December 20, 2019

Curetis GmbH
℅ Gail Radcliffe
President
Radcliffe Consulting, Inc.
231 Fairbanks Street
West Boylston, Massachusetts 01583

Re: K191967

Trade/Device Name: Unyvero LRT BAL Application
Regulation Number: 21 CFR 866.3985
Regulation Name: Device To Detect And Identify Microorganisms And Associated Resistance Marker Nucleic Acids Directly In Respiratory Specimens
Regulatory Class: Class II
Product Code: QBH
Dated: July 22, 2019
Received: July 23, 2019

Dear Gail Radcliffe:

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. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. 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) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.


For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). 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 (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Kristian M. Roth -S

Kristian Roth, Ph.D.
Branch Chief
Bacterial Multiples and Medical Countermeasures
Division of Microbiology Devices
OHT7: Office of In Vitro Diagnostics and Radiological Health
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure
Indications for Use

The Unyvero LRT BAL Application is a qualitative nucleic acid multiplex test intended for the simultaneous detection and identification of nucleic acid sequences from the following microorganisms (N = 20) and antibiotic resistance markers (N = 10) in bronchoalveolar lavage (BAL)-like specimens (BAL or mini-BAL) from adult hospitalized patients with suspected lower respiratory tract infections.

[continued on page 2]
Indications for Use – Unyvero LRT BAL Application

The Unyvero LRT BAL Application performed on the Unyvero System is indicated as an aid in the diagnosis of lower respiratory tract infection in adult hospitalized patients with signs and symptoms of lower respiratory infection; results should be used in conjunction with other clinical and laboratory findings. As BAL specimens may contain colonizing microorganisms, detection of Unyvero LRT BAL microbial targets does not indicate that the microorganism is the cause of the disease. Unyvero positive results do not rule out co-infection with other microorganisms. Negative results do not preclude lower respiratory infection, as the causative agent may be a microorganism not detected by this test.

A negative result for any antibiotic resistance marker does not indicate that detected microorganisms are susceptible to applicable antimicrobial agents. Detected antibiotic resistance markers cannot be definitively linked to specific microorganisms, and may be present in organisms that are not detected by the Unyvero LRT BAL Application.

Microbiology cultures of BALs should be performed to obtain isolates for species identification and antimicrobial susceptibility testing and to identify potential microorganisms not targeted by the Unyvero LRT BAL Application.

### Microorganism & Associated Antibiotic Resistance Marker

<table>
<thead>
<tr>
<th>Microorganism</th>
<th>Associated Antibiotic Resistance Marker</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acinetobacter spp. a</td>
<td>ctx-M b, kpc, ndm, oxa-23, oxa-24, oxa-58, vim</td>
</tr>
<tr>
<td>Chlamydia pneumoniae</td>
<td>-</td>
</tr>
<tr>
<td>Citrobacter freundii</td>
<td>ctx-M b, kpc, ndm, oxa-48, vim</td>
</tr>
<tr>
<td>Enterobacter cloacae complex c</td>
<td>ctx-M b, kpc, ndm, oxa-48, vim</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>ctx-M b, kpc, ndm, oxa-48, vim</td>
</tr>
<tr>
<td>Haemophilus influenzae</td>
<td>tem</td>
</tr>
<tr>
<td>Klebsiella oxytoca</td>
<td>ctx-M b, kpc, ndm, oxa-48, vim</td>
</tr>
<tr>
<td>Klebsiella pneumoniae d</td>
<td>ctx-M b, kpc, ndm, oxa-48, vim</td>
</tr>
<tr>
<td>Klebsiella varicola</td>
<td>ctx-M b, kpc, ndm, oxa-48, vim</td>
</tr>
<tr>
<td>Legionella pneumophila</td>
<td>-</td>
</tr>
<tr>
<td>Moraxella catarrhals</td>
<td>-</td>
</tr>
<tr>
<td>Morganella morganii</td>
<td>ctx-M b, kpc, ndm, oxa-48, vim</td>
</tr>
<tr>
<td>Mycoplasma pneumoniae</td>
<td>-</td>
</tr>
<tr>
<td>Pneumocystis jirovecii</td>
<td>-</td>
</tr>
<tr>
<td>Proteus spp. e</td>
<td>ctx-M b, kpc, ndm, oxa-48, vim</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>ctx-M b, kpc, ndm, vim</td>
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<tr>
<td>Serratia marcescens</td>
<td>ctx-M b, kpc, ndm, oxa-48, vim</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>mecA</td>
</tr>
<tr>
<td>Stenotrophomonas maltophilia</td>
<td>-</td>
</tr>
<tr>
<td>Streptococcus pneumoniae</td>
<td>-</td>
</tr>
</tbody>
</table>

a Acinetobacter spp. includes: A. baumannii, A. calcoaceticus, A. haemolyticus, A. junii, A. lwofili, A. nosocomialis, A. parvus, A. pittii (detected by LRT BAL Application) and A. ursingii (not detected by LRT BAL Application).

b ctx-M1 subgroup.

c Enterobacter cloacae complex includes: E. asburiae, E. chengduensis, E. chuandaensis, E. cloacae, E. hormaechei (incl. ssp. xiangfangensis), E. kobei, E. ludwigii, E. roggenkampii, E. sichuanensis as well as E. hugandensis (not yet recognized as member of the E. cloacae complex).

d Klebsiella pneumoniae includes two variants: K. pneumoniae (variant 1), and K. quasipneumoniae (variant 2).

e Proteus spp. includes P. cibarius, P. hauseri, P. mirabilis, P. penneri and P. vulgaris.
510(k) SUMMARY – LRT BAL Application (K191967)

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92. The assigned 510(k) number is K191967.

807.92 (a)(1): Name: Curetis GmbH
Address: Max-Eyth-Strasse 42
         Holzgerlingen, Germany 71088
Phone: +49 7031 49195-24
Email: regulatory@curetis.com
Contact: Karsten Mueller, Head of Quality and Regulatory Affairs

807.92 (a)(2): Device name - trade name and common name, and classification

Trade name:
Unyvero LRT BAL Application

Common Name: Detection and identification of microorganisms and associated resistance marker nucleic acids directly in respiratory specimens

Classification / Product Code: 21 CFR Part 866.3985 / QBH

807.92 (a)(3): Identification of the legally marketed predicate devices
The Unyvero LRT BAL Application is substantially equivalent to its predecessor test system, the Unyvero LRT Application (Curetis, GmbH, Germany), granted de novo status under DEN170047 on April 3rd, 2018.

807.92 (a)(4): Device Description
The Unyvero LRT BAL Application automates and integrates DNA purification and eight parallel multiplex endpoint PCR reactions. It provides qualitative detection of nucleic acids from multiple lower respiratory pathogens using hybridization on PCR chamber arrays in a single use cartridge from a single bronchoalveolar lavage (BAL)-like specimen (BAL or mini-BAL).

The Unyvero LRT BAL Application identifies 20 microorganisms and 10 antibiotic resistance markers as listed in the Intended Use Statement, below.
Overview
The Unyvero LRT BAL Application uses a multiplex PCR approach following array hybridization which targets 30 individual analytes (microorganisms (N = 20) and antibiotic resistance markers (N = 10) divided into eight separate PCR reactions that are performed in individual reaction chambers simultaneously on a Unyvero LRT BAL Application cartridge. Multiplex compositions are designed to avoid any expected common occurrence of certain analytes within the same multiplex to largely reduce competitive PCR inhibition. Individual analyte assays of the Unyvero LRT BAL panel are designed to exhibit low or absent cross-reactivity with the relevant bronchoalveolar lavage (BAL)-like specimens (BAL or mini-BAL) sample matrix or ‘close neighbor’ strains. Array oligonucleotides are designed for similar hybridization and melting temperatures (approx. 65 – 80 °C, varying by amplicon). Hybridization and melting temperatures are used to exclude non-specific hybridization signals for improved signal specificity.

Instrument, Cartridge, and Other Consumables
The instrumentation consists of one (or more) Unyvero L4 Lysator, one (or more) Unyvero A50 Analyzer, a Unyvero C8 Cockpit, and four single-use consumables: the Unyvero LRT BAL Cartridge, the Unyvero Sample Tube, Sample Tube Cap and the Unyvero Master Mix. A Unyvero Sample Tube Holder is supplied as accessory to simplify the sample filling step.

- Unyvero LRT BAL Cartridge contains DNA isolation and purification reagents, primers, hybridization and wash buffers, and oligonucleotides for detection.
- Unyvero T1 Sample Tube and Transport Cap contains glass beads and buffers to lyse microorganisms and liquefy the sample.
- Unyvero T1 Sample Tube Cap seals the Unyvero Sample Tube and contains Proteinase K and a synthetic control gene for process monitoring.
- Unyvero M1 Master Mix Tube contains reagents for DNA amplification.

Controls
An internal control (a synthetic gene without any homology to known sequences) is processed in every chamber in order to verify the DNA purification, amplification, array hybridization, and detection.

Other than the built-in controls, no external materials are supplied with Unyvero LRT BAL Application devices and consumables. Good laboratory practice recommends running external positive and negative controls using samples cultured in the laboratory.
Reagents
No additional reagents are required to perform the Unyvero LRT BAL Application; all reagents are supplied within the cartridge or within the other consumables with the exception of the polymerase Master Mix, which is provided separately (frozen).

Assay Procedures
How to perform a Unyvero LRT BAL test:

1. Remove the Unyvero Sample Tube from its packaging and slide it in the Unyvero Sample Tube Holder in the upright position with the barcoded end at the bottom.
2. Remove the Transport Cap from the Sample Tube by pulling it upward.
3. Pipette 180 µL of vortexed patient specimen into the Sample Tube and close it using the Unyvero Cap provided in the LRT BAL kit; align the small nodules on the neck of the Sample Tube with the openings on the Cap and press down to lock in place.
4. Scan the Sample Tube and place it into the Lysator. Close the Lysator lid to start the Lysator.
5. Remove Master Mix from freezer and thaw at room temperature (15 °C - 25 °C) for approximately 30 minutes.
6. When lysis is complete, remove the Sample Tube from the Lysator and place it into the labeled position on the left-hand side of the Unyvero LRT BAL Cartridge.
7. Place the thawed Master Mix into the labeled position on the right-hand side of the Cartridge.
8. Scan the Cartridge on the Cockpit and insert it into the position indicated on the Analyzer. The software provides on-screen instructions to start the test.
9. View results after completion of the run.

During the automated analysis (Step 8), which is entirely controlled by the A50 Analyzer, the sample is mixed with ethanol and then transferred onto the DNA purification column, where buffers purify and elute the DNA. Eluted DNA is transferred to a chamber, where mixing with the Master Mix takes place. This mixture is distributed into eight separate PCR reaction chambers each containing multiple primer pairs, consisting of one labeled and one non-labeled primer for the respective multiplex endpoint PCR. After specific amplification, PCR products are hybridized to the corresponding array probes. Each array has been manufactured with probes corresponding to the amplicons for the targeted microorganism sequences described above. A total of up to 49 spots per array allows for redundant detection with at least four spots per analyte, as well as spots for intensity calibration, and orientation markers for the image processing software. Binding of amplicons to specific probes is detected by analyzing fluorescence images of the arrays. Result data are displayed on the C8 Cockpit for visualization, printout, temporary storage and electronic data export.
A test run is completed after 4 to 5 hrs, and results for panel microorganisms and corresponding antibiotic resistance markers are displayed on the Cockpit screen. Four screens are provided:

- **The Result Summary screen** provides a quick overview of all detected LRT BAL panel microorganisms, together with all detected corresponding antibiotic resistance markers.
- **The Microorganisms screen** provides a list of all panel microorganisms grouped in Gram-positive bacteria, non-fermenting bacteria, Enterobacteriaceae and other microorganisms together with the analysis result (reported as detected, not detected or invalid).
- **The Result Details screen** provides a list of all analyzed microorganisms and the corresponding antibiotic resistance markers together with the analysis result (reported as detected, not detected, invalid or NA).
- **Test Details screen** showing user name, lot numbers of used consumables, expiration dates of the consumables and start and stop times and dates of the test.

Results can be reviewed on the cockpit or, optionally, be printed out. All results are saved in a database on the Unyvero Cockpit for later review and printing.

**Software**

The Unyvero software is designed to:

- Manage analysis workflow (Cockpit)
- Carry out sample lysis (Lysator)
- Execute the analysis and generate the analytical result (Analyzer)
- Manage communication among units (Cockpit, Lysator, Analyzer)
- Monitor internal mechanical / electrical actuators (Lysator, Analyzer)
- Present analysis results (Cockpit)
- Store analysis results (Cockpit)

Each device (Cockpit, Lysator, Analyzer) is a subsystem within the overall system, and each consists of hardware and software components. The different devices are interconnected by an Ethernet based communication interface, and system functionality is provided by the interaction of all three device types. Only the Cockpit presents a rich user interface and allows interaction with the operator. The Lysator and Analyzer units include a simple display for showing device status. Optional HIS/LIS connectivity allows transferring results to a hospital or laboratory information system.
**807.92 (a)(5): Intended Use**

The Unyvero LRT BAL Application is a qualitative nucleic acid multiplex test intended for the simultaneous detection and identification of nucleic acid sequences from the following microorganisms (N = 20) and antibiotic resistance markers (N = 10) in bronchoalveolar lavage (BAL)-like specimens (BAL or mini-BAL) from adult hospitalized patients with suspected lower respiratory tract infections.

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<th>Microorganism</th>
<th>Associated Antibiotic Resistance Marker(s)</th>
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</tr>
<tr>
<td><em>Klebsiella variicola</em></td>
<td>ctx-M &lt;sup&gt;b&lt;/sup&gt;, kpc, ndm, oxa-48, vim</td>
</tr>
<tr>
<td><em>Legionella pneumophila</em></td>
<td>-</td>
</tr>
<tr>
<td><em>Moraxella catarrhalis</em></td>
<td>-</td>
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<tr>
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<td><em>Proteus spp.</em></td>
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</tbody>
</table>

<sup>a</sup> *Acinetobacter spp.* includes: *A. baumannii*, *A. calcoaceticus*, *A. haemolyticus*, *A. junii*, *A. lwofii*, *A. nosocomialis*, *A. parvus*, *A. pittii* (detected by LRT BAL Application), and *A. ursingii* (not detected by LRT BAL Application).

<sup>b</sup> ctx-M1 subgroup.

<sup>c</sup> *Enterobacter cloacae* complex includes: *E. asburiae*, *E. chengduensis*, *E. chuandaensis*, *E. cloacae*, *E. hormaechei* (incl. ssp. xiangfangensis), *E. kobei*, *E. ludwigii*, *E. roggenkampii*, *E. sichuanensis* and *E. bugandensis* (not yet recognized as member of the *E. cloacae* complex).

<sup>d</sup> *Klebsiella pneumoniae* includes two variants: *K. pneumoniae* (variant 1), and *K. quasipneumoniae* (variant 2).

<sup>e</sup> *Proteus spp.* includes: *P. cibarius*, *P. hauseri*, *P. mirabilis*, *P. penneri*, and *P. vulgaris*.

The Unyvero LRT BAL Application performed on the Unyvero System is indicated as an aid in the diagnosis of lower respiratory tract infection in adult hospitalized patients with signs and symptoms of lower respiratory infection; results should be used in conjunction with other clinical and laboratory findings. As BAL specimens may contain colonizing microorganisms, detection of Unyvero LRT BAL...
microbial targets does not indicate that the microorganism is the cause of the disease. Unyvero positive results do not rule out co-infection with other microorganisms. Negative results do not preclude lower respiratory infection, as the causative agent may be a microorganism not detected by this test.

A negative result for any antibiotic resistance marker does not indicate that detected microorganisms are susceptible to applicable antimicrobial agents. Detected antibiotic resistance markers cannot be definitively linked to specific microorganisms, and may be present in organisms that are not detected by the Unyvero LRT BAL Application.

Microbiology cultures of BALs should be performed to obtain isolates for species identification and antimicrobial susceptibility testing and to identify potential microorganisms not targeted by the Unyvero LRT BAL Application.

807.92 (a)(6): Technological Similarities and Differences to the Predicate

Table 1: Comparison of the Unyvero LRT Application and the Unyvero LRT BAL Application

<table>
<thead>
<tr>
<th>Element</th>
<th>New Device: Curetis Unyvero LRT BAL Application</th>
<th>Predicate: Curetis Unyvero LRT Application (DEN170047)</th>
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</thead>
<tbody>
<tr>
<td>Specimen Type</td>
<td>Bronchoalveolar lavage (BAL)-like specimens from adult hospitalized patients with suspected lower respiratory tract infections</td>
<td>Endotracheal aspirate specimens from adult hospitalized patients with suspected lower respiratory tract infections</td>
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<tr>
<td>Organisms Detected</td>
<td>Bacteria:</td>
<td>Bacteria:</td>
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<td><em>Acinetobacter</em> spp, <em>Citrobacter freundii</em></td>
<td><em>Acinetobacter</em> spp, <em>Citrobacter freundii</em></td>
</tr>
<tr>
<td></td>
<td><em>Enterobacter cloacae complex</em></td>
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<td><em>Escherichia coli</em></td>
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</tr>
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<td></td>
<td><em>Haemophilus influenzae</em></td>
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<tr>
<td></td>
<td><em>Klebsiella oxytoca</em></td>
<td><em>Klebsiella oxytoca</em></td>
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<td><em>Klebsiella pneumoniae</em></td>
<td><em>Klebsiella pneumoniae</em></td>
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<td><em>Klebsiella variicola</em></td>
<td><em>Klebsiella variicola</em></td>
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<tr>
<td></td>
<td><em>Moraxella catarrhalis</em></td>
<td><em>Moraxella catarrhalis</em></td>
</tr>
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<td><em>Morganella morgani</em></td>
<td><em>Morganella morgani</em></td>
</tr>
<tr>
<td></td>
<td><em>Proteus spp.</em></td>
<td><em>Proteus spp.</em></td>
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<td><em>Pseudomonas aeruginosa</em></td>
<td><em>Pseudomonas aeruginosa</em></td>
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<td><em>Serratia marcescens</em></td>
<td><em>Serratia marcescens</em></td>
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<td><em>Staphylococcus aureus</em></td>
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<td><em>Stenotrophomonas maltophilia</em></td>
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<td></td>
<td><em>Streptococcus pneumoniae</em></td>
<td><em>Streptococcus pneumoniae</em></td>
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<tr>
<td></td>
<td>Atypical Bacteria:</td>
<td>Atypical Bacteria:</td>
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<tr>
<td></td>
<td><em>Chlamydia pneumoniae</em></td>
<td><em>Chlamydia pneumoniae</em></td>
</tr>
<tr>
<td></td>
<td><em>Legionella pneumophila</em></td>
<td><em>Legionella pneumophila</em></td>
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<tr>
<td></td>
<td><em>Mycoplasma pneumoniae</em></td>
<td><em>Mycoplasma pneumoniae</em></td>
</tr>
<tr>
<td></td>
<td>Fungus: <em>Pneumocystis jirovecii</em></td>
<td>Fungus: <em>Pneumocystis jirovecii</em></td>
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<td></td>
<td>Antimicrobial Resistance Genes:</td>
<td>Antimicrobial Resistance Genes:</td>
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<tr>
<td>Analyte</td>
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<td>DNA</td>
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<tr>
<td>-------------</td>
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</tr>
<tr>
<td>Technological Principles</td>
<td>Multiplex nucleic acid</td>
<td>Multiplex nucleic acid</td>
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<tr>
<td>Result Types</td>
<td>Qualitative for all analytes</td>
<td>Qualitative for all analytes</td>
</tr>
<tr>
<td>Instrumentation</td>
<td>Unyvero System</td>
<td>Unyvero System</td>
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<tr>
<td>Time to Result</td>
<td>About 4-5 hrs</td>
<td>About 4-5 hrs</td>
</tr>
<tr>
<td>Reagent Storage</td>
<td>Room temperature (below -20 °C, Master Mix Tube only)</td>
<td>Room temperature (below -20 °C, Master Mix Tube only)</td>
</tr>
<tr>
<td>Controls</td>
<td>Control included in each test to monitor for the presence of PCR inhibitors and enables the system to detect failures in the testing process.</td>
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</tr>
<tr>
<td>User Complexity</td>
<td>Moderate</td>
<td>Moderate</td>
</tr>
</tbody>
</table>

807.92 (b)(1): Brief Description of Nonclinical Data

Limits-of-Detection (LoDs)

Limits-of-Detection were determined for each LRT BAL panel analyte by serial dilutions of reference strains prepared in pooled negative native lavage specimens as test matrix. The lowest test concentration with a positivity rate of 95% or higher was determined as the LoD for each specific panel analyte (e.g., at least 19 of 20 positive results for at least 20 performed test replicates). Tables 2 and 3 summarize LoDs for all LRT BAL panel microorganisms or antibiotic resistance markers, respectively.
### Table 2: LoDs for LRT BAL panel microorganisms.

<table>
<thead>
<tr>
<th>Reference Strain ID</th>
<th>LoD [CFU/mL]</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Acinetobacter spp.</strong> ATCC 19606 (A. baumannii)</td>
<td>2.0 x 10^4</td>
</tr>
<tr>
<td><strong>Chlamydia pneumoniae</strong> ATCC VR-2282</td>
<td>3.2 x 10^2</td>
</tr>
<tr>
<td><strong>Citrobacter freundii</strong> ATCC 8090</td>
<td>8.0 x 10^4</td>
</tr>
<tr>
<td><strong>Enterobacter cloacae complex</strong> ATCC 13047 (E. cloacae)</td>
<td>2.0 x 10^5</td>
</tr>
<tr>
<td><strong>Escherichia coli</strong> ATCC 11775</td>
<td>2.0 x 10^4</td>
</tr>
<tr>
<td><strong>Haemophilus influenzae</strong> ATCC 33391</td>
<td>2.0 x 10^4</td>
</tr>
<tr>
<td><strong>Klebsiella oxytoca</strong> ATCC 13182</td>
<td>1.0 x 10^4</td>
</tr>
<tr>
<td><strong>Klebsiella pneumoniae (var. 1)</strong> ATCC 13883</td>
<td>4.0 x 10^4</td>
</tr>
<tr>
<td><strong>Klebsiella quasipneumoniae (K. pneumoniae, var. 2)</strong> ATCC 700603</td>
<td>4.0 x 10^4</td>
</tr>
<tr>
<td><strong>Klebsiella variicola</strong> ATCC BAA-830</td>
<td>2.0 x 10^4</td>
</tr>
<tr>
<td><strong>Legionella pneumophila</strong> ATCC 33152</td>
<td>8.0 x 10^4</td>
</tr>
<tr>
<td><strong>Moraxella catarrhalis</strong> ATCC 25238</td>
<td>1.5 x 10^5</td>
</tr>
<tr>
<td><strong>Morganella morganii</strong> ATCC 25830</td>
<td>2.0 x 10^4</td>
</tr>
<tr>
<td><strong>Mycoplasma pneumoniae</strong> ATCC 29085</td>
<td>1.6 x 10^3</td>
</tr>
<tr>
<td><strong>Pneumocystis jirovecii</strong> 36 0314</td>
<td>5.0 x 10^3</td>
</tr>
<tr>
<td><strong>Proteus spp.</strong> ATCC 29906 (P. mirabilis) ATCC 29905 (P. vulgaris)</td>
<td>5.0 x 10^3</td>
</tr>
<tr>
<td><strong>Pseudomonas aeruginosa</strong> ATCC 10145</td>
<td>6.3 x 10^2</td>
</tr>
<tr>
<td><strong>Serratia marcescens</strong> ATCC 13880</td>
<td>4.0 x 10^4</td>
</tr>
<tr>
<td><strong>Staphylococcus aureus</strong> ATCC 12600</td>
<td>1.5 x 10^5</td>
</tr>
<tr>
<td><strong>Stenotrophomonas maltophilia</strong> ATCC 13637</td>
<td>5.0 x 10^3</td>
</tr>
<tr>
<td><strong>Streptococcus pneumoniae</strong> ATCC 49619</td>
<td>2.0 x 10^4</td>
</tr>
</tbody>
</table>

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* Cell supernatant (in IFU/mL).
* Bacterial suspension, quantified by qPCR (in copies/mL).
* Positive clinical specimen, quantified by qPCR (in copies/mL). LoD was determined using DNA extracted from a positive clinical specimen, and then confirmed by testing dilutions of this clinical specimen at the LoD concentration (20/20 positive results).
Table 3: LoDs for LRT BAL panel antibiotic resistance markers.

<table>
<thead>
<tr>
<th>Reference Strain ID</th>
<th>Host Microorganism</th>
<th>LoD [CFU/mL]</th>
</tr>
</thead>
<tbody>
<tr>
<td>ets-M</td>
<td>NCTC 13443</td>
<td>Klebsiella pneumonia</td>
</tr>
<tr>
<td>kpc</td>
<td>NCTC 13438</td>
<td>Klebsiella pneumonia</td>
</tr>
<tr>
<td>mecA</td>
<td>NCTC 12493</td>
<td>Staphylococcus aureus</td>
</tr>
<tr>
<td>ndm</td>
<td>NCTC 13443</td>
<td>Klebsiella pneumonia</td>
</tr>
<tr>
<td>oxa-23</td>
<td>NCTC 13301</td>
<td>Acinetobacter baumannii</td>
</tr>
<tr>
<td>oxa-24</td>
<td>NCTC 13302</td>
<td>Acinetobacter baumannii</td>
</tr>
<tr>
<td>oxa-48</td>
<td>NCTC 13442</td>
<td>Klebsiella pneumonia</td>
</tr>
<tr>
<td>oxa-58</td>
<td>NCTC 13305</td>
<td>Acinetobacter baumannii</td>
</tr>
<tr>
<td>tem*</td>
<td>NCTC 13443</td>
<td>Klebsiella pneumonia</td>
</tr>
<tr>
<td>vim</td>
<td>NCTC 13437</td>
<td>Pseudomonas aeruginosa</td>
</tr>
</tbody>
</table>

* Although the LRT BAL Application reports tem results only for H. influenzae as corresponding host microorganism, LoD was determined with a tem positive E. coli strain. Note that inclusivity testing was also successfully performed with tem positive H. influenzae strains.

Inclusivity

LRT BAL Microorganisms

Inclusivity wet testing was performed with reference strains for each microorganism analyte at concentrations near the LoD with contrived samples using pooled native negative lavage specimens as sample matrix (Table 4). Reference strains used for LoD determination are considered inclusive and were used as positive controls. Inclusivity was established near LoD (< 5x LoD) for all but one of the tested reference strains. For one reference strain of M. pneumoniae, tested as genomic DNA extract, inclusivity was demonstrated with a reduced analytical sensitivity at 5x LoD, although no primer or probe deviations to the corresponding LRT BAL assay were present.

Table 4: Inclusivity study results for LRT BAL panel microorganisms.

<table>
<thead>
<tr>
<th>Reference Strain</th>
<th>Strain ID</th>
<th>Test Conc. [CFU/ml]</th>
<th>x-fold LoD</th>
<th># Pos./ # Exp.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acinetobacter baumannii (pos. control/LoD ref. strain)</td>
<td>ATCC 19606</td>
<td>4.0 x 10^4</td>
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<td>6/6</td>
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<tr>
<td>Acinetobacter baumannii NCTC 13305</td>
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<tr>
<td>Acinetobacter baumannii NCTC 13302</td>
<td>4.0 x 10^4</td>
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<td>2/2</td>
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</tr>
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<td>Acinetobacter baumannii Micromyx 6148</td>
<td>4.0 x 10^4</td>
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<td>Acinetobacter calcoaceticus ATCC 23055</td>
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<tr>
<td>Acinetobacter Iwoffi ATCC 15309</td>
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<tr>
<td>Acinetobacter haemolyticus ATCC 17906</td>
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<tr>
<td>Chlamydia pneumoniae ATCC VR-2282</td>
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<td>4/4</td>
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</tr>
<tr>
<td>Reference Strain</td>
<td>Strain ID</td>
<td>Test Conc. [CFU/ml]</td>
<td>x-fold LoD</td>
<td># Pos./# Exp.</td>
</tr>
<tr>
<td>------------------</td>
<td>-----------</td>
<td>---------------------</td>
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<td>--------------</td>
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<tr>
<td><strong>(pos. control/LoD ref. strain)</strong></td>
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<tr>
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<td>0/2</td>
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<td>Chlamydia pneumonia</td>
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<td><strong>Citrobacter freundii</strong></td>
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</tr>
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<td>2/2</td>
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<tr>
<td><strong>analyte: Enterobacter cloacae complex</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enterobacter cloacae</td>
<td>ATCC 13047</td>
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<td>7/7</td>
</tr>
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<td>Enterobacter cloacae</td>
<td>ATCC 23355</td>
<td>4.0 x 10^5</td>
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<tr>
<td>Enterobacter cloacae</td>
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<tr>
<td>Enterobacter asburiae</td>
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<td>ATCC 11775</td>
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<td>2x</td>
<td>4/4</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>ATCC 25922</td>
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<td>ATCC 35218</td>
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<td>2x</td>
<td>4/4</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>ATCC BAA-2523</td>
<td>4.0 x 10^4</td>
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<td>2/2</td>
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<tr>
<td>Escherichia coli</td>
<td>NCTC 13351</td>
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<td>4/4</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>NCTC 13476</td>
<td>4.0 x 10^4</td>
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</tr>
<tr>
<td>Escherichia coli</td>
<td>JMI 50067</td>
<td>4.0 x 10^4</td>
<td>2x</td>
<td>2/2</td>
</tr>
<tr>
<td>Haemophilus influenzae</td>
<td>ATCC 33391</td>
<td>4.0 x 10^4</td>
<td>2x</td>
<td>3/3</td>
</tr>
<tr>
<td>Haemophilus influenzae (serotype a)</td>
<td>ATCC 9006</td>
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<td>2/2</td>
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<tr>
<td>Haemophilus influenzae (serotype c)</td>
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<td>2/2</td>
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<tr>
<td>Haemophilus influenzae (serotype b)</td>
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<td>1/2</td>
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<td>Haemophilus influenzae (serotype b)</td>
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</tr>
<tr>
<td>Haemophilus influenzae (serotype b)</td>
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</tr>
<tr>
<td>Klebsiella oxytoca</td>
<td>ATCC 13182</td>
<td>4.0 x 10^4</td>
<td>4x</td>
<td>3/3</td>
</tr>
<tr>
<td>Klebsiella oxytoca</td>
<td>ATCC 43863</td>
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<td>2/2</td>
</tr>
<tr>
<td>Klebsiella oxytoca</td>
<td>ATCC 8724</td>
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<td>4x</td>
<td>2/2</td>
</tr>
<tr>
<td>Klebsiella oxytoca</td>
<td>ATCC 49131</td>
<td>4.0 x 10^4</td>
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<td>2/2</td>
</tr>
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<td>Klebsiella oxytoca</td>
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<td>4.0 x 10^4</td>
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</tr>
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<td>Klebsiella oxytoca</td>
<td>NRZ-22060</td>
<td>4.0 x 10^4</td>
<td>4x</td>
<td>2/2</td>
</tr>
<tr>
<td><strong>analyte: Klebsiella pneumoniae</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reference Strain</td>
<td>Strain ID</td>
<td>Test Conc. [CFU/ml]</td>
<td>x-fold LoD</td>
<td># Pos./ # Exp.</td>
</tr>
<tr>
<td>---------------------------------------------------------------------------------</td>
<td>-------------</td>
<td>---------------------</td>
<td>------------</td>
<td>---------------</td>
</tr>
<tr>
<td><strong>Klebsiella pneumoniae, variant 1</strong> (pos. control/LoD ref. strain)</td>
<td>ATCC 13883</td>
<td>8.0 x 10⁴</td>
<td>2x</td>
<td>4/4</td>
</tr>
<tr>
<td><strong>Klebsiella quasipneumoniae (K. pneumoniae, variant 2)</strong> (pos. control/LoD ref. strain)</td>
<td>ATCC 700603</td>
<td>8.0 x 10⁴</td>
<td>2x</td>
<td>3/3</td>
</tr>
<tr>
<td><em>Klebsiella pneumoniae</em></td>
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<td></td>
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<tr>
<td>ATCC 13439</td>
<td>NCTC 13439</td>
<td>8.0 x 10⁴</td>
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<td>2/2</td>
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<td>ATCC 13438</td>
<td>NCTC 13442</td>
<td>8.0 x 10⁴</td>
<td>2x</td>
<td>2/2</td>
</tr>
<tr>
<td>ATCC 13443</td>
<td>NCTC 13443</td>
<td>2.0 x 10⁴</td>
<td>0.5x</td>
<td>3/3</td>
</tr>
<tr>
<td><em>Klebsiella pneumoniae</em></td>
<td>Micromyx 4653</td>
<td>8.0 x 10⁴</td>
<td>2x</td>
<td>2/2</td>
</tr>
<tr>
<td><em>Klebsiella pneumoniae</em></td>
<td>Micromyx 4676</td>
<td>8.0 x 10⁴</td>
<td>2x</td>
<td>2/2</td>
</tr>
<tr>
<td><em>Klebsiella pneumoniae</em></td>
<td>JMI 49767</td>
<td>2.0 x 10⁴</td>
<td>0.5x</td>
<td>2/2</td>
</tr>
<tr>
<td><em>Klebsiella pneumoniae</em></td>
<td>NRZ-00002</td>
<td>2.0 x 10⁴</td>
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<td>2/2</td>
</tr>
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<td><em>Klebsiella pneumoniae</em></td>
<td>NRZ-00103</td>
<td>8.0 x 10⁴</td>
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<td>ATCC BAA-830</td>
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<td>3/3</td>
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<tr>
<td><em>Klebsiella variicola</em></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>clinical strain 1</td>
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<td>4.0 x 10⁴</td>
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<tr>
<td>clinical strain 2</td>
<td></td>
<td>4.0 x 10⁴</td>
<td>2x</td>
<td>2/2</td>
</tr>
<tr>
<td>clinical strain 3</td>
<td></td>
<td>4.0 x 10⁴</td>
<td>2x</td>
<td>2/2</td>
</tr>
<tr>
<td>clinical strain 4</td>
<td></td>
<td>4.0 x 10⁴</td>
<td>2x</td>
<td>2/2</td>
</tr>
<tr>
<td><strong>Legionella pneumophila</strong> (serotype 1)** (pos. control/LoD ref. strain)</td>
<td>ATCC 33152</td>
<td>1.6 x 10⁵</td>
<td>2x</td>
<td>7/7</td>
</tr>
<tr>
<td><em>Legionella pneumophila</em> (serotype 2)** (pos. control/LoD ref. strain)</td>
<td>ATCC 33154</td>
<td>1.6 x 10⁵</td>
<td>2x</td>
<td>2/2</td>
</tr>
<tr>
<td><em>Legionella pneumophila</em> (serotype 3)** (pos. control/LoD ref. strain)</td>
<td>ATCC 33155</td>
<td>1.6 x 10⁵</td>
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<td>2/2</td>
</tr>
<tr>
<td><em>Legionella pneumophila</em> (serotype 6)** (pos. control/LoD ref. strain)</td>
<td>ATCC 33215</td>
<td>1.6 x 10⁵</td>
<td>2x</td>
<td>2/2</td>
</tr>
<tr>
<td><em>Legionella pneumophila</em> (serotype 8)** (pos. control/LoD ref. strain)</td>
<td>ATCC 35096</td>
<td>1.6 x 10⁵</td>
<td>2x</td>
<td>2/2</td>
</tr>
<tr>
<td><em>Legionella pneumophila</em> (serotype 10)** (pos. control/LoD ref. strain)</td>
<td>ATCC 43283</td>
<td>1.6 x 10⁵</td>
<td>2x</td>
<td>2/2</td>
</tr>
<tr>
<td><em>Legionella pneumophila</em></td>
<td>UCLA L1</td>
<td>1.6 x 10⁵</td>
<td>2x</td>
<td>2/2</td>
</tr>
<tr>
<td><em>Legionella pneumophila</em></td>
<td>UCLA L5</td>
<td>1.6 x 10⁵</td>
<td>2x</td>
<td>2/2</td>
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<tr>
<td><em>Legionella pneumophila</em></td>
<td>UCLA L6</td>
<td>1.6 x 10⁵</td>
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<td>2/2</td>
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<tr>
<td><strong>Moraxella catarrhalis</strong> (pos. control/LoD ref. strain)</td>
<td>ATCC 25238</td>
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<tr>
<td><em>Morganella morganii ssp. sibonii</em></td>
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<td>ATCC 29085</td>
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</tr>
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<td>Test Conc. [CFU/ml]</td>
<td>x-fold LoD</td>
<td># Pos./# Exp.</td>
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<td>------------------</td>
<td>---------------</td>
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<td>------------</td>
<td>--------------</td>
</tr>
<tr>
<td>Mycoplasma pneumoniae (type 1)</td>
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</tr>
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<td></td>
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<td>3.2 x 10³</td>
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<td>0/2</td>
</tr>
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<td>5.0 x 10³</td>
<td>3x</td>
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</tr>
<tr>
<td>Mycoplasma pneumoniae (type 2)</td>
<td>ATCC 15531</td>
<td>6.4 x 10³</td>
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<td>1/2</td>
</tr>
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<td>7.0 x 10³</td>
<td>4.4x</td>
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</tr>
<tr>
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<td></td>
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</tr>
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<td>analyte: Proteus spp.</td>
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<td>Proteus vulgaris (pos. control/LoD ref. strain)</td>
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<td></td>
<td>ATCC 12453</td>
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<tr>
<td></td>
<td>ATCC 14153</td>
<td>1.0 x 10⁴</td>
<td>2x</td>
<td>2/2</td>
</tr>
<tr>
<td></td>
<td>ATCC 25933</td>
<td>1.0 x 10⁴</td>
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<tr>
<td></td>
<td>ATCC 6380</td>
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<tr>
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<td>ATCC 8427</td>
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<td>1.0 x 10⁴</td>
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<td>ATCC 27853</td>
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<td>NCTC 13437</td>
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<tr>
<td>Serratia marcescens (pos. control/LoD ref. strain)</td>
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<tr>
<td></td>
<td>ATCC 14756</td>
<td>8.0 x 10⁴</td>
<td>2x</td>
<td>2/2</td>
</tr>
<tr>
<td></td>
<td>ATCC 15365</td>
<td>8.0 x 10⁴</td>
<td>2x</td>
<td>2/2</td>
</tr>
<tr>
<td></td>
<td>ATCC 27117</td>
<td>8.0 x 10⁴</td>
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<td>2/2</td>
</tr>
<tr>
<td></td>
<td>ATCC 43861</td>
<td>8.0 x 10⁴</td>
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<td>2/2</td>
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<td>DSM-17174</td>
<td>8.0 x 10⁴</td>
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<td>2/2</td>
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<tr>
<td>Staphylococcus aureus (pos. control/LoD ref. strain)</td>
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<tr>
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<td>ATCC 33591</td>
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<td>Test Conc. [CFU/ml]</td>
<td>x-fold LoD</td>
<td># Pos./# Exp.</td>
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<tr>
<td><em>Staphylococcus aureus</em></td>
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<tr>
<td><em>Staphylococcus aureus</em></td>
<td>ATCC 43300</td>
<td>3.0 x 10^5</td>
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<tr>
<td><em>Stenotrophomonas maltophilia</em> (pos. control/LoD ref. strain)</td>
<td>ATCC 13637</td>
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<td>4/4</td>
</tr>
<tr>
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<td>ATCC 13636</td>
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<tr>
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<td>ATCC 17666</td>
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<tr>
<td><em>Stenotrophomonas maltophilia</em></td>
<td>ATCC 49130</td>
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<tr>
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</tr>
<tr>
<td><em>Stenotrophomonas maltophilia</em></td>
<td>DSM-21874 e</td>
<td>1.0 x 10^4</td>
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<td>0/2</td>
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<tr>
<td><em>Stenotrophomonas maltophilia</em></td>
<td>[NCIMB 9528]</td>
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<tr>
<td><em>Stenotrophomonas maltophilia</em></td>
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<td>2.0 x 10^4</td>
<td>4x</td>
<td>2/2</td>
</tr>
<tr>
<td><em>Streptococcus pneumoniae</em></td>
<td>ATCC 49150 g</td>
<td>4.0 x 10^4</td>
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<td>0/2</td>
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<tr>
<td><em>Streptococcus pneumoniae</em></td>
<td>ATCC 33400 h</td>
<td>8.0 x 10^4</td>
<td>4x</td>
<td>2/2</td>
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<tr>
<td><em>Streptococcus pneumoniae</em></td>
<td>ATCC 6303</td>
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<td><em>Streptococcus pneumoniae</em></td>
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<td>ATCC 6301</td>
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<td><em>Streptococcus pneumoniae</em></td>
<td>DSM-11865</td>
<td>4.0 x 10^4</td>
<td>2x</td>
<td>2/2</td>
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<td><em>Streptococcus pneumoniae</em></td>
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<td>2/2</td>
</tr>
<tr>
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<td>DSM-11867</td>
<td>4.0 x 10^4</td>
<td>2x</td>
<td>2/2</td>
</tr>
</tbody>
</table>

