510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE

A. 510(k) Number:

K181665

B. Purpose for Submission:

Addition of the BD Phoenix CPO detect test to the BD Phoenix Gram negative ID/AST and AST only Phoenix panels.

C. Measurand:

Carbapenemase production

D. Type of Test:

Growth-based detection and algorithm using predetermined thresholds

E. Applicant:

Becton, Dickinson and Company

F. Proprietary and Established Names:

BD Phoenix Automated Microbiology System – BD Phoenix CPO detect - GN

G. Regulatory Information:

1. Regulation section:

   21 CFR 866.1645 Short-Term Antimicrobial Susceptibility Test System

2. Classification:

   Class II

3. Product code:

   LON System, Test, Automated, Antimicrobial Susceptibility, Short Incubation

4. Panel:

   83 Microbiology

H. Intended Use:

1. Intended use(s):

   The BD Phoenix Automated Microbiology System is intended for the in vitro rapid identification (ID) and quantitative determination of antimicrobial susceptibility by minimal inhibitory concentration (MIC) of Gram Negative aerobic and facultative anaerobic bacteria belonging to the family Enterobacteriaceae and non-Enterobacteriaceae.

2. Indication(s) for use:

   BD Phoenix CPO detect is a qualitative confirmatory test that uses a growth-based algorithm intended to phenotypically detect carbapenemase-production in *Enterobacteriaceae*, *Pseudomonas aeruginosa*, and *Acinetobacter baumannii* on Gram-negative ID/AST or AST only Phoenix panels. The test also provides the Ambler classification (Class A, Class B and Class D) of the carbapenemase produced. One of three test configurations are available per panel for carbapenemase detection with/without Ambler classification for the target organism groups. BD Phoenix CPO detect does not report multiple classes of carbapenemases from a single isolate.

3. Special conditions for use statement(s):

   For Prescription Use only

   For *in vitro* diagnostic use

   - Due to the small number of tested isolates identified as harboring carbapenemases from multiple Ambler classes (n=7), there is limited information on the performance of the BD Phoenix CPO detect with organisms co-producing different classes of carbapenemases.
   - Carbapenemase positive isolates that are carbapenem susceptible (*Enterobacteriaceae*, *Pseudomonas aeruginosa*, or *Acinetobacter baumannii*) are rare, as encountered in the clinical study. Additional confirmatory testing should be conducted before reporting carbapenemase activity in a susceptible isolate.
   - Well-established phenotypic carbapenemase tests (e.g. CarbaNP and mCIM) do not include testing of *Acinetobacter baumannii*. End-users should consider other methods for further characterization of *Acinetobacter baumannii* if necessary.
   - *In silico* analysis of carbapenemase gene variants was performed in the validation of the PCR multiplex method for the reference method. Performance with isolates harboring specific carbapenemase gene variants expressing enzymes from various Ambler classes by BD Phoenix CPO detect was not determined.

4. Special instrument requirements:

   BD Phoenix Automated Microbiology System

I. Device Description:

The Phoenix panel is a sealed and self-inoculating molded polystyrene tray, with 136 microwells containing dried reagents. The combination panel includes an ID side with dried substrates for bacterial identification and an AST side with varying concentrations of antimicrobial agents, growth, and fluorescent controls at appropriate well locations. The Phoenix system utilizes an optimized colorimetric redox indicator for AST, and a variety of colorimetric and fluorometric indicators for ID. Phoenix panels are also available in an "ID Only" format where only the 51-well side is filled with substrates and the 85-well side is empty. Phoenix panels are also available in an "AST Only" format where both the 51-well and 85-well sides are filled with antibiotics.

Microorganisms to be tested are isolated from pure culture and preliminarily identified as a Gram-negative bacillus, Gram-positive coccus or Gram-positive bacillus. For each bacterial isolate, the inoculum suspension is prepared in the Phoenix ID broth and vortexed to mix. The appropriate amount of inoculated ID Broth is transferred to the prepared AST Broth tube, so that the resulting AST inoculum contains approximately 5 x 10^5 CFU/ml. The Phoenix ID broth is poured into the inoculation port of the 51-well side (left) of the Phoenix Combo panel (for ID substrates). The Phoenix AST Broth is poured into the inoculation port of the 85-well side (right) of the Phoenix Combo panel (for antimicrobials). The panel barcode is scanned to log-in the panel configuration and the panel is loaded into the Phoenix instrument. The instrument houses the inoculated panels where they are continuously incubated at 35°C. The Phoenix instrument reads and records the results of the biochemical substrates and antimicrobial agents contained in the panel and interprets the reactions to give an ID of the isolate, minimal inhibitory concentration (MIC) values, and category interpretations of S, I, R or N (susceptible, intermediate, resistant or not susceptible).

