium,* and *S. aureus*) UTI pathogens at 2-3x LoD density level were spiked into fresh, culture-negative human urine that had first been spiked with an interfering substance/microorganism. A corresponding unspiked urine control was included for each interfering substance/organism.

There were a total of 17 interfering substances tested:
Albumin, glucose, phenazopyridine, seminal fluid, talcum powder, blood, bilirubin, acetaminophen, ibuprofen, mucin, human Chorionic Gonadotrophin (hCG), testosterone, cortisol, progesterone, leukocytes, fluconazole, and flucytosine.

Acidic urine and alkaline urine were also tested.

Three potentially interfering organisms were tested:
H. influenzae, H. parainfluenzae, and *N. gonorrhoeae*

To confirm that the 216Dx could detect each organism at the densities tested, corresponding urine samples lacking each interfering substance/microorganism were processed in parallel and evaluated in the 216Dx concurrently. All samples were evaluated in replicates of four.

The results indicated that the majority of potential substances that may be found in human urine did not interfere with the 216Dx's performance. The following substances with concentrations were noted to interfere with performance:

- Phenazopyridine >200 µg/mL
- Blood >0.0156%
- Bilirubin >20 µg/mL
- Mucin >0.039%, v/v
- Leukocytes $>10^3$ cells/mL
- Talcum powder of 0.4% w/v and *H. parainfluenzae* at 1.1 x 10^5 CFU/mL demonstrated false positivity in unspiked urine
- Acidic urine (pH 6.0) interfered with the positivity of *Enterobacter cloacae* at density levels of 8 x 10^4 CFU/mL.

The study also showed that there were instances where *S. aureus* did not give positive results at density level of 10^3 CFU/mL which is the LoD for *S. aureus*. Limitation for *S. aureus* is noted in the Limitations section of the package insert:

"*In the analytical studies, there were instances where S. aureus did not give positive results at the Limit of Detection density level*."

Potential sources of interference are specified in the Limitations section of the package insert.

f. Assay cut-off:

$\geq 5x10^4$ CFU/mL

2. Comparison studies:

a. Method comparison with predicate device:

Not Applicable

b. Matrix comparison :

Not Applicable

3. Clinical studies :

Comparative studies were conducted at three geographically diverse sites for urine samples received in the laboratory for routine urine culture. Urine samples were tested in

accordance with BacterioScan instructions for use and compared with the reference culture results. Reference testing was performed using 1 and 10 µL loops. Using each loop, colony count plates were performed in triplicate, and a median result was generated for each loop size. Median colony count was determined to be the reference result and were compared to the 216Dx result. Any colony counts at or above $5x10^4$ CFU/mL are considered a positive result for the primary analysis for evaluating performance. A secondary analysis was also performed by taking into account pathogens commonly associated with UTI (UTI-Associated). Performance was also evaluated for subpopulation with bacterial densities of $\geq 1x10^5$ CFU/mL. Organisms isolated from reference colony counts of $\geq 5x10^4$ CFU/mL were identified by Matrix Assisted Laser Desorption Ionization (MALDI) analysis.

Samples measured and containing bacteriuria of $\geq 5x10^4$ CFU/mL is reported by the BacterioScan 216Dx to be "Presumptive Positive."

The pathogens commonly associated with UTI (UTI Associated) that were encountered in the clinical studies were:
Escherichia coli, Klebsiella pneumoniae, Klebsiella oxytoca, Proteus mirabilis, Enterobacter cloacae, Pseudomonas aeruginosa, Enterococcus faecalis, Enterococcus faecium, Aerococcus urinae, Streptococcus agalactiae, and *Staphylococcus aureus;*

The rare uropathogens encountered were:
Enterobacter aerogenes, Citrobacter freundii, Citrobacter koseri, Acinetobacter baumannii, Morganella morganii, Aerococcus sanguinicola, Corynebacterium striatum, and *Staphylococcus saprophyticus.*

a. *Clinical Sensitivity:*

   Of the 3,153 urine samples tested, 3,052 were evaluable for the primary analysis of bacteriuria at the defined cut-off, $\geq 5x10^4$ CFU/mL. For the secondary analysis, the evaluable specimens were 3,010 for $\geq 5x10^4$ CFU/mL and 3,020 for $\geq 1x10^5$ CFU/mL because the identity of some organisms was not obtained in the reference culture for the secondary analysis of $5x10^4$ CFU/mL.

