Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002
www.fda.gov

510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

I Background Information:

A 510(k) Number

K192355

B Applicant

Beckman Coulter, Inc.

C Proprietary and Established Names

MicroScan Dried Gram Negative MIC/Combo Panels with Meropenem (Mer) (0.004-32ug/mL)

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
JWY	Class II	21 CFR 866.1640 - Antimicrobial Susceptibility Test Powder	MI - Microbiology

II Submission/Device Overview:

A Purpose for Submission:

To obtain a substantial equivalence determination for meropenem at concentrations of 0.004 – 32 µg/mL with the MicroScan Dried Gram-Negative MIC/Combo Panels for susceptibility testing of non-fastidious gram negative organisms.

B Measurand:

Meropenem in the dilution range of 0.004-32 µg/mL

C Type of Test:

Quantitative antimicrobial susceptibility test (AST)

III Intended Use/Indications for Use:

A Intended Use(s):

MicroScan Dried Gram-Negative MIC/Combo Panels are designed for use in determining quantitative and/or qualitative antimicrobial agent susceptibility of colonies grown on solid media of rapidly growing aerobic and facultative gram-negative bacilli.

B Indication(s) for Use:

The MicroScan Dried Gram-Negative MIC/Combo Panel is used to determine quantitative and/or qualitative antimicrobial agent susceptibility of colonies grown on solid media of rapidly growing aerobic and facultative anaerobic gram-negative bacilli. After inoculation, panels are incubated for 16 - 20 hours at 35 °C +/- 1 °C in a non-CO_2 incubator, and read either visually or with MicroScan instrumentation, according to the Package Insert.

This particular submission is for updated breakpoints of *Enterobacteriaceae* and *Pseudomonas aeruginosa* for the antimicrobial meropenem (Mer) at concentrations of 0.004 to 32 ug/mL to the test panel.

Meropenem has been shown to be active in vitro against most strains of microorganisms listed below, as described in the FDA-approved package insert for this antimicrobial agent.

Active in vitro and in clinical infections against:

Escherichia coli
Klebsiella pneumoniae
Proteus mirabilis
Pseudomonas aeruginosa

Active in vitro but clinical significance is unknown:

Citrobacter freundii
Citrobacter koseri
Enterobacter cloacae
Hafnia alvei
Klebsiella oxytoca
Morganella morganii
Proteus vulgaris
Serratia marcescens

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

Limitations
The ability of the MicroScan Dried Gram Negative Panels to detect resistance to meropenem is unknown for the following species because an insufficient number of resistant strains were available at the time of comparative testing: *C. koseri* and *P. vulgaris*. Isolates yielding MIC results suggestive of a resistant interpretive category should be submitted to a reference laboratory.

Due to the occurrence of very major errors with meropenem and tubidity inoculation with all read methods, isolates of *K. pneumoniae* that provide an MIC of 1 µg/mL should be retested using an alternative/reference method.

D Special Instrument Requirements:

MicroScan panels can be read either manually or automatically on the WalkAway or autoSCAN-4 instrument systems.

IV Device/System Characteristics:

A Device Description:

The MicroScan Dried Gram-Negative MIC/Combo panel with meropenem is used to determine the quantitative and/or qualitative antimicrobial agent susceptibility of aerobic and facultatively anaerobic gram-negative bacilli colonies grown on solid media. After inoculation, panels are incubated for 16-20 hours at 35°C ± 1° in a non-CO_2 incubator and read either visually or with MicroScan instrumentation according to the package insert.

Inoculation methods: Turbidity or Prompt Inoculation System

Read methods: Manual, MicroScan WalkAway System and MicroScan autoSCAN-4

B Principle of Operation:

The antimicrobial susceptibility tests are dehydrated miniaturizations of the broth dilution susceptibility test. Various antimicrobial agents are diluted in Mueller Hinton broth supplemented with calcium and magnesium to concentrations spanning the range of clinical interest. Breakpoint Combo panels use concentrations equivalent to the categorical breakpoints of FDA and/or CLSI. After inoculation and rehydration with a standardized suspension of organism and incubation at 35°C for a minimum of 16 hours, the minimum inhibitory concentration (MIC) for the test organism is determined by observing the lowest antimicrobial concentration showing inhibition of growth.