BD Phoenix CPO detect is a qualitative growth-based test intended to phenotypically detect carbapenemase-production in *Enterobacteriaceae, Pseudomonas aeruginosa*, and *Acinetobacter baumannii* on the BD Phoenix Automated Microbiology System. The test also provides the Ambler classification (Class A, Class B and Class D) of the carbapenemase produced. CPO detect uses the principle of carbapenem resistance to detect the presence of the carbapenemase, and it employs the principles of Ambler-class specific beta-lactamase inhibition and Ambler-class specific antibiotic resistance to derive the Ambler class of the carbapenemase.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   BD Phoenix Automated Microbiology System-Confirmatory ESBL test

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

   K033458

3. Comparison with predicate:

Similarities		
Item	**BD Phoenix CPO detect (K181665)**	**Phoenix ESBL test (predicate) (K033458)**
Intended Use	The BD Phoenix Automated Microbiology System is intended for the in vitro rapid identification (ID) and quantitative determination of antimicrobial susceptibility by minimal inhibitory concentration (MIC) of Gram Negative aerobic and facultative anaerobic bacteria belonging to the family Enterobacteriaceae and non-Enterobacteriaceae.	Same
Specimen	Isolated colonies from culture	Same
Inoculum	Inoculum density of 0.5 McFarland standard	Same
Incubation Time	< 16 hours	Same
Technology	Automated growth based	Same
Panels	Panel with dried antibiotics and/or inhibitors	Same
Instrumentation	BD Phoenix Automated Microbiology System	Same

Differences		
Item	**BD Phoenix CPO detect (K181665)**	**Phoenix ESBL test (predicate) (K033458)**
Indications for Use	BD Phoenix CPO detect is a qualitative confirmatory test that uses a growth-based algorithm intended to phenotypically detect carbapenemase-production in *Enterobacteriaceae*, *Pseudomonas aeruginosa*, and *Acinetobacter baumannii* on Gram-negative ID/AST or AST only Phoenix panels. The test also provides the Ambler classification (Class A, Class B and Class D) of the carbapenemase produced. One of three test configurations are available per panel for carbapenemase detection with/without Ambler classification for the target organism groups. BD Phoenix CPO detect does not report multiple classes of carbapenemases from a single isolate.	This submission is for the addition of the confirmatory ESBL Test to Gram-negative ID/AST or AST BD Phoenix panels. The Phoenix Confirmatory ESBL Test is a confirmatory test for the detection of the organisms that produce extended spectrum β-lactamase (ESBL) in *Escherichia coli*, *Klebsiella pneumoniae* and *Klebsiella oxytoca.*
Test Results	Detection of carbapenemase-producing organisms with/without the categorization into one of the Ambler classes	Detection of Extended Spectrum β-Lactamase (ESBL) producing organisms
Reagents as part of determination	Set concentrations of meropenem, doripenem, temocillin, and cloxacillin alone and in combination with various chelators and beta-lactamase inhibitors	Set concentrations of Ceftriaxone, Cefotaxime, Ceftazidime plus screening antibiotics used in a decision tree

Differences		
Item	**BD Phoenix CPO detect (K181665)**	**Phoenix ESBL test (predicate) (K033458)**
	used in a decision tree	

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

Clinical Laboratory Standards Institute: M100 "Performance Standards for Antimicrobial Susceptibility Testing." 28th Edition (January 2018)

L. Test Principle:

The BD Phoenix CPO detect test determines the growth or inhibition of growth with each antimicrobic agent or antimicrobic agent/beta-lactamase inhibitor combination in relation to the growth control well. The classification tree algorithms compare these relative growth rates to a series of thresholds in the decision trees. Based on the resultant profile, the system will produce a particular result. The CPO detect result does not depend on the MIC or SIR of any drug on the panel.