   All BacterioScan 216Dx results are reported as presumptive. The overall performance for bacterial density of $\geq 5x10^4$ CFU/mL is shown in Table 4. The performance for subpopulation with bacterial density of $\geq 1x10^5$ CFU/mL is shown in Table 5.

Table 4: Overall Performance for Bacterial Density of ≥5x10^4 CFU/mL							
		Primary Analysis: Bacteriuria			**Secondary Analysis: UTI Associated** *		
		Reference			Reference		
		Positive	Negative	Total	Positive	Negative	Total
BacterioScan 216Dx	Positive	714	576	1290	592	672	1264
	Negative	87	1675	1762	14	1732	1746
	Total	801	2251	3052	606	2404	3010
Sensitivity	89.1% (714/801) 95% CI: 86.8%; 91.1%				97.7% (592/606) 95% CI: 96.2%; 98.6%		
Specificity	74.4% (1675/2251) 95% CI: 72.6%; 76.2%				72.0 (1732/2404) 95% CI: 70.2%; 73.8%		
PPV	55.3% (714/1290) 95% CI: 52.6%; 58.0%				46.8% (592/1264) 95% CI: 44.1%; 49.6%		
NPV	95.1% (1675/1762) 95% CI: 93.9%; 96.0%				99.2% (1732/1746) 95% CI: 98.7%; 99.5%		

* Limited to bacterial pathogens encountered in the clinical studies

Table 5: Performance for Subpopulation with Bacterial Density of ≥1x10^5 CFU/mL							
		Primary Analysis: Bacteriuria			**Secondary Analysis: UTI Associated** *		
		Reference			Reference		
		Positive	Negative	Total	Positive	Negative	Total
BacterioScan 216Dx	Positive	581	709	1290	501	767	1268
	Negative	40	1722	1762	7	1745	1752
	Total	621	2431	3052	508	2512	3020
Sensitivity	93.6% (581/621) 95% CI: 91.3%; 95.2%				98.6% (501/508) 95% CI: 97.2%; 99.3%		
Specificity	70.8% (1722/2431) 95% CI: 69.0%; 72.6%				69.5% (1745/2512) 95% CI: 67.6%; 71.2%		
PPV	45.0% (581/1290) 95% CI: 42.3%; 47.8%				39.5% (501/1268) 95% CI: 36.9%; 42.2%		
NPV	97.7% (1722/1762) 95% CI: 95% CI: 96.9%; 98.3%				99.6% (1745/1752) 95% CI: 99.2%; 99.8%		

* Limited to bacterial pathogens encountered in the clinical studies

Analysis by study site is shown in Tables 6-8.

Table 6: Site 1 Performance for Bacterial Density of ≥5x10^4 CFU/mL							
		Primary Analysis: Bacteriuria			**Secondary Analysis: UTI Associated** *		
		Reference			Reference		
		Positive	Negative	Total	Positive	Negative	Total
BacterioScan 216Dx	Positive	258	212	470	226	238	464
	Negative	14	524	538	2	531	533
	Total	272	736	1008	228	769	997
Sensitivity	94.9% (258/272) 95% CI: 91.5%; 96.9%				99.1% (226/228) 95% CI: 96.9%; 99.8%		
Specificity	71.2% (524/736) 95% CI: 67.8%; 74.4%				69.1% (531/769) 95% CI: 65.7%; 72.2%		
PPV	54.9% (258/470) 95% CI: 50.4%; 59.3%				48.7% (226/464) 95% CI: 44.2%; 53.2%		
NPV	97.4% (524/538) 95% CI: 95.7%; 98.4%				99.6% (531/533) 95% CI: 98.6%; 99.9%		

