July 6, 2018

bioMérieux SA
Asa Karlsson
Sr. Regulatory Affairs Manager
376 Chemin de l'Orme
Marcy l'Etoile, 69280 Fr

Re: K181092
Trade/Device Name: CHROMID CARBA agar (CARB)
Regulation Number: 21 CFR 866.1700
Regulation Name: Culture medium for antimicrobial susceptibility tests
Regulatory Class: Class II
Product Code: JSO
Dated: April 24, 2018
Received: April 25, 2018

Dear Asa Karlsson:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/) and CDRH Learn (http://www.fda.gov/Training/CDRHLearn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (http://www.fda.gov/DICE) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Ribhi Shawar -S For

Uwe Scherf, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*
K181092

Device Name
CHROMID® CARBA agar (CARB)

Indications for Use *(Describe)*
CHROMID® CARBA agar is a selective and differential chromogenic medium that is intended for the qualitative detection and presumptive identification of carbapenemase-producing Escherichia coli and Klebsiella pneumoniae in rectal swab specimens from patients at risk of colonization. CHROMID® CARBA agar is intended as an aid in the detection, identification of colonization and control of these bacteria in a healthcare setting.

Rectal swabs are inoculated directly onto CHROMID® CARBA agar without enrichment and results can be interpreted after incubation for 18-24 hours. Presumptive carbapenemase-producing colonies of E. coli appear pink to burgundy and those of K. pneumoniae appear blue-green or blue-grey.

Other organisms besides carbapenemase-producing E. coli and K. pneumoniae can also grow on CHROMID® CARBA agar with colonies that appear pink to burgundy or blue-green to blue-grey. Sub-culture to non-selective medium is required to confirm organism identity, for antimicrobial susceptibility testing, confirmation of carbapenemase production and epidemiological typing.

A lack of growth or the absence of pink to burgundy or blue-green to blue-grey colonies does not preclude the carriage of carbapenemase producing organisms.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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SECTION 029. 510(k) SUMMARY

510(k) SUMMARY
CHROMID® CARBA agar

A. 510(k) Submission Information:

510(k) Submission: K181092

Submitter's Name: bioMerieux SA

Address: 376 Chemin de l'Orme
69280 Marcy l'Etoile, FRANCE

Contact Person: Asa Karlsson
Sr. Regulatory Affairs Manager

Phone Number: +33 (0)6 48 61 68 49
Email: asa.karlsson@biomerieux.com

510(k) Summary

Date of Preparation: June 28, 2018

B. Device Name:

Formal/Trade Name: CHROMID® CARBA agar

Classification Name: 21 CFR 866.1700
Culture Medium for Antimicrobial Susceptibility Test

Product Code JSO
Culture Media, Antimicrobial Susceptibility Test, Excluding Mueller Hinton Agar

Common Name: CHROMID® CARBA agar (CARB)

C. Predicate Device: CHROMID® VRE agar (K091025)

D. 510(k) Summary:

Intended Use:

CHROMID® CARBA agar is a selective and differential chromogenic medium that is intended for the qualitative detection and presumptive identification of carbapenemase-producing *Escherichia coli* and *Klebsiella pneumoniae* in rectal swab specimens from

patients at risk of colonization. CHROMID® CARBA agar is intended as an aid in the detection, identification of colonization and control of these bacteria in a healthcare setting.

Rectal swabs are inoculated directly onto CHROMID® CARBA agar without enrichment and results can be interpreted after incubation for 18-24 hours. Presumptive carbapenemase-producing colonies of *E. coli* appear pink to burgundy and those of *K. pneumoniae* appear blue-green or blue-grey.

Other organisms besides carbapenemase-producing *E. coli* and *K. pneumoniae* can also grow on CHROMID® CARBA agar with colonies that appear pink to burgundy or blue-green to blue-grey. Sub-culture to non-selective medium is required to confirm organism identity, for antimicrobial susceptibility testing, confirmation of carbapenemase production and epidemiological typing.

A lack of growth or the absence of pink to burgundy or blue-green to blue-grey colonies does not preclude the carriage of carbapenemase producing organisms.

Indications for use:
See Intended Use

Device Description:
CHROMID® CARBA agar consists of a nutritive base combining different peptones, 3 chromogenic substrates and antibiotics. These components enable the screening and presumptive identification of *E. coli*: spontaneous coloration (pink to burgundy) of strains producing β-glucuronidase (β-GUR) and/or β-galactosidase (β-GAL) and *K. pneumoniae*: spontaneous blue-green to bluish-grey coloration of strains producing β-glucosidase (β-GLU) from rectal swabs.

