



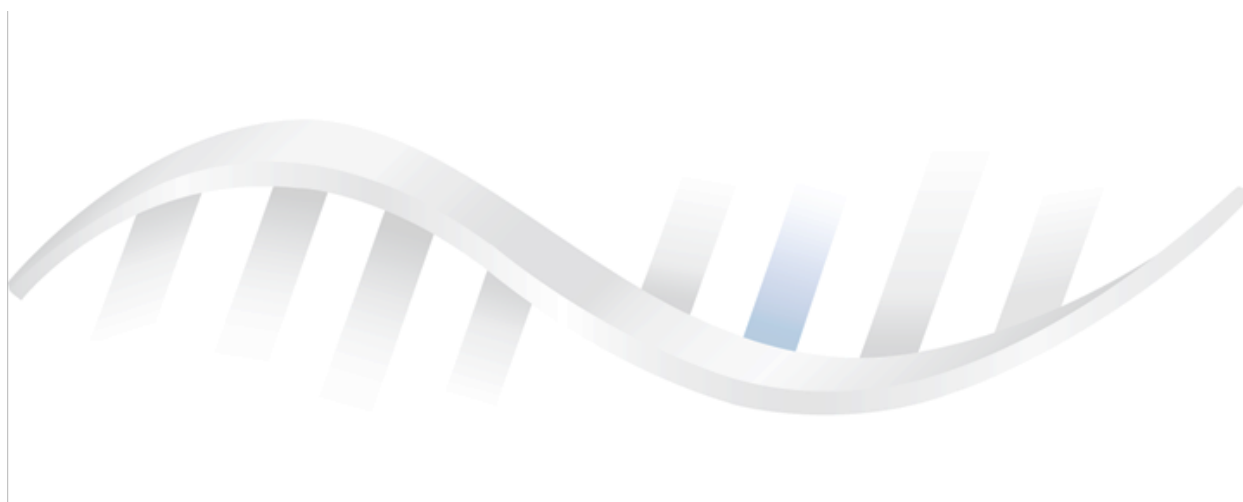
**cobas<sup>®</sup> eplex**  
**blood culture identification**  
**gram-negative (BCID-GN) panel**  
Package Insert



Rx Only

*Designed for the Patient, Optimized for the Lab<sup>®</sup>*

P/N: 09556494001



GenMark Diagnostics, Inc.  
5964 La Place Court  
Carlsbad, CA 92008  
USA  
+1 760 448 4300



EMERGO EUROPE  
Westervoortsedijk 60  
6827 AT Arnhem  
The Netherlands

**UK Responsible Person**

Emergo Consulting (UK) Limited  
c/o Cr360 –UL International  
Compass House, Vision Park Histon  
Cambridge CB24 9BZ, UK

## TABLE OF CONTENTS

Table of Contents .....	2
Intended Use .....	4
Summary and Explanation of Test .....	5
Summary of Detected Organisms .....	6
Bacteria .....	6
Antimicrobial Resistance Markers .....	10
Pan Targets .....	10
Principles of Technology .....	12
Materials Provided .....	13
Composition of Reagents .....	13
Reagent Storage, Stability and Handling .....	14
Materials Not Provided .....	14
Equipment .....	14
Consumables .....	14
Warnings and Precautions .....	14
General .....	14
Safety .....	15
Laboratory .....	15
Specimen Collection, Handling and Storage .....	16
Procedure .....	16
Procedural Notes .....	16
Detailed Procedure .....	17
Quality Control .....	18
Internal Controls .....	18
External Controls .....	18
Results .....	19
Genus and Group Assay Result Interpretation .....	19
Resistance Marker Assay Result Interpretation .....	20
Pan Assay Results .....	20
Test Reports .....	21
Detection Report .....	21
External Control Report .....	21
Summary Report .....	22
Limitations of the Procedure .....	22
Expected Values .....	23
Performance Characteristics .....	26
Clinical Performance .....	26
Comparator Method .....	26
Demographics of Clinical Samples .....	27
Clinical Performance .....	28
Genus and Group Assay Species Stratification .....	42
Resistance Gene Assay Species Stratification .....	45
Resistance Markers and Antimicrobial Resistance Susceptibility .....	54
Co-detections in Clinical Samples .....	56
Clinical Study cobas eplex instrument Performance .....	62
Analytical Performance Characteristics .....	62
Limit of Detection (LoD) .....	62
Analytical Reactivity (Inclusivity) .....	64
Predicted ( <i>in silico</i> ) Reactivity for Genus and Group Assays .....	67
Predicted ( <i>in silico</i> ) Reactivity for Resistance Markers .....	72

Analytical Specificity (Cross-Reactivity and Exclusivity).....	79
Off-panel Exclusivity .....	80
Bottle Positivity.....	82
Reproducibility .....	83
Interfering Substances and Sample Matrix Equivalency (Bottle Evaluation).....	90
Carryover and Cross-Contamination .....	93
Competitive Inhibition Study .....	93
Troubleshooting .....	94
Technical Support (United States).....	95
Technical Support (International).....	95
Glossary of Symbols .....	96
References .....	97
Patents information .....	101

## INTENDED USE

The **cobas eplex** blood culture identification gram-negative (BCID-GN) panel is a qualitative nucleic acid multiplex *in vitro* diagnostic test intended for use on the **cobas eplex** instrument for simultaneous qualitative detection and identification of multiple potentially pathogenic gram-negative bacterial organisms and select determinants associated with antimicrobial resistance in positive blood culture. In addition, the **cobas eplex** BCID-GN panel is capable of detecting several gram-positive bacteria (Pan Gram-Positive assay) and several *Candida* species (Pan *Candida* assay). The **cobas eplex** BCID-GN panel is performed directly on blood culture samples identified as positive by a continuous monitoring blood culture system and which contain gram-negative organism.