V Substantial Equivalence Information

A Predicate Device Name(s):
MicroScan Dried Gram Negative MIC/Combo Panels with Eravacycline (ERV) (0.016-32 ug/mL)

B Predicate 510(k) Number(s):
K190109

C Comparison with Predicate(s):

Table 1. Comparison with Predicate

Device & Predicate Device(s):	**Device: K192355**	**Predicate: K190109**
Device Trade Name	MicroScan Dried Gram Negative MIC/Combo Panels - Meropenem	MicroScan Dried Gram Negative MIC/Combo Panels - Eravacycline
General Device Characteristic Similarities		
Intended Use/Indications For Use	Determination of susceptibility to with gram-negative bacilli	Determination of susceptibility with gram-negative bacilli
Technology	Overnight microdilution MIC susceptibility test	Same
Specimen	Isolated colonies from culture	Same
Incubation Temperature	35 °C ± 1°C	Same
Incubation Atmosphere	Aerobic	Same
Incubation Time	16-20 hours	Same
Reading Method	Automated (WalkAway or autoSCAN-4) or Manual	Same
Result Reported	Report results as minimum inhibitory concentration (MIC) and categorical interpretation (SIR)	Same
General Device Characteristic Differences		
Antimicrobial Agent	Dried Meropenem 0.004 – 32 µg/mL	Dried Eravacycline 0.016 – 32 µg/mL

VI Standards/Guidance Documents Referenced:

1. Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems; Guidance for Industry and FDA
2. CLSI M07-A10. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically. 10th ed. (January 2015)
3. CLSI M100. Performance Standards for Antimicrobial Susceptibility Testing. 29th ed. (January 2019)

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

A reproducibility study was conducted at three external sites using 10 isolates of gram-negative bacilli that were consistent with the intended use. The range of meropenem dilutions tested was 0.004-32 µg/mL. Isolates were tested in triplicate over three days for a total of 270 data points (27 data points per isolate). The isolates tested in the reproducibility study included: *C. freundii* complex (1 isolate), *E. aerogenes* (3 isolates), *E. cloacae* (2 isolates), *E. coli* (1 isolate), *K. oxytoca* (1 isolates) and *P. aeruginosa* (2 isolates).

Inocula were prepared using both the turbidity and Prompt methods and results were read manually (visually) and with the WalkAway and autoSCAN-4 instrument systems. All data points were on-scale and the majority were within ± one doubling dilution of the mode MIC (Table 2). Because all results were on-scale, only a single result is reported for each read method.

The reproducibility results are acceptable.

Table 2. Reproducibility of Meropenem with all Inoculation and Read Methods

Read Method	Reproducibility No. within ±dilution of the mode MIC value (%)	
	Prompt Inoculation	**Turbidity Inoculation**
WalkAway	262/270 (97.0)	266/270 (98.5)
autoSCAN-4	263/270 (97.4)	268/270 (99.3)
Manual	269/270 (99.6)	270/270 (100.0)

2. Linearity:

Not Applicable

3. Analytical Specificity/Interference:

Not Applicable

4. Assay Reportable Range:

Not Applicable

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

Inoculum Density Check. A spectrophotometric device, the MicroScan Turbidity Meter, was used to ensure the accuracy of the turbidity inoculation method. A zero check of the turbidity meter was performed daily. The inocula prepared using the turbidity method were standardized using a reading of 0.08 ± 0.02 (equivalent to a 0.5 McFarland barium sulfate

turbidity standard). The digital reading was recorded for each isolate and was considered acceptable based on recommendations in the *Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems*.

Inoculum density data for the Prompt inoculation system was collected from suspensions of the QC strain *E. coli* ATCC 25922 and for all reproducibility isolates. Average colony counts were within the acceptable range for the QC strain and for all reproducibility isolates except for *K. oxytoca* which showed an elevated colony count at one testing site; however, the reproducibility observed with *K. oxytoca* was acceptable.

Purity Check. Purity checks were performed on all isolates for each inoculum preparation; only results from pure cultures were included.

Growth Failure Rate. Less than 10% of isolates demonstrated no growth on the dried test panel

Quality Control Testing. The CLSI-recommended QC organisms *E. coli* ATCC 25922 and *P. aeruginosa* ATCC 27853 were tested with all inoculation and read methods using fourteen dilutions of meropenem (0.004 – 32 µg/mL). The reference panel was inoculated using the turbidity method only. In this submission, the QC range for *P. aeruginosa* ATCC 27853 is being updated to the current recommended range of 0.12 – 1 µg/mL from the range of 0.25 – 1 µg/mL utilized for the original meropenem clearance (K971376). For both QC strains, quality control results were within the acceptable range for all inoculation and read methods. Results of current QC testing are shown in Table 3 below and demonstrate that acceptable QC results can be obtained with this device for > 95% of tests.