Substantial Equivalence:
The similarities of CHROMID® CARBA agar when compared to the predicate device are described in the following table:

Category	**Predicate Device bioMerieux SA CHROMID® VRE agar K091025**	**Proposed Device bioMerieux SA CHROMID® CARBA agar K181092**	**Substantially equivalent**
Similarities			
Classification, and Product code	Class II, 21 CFR 866.1700 JSO	Class II, 21 CFR 866.1700 JSO	Equivalent
Intended Use	CHROMID® VRE agar is a selective and differential chromogenic medium containing 8 µg/mL vancomycin, for the qualitative detection of *Enterococcus faecium* and *E. faecalis* showing acquired vancomycin resistance (VRE) in stool specimens. CHROMID® VRE agar can be used as an aid to identify, prevent and control	CHROMID® CARBA agar is a selective and differential chromogenic medium that is intended for the qualitative detection and presumptive identification of carbapenemase-producing *Escherichia coli* and *Klebsiella pneumoniae* in rectal swab specimens from patients at risk of colonization. CHROMID® CARBA agar is	Equivalent Both agars are designed to detect resistance mechanisms but for different antimicrobial species.

Category	Predicate Device bioMerieux SA CHROMID® VRE agar K091025	Proposed Device bioMerieux SA CHROMID® CARBA agar K181092	Substantially equivalent
	VRE colonization in healthcare stings. CHROMID® VRE agar is not intended to diagnose VRE infection nor to guide or monitor treatment for infections. Subculture to non-selective media (e.g., trypticase soy agar with 5% sheep blood) is needed for further identification, susceptibility testing and epidemiological typing.	intended as an aid in the detection, identification of colonization and control of these bacteria in a healthcare setting. Rectal swabs are inoculated directly onto CHROMID® CARBA agar without enrichment and results can be interpreted after incubation for 18-24 hours. Presumptive carbapenemase-producing colonies of *E. coli* appear pink to burgundy and those of *K. pneumoniae* appear blue-green or blue-grey. Other organisms besides carbapenemase-producing *E. coli* and *K. pneumoniae* can also grow on CHROMID® CARBA agar with colonies that appear pink to burgundy or blue-green to blue-grey. Sub-culture to non-selective medium is required to confirm organism identity, for antimicrobial susceptibility testing, confirmation of carbapenemase production and epidemiological typing. A lack of growth or the absence of pink to burgundy or blue-green to blue-grey colonies does not preclude the carriage of carbapenemase producing organisms.	
Test method	Manual, culture media	Manual, culture media	Identical
Method of inoculation	Direct inoculation of the sample type without enrichment.	Direct inoculation of the sample type without enrichment.	Identical
Storage of the device	2-8° C in their box until expiry date. Outside the box, plates can be stored for 2 weeks in the dark in the cellophane sachet at 2-8° C.	2-8° C in their box until expiry date. Outside the box, plates can be stored for 2 weeks in the dark in the cellophane sachet at 2-8° C.	Identical
Formula	**Formula / Liter** Casein and meat peptone (bovine or porcine) ……..…18g Heart peptone……..……..3g Corn starch …….……..1g	**Formula/ Liter** Casein and meat peptone (bovine or porcine) ……..…13g Soy peptone……..……..5g Carbohydrates…….……..1g	Equivalent The formulas contain similar ingredients and have

Category	Predicate Device bioMerieux SA CHROMID® VRE agar K091025	Proposed Device bioMerieux SA CHROMID® CARBA agar K181092	Substantially equivalent
	Sodium chloride……6g Agar……..15g Selective mixture……....28.8mg Chromogenic mixture…....0.13g Purified water……..……...1L Final pH: 7.2	L-Tryptophan…….……0.9g Phosphate buffer …..…….1g Nutrient mixture…….2g Agar……..18g Selective mixture……...…1.35g Chromogenic mixture…....1.23g Purified water……..……...1L Final pH: 7.4	a similar final pH. Both formulas can be adjusted and/or supplemented according to the performance criteria required.
Differences			
Analytes	Vancomycin resistant *E. faecium* and *E. faecalis.*	Carbapenemase-producing *E. coli* and *K. pneumoniae.*	Different target species and antimicrobial resistance phenotypes.
Specimen Types	Swabs (stools)	Swabs (rectal)	Different specimen types
Interpretation of positive results	Observe bacterial growth and the appearance of colonies. Positive *E. faecium*: Violet colonies. Positive *E. faecalis*: Blue to green colonies.	Observe bacterial growth and the appearance of colonies. Presumptive positive *E. coli*: Pink to burgundy colonies. Presumptive positive *K. pneumoniae*: Blue-green to bluish-grey colonies.	Equivalent Different color changes depending on bacterial species provide a visual interpretation of positive results. Positive results obtained on CHROMID® CARBA agar are presumptive.
Incubation time and conditions	Incubate at 35-37°C in aerobic conditions. Examined for growth after 24 to 48 hours.	Incubate at 35-37°C in aerobic conditions. Examined for growth after 18 to 24 hours.	Identical. Potential extended incubation time for the predicate.