The following bacterial organisms and genes associated with antibiotic resistance are identified using the **cobas eplex** BCID-GN panel: *Acinetobacter baumannii*, *Bacteroides fragilis*, *Citrobacter*, *Cronobacter sakazakii*, *Enterobacter cloacae* complex, *Enterobacter* (non-cloacae complex), *Escherichia coli*, *Fusobacterium necrophorum*, *Fusobacterium nucleatum*, *Haemophilus influenzae*, *Klebsiella oxytoca*, *Klebsiella pneumoniae* group, *Morganella morganii*, *Neisseria meningitidis*, *Proteus*, *Proteus mirabilis*, *Pseudomonas aeruginosa*, *Salmonella*, *Serratia*, *Serratia marcescens*, *Stenotrophomonas maltophilia*, CTX-M (*bla<sub>CTX-M</sub>*), IMP (*bla<sub>IMP</sub>*), KPC (*bla<sub>KPC</sub>*), NDM (*bla<sub>NDM</sub>*), OXA (*bla<sub>OXA</sub>*) (OXA-23 and OXA-48 groups only), and VIM (*bla<sub>VIM</sub>*).

The **cobas eplex** BCID-GN panel contains assays for the detection of genetic determinants associated with resistance to antimicrobial agents including CTX-M(*bla<sub>CTX-M</sub>*), which is associated with resistance to extended spectrum beta-lactamase (ESBL)-mediated resistance to penicillins, cephalosporins, and monobactams, as well as OXA (*bla<sub>OXA</sub>*) (OXA-23 and OXA-48 groups only), KPC (*bla<sub>KPC</sub>*), and metallo-beta-lactamases IMP (*bla<sub>IMP</sub>*), VIM (*bla<sub>VIM</sub>*), and NDM (*bla<sub>NDM</sub>*), which is associated with carbapenemase-mediated resistance. The antimicrobial resistance gene detected may or may not be associated with the agent responsible for disease. Negative results for these select antimicrobial resistance assays do not indicate susceptibility, as there are multiple mechanisms of resistance in gram-negative bacteria.

The **cobas eplex** BCID-GN panel also contains targets designed to detect a broad range of organisms with a potentially misleading Gram stain result or organisms that may be missed by Gram staining altogether, for example in the case of co-infections. These include a broad Pan Gram-Positive assay (which is designed to detect *Bacillus cereus* group, *Bacillus subtilis* group, *Enterococcus*, *Staphylococcus*, and *Streptococcus*), as well as a Pan *Candida* assay, which is designed to detect four *Candida* species: *Candida albicans*, *Candida glabrata*, *Candida krusei*, and *Candida parapsilosis*.

The detection and identification of specific bacterial and fungal nucleic acids from individuals exhibiting signs and/or symptoms of bloodstream infection aids in the diagnosis of bloodstream infection when used in conjunction with other clinical information. The results from the **cobas eplex** BCID-GN panel are intended to be interpreted in conjunction with Gram stain results and should not be used as the sole basis for diagnosis, treatment, or other patient management decisions.

Negative results in the setting of a suspected bloodstream infection may be due to infection with pathogens that are not detected by this test. Positive results do not rule out co-infection with other organisms; the organism(s) detected by the **cobas eplex** BCID-GN panel may not be the definite cause of disease. Additional laboratory testing (e.g. sub-culturing of positive blood cultures for identification of organisms not detected by **cobas eplex** BCID-GN panel and for susceptibility testing, differentiation of mixed growth, and association of antimicrobial resistance marker genes to a specific organism) and clinical presentation must be taken into consideration in the final diagnosis of bloodstream infection.

## SUMMARY AND EXPLANATION OF TEST

The **cobas eplex** BCID-GN panel is an automated qualitative nucleic acid multiplex *in vitro* diagnostic test for simultaneous detection and identification of multiple potentially pathogenic gram-negative bacterial organisms and select determinants associated with antimicrobial resistance in positive blood culture. The test also detects a wide variety of gram-positive bacteria and several pathogenic *Candida* species. The test is able to detect 21 gram-negative bacterial targets and 6 resistance genes. Multiple *Candida* species are detected as well as the most relevant gram-positive organisms as summarized in **Table 1**. This test is performed on *The True Sample-to-Answer Solution*® **cobas eplex** instrument.

Gram-negative bacteria are a major cause of bacteremia, being isolated from over 60% of positive blood cultures throughout the world.<sup>1</sup> Antimicrobial resistance is common among gram-negative organisms, and multi-drug resistance is increasingly common in many species.<sup>2</sup> When involved in bacteremia, the species belonging to this group have mortality rates ranging from 20% to over 90% in some populations.<sup>3</sup>

**Table 1: Targets Detected by the cobas eplex BCID-GN panel**

Bacterial Targets	
<i>Acinetobacter baumannii</i>	<i>Klebsiella pneumoniae</i> group
<i>Bacteroides fragilis</i>	<i>Morganella morganii</i>
<i>Citrobacter</i>	<i>Neisseria meningitidis</i>
<i>Cronobacter sakazakii</i>	<i>Proteus</i>
<i>Enterobacter cloacae</i> complex	<i>Proteus mirabilis</i>
<i>Enterobacter</i> (non-cloacae complex)	<i>Pseudomonas aeruginosa</i>
<i>Escherichia coli</i>	<i>Salmonella</i>
<i>Fusobacterium necrophorum</i>	<i>Serratia</i>
<i>Fusobacterium nucleatum</i>	<i>Serratia marcescens</i>
<i>Haemophilus influenzae</i>	<i>Stenotrophomonas maltophilia</i>
<i>Klebsiella oxytoca</i>	
Antimicrobial Resistance Markers (See Table 7 For More Detail)	
CTX-M ( <i>bla</i> <sub>CTX-M</sub> )	NDM ( <i>bla</i> <sub>NDM</sub> )
IMP ( <i>bla</i> <sub>IMP</sub> )	OXA ( <i>bla</i> <sub>OXA</sub> )
KPC ( <i>bla</i> <sub>KPC</sub> )	VIM ( <i>bla</i> <sub>VIM</sub> )
Pan Targets	
Pan Gram-Positive	Pan <i>Candida</i>

Local, state, and federal rules and regulations for notification of reportable diseases are continually updated and include a number of organisms that are important for surveillance and outbreak investigations. Laboratories are responsible for following their state and/or local rules pertaining to reportable pathogens and should consult their local and/or state public health laboratories for isolate and/or clinical sample submission guidelines.