a In IFU/mL for *C. pneumoniae*.
b In copies/mL for *M. pneumoniae* and *P. jirovecii*.
c Quantified DNA extract (reference material) from a commercial provider.
d For *M. pneumoniae* ATCC 15531, a positivity rate of 2/2 was obtained at a 5x LoD concentration. Sequencing did not reveal any mismatches to primer and probe binding sites and the observed slightly reduced sensitivity is likely due to the different source material (DNA extract instead of a cell suspension).
e *S. maltophilia* strain DSM-21874 was positive only at a 4x LoD concentration. Sequencing did not reveal any mismatches to primer or probe sequences.
f *S. pneumoniae* LoD reference strain ATCC 46916 did not show consistently positive signals at 2x LoD. ATCC 46916 controls were repeated using a freshly prepared counted culture stock. This time, a positivity rate of 8/8 was obtained at a 2x LoD concentration, as expected.
g *S. pneumoniae* strain ATCC 49150 was only positive at 4x LoD. Sequencing did not reveal any mismatches to primer or probe sequences.
h *S. pneumoniae* strain ATCC 33400 was only consistently positive at 4x LoD. Sequencing did not reveal any mismatches to primer or probe sequences.
To supplement inclusivity testing, in silico GenBank BLAST analyses of LRT BAL panel primer and probe sequences were performed for each LRT BAL panel microorganism (search performed July 2019) for all applicable strain entries. BLAST analyses identified strain entries for which detection by LRT BAL is predicted at LoD (match of relevant primer and probe sequences), only with reduced sensitivity (typically, single relevant mismatches of primer or probe sequences; detection likely at higher than LoD concentrations only), or is not predicted (multiple relevant mismatches in primer and probe sequences).

Table 5 lists microorganisms for which inclusivity was demonstrated by wet testing and are supported by in silico analysis (predicted at LoD or predicted with reduced sensitivity). Note that additional in silico analysis results are provided for strains that have not been wet tested. Such in silico results are provided as supplementary data only. Results are not intended to be a surrogate for wet testing and do not assure that specific strains will be detected.

NOTE: The performance of the Unyvero LRT BAL Application has not been established for those microorganism species that were evaluated by in silico analysis only.

### Table 5: Inclusive LRT BAL panel microorganisms as demonstrated by inclusivity wet testing and/or as predicted by in silico analysis (at LoD concentration or with reduced sensitivity). For strains for which in silico analysis predicts higher than LoD concentrations for one or more applicable entries, numbers of GenBank entries are additionally listed.

<table>
<thead>
<tr>
<th>Microorganism</th>
<th>Wet Testing</th>
<th>In Silico: at LoD</th>
<th>In Silico: Reduced Sensitivity</th>
<th>Comment</th>
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<td><strong>Acinetobacter spp.</strong></td>
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<td>A. calcoaceticus</td>
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<td>-</td>
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<td>A. lwofii</td>
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<td>A. haemolyticus</td>
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<td>A. nosocomialis</td>
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<td>-</td>
<td></td>
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<td>A. pittii</td>
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<td>x</td>
<td>-</td>
<td></td>
</tr>
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<td>A. junii</td>
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<td>x</td>
<td>-</td>
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<tr>
<td>A. parvus</td>
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<td>-</td>
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<td>A. lactucae</td>
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<tr>
<td>A. oleivorans</td>
<td>-</td>
<td>x</td>
<td>-</td>
<td></td>
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<tr>
<td>A. schindleri</td>
<td>-</td>
<td>x</td>
<td>-</td>
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<td>A. guillouiae</td>
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<td>-</td>
<td>x</td>
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<tr>
<td>A. radioresistens</td>
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<td>-</td>
<td>x</td>
<td>3 entries</td>
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<td>A. soli</td>
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<td>-</td>
<td>x</td>
<td>1 entry</td>
</tr>
<tr>
<td>A. ursingii</td>
<td>-</td>
<td>-</td>
<td>x</td>
<td>1 entry</td>
</tr>
</tbody>
</table>

**Chlamydia pneumoniae**               | x           | x                | -                             |         |

**Citrobacter freundii**              | x           | x                | -                             |         |

**Enterobacter cloacae complex**       |             |                  |                               |         |
| E. cloacae                           | x           | x                | -                             |         |

including ssp. dissolvens
<table>
<thead>
<tr>
<th></th>
<th>Wet Testing</th>
<th>In Silico: at LoD</th>
<th>In Silico: Reduced Sensitivity</th>
<th>Comment</th>
</tr>
</thead>
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<td>x</td>
<td>-</td>
<td>including ssp. <em>oharae</em>, <em>steigerwaltii</em>, <em>hoffmannii</em></td>
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<tr>
<td><em>E. hormaechei</em> ssp.</td>
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<tr>
<td><em>xiangfangensis</em></td>
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<tr>
<td><em>E. kobei</em></td>
<td>-</td>
<td>x</td>
<td>-</td>
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<tr>
<td><em>E. ludwigii</em></td>
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<td>x</td>
<td>-</td>
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<tr>
<td><em>E. sichuanensis</em></td>
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<td><em>E. chengduensis</em></td>
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<td>x</td>
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<td><em>E. chuandaensis</em></td>
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<td>-</td>
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<td><em>E. roggenkampii</em></td>
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<td><em>E. asburiae</em></td>
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<td>x</td>
<td>11 entries</td>
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<td><em>E. bugandensis</em></td>
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<td>x</td>
<td>-</td>
<td>not yet recognized as member of the <em>E. cloacae</em> complex</td>
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<td><em>Haemophilus influenzae</em></td>
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<td>x</td>
<td>65 entries</td>
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<td>16 entries</td>
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<td>variant 1 (<em>K. pneumoniae</em>)</td>
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<td>x</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>variant 2 (<em>K. quasipneumoniae</em>)</td>
<td>x</td>
<td>x</td>
<td>11 entries</td>
<td></td>
</tr>
<tr>
<td><em>Klebsiella variicola</em></td>
<td>x</td>
<td>x</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td><em>Legionella pneumophila</em></td>
<td>x</td>
<td>x</td>
<td>-</td>
<td>some entries predict detection at LoD, other entries predict a possible slight performance reduction; strains for both variants were included in inclusivity wet testing and were detected at concentrations near LoD.</td>
</tr>
<tr>
<td><em>Moraxella catarrhalis</em></td>
<td>x</td>
<td>x</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td><em>Morganella morganii</em></td>
<td>x</td>
<td>x</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td><em>Mycoplasma pneumoniae</em></td>
<td>x</td>
<td>x</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td><em>Pneumocystis jirovecii</em></td>
<td>x</td>
<td>x</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td><em>Proteus</em> spp.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>P. mirabilis</em></td>
<td>x</td>
<td>x</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td><em>P. vulgaris</em></td>
<td>x</td>
<td>x</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td><em>P. hauseri</em></td>
<td>x</td>
<td>x</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td><em>P. pennis</em></td>
<td>x</td>
<td>x</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td><em>P. cibarius</em></td>
<td>-</td>
<td>x</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>x</td>
<td>x</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td><em>Serratia</em> marcescens</td>
<td>x</td>
<td>x</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>x</td>
<td>x</td>
<td>&gt; 450 entries</td>
<td></td>
</tr>
<tr>
<td><em>Stenotrophomonas maltophilia</em></td>
<td>x</td>
<td>x</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td><em>Streptococcus pneumoniae</em></td>
<td>x</td>
<td>x</td>
<td>&gt; 240 entries</td>
<td>including serotype 7F</td>
</tr>
</tbody>
</table>
LRT BAL Antibiotic Resistance Markers

Similar to microorganisms, inclusivity wet testing was performed with reference strains carrying antibiotic resistance markers of the LRT BAL panel at concentrations near LoD with contrived samples using pooled negative native lavage specimens as sample matrix (Table 6). Subgroups of antibiotic resistance markers are added, if known (NA: unknown). Where phenotypic antimicrobial susceptibility testing (AST) results are available, this information is also shown (e.g., carbapenem$^R$ = resistant to carbapenems, carbapenem$^S$ = susceptible to carbapenems).

Inclusivity was established near LoD for all tested reference strains.

Table 6: Inclusivity study results for LRT BAL panel antibiotic resistance markers.

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Subgroup</th>
<th>Reference Strain</th>
<th>Strain ID</th>
<th>Test Conc. [CFU/ml]</th>
<th>x-fold LoD</th>
<th># Pos./# Exp.</th>
</tr>
</thead>
<tbody>
<tr>
<td>ctx-M</td>
<td>NA</td>
<td><em>Klebsiella pneumoniae</em> (pos. control/LoD ref. strain)</td>
<td>NCTC 13443</td>
<td>2.0 $\times$ 10^4</td>
<td>2x</td>
<td>3/3</td>
</tr>
<tr>
<td></td>
<td>ctx-M3</td>
<td><em>Klebsiella pneumoniae</em></td>
<td>NRZ-00751</td>
<td>2.0 $\times$ 10^4</td>
<td>2x</td>
<td>2/2</td>
</tr>
<tr>
<td></td>
<td>ctx-M15</td>
<td><em>Klebsiella pneumoniae</em></td>
<td>NRZ-00249</td>
<td>2.0 $\times$ 10^4</td>
<td>2x</td>
<td>2/2</td>
</tr>
<tr>
<td></td>
<td>NA</td>
<td><em>Enterobacter cloacae</em></td>
<td>JMI 46239</td>
<td>2.0 $\times$ 10^4</td>
<td>2x</td>
<td>1/2</td>
</tr>
<tr>
<td></td>
<td>NA</td>
<td><em>Escherichia coli</em></td>
<td>JMI 50067</td>
<td>2.0 $\times$ 10^4</td>
<td>2x</td>
<td>2/2</td>
</tr>
<tr>
<td></td>
<td>NA</td>
<td><em>Klebsiella pneumoniae</em></td>
<td>NRZ-00002</td>
<td>2.0 $\times$ 10^4</td>
<td>1/2</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3.0 $\times$ 10^4</td>
<td>3x</td>
<td>2/2</td>
</tr>
<tr>
<td></td>
<td>NA</td>
<td><em>Enterobacter cloacae</em></td>
<td>ATCC BAA-2468</td>
<td>4.0 $\times$ 10^4</td>
<td>4x</td>
<td>2/2</td>
</tr>
<tr>
<td></td>
<td>NA</td>
<td><em>Klebsiella pneumoniae</em></td>
<td>JMI 49831</td>
<td>4.0 $\times$ 10^4</td>
<td>4x</td>
<td>2/2</td>
</tr>
<tr>
<td></td>
<td>NA</td>
<td><em>Klebsiella pneumoniae</em></td>
<td>JMI 49767</td>
<td>2.0 $\times$ 10^4</td>
<td>2x</td>
<td>2/2</td>
</tr>
<tr>
<td></td>
<td>kpc-3</td>
<td><em>Klebsiella pneumoniae</em> (pos. control/LoD ref. strain)</td>
<td>NCTC 13438</td>
<td>8.0 $\times$ 10^4</td>
<td>2x</td>
<td>5/5</td>
</tr>
<tr>
<td></td>
<td>kpc-2</td>
<td><em>Escherichia coli</em></td>
<td>NRZ-00281</td>
<td>8.0 $\times$ 10^4</td>
<td>2x</td>
<td>2/2</td>
</tr>
<tr>
<td></td>
<td>kpc-2</td>
<td><em>Klebsiella pneumoniae</em></td>
<td>NRZ-00103</td>
<td>8.0 $\times$ 10^4</td>
<td>2x</td>
<td>2/2</td>
</tr>
<tr>
<td></td>
<td>kpc-3</td>
<td><em>Escherichia coli</em></td>
<td>NRZ-00222</td>
<td>8.0 $\times$ 10^4</td>
<td>2x</td>
<td>1/2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.2 $\times$ 10^5</td>
<td>3x</td>
<td>2/2</td>
</tr>
<tr>
<td></td>
<td>kpc-3</td>
<td><em>Klebsiella pneumoniae</em> (carbapenem$^R$)</td>
<td>Micromyx 4653</td>
<td>8.0 $\times$ 10^4</td>
<td>2x</td>
<td>4/4</td>
</tr>
<tr>
<td></td>
<td>kpc-3</td>
<td><em>Klebsiella pneumoniae</em> (carbapenem$^R$)</td>
<td>Micromyx 4676</td>
<td>8.0 $\times$ 10^4</td>
<td>2x</td>
<td>4/4</td>
</tr>
<tr>
<td></td>
<td>NA</td>
<td><em>Staphylococcus aureus</em> (methicillin$^R$, cefoxitin$^R$) (pos. control/LoD ref. strain)</td>
<td>NCTC 12493</td>
<td>8.0 $\times$ 10^5</td>
<td>2x</td>
<td>3/3</td>
</tr>
<tr>
<td></td>
<td>SCCmecI</td>
<td><em>Staphylococcus aureus</em></td>
<td>RKI 07-03165</td>
<td>8.0 $\times$ 10^4</td>
<td>2x</td>
<td>2/2</td>
</tr>
<tr>
<td></td>
<td>SCCmecII</td>
<td><em>Staphylococcus aureus</em></td>
<td>RKI 01-00694</td>
<td>8.0 $\times$ 10^4</td>
<td>2x</td>
<td>2/2</td>
</tr>
<tr>
<td></td>
<td>SCCmecIII</td>
<td><em>Staphylococcus aureus</em> (methicillin$^R$)</td>
<td>ATCC 33591</td>
<td>8.0 $\times$ 10^5</td>
<td>2x</td>
<td>2/2</td>
</tr>
<tr>
<td></td>
<td>SCCmecIV</td>
<td><em>Staphylococcus aureus</em></td>
<td>RKI 09-00187</td>
<td>8.0 $\times$ 10^5</td>
<td>2x</td>
<td>2/2</td>
</tr>
<tr>
<td></td>
<td>SCCmecV</td>
<td><em>Staphylococcus aureus</em></td>
<td>RKI 08-02492</td>
<td>8.0 $\times$ 10^5</td>
<td>2x</td>
<td>2/2</td>
</tr>
<tr>
<td></td>
<td>NA</td>
<td><em>Staphylococcus aureus</em> (methicillin$^R$)</td>
<td>DSM-17091</td>
<td>8.0 $\times$ 10^5</td>
<td>2x</td>
<td>2/2</td>
</tr>
<tr>
<td></td>
<td>SCCmecII</td>
<td><em>Staphylococcus aureus</em> (methicillin$^R$)</td>
<td>ATCC 43300</td>
<td>3.0 $\times$ 10^5</td>
<td>0.8x</td>
<td>2/2</td>
</tr>
<tr>
<td>Analyte</td>
<td>Subgroup</td>
<td>Reference Strain</td>
<td>Strain ID</td>
<td>Test Conc. [CFU/ml]</td>
<td>x-fold LoD</td>
<td># Pos./# Exp.</td>
</tr>
<tr>
<td>---------</td>
<td>----------</td>
<td>------------------</td>
<td>-----------</td>
<td>---------------------</td>
<td>------------</td>
<td>--------------</td>
</tr>
<tr>
<td><strong>ndm</strong></td>
<td>ndm-1</td>
<td><em>Klebsiella pneumoniae</em> (pos. control/LoD ref. strain)</td>
<td>NCTC 13443</td>
<td>$4.0 \times 10^4$</td>
<td>2x</td>
<td>5/5</td>
</tr>
<tr>
<td></td>
<td>ndm-1</td>
<td><em>Acinetobacter baumannii</em></td>
<td>JMI 49755</td>
<td>$4.0 \times 10^4$</td>
<td>2x</td>
<td>4/4</td>
</tr>
<tr>
<td></td>
<td>ndm-1</td>
<td><em>Enterobacter cloacae</em> (imipenem&lt;sup&gt;B&lt;/sup&gt;, ertapenem&lt;sup&gt;B&lt;/sup&gt;)</td>
<td>ATCC BAA-2468</td>
<td>$4.0 \times 10^4$</td>
<td>2x</td>
<td>1/2</td>
</tr>
<tr>
<td></td>
<td>ndm-1</td>
<td><em>Enterobacter cloacae</em></td>
<td>JMI 46239</td>
<td>$4.0 \times 10^4$</td>
<td>2x</td>
<td>4/4</td>
</tr>
<tr>
<td></td>
<td>ndm-1</td>
<td><em>Escherichia coli</em></td>
<td>JMI 50067</td>
<td>$4.0 \times 10^4$</td>
<td>2x</td>
<td>2/2</td>
</tr>
<tr>
<td></td>
<td>ndm-1</td>
<td><em>Klebsiella pneumoniae</em></td>
<td>JMI 49767</td>
<td>$2.0 \times 10^4$</td>
<td>1x</td>
<td>2/2</td>
</tr>
<tr>
<td></td>
<td>ndm-1</td>
<td><em>Klebsiella pneumoniae</em></td>
<td>JMI 49831</td>
<td>$4.0 \times 10^4$</td>
<td>2x</td>
<td>2/2</td>
</tr>
<tr>
<td><strong>oxa-23</strong></td>
<td></td>
<td><em>Acinetobacter baumannii</em> (pos. control/LoD ref. strain)</td>
<td>NCTC 13301</td>
<td>$2.0 \times 10^7$</td>
<td>2x</td>
<td>3/3</td>
</tr>
<tr>
<td></td>
<td>NA</td>
<td><em>Acinetobacter baumannii</em> (carbapenem&lt;sup&gt;B&lt;/sup&gt;)</td>
<td>Micromyx 4410</td>
<td>$2.0 \times 10^7$</td>
<td>2x</td>
<td>2/2</td>
</tr>
<tr>
<td></td>
<td>NA</td>
<td><em>Acinetobacter baumannii</em> (carbapenem&lt;sup&gt;B&lt;/sup&gt;)</td>
<td>Micromyx 6148</td>
<td>$2.0 \times 10^7$</td>
<td>2x</td>
<td>2/2</td>
</tr>
<tr>
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<td>NA</td>
<td><em>Acinetobacter baumannii</em> (carbapenem&lt;sup&gt;B&lt;/sup&gt;)</td>
<td>Micromyx 6149</td>
<td>$2.0 \times 10^7$</td>
<td>2x</td>
<td>2/2</td>
</tr>
<tr>
<td></td>
<td>NA</td>
<td><em>Acinetobacter baumannii</em> (carbapenem&lt;sup&gt;B&lt;/sup&gt;)</td>
<td>Micromyx 6153</td>
<td>$2.0 \times 10^7$</td>
<td>2x</td>
<td>2/2</td>
</tr>
<tr>
<td></td>
<td>NA</td>
<td><em>Acinetobacter baumannii</em> (imipenem&lt;sup&gt;B&lt;/sup&gt;, meropenem&lt;sup&gt;B&lt;/sup&gt;)</td>
<td>UCLA A5</td>
<td>$2.0 \times 10^7$</td>
<td>2x</td>
<td>2/2</td>
</tr>
<tr>
<td><strong>oxa-24</strong></td>
<td></td>
<td><em>Acinetobacter baumannii</em> (pos. control/LoD ref. strain)</td>
<td>NCTC 13302</td>
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<td>2x</td>
<td>3/3</td>
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<tr>
<td></td>
<td>oxa-72</td>
<td><em>Acinetobacter baumannii</em></td>
<td>NRZ-00449</td>
<td>$1.0 \times 10^4$</td>
<td>2x</td>
<td>2/2</td>
</tr>
<tr>
<td></td>
<td>NA</td>
<td><em>Acinetobacter baumannii</em> (imipenem&lt;sup&gt;B&lt;/sup&gt;, meropenem&lt;sup&gt;B&lt;/sup&gt;)</td>
<td>UCLA A4</td>
<td>$1.0 \times 10^4$</td>
<td>2x</td>
<td>2/2</td>
</tr>
<tr>
<td></td>
<td>NA</td>
<td><em>Acinetobacter baumannii</em> (imipenem&lt;sup&gt;B&lt;/sup&gt;, meropenem&lt;sup&gt;B&lt;/sup&gt;)</td>
<td>clinical strain 1</td>
<td>$1.0 \times 10^4$</td>
<td>2x</td>
<td>2/2</td>
</tr>
<tr>
<td></td>
<td>NA</td>
<td><em>Acinetobacter baumannii</em> (imipenem&lt;sup&gt;B&lt;/sup&gt;, meropenem&lt;sup&gt;B&lt;/sup&gt;)</td>
<td>clinical strain 2</td>
<td>$1.0 \times 10^4$</td>
<td>2x</td>
<td>2/2</td>
</tr>
<tr>
<td><strong>oxa-48</strong></td>
<td></td>
<td><em>Klebsiella pneumoniae</em> (pos. control/LoD ref. strain)</td>
<td>NCTC 13442</td>
<td>$6.0 \times 10^4$</td>
<td>2x</td>
<td>3/3</td>
</tr>
<tr>
<td></td>
<td>oxa-48</td>
<td><em>Escherichia coli</em> (ertapenem&lt;sup&gt;B&lt;/sup&gt;)</td>
<td>ATCC BAA-2523</td>
<td>$6.0 \times 10^4$</td>
<td>2x</td>
<td>2/2</td>
</tr>
<tr>
<td></td>
<td>oxa-48</td>
<td><em>Escherichia coli</em></td>
<td>NRZ-00176</td>
<td>$6.0 \times 10^4$</td>
<td>2x</td>
<td>1/2</td>
</tr>
<tr>
<td></td>
<td>oxa-162</td>
<td><em>Escherichia coli</em></td>
<td>NRZ-00361</td>
<td>$6.0 \times 10^4$</td>
<td>3x</td>
<td>2/2</td>
</tr>
<tr>
<td></td>
<td>oxa-232</td>
<td><em>Klebsiella pneumoniae</em></td>
<td>NRZ-22060</td>
<td>$6.0 \times 10^4$</td>
<td>2x</td>
<td>2/2</td>
</tr>
<tr>
<td><strong>oxa-58</strong></td>
<td></td>
<td><em>Acinetobacter baumannii</em> (pos. control/LoD ref. strain)</td>
<td>NCTC 13305</td>
<td>$1.0 \times 10^4$</td>
<td>2x</td>
<td>2/3</td>
</tr>
<tr>
<td></td>
<td>oxa-58</td>
<td><em>Acinetobacter baumannii</em></td>
<td>NRZ-00518</td>
<td>$1.0 \times 10^4$</td>
<td>2x</td>
<td>3/3</td>
</tr>
<tr>
<td><strong>tem</strong></td>
<td></td>
<td><em>Klebsiella pneumoniae</em> (pos. control/LoD ref. strain)</td>
<td>NCTC 13443</td>
<td>$4.0 \times 10^4$</td>
<td>2x</td>
<td>2/2</td>
</tr>
<tr>
<td></td>
<td>tem-1</td>
<td><em>Escherichia coli</em></td>
<td>ATCC 35218</td>
<td>$4.0 \times 10^4$</td>
<td>2x</td>
<td>2/2</td>
</tr>
<tr>
<td></td>
<td>tem-3</td>
<td><em>Escherichia coli</em> (ESBL)</td>
<td>ATCC 13351</td>
<td>$4.0 \times 10^4$</td>
<td>2x</td>
<td>2/2</td>
</tr>
<tr>
<td></td>
<td>NA</td>
<td><em>Citrobacter freundii</em></td>
<td>ATCC 43864</td>
<td>$4.0 \times 10^4$</td>
<td>2x</td>
<td>2/2</td>
</tr>
<tr>
<td></td>
<td>NA</td>
<td><em>Enterobacter cloacae</em></td>
<td>JMI 46239</td>
<td>$4.0 \times 10^4$</td>
<td>2x</td>
<td>2/2</td>
</tr>
<tr>
<td></td>
<td>NA</td>
<td><em>Escherichia coli</em></td>
<td>JMI 50067</td>
<td>$2.0 \times 10^4$</td>
<td>1x</td>
<td>2/2</td>
</tr>
<tr>
<td></td>
<td>NA</td>
<td><em>Klebsiella pneumoniae</em></td>
<td>NRZ-00751</td>
<td>$2.0 \times 10^4$</td>
<td>1x</td>
<td>2/2</td>
</tr>
<tr>
<td></td>
<td>NA</td>
<td><em>Escherichia coli</em></td>
<td>ATCC BAA-2523</td>
<td>$4.0 \times 10^4$</td>
<td>2x</td>
<td>2/2</td>
</tr>
<tr>
<td>Analyte</td>
<td>Subgroup</td>
<td>Reference Strain</td>
<td>Strain ID</td>
<td>Test Conc. [CFU/ml]</td>
<td>x-fold LoD</td>
<td># Pos./# Exp.</td>
</tr>
<tr>
<td>---------</td>
<td>----------</td>
<td>------------------</td>
<td>-----------</td>
<td>------------------</td>
<td>------------</td>
<td>--------------</td>
</tr>
<tr>
<td>Acinetobacter baumannii</td>
<td>NA</td>
<td>JMI 49755</td>
<td>$4 \times 10^4$</td>
<td>2x</td>
<td>2/2</td>
<td></td>
</tr>
<tr>
<td>Haemophilus influenzae (ampicillinR, cefinaseR)</td>
<td>NA</td>
<td>clinical strain 1</td>
<td>$4 \times 10^4$</td>
<td>2x</td>
<td>2/2</td>
<td></td>
</tr>
<tr>
<td>Haemophilus influenzae (cefinaseR)</td>
<td>NA</td>
<td>clinical strain 2</td>
<td>$4 \times 10^4$</td>
<td>2x</td>
<td>2/2</td>
<td></td>
</tr>
<tr>
<td>Klebsiella pneumoniae</td>
<td>NA</td>
<td>Micromyx 4676</td>
<td>$8 \times 10^4$</td>
<td>4x</td>
<td>2/2</td>
<td></td>
</tr>
<tr>
<td>Pseudomonas aeruginosa (pos. control/LoD ref. strain)</td>
<td>vim-10</td>
<td>NCTC 13437</td>
<td>$4 \times 10^4$</td>
<td>2x</td>
<td>3/3</td>
<td></td>
</tr>
<tr>
<td>Citrobacter freundii</td>
<td>vim-1</td>
<td>NRZ-00452</td>
<td>$4 \times 10^4$</td>
<td>2x</td>
<td>2/2</td>
<td></td>
</tr>
<tr>
<td>Pseudomonas aeruginosa (ceftazidimeR, imipenemR)</td>
<td>vim-1</td>
<td>DSM-24600</td>
<td>$4 \times 10^4$</td>
<td>2x</td>
<td>2/2</td>
<td></td>
</tr>
<tr>
<td>Enterobacter cloacae</td>
<td>vim-1</td>
<td>NRZ-00239</td>
<td>$4 \times 10^4$</td>
<td>2x</td>
<td>2/2</td>
<td></td>
</tr>
<tr>
<td>Klebsiella pneumoniae</td>
<td>vim-1</td>
<td>NCTC 13439</td>
<td>$4 \times 10^4$</td>
<td>2x</td>
<td>2/2</td>
<td></td>
</tr>
<tr>
<td>Klebsiella pneumoniae</td>
<td>NA</td>
<td>NCTC 13440</td>
<td>$4 \times 10^4$</td>
<td>2x</td>
<td>2/2</td>
<td></td>
</tr>
<tr>
<td>Pseudomonas aeruginosa (carbapenemR)</td>
<td>NA</td>
<td>UCLA P20</td>
<td>$1.3 \times 10^3$</td>
<td>0.1x</td>
<td>2/2</td>
<td></td>
</tr>
<tr>
<td>Micromyx 2562</td>
<td>NA</td>
<td>Micromyx 2562</td>
<td>$4 \times 10^4$</td>
<td>2x</td>
<td>2/2</td>
<td></td>
</tr>
</tbody>
</table>

To supplement inclusivity testing for further specific antibiotic resistance marker variants, reference sequences for all available variants belonging to individual antibiotic resistance markers or marker subgroups were compiled and analyzed in silico.

Subgroups or variants for applicable LRT BAL panel antibiotic resistance markers for which detection is predicted at LoD (match of relevant primer and probe sequences), with reduced sensitivity (typically, single relevant mismatches of primer or probe sequences; detection likely at higher than LoD concentrations only), or is not predicted (multiple relevant mismatches in primer and probe sequences) are listed in Table 7. Such predictions are provided as supplementary data only. Results are not intended to be a surrogate for wet testing and do not assure that specific variant will be detected.

NOTE: The performance of the Unyvero LRT BAL Application has not been established for antibiotic resistance marker variants other than those listed in the inclusivity test results table above.
Table 7: *In silico* prediction for LRT BAL panel antibiotic resistance markers for applicable subgroups or variants.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ctx-M:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ctx-M:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ctx-M2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ctx-M8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ctx-M9</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ctx-M25</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ctx-M45 subgroups</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>kpc</strong></td>
<td>1 - 39</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ndm</strong></td>
<td>1 - 24, 27</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>oxa:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>oxa-24</td>
<td>24 - 26, 33, 40, 72, 139, 160, 207, 437, 653</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>oxa:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>oxa-48</td>
<td>48, 48b, 162, 163, 181, 199, 232, 244, 245, 247, 252, 370, 405, 416, 438, 439, 484, 505, 514, 515, 517, 519, 538, 546, 547, 566, 567, 731, 788, 793</td>
<td>204</td>
<td>54, 436, 535</td>
</tr>
<tr>
<td>oxa-58</td>
<td>58, 96, 97, 164, 397, 467, 512</td>
<td></td>
<td>420</td>
</tr>
<tr>
<td><strong>vim</strong></td>
<td>1 - 6, 8 - 12, 14 - 20, 23 - 46, 48 - 54, 56, 58, 60, 62</td>
<td></td>
<td>57, 59</td>
</tr>
</tbody>
</table>

NOTE: *H. influenzae* commonly hosts *tem*-1. *tem* will only be reported by the LRT BAL Application if *H. influenzae* is concurrently detected.
Exclusivity and Cross-Reactivity

For each of the LRT BAL panel analytes, cross-reactive species (clinically relevant close neighbor strains) were predicted by GenBank BLAST search. Predictions were complemented with exclusivity wet testing for close-neighbor strains or common respiratory flora microorganisms performed in duplicate at a worst-case concentration (typically: $1.5 \times 10^7$ CFU/mL for bacterial microorganisms, or as indicated) by spiking into 0.25x ARM (artificial respiratory matrix) surrogate as sample matrix.