Both the devices use a selective mixture for the detection of resistance mechanisms and a chromogenic mixture for the presumptive identification of the bacterial species. Their formulas and method of inoculation on the agar are similar. The differences between the new device and the predicate device are related to the bacterial species and antimicrobial resistance mechanisms detected and the associated colony colors, the specimen type and incubation time. The performance data presented in this submission support a substantial equivalence

decision. CHROMID® CARBA agar is substantially equivalent to CHROMID® VRE agar (K091025).

Performance Characteristics:

Analytical Studies

The following analytical studies were conducted to evaluate the performance of the CHROMID® CARBA agar: Interfering Substances, Recovery Study (Limit of Detection), Cross Reactivity (Analytical Specificity), Challenge Testing (Analytical Reactivity), Mixed Infection and Incubation Time. All analytical performance studies demonstrated acceptable results.

Interfering Substances: No interference was observed with 21 interfering substances including Zinc Oxide, Pramocaine hydrochloride, Miconazole nitrate, K-Y Jelly, Loperamide hydrochloride, Playtex Personal wipes, Witch Hazel, Diosmectite, Talc, K-Y Liquibeads vaginal moisturizer, Vaseline, Glycerol, Phenylephrine HCl, Trojan Enz condoms, Physiological saline, Bisacodyl, Ispaghula husk, Benzocaine + Resorcinol, Ruscoside + Lidocaine hydrochloride + Prednacinolone acetonide, Hydrocortisone and Human Blood.

Recovery Study (Limit of Detection (LOD)): Two well-characterized KPC strains *K. pneumoniae* ATCC® 1705™ and *E. coli* ATCC® 2340™ were tested to determine the lowest number of CFU/mL detected on CHROMID® CARBA agar. After 18 to 24 hours of incubation, the lowest dilution for the detection (Limit of Detection (LOD)) of both strains was $1.5x10^3$ CFU/mL.

Cross Reactivity (Analytical Specificity): To evaluate the analytical specificity of CHROMID® CARBA agar, testing was performed with high concentrations (10^6 CFU/mL; 1000 times the LOD) of 59 target and non-target organisms. The strains tested included bacterial and fungal species encountered in stools, CPE and strains of *E. coli* and *K. pneumoniae* that produced other carbapenemases besides KPC type enzyme. After 18 to 24 hours of incubation, growth and colony coloration were analyzed.
Sixteen CPE grew with pink to burgundy or blue-green to blue-grey colonies:

- Six KPC strains belonging to the following species: three *C. freundii* (blue-grey), one *P. rettgerii* (blue-green), one *E. cloacae* (blue-green) and one *K. aerogenes* [*E. aerogenes*] (blue-green),
- Four strains of *K. pneumoniae* with a resistant mechanism other than KPC: one VIM, one IMP, one OXA-48, one NDM (all blue-green),
- Three strains of *E. coli* with a resistant mechanism other than KPC: one NDM, one VIM, one IMP (all pink-to burgundy),
- Two strains of *M. morganii* with NDM (both blue-green),
- One strain of *S. marcescens* with SME (blue-green).

Pseudomonas aeruginosa (VIM), *Stenotrophomonas maltophilia* (VIM), *Pseudomonas putida* and *Acinetobacter baumanii* (NDM) grew on CHROMID® CARBA agar but without a characteristic coloration (colorless).
See Limitations section in the package insert.