## SUMMARY OF DETECTED ORGANISMS

### Bacteria

#### ***Acinetobacter baumannii***

*Acinetobacter baumannii* is a short, rod-shaped, opportunistic bacteria which accounts for about 80% of reported *Acinetobacter* infections in humans. Those at higher risk for infection include persons with open wounds, cardiovascular disease, implanted devices, previous treatment with antimicrobials, and persons who have undergone mechanical ventilation or hemodialysis.<sup>4,5,6</sup> *Acinetobacter baumannii* is inherently resistant to multiple antibiotics including amoxicillin-clavulanic acid, ertapenem, trimethoprim, and chloramphenicol.<sup>7</sup> Isolates carrying CTX-M, IMP, KPC, NDM, OXA, and VIM resistance markers have been reported.<sup>8,9,10</sup>

#### ***Bacteroides fragilis***

*Bacteroides fragilis* is a rod-shaped, obligate anaerobe and may be a part of the normal gastrointestinal flora. It is among the most important anaerobic pathogens involved in human infection.<sup>11</sup> Since *Bacteroides fragilis* is a fastidious organism, it is difficult to isolate and often overlooked.<sup>12</sup> *Bacteroides fragilis* is commonly involved in intra-abdominal infection but is also capable of infecting the bloodstream. Mortality rates for bacteremia due to *Bacteroides fragilis* have been reported at between 24-31%. Studies have also noted rates of beta-lactam resistance as high as 90-98%.<sup>13</sup>

#### ***Citrobacter***

*Citrobacter* species are facultative anaerobic coccobacilli bacteria of the *Enterobacteriaceae* family commonly found in environmental samples as well as the human intestine. *Citrobacter* species are considered opportunistic pathogens causing diseases including diarrhea, urinary tract infections, meningitis, brain abscesses, and sepsis.<sup>14</sup> The **cobas eplex** BCID-GN panel detects *Citrobacter braakii*, *Citrobacter freundii*, *Citrobacter koseri*, *Citrobacter werkmanii*, and *Citrobacter youngae*. Antibiotic resistance markers reported in *Citrobacter* include CTX-M, IMP, KPC, NDM, OXA, and VIM.<sup>15,16,17,18,19,20</sup>

#### ***Cronobacter sakazakii* (formerly *Enterobacter sakazakii*)**

*Cronobacter* are robust bacteria able to survive for long periods of time in a variety of environments ranging from dry foods, like infant formula and dried milk, to sewer water. Though rare, *Cronobacter sakazakii* can cause diarrhea, urinary tract infections, severe bacteremia, and meningitis and is most commonly isolated from infants and the elderly.<sup>21</sup>

#### ***Enterobacter cloacae* complex**

The *Enterobacter cloacae* complex consists of several facultatively anaerobic species including *Enterobacter cloacae*, *Enterobacter asburiae*, and *Enterobacter hormaechei*, with *Enterobacter cloacae* and *Enterobacter hormaechei* being the most prevalent organisms isolated from clinical specimens.<sup>22</sup> In one study over four years and nine hospital wards, *Enterobacter cloacae* alone represented nearly 8% of all gram-negative bloodstream infections.<sup>23</sup> The **cobas eplex** BCID-GN panel *Enterobacter cloacae* complex assay detects *Enterobacter asburiae*, *Enterobacter cloacae*, *Enterobacter cloacae* subsp. *cloacae*, *Enterobacter cloacae* subsp. *dissolvens*, *Enterobacter hormaechei*, *Enterobacter hormaechei* subsp. *hormaechei*, *Enterobacter hormaechei* subsp. *oharae*, *Enterobacter hormaechei* subsp. *steigerwaltii*, and *Enterobacter ludwigii*.

***Enterobacter (non-cloacae complex)***

*Enterobacter* (non-cloacae complex) consists of a number of species including *Enterobacter aerogenes*, *Enterobacter amnigenus*, and *Enterobacter gergoviae*. These species are rod-shaped, non-spore-forming, facultative anaerobes and are important organisms in hospital acquired infections. Though considered opportunistic pathogens, members of this complex have shown the ability to infect even immunocompetent persons.<sup>24</sup> Some have been noted as intrinsically resistant to ampicillin, amoxicillin, and a number of cephalosporins.<sup>7</sup> Multi-drug resistant strains have also begun to circulate with strains of an epidemic clone being detected in many European hospitals.<sup>25</sup> Species have been isolated from drinking water, soil, and clinical specimens. Locations for infection have included the respiratory tract, wounds, blood, and feces. The **cobas eplex** BCID-GN *Enterobacter* (non-cloacae complex) assay detects *Enterobacter aerogenes*, *Enterobacter amnigenus*, and *Enterobacter gergoviae*.

***Escherichia coli***

*Escherichia coli* is a facultatively anaerobic, rod-shaped member of the family *Enterobacteriaceae* commonly found in the human gut. *Escherichia coli* has shown the ability to colonize or infect not only the gastrointestinal tract, but also the urinary tract as well as food products including meat, milk, and vegetables. Infections from *Escherichia coli* have also been traced back to contaminated water sources.<sup>26</sup> *Escherichia coli* is classified into over 150 serotypes based on surface antigens and is the gram-negative species most frequently isolated from blood culture.<sup>23</sup> *Escherichia coli* strains in the gastrointestinal tract are usually commensal, however some strains can cause severe disease, and many carry genes for antibiotic resistance.<sup>27</sup> Resistance markers CTX-M, IMP, KPC, NDM, OXA, and VIM have all been noted in clinical isolates of *Escherichia coli*.<sup>28,29,30,31,32,33</sup>

***Fusobacterium necrophorum, Fusobacterium nucleatum***

*Fusobacterium* species are non-sporulating, anaerobic organisms commonly found in oropharyngeal, gastrointestinal, and urogenital tracts.<sup>34</sup> *Fusobacterium necrophorum* and *Fusobacterium nucleatum* are the two most commonly isolated pathogens within the genus, representing up to 86% of clinical cases of *Fusobacterium* infection. *Fusobacterium* species have been implicated in pharyngotonsillitis, jugular vein septic thrombophlebitis, general sepsis, and metastatic abscesses in the lungs, liver, joints, and pleural spaces. Resistance to erythromycin and other macrolides is common.<sup>35</sup>

***Haemophilus influenzae***

*Haemophilus influenzae* is a coccobacillus that can cause infections including pneumonia, bacteremia and meningitis, with bacteremia causing up to 80% of invasive infections.<sup>36,37</sup> Persons at increased risk for infection with *Haemophilus influenzae* include those with sickle cell disease, asplenia, HIV, recipients of stem cell transplants, chemotherapy/radiation patients, and persons over 65 years of age.<sup>36,37</sup> The mortality rate for persons with invasive disease has been placed at just over 20% overall with rates approaching 30% in persons over 65 years of age.