Exclusivity study results are listed in Table 8. For Haemophilus haemolyticus (ATCC 33390) and Aggregatibacter aphrophilus (ATCC 19415), cross-reactivity to Haemophilus influenzae close to LoD concentrations (for ATCC 33390) or with reduced sensitivity (for ATCC 19415), respectively, was observed. Another strain, Haemophilus parainfluenzae (ATCC 33392) cross-reacted to Haemophilus influenzae only at very high concentrations in some of the tests (>100x LoD, >$10^7$ CFU/mL).

Table 8: Exclusivity study results.

<table>
<thead>
<tr>
<th>Strain</th>
<th>Test Concentration</th>
<th>Cross-Reactivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actinomyces odontolyticus</td>
<td>$1.5 \times 10^7$</td>
<td>no</td>
</tr>
<tr>
<td>Aspergillus fumigatus</td>
<td>$1.5 \times 10^7$</td>
<td>no</td>
</tr>
<tr>
<td>Candida albicans</td>
<td>$1.5 \times 10^7$</td>
<td>no</td>
</tr>
<tr>
<td>Candida dubliniensis</td>
<td>$1.5 \times 10^7$</td>
<td>no</td>
</tr>
<tr>
<td>Candida glabrata</td>
<td>$1.5 \times 10^7$</td>
<td>no</td>
</tr>
<tr>
<td>Candida krusei</td>
<td>$1.5 \times 10^7$</td>
<td>no</td>
</tr>
<tr>
<td>Candida parapsilosis</td>
<td>$1.5 \times 10^7$</td>
<td>no</td>
</tr>
<tr>
<td>Candida tropicalis</td>
<td>$1.5 \times 10^7$</td>
<td>no</td>
</tr>
<tr>
<td>Cardiobacterium hominis</td>
<td>$1.5 \times 10^7$</td>
<td>no</td>
</tr>
<tr>
<td>Eikenella corrodens</td>
<td>$1.5 \times 10^7$</td>
<td>no</td>
</tr>
<tr>
<td>Enterococcus faecalis</td>
<td>$1.5 \times 10^7$</td>
<td>no</td>
</tr>
<tr>
<td>Enterococcus faecium</td>
<td>$1.5 \times 10^7$</td>
<td>no</td>
</tr>
<tr>
<td>Fusobacterium nucleatum</td>
<td>$5.0 \times 10^6$</td>
<td>no</td>
</tr>
<tr>
<td>Granulicatella adiacens</td>
<td>$1.5 \times 10^7$</td>
<td>no</td>
</tr>
<tr>
<td>Kingella kingae</td>
<td>$1.5 \times 10^7$</td>
<td>no</td>
</tr>
<tr>
<td>Lactobacillus acidophilus</td>
<td>$1.5 \times 10^7$</td>
<td>no</td>
</tr>
<tr>
<td>Micrococcus luteus</td>
<td>$1.5 \times 10^7$</td>
<td>no</td>
</tr>
<tr>
<td>Mycobacterium bovis</td>
<td>$1.5 \times 10^7$</td>
<td>no</td>
</tr>
<tr>
<td>Mycoplasma orale</td>
<td>$1.5 \times 10^7$</td>
<td>no</td>
</tr>
<tr>
<td>Neisseria lactamica</td>
<td>$1.5 \times 10^7$</td>
<td>no</td>
</tr>
<tr>
<td>Neisseria sicca</td>
<td>$1.5 \times 10^7$</td>
<td>no</td>
</tr>
<tr>
<td>Pantoae agglomerans</td>
<td>$1.5 \times 10^7$</td>
<td>no</td>
</tr>
<tr>
<td>Peptostreptococcus stomatis</td>
<td>$5.0 \times 10^6$</td>
<td>no</td>
</tr>
<tr>
<td>Porphyromonas gingivalis</td>
<td>$1.5 \times 10^7$</td>
<td>no</td>
</tr>
<tr>
<td>Prevotella buccalis</td>
<td>$1.5 \times 10^7$</td>
<td>no</td>
</tr>
<tr>
<td>Raoultella planticola</td>
<td>$1.5 \times 10^7$</td>
<td>no</td>
</tr>
</tbody>
</table>
For *A. aphrophilus*, cross-reactivity to *H. influenzae* was observed down to a concentration of $2.0 \times 10^5$ CFU/mL (1/2 tests positive). For a concentration of $1.0 \times 10^5$ CFU/mL (equivalent to 5x LoD of *H. influenzae*), cross-reactivity was not observed any more. According to BLAST analysis, cross-reactivity of *A. aphrophilus* to *H. influenzae* is only predicted for some strains (including the tested reference strain ATCC 19415), but not for other strains.

For *H. haemolyticus*, cross-reactivity to *H. influenzae* was observed down to a concentration of $4.0 \times 10^5$ CFU/mL (2/2 tests positive, equivalent to 2x LoD of *H. influenzae*). Sequence comparison by BLAST for *H. haemolyticus* to *H. influenzae* shows a 3’ mismatch to *close neighbor microorganisms* [in CFU/mL]

<table>
<thead>
<tr>
<th>microorganisms</th>
<th>concentration [in CFU/mL]</th>
<th>cross-reactivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acinetobacter ursingii</td>
<td>$1.5 \times 10^7$</td>
<td>no</td>
</tr>
<tr>
<td>Aggregatibacter actinomycetemcomitans</td>
<td>$1.5 \times 10^7$</td>
<td>no</td>
</tr>
<tr>
<td>Aggregatibacter aphrophilus</td>
<td>$1.5 \times 10^7$</td>
<td>yes (<em>H. influenzae</em>) a</td>
</tr>
<tr>
<td>Citrobacter koseri</td>
<td>$1.5 \times 10^7$</td>
<td>no</td>
</tr>
<tr>
<td>Haemophilus haemolyticus</td>
<td>$1.5 \times 10^7$</td>
<td>yes (<em>H. influenzae</em>) b</td>
</tr>
<tr>
<td>Haemophilus parahaemolyticus</td>
<td>$1.5 \times 10^7$</td>
<td>no</td>
</tr>
<tr>
<td>Haemophilus parainfluenzae</td>
<td>$1.5 \times 10^7$</td>
<td>yes (<em>H. influenzae</em>) c</td>
</tr>
<tr>
<td>Legionella longbeachae</td>
<td>$1.5 \times 10^7$</td>
<td>no</td>
</tr>
<tr>
<td>Legionella/Tatlockia micdadei</td>
<td>$1.5 \times 10^7$</td>
<td>no</td>
</tr>
<tr>
<td>Staphylococcus capitis</td>
<td>$1.5 \times 10^7$</td>
<td>no</td>
</tr>
<tr>
<td>Staphylococcus epidermidis</td>
<td>$1.5 \times 10^7$</td>
<td>no</td>
</tr>
<tr>
<td>Staphylococcus haemolyticus</td>
<td>$1.5 \times 10^7$</td>
<td>no</td>
</tr>
<tr>
<td>Staphylococcus lugdunensis</td>
<td>$1.5 \times 10^7$</td>
<td>no</td>
</tr>
<tr>
<td>Staphylococcus saprophyticus</td>
<td>$1.5 \times 10^7$</td>
<td>no</td>
</tr>
<tr>
<td>Streptococcus agalactiae</td>
<td>$1.5 \times 10^7$</td>
<td>no</td>
</tr>
<tr>
<td>Streptococcus anginosus</td>
<td>$1.5 \times 10^7$</td>
<td>no</td>
</tr>
<tr>
<td>Streptococcus dysgalactiae</td>
<td>$1.5 \times 10^7$</td>
<td>no</td>
</tr>
<tr>
<td>Streptococcus gordonii</td>
<td>$1.5 \times 10^7$</td>
<td>no</td>
</tr>
<tr>
<td>Streptococcus intermedius</td>
<td>$1.5 \times 10^7$</td>
<td>no</td>
</tr>
<tr>
<td>Streptococcus mitis</td>
<td>$1.5 \times 10^7$</td>
<td>no</td>
</tr>
<tr>
<td>Streptococcus mutans</td>
<td>$1.5 \times 10^7$</td>
<td>no</td>
</tr>
<tr>
<td>Streptococcus oralis</td>
<td>$1.5 \times 10^7$</td>
<td>no</td>
</tr>
<tr>
<td>Streptococcus parasanguinis</td>
<td>$1.5 \times 10^7$</td>
<td>no</td>
</tr>
<tr>
<td>Streptococcus pseudopneumoniae</td>
<td>$1.5 \times 10^7$</td>
<td>no</td>
</tr>
<tr>
<td>Streptococcus pyogenes</td>
<td>$1.5 \times 10^7$</td>
<td>no</td>
</tr>
<tr>
<td>Streptococcus salivarius</td>
<td>$1.5 \times 10^7$</td>
<td>no</td>
</tr>
<tr>
<td>Streptococcus sanguinis</td>
<td>$1.5 \times 10^7$</td>
<td>no</td>
</tr>
<tr>
<td>Streptococcus vestibularis</td>
<td>$1.5 \times 10^7$</td>
<td>no</td>
</tr>
</tbody>
</table>

**respiratory viruses** [in copies/mL]

<table>
<thead>
<tr>
<th>virus</th>
<th>concentration [in copies/mL]</th>
<th>cross-reactivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenovirus 41</td>
<td>$1.0 \times 10^5$</td>
<td>no</td>
</tr>
<tr>
<td>Enterovirus 68</td>
<td>$1.0 \times 10^5$</td>
<td>no</td>
</tr>
<tr>
<td>Enterovirus 71</td>
<td>$1.0 \times 10^5$</td>
<td>no</td>
</tr>
<tr>
<td>Parainfluenzae Virus 1</td>
<td>$1.0 \times 10^5$</td>
<td>no</td>
</tr>
<tr>
<td>Parainfluenzae Virus 2</td>
<td>$1.0 \times 10^5$</td>
<td>no</td>
</tr>
<tr>
<td>Parainfluenzae Virus 3</td>
<td>$1.0 \times 10^5$</td>
<td>no</td>
</tr>
<tr>
<td>Parainfluenzae Virus 4</td>
<td>$1.0 \times 10^5$</td>
<td>no</td>
</tr>
<tr>
<td>Rhinovirus</td>
<td>$1.0 \times 10^5$</td>
<td>no</td>
</tr>
<tr>
<td>RSV A</td>
<td>$1.0 \times 10^5$</td>
<td>no</td>
</tr>
<tr>
<td>RSV B</td>
<td>$1.0 \times 10^5$</td>
<td>no</td>
</tr>
</tbody>
</table>

* For *A. aphrophilus*, cross-reactivity to *H. influenzae* was observed down to a concentration of $2.0 \times 10^5$ CFU/mL (1/2 tests positive). For a concentration of $1.0 \times 10^5$ CFU/mL (equivalent to 5x LoD of *H. influenzae*), cross-reactivity was not observed any more. According to BLAST analysis, cross-reactivity of *A. aphrophilus* to *H. influenzae* is only predicted for some strains (including the tested reference strain ATCC 19415), but not for other strains.

* For *H. haemolyticus*, cross-reactivity to *H. influenzae* was observed down to a concentration of $4.0 \times 10^5$ CFU/mL (2/2 tests positive, equivalent to 2x LoD of *H. influenzae*). Sequence comparison by BLAST for *H. haemolyticus* to *H. influenzae* shows a 3’ mismatch to...
one of the assay primers, while the second primer and all internal array probes show a full match. Therefore, the observed cross-reactivity is supported by BLAST analysis, although only predicted with reduced sensitivity.

For *H. parainfluenzae*, cross-reactivity to *H. influenzae* was observed only at the tested worst-case concentration of $1.5 \times 10^7$ CFU/mL (2/4 tests positive, equivalent to 750x LoD of *H. influenzae*). Additional tests at $2.0 \times 10^6$ CFU/mL (equivalent to 100x LoD of *H. influenzae*), cross-reactivity was not observed any more.

Table 9 lists predicted possible cross-reactivity of applicable LRT BAL panel microorganisms based on *in silico* analysis, exclusivity wet testing and cases observed during the prospective or archived study.

**Table 9: In silico cross-reactivity prediction, results of exclusivity wet testing and cross-reactive specimens observed for the prospective and archived study.**

<table>
<thead>
<tr>
<th>Close Neighbor Strain a</th>
<th>Cross-Reactivity Prediction (in-silico analysis)</th>
<th>Wet Testing Result</th>
<th>Cross-Reactions Observed in Clinical Study (N = 1,408 prosp. or arch. specimens)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Citrobacter freundii</strong></td>
<td>Detection predicted at higher than LoD concentrations (certain strains) / Detection not predicted (other strains) c</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Citrobacter braakii</td>
<td>Detection predicted at higher than LoD concentrations</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Citrobacter pasteurii</td>
<td>Detection predicted at higher than LoD concentrations</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Citrobacter wekimannii</td>
<td>Detection predicted at higher than LoD concentrations (certain strains) / Detection not predicted (other strains) c</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Citrobacter youngae</td>
<td>Detection predicted at LoD (certain strains) / Detection predicted at higher than LoD concentrations (other strains) c</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Kluyvera georgiana</td>
<td>Detection predicted at higher than LoD concentrations</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Citrobacter koseri</td>
<td>Detection not predicted</td>
<td>negative ATCC 27156</td>
<td>-</td>
</tr>
</tbody>
</table>

**Escherichia coli**

<table>
<thead>
<tr>
<th>Close Neighbor Strain a</th>
<th>Cross-Reactivity Prediction (in-silico analysis)</th>
<th>Wet Testing Result</th>
<th>Cross-Reactions Observed in Clinical Study (N = 1,408 prosp. or arch. specimens)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shigella dysenteriae b</td>
<td>Detection predicted at LoD</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Shigella boydii b</td>
<td>Detection predicted at LoD</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Shigella flexneri b</td>
<td>Detection predicted at LoD</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Shigella sonnei b</td>
<td>Detection predicted at LoD</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Escherichia albertii</td>
<td>Detection predicted at LoD</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Escherichia fergusonii</td>
<td>Detection predicted at LoD</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

**Haemophilus influenzae**

<table>
<thead>
<tr>
<th>Close Neighbor Strain a</th>
<th>Cross-Reactivity Prediction (in-silico analysis)</th>
<th>Wet Testing Result</th>
<th>Cross-Reactions Observed in Clinical Study (N = 1,408 prosp. or arch. specimens)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemophilus haemolyticus</td>
<td>Detection predicted at higher than LoD concentrations</td>
<td>positive ATCC 33390</td>
<td>5</td>
</tr>
<tr>
<td>Haemophilus parahaemolyticus</td>
<td>Detection not predicted</td>
<td>negative ATCC 10014</td>
<td>-</td>
</tr>
<tr>
<td>Haemophilus parainfluenzae</td>
<td>Detection not predicted</td>
<td>positive at worst-case concentration only ATCC 33392</td>
<td>1</td>
</tr>
<tr>
<td>Haemophilus aegyptius b</td>
<td>Detection predicted at LoD</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Aggregatibacter actinomyctetemcomitans</td>
<td>Detection not predicted</td>
<td>negative ATCC 33384</td>
<td>-</td>
</tr>
<tr>
<td>----------------------------------------</td>
<td>------------------------</td>
<td>---------------------</td>
<td>---</td>
</tr>
<tr>
<td>Aggregatibacter aphrophilus</td>
<td>Detection predicted at higher than LoD concentrations (certain strains) / Detection not predicted (other strains)</td>
<td>positive ATCC 19415</td>
<td>3</td>
</tr>
<tr>
<td>Aggregatibacter segnis</td>
<td>Detection predicted at higher than LoD concentrations</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

**Klebsiella oxytica**

| Klebsiella michiganensis | Detection predicted at LoD (certain strains) / Detection predicted at higher than LoD concentrations (other strains) | - | - |

**Klebsiella pneumoniae**

| Klebsiella quasivariicola | Detection predicted at higher than LoD concentrations | - | - |

**Staphylococcus aureus**

<table>
<thead>
<tr>
<th>Staphylococcus argenteus</th>
<th>Detection predicted at LoD</th>
<th>-</th>
<th>-</th>
</tr>
</thead>
<tbody>
<tr>
<td>CNS:</td>
<td>Detection not predicted</td>
<td>negative ATCC 51625 ATCC 27840 ATCC 43809 ATCC 29970 ATCC 15305</td>
<td></td>
</tr>
<tr>
<td>S. epidermidis</td>
<td></td>
<td>ATCC 13813 ATCC 33397</td>
<td></td>
</tr>
<tr>
<td>S. capitis</td>
<td></td>
<td>ATCC 43078 ATCC 10558 ATCC 27335</td>
<td></td>
</tr>
<tr>
<td>S. lugdunensis</td>
<td></td>
<td>ATCC 49456</td>
<td></td>
</tr>
<tr>
<td>S. haemolyticus</td>
<td></td>
<td>ATCC 25175 ATCC 35037</td>
<td></td>
</tr>
<tr>
<td>S. saprophyticus</td>
<td></td>
<td>ATCC 15912 ATCC BAA-960</td>
<td></td>
</tr>
</tbody>
</table>

**Streptococcus pneumoniae**

<table>
<thead>
<tr>
<th>other Streptococcus spp.:</th>
<th>Detection not predicted</th>
<th>negative ATCC 12344 ATCC 7073 ATCC 10556 ATCC 49124</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. agalactiae</td>
<td></td>
<td>ATCC 13813</td>
</tr>
<tr>
<td>S. anginosus</td>
<td></td>
<td>ATCC 33397</td>
</tr>
<tr>
<td>S. dysgalactiae</td>
<td></td>
<td>ATCC 43078</td>
</tr>
<tr>
<td>S. gordonii</td>
<td></td>
<td>ATCC 10558</td>
</tr>
<tr>
<td>S. intermedius</td>
<td></td>
<td>ATCC 27335</td>
</tr>
<tr>
<td>S. mitis</td>
<td></td>
<td>ATCC 49456</td>
</tr>
<tr>
<td>S. mutans</td>
<td></td>
<td>ATCC 25175</td>
</tr>
<tr>
<td>S. oralis</td>
<td></td>
<td>ATCC 35037</td>
</tr>
<tr>
<td>S. parasanguinis</td>
<td></td>
<td>ATCC 15912</td>
</tr>
<tr>
<td>S. pseudopneumoniae</td>
<td></td>
<td>ATCC BAA-960</td>
</tr>
<tr>
<td>S. pyogenes</td>
<td></td>
<td>ATCC 12344</td>
</tr>
<tr>
<td>S. salivarius</td>
<td></td>
<td>ATCC 7073</td>
</tr>
<tr>
<td>S. sanguinis</td>
<td></td>
<td>ATCC 10556</td>
</tr>
<tr>
<td>S. vestibularis</td>
<td></td>
<td>ATCC 49124</td>
</tr>
</tbody>
</table>

\[a\] For several analyte assays, soil, environmental, plant or animal derived close neighbor strains are also predicted at LoD or at higher than LoD concentrations (Citrobacter freundii, C. portucalensis, Enterobacter cloacae complex: E. soli, E. mori, E. nickellidurans; Escherichia coli: E. marmotae; Staphylococcus aureus: S. schweitzeri, S. simiae; Stenotrophomonas maltophilia: S. nitritireducens, S. daejeonensis, S. acidaminiphila, S. koreensis, S. rhizophila, Xanthomonas spp., Pseudoxanthomonas spp.).

\[b\] Clinical relevance unlikely for respiratory infections.

\[c\] Predictions for available strains distribute into different categories.
Interference Testing
Interference testing had already been established with the Unyvero LRT Application (predicate device), which relies on the same DNA extraction procedures and chemistry as the LRT BAL Application. Results are included below for reference. Possible interfering substances, such as respiratory medications, antibiotics, sample storage media, lavage media, sample liquefying agent (DTT), lysis buffer and endogenous substances blood and human DNA were tested. Pools of panel analytes were analyzed with and without interfering substances added at concentrations recommended in the CLSI guideline ‘Interference Testing in Clinical Chemistry’. Representative analytes were pooled and added to PBS as surrogate matrix containing potentially interfering substances at concentrations as indicated in Table 10. No interference was observed at tested concentrations.

Table 10: Tested possible interfering substances (M: test concentration in mol/L).

<table>
<thead>
<tr>
<th>Interferent</th>
<th>Test Concentration</th>
<th>Interference Observed</th>
</tr>
</thead>
<tbody>
<tr>
<td>respiratory drugs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Guaifenesin</td>
<td>1.5 x 10⁻³ M</td>
<td>no</td>
</tr>
<tr>
<td>Dextromethorphan</td>
<td>3.7 x 10⁻⁶ M</td>
<td>no</td>
</tr>
<tr>
<td>Acetyl-Cystein</td>
<td>1.0 x 10⁻³ M</td>
<td>no</td>
</tr>
<tr>
<td>Salbutamol</td>
<td>4.0 x 10⁻⁶ M</td>
<td>no</td>
</tr>
<tr>
<td>Carbocystein</td>
<td>2.8 x 10⁻³ M</td>
<td>no</td>
</tr>
<tr>
<td>Ambroxol</td>
<td>8.0 x 10⁻⁴ M</td>
<td>no</td>
</tr>
<tr>
<td>Beclomethasone</td>
<td>7.0 x 10⁻⁴ M</td>
<td>no</td>
</tr>
<tr>
<td>Theophyllin</td>
<td>2.2 x 10⁻⁴ M</td>
<td>no</td>
</tr>
<tr>
<td>antibiotics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ampicillin</td>
<td>1.5 x 10⁻⁴ M</td>
<td>no</td>
</tr>
<tr>
<td>Cefuroxime</td>
<td>1.4 x 10⁻³ M</td>
<td>no</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>8.2 x 10⁻⁵ M</td>
<td>no</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>3.0 x 10⁻⁵ M</td>
<td>no</td>
</tr>
<tr>
<td>Amikacin</td>
<td>1.4 x 10⁻⁴ M</td>
<td>no</td>
</tr>
<tr>
<td>Imipenem</td>
<td>5.0 x 10⁻⁴ M</td>
<td>no</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>8.9 x 10⁻⁵ M</td>
<td>no</td>
</tr>
<tr>
<td>Trimethoprim</td>
<td>1.4 x 10⁻⁴ M</td>
<td>no</td>
</tr>
<tr>
<td>Sulfamethoxazole</td>
<td>1.6 x 10⁻³ M</td>
<td>no</td>
</tr>
<tr>
<td>lavage sample media</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ringer-Lactate solution</td>
<td>100%</td>
<td>no</td>
</tr>
<tr>
<td>Ringer solution</td>
<td>100%</td>
<td>no</td>
</tr>
<tr>
<td>inhalation agent</td>
<td>sodium chloride</td>
<td>5% w/v</td>
</tr>
<tr>
<td>lysis buffer</td>
<td>lysis buffer DTT, 90% v/v</td>
<td>lysis buffer: 90% v/v (final conc. in lysis tube) or 80% v/v (for added sample), DTT: 40 mM (final conc. in lysis tube) or 35 mM (for added sample)</td>
</tr>
<tr>
<td>sample components</td>
<td>EDTA blood</td>
<td>100% v/v</td>
</tr>
<tr>
<td></td>
<td>human placenta DNA</td>
<td>1 µg/µL</td>
</tr>
<tr>
<td></td>
<td>fish sperm DNA</td>
<td>4 µg/µL</td>
</tr>
<tr>
<td></td>
<td>mucin (pig stomach, type II)</td>
<td>20 mg/ml.</td>
</tr>
</tbody>
</table>
Reproducibility

Assay reproducibility was established with artificial samples (viable strains spiked in ARM surrogate matrix) with a representative strain panel (incl. Gram-positive, Gram-negative and ‘atypical’ microorganisms) covering the following LRT BAL panel analytes: *Acinetobacter* spp., *C. pneumoniae*, *C. freundii*, *H. influenzae*, *K. pneumoniae* (comprising LRT BAL panel antibiotic resistance markers *ctx*-M, *ndm*, and *tem*), *M. morganii*, *Proteus* spp. and, *S. aureus* (comprising LRT BAL panel antibiotic resistance marker *mecA*). Reproducibility testing was performed at a moderate concentration (2.5x - 10x LoD of the corresponding target analyte), at a low concentration (1x - 4x LoD of the corresponding target analyte), and with all analytes negative (surrogate matrix only) on three different Unyvero systems. Each Unyvero system mimicked a different clinical setting, consisted of one Unyvero Cockpit, three Unyvero Lysators, up to six Unyvero Analyzers, and was operated by one of three dedicated operators with different levels of work experience.

Each operator performed 3 ‘moderate’, 3 ‘low’, and 3 ‘negative’ replicates per test shift on his/her Unyvero system (maximum: 18 replicates per test day). Each operator performed a minimum of 30 replicates per concentration level (90 replicates in total per Unyvero system, 270 replicates in total for all three Unyvero systems with 90 replicates for each concentration level) distributed over a minimum of five test days with sample identities blinded to the operator. Samples on individual Analyzer slots were rotated (e.g., ‘moderate’ followed by ‘low’, followed by ‘negative’ etc.) to achieve a non-consecutive testing schedule for each sample type between test shifts. Failed runs as well as runs with single invalid analyte results were repeated to achieve a minimum number of at least 30 valid results for each of the target analytes at all test concentration levels.

Tables 11 to 13 summarize the reproducibility results for each concentration level, along with the agreement rates with the expected result and 95% confidence intervals (95% CI, calculated using the Wilson score method).
Table 11: Reproducibility study results (agreement with expected result) for concentration level ‘moderate’, 5x LoD per test analyte or as indicated.

<table>
<thead>
<tr>
<th>Analyte</th>
<th>x-fold LoD</th>
<th>Unyvero System/Operator</th>
<th>Agreement with Expected Result</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td># Pos. / # Exp.</td>
<td>%</td>
</tr>
<tr>
<td><strong>Acinetobacter baumannii</strong></td>
<td>5</td>
<td>operator 1</td>
<td>30/31</td>
</tr>
<tr>
<td>ATCC 19606</td>
<td></td>
<td>operator 2</td>
<td>31/31</td>
</tr>
<tr>
<td></td>
<td></td>
<td>operator 3</td>
<td>30/30</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>total</strong></td>
<td>91/92</td>
</tr>
<tr>
<td><strong>Chlamydia pneumoniae</strong></td>
<td>5</td>
<td>operator 1</td>
<td>31/31</td>
</tr>
<tr>
<td>ATCC VR-2282</td>
<td></td>
<td>operator 2</td>
<td>31/31</td>
</tr>
<tr>
<td></td>
<td></td>
<td>operator 3</td>
<td>30/30</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>total</strong></td>
<td>92/92</td>
</tr>
<tr>
<td><strong>Citrobacter freundii</strong></td>
<td>5</td>
<td>operator 1</td>
<td>29/30</td>
</tr>
<tr>
<td>ATCC 8090</td>
<td></td>
<td>operator 2</td>
<td>31/31</td>
</tr>
<tr>
<td></td>
<td></td>
<td>operator 3</td>
<td>30/30</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>total</strong></td>
<td>90/91</td>
</tr>
<tr>
<td><strong>Haemophilus influenzae</strong></td>
<td>5</td>
<td>operator 1</td>
<td>31/31</td>
</tr>
<tr>
<td>ATCC 33391</td>
<td></td>
<td>operator 2</td>
<td>31/31</td>
</tr>
<tr>
<td></td>
<td></td>
<td>operator 3</td>
<td>30/30</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>total</strong></td>
<td>90/92</td>
</tr>
<tr>
<td><strong>Klebsiella pneumoniae</strong></td>
<td>2.5</td>
<td>operator 1</td>
<td>31/31</td>
</tr>
<tr>
<td>NCTC 13443</td>
<td></td>
<td>operator 2</td>
<td>31/31</td>
</tr>
<tr>
<td></td>
<td></td>
<td>operator 3</td>
<td>30/30</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>total</strong></td>
<td>92/92</td>
</tr>
<tr>
<td><strong>ctx-M</strong></td>
<td>10</td>
<td>operator 1</td>
<td>29/30</td>
</tr>
<tr>
<td>NCTC 13443</td>
<td></td>
<td>operator 2</td>
<td>31/31</td>
</tr>
<tr>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td></td>
<td><strong>total</strong></td>
<td>92/92</td>
</tr>
<tr>
<td><strong>ndm</strong></td>
<td>5</td>
<td>operator 1</td>
<td>31/31</td>
</tr>
<tr>
<td>NCTC 13443</td>
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<td>operator 2</td>
<td>31/31</td>
</tr>
<tr>
<td></td>
<td></td>
<td>operator 3</td>
<td>30/30</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>total</strong></td>
<td>90/91</td>
</tr>
<tr>
<td><strong>tem</strong></td>
<td>5</td>
<td>operator 1</td>
<td>28/31</td>
</tr>
<tr>
<td>NCTC 13443</td>
<td></td>
<td>operator 2</td>
<td>31/31</td>
</tr>
<tr>
<td></td>
<td></td>
<td>operator 3</td>
<td>30/30</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>total</strong></td>
<td>89/92</td>
</tr>
<tr>
<td><strong>Morganella morganii</strong></td>
<td>5</td>
<td>operator 1</td>
<td>31/31</td>
</tr>
<tr>
<td>ATCC 25830</td>
<td></td>
<td>operator 2</td>
<td>31/31</td>
</tr>
<tr>
<td></td>
<td></td>
<td>operator 3</td>
<td>30/30</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>total</strong></td>
<td>92/92</td>
</tr>
<tr>
<td><strong>Proteus vulgaris</strong></td>
<td>5</td>
<td>operator 1</td>
<td>31/31</td>
</tr>
<tr>
<td>ATCC 29905</td>
<td></td>
<td>operator 2</td>
<td>31/31</td>
</tr>
<tr>
<td></td>
<td></td>
<td>operator 3</td>
<td>30/30</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>total</strong></td>
<td>91/91</td>
</tr>
<tr>
<td><strong>Staphylococcus aureus</strong></td>
<td>8.3</td>
<td>operator 1</td>
<td>31/31</td>
</tr>
<tr>
<td>NCTC 12493</td>
<td></td>
<td>operator 2</td>
<td>31/31</td>
</tr>
<tr>
<td></td>
<td></td>
<td>operator 3</td>
<td>30/30</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>total</strong></td>
<td>92/92</td>
</tr>
<tr>
<td><strong>mecA</strong></td>
<td>3</td>
<td>operator 1</td>
<td>31/31</td>
</tr>
<tr>
<td>NCTC 12493</td>
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<td>operator 2</td>
<td>31/31</td>
</tr>
<tr>
<td></td>
<td></td>
<td>operator 3</td>
<td>30/30</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>total</strong></td>
<td>92/92</td>
</tr>
</tbody>
</table>

*a Reduced number of available results due to invalid analyte results.*
Table 12: Reproducibility study results (agreement with expected result) for concentration level ‘low’, 2x LoD per analyte or as indicated.

<table>
<thead>
<tr>
<th>low</th>
<th>x-fold LoD</th>
<th>Unyvero System/Operator</th>
<th>Agreement with Expected Result</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td># Pos. / # Exp.</td>
<td>%</td>
</tr>
<tr>
<td>Acinetobacter baumannii ATCC 19606</td>
<td>2</td>
<td>operator 1</td>
<td>29/30</td>
</tr>
<tr>
<td></td>
<td></td>
<td>operator 2</td>
<td>31/31</td>
</tr>
<tr>
<td></td>
<td></td>
<td>operator 3</td>
<td>29/30</td>
</tr>
<tr>
<td></td>
<td></td>
<td>total</td>
<td>89/91</td>
</tr>
<tr>
<td>Chlamydia pneumoniae ATCC VR-2282</td>
<td>2</td>
<td>operator 1</td>
<td>30/30</td>
</tr>
<tr>
<td></td>
<td></td>
<td>operator 2</td>
<td>31/31</td>
</tr>
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<td></td>
<td></td>
<td>operator 3</td>
<td>30/30</td>
</tr>
<tr>
<td></td>
<td></td>
<td>total</td>
<td>91/91</td>
</tr>
<tr>
<td>Citrobacter freundii ATCC 8090</td>
<td>2</td>
<td>operator 1</td>
<td>28/30</td>
</tr>
<tr>
<td></td>
<td></td>
<td>operator 2</td>
<td>26/31</td>
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<td>29/30</td>
</tr>
<tr>
<td></td>
<td></td>
<td>total</td>
<td>83/91</td>
</tr>
<tr>
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<td>operator 1</td>
<td>27/30</td>
</tr>
<tr>
<td></td>
<td></td>
<td>operator 2</td>
<td>31/31</td>
</tr>
<tr>
<td></td>
<td></td>
<td>operator 3</td>
<td>29/30</td>
</tr>
<tr>
<td></td>
<td></td>
<td>total</td>
<td>87/91</td>
</tr>
<tr>
<td>Klebsiella pneumoniae NCTC 13443</td>
<td>1</td>
<td>operator 1</td>
<td>30/30</td>
</tr>
<tr>
<td></td>
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<td>31/31</td>
</tr>
<tr>
<td></td>
<td></td>
<td>operator 3</td>
<td>28/30</td>
</tr>
<tr>
<td></td>
<td></td>
<td>total</td>
<td>89/91</td>
</tr>
<tr>
<td>ctx-M NCTC 13443</td>
<td>4</td>
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<td>30/31</td>
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<td>total</td>
<td>89/91</td>
</tr>
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<td>29/30</td>
</tr>
<tr>
<td></td>
<td></td>
<td>operator 2</td>
<td>30/31</td>
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<td>30/30</td>
</tr>
<tr>
<td></td>
<td></td>
<td>total</td>
<td>89/91</td>
</tr>
<tr>
<td>tem NCTC 13443</td>
<td></td>
<td>operator 1</td>
<td>27/30</td>
</tr>
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<td>operator 2</td>
<td>31/31</td>
</tr>
<tr>
<td></td>
<td></td>
<td>operator 3</td>
<td>29/30</td>
</tr>
<tr>
<td></td>
<td></td>
<td>total</td>
<td>87/91</td>
</tr>
<tr>
<td>Morganella morganii ATCC 25830</td>
<td>2</td>
<td>operator 1</td>
<td>30/30</td>
</tr>
<tr>
<td></td>
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<td>30/31</td>
</tr>
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<td></td>
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<td>30/30</td>
</tr>
<tr>
<td></td>
<td></td>
<td>total</td>
<td>90/91</td>
</tr>
<tr>
<td>Proteus vulgaris a ATCC 29905</td>
<td>2</td>
<td>operator 1</td>
<td>25/30</td>
</tr>
<tr>
<td></td>
<td></td>
<td>operator 2</td>
<td>24/31</td>
</tr>
<tr>
<td></td>
<td></td>
<td>operator 3</td>
<td>27/30</td>
</tr>
<tr>
<td></td>
<td></td>
<td>total</td>
<td>76/91</td>
</tr>
<tr>
<td>Staphylococcus aureus NCTC 12493</td>
<td>3</td>
<td>operator 1</td>
<td>29/30</td>
</tr>
<tr>
<td></td>
<td></td>
<td>operator 2</td>
<td>30/30 b</td>
</tr>
<tr>
<td></td>
<td></td>
<td>operator 3</td>
<td>30/30</td>
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<td></td>
<td></td>
<td>total</td>
<td>89/90</td>
</tr>
<tr>
<td>mecA NCTC 12493</td>
<td>1.3</td>
<td>operator 1</td>
<td>30/30</td>
</tr>
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<td></td>
<td></td>
<td>operator 2</td>
<td>31/31</td>
</tr>
<tr>
<td></td>
<td></td>
<td>operator 3</td>
<td>29/30</td>
</tr>
<tr>
<td></td>
<td></td>
<td>total</td>
<td>90/91</td>
</tr>
</tbody>
</table>

*a* Proteus spp. demonstrated a slightly lower than expected positivity rate for the 2x LoD concentration with a positivity rate (for all operators combined) of 83.5% with a 95% CI of 74.6% - 89.7%. However, for an alternative test series performed in parallel for the sample stability study using the same strain and the identical cartridge lot with pooled negative BAL matrix the expected positivity rate at a 2x LoD concentration for Proteus spp. was confirmed (positivity rate: 92/93, 98.9%).