Table 3. Quality Control Results for all Inoculation and Read Methods for Meropenem

Organism	Conc. (µg/mL)	Reference[a]	Prompt Inoculation Method			Turbidity Inoculation Method		
			Manual	WalkAway	AS4	Manual	WalkAway	AS4
E. coli ATCC 25922 Expected Range: 0.008-0.06 µg/mL	≤0.004	1	-	-	-	-	-	-
	0.008	1	-	-	-	-	-	-
	0.015	149	77	57	65	131	139	139
	0.03	36	111	138	130	56	49	47
	0.06	-	9	-	-	-	-	-
	0.12	1	1	1	1	-	-	-
	0.25	-	1	2	2	-	-	-
	0.5	-	-	-	-	-	-	-
	1	-	-	-	-	-	-	-
	2	-	-	-	-	-	-	-
	4	-	-	-	-	1	1	1
	8	1	1	1	1	1	1	1
	16	-	-	-	-	-	-	-
	32	-	-	-	-	-	-	-
	>32	-	-	1	1	-	-	-
P. aeruginosa ATCC 27853	≤0.004	-	-	-	-	-	-	-
	0.008	-	-	-	-	-	-	-
	0.015	-	-	-	-	-	-	-
	0.03	-	-	-	-	-	-	-

Organism	Conc. (µg/mL)	Reference[a]	Prompt Inoculation Method			Turbidity Inoculation Method		
			Manual	WalkAway	AS4	Manual	WalkAway	AS4
Expected Range: 0.12 – 1.0 µg/mL	0.06	-	-	-	-	-	-	-
	0.12	-	-	-	-	1	-	-
	0.25	122	179	142	154	171	132	149
	0.50	59	20	49	38	10	37	24
	1	7	2	11	8	4	16	11
	2	-	-	-	-	-	-	-
	4	-	-	-	-	1	1	1
	8	1	-	-	-	-	-	-
	16	-	-	-	-	-	-	-
	32	-	-	-	-	-	-	-
	>32	-	-	-	-	-	-	-

[a] Reference panel was inoculated using the turbidity method and read manually

6. Detection Limit:

   Not Applicable

7. Assay Cut-Off:

   Not Applicable

8. Accuracy (Instrument):

   No Applicable

9. Carry-Over:

   Not Applicable

B Comparison Studies:

1. Method Comparison with Predicate Device:

   The results obtained with the MicroScan Dried Gram-Negative MIC/Combo Panel with meropenem (dilution range 0.004 – 32 µg/mL) were compared to results obtained using a frozen broth microdilution reference panel (dilution range 0.004 – 32 µg/mL). Clinical isolates were evaluated at three testing sites in the U.S in a single study; challenge isolates were evaluated in two separate studies performed at internal and external sites.

   The reference panel was prepared as described in CLSI document M07-A10 except for the use of Pluronic-F in the inoculum water for the reference panel. A validation study was performed to demonstrate the equivalence between reference panels inoculated with organisms suspended in water supplemented with Pluronic-F and reference panels inoculated with autoclaved deionized water without Pluronic-F. The effect of Pluronic-F in the reference panel was determined with 11 replicates each of the quality control strains *E. coli* ATCC 25922 and *P. aeruginosa* ATCC 27853; 100% of results were within the expected QC range with both inoculum preparations.

For the reference method and MicroScan panels inoculated using the turbidity method, panels were inoculated using the same standardized suspension further diluted into 25 mL of water with Pluronic-D (for the MicroScan dried panels) or Pluronic-F (for the frozen reference panels). MicroScan panels were also inoculated using the Prompt inoculation method with isolates inoculated into the Prompt inoculation bottle. Reference panels were read manually (visually); MicroScan panels inoculated with both inoculation methods were read using the WalkAway and autoSCAN-4 instruments and by manual read.