***Klebsiella oxytoca, Klebsiella pneumoniae group***

*Klebsiella* species are non-motile, rod-shaped members of the *Enterobacteriaceae* family and are among the most common causes of community and hospital-acquired infections.<sup>38</sup> The genus *Klebsiella* consists of at least 11 species,<sup>39</sup> of which the *Klebsiella pneumoniae* group (*K. pneumoniae*, *K. quasipneumoniae*, *K. variicola*) and *Klebsiella oxytoca* species are the most common. *Klebsiella pneumoniae* and *Klebsiella oxytoca* are estimated to account for >95% and 3.5% of *Klebsiella* infections, respectively.<sup>40</sup> Both *Klebsiella pneumoniae* and *Klebsiella oxytoca* are generally resistant to multiple antibiotics,<sup>41</sup> and antibiotic susceptibility and treatment guidelines for infection are virtually identical.<sup>41</sup> Resistance markers CTX-M, IMP, KPC, NDM, OXA, and VIM have all been noted in clinical isolates of both *Klebsiella oxytoca* and *Klebsiella pneumoniae*.<sup>42,43,44,45,46,47,48,49,50,51,52,53</sup>



### ***Morganella morganii***

*Morganella morganii* is a rod-shaped member of the *Enterobacteriaceae* family commonly found in the human gastrointestinal tract as well as in the environment. It has been shown to cause infection in the urinary tract as well as in the bloodstream and is most often implicated in nosocomial, post-operative, or wound infections. *Morganella morganii* has intrinsic resistance to many beta-lactams,<sup>54</sup> while some isolates have shown the ability to produce extended spectrum beta-lactamases (ESBLs).<sup>55</sup> Resistance markers CTX-M, IMP, KPC, NDM, OXA, and VIM have all been noted in clinical isolates of *Morganella morganii*.<sup>56,57,58,59,60,61</sup>

### ***Neisseria meningitidis***

*Neisseria meningitidis* is found in the upper respiratory tract of approximately 10% of the population, with the highest rates in sub-Saharan Africa. *Neisseria meningitidis* is an opportunistic pathogen, can be spread from close person to person contact and may cause bloodstream infection as well as meningitis. Death due to meningococcal septicemia may occur in as little as a few hours.<sup>62,63</sup> Nearly all isolates recovered from patients with invasive disease are encapsulated. Meningococci obtained from healthy/asymptomatic carriers are often non-serogroupable, due either to phase variation of capsule expression, inactivation or absence of genes involved in capsule synthesis/production/transport. The capsule transport to cell surface gene, *ctrA*, is highly conserved among isolates responsible for invasive meningococcal infections.<sup>64</sup> The **cobas eplex** BCID-GN panel detects only encapsulated *N. meningitidis*.

### ***Proteus***

*Proteus* species are members of the *Enterobacteriaceae* family which consists of several species including *Proteus mirabilis*, *Proteus cibarius*, *Proteus penneri*, and *Proteus vulgaris*.<sup>65</sup> *Proteus* species are a common part of the human intestinal flora and can also be found as colonizers of the skin and oral mucosa.<sup>66</sup> They are present in soil, water, and often in seafood, and they are the most prevalent bacteria isolated from kidney stones.<sup>65</sup> *Proteus* species are a common cause of bacteremia, especially following catheter-associated urinary tract infections.<sup>67</sup> Resistance markers CTX-M, IMP, KPC, NDM, OXA, and VIM have all been noted in clinical isolates of *Proteus* species.<sup>68, 69,70,71,72,73</sup>

### ***Proteus mirabilis***

*Proteus mirabilis* is by far the most common species of *Proteus* implicated in disease, accounting for 90% of all *Proteus* infections.<sup>66</sup> Multi-drug resistant strains have been commonly isolated from patients with bacteremia, increasing mortality from ~20% to nearly 40% over susceptible strains.<sup>3</sup> Resistance markers CTX-M, IMP, KPC, NDM, OXA, and VIM have all been noted in clinical isolates of *Proteus mirabilis*.<sup>68,69,70,71,72,73</sup>

### ***Pseudomonas aeruginosa***

*Pseudomonas aeruginosa* is an important pathogen capable of causing infections in a number of organs and organ systems including the skin, eyes, ears, respiratory tract, urinary tract, gastrointestinal tract, bones, heart, bloodstream, and cerebrospinal fluid.<sup>74</sup> It has been implicated in 7-9% of all healthcare-associated infections in countries throughout the world and is frequently associated with multi-drug resistance. Mortality from *Pseudomonas aeruginosa* bloodstream infection has been reported as high as 42%.<sup>75</sup> Resistance markers CTX-M, IMP, KPC, NDM, OXA, and VIM have all been noted in clinical isolates of *Pseudomonas aeruginosa*.<sup>76,77,78</sup>



### **Salmonella**

Both typhoidal and non-typhoidal *Salmonella* species are members of the *Enterobacteriaceae* family and are major causes of invasive infections worldwide. Non-typhoidal *Salmonella* species most often manifest as severe disease in malnourished children as well as HIV and malaria-infected persons and are most prevalent in Africa.<sup>79,80</sup> Mortality rates for invasive non-typhoidal *Salmonella* (iNTS) have been reported as high as 28%,<sup>81</sup> while bacteremia from typhoidal *Salmonella* (also known as typhoid or paratyphoid fever depending on the infecting serovar) has been reported between 10-30% when left untreated and 1-4% with proper treatment.<sup>82</sup> Resistance markers CTX-M, IMP, KPC, NDM, OXA, and VIM have all been noted in clinical isolates of *Salmonella* species.<sup>83,84,85,86,87</sup>

### **Serratia**

The bacteria in the genus *Serratia* belong to the *Enterobacteriaceae* family and have emerged as important pathogens over the last 30 years, representing 6.5% of gram-negative infections in ICUs.<sup>88</sup> In some cases, *Serratia* infection can develop into meningitis or bacteremia, where it has a mortality rate of up to 37% in some populations.<sup>89,90</sup> Sources of infection have included baby shampoo, liquid soap dispensers, saline solutions, prefilled heparin syringes, inhalation medications, parenteral nutrition, urine collection basins, tap water, and a wide variety of medical devices and antiseptics; however, the most common mode of transmission is the hands of hospital personnel.<sup>91,92,88</sup> *Serratia* species are intrinsically resistant to several beta-lactams,<sup>93</sup> and resistance markers CTX-M, IMP, KPC, NDM, OXA, and VIM have all been noted in clinical isolates of *Serratia* species.<sup>94,95,96,97,98,99</sup> The **cobas eplex BCID-GN *Serratia*** assay detects *Serratia ficaria*, *Serratia fonticola*, *Serratia grimesii*, *Serratia liquefaciens*, *Serratia marcescens*, *Serratia plymuthica*, and *Serratia rubidaea*.