The test is offered to users as a choice of multiple configurations—9-well, 6-well, and 2-well (See **Table 1** below). There are different classification tree algorithms for *Enterobacteriaceae* and non-fermenters. The Phoenix instrument calculates both of these results simultaneously and then reports the appropriate result based on the isolate identification. The wells for the CPO detect test are specific for the test and are not part of any drug MIC determination.

If the test is unable to classify the carbapenemase into an Ambler class, then it reports only the presence of a carbapenemase. When two different Ambler class carbapenemases are present, BD Phoenix CPO detect will not report multiple classes; e.g., it will not report both Class A and Class B. For bacteria that produce more than one class of carbapenemase, the Phoenix test is expected to give a result of positive with no classification.

Table 1. Interpretation of Results for the (3) Possible Configurations of the BD Phoenix CPO Detect Test

Test Configuration	Organism Group	Possible Test Results
2-Well	*Enterobacteriaceae, Pseudomonas aeruginosa,* or *Acinetobacter baumannii*	Carbapenemase Producer
6-Well	*Enterobacteriaceae*	Carbapenemase Producer[1]
		Carbapenemase Producer, Class A, B, or D
	Pseudomonas aeruginosa and Acinetobacter baumannii	Carbapenemase Producer
9-Well	*Enterobacteriaceae, Pseudomonas aeruginosa,* or *Acinetobacter baumannii*	Carbapenemase Producer[1]
		Carbapenemase Producer, Class A, B, or D

[1] *Ambler class could not be determined; therefore, no Ambler class is reported.*

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Intra- and inter-site reproducibility of the BD Phoenix CPO detect test on the BD Phoenix System was evaluated at three sites using a panel of Gram-negative isolates. Thirteen gram-negative organisms were tested, where each site tested the isolates in triplicate on three different days using Gram Negative Phoenix panels containing CPO detect and associated reagents. There were two QC isolates included on the reproducibility panel. Results of the study demonstrated that the BD Phoenix CPO detect test showed acceptable reproducibility at ≥ 95% with the expected results for Gram-negative organisms prepared by both manual and Phoenix AP inoculations. **Table 2** below presents the reproducibility of the organism panels with and without the QC organism data included in the performance calculations.

Table 2. BD Phoenix CPO Detect Reproducibility Summary (Manual and Phoenix AP Inoculation)

Organism	Expected Result		BD Phoenix CPO Detect Result			
			Manual		BD Phoenix AP	
	CPO Detection (P/N)[1]	Ambler Class (A, B, D)[2]	CPO Detection (Observed/Expected)	Ambler Class (Observed/Expected)	CPO Detection (Observed/Expected)	Ambler Class (Observed/Expected)
E. coli	P	A	27/27 (100%)	27/27 (100%)	27/27 (100%)	27/27 (100%)
K. pneumo. spp. *pneumo.*	P	B	27/27 (100%)	27/27 (100%)	27/27 (100%)	27/27 (100%)
E. coli ATCC 25922[3]	N[4]	--	27/27 (100%)	27/27 (100%)	27/27 (100%)	27/27 (100%)
K. pneumo. spp. *pneumo.*	N[4]	--	27/27 (100%)	27/27 (100%)	27/27 (100%)	27/27 (100%)
K. pneumo. spp. *pneumo.*	P	D	27/27 (100%)	25/27 (92.6%)	27/27 (100%)	24/27 (88.9%)
Klebsiella aerogenes	N[4]	--	27/27 (100%)	27/27 (100%)	26/27 (96.3%)	26/27 (96.3%)
K. pneumo. spp. *pneumo.* ATCC BAA-1705[3]	P	A	27/27 (100%)	27/27 (100%)	27/27 (100%)	27/27 (100%)
E. coli	P	B	27/27 (100%)	27/27 (100%)	27/27 (100%)	27/27 (100%)
A. baumannii	P	B	27/27 (100%)	27/27 (100%)	27/27 (100%)	27/27 (100%)
P. aeruginosa	P	A	27/27 (100%)	26/27 (96.3%)	27/27 (100%)	27/27 (100%)
P. aeruginosa ATCC 27853	N[4]	--	26/27 (96.3%)	26/27 (96.3%)	27/27 (100%)	27/27 (100%)
A. baumannii	P	D	27/27 (100%)	27/27 (100%)	27/27 (100%)	26/27 (96.3%)
P. aeruginosa	P	B	27/27 (100%)	27/27 (100%)	27/27 (100%)	27/27 (100%)
All (with QC isolates)			350/351 (99.7%)	347/351 (98.9%)	350/351 (99.7%)	346/351 (98.6%)
w/o QC Isolates			296/297 (99.7%)	293/297 (98.7%)	296/297 (99.7%)	292/297 (98.3%)

