DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
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BIOMERIEUX SA
ASA KARLSSON
SR. MANAGER, REGULATORY AFFAIRS MICROBIOLOGY
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CRAPONNE 69290
FRANCE

Re: K162385
Trade/Device Name: RAPIDEC CARBA NP
Regulation Number: 21 CFR 866.1640
Regulation Name: Antimicrobial Susceptibility Test Powder
Regulatory Class: II
Product Code: PTJ
Dated: March 27, 2017
Received: March 28, 2017

Dear Ms. 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 Parts 801 and 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.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. 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 the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Ribhi Shawar -A
For

Uwe Scherf, M.Sc., Ph.D.
Director
Division of Microbiology Devices
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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: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K162385

Device Name
RAPIDEC® CARBA NP

Indications for Use *(Describe)*
RAPIDEC® CARBA NP is a phenotypic (colorimetric) *in vitro* diagnostic test for the qualitative detection of carbapenemase enzymes in *Enterobacteriaceae* and *Pseudomonas aeruginosa* colonies that have elevated MIC values to any carbapenem. RAPIDEC® CARBA NP is performed on pure colonies grown on non-selective sheep blood agar culture media.

RAPIDEC® CARBA NP is intended as an aid in the prevention and control of infection caused by carbapenemase-producing *Enterobacteriaceae* and *Pseudomonas aeruginosa.*

RAPIDEC® CARBA NP is not intended to guide or monitor the treatment for these bacterial infections. A negative result does not preclude the presence of carbapenemase enzymes. The ability of RAPIDEC® CARBA NP to detect carbapenemase enzymes encoded by genetic markers other than KPC, NDM, OXA-48, VIM, and IMP has not been established. RAPIDEC® CARBA NP testing should be used in conjunction with other laboratory tests including antimicrobial susceptibility testing.

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 8. 510(k) SUMMARY

510(k) SUMMARY
RAPIDEC® CARBA NP

510(k) Submission Information:

Submitter's Name: bioMerieux SA

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Date of Preparation: July 29, 2016

Device:

Formal/Trade Name: RAPIDEC® CARBA NP
Classification: II
Regulation Number: 21 CFR 866.1640
Regulation Name: Antimicrobial Susceptibility Test Powder

Product Code: PTJ

Common Name: RAPIDEC® CARBA NP

Predicate Device: Clearview® Exact PBP2a Test (K091766)

510(k) Summary:

Intended use:

RAPIDEC® CARBA NP is a phenotypic (colorimetric) *in vitro* diagnostic test for the qualitative detection of carbapenemase enzymes in *Enterobacteriaceae* and *Pseudomonas aeruginosa* colonies that have elevated MIC values to any carbapenem. RAPIDEC® CARBA NP is performed on pure colonies grown on non-selective sheep blood agar culture media.
RAPIDEC® CARBA NP is intended as an aid in the prevention and control of infection caused by carbapenemase-producing *Enterobacteriaceae* and *Pseudomonas aeruginosa.*

RAPIDEC® CARBA NP is not intended to guide or monitor the treatment for these bacterial infections. A negative result does not preclude the presence of carbapenemase enzymes. The ability of RAPIDEC® CARBA NP to detect carbapenemase enzymes encoded by genetic markers other than KPC, NDM, OXA-48, VIM and IMP has not been established. RAPIDEC® CARBA NP testing should be used in conjunction with other laboratory tests including antimicrobial susceptibility testing.

Device Description:

The RAPIDEC® CARBA NP strip is composed of 5 wells prepared with premeasured portions of the necessary substrates for the reactions. In addition, the kit contains the necessary accessories for performing the test.

In order to rehydrate the dry reagents and initiate the reactions, wells **a**, **b** and **c** are filled with 100 µL of API Suspension Medium (purified water). The strip is left at room temperature for 4-10 minutes to allow the dry reagents to reconstitute in the wells. The bacterial inoculum suspension is prepared in well **c** until the turbidity equals well **b**. Well **c** contains the lysis buffer. In order to achieve lysis of the inoculum suspension, which enables the extraction of the enzyme, the strip is left at room temperature for additionally 30 minutes.
As the next step, 25 µL of the lysed inoculum suspension is transferred to wells **d** and **e** and 25 µL from well **a** (phenol red solution) is also transferred to wells **d** and **e**. The strip is incubated for 30 minutes at 33-38°C to allow for the hydrolysis to occur and change in color of the phenol red solution in case of presence of a carbapenemase enzyme. The initial reading is performed after 30 minutes of incubation. In case of a negative or doubtful reaction, the strip is re-incubated for an additional 1 hour and 30 minutes before performing the final reading.
The hydrolysis acidifies the medium which results in the change in color of the pH indicator. Reading is performed by comparing the colors in wells **d** and **e**. The test is positive when a significant variation in color is observed between the two wells. For example, the control well is red and the test well has changed to yellow.