*b* Reduced number of available results due to invalid analyte results.
Table 13: Reproducibility study results (agreement with expected result) for negative samples.

<table>
<thead>
<tr>
<th>negative</th>
<th>Unyvero System/Operator</th>
<th>Agreement with Expected Result # Neg./# Exp.</th>
<th>%</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Acinetobacter baumannii</em> ATCC 19606</td>
<td>operator 1</td>
<td>31/31</td>
<td>100.0</td>
<td>89.0 - 100.0</td>
</tr>
<tr>
<td></td>
<td>operator 2</td>
<td>31/31</td>
<td>100.0</td>
<td>89.0 - 100.0</td>
</tr>
<tr>
<td></td>
<td>operator 3</td>
<td>30/30</td>
<td>100.0</td>
<td>88.7 - 100.0</td>
</tr>
<tr>
<td></td>
<td>total</td>
<td>92/92</td>
<td>100.0</td>
<td>96.0 - 100.0</td>
</tr>
<tr>
<td><em>Chlamydia pneumoniae</em> ATCC VR-2282</td>
<td>operator 1</td>
<td>31/31</td>
<td>100.0</td>
<td>89.0 - 100.0</td>
</tr>
<tr>
<td></td>
<td>operator 2</td>
<td>31/31</td>
<td>100.0</td>
<td>89.0 - 100.0</td>
</tr>
<tr>
<td></td>
<td>operator 3</td>
<td>30/30</td>
<td>100.0</td>
<td>88.7 - 100.0</td>
</tr>
<tr>
<td></td>
<td>total</td>
<td>92/92</td>
<td>100.0</td>
<td>96.0 - 100.0</td>
</tr>
<tr>
<td><em>Citrobacter freundii</em> ATCC 8090</td>
<td>operator 1</td>
<td>31/31</td>
<td>100.0</td>
<td>89.0 - 100.0</td>
</tr>
<tr>
<td></td>
<td>operator 2</td>
<td>31/31</td>
<td>100.0</td>
<td>89.0 - 100.0</td>
</tr>
<tr>
<td></td>
<td>operator 3</td>
<td>30/30</td>
<td>100.0</td>
<td>88.7 - 100.0</td>
</tr>
<tr>
<td></td>
<td>total</td>
<td>92/92</td>
<td>100.0</td>
<td>96.0 - 100.0</td>
</tr>
<tr>
<td><em>Haemophilus influenzae</em> ATCC 33391</td>
<td>operator 1</td>
<td>31/31</td>
<td>100.0</td>
<td>89.0 - 100.0</td>
</tr>
<tr>
<td></td>
<td>operator 2</td>
<td>31/31</td>
<td>100.0</td>
<td>89.0 - 100.0</td>
</tr>
<tr>
<td></td>
<td>operator 3</td>
<td>30/30</td>
<td>100.0</td>
<td>88.7 - 100.0</td>
</tr>
<tr>
<td></td>
<td>total</td>
<td>92/92</td>
<td>100.0</td>
<td>96.0 - 100.0</td>
</tr>
<tr>
<td><em>Klebsiella pneumoniae</em> NCTC 13443</td>
<td>operator 1</td>
<td>31/31</td>
<td>100.0</td>
<td>89.0 - 100.0</td>
</tr>
<tr>
<td></td>
<td>operator 2</td>
<td>30/30 a</td>
<td>100.0</td>
<td>88.7 - 100.0</td>
</tr>
<tr>
<td></td>
<td>operator 3</td>
<td>30/30</td>
<td>100.0</td>
<td>88.7 - 100.0</td>
</tr>
<tr>
<td></td>
<td>total</td>
<td>91/91</td>
<td>100.0</td>
<td>96.0 - 100.0</td>
</tr>
<tr>
<td><em>ctx-M</em> NCTC 13443</td>
<td>operator 1</td>
<td>31/31</td>
<td>100.0</td>
<td>89.0 - 100.0</td>
</tr>
<tr>
<td></td>
<td>operator 2</td>
<td>30/30 a</td>
<td>100.0</td>
<td>88.7 - 100.0</td>
</tr>
<tr>
<td></td>
<td>operator 3</td>
<td>30/30</td>
<td>100.0</td>
<td>88.7 - 100.0</td>
</tr>
<tr>
<td></td>
<td>total</td>
<td>91/91</td>
<td>100.0</td>
<td>96.0 - 100.0</td>
</tr>
<tr>
<td><em>ndm</em> NCTC 13443</td>
<td>operator 1</td>
<td>31/31</td>
<td>100.0</td>
<td>89.0 - 100.0</td>
</tr>
<tr>
<td></td>
<td>operator 2</td>
<td>31/31</td>
<td>100.0</td>
<td>89.0 - 100.0</td>
</tr>
<tr>
<td></td>
<td>operator 3</td>
<td>30/30</td>
<td>100.0</td>
<td>88.7 - 100.0</td>
</tr>
<tr>
<td></td>
<td>total</td>
<td>92/92</td>
<td>100.0</td>
<td>96.0 - 100.0</td>
</tr>
<tr>
<td><em>tem</em> NCTC 13443</td>
<td>operator 1</td>
<td>31/31</td>
<td>100.0</td>
<td>89.0 - 100.0</td>
</tr>
<tr>
<td></td>
<td>operator 2</td>
<td>31/31</td>
<td>100.0</td>
<td>89.0 - 100.0</td>
</tr>
<tr>
<td></td>
<td>operator 3</td>
<td>30/30</td>
<td>100.0</td>
<td>88.7 - 100.0</td>
</tr>
<tr>
<td></td>
<td>total</td>
<td>92/92</td>
<td>100.0</td>
<td>96.0 - 100.0</td>
</tr>
<tr>
<td><em>Morganella morganii</em> ATCC 25830</td>
<td>operator 1</td>
<td>31/31</td>
<td>100.0</td>
<td>89.0 - 100.0</td>
</tr>
<tr>
<td></td>
<td>operator 2</td>
<td>30/30 a</td>
<td>100.0</td>
<td>88.7 - 100.0</td>
</tr>
<tr>
<td></td>
<td>operator 3</td>
<td>30/30</td>
<td>100.0</td>
<td>88.7 - 100.0</td>
</tr>
<tr>
<td></td>
<td>total</td>
<td>91/91</td>
<td>100.0</td>
<td>96.0 - 100.0</td>
</tr>
<tr>
<td><em>Proteus vulgaris</em> ATCC 29905</td>
<td>operator 1</td>
<td>30/30 a</td>
<td>100.0</td>
<td>88.7 - 100.0</td>
</tr>
<tr>
<td></td>
<td>operator 2</td>
<td>31/31</td>
<td>100.0</td>
<td>89.0 - 100.0</td>
</tr>
<tr>
<td></td>
<td>operator 3</td>
<td>30/30</td>
<td>100.0</td>
<td>88.7 - 100.0</td>
</tr>
<tr>
<td></td>
<td>total</td>
<td>91/91</td>
<td>100.0</td>
<td>96.0 - 100.0</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em> NCTC 12493</td>
<td>operator 1</td>
<td>31/31</td>
<td>100.0</td>
<td>89.0 - 100.0</td>
</tr>
<tr>
<td></td>
<td>operator 2</td>
<td>31/31</td>
<td>100.0</td>
<td>89.0 - 100.0</td>
</tr>
<tr>
<td></td>
<td>operator 3</td>
<td>30/30</td>
<td>100.0</td>
<td>88.7 - 100.0</td>
</tr>
<tr>
<td></td>
<td>total</td>
<td>92/92</td>
<td>100.0</td>
<td>96.0 - 100.0</td>
</tr>
<tr>
<td><em>mecA</em> NCTC 12493</td>
<td>operator 1</td>
<td>31/31</td>
<td>100.0</td>
<td>89.0 - 100.0</td>
</tr>
<tr>
<td></td>
<td>operator 2</td>
<td>30/30 a</td>
<td>100.0</td>
<td>88.7 - 100.0</td>
</tr>
<tr>
<td></td>
<td>operator 3</td>
<td>30/30</td>
<td>100.0</td>
<td>88.7 - 100.0</td>
</tr>
<tr>
<td></td>
<td>total</td>
<td>91/91</td>
<td>100.0</td>
<td>96.0 - 100.0</td>
</tr>
</tbody>
</table>

* Reduced number of available results due to invalid analyte results.

For three cartridge runs, unexpected positive results were reported with weak signals close to the assay thresholds on different test days and different operators/test systems (2x *E. coli*, for one ‘moderate’ and one ‘low’ test sample, 1x *oxa*-23, for one ‘moderate’ test sample).
Fresh-Frozen Study
Assay reproducibility between fresh samples and samples stored frozen was established with artificial samples (viable strains spiked in pooled native negative BAL specimens as test matrix) with the representative strain panel as described for the reproducibility study above. Testing was performed at a moderate concentration (2.5x - 10x LoD of the corresponding target analyte, at least 10 replicates per condition), at a low concentration (1x - 4x LoD of the corresponding target analyte, at least 30 replicates per condition) and with all target analytes negative (at least 10 replicates per condition).

Pair-wise tests with the LRT BAL Application were performed for samples tested within 2 hrs after test sample preparation (Time 0) and samples tested after freezing below -70 °C for at least 1 day and thawing immediately before testing.

Tables 14 to 16 summarize the fresh-frozen test results for each of the tested concentration levels (moderate, low, negative) for both storage conditions (tested freshly, tested frozen), along with the agreement rates with the expected result and 95% confidence intervals (95% CI, calculated using the Wilson score method).

Comparable agreement rates with the expected result were obtained for all test analytes for both test conditions.
### Table 14: Fresh-frozen study test results for concentration level ‘moderate’, approx. 5x LoD per test analyte.

<table>
<thead>
<tr>
<th>moderate</th>
<th>x-fold LoD</th>
<th>Test Condition</th>
<th>Agreement with Expected Result</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td># Pos. /# Exp.</td>
</tr>
<tr>
<td><strong>Acinetobacter baumannii</strong></td>
<td>5</td>
<td>fresh</td>
<td>11/11</td>
</tr>
<tr>
<td>ATCC 19606</td>
<td></td>
<td>frozen</td>
<td>11/11</td>
</tr>
<tr>
<td><strong>Chlamydia pneumoniae</strong></td>
<td>5</td>
<td>fresh</td>
<td>11/11</td>
</tr>
<tr>
<td>ATCC VR-2282</td>
<td></td>
<td>frozen</td>
<td>11/11</td>
</tr>
<tr>
<td><strong>Citrobacter freundii</strong></td>
<td>5</td>
<td>fresh</td>
<td>11/11</td>
</tr>
<tr>
<td>ATCC 8090</td>
<td></td>
<td>frozen</td>
<td>11/11</td>
</tr>
<tr>
<td><strong>Haemophilus influenzae</strong></td>
<td>5</td>
<td>fresh</td>
<td>10/11</td>
</tr>
<tr>
<td>ATCC 33391</td>
<td></td>
<td>frozen</td>
<td>11/11</td>
</tr>
<tr>
<td><strong>Klebsiella pneumoniae</strong></td>
<td>2.5</td>
<td>fresh</td>
<td>11/11</td>
</tr>
<tr>
<td>NCTC 13443</td>
<td></td>
<td>frozen</td>
<td>11/11</td>
</tr>
<tr>
<td><strong>ctx-M</strong></td>
<td>10</td>
<td>fresh</td>
<td>11/11</td>
</tr>
<tr>
<td>NCTC 13443</td>
<td></td>
<td>frozen</td>
<td>11/11</td>
</tr>
<tr>
<td><strong>ndm</strong></td>
<td>5</td>
<td>fresh</td>
<td>11/11</td>
</tr>
<tr>
<td>NCTC 13443</td>
<td></td>
<td>frozen</td>
<td>11/11</td>
</tr>
<tr>
<td><strong>tem</strong></td>
<td>5</td>
<td>fresh</td>
<td>10/11</td>
</tr>
<tr>
<td>NCTC 13443</td>
<td></td>
<td>frozen</td>
<td>11/11</td>
</tr>
<tr>
<td><strong>Morganella morganii</strong></td>
<td>5</td>
<td>fresh</td>
<td>11/11</td>
</tr>
<tr>
<td>ATCC 25830</td>
<td></td>
<td>frozen</td>
<td>11/11</td>
</tr>
<tr>
<td><strong>Proteus vulgaris</strong></td>
<td>5</td>
<td>fresh</td>
<td>11/11</td>
</tr>
<tr>
<td>ATCC 29905</td>
<td></td>
<td>frozen</td>
<td>11/11</td>
</tr>
<tr>
<td><strong>Staphylococcus aureus</strong></td>
<td>8.3</td>
<td>fresh</td>
<td>10/10 a</td>
</tr>
<tr>
<td>NCTC 12493</td>
<td></td>
<td>frozen</td>
<td>11/11</td>
</tr>
<tr>
<td><strong>mecA</strong></td>
<td>3</td>
<td>fresh</td>
<td>11/11</td>
</tr>
<tr>
<td>NCTC 12493</td>
<td></td>
<td>frozen</td>
<td>11/11</td>
</tr>
<tr>
<td><strong>total (all analytes)</strong></td>
<td></td>
<td><strong>fresh</strong></td>
<td>129/131</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>frozen</strong></td>
<td>132/132</td>
</tr>
</tbody>
</table>

*a Reduced number of available results due to invalid analyte results.*
Table 15: Fresh-frozen study test results for concentration level ‘low’, approx. 2x LoD per test analyte.

<table>
<thead>
<tr>
<th>low</th>
<th>x-fold LoD</th>
<th>Test Condition</th>
<th>Agreement with Expected Result</th>
<th># Pos. /# Exp.</th>
<th>%</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acinetobacter baumannii</td>
<td>2</td>
<td>fresh</td>
<td>31/32</td>
<td>96.9</td>
<td>84.3 - 99.4</td>
<td></td>
</tr>
<tr>
<td>ATCC 19606</td>
<td>2</td>
<td>frozen</td>
<td>31/31</td>
<td>100.0</td>
<td>89.0 - 100.0</td>
<td></td>
</tr>
<tr>
<td>Chlamydia pneumoniae</td>
<td>2</td>
<td>fresh</td>
<td>32/32</td>
<td>100.0</td>
<td>89.3 - 100.0</td>
<td></td>
</tr>
<tr>
<td>ATCC VR-2282</td>
<td>2</td>
<td>frozen</td>
<td>31/31</td>
<td>100.0</td>
<td>89.0 - 100.0</td>
<td></td>
</tr>
<tr>
<td>Citrobacter freundii</td>
<td>2</td>
<td>fresh</td>
<td>31/32</td>
<td>96.9</td>
<td>84.3 - 99.4</td>
<td></td>
</tr>
<tr>
<td>ATCC 8090</td>
<td>2</td>
<td>frozen</td>
<td>30/31</td>
<td>96.8</td>
<td>83.8 - 99.4</td>
<td></td>
</tr>
<tr>
<td>Haemophilus influenzae</td>
<td>2</td>
<td>fresh</td>
<td>29/31</td>
<td>93.5</td>
<td>79.3 - 98.2</td>
<td></td>
</tr>
<tr>
<td>ATCC 33391</td>
<td>2</td>
<td>frozen</td>
<td>28/30 a</td>
<td>93.3</td>
<td>78.7 - 98.2</td>
<td></td>
</tr>
<tr>
<td>Klebsiella pneumoniae</td>
<td>2</td>
<td>fresh</td>
<td>31/32</td>
<td>96.9</td>
<td>84.3 - 99.4</td>
<td></td>
</tr>
<tr>
<td>ATCC 13443</td>
<td>2</td>
<td>frozen</td>
<td>31/31</td>
<td>100.0</td>
<td>89.0 - 100.0</td>
<td></td>
</tr>
<tr>
<td>ctx-M</td>
<td>4</td>
<td>fresh</td>
<td>32/32</td>
<td>100.0</td>
<td>89.3 - 100.0</td>
<td></td>
</tr>
<tr>
<td>NCTC 13443</td>
<td>4</td>
<td>frozen</td>
<td>31/31</td>
<td>100.0</td>
<td>89.0 - 100.0</td>
<td></td>
</tr>
<tr>
<td>ndm</td>
<td>2</td>
<td>fresh</td>
<td>31/32</td>
<td>96.9</td>
<td>84.3 - 99.4</td>
<td></td>
</tr>
<tr>
<td>NCTC 13443</td>
<td>2</td>
<td>frozen</td>
<td>31/31</td>
<td>100.0</td>
<td>89.0 - 100.0</td>
<td></td>
</tr>
<tr>
<td>tem</td>
<td>2</td>
<td>fresh</td>
<td>30/31</td>
<td>96.8</td>
<td>83.8 - 99.4</td>
<td></td>
</tr>
<tr>
<td>NCTC 13443</td>
<td>2</td>
<td>frozen</td>
<td>29/30 a</td>
<td>96.7</td>
<td>83.3 - 99.4</td>
<td></td>
</tr>
<tr>
<td>Morganella morganii</td>
<td>2</td>
<td>fresh</td>
<td>32/32</td>
<td>100.0</td>
<td>89.3 - 100.0</td>
<td></td>
</tr>
<tr>
<td>ATCC 25830</td>
<td>2</td>
<td>frozen</td>
<td>31/31</td>
<td>100.0</td>
<td>89.0 - 100.0</td>
<td></td>
</tr>
<tr>
<td>Proteus vulgaris</td>
<td>2</td>
<td>fresh</td>
<td>32/32</td>
<td>100.0</td>
<td>89.3 - 100.0</td>
<td></td>
</tr>
<tr>
<td>ATCC 29905</td>
<td>2</td>
<td>frozen</td>
<td>30/31</td>
<td>96.8</td>
<td>83.8 - 99.4</td>
<td></td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>3</td>
<td>fresh</td>
<td>32/32</td>
<td>100.0</td>
<td>89.3 - 100.0</td>
<td></td>
</tr>
<tr>
<td>NCTC 12493</td>
<td>3</td>
<td>frozen</td>
<td>31/31</td>
<td>100.0</td>
<td>89.0 - 100.0</td>
<td></td>
</tr>
<tr>
<td>mecA</td>
<td>1.3</td>
<td>fresh</td>
<td>32/32</td>
<td>100.0</td>
<td>89.3 - 100.0</td>
<td></td>
</tr>
<tr>
<td>NCTC 12493</td>
<td>1.3</td>
<td>frozen</td>
<td>31/31</td>
<td>100.0</td>
<td>89.0 - 100.0</td>
<td></td>
</tr>
<tr>
<td>total (all analytes)</td>
<td></td>
<td>fresh</td>
<td>375/382</td>
<td>98.2</td>
<td>96.3 - 99.1</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>frozen</td>
<td>365/370</td>
<td>98.6</td>
<td>96.9 - 99.4</td>
<td></td>
</tr>
</tbody>
</table>

*a Reduced number of available results due to invalid analyte results.
**Table 16: Fresh-frozen study test results for samples negative for all analytes.**

<table>
<thead>
<tr>
<th>negative</th>
<th>Test Condition</th>
<th>Agreement with Expected Result</th>
<th># Neg./# Exp.</th>
<th>%</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Acinetobacter baumannii</em> ATCC 19606</td>
<td>fresh</td>
<td>10/10</td>
<td>100.0</td>
<td>72.3</td>
<td>- 100.0</td>
</tr>
<tr>
<td></td>
<td>frozen</td>
<td>11/11</td>
<td>100.0</td>
<td>74.1</td>
<td>- 100.0</td>
</tr>
<tr>
<td><em>Chlamydia pneumoniae</em> ATCC VR-2282</td>
<td>fresh</td>
<td>10/10</td>
<td>100.0</td>
<td>72.3</td>
<td>- 100.0</td>
</tr>
<tr>
<td></td>
<td>frozen</td>
<td>11/11</td>
<td>100.0</td>
<td>74.1</td>
<td>- 100.0</td>
</tr>
<tr>
<td><em>Citrobacter freundii</em> ATCC 8090</td>
<td>fresh</td>
<td>10/10</td>
<td>100.0</td>
<td>72.3</td>
<td>- 100.0</td>
</tr>
<tr>
<td></td>
<td>frozen</td>
<td>11/11</td>
<td>100.0</td>
<td>74.1</td>
<td>- 100.0</td>
</tr>
<tr>
<td><em>Haemophilus influenzae</em> ATCC 33391</td>
<td>fresh</td>
<td>10/10</td>
<td>100.0</td>
<td>72.3</td>
<td>- 100.0</td>
</tr>
<tr>
<td></td>
<td>frozen</td>
<td>11/11</td>
<td>100.0</td>
<td>74.1</td>
<td>- 100.0</td>
</tr>
<tr>
<td><em>Klebsiella pneumoniae</em> NCTC 13443</td>
<td>fresh</td>
<td>10/10</td>
<td>100.0</td>
<td>72.3</td>
<td>- 100.0</td>
</tr>
<tr>
<td></td>
<td>frozen</td>
<td>11/11</td>
<td>100.0</td>
<td>74.1</td>
<td>- 100.0</td>
</tr>
<tr>
<td><em>ctx-M</em> NCTC 13443</td>
<td>fresh</td>
<td>10/10</td>
<td>100.0</td>
<td>72.3</td>
<td>- 100.0</td>
</tr>
<tr>
<td></td>
<td>frozen</td>
<td>11/11</td>
<td>100.0</td>
<td>74.1</td>
<td>- 100.0</td>
</tr>
<tr>
<td><em>ndm</em> NCTC 13443</td>
<td>fresh</td>
<td>10/10</td>
<td>100.0</td>
<td>72.3</td>
<td>- 100.0</td>
</tr>
<tr>
<td></td>
<td>frozen</td>
<td>11/11</td>
<td>100.0</td>
<td>74.1</td>
<td>- 100.0</td>
</tr>
<tr>
<td><em>tem</em> NCTC 13443</td>
<td>fresh</td>
<td>10/10</td>
<td>100.0</td>
<td>72.3</td>
<td>- 100.0</td>
</tr>
<tr>
<td></td>
<td>frozen</td>
<td>11/11</td>
<td>100.0</td>
<td>74.1</td>
<td>- 100.0</td>
</tr>
<tr>
<td><em>Morganella morganii</em> ATCC 25830</td>
<td>fresh</td>
<td>10/10</td>
<td>100.0</td>
<td>72.3</td>
<td>- 100.0</td>
</tr>
<tr>
<td></td>
<td>frozen</td>
<td>11/11</td>
<td>100.0</td>
<td>74.1</td>
<td>- 100.0</td>
</tr>
<tr>
<td><em>Proteus vulgaris</em> ATCC 29905</td>
<td>fresh</td>
<td>10/10</td>
<td>100.0</td>
<td>72.3</td>
<td>- 100.0</td>
</tr>
<tr>
<td></td>
<td>frozen</td>
<td>11/11</td>
<td>100.0</td>
<td>74.1</td>
<td>- 100.0</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em> NCTC 12493</td>
<td>fresh</td>
<td>9/9 a</td>
<td>100.0</td>
<td>70.1</td>
<td>- 100.0</td>
</tr>
<tr>
<td></td>
<td>frozen</td>
<td>11/11</td>
<td>100.0</td>
<td>74.1</td>
<td>- 100.0</td>
</tr>
<tr>
<td><em>mecA</em> NCTC 12493</td>
<td>fresh</td>
<td>10/10</td>
<td>100.0</td>
<td>72.3</td>
<td>- 100.0</td>
</tr>
<tr>
<td></td>
<td>frozen</td>
<td>11/11</td>
<td>100.0</td>
<td>74.1</td>
<td>- 100.0</td>
</tr>
<tr>
<td><strong>total (all analytes)</strong></td>
<td>fresh</td>
<td>119/119</td>
<td>100.0</td>
<td>96.9</td>
<td>- 100.0</td>
</tr>
<tr>
<td></td>
<td>frozen</td>
<td>132/132</td>
<td>100.0</td>
<td>97.2</td>
<td>- 100.0</td>
</tr>
</tbody>
</table>

*a Reduced number of available results due to invalid analyte results.

**Sample Stability Study**

Assay reproducibility between fresh samples and samples stored refrigerated for at least 24 hrs was established with artificial samples using the same experimental approach as for the fresh-frozen study.

Pair-wise tests with the LRT BAL Application were performed for samples tested within 2 hrs after test sample preparation (Time 0) and samples tested after at total storage of at least 24 hrs including at least 2 hrs at a worst-case ambient temperature of 30 °C and at least 22 hrs stored in a refrigerator.

Tables 17 to 19 summarize the sample stability test results for each of the tested concentration levels (moderate, low, negative) for both test conditions (tested freshly, tested after storage), along with the agreement rates with the expected result and 95% confidence intervals (95% CI, calculated using the
Wilson score method). Comparable agreement rates with the expected result were obtained for all test analytes for both test conditions.

Table 17: Sample stability study test results for concentration level ‘moderate’, approx. 5x LoD per test analyte, and a storage time of at least 24 hrs.

<table>
<thead>
<tr>
<th>moderate</th>
<th>x-fold LoD</th>
<th>Test Condition</th>
<th>Agreement with Expected Result</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td># Pos. / # Exp.</td>
</tr>
<tr>
<td><em>Acinetobacter baumannii</em></td>
<td>5</td>
<td>fresh</td>
<td>10/10</td>
</tr>
<tr>
<td>ATCC 19606</td>
<td></td>
<td>24 hrs</td>
<td>11/11</td>
</tr>
<tr>
<td><em>Chlamydia pneumoniae</em></td>
<td>5</td>
<td>fresh</td>
<td>10/10</td>
</tr>
<tr>
<td>ATCC VR-2282</td>
<td></td>
<td>24 hrs</td>
<td>11/11</td>
</tr>
<tr>
<td><em>Citrobacter freundii</em></td>
<td>5</td>
<td>fresh</td>
<td>10/10</td>
</tr>
<tr>
<td>ATCC 8090</td>
<td></td>
<td>24 hrs</td>
<td>11/11</td>
</tr>
<tr>
<td><em>Haemophilus influenzae</em></td>
<td>5</td>
<td>fresh</td>
<td>10/10</td>
</tr>
<tr>
<td>ATCC 33391</td>
<td></td>
<td>24 hrs</td>
<td>11/11</td>
</tr>
<tr>
<td><em>Klebsiella pneumoniae</em></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ctx-M</td>
<td>10</td>
<td>fresh</td>
<td>10/10</td>
</tr>
<tr>
<td>NCTC 13443</td>
<td></td>
<td>24 hrs</td>
<td>11/11</td>
</tr>
<tr>
<td>ndm</td>
<td>5</td>
<td>fresh</td>
<td>9/10</td>
</tr>
<tr>
<td>NCTC 13443</td>
<td></td>
<td>24 hrs</td>
<td>11/11</td>
</tr>
<tr>
<td>tem</td>
<td>5</td>
<td>fresh</td>
<td>10/10</td>
</tr>
<tr>
<td>NCTC 13443</td>
<td></td>
<td>24 hrs</td>
<td>11/11</td>
</tr>
<tr>
<td><em>Morganella morganii</em></td>
<td>5</td>
<td>fresh</td>
<td>10/10</td>
</tr>
<tr>
<td>ATCC 25830</td>
<td></td>
<td>24 hrs</td>
<td>11/11</td>
</tr>
<tr>
<td><em>Proteus vulgaris</em></td>
<td>5</td>
<td>fresh</td>
<td>10/10</td>
</tr>
<tr>
<td>ATCC 29905</td>
<td></td>
<td>24 hrs</td>
<td>11/11</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>8.3</td>
<td>fresh</td>
<td>9/9 *</td>
</tr>
<tr>
<td>NCTC 12493</td>
<td></td>
<td>24 hrs</td>
<td>11/11</td>
</tr>
<tr>
<td><em>mecA</em></td>
<td>3</td>
<td>fresh</td>
<td>10/10</td>
</tr>
<tr>
<td>NCTC 12493</td>
<td></td>
<td>24 hrs</td>
<td>11/11</td>
</tr>
<tr>
<td>total (all analytes)</td>
<td></td>
<td></td>
<td>118/119</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>132/132</td>
</tr>
</tbody>
</table>

* Reduced number of available results due to invalid analyte results.
Table 18: Sample stability study test results for concentration level ‘low’, approx. 2x LoD per test analyte, and a storage time of at least 24 hrs.

<table>
<thead>
<tr>
<th>Low</th>
<th>x-fold LoD</th>
<th>Test Condition</th>
<th>Agreement with Expected Result</th>
<th># Pos. /# Exp.</th>
<th>%</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acinetobacter baumannii</td>
<td>2</td>
<td>fresh</td>
<td>31/32</td>
<td>96.9</td>
<td>84.3 - 99.4</td>
<td></td>
</tr>
<tr>
<td>ATCC 19606</td>
<td></td>
<td>24 hrs</td>
<td>31/32</td>
<td>96.9</td>
<td>84.3 - 99.4</td>
<td></td>
</tr>
<tr>
<td>Chlamydia pneumoniae</td>
<td>2</td>
<td>fresh</td>
<td>32/32</td>
<td>100.0</td>
<td>89.3 - 100.0</td>
<td></td>
</tr>
<tr>
<td>ATCC VR-2282</td>
<td></td>
<td>24 hrs</td>
<td>32/32</td>
<td>100.0</td>
<td>89.3 - 100.0</td>
<td></td>
</tr>
<tr>
<td>Citrobacter freundii</td>
<td>2</td>
<td>fresh</td>
<td>31/32</td>
<td>96.9</td>
<td>84.3 - 99.4</td>
<td></td>
</tr>
<tr>
<td>ATCC 8090</td>
<td></td>
<td>24 hrs</td>
<td>29/32</td>
<td>90.6</td>
<td>75.8 - 96.8</td>
<td></td>
</tr>
<tr>
<td>Haemophilus influenzae</td>
<td>2</td>
<td>fresh</td>
<td>29/31</td>
<td>93.5</td>
<td>79.3 - 98.2</td>
<td></td>
</tr>
<tr>
<td>ATCC 33391</td>
<td></td>
<td>24 hrs</td>
<td>31/31&lt;sup&gt;a&lt;/sup&gt;</td>
<td>100.0</td>
<td>89.0 - 100.0</td>
<td></td>
</tr>
<tr>
<td>Klebsiella pneumoniae</td>
<td>1</td>
<td>fresh</td>
<td>31/32</td>
<td>96.9</td>
<td>84.3 - 99.4</td>
<td></td>
</tr>
<tr>
<td>NCTC 13443</td>
<td></td>
<td>24 hrs</td>
<td>32/32</td>
<td>100.0</td>
<td>89.3 - 100.0</td>
<td></td>
</tr>
<tr>
<td>ctx-M</td>
<td>4</td>
<td>fresh</td>
<td>32/32</td>
<td>100.0</td>
<td>89.3 - 100.0</td>
<td></td>
</tr>
<tr>
<td>NCTC 13443</td>
<td></td>
<td>24 hrs</td>
<td>32/32</td>
<td>100.0</td>
<td>89.3 - 100.0</td>
<td></td>
</tr>
<tr>
<td>ndm</td>
<td>2</td>
<td>fresh</td>
<td>31/32</td>
<td>96.9</td>
<td>84.3 - 99.4</td>
<td></td>
</tr>
<tr>
<td>NCTC 13443</td>
<td></td>
<td>24 hrs</td>
<td>31/32</td>
<td>96.9</td>
<td>84.3 - 99.4</td>
<td></td>
</tr>
<tr>
<td>tem</td>
<td>2</td>
<td>fresh</td>
<td>30/31</td>
<td>96.8</td>
<td>83.8 - 99.4</td>
<td></td>
</tr>
<tr>
<td>NCTC 13443</td>
<td></td>
<td>24 hrs</td>
<td>30/31&lt;sup&gt;a&lt;/sup&gt;</td>
<td>96.8</td>
<td>83.8 - 99.4</td>
<td></td>
</tr>
<tr>
<td>Morganella morganii</td>
<td>2</td>
<td>fresh</td>
<td>32/32</td>
<td>100.0</td>
<td>89.3 - 100.0</td>
<td></td>
</tr>
<tr>
<td>ATCC 25830</td>
<td></td>
<td>24 hrs</td>
<td>31/32</td>
<td>96.9</td>
<td>84.3 - 99.4</td>
<td></td>
</tr>
<tr>
<td>Proteus vulgaris</td>
<td>2</td>
<td>fresh</td>
<td>32/32</td>
<td>100.0</td>
<td>89.3 - 100.0</td>
<td></td>
</tr>
<tr>
<td>ATCC 29905</td>
<td></td>
<td>24 hrs</td>
<td>30/30</td>
<td>100.0</td>
<td>88.7 - 100.0</td>
<td></td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>3</td>
<td>fresh</td>
<td>32/32</td>
<td>100.0</td>
<td>89.3 - 100.0</td>
<td></td>
</tr>
<tr>
<td>NCTC 12493</td>
<td></td>
<td>24 hrs</td>
<td>32/32</td>
<td>100.0</td>
<td>89.3 - 100.0</td>
<td></td>
</tr>
<tr>
<td>mecA</td>
<td>1,3</td>
<td>fresh</td>
<td>32/32</td>
<td>100.0</td>
<td>89.3 - 100.0</td>
<td></td>
</tr>
<tr>
<td>NCTC 12493</td>
<td></td>
<td>24 hrs</td>
<td>32/32</td>
<td>100.0</td>
<td>89.3 - 100.0</td>
<td></td>
</tr>
<tr>
<td>total (all analytes)</td>
<td>fresh</td>
<td>375/382</td>
<td>98.2</td>
<td>96.3 - 99.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>24 hrs</td>
<td>373/380</td>
<td>98.2</td>
<td>96.2 - 99.1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> Reduced number of available results due to invalid analyte results.
### Table 19: Sample stability study test results for samples negative for all analytes for a total storage time of at least 24 hrs.