[1]P: carbapenemase detected; N: carbapenemase not detected. The reproducibility set included nine carbapenemase producers.
[2]The nine carbapenemase producers covered three Class A, four Class B, and two Class D carbapenemases. (--) represents no Ambler class reported for this organism.
[3]QC isolates were E. coli ATCC 25922 and K. pneumo. spp. pneumo. ATCC BAA-1705.
[4]Numbers in table for organisms negative for carbapenemase show observed negatives/expected negatives.

b. Linearity/assay reportable range:

Not Applicable

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

Quality Control (QC) strains recommended for carbapenemase testing were evaluated using both the Manual and Phoenix AP Inoculation procedures. The BD Phoenix CPO detect test gave the expected results > 95% of the time, demonstrating that the system can produce the expected QC results with this test (**Table 3**).

Table 3. QC Performance Summary

Organism	Expected Result		BD Phoenix CPO Detect Result			
			Manual		BD Phoenix AP	
	CPO Detection (P/N) [1]	Ambler Class (A, B, D)[2]	CPO Detection (Observed/Expected)	Ambler Class (Observed/Expected)	CPO Detection (Observed/Expected)	Ambler Class (Observed/Expected)
E. coli ATCC 25922	N[3]	--	118/118	118/118	71/71	71/71
K. pneumoniae ATCC BAA-1705	P	A	117/117	115/117	71/71	71/71
All			100% (235/235)	99.1% (233/235)	100% (142/142)	100% (142/142)

[1] *P: carbapenemase detected; N: carbapenemase not detected*
[2] *Ambler Class A, B, or D expected. (--) represents no Ambler Class reported for this organism.*
[3] *Numbers in table for organism negative for carbapenemase show observed negatives/expected negatives.*

d. Detection limit:

Not Applicable

e. Analytical specificity:

Not Applicable

f. Assay cut-off:

Not Applicable

2. Comparison studies:

a. Method comparison with predicate device:

Not Applicable

b. Matrix comparison:

Not Applicable

3. Clinical studies:

a. Clinical Sensitivity:

Clinical fresh and stock isolates were tested across three sites to demonstrate the performance of the BD Phoenix CPO detect test with multiple lots of BD Phoenix Gram Negative panels. Challenge isolates obtained from domestic and international sources were also tested at these sites. All studies were conducted with the 9-well configuration of the BD Phoenix CPO detect test. For the challenge isolates, Phoenix System results with the CPO detect test were compared to the expected results. Phoenix System results for clinical isolates were compared to the results obtained from the Composite Reference Method, which was based on results from three different and independent tests. The tests included the following: 1) Phenotypic testing to detect the presence of carbapenemase expression according to the CLSI-recommended modified Carbapenem Inactivation Method (mCIM), 2) carbapenem MIC results obtained by the BD Phoenix cleared system and 3) Molecular (multiplex PCR amplification) testing to assign the Ambler classification of the enzyme based on detection of gene or genes associated with each class. All strains were tested using the mCIM assay and on the BD Phoenix panel. PCR testing was performed as appropriate based on the reference decision flowchart. Under certain conditions, and to lessen the burden of extensive PCR testing, the MIC screen was applied for each organism group (**Table 4)** and used to determine whether an isolate would proceed to PCR testing. The possible outcomes for the Composite Reference Method are shown in **Table 5**.