Substantial Equivalence:

The similarities and differences of the RAPIDEC® CARBA NP when compared to the predicate device, Clearview® Exact PBP2a Test (K091766), are described in the following table.

Item	**Device:** **RAPIDEC® CARBA NP**	**Predicate:** **Clearview® Exact PBP2a Test (K091766)**
Similarities		
Intended Use	RAPIDEC® CARBA NP is a phenotypic (colorimetric) *in vitro* diagnostic test for the qualitative	The Clearview® Exact PBP2a Test is a qualitative, *in vitro*, immunochromatographic assay

Item	Device: RAPIDEC® CARBA NP	Predicate: Clearview® Exact PBP2a Test (K091766)
	detection of carbapenemase enzymes in *Enterobacteriaceae* and *Pseudomonas aeruginosa* colonies that have elevated MIC values to any carbapenem. RAPIDEC® CARBA NP is performed on pure colonies grown on non-selective sheep blood agar culture media. RAPIDEC® CARBA NP is intended as an aid in the prevention and control of infection caused by carbapenemase-producing *Enterobacteriaceae* and *Pseudomonas aeruginosa*. RAPIDEC® CARBA NP is not intended to guide or monitor the treatment for these bacterial infections. A negative result does not preclude the presence of carbapenemase enzymes. The ability of the RAPIDEC® CARBA NP to detect carbapenemase enzymes encoded by genetic markers other than KPC, NDM, OXA-48, VIM and IMP has not been established. RAPIDEC® CARBA NP testing should be used in conjunction with other laboratory tests including antimicrobial susceptibility testing	for the detection of penicillin-binding protein 2a (PBP2a) in isolates identified as *Staphylococcus aureus*, as an aid in detecting methicillin-resistant *Staphylococcus aureus* (MRSA). The Clearview® Exact PBP2a Test is not intended to diagnose MRSA nor to guide or monitor treatment for MRSA infections.
Capability	Marker of antimicrobial resistance	Same
Interpretation	Does not provide MIC information	Same
Sample type	Bacterial isolates/colonial growth	Same
Culture media	Sheep blood agar	Same
Inoculum preparation	By touching well isolated colonies with an applicator stick	Same
Reaction	Lysis of bacterial cell wall	Same

Item	Device: RAPIDEC® CARBA NP	Predicate: Clearview® Exact PBP2a Test (K091766)
preparation		
Controls	Built-in procedural control on every test strip	Same
Reading	Visual based on color change	Same
Differences		
Technology	Manual hydrolyzing test for qualitative detection of carbapenemase enzymes (KPC, NDM, OXA-48, VIM and IMP) in *Enterobacteriaceae* and *Pseudomonas aeruginosa* based on change in color of a pH indicator.	Immunochromatographic assay for detection of penicillin-binding protein 2a (PBP2a) in isolates identified as *Staphylococcus aureus.*

RAPIDEC® CARBA NP demonstrated substantially equivalence when compared to the predicate device, Clearview® Exact PBP2a Test (K091766) and substantially equivalent performance when compared to the composite reference method (CLSI Carba NP test, PCR characterization and carbapenemase MIC determinations). The performance was evaluated following information in the FDA Class II Special Controls Guidance Document: *Antimicrobial Susceptibility Test (AST) Systems; Guidance for Industry and FDA, issued August 28, 2009*.

The Premarket Notification 510(k) presents data in support of RAPIDEC® CARBA NP.

Performance Characteristics:

Non-clinical (analytical) and clinical studies were performed for RAPIDEC® CARBA NP.

Analytical Performance

Quality Control
Two quality control organisms were tested at each study site by RAPIDEC® CARBA NP on each day of testing. The organisms tested were:

Klebsiella pneumoniae ATCC® BAA-1705™ (positive reaction)
Klebsiella pneumoniae ATCC® BAA-1706™ (negative reaction)

The results of QC testing with RAPIDEC® CARBA NP met the pre-defined acceptance criteria (≥95% agreement) when compared to the expected results as determined for the recommended QC strains.