Clinical Study
To determine the performance of the MicroScan Dried Gram-Negative MIC/Combo Panel with Meropenem, a total of 528 *Enterobacteriaceae* clinical isolates were evaluated with all inoculation and read methods (Tables 4 and 5). The testing included the following indicated species: *C. freundii* (15 isolates), *C. koseri* (3 isolates), *E. cloacae* complex (41 isolates), *E. coli* (214 isolates), *H. alvei* (1 isolate), *K. oxytoca* (14 isolates), *K. pneumoniae* (71 isolates), *M. morganii* (16 isolates), *P. mirabilis* (89 isolates), *P. vulgaris* (2 isolates) and *S. marcescens* (34 isolates). An additional 28 isolates of non-indicated *Enterobacteriaceae* species (10% of the total number of isolates tested) were also evaluated. Of the *Enterobacteriaceae* isolates, 448 (84.8%) were fresh isolates (tested within seven days of isolation) and 80 (15.2%) were stock isolates.

A total of 87 clinical isolates of *P. aeruginosa* were evaluated, 77 of which (88.5%) were fresh isolates and 10 (11.5%) were stock isolates (Tables 4 and 5).

Challenge Study
A total of 122 *Enterobacteriaceae* challenge isolates were evaluated. These included: *C. freundii* (4 isolates), *C. koseri* (9 isolates), *E. cloacae* complex (13 isolates), *E. coli* (15 isolates), *H. alvei* (10 isolates), *K. oxytoca* (3 isolates), *K. pneumoniae* (29 isolates), *M. morganii* (3 isolates), *P. mirabilis* (6 isolates), P. vulgaris (21 isolates) and *S. marcescens* (5 isolates). In addition, four isolates of the non-indicated species, *K. aerogenes,* were evaluated.

A total of 44 challenge isolates of *P. aeruginosa* were evaluated. See Tables 4 and 5.

Results for EA, CA and categorical errors for *Enterobacteriaceae* and *P. aeruginosa* for all inoculation and read methods are shown in Tables 4 and 5 below. Essential agreement of evaluable results was calculated considering MIC results that were clearly identical to reference method results or clearly ≥ one doubling dilution higher or lower than the reference method results. Overall results for *Enterobacteriaceae* and for *P. aeruginosa* with all inoculation and read methods were acceptable.

For *C. koseri* and *P. vulgaris,* no resistant isolates were available for evaluation during clinical or challenge testing. The sponsor included the following limitation in the device labeling:

> *The ability of the MicroScan Dried Gram Negative Panels to detect resistance to meropenem is unknown for the following species because an insufficient number of resistant strains were available at the time of comparative testing: C. koseri and P.*

vulgaris. Isolates yielding MIC results suggestive of a resistant interpretive category should be submitted to a reference laboratory.

For *K. pneumoniae* inoculated with the turbidity method, one very major error was observed with the WalkAway and autoSCAN-4 read method for a very major error rate of 3.3%. With the turbidity inoculation method and manual read, two very major errors with *K. pneumoniae* were observed (6.7%). The sponsor included the following limitation in the device labeling to address the potential for very major errors with this species:

Due to the occurrence of very major errors with meropenem and turbidity inoculation with all read methods, isolates of K. pneumoniae that provide an MIC of 1 µg/mL should be retested using an alternative/reference method.

One of two resistant isolates of *H. alvei* showed a very major error (50.0%) with the turbidity inoculation method and manual read. The sponsor included the following footnote to the performance table in the device labeling:

One of the two resistant Hafnia alvei strains had a discrepant result compared to the reference method when using the manual read and turbidity inoculation method.

To address the testing and reporting of meropenem results for non-indicated species, the sponsor included the following statement in the Warnings and Precautions section of the device labeling:

The safety and efficacy of antimicrobial agents tested by this device, may or may not have been established in adequate and well-controlled clinical trials for treating clinical infections due to microorganisms outside of those found in the indications and usage section in the drug label. The clinical significance in those instances is unknown. The approved labeling for specific antimicrobial agents provides the uses for which the antimicrobial drug is approved.