* Limited to bacterial pathogens encountered in the clinical studies

Table 7: Site 2 Performance for Bacterial Density of ≥5x10^4 CFU/mL							
		Primary Analysis: Bacteriuria			**Secondary Analysis: UTI Associated** *		
		Reference			Reference		
		Positive	Negative	Total	Positive	Negative	Total
BacterioScan 216Dx	Positive	180	162	342	139	191	330
	Negative	36	655	691	4	681	685
	Total	216	817	1033	143	872	1015
Sensitivity	83.3% (180/216) 95% CI: 77.8%; 87.7%				97.2% (139/143) 95% CI: 93.0%; 98.9%		
Specificity	80.2% (655/817) 95% CI: 77.3%; 82.8%				78.1% (681/872) 95% CI: 75.2%; 80.7%		
PPV	52.6% (180/342) 95% CI: 47.3%; 57.9%				42.1% (139/330) 95% CI: 36.9%; 47.5%		
NPV	94.8% (655/691) 95% CI: 92.9%; 96.2%				99.4% (681/685) 95% CI: 98.5%; 99.8%		

* Limited to bacterial pathogens encountered in the clinical studies

Table 8: Site 3 Performance for Bacterial Density of ≥5x10^4 CFU/mL							
		Primary Analysis: Bacteriuria			**Secondary Analysis: UTI Associated** *		
		Reference			Reference		
		Positive	Negative	Total	Positive	Negative	Total
BacterioScan 216Dx	Positive	276	202	478	227	243	470
	Negative	37	496	533	8	520	528
	Total	313	698	1011	235	763	998
Sensitivity	88.2% (276/313) 95% CI: 84.1%; 91.3%				96.6% (227/235) 95% CI: 93.4%; 98.3%		
Specificity	71.1% (496/698) 95% CI: 67.6%; 74.3%				68.2% (520/763) 95% CI: 64.8%; 71.4%		
PPV	57.7% (276/4783) 95% CI: 53.3%; 62.1%				48.3% (227/470) 95% CI: 43.8%; 52.8%		
NPV	93.1% (496/533) 95% CI: 90.6%; 94.9%				98.5% (520/528) 95% CI: 97.0%; 99.2%		

* Limited to bacterial pathogens encountered in the clinical studies

Analysis by gender is shown in Tables 9-10.

Table 9: Performance for Bacterial Density of ≥5x10^4 CFU/mL (Male)							
		Primary Analysis: Bacteriuria			**Secondary Analysis: UTI Associated** *		
		Reference			Reference		
		Positive	Negative	Total	Positive	Negative	Total
BacterioScan 216Dx	Positive	127	154	281	101	172	273
	Negative	6	577	583	3	580	583
	Total	133	731	864	104	752	856
Sensitivity	95.6% (127/133) 95% CI: 90.5%; 97.9%				97.1% (101/104) 95% CI: 91.9%; 99.0%		
Specificity	78.9% (577/731) 95% CI: 75.8%; 81.7%				77.1% (580/752) 95% CI: 74.0%; 80.0%		
PPV	45.2% (127/281) 95% CI: 39.5%; 51.0%				37.0% (101/273) 95% CI: 31.5%; 42.9%		
NPV	99.0% (577/583) 95% CI: 97.8%; 99.5%				99.5% (580/583) 95% CI: 98.5%; 99.8%		