<table>
<thead>
<tr>
<th>negative</th>
<th>Test Condition</th>
<th>Agreement with Expected Result</th>
<th># Neg./# Exp.</th>
<th>%</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acinetobacter baumannii</td>
<td>fresh</td>
<td>11/11</td>
<td>100.0</td>
<td>74.1 - 100.0</td>
<td></td>
</tr>
<tr>
<td>ATCC 19606</td>
<td>24 hrs</td>
<td>11/11</td>
<td>100.0</td>
<td>74.1 - 100.0</td>
<td></td>
</tr>
<tr>
<td>Chlamydia pneumoniae</td>
<td>fresh</td>
<td>11/11</td>
<td>100.0</td>
<td>74.1 - 100.0</td>
<td></td>
</tr>
<tr>
<td>ATCC VR-2282</td>
<td>24 hrs</td>
<td>11/11</td>
<td>100.0</td>
<td>74.1 - 100.0</td>
<td></td>
</tr>
<tr>
<td>Citrobacter freundii</td>
<td>fresh</td>
<td>11/11</td>
<td>100.0</td>
<td>74.1 - 100.0</td>
<td></td>
</tr>
<tr>
<td>ATCC 8090</td>
<td>24 hrs</td>
<td>11/11</td>
<td>100.0</td>
<td>74.1 - 100.0</td>
<td></td>
</tr>
<tr>
<td>Haemophilus influenzae</td>
<td>fresh</td>
<td>11/11</td>
<td>100.0</td>
<td>74.1 - 100.0</td>
<td></td>
</tr>
<tr>
<td>ATCC 33391</td>
<td>24 hrs</td>
<td>11/11</td>
<td>100.0</td>
<td>74.1 - 100.0</td>
<td></td>
</tr>
<tr>
<td>Klebsiella pneumoniae</td>
<td>fresh</td>
<td>11/11</td>
<td>100.0</td>
<td>74.1 - 100.0</td>
<td></td>
</tr>
<tr>
<td>NCTC 13443</td>
<td>24 hrs</td>
<td>11/11</td>
<td>100.0</td>
<td>74.1 - 100.0</td>
<td></td>
</tr>
<tr>
<td>ctx-M</td>
<td>fresh</td>
<td>10/10 *</td>
<td>100.0</td>
<td>72.3 - 100.0</td>
<td></td>
</tr>
<tr>
<td>NCTC 13443</td>
<td>24 hrs</td>
<td>11/11</td>
<td>100.0</td>
<td>74.1 - 100.0</td>
<td></td>
</tr>
<tr>
<td>ndm</td>
<td>fresh</td>
<td>11/11</td>
<td>100.0</td>
<td>74.1 - 100.0</td>
<td></td>
</tr>
<tr>
<td>NCTC 13443</td>
<td>24 hrs</td>
<td>11/11</td>
<td>100.0</td>
<td>74.1 - 100.0</td>
<td></td>
</tr>
<tr>
<td>tem</td>
<td>fresh</td>
<td>11/11</td>
<td>100.0</td>
<td>74.1 - 100.0</td>
<td></td>
</tr>
<tr>
<td>NCTC 13443</td>
<td>24 hrs</td>
<td>11/11</td>
<td>100.0</td>
<td>74.1 - 100.0</td>
<td></td>
</tr>
<tr>
<td>Morganella morganii</td>
<td>fresh</td>
<td>10/10 *</td>
<td>100.0</td>
<td>72.3 - 100.0</td>
<td></td>
</tr>
<tr>
<td>ATCC 25830</td>
<td>24 hrs</td>
<td>11/11</td>
<td>100.0</td>
<td>74.1 - 100.0</td>
<td></td>
</tr>
<tr>
<td>Proteus vulgaris</td>
<td>fresh</td>
<td>11/11</td>
<td>100.0</td>
<td>74.1 - 100.0</td>
<td></td>
</tr>
<tr>
<td>ATCC 29905</td>
<td>24 hrs</td>
<td>11/11</td>
<td>100.0</td>
<td>74.1 - 100.0</td>
<td></td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>fresh</td>
<td>11/11</td>
<td>100.0</td>
<td>74.1 - 100.0</td>
<td></td>
</tr>
<tr>
<td>NCTC 12493</td>
<td>24 hrs</td>
<td>11/11</td>
<td>100.0</td>
<td>74.1 - 100.0</td>
<td></td>
</tr>
<tr>
<td>mecA</td>
<td>fresh</td>
<td>11/11</td>
<td>100.0</td>
<td>74.1 - 100.0</td>
<td></td>
</tr>
<tr>
<td>NCTC 12493</td>
<td>24 hrs</td>
<td>11/11</td>
<td>100.0</td>
<td>74.1 - 100.0</td>
<td></td>
</tr>
<tr>
<td>total (all analytes)</td>
<td>fresh</td>
<td>130/130</td>
<td>100.0</td>
<td>97.1 - 100.0</td>
<td></td>
</tr>
<tr>
<td>24 hrs</td>
<td>132/132</td>
<td>100.0</td>
<td>97.2 - 100.0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
807.92 (b)(2): Brief Description of Clinical Data

Introduction
Clinical performance of the LRT BAL Application was established by a prospective study cohort using 1,016 lavage specimens that had been collected at nine US clinical sites from hospitalized patients suspected for lower respiratory infections, by an archived study comprising 392 confirmed positive lavage specimens predominantly collected at US clinical sites, as well as by a contrived study using artificial positive samples to augment for rare LRT BAL panel analytes.

Performance characteristics of LRT BAL antibiotic resistance markers was evaluated for the prospective study cohort. Furthermore, antibiotic resistance markers detected by LRT BAL were correlated to resistance phenotypes of corresponding strain isolates using antimicrobial susceptibility test (AST) results collected for the prospective and archived study cohorts. Finally, rare antibiotic resistance markers were also included for contrived study testing.

A. Prospective Study with Frozen Specimens

Specimen Cohort: Inclusion/Exclusion Criteria, Demographics
BAL and mini-BAL specimens from hospitalized patients, age 18 or older, suspected of a lower respiratory infection, were eligible for the prospective study. Specimens had been collected at nine US clinical sites between June 2015 and July 2016 for a previous clinical study. Specimens were stored frozen within 24 hrs after arrival of the specimen in the lab.

Demographic information for prospective specimens included into the LRT BAL prospective study is described in Table 20.

Table 20: Demographic patient data for the LRT BAL prospective study.

<table>
<thead>
<tr>
<th>Included Specimens</th>
<th>1,016</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>male</td>
<td>598</td>
</tr>
<tr>
<td>female</td>
<td>418</td>
</tr>
<tr>
<td>Age</td>
<td></td>
</tr>
<tr>
<td>18 - 30 years</td>
<td>69</td>
</tr>
<tr>
<td>31 - 60 years</td>
<td>367</td>
</tr>
<tr>
<td>&gt; 60 years</td>
<td>580</td>
</tr>
<tr>
<td>Clinical Setting</td>
<td></td>
</tr>
<tr>
<td>ICU</td>
<td>505</td>
</tr>
<tr>
<td>ward</td>
<td>511</td>
</tr>
</tbody>
</table>
Reference Methods – Microorganisms

For ‘typical’ microorganisms, LRT BAL Application results were compared to standard-of-care (SoC) culture results as the reference. SoC culture results had been reported either qualitatively or quantitatively. For quantitative cultures, a reporting threshold of $10^3$ CFU/mL or higher for mini-BAL specimens and of $10^4$ CFU/mL or higher for BAL specimens was applied, following recommendations by the Infectious Diseases Society of America (IDSA) and the American Thoracic Society (ATS). For ‘atypical’ microorganisms *Chlamydia pneumoniae*, *Mycoplasma pneumoniae*, *Legionella pneumophila* and *Pneumocystis jirovecii*, no common SoC reference test was performed. Instead, SoC testing had only been performed on special request by the physician for a limited subset of patients.

In addition, LRT BAL Application results for ‘typical’ microorganisms were compared to a composite comparator as a second reference method. This composite comparator consists of the results of SoC culture combined with a molecular multiplex PCR comparator assay for which all positive PCR results were followed by bi-directional sequencing. For the composite comparator, any specimen that was positive by either SoC culture and/or positive by PCR and bi-directional sequencing was considered positive for the respective microorganism. Any specimen that was negative for both SoC culture and PCR was considered negative (Table 21A). Validated comparator PCR assays with analytical sensitivities in a similar range to the corresponding LRT BAL assays were included into the multiplex PCR comparator assay. These primers target different genetic loci than those used for the LRT BAL Application.

For ‘atypical’ microorganisms, a combination of two different validated PCR comparator assays was used as composite comparator, each targeting different genetic loci compared to the corresponding LRT BAL assays. As shown in Table 21B, specimens that were positive for either of the PCR/sequencing comparator assays were considered positive and specimens that were negative for both PCR/sequencing assays were considered negative.
Table 21: Result determination algorithms for the composite comparator: (A) for ‘typical’ microorganisms, (B) for ‘atypical’ microorganisms.

<table>
<thead>
<tr>
<th>Comparator 1: SoC (culture)</th>
<th>Comparator 2: PCR assay (included in multiplex PCR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>positive result</td>
<td>positive result</td>
</tr>
<tr>
<td>negative result</td>
<td>negative result</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Comparator 1: PCR assay 1 (included in multiplex PCR)</th>
<th>Comparator 2: PCR assay 2 (included in multiplex PCR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>positive result</td>
<td>positive result</td>
</tr>
<tr>
<td>negative result</td>
<td>negative result</td>
</tr>
</tbody>
</table>

Reference Methods – Antibiotic Resistance Markers
PCR assays corresponding to each LRT BAL antibiotic resistance marker assay were included into the multiplex PCR comparator assay as a (single) molecular reference. Positive PCRs were followed by bi-directional sequencing.

Cultured isolates had been collected for positive prospective specimens whenever possible. Isolates were regrown and evaluated by MALDI-TOF to confirm strain identities and by whole genome sequencing using a next generation sequencing (NGS) approach to screen for presence or absence of LRT BAL panel antibiotic resistance markers. A few isolates that failed to grow were evaluated by PCR/bi-directional sequencing from frozen isolate stocks to confirm identity and to screen for presence or absence of such markers.

Phenotypic AST results for positive specimens as reported by SoC culture were collected to correlate antibiotic resistance markers detected by the LRT BAL Application to resistance phenotypes.

Discrepant Result Analysis
False positive discrepant results were analyzed by performing singleplex PCRs/bi-directional sequencing using primer pairs targeting different genetic loci compared to the corresponding LRT BAL assays on specimen DNA extracts for each discrepant LRT BAL analyte.

Microorganism Results – Comparison to SoC Culture Reference, PPA/NPA
For the prospective clinical study cohort, 1,016 previously collected specimens were tested with the LRT BAL Application. For ‘typical’ microorganisms, LRT BAL results were compared to the SoC culture result as reference (Table 22) to determine true positives (TP), false negatives (FN), false
positives (FP) and true negatives (TN), as well as positive percent agreements (PPA, TP / (TP + FN)), negative percent agreements (NPA, TN / (TN + FP)), positive predictive values (PPV, TP / (TP + FP)) and negative predictive values (NPV, TN / (TN + FN)), calculated together with their two-sided 95% confidence intervals (95% CI), determined according to the Wilson score method.

Table 22: Prospective study (N = 1,016 specimens *), comparison to SoC microbiology culture results.

<table>
<thead>
<tr>
<th></th>
<th>TP</th>
<th>FN</th>
<th>FP e d</th>
<th>TN</th>
<th>PPA [ %] (95% CI)</th>
<th>NPA [ %] (95% CI)</th>
<th>PPV [ %] (95% CI)</th>
<th>NPV [ %] (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Acinetobacter spp.</em></td>
<td>10</td>
<td>1</td>
<td>11</td>
<td>993</td>
<td>90.9 (62.3 - 98.4)</td>
<td>98.9 (98.0 - 99.4)</td>
<td>47.6 (28.3 - 67.6)</td>
<td>99.9 (99.4 - 100.0)</td>
</tr>
<tr>
<td><em>Citrobacter freundii</em></td>
<td>1</td>
<td>0</td>
<td>3</td>
<td>1,011</td>
<td>100.0 (20.7 - 100.0)</td>
<td>99.7 (99.1 - 99.9)</td>
<td>25.0 (4.6 - 69.9)</td>
<td>100.0 (99.6 - 100.0)</td>
</tr>
<tr>
<td><em>Enterobacter cloacae complex</em></td>
<td>13</td>
<td>4 e</td>
<td>7</td>
<td>991</td>
<td>76.5 (52.7 - 90.4)</td>
<td>99.3 (98.6 - 99.7)</td>
<td>65.0 (43.3 - 81.9)</td>
<td>99.9 (99.0 - 99.8)</td>
</tr>
<tr>
<td><em>Escherichia coli</em></td>
<td>17</td>
<td>1</td>
<td>30</td>
<td>968</td>
<td>94.4 (74.2 - 99.0)</td>
<td>97.0 (95.7 - 97.9)</td>
<td>36.2 (24.0 - 50.5)</td>
<td>99.9 (99.4 - 100.0)</td>
</tr>
<tr>
<td><em>Haemophilus influenzae</em></td>
<td>8</td>
<td>1</td>
<td>48</td>
<td>958</td>
<td>88.9 (56.5 - 98.0)</td>
<td>95.2 (93.7 - 96.4)</td>
<td>14.3 (7.4 - 25.7)</td>
<td>99.9 (99.4 - 100.0)</td>
</tr>
<tr>
<td><em>Klebsiella oxytoca</em></td>
<td>6</td>
<td>1</td>
<td>8</td>
<td>1,001</td>
<td>85.7 (48.7 - 97.4)</td>
<td>99.2 (98.4 - 99.6)</td>
<td>42.9 (21.4 - 67.4)</td>
<td>99.9 (99.4 - 100.0)</td>
</tr>
<tr>
<td><em>Klebsiella pneumoniae</em> b</td>
<td>20</td>
<td>4 f</td>
<td>10</td>
<td>982</td>
<td>83.3 (64.1 - 93.3)</td>
<td>99.0 (98.2 - 99.5)</td>
<td>66.7 (48.8 - 80.8)</td>
<td>99.6 (99.0 - 99.8)</td>
</tr>
<tr>
<td><em>Klebsiella variicola</em> b</td>
<td>0</td>
<td>2</td>
<td>2</td>
<td>1,012</td>
<td>0.0 (0.0 - 65.8)</td>
<td>99.8 (99.3 - 99.9)</td>
<td>0.0 (0.0 - 65.8)</td>
<td>99.8 (99.3 - 99.9)</td>
</tr>
<tr>
<td><em>Moraxella catarrhalis</em></td>
<td>2</td>
<td>0</td>
<td>13</td>
<td>997</td>
<td>100.0 (34.2 - 100.0)</td>
<td>98.7 (97.8 - 99.2)</td>
<td>13.3 (3.7 - 37.9)</td>
<td>100.0 (99.6 - 100.0)</td>
</tr>
<tr>
<td><em>Morganella morganii</em></td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>1,009</td>
<td>NA</td>
<td>99.7 (99.1 - 99.9)</td>
<td>0.0 (0.0 - 56.1)</td>
<td>100.0 (99.6 - 100.0)</td>
</tr>
<tr>
<td><em>Proteus spp.</em></td>
<td>4</td>
<td>0</td>
<td>6</td>
<td>1,006</td>
<td>100.0 (51.0 - 100.0)</td>
<td>99.4 (98.7 - 99.7)</td>
<td>40.0 (16.8 - 68.7)</td>
<td>100.0 (99.6 - 100.0)</td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>69</td>
<td>3</td>
<td>43</td>
<td>900</td>
<td>95.8 (88.5 - 98.6)</td>
<td>95.4 (93.9 - 96.6)</td>
<td>61.6 (52.4 - 70.1)</td>
<td>99.7 (99.0 - 99.9)</td>
</tr>
<tr>
<td><em>Serratia marcescens</em></td>
<td>12</td>
<td>0</td>
<td>5</td>
<td>998</td>
<td>100.0 (75.8 - 100.0)</td>
<td>99.5 (98.8 - 99.8)</td>
<td>70.6 (46.9 - 86.7)</td>
<td>100.0 (99.6 - 100.0)</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>63</td>
<td>8</td>
<td>41</td>
<td>904</td>
<td>88.7 (79.3 - 94.2)</td>
<td>95.7 (94.2 - 96.8)</td>
<td>60.6 (51.0 - 69.4)</td>
<td>99.1 (98.3 - 99.6)</td>
</tr>
<tr>
<td><em>Stenotrophomonas maltophilia</em></td>
<td>19</td>
<td>2</td>
<td>22</td>
<td>972</td>
<td>90.5 (71.1 - 97.4)</td>
<td>97.8 (96.7 - 98.5)</td>
<td>46.3 (32.1 - 61.3)</td>
<td>99.8 (99.3 - 99.9)</td>
</tr>
<tr>
<td><em>Streptococcus pneumoniae</em></td>
<td>3</td>
<td>0</td>
<td>10</td>
<td>1,003</td>
<td>100.0 (43.9 - 100.0)</td>
<td>99.0 (98.2 - 99.5)</td>
<td>23.1 (8.2 - 50.3)</td>
<td>100.0 (99.6 - 100.0)</td>
</tr>
</tbody>
</table>

*Observed invalid LRT BAL analyte results: *Acinetobacter spp.* (1), *C. freundii* (1), *E. cloacae complex* (1), *H. influenzae* (1), *M. catarrhalis* (4), *M. morganii* (4), *P. aeruginosa* (1), *S. marcescens* (1) and *S. maltophilia* (1). *K. variicola* is typically reported by culture as *K. pneumoniae*. To discriminate *K. variicola* from *K. pneumoniae*, *K. pneumoniae* strain isolates were sequenced. For a few cases, for which no isolates were provided, sequencing was performed from specimen DNA extracts instead. Two of 26 cases were identified as *K. variicola* and confirmed by both isolate and DNA extract sequencing. Results for *K. pneumoniae* and *K. variicola* performance are calculated based on the species identified by sequencing. *Note that many of the FP detections are confirmed when comparing against the composite comparator reference that includes molecular reference assays (see section ‘Comparison to Composite Comparator Reference’). Specimens with false positive LRT BAL results were analyzed with molecular assays (PCR/bi-directional sequencing) using specimen DNA extracts for presence or absence of the corresponding microorganism: presence was confirmed in 11 of 11 cases for *Acinetobacter spp.*, 3 of 3 cases for *C. freundii*, 7 of 7 cases for *E. cloacae complex*, 18 of 30 cases for *E. coli*, 42 of 48 cases for *H. influenzae*, 7 of 8 cases for *K. oxytoca*, 5 of 10 cases for *K. pneumoniae*, 2 of 2 cases for *K. variicola*, 13 of 13 cases for *M. catarrhalis*, 3 of 3 cases for *M. morganii*, 6 of 6 cases for *Proteus spp.*, 41 of 43 cases for *P. aeruginosa*, 4 of 5 cases for *S. marcescens*, 31 of 41 cases for *S. aureus*, 21 of 22 cases for *S. maltophilia*, and 10 of 10 cases for *S. pneumoniae*. For cases that were not confirmed for *H. influenzae*, sequencing...
results identified *H. haemolyticus* (3x), *H. parainfluenzae* (1x) and *Aggregatibacter aphrophilus* (1x). For all other cases, PCRs did not amplify sufficient amounts for sequencing.

Two of the four specimens that were FN for *E. cloacae* complex contained multiple host microorganisms identified by culture, and/or LRT BAL. For one specimen, *Acinetobacter* spp. was additionally reported by both LRT BAL and culture. For the other specimen, *S. maltophilia* was additionally reported by LRT BAL only.

Two of the four specimens that were FN for *K. pneumoniae* contained multiple host microorganisms identified by culture and/or the molecular reference testing. For one FN specimen, *P. aeruginosa* was additionally reported by both LRT BAL and culture. For the other specimen, *E. cloacae* complex was additionally reported by both LRT BAL and culture and *S. maltophilia* was additionally reported by LRT BAL only.

As no common SoC reference method was performed for the ‘atypical’ microorganisms reported by the LRT BAL panel, Table 23 lists positive and negative detections by the LRT BAL Application, compared to the subset of cases for which a SoC test was performed on special request by the physician. For *C. pneumoniae*, only one SoC test with a negative result was performed. For the three other ‘atypical’ microorganisms, the following PPA/NPA estimates when compared against SoC tests were observed: *L. pneumophila* PPA 0/1 (0%), NPA 237/237 (100%); *M. pneumoniae* PPA 0/0, NPA 28/28 (100%); *P. jirovecii* PPA 5/5 (100%), NPA 99/100 (99%).

Table 23: Summary of LRT BAL results for 'atypical' microorganisms for the prospective study.

<table>
<thead>
<tr>
<th>Soc Test (tested on request only)</th>
<th>LRT BAL result</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>positive</td>
</tr>
<tr>
<td><strong>Chlamydia pneumoniae</strong></td>
<td></td>
</tr>
<tr>
<td>not tested</td>
<td>1,015 (99.9%)</td>
</tr>
<tr>
<td>tested</td>
<td>1 (0.1%)</td>
</tr>
<tr>
<td>positive result</td>
<td>0</td>
</tr>
<tr>
<td>negative result</td>
<td>1</td>
</tr>
<tr>
<td><strong>Legionella pneumophila</strong></td>
<td></td>
</tr>
<tr>
<td>not tested</td>
<td>778 (76.6%)</td>
</tr>
<tr>
<td>tested</td>
<td>238 (23.4%)</td>
</tr>
<tr>
<td>positive result</td>
<td>1</td>
</tr>
<tr>
<td>negative result</td>
<td>237</td>
</tr>
<tr>
<td><strong>Mycoplasma pneumoniae</strong></td>
<td></td>
</tr>
<tr>
<td>not tested</td>
<td>988 (97.2%)</td>
</tr>
<tr>
<td>tested</td>
<td>28 (2.8%)</td>
</tr>
<tr>
<td>positive result</td>
<td>0</td>
</tr>
<tr>
<td>negative result</td>
<td>28</td>
</tr>
<tr>
<td><strong>Pneumocystis jirovecii</strong></td>
<td></td>
</tr>
<tr>
<td>not tested</td>
<td>911 (89.7%)</td>
</tr>
<tr>
<td>tested&lt;sup&gt;c&lt;/sup&gt;</td>
<td>105 (10.3%)</td>
</tr>
<tr>
<td>positive result</td>
<td>5</td>
</tr>
<tr>
<td>negative result</td>
<td>100</td>
</tr>
</tbody>
</table>

<sup>a</sup> Reduced number of available LRT BAL results due to one invalid analyte result.

<sup>b</sup> *L. pneumophila* was only reported positive by culture after 13 days.

<sup>c</sup> Applied *Pneumocystis* SoC methods for 105 specimens were DFA (63 specimens), IFA (29 specimens), and PCR (13 specimens).

<sup>d</sup> Positive by DFA (three specimens) or IFA (two specimens).

<sup>e</sup> Negative by DFA, confirmed positive by molecular reference tests.
Microorganisms - Stratification by Qualitative and Quantitative Culture Result

For all prospective specimens with positive culture results, true positive and false negative LRT BAL results were stratified by the semi-quantitative result reported by qualitative SoC culture (categories: rare, few, moderate, numerous) or by quantitative SoC culture (categories: 10^3 - < 10^4, 10^4 - < 10^5, 10^5 - < 10^6, > 10^6, in CFU/mL) as shown in Table 24.

Table 24: Prospective study, comparison to SoC culture, stratification by qualitative or quantitative culture result.

<table>
<thead>
<tr>
<th>Microorganism</th>
<th>Qualitative Culture Result</th>
<th>Quantitative Culture Result</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Category</td>
<td>Total</td>
</tr>
<tr>
<td>Acinetobacter spp.</td>
<td>rare</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>few</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>moderate</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>numerous</td>
<td>1</td>
</tr>
<tr>
<td>Citrobacter freundii</td>
<td>rare</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>few</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>moderate</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>numerous</td>
<td>0</td>
</tr>
<tr>
<td>Enterobacter cloacae</td>
<td>rare</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>few</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>moderate</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>numerous</td>
<td>1</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>rare</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>few</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>moderate</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>numerous</td>
<td>3</td>
</tr>
<tr>
<td>Haemophilus influenzae</td>
<td>rare</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>few</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>moderate</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>numerous</td>
<td>0</td>
</tr>
<tr>
<td>Klebsiella oxytoca</td>
<td>rare</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>few</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>moderate</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>numerous</td>
<td>1</td>
</tr>
<tr>
<td>Klebsiella pneumoniae</td>
<td>rare</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>few</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>moderate</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>numerous</td>
<td>1</td>
</tr>
<tr>
<td>Klebsiella varicola</td>
<td>rare</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>few</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>moderate</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>numerous</td>
<td>2</td>
</tr>
<tr>
<td>Moraxella catarrhalis</td>
<td>rare</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>few</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>moderate</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>numerous</td>
<td>0</td>
</tr>
<tr>
<td>Morganella morganii</td>
<td>rare</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>few</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>moderate</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>numerous</td>
<td>0</td>
</tr>
<tr>
<td>Proteus spp.</td>
<td>rare</td>
<td>0</td>
</tr>
<tr>
<td>Qualitative Culture Result</td>
<td>Quantitative Culture Result</td>
<td></td>
</tr>
<tr>
<td>----------------------------</td>
<td>----------------------------</td>
<td></td>
</tr>
<tr>
<td>Category</td>
<td>Total</td>
<td>TP</td>
</tr>
<tr>
<td>few</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>moderate</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>numerous</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Pseudomonas aeruginosa</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>rare</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>moderate</td>
<td>16</td>
<td>16</td>
</tr>
<tr>
<td>numerous</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td><strong>Serratia marcescens</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>rare</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>few</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>moderate</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>numerous</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Staphylococcus aureus</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>rare</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>few</td>
<td>11</td>
<td>10</td>
</tr>
<tr>
<td>moderate</td>
<td>11</td>
<td>10</td>
</tr>
<tr>
<td>numerous</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td><strong>Stenotrophomonas maltophilia</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>rare</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>few</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>moderate</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>numerous</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td><strong>Streptococcus pneumoniae</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>rare</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>few</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>moderate</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>numerous</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

^ One *P. aeruginosa* and one *S. aureus* case were reported positive by SoC culture without any qualitative or quantitative information, and were therefore not included in this table.
Microorganism Results – Comparison to SoC Culture Reference, Concordance Rates for the Prospective Study

For 212 specimens, at least one LRT BAL panel microorganism was reported by both the LRT BAL Application and SoC; for 21 specimens, a positive SoC result was missed by LRT BAL. For 632 specimens, both the LRT BAL Application and SoC reported a negative result (no growth or normal/mixed flora result). For 151 specimens, the LRT BAL Application reported a positive result while SoC was negative. For 65 of these 151 specimens, SoC reported normal/mixed flora, while for 81 of 151 specimens, no growth was reported (Table 25).

Table 25: Comparison of positive and negative SoC results to LRT BAL.

<table>
<thead>
<tr>
<th>LRT BAL Result</th>
<th>Positive SoC Result (N = 233)</th>
<th>Negative SoC Results (N = 783)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Microorganism(s) Reported</td>
<td>No Growth</td>
<td>Normal/Mixed Flora</td>
</tr>
<tr>
<td>any positive (N = 363)</td>
<td>212</td>
<td>81</td>
</tr>
<tr>
<td>all negative (N = 653)</td>
<td>21</td>
<td>358</td>
</tr>
</tbody>
</table>

* Presence or absence of flora not reported.

For 1,016 prospective specimens, the LRT BAL Application reported 363 specimens with at least one LRT BAL panel microorganism. For 113 specimens, multi-detections with two or more LRT BAL panel microorganisms were reported. SoC culture reported 233 specimens with at least one LRT BAL panel microorganism. For 40 specimens, multi-detections with two or more LRT BAL panel microorganisms were reported (Table 26).

Table 26: Numbers of detected LRT BAL panel microorganisms as reported by LRT BAL or SoC.

<table>
<thead>
<tr>
<th>Number of Detected Microorganisms</th>
<th>LRT BAL</th>
<th>SoC</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td># specimens [%]</td>
<td># specimens [%]</td>
</tr>
<tr>
<td>0</td>
<td>653 [64.3]</td>
<td>783 [77.1]</td>
</tr>
<tr>
<td>any positive</td>
<td>363 [35.7]</td>
<td>233 [22.9]</td>
</tr>
<tr>
<td>1</td>
<td>250 [24.6]</td>
<td>194 [19.1]</td>
</tr>
<tr>
<td>2</td>
<td>78 [7.7]</td>
<td>31 [3.1]</td>
</tr>
<tr>
<td>3</td>
<td>19 [1.9]</td>
<td>5 [0.5]</td>
</tr>
<tr>
<td>4</td>
<td>7 [0.7]</td>
<td>3 [0.3]</td>
</tr>
<tr>
<td>5</td>
<td>7 [0.7]</td>
<td>0 [0.0]</td>
</tr>
<tr>
<td>6</td>
<td>2 [0.2]</td>
<td>0 [0.0]</td>
</tr>
</tbody>
</table>
Table 27 lists all LRT BAL results compared to SoC culture results stratified into the following categories:

category 1: concordant result for both LRT BAL and SoC
- category 1a: both negative,
- category 1b: both positive with a fully concordant result,

category 2: LRT BAL reported additional microorganisms compared to SoC
- category 2a: for specimens with a negative SoC result,
- category 2b: for specimens with a positive SoC result,

category 3: LRT BAL reported fewer microorganisms compared to SoC
- category 3a: for specimens with a negative LRT BAL result,
- category 3b: for specimens with a positive LRT BAL result,

category 4: LRT BAL and SoC report discordant results with different microorganisms
- category 4a: LRT BAL and SoC reportings share at least one concordant microorganism,
- category 4b: LRT BAL and SoC results are fully discordant.

When comparing LRT BAL to SoC culture results, an overall concordance rate of 75.9% (632 negative specimens (62.2%), 139 positive specimens (13.7%)) was observed; discrepancies were mostly due to LRT BAL detection of additional microorganisms. For 214 of all specimens (21.1%), LRT BAL reported one or more additional microorganisms compared to SoC. 151 of these specimens (14.9%) were reported fully negative by SoC, while for 63 specimens (6.2%) at least one LRT BAL panel microorganism was reported by SoC. For 25 of all specimens (2.5%), one or more positive SoC results were not reported by LRT BAL. 21 of these specimens (2.1%) were reported fully negative by LRT BAL, while four specimens (0.4%) were reported with at least one positive LRT BAL result. For 0.4% of all specimens, LRT BAL and SoC reported different microorganisms. Two of these specimens (0.2%) shared at least one concordant microorganism result, while for four specimens (0.4%) results were fully discordant.

### Table 27: Comparison of LRT BAL and SoC results, full listing.

<table>
<thead>
<tr>
<th>LRT BAL Result</th>
<th>SoC Result</th>
<th># Cases</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Category 1: concordant LRT BAL and SoC results</td>
<td>concordant results:</td>
<td></td>
<td>75.9%</td>
</tr>
<tr>
<td>Category 1a: both negative</td>
<td></td>
<td>632</td>
<td>62.2</td>
</tr>
<tr>
<td>Category 1b: concordant positive results</td>
<td></td>
<td>139</td>
<td>13.7</td>
</tr>
<tr>
<td>Acinetobacter spp.</td>
<td>Acinetobacter spp.</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Enterobacter cloacae complex</td>
<td>Enterobacter cloacae complex</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>Escherichia coli</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Haemophilus influenzae</td>
<td>Haemophilus influenzae</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Klebsiella pneumoniae</td>
<td>Klebsiella pneumoniae</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Moraxella catarrhalis</td>
<td>Moraxella catarrhalis</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Pneumocystis jirovecii</td>
<td>Pneumocystis jirovecii</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>Pseudomonas aeruginosa</td>
<td>31</td>
<td></td>
</tr>
<tr>
<td>Serratia marcescens</td>
<td>Serratia marcescens</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>Staphylococcus aureus</td>
<td>39</td>
<td></td>
</tr>
<tr>
<td>Stenotrophomonas maltophilia</td>
<td>Stenotrophomonas maltophilia</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Streptococcus pneumoniae</td>
<td>Streptococcus pneumoniae</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>
### LRT BAL Result vs. SoC Result

<table>
<thead>
<tr>
<th>LRT BAL Result</th>
<th>SoC Result</th>
<th># Cases</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acinetobacter spp., Citrobacter freundii</td>
<td>Acinetobacter spp., Citrobacter freundii</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Acinetobacter spp., Stenotrophomonas maltophilia</td>
<td>Acinetobacter spp., Stenotrophomonas maltophilia</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Enterobacter cloacae complex, Staphylococcus aureus</td>
<td>Enterobacter cloacae complex, Staphylococcus aureus</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Escherichia coli, Klebsiella oxytoca</td>
<td>Escherichia coli, Klebsiella oxytoca</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Klebsiella oxytoca, Staphylococcus aureus</td>
<td>Klebsiella oxytoca, Staphylococcus aureus</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Klebsiella pneumoniae, Pseudomonas aeruginosa</td>
<td>Klebsiella pneumoniae, Pseudomonas aeruginosa</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Proteus spp., Pseudomonas aeruginosa</td>
<td>Proteus spp., Pseudomonas aeruginosa</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Pseudomonas aeruginosa, Staphylococcus aureus</td>
<td>Pseudomonas aeruginosa, Staphylococcus aureus</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Pseudomonas aeruginosa, Stenotrophomonas maltophilia</td>
<td>Pseudomonas aeruginosa, Stenotrophomonas maltophilia</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Proteus spp., Pseudomonas aeruginosa, Staphylococcus aureus</td>
<td>Proteus spp., Pseudomonas aeruginosa, Staphylococcus aureus</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Category 2: LRT BAL detects additional microorganisms</td>
<td>additional detections: 21.1 %</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Category 2: negative SoC result

<table>
<thead>
<tr>
<th>Category 2a: negative SoC result</th>
<th>151</th>
<th>14.9</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acinetobacter spp. negative</td>
<td>3</td>
<td>14.9</td>
</tr>
<tr>
<td>Citrobacter freundii negative</td>
<td>1</td>
<td>14.9</td>
</tr>
<tr>
<td>Enterobacter cloacae complex</td>
<td>4</td>
<td>26.3</td>
</tr>
<tr>
<td>Escherichia coli negative</td>
<td>14</td>
<td>93.0</td>
</tr>
<tr>
<td>Haemophilus influenzae negative</td>
<td>24</td>
<td>93.0</td>
</tr>
<tr>
<td>Klebsiella oxytoca negative</td>
<td>2</td>
<td>13.4</td>
</tr>
<tr>
<td>Klebsiella pneumoniae negative</td>
<td>3</td>
<td>19.8</td>
</tr>
<tr>
<td>Legionella pneumophila negative</td>
<td>1</td>
<td>6.6</td>
</tr>
<tr>
<td>Moraxella catarrhalis negative</td>
<td>3</td>
<td>19.8</td>
</tr>
<tr>
<td>Mycoplasma pneumonae negative</td>
<td>4</td>
<td>26.3</td>
</tr>
<tr>
<td>Pneumocystis jirovecii negative</td>
<td>9</td>
<td>59.3</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa negative</td>
<td>27</td>
<td>17.9</td>
</tr>
<tr>
<td>Staphylococcus aureus negative</td>
<td>21</td>
<td>13.9</td>
</tr>
<tr>
<td>Stenotrophomonas maltophilia</td>
<td>2</td>
<td>13.9</td>
</tr>
<tr>
<td>Streptococcus pneumoniae negative</td>
<td>6</td>
<td>3.9</td>
</tr>
<tr>
<td>Enterobacter cloacae complex, Staphylococcus aureus</td>
<td>negative</td>
<td>1</td>
</tr>
<tr>
<td>Escherichia coli, Klebsiella pneumoniae negative</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Escherichia coli, Serratia marcescens negative</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Haemophilus influenzae, Moraxella catarrhalis negative</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Haemophilus influenzae, Mycoplasma pneumonae negative</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Haemophilus influenzae, Staphylococcus aureus negative</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Haemophilus influenzae, Streptococcus pneumoniae negative</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Klebsiella oxytoca, negative</td>
<td>1</td>
<td>1.3</td>
</tr>
<tr>
<td>LRT BAL Result</td>
<td>SoC Result</td>
<td># Cases</td>
</tr>
<tr>
<td>----------------------------------------</td>
<td>--------------------</td>
<td>---------</td>
</tr>
<tr>
<td><em>Proteus</em> spp.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Klebsiella pneumoniae</em>, <em>Staphylococcus aureus</em></td>
<td>negative</td>
<td>1</td>
</tr>
<tr>
<td><em>Moraxella catarrhalis</em>, <em>Pneumocystis jirovecii</em></td>
<td>negative</td>
<td>1</td>
</tr>
<tr>
<td><em>Moraxella catarrhalis</em>, <em>Streptococcus pneumoniae</em></td>
<td>negative</td>
<td>1</td>
</tr>
<tr>
<td><em>Pneumocystis jirovecii</em>, <em>Staphylococcus aureus</em></td>
<td>negative</td>
<td>1</td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa</em>, <em>Staphylococcus aureus</em></td>
<td>negative</td>
<td>6</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em>, <em>Serratia marcescens</em></td>
<td>negative</td>
<td>1</td>
</tr>
<tr>
<td><em>Enterobacter cloacae complex</em>, <em>Haemophilus influenzae</em>, <em>Moraxella catarrhalis</em></td>
<td>negative</td>
<td>1</td>
</tr>
<tr>
<td><em>Escherichia coli</em>, <em>Haemophilus influenzae</em>, <em>Staphylococcus aureus</em></td>
<td>negative</td>
<td>1</td>
</tr>
<tr>
<td><em>Klebsiella oxytoca</em>, <em>Pseudomonas aeruginosa</em>, <em>Staphylococcus aureus</em></td>
<td>negative</td>
<td>1</td>
</tr>
<tr>
<td><em>Enterobacter cloacae complex</em>, <em>Haemophilus influenzae</em>, <em>Moraxella catarrhalis</em>, <em>Morganella morganii</em>, <em>Staphylococcus aureus</em>, <em>Serratia marcescens</em></td>
<td>negative</td>
<td>1</td>
</tr>
</tbody>
</table>