Table 4. Performance of MicroScan Dried Gram-Negative Panels with Meropenem, Using <u>Prompt</u> Inoculation and All Read Methods

	Tot	No. EA	EA %	Eval EA Tot	No. Eval EA	Eval EA %	No. CA	CA %	No. R	No. S	min	maj	vmj
WalkAway Read													
Enterobacteriaceae													
Clinical	528	506	95.8	526	504	95.8	528	100.0	18	510	0	0	0
Challenge	122	115	94.3	109	103	94.5	114	93.4	51	65	8	0	0
Combined	650	621	95.5	635	607	95.6	642	98.8	69	575	8	0	0
P. aeruginosa													
Clinical	87	79	90.8	82	75	91.5	81	93.1	12	71	5	1	0
Challenge	44	43	97.7	20	19	95.0	40	90.9	34	7	3	1	0
Combined	131	122	93.1	102	94	92.2	121	92.4	46	78	8	2	0
autoSCAN-4 Read													
Enterobacteriaceae													
Clinical	528	508	96.2	526	506	96.2	528	100.0	18	510	0	0	0
Challenge	122	115	94.3	109	103	94.5	114	93.4	51	65	8	0	0
Combined	650	623	95.8	635	609	95.9	642	98.8	69	575	8	0	0
P. aeruginosa													
Clinical	87	76	87.4	84	73	86.9	80	92.0	12	71	6	0	1
Challenge	44	43	97.7	21	20	95.2	40	90.9	34	7	3	1	0
Combined	131	119	90.8	105	93	88.6	120	91.6	46	78	9	1	1
Manual Read													
Enterobacteriaceae													
Clinical	528	507	96.0	526	505	96.0	527	99.8	18	510	1	0	0
Challenge	122	114	93.4	108	101	93.5	113	92.6	51	65	9	0	0
Combined	650	621	95.5	634	606	95.6	640	98.5	69	575	10	0	0
P. aeruginosa													
Clinical	87	79	90.8	85	77	90.6	82	94.3	12	71	5	0	0
Challenge	44	43	97.7	21	20	95.2	40	90.9	34	7	3	1	0
Combined	131	122	93.1	106	97	91.5	122	93.1	46	78	8	1	0

EA – Essential Agreement (± 1 dilution)
CA – Category Agreement
EVAL – Evaluable isolates
NS – Non-Susceptible isolates

min – minor discrepancies
maj – major discrepancies
vmj – very major discrepancies

Essential agreement (EA) occurs when the result of the reference method and that of the MicroScan Dried Gram-Negative MIC/Combo Panel are within plus or minus one serial two-fold dilution of the antibiotic. Evaluable results are those that are on scale for both the reference method and the MicroScan Dried Gram-Negative MIC/Combo Panel. Category agreement (CA) occurs when the interpretation of the result of the reference method agrees exactly with the interpretation provided by the MicroScan Dried Gram-Negative MIC/Combo Panel.

Table 5. Performance of MicroScan Dried Gram-Negative Panels with Meropenem, Using Turbidity Inoculation and All Read Methods

	Tot	No. EA	EA %	Eval EA Tot	No. Eval EA	Eval EA %	No. CA	CA %	No. R	No. S	min	maj	vmj
WalkAway Read													
Enterobacteriaceae													
Clinical	528	518	98.1	526	516	98.1	525	99.4	18	510	2	1	0
Challenge	122	112	91.8	110	101	91.8	112	91.8	51	65	8	1	1
Combined	650	630	96.9	636	617	97.0	637	98.0	69	575	10	2	1
P. aeruginosa													
Clinical	87	80	92.0	84	77	91.7	85	97.7	12	71	2	0	0
Challenge	45	45	100.0	21	21	100.0	42	93.3	35	7	3	0	0
Combined	132	125	94.7	105	98	93.3	127	96.2	47	78	5	0	0
autoSCAN-4 Read													
Enterobacteriaceae													
Clinical	528	517	97.9	526	515	97.9	526	99.6	18	510	1	1	0
Challenge	122	114	93.4	110	102	92.7	112	91.8	51	65	8	1	1
Combined	650	631	97.1	636	617	97.0	638	98.2	69	575	9	2	1
P. aeruginosa													
Clinical	87	78	89.7	85	76	89.4	84	96.6	12	71	3	0	0
Challenge	45	45	100.0	23	23	100.0	42	93.3	35	7	3	0	0
Combined	132	123	93.2	108	99	91.7	126	95.5	47	78	6	0	0
Manual Read													
Enterobacteriaceae													
Clinical	528	519	98.3	526	517	98.3	523	99.1	18	510	2	1	2
Challenge	122	115	94.3	110	103	93.6	114	93.4	51	65	6	1	1
Combined	650	634	97.5	636	620	97.5	637	98.0	69	575	8	2	3
P. aeruginosa													
Clinical	87	80	92.0	84	77	91.7	85	97.7	12	71	2	0	0
Challenge	45	45	100.0	24	24	100.0	40	88.9	35	7	5	0	0
Combined	132	125	94.7	108	101	93.5	125	94.7	47	78	7	0	0