### ***Serratia marcescens***

*Serratia marcescens* is the most common *Serratia* species implicated in disease and is known for the characteristic pink to red coloration of many isolates. It is a member of the *Enterobacteriaceae* family and is commonly isolated in bathrooms, often persisting in locations where water is present. In humans, *Serratia marcescens* has been shown to cause infection of the eye, respiratory tract, gastrointestinal tract, urinary tract, and wounds. It has further been implicated in endocarditis and osteomyelitis, along with pneumonia and meningitis, in addition to bacteremia.<sup>100</sup> Mortality rates of between 20-58% have been reported in cases of bacteremia caused by *Serratia marcescens*, and epidemiologic data indicates that antimicrobial resistance is increasing. Resistance markers CTX-M, IMP, KPC, NDM, OXA, and VIM have all been noted in clinical isolates of *Serratia* species.<sup>94,95,96,97,98,99</sup>

### ***Stenotrophomonas maltophilia***

*Stenotrophomonas maltophilia* is an aerobic, non-fermenting bacillus commonly found in water, soil, plant material, animals, and on hospital equipment. It has been implicated in bacteremia, endocarditis, and meningitis, as well as ocular, urinary tract, respiratory tract, skin, and soft tissue infections.<sup>101</sup> Treatment of *Stenotrophomonas maltophilia* is challenging due to its intrinsic multi-drug resistance, including the use of efflux systems, the presence of a thermo-dependent outer membrane, which protects against aminoglycosides, and two chromosomal beta-lactamases, which grant resistance to carbapenems, cephalosporins, and imipenem.<sup>7,102</sup> Mortality rates for bacteremia caused by *Stenotrophomonas maltophilia* range broadly between 10-60%, with underlying disease playing a large role in the mortality rate.<sup>103</sup> The resistance marker CTX-M has been noted in clinical isolates of *Stenotrophomonas maltophilia*.<sup>76</sup>

## Antimicrobial Resistance Markers

### **ctx-M (*bla*<sub>CTX-M</sub>) (cefotaxime-hydrolyzing beta-lactamase, CTX-M)**

CTX-M enzymes are plasmid-mediated, class A extended spectrum beta-lactamases (ESBLs). These enzymes are commonly found in *Escherichia coli* and *Klebsiella* species and consist of at least five types and over eighty different individual enzymes.<sup>104</sup>

### **imp (*bla*<sub>IMP</sub>) (imipenem-resistant metallo-beta-lactamase, IMP)**

Imipenem-resistant metallo-beta-lactamases are class D beta-lactamases (MBL) which are typically encoded on plasmids. There are currently over 50 IMP enzymes which can be found in a broad range of gram-negative organisms throughout the world.<sup>105</sup>

### **kpc (*bla*<sub>KPC</sub>) (*Klebsiella pneumoniae* carbapenemase, KPC)**

KPC, or *Klebsiella pneumoniae* carbapenemase, is found in a number of gram-negative organisms, though it is most commonly found on plasmids in *Klebsiella pneumoniae*.<sup>105</sup>

### **ndm (*bla*<sub>NDM</sub>) (New Delhi metallo-beta-lactamase, NDM)**

NDM, or New Delhi beta-lactamase, is a carbapenemase with the ability to hydrolyze most penicillins and cephalosporins as well as carbapenems.<sup>106</sup> Originally isolated from an Indian patient in 2008, it has now been isolated throughout the world.<sup>107</sup>

### **oxa (*bla*<sub>OXA</sub>) (oxacillin-hydrolyzing beta-lactamase, OXA)**

OXA enzymes are class D beta-lactamases and confer resistance to cefpirome, cephalothin, and oxacillin.<sup>78</sup> There are over 500 OXA enzymes to date,<sup>108</sup> with some but not all being considered ESBLs. The **cobas eplex** BCID-GN panel was designed to detect but not differentiate the OXA-23 and OXA-48 groups, which confer carbapenem resistance.

### **vim (*bla*<sub>VIM</sub>) (Verona integron-encoded metallo-beta-lactamase, VIM)**

VIM, or Verona integron–encoded metallo-beta-lactamases (MBL), are among the most widely distributed MBLs and are comprised of more than 40 individual enzymes. VIM is a part of the most clinically relevant B1 sub-group of MBLs along with IMP and NDM.<sup>109</sup>

## Pan Targets

Gram staining is highly accurate, however some organisms are known to be gram-variable, meaning that the Gram stain may produce misleading results. Additionally, inaccurate Gram stains have also been noted in the instance of polymicrobial infections.<sup>110</sup> The BCID-GN panel includes two pan targets designed to detect but not differentiate organisms that may be missed by Gram stain.

### **Pan Gram-Positive**

The Pan Gram-Positive assay is designed to detect several gram-positive organisms, including those with a potentially misleading Gram stain result. The Pan Gram-Positive assay may provide data to facilitate the correct testing algorithm. If a Pan Gram-Positive target is detected, supplementary testing to determine the identity of the gram-positive organism is recommended.