**Category 2b: positive result for both LRT BAL and SoC**

<table>
<thead>
<tr>
<th>LRT BAL Result</th>
<th>SoC Result</th>
<th># Cases</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Acinetobacter</em> spp., <em>Klebsiella pneumoniae</em></td>
<td><em>Klebsiella pneumoniae</em></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td><em>Acinetobacter</em> spp., <em>Pseudomonas aeruginosa</em></td>
<td><em>Pseudomonas aeruginosa</em></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td><em>Enterobacter cloacae complex</em>, <em>Mycoplasma pneumoniae</em></td>
<td><em>Enterobacter cloacae complex</em></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td><em>Escherichia coli</em>, <em>Haemophilus influenzae</em></td>
<td><em>Escherichia coli</em></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td><em>Escherichia coli</em>, <em>Pseudomonas aeruginosa</em></td>
<td><em>Pseudomonas aeruginosa</em></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td><em>Escherichia coli</em>, <em>Serratia marcescens</em></td>
<td><em>Escherichia coli</em></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td><em>Escherichia coli</em>, <em>Staphylococcus aureus</em></td>
<td><em>Escherichia coli</em></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td><em>Escherichia coli</em>, <em>Staphylococcus aureus</em></td>
<td><em>Staphylococcus aureus</em></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td><em>Haemophilus influenzae</em>, <em>Klebsiella oxytoca</em></td>
<td><em>Klebsiella oxytoca</em></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td><em>Haemophilus influenzae</em>, <em>Moraxella catarrhalis</em></td>
<td><em>Haemophilus influenzae</em></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td><em>Haemophilus influenzae</em>, <em>Pseudomonas aeruginosa</em></td>
<td><em>Pseudomonas aeruginosa</em></td>
<td>3</td>
<td></td>
</tr>
<tr>
<td><em>Haemophilus influenzae</em>, <em>Staphylococcus aureus</em></td>
<td><em>Haemophilus influenzae</em></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td><em>Haemophilus influenzae</em>, <em>Staphylococcus aureus</em></td>
<td><em>Staphylococcus aureus</em></td>
<td>2</td>
<td></td>
</tr>
<tr>
<td><em>Klebsiella oxytoca</em>, <em>Klebsiella pneumoniae</em></td>
<td><em>Klebsiella pneumoniae</em></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td><em>Klebsiella oxytoca</em>, <em>Serratia marcescens</em></td>
<td><em>Klebsiella oxytoca</em></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>LRT BAL Result</td>
<td>SoC Result</td>
<td># Cases</td>
<td>%</td>
</tr>
<tr>
<td>-------------------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------------</td>
<td>---------</td>
<td>----</td>
</tr>
<tr>
<td>Klebsiella oxytoca, Stenotrophomonas maltophilia</td>
<td>Klebsiella oxytoca</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Klebsiella pneumoniae, Pseudomonas aeruginosa</td>
<td>Klebsiella pneumoniae</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Klebsiella pneumoniae, Staphylococcus aureus</td>
<td>Klebsiella pneumoniae</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Klebsiella pneumoniae, Staphylococcus aureus</td>
<td>Staphylococcus aureus</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Pneumocystis jiroveci, Pseudomonas aeruginosa</td>
<td>Staphylococcus aureus</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Pneumocystis jiroveci, Stenotrophomonas maltophilia</td>
<td>Stenotrophomonas maltophilia</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Proteus spp., Staphylococcus aureus</td>
<td>Proteus spp.</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Pseudomonas aeruginosa, Serratia marcescens</td>
<td>Pseudomonas aeruginosa</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Pseudomonas aeruginosa, Staphylococcus aureus</td>
<td>Pseudomonas aeruginosa</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Pseudomonas aeruginosa, Staphylococcus aureus</td>
<td>Staphylococcus aureus</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Pseudomonas aeruginosa, Stenotrophomonas maltophilia</td>
<td>Pseudomonas aeruginosa</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Staphylococcus aureus, Stenotrophomonas maltophilia</td>
<td>Staphylococcus aureus</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Acinetobacter spp., Klebsiella pneumoniae, Staphylococcus aureus</td>
<td>Klebsiella pneumoniae, Staphylococcus aureus</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Acinetobacter spp., Klebsiella pneumoniae, Stenotrophomonas maltophilia</td>
<td>Klebsiella pneumoniae</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Acinetobacter spp., Pseudomonas aeruginosa, Stenotrophomonas maltophilia</td>
<td>Acinetobacter spp., Pseudomonas aeruginosa</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Enterobacter cloacae complex, Klebsiella pneumoniae, Moraxella catarrhalis</td>
<td>Enterobacter cloacae complex</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Enterobacter cloacae complex, Klebsiella pneumoniae, Moraxella catarrhalis</td>
<td>Enterobacter cloacae complex</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Escherichia coli, Morganella morganii, Pseudomonas aeruginosa</td>
<td>Pseudomonas aeruginosa</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Escherichia coli, Pneumocystis jirovecii, Pseudomonas aeruginosa</td>
<td>Escherichia coli</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Escherichia coli, Pseudomonas aeruginosa, Serratia marcescens</td>
<td>Pseudomonas aeruginosa, Serratia marcescens</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus</td>
<td>Staphylococcus aureus</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Haemophilus influenzae, Moraxella catarrhalis, Streptococcus pneumoniae</td>
<td>Moraxella catarrhalis, Streptococcus pneumoniae</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Klebsiella oxytoca, Pseudomonas aeruginosa, Stenotrophomonas maltophilia</td>
<td>Pseudomonas aeruginosa</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Klebsiella pneumoniae, Pseudomonas aeruginosa, Stenotrophomonas maltophilia</td>
<td>Klebsiella pneumoniae, Pseudomonas aeruginosa</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>LRT BAL Result</td>
<td>SoC Result</td>
<td># Cases</td>
<td>%</td>
</tr>
<tr>
<td>------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------------------------</td>
<td>---------</td>
<td>------</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa, Serratia marcescens, Stenotrophomonas maltophilia</td>
<td>Pseudomonas aeruginosa</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Pseudomonas aeruginosa, Serratia marcescens, Stenotrophomonas maltophilia</td>
<td>Pseudomonas aeruginosa, Serratia marcescens</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Acinetobacter spp., Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa</td>
<td>Klebsiella pneumoniae, Pseudomonas aeruginosa</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Acinetobacter spp., Escherichia coli, Klebsiella pneumoniae, Stenotrophomonas maltophilia</td>
<td>Acinetobacter spp.</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Acinetobacter spp., Escherichia coli, Proteus spp., Pseudomonas aeruginosa</td>
<td>Pseudomonas aeruginosa</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Enterobacter cloacae complex, Escherichia coli, Klebsiella oxytoca, Stenotrophomonas maltophilia</td>
<td>Enterobacter cloacae complex, Escherichia coli, Klebsiella oxytoca</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Acinetobacter spp., Enterobacter cloacae complex, Haemophilus influenzae, Klebsiella pneumoniae, Streptococcus pneumoniae</td>
<td>Enterobacter cloacae complex, Klebsiella pneumoniae, Streptococcus pneumoniae</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Escherichia coli, Haemophilus influenzae, Pseudomonas aeruginosa, Staphylococcus aureus</td>
<td>Staphylococcus aureus</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Haemophilus influenzae, Proteus spp., Pseudomonas aeruginosa, Stenotrophomonas maltophilia</td>
<td>Pseudomonas aeruginosa</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Pseudomonas aeruginosa, Serratia marcescens, Staphylococcus aureus, Stenotrophomonas maltophilia</td>
<td>Pseudomonas aeruginosa, Serratia marcescens, Staphylococcus aureus</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Acinetobacter spp., Enterobacter cloacae complex, Haemophilus influenzae, Klebsiella pneumoniae, Streptococcus pneumoniae</td>
<td>Enterobacter cloacae complex, Klebsiella pneumoniae, Streptococcus pneumoniae</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Citrobacter freundii, Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Serratia marcescens</td>
<td>Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Serratia marcescens</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Enterobacter cloacae complex, Escherichia coli, Klebsiella oxytoca, Klebsiella varicola, Proteus spp.</td>
<td>Enterobacter cloacae complex</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Serratia marcescens, Stenotrophomonas maltophilia</td>
<td>Klebsiella pneumoniae, Pseudomonas aeruginosa, Serratia marcescens, Stenotrophomonas maltophilia</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Escherichia coli, Morganella morganii, Proteus spp., Pseudomonas aeruginosa, Stenotrophomonas maltophilia</td>
<td>Pseudomonas aeruginosa</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Haemophilus influenzae, Klebsiella pneumoniae, Klebsiella pneumoniae, Haemophilus influenzae</td>
<td>Haemophilus influenzae, Klebsiella pneumoniae</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>LRT BAL Result</td>
<td>SoC Result</td>
<td># Cases</td>
<td>%</td>
</tr>
<tr>
<td>---------------------------------------------------</td>
<td>----------------------------------------------</td>
<td>---------</td>
<td>----</td>
</tr>
<tr>
<td>Klebsiella variicola, Proteus spp., Staphylococcus aureus</td>
<td>Proteus spp., Staphylococcus aureus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haemophilus influenzae, Klebsiella pneumoniae, Moraxella catarrhalis, Pneumocystis jirovecii, Serratia marcescens</td>
<td>Serratia marcescens</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Acinetobacter spp., Escherichia coli, Klebsiella pneumoniae, Proteus spp., Pseudomonas aeruginosa, Staphylococcus aureus</td>
<td>Klebsiella pneumoniae</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

**Category 3: LRT BAL detects fewer microorganisms**

<table>
<thead>
<tr>
<th>Category 3a: LRT BAL negative</th>
<th>fewer detections: 2.5 %</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>negative</td>
<td>Enterobacter cloacae complex</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>negative</td>
<td>Escherichia coli</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>negative</td>
<td>Klebsiella oxytoca</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>negative</td>
<td>Klebsiella pneumoniae</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>negative</td>
<td>Klebsiella varicola</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>negative</td>
<td>Legionella pneumophila</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>negative</td>
<td>Pneumocystis jirovecii</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>negative</td>
<td>Pseudomonas aeruginosa</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>negative</td>
<td>Staphylococcus aureus</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>negative</td>
<td>Stenotrophomonas maltophilia</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

**Category 3b: positive result for both LRT BAL and SoC**

| Acinetobacter spp. | Acinetobacter spp., Enterobacter cloacae complex | 1       |    |
| Pseudomonas aeruginosa | Klebsiella pneumoniae, Pseudomonas aeruginosa | 1       |    |
| Stenotrophomonas maltophilia | Haemophilus influenzae, Stenotrophomonas maltophilia | 1       |    |
| Acinetobacter spp., Enterobacter cloacae complex | Acinetobacter spp., Enterobacter cloacae complex, Klebsiella varicola | 1       |    |

**Category 4 LRT BAL and SoC detect different microorganisms**

<table>
<thead>
<tr>
<th>Category 4a: partially concordant positive results</th>
<th>discordant microorganism results: 0.6 %</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Citrobacter freundii, Pseudomonas aeruginosa</td>
<td>Pseudomonas aeruginosa, Staphylococcus aureus</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Enterobacter cloacae complex, Klebsiella oxytoca, Stenotrophomonas maltophilia</td>
<td>Enterobacter cloacae complex, Klebsiella pneumoniae</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

**Category 4b: fully discordant results**

| Haemophilus influenzae | Staphylococcus aureus | 1       |    |
| Pseudomonas aeruginosa | Acinetobacter spp. | 1       |    |
| Pseudomonas aeruginosa | Staphylococcus aureus | 1       |    |
| Stenotrophomonas maltophilia | Enterobacter cloacae complex | 1       |    |
Microorganism Results – Comparison to Composite Comparator Reference

LRT BAL results from the prospective clinical study were also compared to a composite comparator reference consisting of SoC culture results combined with a validated molecular test (PCR/sequencing, being part of a multiplex PCR assay). For ‘atypical’ microorganisms (for which SoC testing was not performed for all specimens), the composite comparator reference consists of two validated molecular tests for each microorganism (PCR/sequencing, also being part of the multiplex PCR assay). Table 28 summarizes comparison results together with their 95% confidence intervals.

Table 28: Prospective study (N = 1,016 specimens *), comparison to composite comparator.

<table>
<thead>
<tr>
<th>Microorganism</th>
<th>TP</th>
<th>FN</th>
<th>FP</th>
<th>TN</th>
<th>PPA [%] (95% CI)</th>
<th>NPA [%] (95% CI)</th>
<th>PPV [%] (95% CI)</th>
<th>NPV [%] (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acinetobacter spp.</td>
<td>16</td>
<td>2</td>
<td>5</td>
<td>992</td>
<td>88.9 (67.2 - 96.9)</td>
<td>99.5 (98.8 - 99.8)</td>
<td>76.2 (54.9 - 89.4)</td>
<td>99.8 (99.3 - 99.9)</td>
</tr>
<tr>
<td>Chlamydia pneumoniae b</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1,016</td>
<td>NA</td>
<td>100.0 (99.6 - 100.0)</td>
<td>NA</td>
<td>100.0 (99.6 - 100.0)</td>
</tr>
<tr>
<td>Citrobacter freundii</td>
<td>1</td>
<td>0</td>
<td>3</td>
<td>1,011</td>
<td>100.0 (20.7 - 100.0)</td>
<td>99.7 (99.1 - 99.9)</td>
<td>25.0 (4.6 - 69.9)</td>
<td>100.0 (99.6 - 100.0)</td>
</tr>
<tr>
<td>Enterobacter cloacae complex</td>
<td>18</td>
<td>4</td>
<td>2</td>
<td>991</td>
<td>81.8 (61.5 - 92.7)</td>
<td>99.8 (99.3 - 99.9)</td>
<td>90.0 (69.9 - 97.2)</td>
<td>99.6 (99.0 - 99.8)</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>28</td>
<td>6</td>
<td>19</td>
<td>963</td>
<td>82.4 (66.5 - 91.7)</td>
<td>98.1 (97.0 - 98.8)</td>
<td>59.6 (45.3 - 72.4)</td>
<td>99.4 (98.7 - 99.7)</td>
</tr>
<tr>
<td>Haemophilus influenzae</td>
<td>20</td>
<td>2</td>
<td>36</td>
<td>957</td>
<td>90.9 (72.2 - 97.5)</td>
<td>96.4 (95.0 - 97.4)</td>
<td>35.7 (24.5 - 48.8)</td>
<td>99.8 (99.2 - 99.9)</td>
</tr>
<tr>
<td>Klebsiella oxytoca</td>
<td>8</td>
<td>2</td>
<td>6</td>
<td>1,000</td>
<td>80.0 (49.0 - 94.3)</td>
<td>99.4 (98.7 - 99.7)</td>
<td>57.1 (32.6 - 78.6)</td>
<td>99.8 (99.3 - 99.9)</td>
</tr>
<tr>
<td>Klebsiella pneumoniae b</td>
<td>21</td>
<td>4</td>
<td>9</td>
<td>981</td>
<td>84.0 (65.3 - 93.6)</td>
<td>99.1 (98.3 - 99.5)</td>
<td>70.0 (52.1 - 83.3)</td>
<td>99.6 (99.0 - 99.8)</td>
</tr>
<tr>
<td>Klebsiella variicola b</td>
<td>0</td>
<td>2</td>
<td>1</td>
<td>1,012</td>
<td>0.0 (0.0 - 65.8)</td>
<td>99.9 (99.4 - 100.0)</td>
<td>0.0 (0.0 - 79.3)</td>
<td>99.8 (99.3 - 99.9)</td>
</tr>
<tr>
<td>Legionella pneumophila b</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1,014</td>
<td>100.0 (20.7 - 100.0)</td>
<td>100.0 (99.6 - 100.0)</td>
<td>100.0 (20.7 - 100.0)</td>
<td>100.0 (99.6 - 100.0)</td>
</tr>
<tr>
<td>Moraxella catarrhalis</td>
<td>12</td>
<td>4</td>
<td>3</td>
<td>993</td>
<td>75.0 (50.5 - 89.8)</td>
<td>99.7 (99.1 - 99.9)</td>
<td>80.0 (54.8 - 93.0)</td>
<td>99.6 (99.0 - 99.8)</td>
</tr>
<tr>
<td>Morganella morganii</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>1,009</td>
<td>100.0 (43.9 - 100.0)</td>
<td>100.0 (99.6 - 100.0)</td>
<td>100.0 (43.9 - 100.0)</td>
<td>100.0 (99.6 - 100.0)</td>
</tr>
<tr>
<td>Mycoplasma pneumoniae b</td>
<td>3</td>
<td>0</td>
<td>3</td>
<td>1,010</td>
<td>100.0 (43.9 - 100.0)</td>
<td>99.7 (99.1 - 99.9)</td>
<td>50.0 (18.8 - 81.2)</td>
<td>100.0 (99.6 - 100.0)</td>
</tr>
<tr>
<td>Pneumocystis jirovecii b</td>
<td>20</td>
<td>5</td>
<td>2</td>
<td>989</td>
<td>80.0 (60.9 - 91.1)</td>
<td>99.8 (99.3 - 99.9)</td>
<td>90.9 (72.2 - 97.5)</td>
<td>99.5 (98.8 - 99.8)</td>
</tr>
<tr>
<td>Proteus spp.</td>
<td>10</td>
<td>0</td>
<td>0</td>
<td>1,006</td>
<td>100.0 (72.3 - 100.0)</td>
<td>100.0 (99.6 - 100.0)</td>
<td>100.0 (72.3 - 100.0)</td>
<td>100.0 (99.6 - 100.0)</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>100</td>
<td>7</td>
<td>12</td>
<td>896</td>
<td>93.5 (87.1 - 96.8)</td>
<td>98.7 (97.7 - 99.2)</td>
<td>89.3 (82.2 - 93.8)</td>
<td>99.2 (98.4 - 99.6)</td>
</tr>
<tr>
<td>Serratia marcescens</td>
<td>15</td>
<td>1</td>
<td>2</td>
<td>997</td>
<td>93.8 (71.7 - 98.9)</td>
<td>99.8 (99.3 - 99.9)</td>
<td>88.2 (65.7 - 96.7)</td>
<td>99.9 (99.4 - 100.0)</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>80</td>
<td>16</td>
<td>24</td>
<td>896</td>
<td>83.3 (74.6 - 89.5)</td>
<td>97.4 (96.1 - 98.2)</td>
<td>76.9 (68.0 - 84.0)</td>
<td>98.2 (97.2 - 98.9)</td>
</tr>
<tr>
<td>Stenotrophomonas maltophilia</td>
<td>34</td>
<td>7</td>
<td>7</td>
<td>967</td>
<td>82.9 (68.7 - 91.5)</td>
<td>99.3 (98.5 - 99.7)</td>
<td>82.9 (68.7 - 91.5)</td>
<td>99.3 (98.5 - 99.7)</td>
</tr>
<tr>
<td>Streptococcus pneumoniae</td>
<td>11</td>
<td>0</td>
<td>2</td>
<td>1,003</td>
<td>100.0 (74.1 - 100.0)</td>
<td>99.8 (99.3 - 99.9)</td>
<td>84.6 (57.8 - 95.7)</td>
<td>100.0 (99.6 - 100.0)</td>
</tr>
</tbody>
</table>
Observed invalid LRT BAL analyte results: *Acinetobacter* spp. (1), *C. freundii* (1), *E. cloacae* complex (1), *H. influenzae* (1), *M. catarrhalis* (4), *M. morganii* (4), *P. aeruginosa* (1), *S. marcescens* (1) and *S. maltophilia* (1). For one SoC negative specimen, *K. pneumoniae* and *K. variicola* were simultaneously reported by the molecular test of the composite comparator, but were negative by SoC culture. As it was not feasible to resolve whether these analytes exceeded the molecular reporting threshold, both were set to ‘invalid’. For this specimen, LRT BAL had reported a positive result for *K. variicola* and a negative result for *K. pneumoniae.*

b. ‘Atypical’ microorganisms *C. pneumoniae*, *L. pneumophila*, *M. pneumoniae*, and *P. jirovecii* were compared to two independent molecular tests (PCR/bi-directional sequencing) as composite comparator.

c. *K. variicola* is typically reported by culture as *K. pneumoniae*. To discriminate *K. variicola* from *K. pneumoniae*, provided *K. pneumoniae* strain isolates were sequenced. For a few cases, no isolate was provided and sequencing was performed from specimen DNA extracts instead. Two of 27 cases were identified as *K. variicola* and confirmed by both isolate and DNA extract sequencing. Results for *K. pneumoniae* and *K. variicola* performance are calculated based on the species identified by sequencing.

d. For two of five FN *P. jirovecii* cases, repeat comparator testing results indicating specimen degradation during prolonged storage as likely reason for observed failures.

**Antibiotic Resistance Marker Results – Comparison to Molecular Reference**

Performance characteristics of LRT BAL panel antibiotic resistance markers were evaluated for the prospective study (1,016 specimens) by comparing to corresponding molecular reference assays to determine PPAs (TP / (TP + FN)) and NPAs (FN / (FN + FP)) together with 95% confidence intervals. For each antibiotic resistance marker, one PCR assay was performed followed by bi-directional sequencing.

Antibiotic resistance marker results are only reported by the LRT BAL Application if at least one corresponding host microorganism is simultaneously detected. Results for antibiotic resistance markers detected without a positive corresponding host microorganism result are masked on the results screen. Table 29 reports antibiotic resistance markers as displayed on the LRT BAL results screen, i.e., all antibiotic resistance markers for which a corresponding host microorganism was simultaneously detected. Note that PPA/NPA performance data are driven by LRT BAL microorganism results.
Table 29: Comparison of antibiotic resistance markers to corresponding molecular reference assays (PCR/sequencing) for the prospective study (N = 1,016 specimens) for markers as displayed and reported on the LRT BAL results screen (number of detected host microorganisms for each marker in brackets).

<table>
<thead>
<tr>
<th>Antibiotic Resistance Marker</th>
<th>TP</th>
<th>FN</th>
<th>FP</th>
<th>TN</th>
<th>PPA [%] (95% CI)</th>
<th>NPA [%] (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ctx-M (N = 208)</td>
<td>8</td>
<td>1</td>
<td>1</td>
<td>197</td>
<td>88.9 (56.5 - 98.0)</td>
<td>99.5 (97.2 - 99.9)</td>
</tr>
<tr>
<td>kpc (N = 208)</td>
<td>3</td>
<td>0</td>
<td>1</td>
<td>204</td>
<td>100.0 (43.9 - 100.0)</td>
<td>99.5 (97.3 - 99.9)</td>
</tr>
<tr>
<td>mecA (N = 104)</td>
<td>22</td>
<td>0</td>
<td>25</td>
<td>57</td>
<td>100.0 (85.1 - 100.0)</td>
<td>69.5 (58.9 - 78.4)</td>
</tr>
<tr>
<td>ndm (N = 208)</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>207</td>
<td>100.0 (20.7 - 100.0)</td>
<td>100.0 (98.2 - 100.0)</td>
</tr>
<tr>
<td>oxa-23 (N = 21)</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>18</td>
<td>100.0 (43.9 - 100.0)</td>
<td>100.0 (82.4 - 100.0)</td>
</tr>
<tr>
<td>oxa-24 (N = 21)</td>
<td>3</td>
<td>0</td>
<td>1</td>
<td>16</td>
<td>100.0 (43.9 - 100.0)</td>
<td>94.1 (73.0 - 99.0)</td>
</tr>
<tr>
<td>oxa-48 (N = 112)</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>111</td>
<td>100.0 (20.7 - 100.0)</td>
<td>100.0 (96.7 - 100.0)</td>
</tr>
<tr>
<td>oxa-58 (N = 21)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>21</td>
<td>NA</td>
<td>100.0 (84.5 - 100.0)</td>
</tr>
<tr>
<td>tem (N = 56)</td>
<td>9</td>
<td>0</td>
<td>7</td>
<td>40</td>
<td>100.0 (70.1 - 100.0)</td>
<td>85.1 (72.3 - 92.6)</td>
</tr>
<tr>
<td>vim (N = 208)</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>207</td>
<td>NA</td>
<td>99.5 (97.3 - 99.9)</td>
</tr>
</tbody>
</table>

* Observed invalid LRT BAL analyte results: ctx-M (1) and oxa-24 (1).
* One false negative result belongs to the ctx-M9 subgroup that is not covered by the ctx-M assay of the LRT BAL Application (targeted against ctx-M1 subgroup).
* Note that molecular reference assays use cutoffs to achieve analytical sensitivities in a similar range to LRT BAL. Negative results by molecular reference assays do not preclude the presence of the antibiotic resistance marker in the specimen at a low concentration, nor its possible clinical relevance. Please refer to section ‘Correlation of Detected Antibiotic Resistance Markers to Strain Genotypes and Phenotypes’, p. 68 for genotypic and phenotypic correlation of reported antibiotic resistance markers.
* Specimens with false positive LRT BAL results were analyzed with additional molecular assays (PCR/bi-directional sequencing) using specimen DNA extracts for presence or absence of antibiotic resistance markers. Presence of antibiotic resistance markers was confirmed in 0 of 1 case for ctx-M, 1 of 1 case of kpc, 10 of 25 cases for mecA, 1 of 1 case for oxa-24, 6 of 7 cases for tem and 1 of 1 case for vim. Cross-reactivity to other off-panel analytes has not been observed. For all not confirmed cases, PCRs did not amplify sufficient amounts for sequencing.
* Note that Staphylococci other than S. aureus commonly harbor mecA. Positive mecA results can, therefore, be due to the presence of this marker in such microorganisms.
* Although tem is reported by LRT BAL for H. influenzae only, other Gram-negative microorganisms (e.g., Enterobacteriaceae, Acinetobacter spp., P. aeruginosa) can harbor tem. Positive tem results can, therefore, be due to the presence of this marker in such microorganisms.

Antibiotic Resistance Marker Results – Agreement Rates to Positive and Negative Microorganisms as Detected by Culture/Isolate Sequencing or Composite Comparator Testing

In order to determine agreement rates of antibiotic resistance markers reported by LRT BAL to positive and negative reference results, a comparison to the following references was performed: (A) SoC culture result for microorganisms, combined with sequencing results/marker screenings of provided strain isolates, and (B) composite comparator result for microorganisms and molecular reference results (PCR/sequencing) for antibiotic resistance markers. Note that an isolate was not provided for all SoC positive microorganisms, thereby limiting the dataset for comparison (A). Comparison (B) evaluates the entire specimen cohort, including all positive LRT BAL results that were negative by 510(k) Summary – LRT BAL Application K191967 Rev 3.0.
SoC culture. Molecular reference assays use cutoffs that were set to achieve an analytical assay sensitivity in a comparable range to LRT BAL.

For both comparisons, the following agreement rates are evaluated for ctx-M, kpc, ndm, and vim (for Enterobacteriaceae, Acinetobacter spp. and/or P. aeruginosa as possible host microorganisms), for oxa-48 (for Enterobacteriaceae), for tem (for H. influenzae), and for mecA (for S. aureus) in Tables 30 - 38:

1. Agreement of one (or more) detected host microorganisms in combination with an antibiotic resistance marker (Org+/Res+) between LRT BAL and reference methods (A) or (B).

2. Agreement of one (or more) detected host microorganisms without reported antibiotic resistance marker (Org+/Res-) between LRT BAL and reference methods (A) or (B).

3. Agreement of a negative result for one (or more) host microorganisms (Org-) between LRT BAL and reference methods (A) and (B).

As presence of mecA is expected to directly correlate with cefoxitin/oxacillin resistance in S. aureus strains (MRSA, methicillin-resistant S. aureus), while the absence of mecA is expected to correlate with susceptible S. aureus strains (MSSA, methicillin-sensitive S. aureus), mecA was furthermore compared to the MRSA/MSSA status of the isolate as reported by SoC culture as a third reference (C) in Table 38:

1. Agreement of a detected S. aureus in combination with a detected mecA as reported by LRT BAL (Org+/Res+) to S. aureus reported with an MRSA phenotype by SoC culture (Org+/MRSA).

2. Agreement of a detected S. aureus together with a negative result for mecA (Org+/Res-) as reported by LRT BAL to S. aureus reported with an MSSA phenotype by SoC culture (Org+/MSSA).

3. Agreement of a negative result for S. aureus between LRT BAL and SoC culture.

No agreement tables are included for oxa-58 for which positive results were reported neither by the LRT BAL Application, nor by the reference methods.
Table 30: Agreement rates for *oxa*-23 between LRT BAL and reference methods A (culture) and B (composite comparator) for *Acinetobacter* spp. as host microorganism.

### A

<table>
<thead>
<tr>
<th>LRT BAL Result</th>
<th><em>Acinetobacter</em> spp. <em>oxa</em>-23</th>
<th>Culture Result for <em>Acinetobacter</em> spp. + Isolate Sequencing/Marker Screening for <em>oxa</em>-23</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Org+/Res+</td>
<td>Org+/Res-</td>
</tr>
<tr>
<td>LRT BAL Result</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><em>Acinetobacter</em> spp./<em>oxa</em>-23</th>
<th>rate [%]</th>
<th>positivity</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agreement (Org+/Res+)</td>
<td>100.0</td>
<td>1/1</td>
<td>20.7 - 100.0</td>
</tr>
<tr>
<td>Agreement (Org+/Res-)</td>
<td>100.0</td>
<td>7/7</td>
<td>64.6 - 100.0</td>
</tr>
<tr>
<td>Agreement (Org-)</td>
<td>98.9</td>
<td>993/1,004</td>
<td>98.0 - 99.4</td>
</tr>
</tbody>
</table>

### B

<table>
<thead>
<tr>
<th>LRT BAL Result</th>
<th><em>Acinetobacter</em> spp. <em>oxa</em>-23</th>
<th>Composite Comparator Result for <em>Acinetobacter</em> spp. + Mol. Reference (PCR/Seq.) for <em>oxa</em>-23</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Org+/Res+</td>
<td>Org+/Res-</td>
</tr>
<tr>
<td>LRT BAL Result</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><em>Acinetobacter</em> spp./<em>oxa</em>-23</th>
<th>rate [%]</th>
<th>positivity</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agreement (Org+/Res+)</td>
<td>100.0</td>
<td>3/3</td>
<td>43.9 - 100.0</td>
</tr>
<tr>
<td>Agreement (Org+/Res-)</td>
<td>86.7</td>
<td>13/15</td>
<td>62.1 - 96.3</td>
</tr>
<tr>
<td>Agreement (Org-)</td>
<td>99.5</td>
<td>992/997</td>
<td>98.8 - 99.8</td>
</tr>
</tbody>
</table>

* One invalid LRT BAL result for *Acinetobacter* spp.
Table 31: Agreement rates for *oxa*-24 between LRT BAL and reference methods A (culture) and B (composite comparator) for *Acinetobacter* spp. as host microorganism.

### A

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>4</td>
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<td></td>
<td></td>
<td>0</td>
<td>4</td>
<td>2</td>
<td>10</td>
<td>16</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>993</td>
<td>994</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>Total</strong></td>
<td><strong>3</strong></td>
<td><strong>4</strong></td>
<td><strong>3</strong></td>
<td><strong>1,004</strong></td>
</tr>
</tbody>
</table>

**Agreement (Org+/Res+)** 100.0 3/3 43.9 - 100.0  
**Agreement (Org+/Res-)** 100.0 4/4 51.0 - 100.0  
**Agreement (Org-)** 98.9 993/1,004 98.0 - 99.4

### B

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>3</td>
<td>0</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0</td>
<td>12</td>
<td>4</td>
<td>16</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1</td>
<td>1</td>
<td>992</td>
<td>994</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>Total</strong></td>
<td><strong>4</strong></td>
<td><strong>13</strong></td>
<td><strong>997</strong></td>
</tr>
</tbody>
</table>

**Agreement (Org+/Res+)** 75.0 3/4 30.1 - 95.4  
**Agreement (Org+/Res-)** 92.3 12/13 66.7 - 98.6  
**Agreement (Org-)** 99.5 992/997 98.8 - 99.8

* One invalid LRT BAL result for *Acinetobacter* spp. and one for *oxa*-24.
Table 32: Agreement rates for ctx-M between LRT BAL and reference methods A (culture) and B (composite comparator) for combined possible host microorganisms: Enterobacteriaceae, Acinetobacter spp., P. aeruginosa.