Analytical Reactivity (Challenge testing)
A total of 43 carbapenemase producers as determined by the reference composite method were tested by the RAPIDEC® CARBA NP. There were (2) VIM producing *Pseudomonas aeruginosa* and 41 carbapenemase producing *Enterobactericeae* consisting of (16) KPC, (10) NDM, (7) OXA-48, (5) VIM and (3) IMP.
An initial reading was performed at 30 minutes and when the result was negative, the final reading was performed at a total of 2 hours of 33-38°C incubation.
All 43 strains were detected positive by RAPIDEC® CARBA NP following the reading protocol, with an analytical sensitivity of 100% (43/43)*.

* There were four negative results at the initial 30-minute read but became positive at the final 2–hour read; there were eight initial positive results that changed back to negatives when read again at 2 hours incubation.

Cross-reactivity
A total of 93 non-carbapenemase producing strains with elevated carbapenem MICs were tested on the RAPIDEC® CARBA NP test. The strains tested include 67 strains (i.e., 59 *Enterobacteriaceae,* 8 *Pseudomonas aeruginosa*) related to the intended use, 26 other organisms including non-fermenting gram negative rods, gram positive organisms and yeast. All strains were well-characterized. The resistance mechanisms were AmpC, high level AmpC, porin loss, ESBL, porin loss/ESBL, porin loss/AmpC, MRSA, and VRE. An initial reading was performed at 30 minutes and if the result was negative a final reading was performed at a total of 2 hours of 33-38°C incubation.
The analytical specificity was 97.9% (91/93) at 30 minutes of incubation due to the two intrinsic resistant *Stenotrophomonas maltophilia*. The analytical specificity was 93.6% (87/93) at 2 hours of incubation. The results demonstrated one *Enterobacteriaceae* (*Morganella morganii*) with an AmpC resistance and 5 non-fermenting gram negative rods (three intrinsic resistant *Stenotrophomonas maltophilia*, one each for *Burkholderia cepaciae* and *Sphingomonas paucimobilis*) have given a positive reaction with the RAPIDEC® CARBA NP.
For intended *Enterobacteriaceae* and *Pseudomonas aeruginosa* strains, the analytical specificity was 100% (67/67) at 30 minutes of incubation and 98.5% (66/67) at 2 hours of incubation because of the AmpC producing *Morganella morganii*.

Agar Culture Media Compatibility Studies
RAPIDEC® CARBA NP results with strains isolated on Columbia agar + 5% sheep blood (COS) were compared with those strains isolated on Trypticase Soy agar + 5% sheep blood (TSS). A total of 106 strains (92 carbapenemase producers and 14 non-carbapenemase producers) were tested. The carbapenemase producers included 19 IMP, 20 KPC, 20 VIM, 17 NDM, and 16 OXA-48. The positive rate for the carbapenemase producers was 94.6% (87/92) and 92.4% (85/92) for TSS and COS

respectively at the initial 30-minute read. There were five (4 OXA-48 producing *K. pneumoniae* and one KPC producing *K. pneumoniae*) that were negative for both media and two NDM producing *Providencia* spp. for COS at the 30-minute read. The positive rate was 98.9% (91/92) for both media due to one negative KPC producing *K. pneumoniae* at the final 2-hour read. The negative rate for non-carbapenemase producers was 100% for both media at 30-minute and 2-hour reads. The results indicates no significant differences between TSS and COS.

Clinical Studies

In the RAPIDEC® CARBA NP clinical study, a total of 457 strains consisting of 394 *Enterobacteriaceae* and 63 *P. aeruginosa* were evaluated across 5 sites using both the routine and the short subculture procedures.

Carbapenemase determination was determined by a composite reference method composed of three tests: carbapenem MIC (Imipenem, Meropenem, Ertapenem and/or Doripenem), CLSI® Carba NP and carbapenemase genetic markers by Polymerase Chain Reaction (PCR).

Results from the three different tests were used to determine the carbapenemase positive/negative status of an isolate, with the final composite reference result based on agreement of at least two of the three tests. Agreement between RAPIDEC® CARBA NP and composite reference method was assessed. When a RAPIDEC® CARBA NP result was not in agreement with the composite reference result, it was further evaluated. A negative RAPIDEC® CARBA NP result was considered as a false negative when the composite reference result was determined to be positive, indicating a false non-carbapenemase producer. A positive RAPIDEC® CARBA NP result was considered as a false positive when the composite reference result was determined to be negative, indicating a false carbapenemase producer. The comparative performance is shown in Table 1. The performance of RAPIDEC® CARBA NP with *Enterobacteriaceae* and *Pseudomonas aeruginosa* expressing the indicated carbapenemase genetic markers is shown in Table 2.