The **cobas eplex** BCID-GN panel Pan Gram-Positive assay detects the following gram-positive organisms: *Bacillus cereus* group (including *B. cereus* and *B. thuringiensis*), *Bacillus subtilis* group (including *B. amyloliquefaciens*, *B. atrophaeus*, *B. licheniformis*, and *B. subtilis*), *Enterococcus* (including *E. avium*, *E. casseliflavus*, *E. cecorum*, *E. dispar*, *E. durans*, *E. faecalis*, *E. faecium*, *E. gallinarum*, *E. hirae*, *E. italicus*, *E. malodoratus*, *E. pseudoavium*, *E. raffinosus*, *E. saccharolyticus*, and *E. sanguinicola*), *Staphylococcus* (including *S. arlettae*, *S. aureus*, *S. auricularis*, *S. capitis*, *S. caprae*, *S. carnosus*, *S. chromogenes*, *S. cohnii*, *S. epidermidis*, *S. gallinarum*, *S. haemolyticus*, *S. hominis*, *S. hyicus*, *S. intermedius*, *S. lentus*, *S. lugdunensis*, *S. muscae*, *S. pasteurii*, *S. pettenkoferi*, *S. pseudintermedius*, *S. saccharolyticus*, *S. saprophyticus*, *S. schleiferi*, *S. sciuri*, *S. simulans*, *S. vitulinus*, *S. warneri*, and *S. xylosus*) and/or *Streptococcus* (including *S. agalactiae*, *S. anginosus*, *S. bovis*, *S. constellatus*, *S. cricetid*, *S. dysgalactiae*, *S. equi*, *S. equinus*, *S. gallolyticus*, *S. gordonii*, *S. infantarius*, *S. infantis*, *S. intermedius*, *S. mitis*, *S. oralis*, *S. parasanguinis*, *S. peroris*, *S. pneumoniae*, *S. pyogenes*, *S. salivarius*, *S. sanguinis*, and *S. thoraltensis*).

### **Pan Candida**

The Pan *Candida* assay is designed to detect four of the most prevalent *Candida* species: *Candida albicans*, *Candida glabrata*, *Candida krusei*, and *Candida parapsilosis*. Since some fungal organisms, like *Candida*, are known to grow slowly, they may go unnoticed on Gram stains, especially in the case of mixed infection. The Pan *Candida* target may provide data to facilitate the correct testing algorithm. If the Pan *Candida* assay is positive, supplementary testing to determine the identity of the *Candida* species is recommended.

## PRINCIPLES OF TECHNOLOGY

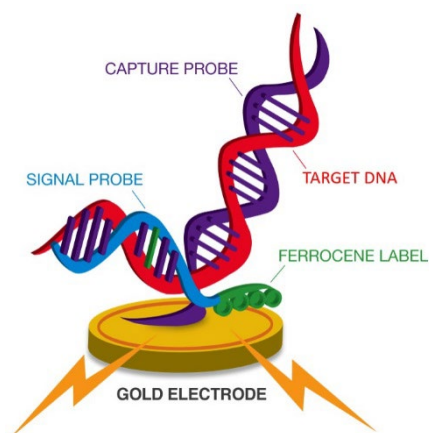
*The True Sample-to-Answer Solution®* **cobas eplex** instrument automates all aspects of nucleic acid testing including extraction, amplification, and detection, combining electrowetting and the eSensor® technology in a single-use cartridge. eSensor technology is based on the principles of competitive DNA hybridization and electrochemical detection, which is highly specific and is not based on fluorescent or optical detection.

Electrowetting, or digital microfluidics, uses electrical fields to directly manipulate discrete droplets on the surface of a hydrophobically coated printed circuit board (PCB). Sample and reagents are moved in a programmable fashion in the **cobas eplex** cartridge to complete all portions of the sample processing from nucleic acid extraction to detection.

A sample is loaded into the **cobas eplex** cartridge and the cartridge is placed into the **cobas eplex** instrument. Nucleic acids are extracted and purified from the specimen via magnetic solid phase extraction. PCR is used to create double-stranded DNA, which is treated with exonuclease to create single-stranded DNA in preparation for eSensor detection.

The target DNA is mixed with ferrocene-labeled signal probes that are complementary to the specific targets on the panel. Target DNA hybridizes to its complementary signal probe and capture probes, which are bound to gold-plated electrodes, as shown below in **Figure 1**. The presence of each target is determined by voltammetry which generates specific electrical signals from the ferrocene-labeled signal probe.

**Figure 1:** Hybridization complex. Target-specific capture probes are bound to the gold electrodes in the eSensor microarray on the **cobas eplex** cartridge. The amplified target DNA hybridizes to the capture probe and to a complementary ferrocene-labeled signal probe. Electrochemical analysis determines the presence or absence of targets using voltammetry.



## MATERIALS PROVIDED

**Table 2: The True Sample-to-Answer Solution®**  
cobas eplex blood culture identification Gram-Negative panel Kit Contents

Product	Item number	Components (quantity)	Storage
cobas eplex blood culture identification Gram-Negative (BCID-GN) panel	GenMark: EA002012 Roche: 9556494001	cobas eplex BCID-GN panel Cartridge (12)	2–8 °C

## COMPOSITION OF REAGENTS

Component	Concentration (w/v)
Salting Buffer	
Guanidine hydrochloride	≤ 45%
Sodium perchlorate	≤ 14%
Binding Buffer	
PEG 8000	≤ 20%
NaH <sub>2</sub> PO <sub>4</sub>	≤ 1.0%
EDTA	≤ 0.1%
NaCl	≤ 5.0%
NaN <sub>3</sub>	≤ 0.2%
Cysteamine HCl	≤ 1.0%
MTG	≤ 1.0%
Lysis Buffer	
Tris-HCl	≤ 5.0%
Urea	25% - 50%
Guanidine hydrochloride	≤ 2.0%
Calcium Chloride	≤ 1.0%
SDS	≤ 5.0%
Tween-20	10% - 20% (v/v)
Oil Component	
Polydimethylsiloxane, Trimethylsiloxy Terminated, 5 cSt	≥ 95%

Component	Concentration (w/v)
Recon/Elution Buffer	
Sodium azide	≤ 0.2%
Tween-20	≤ 2.0% (v/v)
Wash Buffer	
PEG 8000	≤ 20%
NaH <sub>2</sub> PO <sub>4</sub>	≤ 1.0%
EDTA	≤ 0.1%
NaCl	≤ 5.0%
NaN <sub>3</sub>	≤ 0.2%
Cysteamine HCl	≤ 1.0%
MTG	≤ 1.0%
Tween-20	≤ 2.0% (v/v)
PCR Reaction	
Tris-HCl	≤ 5.0%
KCl	≤ 5.0%
Trehalose	10% - 50%
Bovine Serum Albumin	≤ .05%
dNTPs	Trace
MgCl <sub>2</sub>	≤ 0.1%
Oligonucleotides	Trace

Upon receipt, reagents should be stored at 2–8 °C. SDSs are available on request from your local Roche representative or can be accessed via eLabDoc.