Table 4. MIC Screen Cut-Offs Set for Each Organism Group

Organism Group	Drug	MIC Screen Cut-Off *(considered positive result)*
Enterobacteriaceae (other than *Proteus* spp).	Meropenem	>0.25µg/ml
Proteus spp.	Ertapenem	>0.5µg/ml
Pseudomonas aeruginosa	Meropenem	>4µg/ml
Acinetobacter baumannii	Imipenem	>2µg/ml

Table 5. Possible Outcomes of Composite Reference Method

mCIM Result	MIC Screen	PCR	Composite Reference Method Result
Positive	N/A	Positive	Positive with Class
Positive	N/A	Negative	Positive no Class
Negative	Positive	Positive	Positive with Class
Negative	Positive	Negative	Negative
Negative	Negative	N/A	Negative
Indeterminate	Negative	Negative	Negative
Indeterminate	Negative	Positive	No Result
Indeterminate	Positive	Negative	No Result
Indeterminate	Positive	Positive	Positive with Class

There were 1641 Gram-negative clinical and challenge isolates enrolled in the study. A total of 189 isolates were excluded for the following reasons:

- (30) related to isolate characterization (e.g. failed or incomplete challenge screen, mixed purity plates, organisms not in inclusion criteria)
- (17) due to non-compliance with the Phoenix System procedure (incorrect amount of indicator, uninoculated panels, no growth)
- (142) due to non-compliance with the reference system results (QC failure, protocol deviation, no reference/expected result)

Results from these 1452 compliant Gram-negative Phoenix and reference isolates were used to calculate the performance for BD Phoenix CPO detect test for carbapenemase detection. Of these 1452 isolates, 317 (21.8%) were challenge isolates and 1135 (78.2%) were clinical isolates. Clinical isolates were comprised of 416 fresh isolates (28.7% of total isolates tested) and 719 stock isolates (49.5% of the total isolates tested). A total of 155 isolates were used from the CDC/FDA AR Bank. The distribution of isolates according to the Reference Method and BD Phoenix CPO detect test result is displayed in **Table 6**. **Table 7** and **Table 8** show the ability of the BD Phoenix CPO detect test to identify carbapenemase-producing isolates for all organisms, and for each organism group, respectively. The classification performance of the BD Phoenix CPO detect test (Class A, Class B, or Class D) for all isolates (n=1452) is presented in **Table 9**.

Table 6. Distribution of Isolates for the Clinical Study Based on Test Results

Combined (Clinical and Challenge)									
		Reference Method Results							**Total**
		A[1] only	**Multiple, A and B[2]**	**B only**	**Multiple, B and D[2]**	**D only**	**CPO, unclass[3]**	**No CPO[4]**	
BD Phoenix CPO Detect Results	**CPO, A[5]**	122	0	0	0	4	7	4	137
	CPO, B	3	0	126	0	3	1	12	145
	CPO, D	0	0	2	5	134	5	6	152
	CPO, unclass.[6]	18	1	27	1	10	7	12	76
	No CPO[7]	3	0	6	0	0	1	932	942
Total		146	1	161	6	151	21	966	1452

[1]Carbapenemase-positive with Ambler Class A gene identified by Reference Method
[2]Carbapenemase-positive with multiple Ambler Class genes identified by Reference Method
[3]Carbapenemase-positive, but no Ambler Class identified by Reference Method
[4]No carbapenemase detected by Reference Method
[5]Carbapenemase-positive with Ambler Class detected (Class A) by the BD Phoenix CPO detect test
[6]Carbepenemase-positve, but no Ambler Class identified by the BD Phoenix CPO detect test
[7]No carbapenemase detected by the BD Phoenix CPO detect test

Table 7. BD Phoenix CPO Detect Test Performance [Carbapenemase Detection] vs the Composite Reference Method.

Isolate Type	Total # Isolates	TP	FP	TN	FN	PPA [95% CI]	NPA [95% CI]
Clinical	1135	245	20	864	6	97.6% (245/251) [94.9%; 98.9%]	97.7% (864/884) [96.5%; 98.5%]
Challenge[1,2]	317	231	14	68	4	98.3% (231/235) [95.7%; 99.3%]	82.9% (68/82) [73.4%; 89.6%]
Combined[3]	1452	476	34	932	10	97.9% (476/486) [96.3%; 98.9%]	96.5% (932/966) [95.1%; 97.4%]

[1]*The challenge set isolates were well-characterized and compared to the expected results.*