### A

<table>
<thead>
<tr>
<th>Combined Hosts ctx-M</th>
<th>Culture Result for Host Microorganism(s) + Isolate Sequencing/Marker Screening for ctx-M</th>
<th>LRT BAL Result</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Org+/Res+</td>
<td>Org+/Res-</td>
</tr>
<tr>
<td>Org+/Res+</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Org+/Res-</td>
<td>0</td>
<td>92</td>
</tr>
<tr>
<td>Org-</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>3</td>
<td>99</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Combined Hosts/ctx-M</th>
<th>rate [%]</th>
<th>positivity</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agreement (Org+/Res+)</td>
<td>100.0</td>
<td>3/3</td>
<td>43.9 - 100.0</td>
</tr>
<tr>
<td>Agreement (Org+/Res-)</td>
<td>92.9</td>
<td>92/99</td>
<td>86.1 - 96.5</td>
</tr>
<tr>
<td>Agreement (Org-)</td>
<td>91.4</td>
<td>794/869</td>
<td>89.3 - 93.1</td>
</tr>
</tbody>
</table>

### B

<table>
<thead>
<tr>
<th>Combined Hosts ctx-M</th>
<th>Composite Comparator Result for Host Microorganism(s) + Mol. Reference (PCR/Seq.) for ctx-M</th>
<th>LRT BAL Result</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Org+/Res+</td>
<td>Org+/Res-</td>
</tr>
<tr>
<td>Org+/Res+</td>
<td>8</td>
<td>1</td>
</tr>
<tr>
<td>Org+/Res-</td>
<td>1</td>
<td>161</td>
</tr>
<tr>
<td>Org-</td>
<td>0</td>
<td>20</td>
</tr>
<tr>
<td>total</td>
<td>9</td>
<td>182</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Combined Hosts/ctx-M</th>
<th>rate [%]</th>
<th>positivity</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agreement (Org+/Res+)</td>
<td>88.9</td>
<td>8/9</td>
<td>56.5 - 98.0</td>
</tr>
<tr>
<td>Agreement (Org+/Res-)</td>
<td>88.5</td>
<td>161/182</td>
<td>83.0 - 92.3</td>
</tr>
<tr>
<td>Agreement (Org-)</td>
<td>95.6</td>
<td>785/821</td>
<td>94.0 - 96.8</td>
</tr>
</tbody>
</table>

---

a Specimens with multiple detected possible host microorganisms by culture: 1 of 3, by the composite comparator: 6 of 9.
b For one ‘Org+/Res-’ and for one ‘Org+/No Isolate’ case, presence of the ctx-M gene was confirmed for an off-panel isolate of Providencia stuartii.
c Four invalid LRT BAL ctx-M results.
d SoC reported the following possible corresponding host microorganisms for three Org+/Res+ cases: *E. coli, K. pneumoniae, K. pneumoniae/P. aeruginosa.*
e SoC reported the following possible corresponding host microorganisms for four Org+/Res- cases: *E. coli, P. aeruginosa (2x), K. pneumoniae/P. aeruginosa/S. marcescens.*
f SoC reported the following possible corresponding host microorganisms for one Org+/No Isolate case: *K. pneumoniae.*
Table 33: Agreement rates for \textit{kpc} between LRT BAL and reference methods A (culture) and B (composite comparator) for combined possible host microorganisms: Enterobacteriaceae, \textit{Acinetobacter} spp., \textit{P. aeruginosa}.

<table>
<thead>
<tr>
<th>Combined Hosts (kpc)</th>
<th>Culture Result for Host Microorganism(s) + Isolate Sequencing/Marker Screening for (kpc)</th>
<th>Org+/Res+</th>
<th>Org+/Res-</th>
<th>Org+/No Isolate</th>
<th>Org-</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>LRT BAL Result</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Org+/Res+</td>
<td>1 \textsuperscript{a}</td>
<td>2 \textsuperscript{c}</td>
<td>1 \textsuperscript{d}</td>
<td>0</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Org+/Res-</td>
<td>0</td>
<td>96</td>
<td>32</td>
<td>76</td>
<td>204</td>
<td></td>
</tr>
<tr>
<td>Org-</td>
<td>0</td>
<td>3</td>
<td>8</td>
<td>797</td>
<td>808</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>1 \textsuperscript{a}</td>
<td>101</td>
<td>41</td>
<td>873</td>
<td>1,016</td>
<td></td>
</tr>
<tr>
<td>Combined Hosts/(kpc)</td>
<td>rate [%]</td>
<td>positivity</td>
<td>95% CI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Agreement (Org+/Res+)</td>
<td>100.0</td>
<td>1/1</td>
<td>20.7 - 100.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Agreement (Org+/Res-)</td>
<td>95.0</td>
<td>96/101</td>
<td>88.9 - 97.9</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Agreement (Org-)</td>
<td>91.3</td>
<td>797/873</td>
<td>89.2 - 93.0</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Combined Hosts (kpc)</th>
<th>Composite Comparator Result for Host Microorganism(s) + Mol. Reference (PCR/Seq.) for (kpc)</th>
<th>Org+/Res+</th>
<th>Org+/Res-</th>
<th>Org-</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>LRT BAL Result</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Org+/Res+</td>
<td>3</td>
<td>1</td>
<td>0</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Org+/Res-</td>
<td>0</td>
<td>167</td>
<td>37</td>
<td>204</td>
<td></td>
</tr>
<tr>
<td>Org-</td>
<td>0</td>
<td>20</td>
<td>788</td>
<td>808</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>3 \textsuperscript{a}</td>
<td>188</td>
<td>825</td>
<td>1,016</td>
<td></td>
</tr>
<tr>
<td>Combined Hosts/(kpc)</td>
<td>rate [%]</td>
<td>positivity</td>
<td>95% CI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Agreement (Org+/Res+)</td>
<td>100.0</td>
<td>3/3</td>
<td>43.9 - 100.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Agreement (Org+/Res-)</td>
<td>88.8</td>
<td>167/188</td>
<td>83.5 - 92.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Agreement (Org-)</td>
<td>95.5</td>
<td>788/825</td>
<td>93.9 - 96.7</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\textsuperscript{a} Specimens with multiple detected possible host microorganisms by culture: 0 of 1, by the composite comparator: 2 of 3.

\textsuperscript{b} SoC reported the following possible corresponding host microorganisms for one Org+/Res+ case: \textit{E. cloacae} complex.

\textsuperscript{c} SoC reported the following possible corresponding host microorganisms for two Org+/Res- cases: \textit{Acinetobacter} spp., \textit{K. pneumoniae/P. aeruginosa}.

\textsuperscript{d} SoC reported the following possible corresponding host microorganisms for one Org+/No Isolate case: \textit{K. pneumoniae}.
Table 34: Agreement rates for ndm between LRT BAL and reference methods A (culture) and B (composite comparator) for combined possible host microorganisms: Enterobacteriaceae, Acinetobacter spp., P. aeruginosa.

### A

<table>
<thead>
<tr>
<th>Combined Hosts ndm</th>
<th>Culture Result for Host Microorganism(s) + Isolate Sequencing/Marker Screening for ndm</th>
<th>Org+/Res+</th>
<th>Org+/Res-</th>
<th>Org+/No Isolate</th>
<th>Org-</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>LRT BAL Result</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Org+/Res+</td>
<td>1 c</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Org+/Res-</td>
<td>0</td>
<td>98</td>
<td>33</td>
<td>76</td>
<td>207</td>
<td></td>
</tr>
<tr>
<td>Org-</td>
<td>0</td>
<td>3</td>
<td>8</td>
<td>796</td>
<td>807</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>1 a</td>
<td>101</td>
<td>41</td>
<td>872</td>
<td>1,015 b</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Combined Hosts ndm</th>
<th>rate [%]</th>
<th>positivity</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agreement (Org+/Res+)</td>
<td>100.0</td>
<td>1/1</td>
<td>20.7 - 100.0</td>
</tr>
<tr>
<td>Agreement (Org+/Res-)</td>
<td>97.0</td>
<td>98/101</td>
<td>91.6 - 99.0</td>
</tr>
<tr>
<td>Agreement (Org-)</td>
<td>91.3</td>
<td>796/872</td>
<td>89.2 - 93.0</td>
</tr>
</tbody>
</table>

### B

<table>
<thead>
<tr>
<th>Combined Hosts ndm</th>
<th>Composite Comparator Result for Host Microorganism(s) + Mol. Reference (PCR/Seq.) for ndm</th>
<th>Org+/Res+</th>
<th>Org+/Res-</th>
<th>Org-</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>LRT BAL Result</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Org+/Res+</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Org+/Res-</td>
<td>0</td>
<td>170</td>
<td>37</td>
<td>207</td>
<td></td>
</tr>
<tr>
<td>Org-</td>
<td>0</td>
<td>20</td>
<td>787</td>
<td>807</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>1 a</td>
<td>190</td>
<td>824</td>
<td>1,015 b</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Combined Hosts ndm</th>
<th>rate [%]</th>
<th>positivity</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agreement (Org+/Res+)</td>
<td>100.0</td>
<td>1/1</td>
<td>20.7 - 100.0</td>
</tr>
<tr>
<td>Agreement (Org+/Res-)</td>
<td>89.5</td>
<td>170/190</td>
<td>84.3 - 93.1</td>
</tr>
<tr>
<td>Agreement (Org-)</td>
<td>95.5</td>
<td>787/824</td>
<td>93.9 - 96.7</td>
</tr>
</tbody>
</table>

- Specimens with multiple detected possible host microorganisms by culture: 1 of 1, by the composite comparator: 1 of 1.
- One invalid LRT BAL result for ndm.
- SoC reported the following possible corresponding host microorganisms for one Org+/Res+ case: K. pneumoniae/P. aeruginosa.
Table 35: Agreement rates for *vim* between LRT BAL and reference methods A (culture) and B (composite comparator) for combined possible host microorganisms: Enterobacteriaceae, *Acinetobacter* spp., *P. aeruginosa*.

<table>
<thead>
<tr>
<th>Combined Hosts/ <em>vim</em></th>
<th>Culture Result for Host Microorganism(s) + Isolate Sequencing/Marker Screening for <em>vim</em></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Org+/Res+</td>
<td>Org+/Res-</td>
</tr>
<tr>
<td>LRT BAL Result</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Org+/Res+</td>
<td>0</td>
<td>1*</td>
</tr>
<tr>
<td>Org+/Res-</td>
<td>0</td>
<td>98</td>
</tr>
<tr>
<td>Org-</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>0</td>
<td>102</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Combined Hosts/ <em>vim</em></th>
<th>rate [%]</th>
<th>positivity</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agreement (Org+/Res+)</td>
<td>NA</td>
<td>0/0</td>
<td>NA</td>
</tr>
<tr>
<td>Agreement (Org+/Res-)</td>
<td>96.1</td>
<td>98/102</td>
<td>90.3 - 98.5</td>
</tr>
<tr>
<td>Agreement (Org-)</td>
<td>91.3</td>
<td>797/873</td>
<td>89.2 - 93.0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Combined Hosts/ <em>vim</em></th>
<th>Composite Comparator Result for Host Microorganism(s) + Mol. Reference (PCR/Seq.) for <em>vim</em></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Org+/Res+</td>
<td>Org+/Res-</td>
</tr>
<tr>
<td>LRT BAL Result</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Org+/Res+</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Org+/Res-</td>
<td>0</td>
<td>170</td>
</tr>
<tr>
<td>Org-</td>
<td>0</td>
<td>20</td>
</tr>
<tr>
<td>Total</td>
<td>0</td>
<td>191</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Combined Hosts/ <em>vim</em></th>
<th>rate [%]</th>
<th>positivity</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agreement (Org+/Res+)</td>
<td>NA</td>
<td>0/0</td>
<td>NA</td>
</tr>
<tr>
<td>Agreement (Org+/Res-)</td>
<td>89.0</td>
<td>170/191</td>
<td>83.8 - 92.7</td>
</tr>
<tr>
<td>Agreement (Org-)</td>
<td>95.5</td>
<td>788/825</td>
<td>93.9 - 96.7</td>
</tr>
</tbody>
</table>

* SoC reported the following possible corresponding host microorganisms for one Org+/Res- case: *P. aeruginosa.*
Table 36: Agreement rates for *oxa*-48 between LRT BAL and reference methods A (culture) and B (composite comparator) for combined possible host microorganisms: Enterobacteriaceae.

### A

<table>
<thead>
<tr>
<th>Combined Hosts <em>oxa</em>-48</th>
<th>Culture Result for Host Microorganism(s) + Isolate Sequencing/Marker Screening for <em>oxa</em>-48</th>
<th>Org+/Res+</th>
<th>Org+/Res-</th>
<th>Org+/ No Isolate</th>
<th>Org-</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>LRT BAL Result</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Org+/Res+</td>
<td></td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Org+/Res-</td>
<td></td>
<td>0</td>
<td>51</td>
<td>13</td>
<td>47</td>
<td>111</td>
</tr>
<tr>
<td>Org-</td>
<td></td>
<td>0</td>
<td>4</td>
<td>6</td>
<td>890</td>
<td>900</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>1</td>
<td>55</td>
<td>19</td>
<td>937</td>
<td>1,012</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Combined Hosts/<em>oxa</em>-48</th>
<th>rate [%]</th>
<th>positivity</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agreement (Org+/Res+)</td>
<td>100.0</td>
<td>1/1</td>
<td>20.7 - 100.0</td>
</tr>
<tr>
<td>Agreement (Org+/Res-)</td>
<td>92.7</td>
<td>51/55</td>
<td>82.7 - 97.1</td>
</tr>
<tr>
<td>Agreement (Org-)</td>
<td>95.0</td>
<td>890/937</td>
<td>93.4 - 96.2</td>
</tr>
</tbody>
</table>

### B

<table>
<thead>
<tr>
<th>Combined Hosts <em>oxa</em>-48</th>
<th>Composite Comparator Result for Host Microorganism(s) + Mol. Reference (PCR/Seq.) for <em>oxa</em>-48</th>
<th>Org+/Res+</th>
<th>Org+/Res-</th>
<th>Org-</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>LRT BAL Result</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Org+/Res+</td>
<td></td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Org+/Res-</td>
<td></td>
<td>0</td>
<td>84</td>
<td>27</td>
<td>111</td>
</tr>
<tr>
<td>Org-</td>
<td></td>
<td>0</td>
<td>14</td>
<td>886</td>
<td>900</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>1</td>
<td>98</td>
<td>913</td>
<td>1,012</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Combined Hosts/<em>oxa</em>-48</th>
<th>rate [%]</th>
<th>positivity</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agreement (Org+/Res+)</td>
<td>100.0</td>
<td>1/1</td>
<td>20.7 - 100.0</td>
</tr>
<tr>
<td>Agreement (Org+/Res-)</td>
<td>85.7</td>
<td>84/98</td>
<td>77.4 - 91.3</td>
</tr>
<tr>
<td>Agreement (Org-)</td>
<td>97.0</td>
<td>886/913</td>
<td>95.7 - 98.0</td>
</tr>
</tbody>
</table>

---

*a Specimens with multiple detected possible host microorganisms by culture: 0 of 1, by the composite comparator: 0 of 1.

*b Four invalid LRT BAL results for *oxa*-48.

*c SoC reported the following possible corresponding host microorganisms for one Org+/Res+ case: *K. pneumoniae*/*P. aeruginosa.*
Table 37: Agreement rates for *tem* between LRT BAL and reference methods A (culture) and B (composite comparator) for *H. influenzae* as host microorganism.

### A

<table>
<thead>
<tr>
<th><em>H. influenzae</em> tem</th>
<th>Culture Result for <em>H. influenzae</em> + Isolate Sequencing/Marker Screening for <em>tem</em></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Org+/Res+</td>
</tr>
<tr>
<td>LRT BAL Result</td>
<td></td>
</tr>
<tr>
<td>Org+/Res+</td>
<td>2</td>
</tr>
<tr>
<td>Org+/Res-</td>
<td>0</td>
</tr>
<tr>
<td>Org-</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>2</td>
</tr>
</tbody>
</table>

**H. influenzae/tem** rate [%] positivity 95% CI

- Agreement (Org+/Res+): 100.0 2/2 34.2 - 100.0
- Agreement (Org+/Res-): 100.0 3/3 43.9 - 100.0
- Agreement (Org-): 95.2 958/1,006 93.7 - 96.4

### B

<table>
<thead>
<tr>
<th><em>H. influenzae</em> tem</th>
<th>Composite Comparator Result for <em>H. influenzae</em> + Mol. Reference (PCR/Seq.) for <em>tem</em></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Org+/Res+</td>
</tr>
<tr>
<td>LRT BAL Result</td>
<td></td>
</tr>
<tr>
<td>Org+/Res+</td>
<td>6</td>
</tr>
<tr>
<td>Org+/Res-</td>
<td>0</td>
</tr>
<tr>
<td>Org-</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>6</td>
</tr>
</tbody>
</table>

**H. influenzae/tem** rate [%] positivity 95% CI

- Agreement (Org+/Res+): 100.0 6/6 61.0 - 100.0
- Agreement (Org+/Res-): 87.5 14/16 64.0 - 96.5
- Agreement (Org-): 96.4 957/993 95.0 - 97.4

* One LRT BAL run with an invalid result for both *H. influenzae* and *tem*. 
Table 38: Agreement rates for mecA between LRT BAL and reference methods A (culture) and B (composite comparator) and C (phenotypic resistance as reported by AST for the culture isolate) for S. aureus as host microorganism.

<table>
<thead>
<tr>
<th>S. aureus mecA</th>
<th>Culture Result for S. aureus + Isolate Sequencing/Marker Screening for mecA</th>
<th>S. aureus/mecA rate [%]</th>
<th>positivity</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>LRT BAL Result</td>
<td>Org+/Res+</td>
<td>Org+/Res-</td>
<td>Org+/No Isolate</td>
<td>Org-</td>
</tr>
<tr>
<td>Org+/Res+</td>
<td>17</td>
<td>4</td>
<td>9</td>
<td>17</td>
</tr>
<tr>
<td>Org+/Res-</td>
<td>1</td>
<td>23</td>
<td>9</td>
<td>24</td>
</tr>
<tr>
<td>Org-</td>
<td>3</td>
<td>2</td>
<td>3</td>
<td>904</td>
</tr>
<tr>
<td>Total</td>
<td>21</td>
<td>29</td>
<td>21</td>
<td>945</td>
</tr>
</tbody>
</table>

| Agreement (Org+/Res+) | 81.0 | 17/21 | 60.0 - 92.3 |
| Agreement (Org+/Res-) | 79.3 | 23/29 | 61.6 - 90.2 |
| Agreement (Org-) | 95.7 | 904/945 | 94.2 - 96.8 |

<table>
<thead>
<tr>
<th>S. aureus mecA</th>
<th>Composite Comparator Result for S. aureus + Mol. Reference (PCR/Seq.) for mecA</th>
<th>S. aureus/mecA rate [%]</th>
<th>positivity</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>LRT BAL Result</td>
<td>Org+/Res+</td>
<td>Org+/Res-</td>
<td>Org-</td>
<td>Total</td>
</tr>
<tr>
<td>Org+/Res+</td>
<td>20</td>
<td>18</td>
<td>9</td>
<td>47</td>
</tr>
<tr>
<td>Org+/Res-</td>
<td>0</td>
<td>42</td>
<td>15</td>
<td>57</td>
</tr>
<tr>
<td>Org-</td>
<td>5</td>
<td>11</td>
<td>896</td>
<td>912</td>
</tr>
<tr>
<td>Total</td>
<td>25</td>
<td>71</td>
<td>920</td>
<td>1,016</td>
</tr>
</tbody>
</table>

| Agreement (Org+/Res+) | 80.0 | 20/25 | 60.9 - 91.1 |
| Agreement (Org+/Res-) | 59.2 | 42/71 | 47.5 - 69.8 |
| Agreement (Org-) | 97.4 | 896/920 | 96.1 - 98.2 |

<table>
<thead>
<tr>
<th>S. aureus mecA</th>
<th>Culture Result for S. aureus + and Cefoxitin/Oxacillin AST Results</th>
<th>S. aureus/MRSA status rate [%]</th>
<th>positivity</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>LRT BAL Result</td>
<td>Org+/MRSA</td>
<td>Org+/MSSA</td>
<td>Org+/No AST</td>
<td>Org-</td>
</tr>
<tr>
<td>Org+/Res+</td>
<td>23</td>
<td>6</td>
<td>1</td>
<td>17</td>
</tr>
<tr>
<td>Org+/Res-</td>
<td>1</td>
<td>27</td>
<td>5</td>
<td>24</td>
</tr>
<tr>
<td>Org-</td>
<td>3</td>
<td>4</td>
<td>1</td>
<td>904</td>
</tr>
<tr>
<td>Total</td>
<td>27</td>
<td>37</td>
<td>7</td>
<td>945</td>
</tr>
</tbody>
</table>

| Agreement (Org+/Res+) | 85.1 | 23/27 | 67.5 - 94.1 |
| Agreement (Org+/Res-) | 73.0 | 27/37 | 57.0 - 84.6 |
| Agreement (Org-) | 95.7 | 904/945 | 94.2 - 96.8 |

18 cases were determined as Org+/Res- negative by the molecular reference assay using cutoffs set to achieve an analytical sensitivity in a comparable range to LRT BAL. For 10 of these 18 cases, presence of mecA was confirmed by alternate molecular tests (PCR/sequencing).

One strain was reported by the clinical site as MRSA, although this was not supported by the provided oxacillin Kirby-Bauer zone diameter. Independent cefoxitin AST confirmed the MRSA phenotype for this strain.
B. Archived Study

Specimen Cohort: Inclusion/Exclusion Criteria, Demographics

Lavage specimens from patients, age 18 or older, suspected of a lower respiratory infection, with at least one LRT BAL panel microorganism reported positive by standard-of-care (SoC) were eligible for the archived study. Specimens were collected at 11 US clinical sites between 2015 and 2019, complemented with few specimens collected from other sites. In contrast to the prospective study, where specimens were only from hospitalized patients (inpatients), specimens from outpatients or from patients with an unknown status were also accepted. Confirmatory testing (PCR/bi-directional sequencing using two independent PCR assays per analyte) to exclude specimens that may have degraded during storage was performed for the reported SoC results prior to the study. Only specimens with at least one confirmed SoC result were included.

The archived cohort included 197 specimens from a previous study. These specimens were supplemented with 195 specimens meeting inclusion criteria that had been collected over time to achieve a total set of 392 archived study specimens.

Demographic information for specimens included into the LRT BAL archived study is described in Table 39.

Table 39: Demographic patient data for the LRT BAL archived study.

<table>
<thead>
<tr>
<th>Included Specimens</th>
<th>392</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong> a</td>
<td></td>
</tr>
<tr>
<td>male</td>
<td>198</td>
</tr>
<tr>
<td>female</td>
<td>122</td>
</tr>
<tr>
<td><strong>Age</strong> b</td>
<td></td>
</tr>
<tr>
<td>18 - 30 years</td>
<td>18</td>
</tr>
<tr>
<td>31 - 60 years</td>
<td>106</td>
</tr>
<tr>
<td>&gt; 60 years</td>
<td>190</td>
</tr>
<tr>
<td><strong>Clinical Setting</strong> c</td>
<td></td>
</tr>
<tr>
<td>ICU</td>
<td>112</td>
</tr>
<tr>
<td>ward</td>
<td>101</td>
</tr>
<tr>
<td>in-patient (not specified)</td>
<td>69</td>
</tr>
<tr>
<td>out-patient</td>
<td>32</td>
</tr>
</tbody>
</table>

a Not reported: 72 patients.
b Not reported: 78 patients.
c Not reported: 78 patients.
Reference Methods
For all archived specimens, LRT BAL Application microorganism results were compared to confirmed positive results from SoC microbiology culture (for ‘typical’ microorganism) or other SoC methods (for ‘atypical’ microorganisms) as reference. SoC culture results were reported either qualitatively or quantitatively. For quantitative cultures, a reporting threshold of $10^3$ CFU/mL or higher for mini-BAL specimens and of $10^4$ CFU/mL or higher for BAL specimens was applied, following recommendations by the Infectious Diseases Society of America (IDSA) and the American Thoracic Society (ATS).

Evaluation of collected isolates and AST results, as well as discrepant result resolution was performed as for the prospective study.

Microorganism Results – Comparison to confirmed SoC reference, PPA/NPA
LRT BAL Application results were compared to confirmed SoC results as reference (Tables 40 and 41) to determine true positives (TP), false negatives (FN), false positives (FP) and true negatives (TN) and to calculate positive percent agreements (PPA, TP / (TP + FN)) and negative percent agreements (NPA, TN / (TN + FP)), together with their two-sided 95% confidence intervals (95% CI), determined according to the Wilson score method.

Note that SoC testing for ‘atypical’ microorganisms was only performed on special request by the physician. Other specimens besides the ones collected because of a positive SoC result for any of the ‘atypical’ microorganisms, were typically not tested, and, therefore, the NPA cannot be determined.

Table 40: Archived study (N = 392), comparison to confirmed SoC results, ‘typical’ microorganisms.

<table>
<thead>
<tr>
<th>Microorganism</th>
<th>TP</th>
<th>FN</th>
<th>FP</th>
<th>TN</th>
<th>PPA [%] (95% CI)</th>
<th>NPA [%] (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acinetobacter spp.</td>
<td>18</td>
<td>0</td>
<td>3</td>
<td>371</td>
<td>100.0 (82.4 - 100.0)</td>
<td>99.2 (97.7 - 99.7)</td>
</tr>
<tr>
<td>Citrobacter freundii</td>
<td>5</td>
<td>0</td>
<td>5</td>
<td>382</td>
<td>100.0 (56.6 - 100.0)</td>
<td>98.7 (97.0 - 99.4)</td>
</tr>
<tr>
<td>Enterobacter cloacae complex</td>
<td>15</td>
<td>4</td>
<td>0</td>
<td>373</td>
<td>78.9 (56.7 - 91.5)</td>
<td>100.0 (99.0 - 100.0)</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>46</td>
<td>3</td>
<td>17</td>
<td>326</td>
<td>93.9 (83.5 - 97.9)</td>
<td>95.0 (92.2 - 96.9)</td>
</tr>
<tr>
<td>Haemophilus influenzae</td>
<td>50</td>
<td>0</td>
<td>21</td>
<td>321</td>
<td>100.0 (92.9 - 100.0)</td>
<td>93.9 (90.8 - 95.9)</td>
</tr>
<tr>
<td>Klebsiella oxytoca</td>
<td>16</td>
<td>1</td>
<td>6</td>
<td>369</td>
<td>94.1 (73.0 - 99.0)</td>
<td>98.4 (96.6 - 99.3)</td>
</tr>
<tr>
<td>Klebsiella pneumoniae *</td>
<td>29</td>
<td>2</td>
<td>10</td>
<td>351</td>
<td>93.5 (79.3 - 98.2)</td>
<td>97.2 (95.0 - 98.5)</td>
</tr>
<tr>
<td>Klebsiella variicola *</td>
<td>2</td>
<td>0</td>
<td>4</td>
<td>386</td>
<td>100.0 (34.2 - 100.0)</td>
<td>99.0 (97.4 - 99.6)</td>
</tr>
<tr>
<td>Moraxella catarrhalis</td>
<td>21</td>
<td>0</td>
<td>9</td>
<td>362</td>
<td>100.0 (84.5 - 100.0)</td>
<td>97.6 (95.5 - 98.7)</td>
</tr>
<tr>
<td>Morganella morganii</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>391</td>
<td>100.0 (20.7 - 100.0)</td>
<td>100.0 (99.0 - 100.0)</td>
</tr>
<tr>
<td>Proteus spp.</td>
<td>15</td>
<td>0</td>
<td>7</td>
<td>370</td>
<td>100.0 (79.6 - 100.0)</td>
<td>98.1 (96.2 - 99.1)</td>
</tr>
</tbody>
</table>
Pseudomonas aeruginosa | 54 | 2 | 2 | 334 | 96.4 (87.9 - 99.0) | 99.4 (97.9 - 99.8)
Serratia marcescens | 23 | 2 | 3 | 364 | 92.0 (75.0 - 97.8) | 99.2 (97.6 - 99.7)
Staphylococcus aureus | 56 | 2 | 21 | 313 | 96.6 (88.3 - 99.1) | 93.7 (90.6 - 95.9)
Stenotrophomonas maltophilia | 37 | 3 | 10 | 342 | 92.5 (80.1 - 97.4) | 97.2 (94.9 - 98.4)
Streptococcus pneumoniae | 34 | 1 | 5 | 352 | 97.1 (85.5 - 99.5) | 98.6 (96.8 - 99.4)

*K. variicola* is typically reported by culture as *K. pneumoniae*. To discriminate *K. variicola* from *K. pneumoniae*, *K. pneumoniae* strain isolates, if available, were sequenced. If no isolate was provided, sequencing was performed from specimen DNA extracts instead. Results for *K. pneumoniae* and *K. variicola* performance are calculated based on the species identified by sequencing.

Specimens with false positive LRT BAL results were analyzed with molecular assays (PCR/bi-directional sequencing) using specimen DNA extracts for presence or absence of microorganisms. Presence of microorganisms was confirmed in 3 of 3 cases for *Acinetobacter* spp., 4 of 5 cases for *C. freundii* (one confirmed case was reported as *C. youngae* by SoC), 15 of 17 cases for *E. coli*, 17 of 21 cases for *H. influenzae*, 6 of 6 cases for *K. oxytoca*, 7 of 10 cases for *K. pneumoniae*, 2 of 4 cases for *K. variicola*, 8 of 9 cases for *M. catarrhalis*, 6 of 7 cases for *Proteus* spp., 2 of 2 cases for *P. aeruginosa*, 1 of 3 cases for *S. marcescens*, 18 of 21 cases for *S. aureus*, 10 of 10 cases for *S. maltophilia*, and 4 of 5 cases for *S. pneumoniae*. For cases that were not confirmed for *H. influenzae*, sequencing results identified *H. haemolyticus* (2x), *A. aphrophilus* (2x). For all other cases, PCRs did not amplify sufficient amounts for sequencing.

Three of the four specimens that were FN for *E. cloacae* complex contained multiple host microorganisms identified by culture, and/or LRT BAL. For one specimen, *Klebsiella oxytoca* was additionally reported by both LRT BAL and culture. For the two other specimens, *Proteus* spp. or *E. coli*, respectively, were additionally reported by LRT BAL only.

Table 41: Archived study (N = 392), comparison to confirmed SoC results, ‘atypical’ microorganisms.

<table>
<thead>
<tr>
<th>Microorganism</th>
<th>TP</th>
<th>FN</th>
<th>add. pos.</th>
<th>add. neg.</th>
<th>PPA [%] (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlamydia pneumoniae</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>392</td>
<td>NA</td>
</tr>
<tr>
<td>Legionella pneumophila</td>
<td>17</td>
<td>2</td>
<td>0</td>
<td>373</td>
<td>89.5 (68.6 - 97.1)</td>
</tr>
<tr>
<td>Mycoplasma pneumoniae</td>
<td>5</td>
<td>1</td>
<td>3</td>
<td>383</td>
<td>83.3 (43.7 - 97.0)</td>
</tr>
<tr>
<td>Pneumocystis jirovecii</td>
<td>16</td>
<td>3</td>
<td>13</td>
<td>360</td>
<td>84.2 (62.4 - 94.5)</td>
</tr>
</tbody>
</table>

For all archived specimens, true positive and false negative LRT BAL results were stratified by the semi-quantitative result reported by qualitative SoC culture (categories: rare, few, moderate, numerous) or by quantitative SoC culture (categories: 103 - < 104, 104 - < 105, 105 - < 106, > 106, in CFU/mL) as shown in Table 42.
Table 42: Archived study, comparison to confirmed SoC results, stratification by qualitative or quantitative SoC culture result.

<table>
<thead>
<tr>
<th>Category</th>
<th>Qualitative Culture Result</th>
<th>Quantitative Culture Result</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>TP</td>
</tr>
<tr>
<td><strong>Acinetobacter spp.</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>rare</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>few</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>moderate</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>numerous</td>
<td>3</td>
<td>3</td>
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<td></td>
</tr>
<tr>
<td><strong>Citrobacter freundii</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td><strong>Enterobacter cloacae complex</strong></td>
<td></td>
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<td></td>
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<tr>
<td><strong>Escherichia coli</strong></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Haemophilus influenzae</strong></td>
<td></td>
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<td></td>
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<td></td>
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<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Klebsiella oxytoca</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
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<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Klebsiella pneumoniae</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td><strong>Klebsiella varicola</strong></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Moraxella catarrhalis</strong></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Morganella morganii</strong></td>
<td></td>
<td></td>
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<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Proteus spp.</strong></td>
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<tr>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Pseudomonas aeruginosa</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Serratia marcescens</strong></td>
<td></td>
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</tr>
<tr>
<td></td>
<td></td>
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<tr>
<td></td>
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<tr>
<td>Category</td>
<td>Total</td>
<td>TP</td>
</tr>
<tr>
<td>-----------</td>
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<td>-----</td>
</tr>
<tr>
<td>few</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>moderate</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>numerous</td>
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<td>2</td>
</tr>
<tr>
<td>rare</td>
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<td>5</td>
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<tr>
<td>few</td>
<td>14</td>
<td>13</td>
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<tr>
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<td>18</td>
<td>16</td>
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<tr>
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</tr>
<tr>
<td>numerous</td>
<td>11</td>
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</table>

<table>
<thead>
<tr>
<th>Category</th>
<th>Total</th>
<th>TP</th>
<th>FN</th>
<th>PPA [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>10^4 - &lt; 10^5</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>100.0</td>
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</tr>
<tr>
<td>&gt; 10^6</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td>10^4 - &lt; 10^5</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td>10^5 - &lt; 10^6</td>
<td>6</td>
<td>6</td>
<td>0</td>
<td>100.0</td>
</tr>
<tr>
<td>&gt; 10^6</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td>10^4 - &lt; 10^5</td>
<td>4</td>
<td>4</td>
<td>0</td>
<td>100.0</td>
</tr>
<tr>
<td>10^5 - &lt; 10^6</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>100.0</td>
</tr>
<tr>
<td>&gt; 10^6</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td>10^4 - &lt; 10^5</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td>10^5 - &lt; 10^6</td>
<td>6</td>
<td>6</td>
<td>0</td>
<td>100.0</td>
</tr>
<tr>
<td>&gt; 10^6</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>100.0</td>
</tr>
</tbody>
</table>

* One Acinetobacter spp., 4 E. cloacae complex, 7. E. coli, 4 H. influenzae, 4 K. oxytoca, 5 K. pneumoniae, 1 M. catarrhalis, 2 Proteus spp., 11 P. aeruginosa, 4 S. marcescens, 9 S. aureus, 3 S. maltophilia and 1 S. pneumoniae case were reported as positive by SoC culture without qualitative or quantitative results, and were therefore not included in this table.

**Antibiotic Resistance Markers**

Antibiotic resistance markers reported by LRT BAL for the archived study are listed in Table 43. Note that antibiotic resistance markers are only reported and displayed on the Unyvero results screen, if a corresponding host microorganism was simultaneously detected. Results for ctx-M, kpc, ndm, and vim are reported for LRT BAL positive specimens for Enterobacteriaceae, Acinetobacter spp., and P. aeruginosa (N = 212); results for oxa-48 are reported for LRT BAL positive specimens for Enterobacteriaceae (N = 166); results for oxa-23, oxa-24, and oxa-58 are reported for LRT BAL positive specimens for Acinetobacter spp. (N = 21); results for tem are reported for LRT BAL positive specimens for H. influenzae (N = 71); and results for mecA are reported for LRT BAL positive specimens for S. aureus (N = 77). Only specimens with antibiotic resistance markers reported positive by LRT BAL were tested for such markers by molecular reference assays (PCR/sequencing).
Table 43: Archived study (N = 392), listing of antibiotic resistance marker results as reported by LRT BAL.

<table>
<thead>
<tr>
<th>Antibiotic Resistance Marker</th>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>ctx-M (N = 212)</td>
<td>14</td>
<td>198</td>
</tr>
<tr>
<td>kpc (N = 212)</td>
<td>2</td>
<td>210</td>
</tr>
<tr>
<td>mecA (N = 77)</td>
<td>44</td>
<td>33</td>
</tr>
<tr>
<td>ndm (N = 212)</td>
<td>0</td>
<td>212</td>
</tr>
<tr>
<td>oxa-23 (N = 21)</td>
<td>4</td>
<td>17</td>
</tr>
<tr>
<td>oxa-24 (N = 21)</td>
<td>3</td>
<td>18</td>
</tr>
<tr>
<td>oxa-48 (N = 166)</td>
<td>0</td>
<td>166</td>
</tr>
<tr>
<td>oxa-58 (N = 21)</td>
<td>1</td>
<td>20</td>
</tr>
<tr>
<td>tem (N = 71)</td>
<td>24</td>
<td>47</td>
</tr>
<tr>
<td>vim (N = 212)</td>
<td>0</td>
<td>212</td>
</tr>
</tbody>
</table>

* Specimens with false positive LRT BAL results were analyzed with molecular assays (PCR/bi-directional sequencing) using specimen DNA extracts for presence or absence of microorganisms: presence of microorganisms was confirmed in 14 of 14 cases for ctx-M, 2 of 2 cases for kpc, 34 of 44 cases for mecA, 4 of 4 cases for oxa-23, 3 of 3 cases for oxa-24, 1 of 1 case for oxa-58, and 22 of 24 cases for tem. For all other cases, PCRs did not amplify sufficient amounts for sequencing.