* Limited to bacterial pathogens encountered in the clinical studies

Table 10: Performance for Bacterial Density of ≥5x10^4 CFU/mL (Female)							
		Primary Analysis: Bacteriuria			**Secondary Analysis: UTI Associated** *		
		Reference			Reference		
		Positive	Negative	Total	Positive	Negative	Total
BacterioScan 216Dx	Positive	587	422	1009	491	500	991
	Negative	81	1094	1179	11	1152	1163
	Total	668	1520	2188	502	1652	2154
Sensitivity	87.9% (587/668) 95% CI: 85.2%; 90.1%				97.8% (491/502) 95% CI: 96.1%; 98.8%		
Specificity	72.2% (1094/1520) 95% CI: 69.9%; 74.4%				69.7% (1152/1652) 95% CI: 67.5%; 71.9%		
PPV	58.2% (587/1009) 95% CI: 55.1%; 61.2%				49.5% (491/991) 95% CI: 46.4%; 52.7%		
NPV	93.1% (1094/1179) 95% CI: 91.5%; 94.4%				99.1% (1152/1163) 95% CI: 98.3%; 99.5%		

* Limited to bacterial pathogens encountered in the clinical studies

Preserved and unpreserved urine samples were collected during the clinical studies. Urine samples collected in container without preservatives (e.g., boric acid) were unpreserved while those collected in container with preservatives were preserved. They were stratified for analysis. Most of the urine samples were preserved (76.2%, 2326/3052). The performance is shown in Tables 11-14.

Table 11: Overall Performance for Bacterial Density of ≥5x10^4 CFU/mL (Unpreserved Samples)							
		Primary Analysis: Bacteriuria			**Secondary Analysis: UTI Associated** *		
		Reference			Reference		
		Positive	Negative	Total	Positive	Negative	Total
BacterioScan 216Dx	Positive	131	120	251	97	143	240
	Negative	29	446	475	4	465	469
	Total	160	566	726	101	608	709
Sensitivity	81.9% (131/160) 95% CI: 75.2%; 87.1%				96.0% (97/101) 95% CI: 90.3%; 98.4%		
Specificity	78.8% (446/566) 95% CI: 75.2%; 82.0%				76.5% (465/608) 95% CI: 72.9%; 79.7%		
PPV	52.2% (131/251) 95% CI: 46.0%; 58.3%				40.4% (97/240) 95% CI: 34.4%; 46.7%		
NPV	93.9% (446/475) 95% CI: 91.4%; 95.7%				99.1% (465/469) 95% CI: 97.8%; 99.7%		

* Limited to bacterial pathogens encountered in the clinical studies

Table 12: Performance for Subpopulation of ≥1x10^5 CFU/mL (Unpreserved Samples)							
		Primary Analysis: Bacteriuria			**Secondary Analysis: UTI Associated** *		
		Reference			Reference		
		Positive	Negative	Total	Positive	Negative	Total
BacterioScan 216Dx	Positive	106	145	251	78	162	240
	Negative	14	461	475	2	469	471
	Total	120	606	726	80	631	711
Sensitivity	88.3% (106/120) 95% CI: 81.4%; 92.9%				97.5% (78/80) 95% CI: 91.3%; 99.3%		
Specificity	76.1% (461/606) 95% CI: 72.5%; 79.3%				74.3% (469/631) 95% CI: 70.8%; 77.6%		
PPV	42.2% (106/251) 95% CI: 36.3%; 48.4%				32.5% (78/240) 95% CI: 26.9%; 38.7%		
NPV	97.1% (461/475) 95% CI: 95.1%; 98.2%				99.6% (469/471) 95% CI: 98.5%; 99.9%		

* Limited to bacterial pathogens encountered in the clinical studies

Table 13: Overall Performance or Bacterial Density of ≥5x10^4 CFU/mL (Preserved Samples)							
		Primary Analysis: Bacteriuria			**Secondary Analysis: UTI Associated** *		
		Reference			Reference		
		Positive	Negative	Total	Positive	Negative	Total
BacterioScan 216Dx	Positive	583	456	1039	495	529	1024
	Negative	58	1229	1287	10	1267	1277
	Total	641	1685	2326	505	1796	2301
Sensitivity	91.0% (583/641) 95% CI: 88.5%; 92.9%				98.0% (495/505) 95% CI: 96.4%; 98.9%		
Specificity	72.9% (1229/1685) 95% CI: 70.8%; 75.0%				70.5% (1267/1796) 95% CI: 68.4%; 72.6%		
PPV	56.1% (583/1039) 95% CI: 53.1%; 59.1%				48.3% (495/1024) 95% CI: 45.3%; 51.4%		
NPV	95.5% (1229/1287) 95% CI: 94.2%; 96.5%				99.2% (1267/1277) 95% CI: 98.6%; 99.6%		