Table 1: Comparative Performance of RAPIDEC® CARBA NP *Enterobacteriaceae* and *Pseudomonas aeruginosa*

Incubation	Total #	Agreement #	Agreement %	Negative #	Positive #	False Positive[a] # (%)	False Negative[b] # (%)
Routine Subculture	457	451	98.7	192	265	5 (2.6)	1 (0.4)
Short Subculture	449	440	98.0	188	261	5 (2.7)	4 (1.5)

[a] False positive for carbapenemase; RAPIDEC CARBA NP positive result for a non-carbapenemase producing *Enterobacteriaceae* or *P. aeruginosa*

[b] False negative for carbapenemase; RAPIDEC CARBA NP negative result for a carbapenemase producing *Enterobacteriaceae* or *P. aeruginosa*

Table 2: Performance of RAPIDEC® CARBA NP with *Enterobacteriaceae* and *Pseudomonas aeruginosa* Expressing the Indicated Carbapenemase Genetic Markers

Carbapenemase determination by composite reference method		**RAPIDEC® CARBA NP performance**			
		Routine subculture/incubation		**Short subculture/incubation**	
		N	**Agreement (%)**	**N***	**Agreement (%)**
Enterobacteriaceae		388/394	98.5%	383/392	97.7%
Pseudomonas aeruginosa		63/63	100%	57/57	100%
All samples		**451/457**	**98.7%**	**440/449**	**98.0%**
Positive samples		**264/265[a]**	**99.6%**	**257/261 [c]**	**98.5%**
Enterobacteriaceae	KPC	143/144 [a]	99.3%	142/143 [c]	99.3%
	NDM	51/51	100%	50/51 [c]	98.0%
	VIM	15/15	100%	14/15 [c]	93.3%
	IMP	12/12	100%	12/12	100%
	OXA-48	23/23	100%	22/23 [c]	95.7%
	Total	244/245	99.6%	240/244	98.4%
Pseudomonas aeruginosa	KPC	3/3	100%	3/3	100%
	NDM	1/1	100%	1/1	100%
	VIM	11/11	100%	8/8	100%
	IMP	5/5	100%	5/5	100%
	Total	20/20	100%	17/17	100%
Negative samples		**187/192[b]**	**97.4%**	**183/188[d]**	**97.3%**
Enterobacteriaceae		144/149 [b]	96.6%	143/148 [d]	96.6%
Pseudomonas aeruginosa		43/43	100%	40/40	100%

* Insufficient growth/biomass for six *P. aeruginosa* and two *K. pneumoniae* in the short subculture procedure. They were three VIM producing *P. aeruginosa*, and one KPC producing *K. pneumoniae*; four negative samples including three *P. aeruginosa* and one *K. pneumoniae*.

[a] Routine subculture false negative (false non-carbapenemase producer) rate was 0.4% (1/265) for claimed carbapenemases; the false negative was KPC-producing *Enterobacteriaceae*

[b] Routine subculture false positive (false carbapenemase producer) rate was 2.6% (5/192) for *P. aeruginosa* and *Enterobacteriaceae*; the five false positives were from *Enterobactericeae*

[c] Short subculture false negative (false non-carbapenemase producer) rate was 1.5% (4/257) for claimed carbapenemases; one false negative each for KPC, NDM, VIM, and OXA-48 from *Enterobacteriaceae*

[d] Short subculture false positive (false carbapenemase producer) rate was 2.7% (5/188); the five false positives were from *Enterobacteriaceae*

Reproducibility

A panel of 9 *Enterobacteriaceae* and 1 *P. aeruginosa* including 4 negative and 6 positive carbapenemases was tested. Each organism was subcultured onto sheep blood agar and incubated for 18-24 hours for the routine subculture procedure and at least 4 hours for the

short subculture procedure. RAPIDEC® CARBA NP was performed on each organism in triplicates for 5 days at 3 sites and interpreted by 2 operators with the RAPIDEC® CARBA NP results blinded to each other.
The reproducibility was 98.2% (884/900) with the routine subculture procedure and 99.1% (892/900) with the short subculture procedure.

Conclusion

The results of the non-clinical and clinical performance studies support that RAPIDEC® CARBA NP is substantially equivalent to the composite reference method composed of three tests: carbapenem MIC (Imipenem, Meropenem, Ertapenem and/or Doripenem), CLSI® Carba NP and carbapenemase genetic markers by Polymerase Chain Reaction (PCR).