Resistance Mechanism Characterization

Challenge isolates of *Enterobacteriaceae* and *P. aeruginosa* harboring various molecular mechanisms of resistance noted in the FDA approved drug label were tested with meropenem. Isolates from the following CDC and FDA Antibiotic Resistance Isolate Bank panels were evaluated: *Enterobacteriaceae* Carbapenem Breakpoint Panel, *Enterobacteriaceae* Carbapenemase Diversity Panel and the Gram Negative Carbapenemase Detection Panel.

Trending

An analysis of trending was conducted using the combined clinical and challenge data for each organism group and for each inoculation and read method. This trending calculation takes into account MIC values that are determined to be one or more doubling dilution lower or higher compared to the reference method irrespective of whether the device MIC values are on scale or not. Results that are not clearly at least one dilution lower, at least one dilution higher or in exact agreement with the CLSI reference method are not considered in the trending analysis.

Trending results for indicated species were evaluated to determine if species-specific trends were observed. Species or organism groups for which the difference between the percentage of isolates with higher vs. lower readings was >30% and for which the confidence interval was determined to be statistically significant were considered to show evidence of trending. Trending that provides higher or lower MIC values compared to the reference is addressed in labeling.

A trend toward lower MIC readings was observed for *P. aeruginosa* using the manual read method with the turbidity inoculation method. While no trending was observed overall for *Enterobacteriaceae*, a trend toward higher readings was observed for *C. koseri* and *E. coli* with Prompt inoculation and all read methods, for *P. mirabilis* with Prompt inoculation and WalkAway and manual reads and for P. vulgaris with Prompt and manual read. A trend toward lower readings was observed for *M. morganii* with turbidity inoculation and all read methods and for P. vulgaris with turbidity and autoScan-4 read. The sponsor included the following footnote to the performance table in the device labeling:

> *Meropenem MIC values for Enterobacteriaceae and Pseudomonas aeruginosa were most frequently in exact agreement with the reference method. When not in agreement, results tended to be one doubling dilution lower for P. aeruginosa (turbidity, manual read), P. vulgaris (Turbidity, AutoScan-4 read) and M. morganii (Turbidity, all read methods). Results tended to be one doubling dilution higher for C. koseri and E. coli (Prompt, all read methods, P. vulgaris (Prompt, manual read) and P. mirabilis (Prompt, WalkAway and manual read).*

Table 6. Trending for all Species with all Inoculation and Read Methods

Inoculation/ Read Method	Organism	Total Evaluable for Trending	≥ 1 Dilution lower No. (%)	Exact No. (%)	≥ 1 Dilution Higher No. (%)	Percent Difference (CI)	Trending Noted
Prompt/ WalkAway	*Enterobacteriaceae*	603	41 (6.8)	367 (60.9)	195 (32.3)	25.5	No
	C. freundii	19	2 (10.5)	15 (79.0)	2 (10.5)	0	No
	C. koseri	12	0	7 (58.3)	5 (41.7)	41.7	Yes
	E. cloacae complex	53	8 (15.1)	30 (56.6)	15 (28.3)	13.2	No
	E. coli	225	7 (3.1)	133 (59.1)	85 (37.8)	34.7	Yes
	H. alvei	11	1 (9.1)	6 (54.6)	4 (36.4)	27.3	No
	K. oxytoca	17	0	13 (76.5)	4 (23.5)	23.5	No
	K. pneumoniae	95	7 (7.4)	68 (71.6)	20 (21.1)	13.7	No
	M. morganii	19	3 (15.8)	12 (63.2)	4 (21.1)	5.3	No
	P. mirabilis	94	9 (9.6)	43 (45.7)	42 (44.7)	35.1	Yes
	P. vulgaris	23	4 (17.4)	12 (52.2)	7 (30.4)	13.0	No
	S. marcescens	35	0	28 (80.0)	7 (20.0)	20.0	No
	P. aeruginosa	103	33 (32.0)	45 (43.7)	25 (24.3)	-7.8	No
Prompt/ autoSCAN-4	*Enterobacteriaceae*	603	55 (9.1)	357 (59.2)	191 (31.7)	22.6	No
	C. freundii	19	2 (10.5)	15 (79.0)	2 (10.5)	0	No
	C. koseri	12	0	7 (58.3)	5 (41.7)	41.7	Yes
	E. cloacae complex	53	7 (13.2)	29 (54.7)	17 (32.1)	18.9	No
	E. coli	225	7 (3.1)	127 (56.4)	91 (40.4)	37.3	Yes
	H. alvei	11	1 (9.1)	7 (63.6)	3 (27.3)	18.2	No
	K. oxytoca	17	0	13 (76.5)	4 (23.5)	23.5	No
	K. pneumoniae	95	7 (7.4)	66 (69.5)	22 (23.2)	15.8	No
	M. morganii	19	4 (21.1)	12 (63.2)	3 (15.8)	-5.3	No
	P. mirabilis	94	11 (11.7)	45 (47.9)	38 (40.4)	28.7	No
	P. vulgaris	23	8 (34.8)	13 (56.5)	2 (8.7)	-26.1	No