* Limited to bacterial pathogens encountered in the clinical studies

Table 14: Performance for Subpopulation of ≥1x10^5 CFU/mL (Preserved Samples)							
		Primary Analysis: Bacteriuria			**Secondary Analysis: UTI Associated** *		
		Reference			Reference		
		Positive	Negative	Total	Positive	Negative	Total
BacterioScan 216Dx	Positive	475	564	1039	423	605	1028
	Negative	26	1261	1287	5	1276	1281
	Total	501	1825	2326	428	1881	2309
Sensitivity	94.8% (475/501) 95% CI: 92.5%; 96.4%				98.8% (423/428) 95% CI: 97.3%; 99.5%		
Specificity	69.1% (1261/1825) 95% CI: 66.9%; 71.2%				67.8% (1276/1881) 95% CI: 65.7%; 69.9%		
PPV	45.7% (475/1039) 95% CI: 42.7%; 48.8%				41.1% (423/1028) 95% CI: 38.2%; 44.2%		
NPV	98.0% (1261/1287) 95% CI: 97.1%; 98.6%				99.6% (1276/1281) 95% CI: 99.1%; 99.8%		

* Limited to bacterial pathogens encountered in the clinical studies

The reporting results for the BacterioScan 216Dx is for bacteriuria of 5x10^4 CFU/mL; presumptive positive is for bacteriuria ≥5x10^4 CFU/mL and presumptive negative is for bacteriuria <5x10^4 CFU/mL. The performance supports the intended use of "*Presumptive positive urine samples must be cultured. Presumptive negative urine samples must be cultured if a low level of bacteriuria is suspected and is clinically relevant*."

b. Clinical specificity:

Same as demonstrated in item a. above

c. Other clinical supportive data (when a. and b. are not applicable):

Not applicable

4. Clinical cut-off:

Non-applicable

5. Expected values/Reference range:

There were 3,052 urine samples from three geographically dispersed clinical sites. The percentage of positive cases (positivity rate) determined by the reference culture method was 26.2% (801/3052) and 42.3% (1290/3052) by the 216Dx instrument. It was consistent across the U.S. sites.

N. Instrument Name:

BacterioScan 216Dx System

O. System Descriptions:

1. Modes of Operation:

   Does the applicant's device contain the ability to transmit data to a computer, webserver, or mobile device?

   Yes ____X____ or No _____

   Does the applicant's device transmit data to a computer, webserver, or mobile device using wireless transmission?

   Yes _____ or No ____X____

2. Software:

   FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

   Yes ___X_____ or No _____

3. Specimen Identification:

   The user logs into the 216Dx interface and is prompted to associate a patient sample ID with a multicuvette serial number and well location. Briefly, the user scans or manually enters the multicuvette serial number. Next, the user enters and saves the individual sample IDs for each of the four well positions.

4. Specimen Sampling and Handling:

   The user pipettes 2.5 mL of sterile TSB into each multicuvette well using a sterile 5 mL pipette tip. A 360 µl aliquot of an individual urine sample is transferred to the corresponding multicuvette well. Once specimens are pipetted into the multicuvette, it is ready to be run in the 216Dx instrument.

5. Calibration:

   No calibration by the user is required.

6. Quality Control:

   Negative and positive quality controls should be tested on board the instrument in accordance with the instructions provided in the product labeling.

P. Other Supportive Instrument Performance Characteristics Data Not Covered In The "Performance Characteristics" Section above:

Not applicable

Q. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Parts 809.10.

R. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.