Challenge Testing (Analytical Reactivity): Fifty-two well-characterized KPC-EK strains were tested on CHROMID® CARBA agar using a calibrated inoculum at $4.5x10^3$ CFU/mL (3 times the LOD).
After 18 to 24 hours of incubation, all the *K. pneumoniae* strains were recovered with characteristic blue-green color. Among the 11 *E. coli* studied, 9 of them grew with a

characteristic burgundy color. The two other *E. coli* failed to grow; of these, one had an MIC in the susceptible range for ertapenem and was intermediate for imipenem and meropenem and the other was susceptible to all three carbapenems tested.

Mixed Infection: Four carbapenemase-producing strains including two *E. coli* and two *K. pneumoniae* that each harbored KPC carbapenemase were tested at three times the LOD value in mixtures with other target and non-target organisms at 10^4 to 10^8 CFU/mL:

- one carbapenem non-susceptible carbapenemase-negative *K. pneumoniae*,
- one carbapenem non-susceptible *Pseudomonas aeruginosa* with VIM carbapenemase,
- one carbapenem non-susceptible *E. coli* with NDM carbapenemase,
- one carbapenem susceptible *K. pneumoniae*.
- one carbapenem non-susceptible *Enterobacter cloacae* with KPC carbapenemase
- one carbapenem non-susceptible *Morganella morganii* with NDM carbapenemase
- one carbapenem non-susceptible *Providencia rettgeri* with KPC carbapenemase

After 18 to 24 hours of incubation, the results obtained showed that when the competitive species were present at $<10^8$ CFU/mL, colonies of the four KPC producing target organisms grew with the characteristic color (either pink-burgundy for *E. coli* or blue-green/blue-grey for *K. pneumoniae*). However, when present at 10^8 CFU/mL, KPC-producing *E. cloacae*, NDM-producing *M. morganii*, VIM-producing *P. aeruginosa* and NDM-producing *E. coli* inhibited or masked the growth of one or more KPC-producing target organisms. Please refer to the Limitations section of the package insert.

Incubation: Ten well-characterized isolates representing KPC-EK strains were tested every two hours between 16 and 28 hours of incubation at +35°C ± 2°C. The 10 strains were recovered with the expected colony colors after 16 hours of incubation and at each reading interval until 28 hours. The results of the study support the ability to recover carbapenemase-producing *E. coli* and *K. pneumoniae* on CHROMID® CARBA agar after incubation for 18-24 hours as stipulated in the device labeling.

Clinical Studies including Challenge, Reproducibility and Quality Control

Challenge Study: Fifty well characterized isolates were tested at one external site at two times the LOD in saline matrix.
The following strains were tested:
11 KPC negative strains: 6 *K. pneumoniae* and 5 *E. coli*,
39 KPC positive strains: 27 *K. pneumoniae* and 12 *E. coli.*
KPC positive strains included KPC-2, KPC-3 and KPC-4 gene variants.
Other resistance mechanisms were tested among the negative strains, including ESBL, AmpC and carbapenem non-susceptible carbapenemase-negative strains.

CHROMID® CARBA agar at 24 hours compared to expected status

K. pneumoniae			
CHROMID® CARBA	**Expected status**		
	Negative	Positive	Total
Negative	23	0	23
Positive	0	27	27
Total	23	27	50

Positive Percent Agreement 100.0% (95% CI: [87.5 - 100.0] %)
Negative Percent Agreement 100.0% (95% CI: [85.7 - 100.0] %)

E. coli			
CHROMID® CARBA	**Expected status**		
	Negative	Positive	Total
Negative	38	0	38
Positive	0	12	12
Total	38	12	50

Positive Percent Agreement 100.0% (95% CI: [75.8 - 100.0] %)
Negative Percent Agreement 100.0% (95% CI: [90.8 - 100.0] %)

Reproducibility and Quality Control:

Ten well-characterized isolates of carbapenemase-producing *E. coli* (4) and *K. pneumoniae* (6) that harbored bla_{KPC} were tested in a blinded fashion in triplicate each day for five days at three sites, and by two different operators at each site. Isolates were tested at approximately the LOD target level and plates were read at 24 hours. The overall between-site reproducibility was 99.3% (894/900).

Quality Control was performed with three quality control organisms tested at each study site by CHROMID® CARBA agar on each day of comparative and reproducibility testing:

Species	Strain	Expected Result	Agreement (%)
K. pneumoniae	ATCC® BAA-1705™	Blue-green/blue-grey colonies	190/190 (100)
E. coli	ATCC® BAA-2340™	Pink-burgundy colonies	190/190 (100)
K. pneumoniae	ATCC® 700603™	No growth	189/190 (99.5)

Overall, 569/570 (99.8%) of Quality Control test results for CHROMID® CARBA agar were as expected.