Inoculation/ Read Method	Organism	Total Evaluable for Trending	≥ 1 Dilution lower No. (%)	Exact No. (%)	≥ 1 Dilution Higher No. (%)	Percent Difference (CI)	Trending Noted
	S. marcescens	35	8 (22.9)	23 (65.7)	4 (11.4)	-11.4	No
	P. aeruginosa	105	35 (34.7)	49 (46.7)	21 (20.0)	-13.3	No
Prompt/ Manual	*Enterobacteriaceae*	603	42 (7.0)	366 (60.8)	194 (32.2)	25.3	No
	C. freundii	19	3 (15.8)	14 (73.7)	2 (10.5)	-5.3	No
	C. koseri	12	0	7 (58.3)	5 (41.7)	41.7	Yes
	E. cloacae complex	53	8 (15.1)	29 (54.7)	16 (30.2)	15.1	No
	E. coli	224	6 (2.7)	132 (59.0)	86 (38.4)	35.7	Yes
	H. alvei	11	1 (9.1)	7 (63.6)	3 (27.3)	18.2	No
	K. oxytoca	17	0	12 (70.6)	5 (29.4)	29.4	No
	K. pneumoniae	95	8 (8.4)	68 (71.6)	19 (20.0)	11.6	No
	M. morganii	19	4 (21.1)	12 (63.2)	3 (15.8)	-5.3	No
	P. mirabilis	94	6 (6.4)	51 (54.3)	37 (39.4)	33.0	Yes
	P. vulgaris	23	2 (8.7)	9 (39.1)	12 (52.2)	43.5	Yes
	S. marcescens	35	4 (11.4)	25 (71.4)	6 (17.1)	5.7	No
	P. aeruginosa	105	48 (45.7)	39 (37.1)	18 (17.1)	-28.6	No
Turbidity/ WalkAway	*Enterobacteriaceae*	604	77 (12.8)	410 (67.9)	117 (19.4)	6.6	No
	C. freundii	19	3 (15.8)	14 (73.7)	2 (10.5)	-5.26	No
	C. koseri	12	1 (8.3)	9 (75.0)	2 (16.7)	8.3	No
	E. cloacae complex	54	12 (22.2)	36 (66.7)	6 (11.1)	-11.1	No
	E. coli	225	17 (7.6)	157 (69.8)	51 (22.7)	15.1	No
	H. alvei	11	2 (18.2)	7 (63.6)	2 (18.2)	0	No
	K. oxytoca	17	1 (5.9)	14 (82.4)	2 (11.8)	5.9	No
	K. pneumoniae	95	16 (16.8)	66 (69.5)	13 (13.7)	-3.2	No
	M. morganii	19	7 (36.8)	11 (57.9)	1 (5.3)	-31.6	Yes
	P. mirabilis	94	11(11.7)	53 (56.4)	30 (31.9)	20.2	No
	P. vulgaris	23	5 (21.7)	14 (60.9)	4 (17.4)	-4.4	No
	S. marcescens	35	2 (5.7)	29 (82.9)	4 (11.4)	5.7	No
	P. aeruginosa	105	32 (30.5)	52 (49.5)	21 (20.0)	-10.5	No
Turbidity/ autoSCAN-4	*Enterobacteriaceae*	607	89 (14.7)	409 (67.1)	111 (18.3)	3.6	No
	C. freundii	19	3 (15.8)	14 (73.7)	2 (10.5)	-5.26	No
	C. koseri	12	1 (8.3)	9 (75.0)	2 (16.7)	8.3	No
	E. cloacae complex	54	10 (18.5)	38 (70.4)	6 (11.1)	-7.4	No
	E. coli	225	17 (7.6)	155 (68.9)	53 (23.6)	16.0	No
	H. alvei	11	3 (27.3)	8 (72.7)	0	-27.3	No
	K. oxytoca	17	1 (5.9)	14 (82.4)	2 (11.8)	5.9	No
	K. pneumoniae	95	15 (15.8)	68 (71.6)	12 (12.6)	-3.2	No
	M. morganii	19	7 (36.8)	11 (57.9)	1 (5.3)	-31.6	Yes
	P. mirabilis	94	13 (13.8)	50 (53.2)	31 (33.0)	19.2	No
	P. vulgaris	23	11 (47.8)	12 (52.2)	0	-47.8	Yes
	S. marcescens	38	8 (21.1)	28 (73.7)	2 (5.3)	-15.8	No
	P. aeruginosa	108	32 (29.6)	60 (55.6)	16 (14.8)	-14.8	No
Turbidity/ Manual	*Enterobacteriaceae*	604	72 (11.9)	423 (70.0)	109 (18.1)	6.1	No
	C. freundii	19	4 (21.1)	14 (73.7)	1 (5.3)	-15.8	No
	C. koseri	12	1 (8.3)	9 (75.0)	2 (16.7)	8.3	No
	E. cloacae complex	54	14 (25.9)	34 (63.0)	6 (11.1)	-14.8	No
	E. coli	225	14 (6.2)	159 (70.7)	52 (23.1)	16.9	No
	H. alvei	11	3 (27.3)	8 (72.7)	0	-27.3	No
	K. oxytoca	17	1 (5.9)	13 (76.5)	3 (17.7)	11.8	No
	K. pneumoniae	95	15 (15.8)	66 (69.5)	14 (14.7)	-1.1	No
	M. morganii	19	7 (36.8)	11 (57.9)	1 (5.3)	-31.6	Yes
	P. mirabilis	94	6 (6.4)	65 (69.2)	23 (24.5)	18.1	No
	P. vulgaris	23	3 (13.0)	18 (78.3)	2 (8.7)	-4.4	No
	S. marcescens	35	4 (11.4)	26 (74.3)	5 (14.3)	2.9	No
	P. aeruginosa	107	47 (43.9)	51 (47.7)	9 (8.4)	-35.5	Yes