## REAGENT STORAGE, STABILITY AND HANDLING

- Store the **cobas eplex** BCID-GN panel kit at 2–8 °C.
- Do not use **cobas eplex** BCID-GN panel kit beyond the expiration date.
- Do not open a cartridge pouch until you are ready to perform testing.

## MATERIALS NOT PROVIDED

### Equipment

- **cobas eplex** instrument and Software
- Pipettes capable of delivering 50 µL
- Printer (optional) - See **cobas eplex** Operator Manual for compatibility guidelines

### Consumables

- Pipette tips, aerosol resistant, RNase/DNase-free
- Disposable, powder free gloves
- 10% bleach for appropriate surfaces
- 70% ethanol or isopropyl alcohol (or equivalent) for appropriate surfaces
- 1.5 mL RNase/DNase-free microcentrifuge tube or equivalent (optional)

## WARNINGS AND PRECAUTIONS

### General

- For *in vitro* diagnostic use only, by laboratory professionals.
- A trained healthcare professional should carefully interpret the results from the **cobas eplex** BCID-GN panel in conjunction with a patient's signs and symptoms and results from other diagnostic tests.
- Positive results do not rule out co-infection with other viruses, bacteria, or fungi. The agent(s) detected may not be the definitive cause of disease. The use of additional laboratory testing (e.g., bacterial, fungal, and viral culture, immunofluorescence and radiography) and clinical presentation must be taken into consideration in the final diagnosis of a blood infection.
- Do not reuse **cobas eplex** BCID-GN panel kit components.
- Do not use reagents beyond the expiration date printed on the labeling.
- Follow the procedure as described in this package insert. Read all instructions before starting the test.
- Inform your local competent authority and the manufacturer about any serious incidents which may occur when using this assay.

## Safety

- Handle all specimens and waste materials as if they were capable of transmitting infectious agents in accordance with Universal Precautions. Observe safety guidelines such as those outlined in CDC/NIH *Biosafety in Microbiological and Biomedical Laboratories*, CLSI Document M29 *Protection of Laboratory Workers from Occupationally Acquired Infections*, or other appropriate guidelines.
- Follow routine laboratory safety procedures for handling of reagents (e.g., do not pipette by mouth, wear appropriate protective clothing and eye protection).
- Follow your institution's safety procedures for handling biological samples.
- Dispose materials used in this test, including reagents, specimens and used vials, in accordance with all federal, state and local regulations.
- Do not stick fingers or other objects inside the **cobas eplex** instrument bays.
- Wash hands thoroughly with soap and water after handling reagents. Launder contaminated clothing prior to re-use.
- Do not puncture or pierce reagent blisters on the **cobas eplex** cartridge. Reagents may cause irritation to skin, eyes and respiratory tract. Harmful if swallowed or inhaled. Contains oxidizing liquids.
- The **cobas eplex** BCID-GN panel cartridge contains chemicals that are classified as hazardous. Review the Safety Data Sheet (SDS) before use and in cases of exposure, refer to the SDS for more information. Safety Data Sheets (SDS) are available on request from your local Roche representative or can be accessed via eLabDoc.
- Contamination of the sample may occur if laboratory personnel processing the sample are colonized with any number of commensal organisms. To avoid this, specimens should be processed in biosafety cabinets utilizing proper personal protective equipment. If a biosafety cabinet is not used, a splash shield or face mask should be worn when processing samples.
- Change gloves frequently during testing to reduce the risk of contamination.
- Thoroughly decontaminate the lab and all equipment with 10% bleach followed by 70% ethanol or isopropyl alcohol (or equivalent).

## Laboratory

- Contamination of the sample may occur if laboratory personnel processing the sample carry common pathogens and contaminants. To avoid this, specimens should be processed in biosafety cabinets. If a biosafety cabinet is not used, a splash shield or face mask should be used when processing samples.
- A biosafety cabinet that is used for bacterial or fungal culture should not be used for sample preparation.
- Samples and cartridges should be handled and/or tested one at a time. To mitigate the risk of sample-to-sample contamination, change gloves after dispensing sample into the cartridge.
- Thoroughly decontaminate the lab and all equipment with 10% bleach followed by 70% ethanol or isopropyl alcohol (or equivalent) prior to processing a specimen.
- Contamination of the sample may occur if the sample is loaded in an area where PCR amplicons are generated. Avoid loading sample in areas that are potentially contaminated with PCR amplicon.



## SPECIMEN COLLECTION, HANDLING AND STORAGE

- Blood culture bottles should be handled according to manufacturer's recommended procedure.
- Clinical specimens can remain in the incubator for up to 12 hours beyond bottle positivity.
- Clinical specimens can be stored at room temperature for up to 7 days.
- Clinical specimens can be stored at 2°C to 8°C for up to 1 month.
- Clinical specimens can be stored at -80°C to -20°C for up to 18 months.
- Clinical specimens can be subjected to up to two freeze/thaw cycles.