[2]*Of the (19) challenge isolates with carbapenemase genes other than bla$_{IMP}$, bla$_{VIM}$, bla$_{KPC}$, bla$_{NDM}$, bla$_{OXA-48}$, bla$_{OXA-24}$, bla$_{OXA-23}$, and bla$_{OXA-58}$, all (19) were reported as carbapenemase producers by the BD Phoenix CPO detect test. These included: (3) bla$_{GES}$, (3) bla$_{IMI}$, (12) bla$_{SME}$, and (1) bla$_{SPM}$.*

[3]*The specificity of the BD Phoenix CPO detect when testing isolates with known carbapenem resistance by cephalosporinase or ESBL coupled with decreased permeability through porin mutations among Enterobacteriaceae, Pseudomonas aeruginosa, and Acinetobacter baumannii has not been fully evaluated. Out of 735 carbapenem "not susceptible" isolates in the clinical study, only four were well-characterized strains with such a known resistance mechanism. All four strains were falsely reported as carbapenemase producers by the BD Phoenix CPO detect test.*

Table 8. BD Phoenix CPO Detect Test Performance [Carbapenemase Detection] vs the Composite Reference Method (by Organism Group)

Organism Group	Isolate Type	Total #	TP	FP	TN	FN	PPA [95% CI]	NPA [95% CI]
Enterobacteriaceae	Clinical	889	189	8	691	1	99.5% (189/190) [97.1%; 99.9%]	98.9% (691/699) [97.8%; 99.4%]
	Challenge	210	149	13	44	4	97.4% (149/153) [93.5%; 99.0%]	77.2%[1] (44/57) [64.8%; 86.2%]
	Combined	1099	338	21	735	5	98.5% (338/343) [96.6%-99.4%]	97.2% (735/756) [95.8%-98.2%]
Acinetobacter baumannii	Clinical	82	27	2	51	2	93.1% (27/29) [78.0%; 98.1%]	96.2% (51/53) [87.3%; 99.0%]
	Challenge	56	41	0	15	0	100% (41/41) [91.4%; 100%]	100% (15/15) [79.6%; 100%]
	Combined	138	68	2	66	2	97.1% (68/70) (90.2%-99.2%)	97.1% (66/68) (89.9%-99.2%)
Pseudomonas aeruginosa	Clinical	164	29	10	122	3	90.6% (29/32) [75.8%; 98.8%]	92.4% (122/132) [86.6%; 95.8%]
	Challenge	51	41	1	9	0	100% (41/41) [91.4%; 100%]	90.0% (9/10) [59.6%; 98.2%]
	Combined	215	70	11	131	3	95.9% (70/73) [88.6%-98.6%]	92.3% (131/142) [86.7%-95.6%]

[1]*For Enterobacteriacea challenge isolates, (13) false positives were observed from 57 isolates that were negative for carbapenemase-production by the Reference Method. These isolates included the following organisms—(8) K. penumoniae spp, (1) P. stuartii, (1) P. mirabilis, (1) K. oxytoca, (1) E. coli, and (1). K. aerogenes.*

Table 9. BD Phoenix CPO Detect Test Performance [Ambler Classification] vs the Composite Reference Method

Ambler Class	Isolate Type	Total #	TP	FP	TN	FN	PPA [95% CI]	NPA [95% CI]
Class A	Clinical	1135	64	14	1043	14	82.1% (64/78) [72.1%; 89.0%]	98.7% (1043/1057) [97.8%; 99.2%]
	Challenge	317	59	1	247	10	85.5% (59/69) [75.3%; 91.9%]	99.6% (247/248) [97.8%; 99.9%]
	Combined	1452	123	15	1290	24	83.7% (123/147) [76.9%; 88.8%]	98.9% (1290/1305) [98.1%; 99.3%]
Class B	Clinical	1135	52	10	1051	22	70.3% (52/74) [59.1%; 79.5%]	99.1% (1051/1061) [98.3%; 99.5%]
	Challenge	317	76	9	214	18	80.9% (76/94) [71.8%; 87.5%]	96.0% (214/223) [92.5%; 97.9%]
	Combined	1452	128	19	1265	40	76.2% (128/168) [69.2%; 82%]	98.5% (1265/1284) [97.7%; 99.1%]
Class D	Clinical	1135	65	11	1042	17	79.3% (65/82) [69.3%; 86.6%]	99.0% (1042/1053) [98.1%; 99.4%]
	Challenge	317	70	2	240	5	93.3% (70/75) [85.3%; 97.1%]	99.2% (240/242) [97.0%; 99.8%]
	Combined	1452	135	13	1282	22	86.0% (135/157) [79.7%; 90.6%]	99.0% (1282/1295) [98.3%; 99.4%]