2. Matrix Comparison:

Not Applicable

C Clinical Studies:

1. Clinical Sensitivity:

Not Applicable

2. Clinical Specificity:

Not Applicable

3. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

Not Applicable

D Clinical Cut-Off:

Not Applicable

E Expected Values/Reference Range:

Table 7. FDA-Recognized Interpretive Criteria for Meropenem

Organism	Interpretive Criteria for Meropenem MIC (µg/mL)[a]		
	Susceptible	Intermediate	Resistant
Enterobacteriaceae	**≤1**	**2**	**≥4**
P. aeruginosa	**≤2**	**4**	**≥8**

[a] FDA STIC Webpage
https://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/ucm410971.htm

F Other Supportive Instrument Performance Characteristics Data:

Not applicable

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

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

To support the implementation of changes to FDA-recognized susceptibility test interpretive criteria (i.e., breakpoints), this submission included a breakpoint change protocol that was reviewed and accepted by FDA. This protocol addresses future revisions to device labeling in response to breakpoint changes that are recognized on the FDA STIC webpage (https://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/ucm410971.htm). The protocol outlined the specific procedures and acceptance criteria that Beckman Coulter intends to use to evaluate the MicroScan Dried Gram-Negative MIC/Combo Panels with Meropenem (Mer) (0.004 - 32 µg/mL) when revised breakpoints for meropenem are published on the FDA STIC webpage. The breakpoint change protocol included with the submission indicated that if specific criteria are met, Beckman Coulter will update the meropenem device label to include (1) the new breakpoints, (2) an updated performance section after re-evaluation of data in this premarket notification with the new breakpoints, and (3) any new limitations as determined by their evaluation.