CLINICAL PERFORMANCE

Method Comparison

Prospective study on fresh clinical samples:

The performance of CHROMID® CARBA agar was evaluated at three external laboratories (2 in the US, 1 in Europe) using prospectively collected rectal swabs. A total of 1099 swabs from unique subjects were initially enrolled, of which 390 were excluded from the analysis of performance due to quality control failure (343), missing data (42) or questionable data reliability (5). Results from 709 swabs were therefore included in the analysis of performance. The characteristics of all colonies growing on CHROMID® CARBA medium (pink-to-burgundy, blue-green to blue-grey, colorless, and colors other than pink-to-burgundy or blue-green to blue-grey) at 18 to 24 hours were compared to the results obtained from the CDC enrichment culture method using selective Trypticase Soy broth, followed by subculture to MacConkey agar and phenotypic and genetic characterization of isolated lactose fermenting colonies.[9]
Isolates from both the reference method and CHROMID® CARBA agar were identified biochemically and their carbapenemase status was determined by carbapenem susceptibility and CARBA NP testing, as well as PCR for carbapenemase resistance markers (**Table 1**).

Table 1. Algorithm for determining carbapenemase status of isolates

Carbapenem MIC [a]	**Carba NP Test**	**Carbapenemase PCR** [b]	**Carbapenemase Status**
Non-susceptible	Positive	Positive	Positive
Non-susceptible	Positive	Negative	Negative
Non-susceptible	Negative	Positive	Positive
Non-susceptible	Negative	Negative	Negative
Susceptible	Positive	Positive	Positive
Susceptible	Positive	Negative	Negative
Susceptible	Negative	Positive	Negative [c]
Susceptible	Negative	Negative	Negative

[a] Non-susceptible: Intermediate or Resistant to one or more of the carbapenem antimicrobial agents tested (ertapenem, imipenem and meropenem)

[b] Multiplex PCR for *bla*$_{IMP}$, *bla*$_{KPC}$, *bla*$_{NDM}$, *bla*$_{OXA-48}$ or *bla*$_{VIM}$

[c] Phenotypic evidence of non-susceptibility to carbapenems in addition to a positive PCR result was required to establish the Carbapenemase Status as positive

The results of the study are presented in **Tables 2** and **3** for carbapenemase-producing *E. coli* and *K. pneumoniae*, respectively.

Table 2. Detection of carbapenemase-producing *E. coli* in the Prospective Clinical Study

		CDC Reference Culture Method		
		Positive	**Negative**	**Total**
CHROMID® CARBA agar	**Positive** [a]	0	2 [c]	**2**
	Negative [b]	0	707	**707**
	Total	**0**	**709**	**709**
Positive Percent Agreement		Not applicable		
Negative Percent Agreement		99.7% (707/709); 95% CI 99.0-99.9%		

95% CI: 95% score confidence interval

[a] Pink-burgundy colonies

[b] No growth or colonies not pink-burgundy

[c] Colonies from 1/2 specimens confirmed as carbapenem non-susceptible, carbapenemase negative *K. pneumoniae*; colonies from 1/2 specimens identified as *Enterococcus faecalis*

Table 3. Detection of carbapenemase-producing *K. pneumoniae* in the Prospective Clinical Study

		CDC Reference Culture Method		
		Positive	**Negative**	**Total**
CHROMID® CARBA agar	**Positive** [a]	43	15 [e, f]	**58**
	Negative [b]	8 [c, d]	643	**651**
	Total	**51**	**658**	**709**
Positive Percent Agreement		84.3% (43/51); 95% CI 72.0-91.8%		
Negative Percent Agreement		97.7% (643/658); 95% CI 96.3-98.6%		

95% CI: 95% score confidence interval

[a] Blue-green/blue-grey colonies

[b] No growth or colonies not blue-green/blue-grey

[c] Includes 1 specimen from which carbapenemase-positive *K. pneumoniae* was recovered by the Reference Method but which yielded blue-green to blue-grey colonies on CHROMID® CARBA agar that were identified biochemically as *P. aeruginosa*

[d] 8/8 isolates grew on CHROMID® CARBA agar when inoculated at approximately the LoD target level (10^3 CFU/mL in stool); all 8 carried bla_{KPC}, were Carba NP Test positive and carbapenem non-susceptible (resistant to ertapenem, imipenem and meropenem)