The percent of unclassified isolates as determined by the BD Phoenix CPO detect test was 5.2% (76/1452). For those isolates identified as carbapenemase producers by the Reference Method, 13.2% (64/486) were not assigned to an Ambler class by BD Phoenix CPO detect. Performance of the device for isolates in which BD Phoenix CPO detect yielded a CPO detection result with Ambler classification is presented in the **Table 10** (n=1357), where the PPA and NPA for each classification is shown with (95) isolates excluded. Using the data in **Table 10** below, the Ambler class for the carbapenemase was correctly reported by the BD Phoenix CPO detect test the following % of times—Class A: 93.8% (122/130), Class B: 87.5% (126/144), and Class D: 94.4% (134/142).

Table 10. BD Phoenix CPO Detect Ambler Classification Performance vs the Composite Reference Method (Clinical and Challenge Isolates Combined with Exclusions)[1]

Ambler Class	Total #	TP	FP	TN	FN	PPA	NPA
Class A	1357	122	8	1221	6	95.3% (122/128) [90.2%; 97.8%]	99.3% (1221/1229) [98.7%; 99.7%]
Class B	1357	126	18	1205	8	94.0% (126/134) [88.6%; 96.9%]	98.5% (1205/1223) [97.7%; 99.1%]
Class D	1357	134	8	1208	7	95.0% (134/141) [90%; 98%]	99.3% (1208/1216) [98.7%; 99.7%]

[1]*A total of 95 isolates were excluded in this analysis—(76) BD Phoenix CPO detect test unclassified isolates, (21) isolates where the Reference Method results were carbapenemase positive, but no Ambler class could be assigned, and (7) isolates containing multiple carbapenemase genes.*

b. Clinical specificity:

See above

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

Not Applicable

4. Clinical cut-off:

Not Applicable

5. Expected values/Reference range:

Of the 735 isolates included in the analysis for carbapenemase detection and reported as *'not susceptible'* based on conventional phenotypic (AST) results, 506 isolates were determined to be carbapenemase producers by the BD Phoenix CPO detect test. For the 717 carbapenem susceptible isolates tested, 713 isolates were determined to be negative for carbapenemase production by the BD Phoenix CPO detect test. **Tables 11-14** show the results of the BD Phoenix CPO detect test compared to susceptibility test results for the 1452 isolates included in the clinical study (combined and separately by organism group).

Table 11. All Samples (*Enterobacteriaceae* + *Pseudomonas aeruginosa* + *Acinetobacter baumannii*), n=1452

BD Phoenix CPO Detect Test		Phenotype (AST)		
		NS[1] (not susceptible)	S[1] (susceptible)	Total
	CPO Detected	506	4	510
	CPO Not Detected	229	713	942
	Total	735	717	1452

[1]NS denotes that the isolate was 'not susceptible' to at least one of the carbapenems tested. S means the isolate was susceptible to all relevant carbapenems tested. For Pseudomonas aeruginosa and Acinetobacter baumannii/Acinetobacter calcoaceticus complex, ertapenem was not used to determine NS as these organisms are intrinsically resistant to ertapenem.

Table 12. *Enterobacteriaceae* Only, n=1099

BD Phoenix CPO Detect Test		Phenotype (AST)		
		NS (not susceptible)	S (susceptible)	Total
	CPO Detected	357	2	359
	CPO Not Detected	174	566	740
	Total	531	568	1099

Table 13. *Pseudomonas aeruginosa* Only, n=215

BD Phoenix CPO Detect Test		Phenotype (AST)		
		NS (not susceptible)	S (susceptible)	Total
	CPO Detected	79	2	81
	CPO Not Detected	44	90	134
	Total	123	92	215

Table 14. *Acinetobacter baumannii* Only, n=138

BD Phoenix CPO Detect Test		Phenotype (AST)		
		NS (not susceptible)	S (susceptible)	Total
	CPO Detected	70	0	70
	CPO Not Detected	11	57	68
	Total	81	57	138

N. Proposed Labeling:

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

O. Conclusion:

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