Correlation of Detected Antibiotic Resistance Markers to Strain Genotypes and Phenotypes

As described in the previous sections, isolates that had been collected for most of the prospective and part of archived study specimens were screened for presence or absence of antibiotic resistance markers of the LRT BAL panel. Furthermore, corresponding AST results were collected to predict resistance phenotypes of such isolates using one or more of the drug assays listed in Table 44. AST results were reported as MIC values or zone diameters (for Kirby-Bauer tests). Strain phenotypes across all test sites were standardized according to breakpoints listed in CLSI guidance M100S (Performance Standards for Antimicrobial Susceptibility Testing, 26th Edition 2016). ‘Intermediate’ calls were regarded as ‘resistant’ calls for this study. For the analysis, any strain was regarded as ‘resistant’ if at least one of the corresponding drugs resulted in an ‘intermediate’ or ‘resistant’ call. Any strain was regarded as ‘susceptible’ if a ‘sensitive’ call was obtained for all applicable tested drugs.
Table 44: AST assays used for evaluation of antibiotic resistance markers detected by LRT BAL.

<table>
<thead>
<tr>
<th>Antibiotic Resistance Marker(s)</th>
<th>Associated Resistance</th>
<th>AST Assay</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>tem</em></td>
<td>penicillins</td>
<td><em>H. influenzae</em>: ampicillin, cefinase</td>
</tr>
<tr>
<td><em>ctx-M</em></td>
<td>3rd generation cephalosporins, cefepime</td>
<td>Enterobacteriaceae: cefotaxime, ceftazidime, ceftriaxone</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>Acinetobacter spp.</em>: cefotaxime, ceftazidime, ceftriaxone, cefepime</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>P. aeruginosa</em>: cefazidine, cefepime</td>
</tr>
<tr>
<td><em>kpc, ndm, oxa-48, vim</em></td>
<td>carabapenems</td>
<td>Enterobacteriaceae: meropenem, ertapenem, imipenem</td>
</tr>
<tr>
<td><em>kpc, ndm, oxa-23, oxa-24, oxa-58, vim</em></td>
<td>carabapenems</td>
<td>Acinetobacter spp.: meropenem, imipenem</td>
</tr>
<tr>
<td><em>kpc, ndm, vim</em></td>
<td>carabapenems</td>
<td><em>P. aeruginosa</em>: meropenem, imipenem</td>
</tr>
<tr>
<td><em>mecaA</em></td>
<td>oxacillin/cefoxitin</td>
<td><em>S. aureus</em>: oxacillin, cefoxitin</td>
</tr>
</tbody>
</table>

Antibiotic resistance markers reported by LRT BAL were correlated to available isolates for:

1. Genotypic agreement of reported antibiotic resistance markers to presence of such markers in cultured isolates for a specific specimen.

2. Phenotypic agreement of reported antibiotic resistance markers with associated phenotypic culture results to provided isolates as determined by antimicrobial susceptibility tests (AST).

Note that antibiotic resistance marker results are only reported by the LRT BAL Application if a corresponding host microorganism is simultaneously reported. Otherwise, such results are masked on the Unyvero results screen. Antibiotic resistance marker results reported together with a corresponding host microorganism may not be linked to this organism, but may have originated from other on-panel or off-panel microorganisms, e.g., *mecaA* may not only originate from *S. aureus*, but also originate from coagulase-negative Staphylococci present in respiratory flora; *tem* may not only originate from *H. influenzae*, but also from other on-panel or off-panel Enterobacteriaceae. If multiple corresponding microorganisms are simultaneously reported for a certain antibiotic resistance marker, one or more than one of these microorganisms could be the host of such marker.

Genotypic and phenotypic agreements were evaluated for all relevant resistance phenotypes including all applicable specimens from the prospective and archived study combined (Tables 45 to 49).
**Oxacillin/Cefoxitin Resistance for *S. aureus* (**mecA**)**

Table 45: Correlation of positive **mecA** results reported by LRT BAL for the prospective (‘p’) or archived (‘a’) study to available *S. aureus* isolates (genotypic agreement, ‘yes’: presence of **mecA** confirmed by sequencing of isolate, ‘no’: **mecA** not confirmed, ‘not prov.’: no isolate provided) and to AST results indicating oxacillin/cefoxitin resistance for isolates with confirmed **mecA** (phenotypic agreement; R: resistant phenotype, S: sensitive phenotype, NA: AST results not reported).

<table>
<thead>
<tr>
<th># Cases</th>
<th>LRT BAL Result (relevant hosts only)</th>
<th>SoC Result (relevant hosts only)</th>
<th>Genotypic Agreement (for available isolates)</th>
<th>Phenotypic Agreement (for isolates with conf. <strong>mecA</strong>)</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>total</td>
<td>p</td>
<td>a</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>17</td>
<td>4</td>
<td><em>S. aureus</em></td>
<td><em>S. aureus</em></td>
<td>yes</td>
</tr>
<tr>
<td>4</td>
<td>4</td>
<td>-</td>
<td><em>S. aureus</em></td>
<td><em>S. aureus</em></td>
<td>no</td>
</tr>
</tbody>
</table>

* One prospective strain was reported by the clinical site as MRSA, although this was not supported by the provided oxacillin Kirby-Bauer zone diameter. An independent cefoxitin AST confirmed the MRSA phenotype for this strain. For another archived strain, no AST results were reported by the clinical site. The MRSA phenotype was determined by an independent cefoxitin AST instead.

**Penicillin Resistance for *H. influenzae** (**tem**)**

Table 46: Correlation of positive **tem** results reported by LRT BAL for the prospective (‘p’) or archived (‘a’) study to available *H. influenzae* isolates (genotypic agreement, ‘yes’: presence of **tem** confirmed by sequencing of isolate, ‘no’: **tem** not confirmed, ‘not prov.’: no isolate provided) and to AST results indicating penicillin resistance for isolates with confirmed **tem** (phenotypic agreement; R: resistant phenotype, S: sensitive phenotype, NA: AST results not reported).

<table>
<thead>
<tr>
<th># Cases</th>
<th>LRT BAL Result (relevant hosts only)</th>
<th>SoC Result (relevant hosts only)</th>
<th>Genotypic Agreement (for available isolates)</th>
<th>Phenotypic Agreement (for isolates with conf. <strong>tem</strong>)</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>total</td>
<td>p</td>
<td>a</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>2</td>
<td>2</td>
<td><em>H. influenzae</em></td>
<td><em>H. influenzae</em></td>
<td>yes</td>
</tr>
</tbody>
</table>

**510(k) Summary – LRT BAL Application K191967 Rev 3.0**
Third Generation Cephalosporin Resistance for Enterobacteriaceae, Acinetobacter spp., and *P. aeruginosa* (ctx-M)

Table 47: Correlation of positive *ctx*-M results reported by LRT BAL for the prospective (‘p’) or archived (‘a’) study to available isolates of Enterobacteriaceae, *Acinetobacter* spp., or *P. aeruginosa* (genotypic agreement, ‘yes’: presence of *ctx*-M confirmed by sequencing of isolate, ‘no’: *ctx*-M not confirmed, ‘not prov.’: no isolate provided) and to AST results indicating third generation cephalosporin resistance for isolates with confirmed *ctx*-M (phenotypic agreement; R: resistant phenotype, S: sensitive phenotype, NA: AST results not reported).

| Genotypic Agreement for Specimens with at Least One Available Isolate: 5/8, 62.5% (95% CI: 30.6 - 86.3) |
| Phenotypic Agreement for Isolates with Confirmed Marker: 4/4, 100.0% (95% CI: 51.0 - 100.0) |

<table>
<thead>
<tr>
<th>Study</th>
<th>LRT BAL Result (relevant hosts only)</th>
<th>SoC Result (relevant hosts only)</th>
<th>Genotypic Agreement (for available isolates)</th>
<th>Phenotypic Agreement (for isolates with conf. <em>ctx</em>-M)</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>p</td>
<td><em>Acinetobacter</em> spp. -</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>p</td>
<td><em>E. coli</em></td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>p</td>
<td><em>K. pneumoniae</em></td>
<td><em>K. pneumoniae</em></td>
<td>yes R</td>
<td></td>
<td></td>
</tr>
<tr>
<td>p</td>
<td><em>P. aeruginosa</em></td>
<td><em>P. aeruginosa</em></td>
<td>no</td>
<td></td>
<td></td>
</tr>
<tr>
<td>p</td>
<td><em>K. pneumoniae</em></td>
<td><em>K. pneumoniae</em></td>
<td>yes R</td>
<td></td>
<td></td>
</tr>
<tr>
<td>p</td>
<td><em>P. aeruginosa</em></td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>p</td>
<td><em>E. coli</em></td>
<td><em>E. coli</em></td>
<td>yes R</td>
<td></td>
<td></td>
</tr>
<tr>
<td>p</td>
<td><em>P. aeruginosa</em></td>
<td>-</td>
<td>-</td>
<td></td>
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</tr>
<tr>
<td>p</td>
<td><em>E. coli</em></td>
<td><em>E. coli</em></td>
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<td>R</td>
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</tr>
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<td><em>Acinetobacter</em> spp. -</td>
<td>-</td>
<td>-</td>
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<td></td>
</tr>
<tr>
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</tr>
<tr>
<td>p</td>
<td><em>K. pneumoniae</em></td>
<td><em>K. pneumoniae</em></td>
<td>(not. prov.) R</td>
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</tr>
<tr>
<td>p</td>
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<tr>
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<tr>
<td>p</td>
<td><em>K. pneumoniae</em></td>
<td><em>K. pneumoniae</em></td>
<td>(not. prov.) R</td>
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<td>(not. prov.) R</td>
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<tr>
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<td><em>P. aeruginosa</em></td>
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Carbapenem Resistance for Enterobacteriaceae, Acinetobacter spp., and P. aeruginosa (kpc, ndm, oxa-48, vim)

Table 48: Correlation of positive results for kpc, ndm, vim reported by LRT BAL for the prospective (‘p’) or archived (‘a’) study to available isolates of Enterobacteriaceae, Acinetobacter spp., or P. aeruginosa, or positive results for oxa-48 to available Enterobacteriaceae isolates (genotypic agreement, ‘yes’: presence of any of these markers confirmed by sequencing, ‘no’: presence not confirmed, ‘not prov.’: no isolate provided) and to AST results indicating carbapenem resistance for isolates with confirmed marker (phenotypic agreement; R: resistant phenotype, S: sensitive phenotype, NA: AST results not reported).

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<th>Marker</th>
<th>LRT BAL Result (relevant hosts only)</th>
<th>SoC Result (relevant hosts only)</th>
<th>Genotypic Agreement (for available isolates)</th>
<th>Phenotypic Agreement (for isolates with conf. marker)</th>
<th>Comment</th>
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<td></td>
<td>P. aeruginosa</td>
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<tr>
<td>p</td>
<td>ndm, oxa-48</td>
<td>Acinetobacter spp.</td>
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<td>E. coli</td>
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<td></td>
<td></td>
<td>K. pneumoniae</td>
<td></td>
<td>yes (both)</td>
<td>R</td>
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<td>P. aeruginosa</td>
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<tr>
<td>p</td>
<td>kpc</td>
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<tr>
<td>p</td>
<td>vim</td>
<td>Proteus spp.</td>
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<td>P. aeruginosa</td>
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a For K. pneumoniae, SoC reported a concentration < 10³ CFU/mL (considered a negative, ‘subclinical’ result below the reporting threshold for mini-BAL specimens).
Table 49: Correlation of positive results for oxa-23, oxa-24, oxa-58, reported by LRT BAL for the prospective (‘p’) or archived (‘a’) study to available Acinetobacter spp. isolates (genotypic agreement, ‘yes’: presence of any of these markers confirmed by sequencing, ‘no’: presence not confirmed, ‘not prov.’: no isolate provided) and to AST results indicating carbapenem resistance for isolates with confirmed marker (phenotypic agreement; R: resistant phenotype, S: sensitive phenotype, NA: AST results not reported).

<table>
<thead>
<tr>
<th>Study</th>
<th>Marker</th>
<th>LRT BAL Result (relevant hosts only)</th>
<th>SoC Result (relevant hosts only)</th>
<th>Genotypic Agreement (for available isolates)</th>
<th>Phenotypic Agreement (isolates with conf. marker)</th>
<th>Comment</th>
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</thead>
<tbody>
<tr>
<td>p</td>
<td>oxa-23</td>
<td>Acinetobacter spp.</td>
<td>Acinetobacter spp.</td>
<td>yes</td>
<td>R</td>
<td>-</td>
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<tr>
<td>a</td>
<td>oxa-23</td>
<td>Acinetobacter spp.</td>
<td>Acinetobacter spp.</td>
<td>yes</td>
<td>R</td>
<td>-</td>
</tr>
<tr>
<td>p</td>
<td>oxa-24</td>
<td>Acinetobacter spp.</td>
<td>Acinetobacter spp.</td>
<td>yes</td>
<td>R</td>
<td>-</td>
</tr>
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<td>a</td>
<td>oxa-23</td>
<td>Acinetobacter spp.</td>
<td>Acinetobacter spp.</td>
<td>yes</td>
<td>R</td>
<td>-</td>
</tr>
<tr>
<td>p</td>
<td>oxa-24</td>
<td>Acinetobacter spp.</td>
<td>Acinetobacter spp.</td>
<td>yes</td>
<td>R</td>
<td>-</td>
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</tbody>
</table>

* For one prospective strain, a resistant phenotype to meropenem was reported by the clinical site, although this was not supported by the provided Kirby-Bauer zone diameter. Independent AST for meropenem and imipenem confirmed resistance to carbapenems for this strain.

C. Contrived Study

The clinical performance evaluation of rare LRT BAL analytes was supplemented by a contrived study, i.e., by testing artificial clinical specimens that were prepared by spiking pooled microorganisms at concentrations close to their respective analyte LoD or at clinically relevant concentrations into unique negative lavage specimens. LRT BAL microorganisms, for which, due to limited specimen numbers, a PPA of 90% or higher with a lower bound of the two-sided 95% confidence interval of 80% or higher was not demonstrated for the clinical performance evaluation using archived specimens, were selected for contrived specimen testing (C. pneumoniae, C. freundii, E. cloacae complex, K. oxytoca, K. pneumoniae, K. variicola, L. pneumophila, M. morganii, M. pneumoniae, P. jirovecii, Proteus spp., S. marcescens). In addition, all low prevalence LRT BAL antibiotic resistance markers (ctx-M, kpc, ndm, oxa-23, oxa-24, oxa-48, oxa-58, vim) were also included. For each target analyte a total of 60 contrived specimens with up to five different spiked reference strains was tested at a low concentration (2x LoD, 30 specimens) and at two moderate concentrations (3.5x LoD and 5x LoD, 15 specimens each) spanning the clinically relevant concentration range. For P. jirovecii, a positive clinical specimen was used for spiking, and all 60 contrived specimens were tested at a 2x LoD concentration.
Agreement rates to the expected results were determined for each target analyte and stratified by actual test concentrations. Tables 50 and 51 show agreement rates for expected positive results (positive results / expected positive results) and expected negative results (negative results / number of expected negative results) together with two-sided 95% confidence intervals (95% CI) for included LRT BAL microorganisms or antibiotic resistance markers, respectively.

Table 50: Contrived study results for targeted LRT BAL microorganism analytes.

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<th>%</th>
<th>95% CI</th>
<th># Neg./# Exp.</th>
<th>%</th>
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### Agreement with Expected Results

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<th>95% CI</th>
<th># Neg./ # Exp.</th>
<th>%</th>
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*Serratia marcescens* 59/60 98.3 91.1 - 99.7 180/180 100.0 97.9 - 100.0

8.0 x 10^4/2x LoD 29/30 96.7 83.3 - 99.4

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*Morganella morganii* strains ATCC 25829 and DSM-46262 strains were retested with pooled negative BAL matrix at 2x LoD both showing 10/10 results.

*Mycoplasma pneumoniae* strains ATCC 29085 and ATCC 49894 were retested with pooled negative BAL matrix at 2x LoD showing 19/20 or 18/20 positive results, respectively. For three of four unexpected negative cases of ATCC 29085, used unique matrices correlated with reduced signals or false negative results also for other analytes and therefore such failures may be matrix-related.

### Table 51: Contrived study results for targeted LRT BAL antibiotic resistance marker analytes.

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### Agreement with Expected Results

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For other LRT BAL panel analytes not evaluated in the contrived study, the following agreement rates with the expected negative result were observed: 120/120 (100.0%, 95% CI 96.9 - 100.0) for *Acinetobacter* spp., 200/200 (100.0%, 95% CI 98.1 - 100.0) for *E. coli*, 228/228 (100.0%, 95% CI 98.3 - 100.0) for *H. influenzae*, 232/232 (100.0%, 95% CI 98.4 - 100.0) for mecA, 239/239 (100.0%, 95% CI 98.4 - 100.0) for *M. catarrhalis*, 208/208 (100.0%, 95% CI 98.2 - 100.0) for *P. aeruginosa*, 179/180 (99.4%, 95% CI 96.9 - 99.9) for *S. aureus*, 240/240 (100.0%, 95% CI 98.4 - 100.0) for *S. maltophilia*, 239/240 (99.6%, 95% CI 97.7 - 99.9) for *S. pneumoniae*, and 82/82 (100%, 95% CI 95.5 - 100.0) for tem.

### Expected Values

Expected values were determined for the prospective study cohort with 1,016 evaluable BAL specimens collected from hospitalized patients suspected for lower respiratory tract infection at nine US sites between June 2015 and July 2016. The LRT BAL Application reported 363 specimens with at least one positive LRT BAL panel microorganism, including 113 specimens with multi-detections of two or more LRT BAL panel microorganisms.

Table 52 lists expected values for microorganisms; Tables 53 and 54 list expected values for antibiotic resistance markers of the LRT BAL panel (for all specimens and stratified for each host microorganism). Note that antibiotic resistance markers are reported by LRT BAL only for specimens positive for a corresponding host microorganism.
Table 52: Expected values of LRT BAL panel microorganisms as reported for the prospective study stratified by all specimens (N = 1,016), as well as by single-detection (N = 250) or multi-detection specimens (N = 113). Expected value rates are given as percentage of 1,016 prospective study specimens.

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<th>Microorganism</th>
<th># Spec.</th>
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Table 53: Expected values of LRT BAL panel antibiotic resistance markers as determined by the LRT BAL Application for the prospective study.

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| ctx-M                        | 9       | 0.9%
| kpc                          | 4       | 0.4%
| mecA                         | 47      | 4.6%
| ndm                          | 1       | 0.1%
| oxa-23                       | 3       | 0.3%
| oxa-24                       | 4       | 0.4%
| oxa-48                       | 1       | 0.1%
| oxa-58                       | 0       | 0.0%
| tem                          | 16      | 1.6%
| vim                          | 1       | 0.1%
Table 54: Expected values of LRT BAL panel antibiotic resistance markers, stratified by reported host microorganism.

<table>
<thead>
<tr>
<th>Total reported multi host detections</th>
<th>ctx-M</th>
<th>kpc</th>
<th>ndm</th>
<th>oxa-23</th>
<th>oxa-24</th>
<th>oxa-48</th>
<th>oxa-58</th>
<th>vim</th>
<th>tem</th>
<th>mecA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>9</td>
<td>4</td>
<td>1</td>
<td>3</td>
<td>4</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>16</td>
<td>47</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>4</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>-</td>
<td>1</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Acinetobacter spp.</strong> (N = 21)</td>
<td>2/21</td>
<td>2/21</td>
<td>1/21</td>
<td>4/21</td>
<td>3/21</td>
<td>4/21</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>9.5%</td>
<td>9.5%</td>
<td>4.8%</td>
<td>14.3%</td>
<td>19.0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Citrobacter freundii</strong> (N = 4)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
<td>-</td>
</tr>
<tr>
<td><strong>Enterobacter cloacae complex</strong> (N = 20)</td>
<td>-</td>
<td>1/20</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
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</tr>
<tr>
<td><strong>Escherichia coli</strong> (N = 47)</td>
<td>8/47</td>
<td>1/47</td>
<td>1/47</td>
<td>1/47</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>17.0%</td>
<td>2.1%</td>
<td>2.1%</td>
<td>2.1%</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
<td>-</td>
</tr>
<tr>
<td><strong>Klebsiella oxytoca</strong> (N = 14)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
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<td>-</td>
</tr>
<tr>
<td><strong>Klebsiella pneumoniae</strong> (N = 30)</td>
<td>4/30</td>
<td>4/30</td>
<td>1/30</td>
<td>1/30</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>13.3%</td>
<td>13.3%</td>
<td>3.3%</td>
<td>3.3%</td>
<td>-</td>
<td>-</td>
<td>-</td>
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</tr>
<tr>
<td><strong>Klebsiella variicola</strong> (N = 2)</td>
<td>-</td>
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<td>-</td>
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<td>-</td>
<td>-</td>
<td></td>
<td></td>
<td>-</td>
</tr>
<tr>
<td><strong>Morganella morganii</strong> (N = 3)</td>
<td>1/3</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<td>-</td>
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<td>-</td>
</tr>
<tr>
<td></td>
<td>33.3%</td>
<td>-</td>
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<td>-</td>
<td>-</td>
<td>-</td>
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<td></td>
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</tr>
<tr>
<td><strong>Proteus spp.</strong> (N = 10)</td>
<td>2/10</td>
<td>-</td>
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<td>-</td>
<td>1/10</td>
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<tr>
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<td>-</td>
<td>-</td>
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<td>10.0%</td>
<td></td>
<td></td>
<td></td>
<td>-</td>
</tr>
<tr>
<td><strong>Pseudomonas aeruginosa</strong> (N = 112)</td>
<td>7/112</td>
<td>2/112</td>
<td>1/112</td>
<td>1/112</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>6.3%</td>
<td>1.8%</td>
<td>0.9%</td>
<td>0.9%</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
<td>-</td>
</tr>
<tr>
<td><strong>Serratia marcescens</strong> (N = 17)</td>
<td>2/17</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
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</tr>
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<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
<td>-</td>
</tr>
<tr>
<td><strong>Haemophilus influenzae</strong> (N = 56)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<td>-</td>
</tr>
<tr>
<td></td>
<td>16/56</td>
<td>28.6%</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
<td>-</td>
</tr>
<tr>
<td><strong>Staphylococcus aureus</strong> (N = 104)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>47/104</td>
<td>45.2%</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<td>-</td>
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<td>-</td>
</tr>
</tbody>
</table>
Specimens reported as negative, as single detection, or as multi-detection, together with reported antibiotic resistance markers are listed in Table 55. For example, for eight specimens, LRT BAL reported a single detection of Acinetobacter spp. For four of these specimens (50%), an antibiotic resistance marker indicating a possible carbapenem resistance was simultaneously reported, while for four other specimens, no corresponding antibiotic resistance marker was reported. Similarly, for 60 specimens, LRT BAL reported a single detection of S. aureus. For 32 of these specimens (53%), a mecA was simultaneously reported, while for the remaining 28 specimens, mecA was not reported.

Table 55: Rates of negative, single detection and multi-detection specimens together with reported antibiotic resistance markers as detected by the LRT BAL Application for the prospective study (N = 1,016 specimens). Note that resistance marker oxa-58 was not detected in the prospective study cohort.

<table>
<thead>
<tr>
<th>Microorganism Result</th>
<th># cases</th>
<th>Antibiotic Resistance Marker Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative</td>
<td>653 (64.3%)</td>
<td>tem ctx-M kpc oxa-23 oxa-24 mecA ctx-M mecA tem, vim ctx-M mecA, oxa-23 ctx-M ndm, oxa-48 kpc mecA, oxa-24</td>
</tr>
<tr>
<td>Single Organism Detected</td>
<td>250 (24.6%)</td>
<td></td>
</tr>
<tr>
<td>Acinetobacter spp.</td>
<td>8</td>
<td>4 - - - 1 3 - - - - - - - -</td>
</tr>
<tr>
<td>Citrobacter freundii</td>
<td>1</td>
<td>1 - - - - - - - - - - - -</td>
</tr>
<tr>
<td>Enterobacter cloacae complex</td>
<td>8</td>
<td>8 - - - - - - - - - - - -</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>24</td>
<td>24 - - - - - - - - - - - -</td>
</tr>
<tr>
<td>Haemophilus influenzae</td>
<td>30</td>
<td>26 4 - - - - - - - - - - - -</td>
</tr>
<tr>
<td>Klebsiella oxytoca</td>
<td>2</td>
<td>2 - - - - - - - - - - - -</td>
</tr>
<tr>
<td>Klebsiella pneumoniae</td>
<td>9</td>
<td>9 - - - - - - - - - - - -</td>
</tr>
<tr>
<td>Legionella pneumophila</td>
<td>1</td>
<td>1 - - - - - - - - - - - -</td>
</tr>
<tr>
<td>Moraxella catarrhalis</td>
<td>4</td>
<td>4 - - - - - - - - - - - -</td>
</tr>
<tr>
<td>Mycoplasma pneumoniae</td>
<td>4</td>
<td>4 - - - - - - - - - - - -</td>
</tr>
<tr>
<td>Pneumocystis jirovecii</td>
<td>14</td>
<td>14 - - - - - - - - - - - -</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>61</td>
<td>61 - - - - - - - - - - - -</td>
</tr>
<tr>
<td>Serratia marcescens</td>
<td>5</td>
<td>5 - - - - - - - - - - - -</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>60</td>
<td>32 - - - - - 28 - - - - - -</td>
</tr>
<tr>
<td>Streptococcus pneumoniae</td>
<td>12</td>
<td>12 - - - - - - - - - - - -</td>
</tr>
<tr>
<td>Two Organisms Detected</td>
<td>78 (7.7%)</td>
<td></td>
</tr>
<tr>
<td>Acinetobacter spp., Citrobacter freundii</td>
<td>1</td>
<td>1 - - - - - - - - - - - -</td>
</tr>
<tr>
<td>Acinetobacter spp., Enterobacter cloacae complex</td>
<td>1</td>
<td>1 - - - - - - - - - - - -</td>
</tr>
<tr>
<td>Acinetobacter spp., Klebsiella pneumoniae</td>
<td>1</td>
<td>1 - - - - - - - - - - - -</td>
</tr>
<tr>
<td>Acinetobacter spp., Pseudomonas aeruginosa</td>
<td>1</td>
<td>1 - - - - - - - - - - - -</td>
</tr>
<tr>
<td>Acinetobacter spp., Stenotrophomonas maltophilia</td>
<td>1</td>
<td>1 - - - - - - - - - - - -</td>
</tr>
<tr>
<td>Citrobacter freundii, Pseudomonas aeruginosa</td>
<td>1</td>
<td>1 - - - - - - - - - - - -</td>
</tr>
<tr>
<td>Enterobacter cloacae complex, Mycoplasma pneumoniae</td>
<td>1</td>
<td>1 - - - - - - - - - - - -</td>
</tr>
<tr>
<td>Enterobacter cloacae complex, Staphylococcus aureus</td>
<td>2</td>
<td>2 - - - - - - - - - - - -</td>
</tr>
<tr>
<td>Escherichia coli, Haemophilus influenzae</td>
<td>1</td>
<td>0 1 - - - - - - - - - - - -</td>
</tr>
<tr>
<td>Escherichia coli, Klebsiella oxytoca</td>
<td>1</td>
<td>1 - - - - - - - - - - - -</td>
</tr>
<tr>
<td>Microorganism Result</td>
<td># cases</td>
<td>no</td>
</tr>
<tr>
<td>----------------------</td>
<td>---------</td>
<td>----</td>
</tr>
<tr>
<td>Escherichia coli, Klebsiella pneumoniae</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Escherichia coli, Pseudomonas aeruginosa</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Escherichia coli, Serratia marcescens</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Escherichia coli, Staphylococcus aureus</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Haemophilus influenzae, Klebsiella oxytoca</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Haemophilus influenzae, Moraxella catarrhalis</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Haemophilus influenzae, Mycoplasma pneumoniae</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Haemophilus influenzae, Pseudomonas aeruginosa</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Haemophilus influenzae, Staphylococcus aureus</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Haemophilus influenzae, Streptococcus pneumoniae</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Klebsiella oxytoca, Klebsiella pneumoniae</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Klebsiella oxytoca, Proteus spp.</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Klebsiella oxytoca, Serratia marcescens</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Klebsiella oxytoca, Stenotrophomonas maltophilia</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Klebsiella pneumoniae, Pseudomonas aeruginosa</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Klebsiella pneumoniae, Staphylococcus aureus</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Moraxella catarrhalis, Pneumocystis jiroveci</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Moraxella catarrhalis, Streptococcus pneumoniae</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Pneumocystis jiroveci, Pseudomonas aeruginosa</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Pneumocystis jiroveci, Staphylococcus aureus</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Proteus spp., Pseudomonas aeruginosa</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Proteus spp., Staphylococcus aureus</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa, Serratia marcescens</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa, Staphylococcus aureus</td>
<td>14</td>
<td>4</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa, Stenotrophomonas maltophilia</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Serratia marcescens, Staphylococcus aureus</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Staphylococcus aureus, Stenotrophomonas maltophilia</td>
<td>5</td>
<td>3</td>
</tr>
</tbody>
</table>

Three Organisms Detected **19** (1.9%)
<table>
<thead>
<tr>
<th>Microorganism Result</th>
<th># cases</th>
<th>Single Marker Detected</th>
<th>Multiple Markers Detected</th>
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</thead>
<tbody>
<tr>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>no markers</td>
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</tr>
<tr>
<td><strong>Single Marker Detected</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>tem</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ctx-M</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>kpc</td>
<td></td>
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<tr>
<td>oxa-23</td>
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<td>oxa-24</td>
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</tr>
<tr>
<td>mecA</td>
<td></td>
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<td></td>
</tr>
<tr>
<td><strong>Multiple Markers Detected</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ctx-M, mecA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ctx-M, mecA, ndm, oxa-23</td>
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</tr>
<tr>
<td>ctx-M, mecA, oxa-48, oxa-24</td>
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<tr>
<td><strong>Microorganism Result</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acinetobacter spp., Klebsiella pneumoniae, Stenotrophomonas maltophilia</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acinetobacter spp., Pseudomonas aeruginosa</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enterobacter cloacae complex, Haemophilus influenzae, Moraxella catarrhalis</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enterobacter cloacae complex, Klebsiella oxytoca, Stenotrophomonas maltophilia</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enterobacter cloacae complex, Klebsiella pneumoniae, Moraxella catarrhalis</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enterobacter cloacae complex, Klebsiella pneumoniae, Pseudomonas aeruginosa</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Escherichia coli, Haemophilus influenzae, Staphylococcus aureus</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Escherichia coli, Morganella morganii, Pseudomonas aeruginosa</td>
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<td></td>
</tr>
<tr>
<td>Escherichia coli, Pseudomonas aeruginosa</td>
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<td></td>
</tr>
<tr>
<td>Escherichia coli, Pneumocystis jirovecii, Pseudomonas aeruginosa</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Escherichia coli, Pseudomonas aeruginosa, Serratia marcescens</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Escherichia coli, Staphylococcus aureus</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haemophilus influenzae, Moraxella catarrhalis, Streptococcus pneumoniae</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Klebsiella oxytoca, Pseudomonas aeruginosa, Staphylococcus aureus</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Klebsiella oxytoca, Pseudomonas aeruginosa, Staphylococcus aureus</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Klebsiella pneumoniae, Pseudomonas aeruginosa, Stenotrophomonas maltophilia</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Klebsiella pneumoniae, Stenotrophomonas maltophilia</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proteus spp., Pseudomonas aeruginosa, Staphylococcus aureus</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pseudomonas aeruginosa, Serratia marcescens, Stenotrophomonas maltophilia</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Four Organisms Detected</strong></td>
<td>7</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Four Organisms Detected (0.7%)**

- Acinetobacter spp., Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa
- Acinetobacter spp., Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa
- Acinetobacter spp., Escherichia coli, Klebsiella pneumoniae, Stenotrophomonas maltophilia
- Acinetobacter spp., Escherichia coli,
<table>
<thead>
<tr>
<th>Microorganism Result</th>
<th># cases</th>
<th>Single Marker Detected</th>
<th>Multiple Markers Detected</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>tem</td>
<td>ctx-M</td>
</tr>
<tr>
<td>Proteus spp.,</td>
<td>1</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enterobacter cloacae complex,</td>
<td>1</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Escherichia coli,</td>
<td>1</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Klebsiella oxytoca,</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stenotrophomonas maltophilia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haemophilus influenzae,</td>
<td>1</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>Proteus spp.,</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pseudomonas aeruginosa,</td>
<td>1</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Stenotrophomonas maltophilia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Escherichia coli,</td>
<td>1</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa, Serratia marcescens, Staphylococcus aureus, Stenotrophomonas maltophilia</td>
<td>1</td>
<td>1</td>
<td>-</td>
</tr>
</tbody>
</table>

**Five Organisms Detected**

7 (0.7%)

| Acinetobacter spp., Enterobacter cloacae complex, Haemophilus influenzae, Klebsiella pneumoniae, Streptococcus pneumoniae | 1 | 1 | - | - | - | - | - | - | - | - |
| Citrobacter freundii, Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Serratia marcescens | 1 | 0 | 1 | - | - | - | - | - | - | - |
| Enterobacter cloacae complex, Escherichia coli, Klebsiella oxytoca, Klebsiella varicola, Proteus spp. | 1 | 1 | - | - | - | - | - | - | - | - |
| Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Serratia marcescens, Stenotrophomonas maltophilia | 1 | 0 | 1 | - | - | - | - | - | - | - |
| Escherichia coli, Morganella morganii, Proteus spp., Pseudomonas aeruginosa, Stenotrophomonas maltophilia | 1 | 0 | - | 1 | - | - | - | - | - | - |
| Haemophilus influenzae, Klebsiella pneumoniae, Klebsiella varicola, Proteus spp., Staphylococcus aureus | 1 | 0 | 1 | - | - | - | - | - | - | - |
| Haemophilus influenzae, Klebsiella pneumoniae, Moraxella catarrhalis, Pneumocystis jiroveci, Serratia marcescens | 1 | 1 | - | - | - | - | - | - | - | - |

**Six Organisms Detected**

2 (0.2%)

| Acinetobacter spp., Escherichia coli, Klebsiella pneumoniae, Proteus spp., Pseudomonas aeruginosa, Staphylococcus aureus | 1 | 0 | 1 | - | - | - | - | - | - | - |
| Enterobacter cloacae complex, | 1 | 0 | 1 | - | - | - | - | - | - | - |
### Antibiotic Resistance Marker Result

<table>
<thead>
<tr>
<th>Microorganism Result</th>
<th># cases</th>
<th>Single Marker Detected</th>
<th>Multiple Markers Detected</th>
</tr>
</thead>
<tbody>
<tr>
<td>H. influenzae, M. catarrhalis, M. morganii, S. aureus, S. maltophilia</td>
<td>1,016</td>
<td>938</td>
<td>15</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td>1,016</td>
<td>938</td>
</tr>
</tbody>
</table>

### 807.92 (b)(3): Conclusions from Nonclinical and Clinical Data

The conclusions drawn from the analytical and clinical data demonstrate that the device is safe and effective for its intended use.