[e] 5/15 isolates on CHROMID® CARBA agar were confirmed as carbapenem non-susceptible *K. pneumoniae* that carried: 4/5 isolates were Carbapenemase Status-positive and carried bla_{KPC} and 1/5 isolates was Carbapenemase Status-negative

[f] 10/15 specimens produced blue-green/blue-grey colonies that were identified as Enterobacteriaceae other than *K. pneumoniae* (*Serratia marcescens* (6), *Citrobacter freundii* (2) and *Enterobacter cloacae* (2))

Analysis of contrived samples:

To supplement the prospective clinical study, testing was also performed using contrived specimens consisting of well-characterized isolates in simulated rectal swab matrix (stool diluted in saline).

A total of 210 contrived samples inoculated with one of the following concentrations of organisms: 1x LOD, 3x LOD, 10x LOD, were included in the study. The samples were blinded and tested at four different sites.

The results of the study are summarized in **Tables 4** and **5** for carbapenemase-producing *E. coli* and *K. pneumoniae*, respectively.

Table 4. Detection of carbapenemase-producing *E. coli* in contrived specimens

		Organism Identity & Carbapenemase Status		
		Positive	**Negative**	**Total**
CHROMID CARBA agar	**Positive** [a]	16	2 [c]	**18**
	Negative [b]	4 [d]	188	**192**
	Total	**20**	**190**	**210**
Positive Percent Agreement		80.0% (16/20); 58.4-91.9%		
Negative Percent Agreement		98.9% (188/190); 95% CI 96.2-99.7%		

95% CI: 95% score confidence interval

[a] Pink-burgundy colonies

[b] No growth or colonies not pink-burgundy

[c] 2/2 isolates were carbapenem non-susceptible *E. coli* (resistant to meropenem and ertapenem and an intermediate MIC for imipenem); both isolates were positive for Extended Spectrum β-Lactamase (ESBL)

[d] False negative results were obtained with 4 strains of carbapenem non-susceptible *E. coli* that harbored $bla_{\text{OXA-48}}$ (2), bla_{NDM} (1) and bla_{VIM} (1) and which were spiked at target levels ranging from 1X to 10X LoD; 2/4 strains had an intermediate MIC to at least one carbapenem including 1 strain that was also susceptible to ertapenem

Table 5. Detection of carbapenemase-producing *K. pneumoniae* in contrived specimens

		Organism Identity & Carbapenemase Status		
		Positive	**Negative**	**Total**
CHROMID® CARBA agar	**Positive** [a]	84	11 [c, d]	**95**
	Negative [b]	3 [e]	112 [f]	**115**
	Total	**87**	**123**	**210**
Positive Percent Agreement		96.6% (84/87); 95% CI % 90.3-98.8%		
Negative Percent Agreement		91.1% (112/123); 95% CI 84.7-94.9%		

95% CI: 95% score confidence interval

[a] Blue-green/blue-grey colonies

[b] No growth or colonies not blue-green/blue-grey

[c] 5/11 false positive results were obtained with carbapenem non-susceptible *K. pneumoniae*, all of which were positive for ESBL (3) or ESBL and AmpC (2)

[d] 6/11 false positive results were due to Carbapenemase Status-positive species of Enterobacteriaceae other than *K. pneumoniae* that harbored bla_{KPC}: *E. cloacae* (4), *K. oxytoca* (1) and *K. ozaenae* (1)

[e] 3/3 false negative results were obtained with Carbapenemase Status positive isolates at the LoD target level; the strains carried carbapenemase resistance markers as follows: bla_{IMP} (1), bla_{KPC} (1) or bla_{OXA-48} (1); 2/3 strains had a susceptible or intermediate MIC to at least one of the three carbapenems tested (ertapenem, imipenem or meropenem)

[f] 18/112 samples contained carbapenem non-susceptible strains of *K. pneumoniae* of which 17 were phenotypically carbapenemase negative; 11/18 were positive for ESBL and 6/18 were positive for AmpC

The clinical study which was performed under CLSI M100-S25, S26, S27 and S28, between April, 2016 through October, 2017 is also compliant to CLSI M100-S28, except the new requirement regarding the integrity check by a disk diffusion or MIC method for the QC strain ATCC® 700603™ which was not required by S26 and as such was not done. No impact on the performances is expected.