## PROCEDURE

### Procedural Notes

- The detection of bacterial or fungal nucleic acid is dependent upon proper specimen collection, handling, transportation, storage, and preparation. Failure to observe proper procedures in any one of these steps can lead to incorrect results. There is a risk of both false positive and false negative results due to improperly collected, transported, or handled specimens.
- Not Detected results may occur due to the presence of inhibitors, technical error, sample mix-up, or an infection caused by an organism not detected by the panel.
- Samples should be positive blood culture containing gram negative organisms as confirmed by Gram stain.
- Samples, consumables, and lab areas should be protected from aerosol or direct contamination with amplicon. Decontaminate laboratory areas and affected equipment with 10% bleach followed by 70% ethanol or isopropyl alcohol (or equivalent).
- Samples should be loaded to the **cobas eplex** BCID-GN panel cartridge in an amplicon-free, clean environment.
- Samples should be processed in biosafety cabinets. If a biosafety cabinet is not used, a splash shield or face mask should be worn when processing samples.
- Change gloves frequently during testing to reduce the risk of contamination.
- Once a cartridge is removed from foil pouch, it should be used within 2 hours. Do not open the test cartridge pouch until the sample is ready to be tested.
- Once the sample is loaded onto the **cobas eplex** BCID-GN panel cartridge, the sample should be processed as soon as possible, but if needed, may be run within 2 hours.
- All frozen samples should be thawed completely and mixed well before testing.
- The blood culture bottle should be inverted several times to mix.
- Allow approximately 10 seconds for the resin to settle.
- The septum of the positive blood culture bottle should be wiped with 70% ethanol or isopropyl alcohol (or equivalent) prior to withdrawing the sample.
- Use sterile materials for transfer and loading of each sample. Ensure that no part of the transfer device touches the inside of any transfer container that may be used. A shallow vessel such as a 1.5 mL microcentrifuge tube is recommended for transfer.
- Do not insert a wet cartridge into the **cobas eplex** instrument. If liquid is present on outside of test cartridge, use a low lint lab wipe (e.g. Kimwipes™) to remove liquid prior to inserting into **cobas eplex** bay.
- Dispose materials used in this test, including reagents, specimens and used vials, in accordance with all regulations.
- Do not re-use cartridges.

## Detailed Procedure

1. Decontaminate the area used for setting up the **cobas eplex** BCID-GN panel with 10% bleach followed by 70% ethanol or isopropyl alcohol (or equivalent).
2. Remove one **cobas eplex** BCID-GN panel cartridge pouch from kit packaging.
3. Open **cobas eplex** BCID-GN panel cartridge pouch.
4. Write the accession ID or place a barcode label with accession ID on the **cobas eplex** BCID-GN panel cartridge.
5. Invert the blood culture bottle several times to mix.
6. Allow approximately 10 seconds for the resin to settle.
7. Wipe the septum of the positive blood culture bottle with 70% ethanol or isopropyl alcohol (or equivalent) prior to withdrawing the sample.
8. Using a loading device capable of accurately delivering 50 µL, aspirate 50 µL of blood culture sample and load into the sample loading port of the **cobas eplex** BCID-GN panel cartridge.  
**NOTE:** a 1.5 mL microcentrifuge tube is recommended for transfer of sample from the blood culture bottle prior to loading **cobas eplex** cartridge.
9. Close the sample loading port immediately by sliding the cap over the port and firmly pushing down on the cap to securely seal the sample delivery port.  
**NOTE:** Bubbles can be present when closing the cap.
10. Scan the **cobas eplex** BCID-GN panel cartridge using the barcode reader provided with the **cobas eplex** instrument.  
**NOTE:** If an accession ID barcode label is not used, manually enter accession ID with the on-screen keyboard.  
**NOTE:** The barcode scanner will read both the accession ID barcode (if placed on the cartridge by the operator) and the 2D barcode printed on the cartridge label; however, the barcode scanner will only beep once to indicate that both barcodes have been read.
11. Insert the **cobas eplex** BCID-GN panel cartridge into any available bay, indicated by a flashing, white LED light. The test will begin automatically when the cartridge has been inserted into the bay and the pre-run check is completed, as indicated by a blue LED light.

## QUALITY CONTROL

### Internal Controls

Each cartridge includes internal controls that monitor performance of each step of the testing process, including extraction, amplification, and detection of targets.

Each amplification reaction on the cartridge has an internal control, and in each reaction, either the internal control or a target must generate signal above the defined threshold for a valid test result. Internal control results are interpreted by the **cobas eplex** Software and displayed on the **cobas eplex** BCID-GN panel Reports as Internal Control with a result of PASS, FAIL, N/A, or INVALID. **Table 3** includes details on the interpretation of Internal Control results.

**Table 3: Internal Control Results**

Internal Control Result	Explanation	Action
<b>PASS</b>	Signal above threshold has been detected from each amplification reaction.  The test was completed and internal controls were successful, indicating valid results were generated.	All results are displayed on the <b>cobas eplex</b> BCID-GN panel Detection Report.  Test is valid, report results.
<b>FAIL</b>	Signal above threshold has not been detected from at least one amplification reaction.  The test was completed but internal controls were not detected, indicating that results may not be valid.	No results are displayed on the <b>cobas eplex</b> BCID-GN panel Detection Report.  Test is not valid, repeat the test using a new cartridge.
<b>N/A</b>	The internal control in every amplification reaction does not generate signal above the threshold, but a target in every amplification reaction does generate signal above the threshold.  The test was completed and internal controls were not successful, however detection of signal above the threshold for a target in every amplification reaction indicates valid results were generated.	All results are displayed on the <b>cobas eplex</b> BCID-GN panel Detection Report.  Test is valid, report results.
<b>INVALID</b>	An error has occurred during processing that prevents analysis of signal data.  The test has not successfully completed and results for this test are not valid. This may be due to an instrument or software error.	No results are displayed on the <b>cobas eplex</b> BCID-GN panel Detection Report.  Test is not valid, repeat the test using a new cartridge.

### External Controls

Positive and negative external controls should be tested as part of good laboratory practice, in accordance with the appropriate accrediting organization as applicable and following the user's laboratory standard quality control procedures. Blood culture medium can be used as the negative control. Previously characterized positive samples or blood culture medium spiked with well characterized organisms can be used as the external positive control. External controls should be run in accordance with laboratory protocols and accrediting organizations, as applicable.

## RESULTS

**Table 4: Interpretation of Results on the cobas eplex BCID-GN panel Detection Report**

Target Result	Explanation	Action
Detected	The test was completed successfully and the target has generated signal above its defined threshold and the Internal Control was reported as PASS.	All results are displayed on the <b>cobas eplex</b> BCID-GN panel Detection Report.  Test is valid, report results.
Not Detected	The test was completed successfully and the target did not generate signal above its defined threshold and the Internal Control was reported as PASS.	All results are displayed on the <b>cobas eplex</b> BCID-GN panel Detection Report.  Test is valid, report results.
N/A	The test was completed successfully and an associated organism for the antibiotic resistance gene target was not detected (see <b>Table 7</b> for resistance marker organism associations).	All results are displayed on the <b>cobas eplex</b> BCID-GN panel Detection Report.  Test is valid, report results.
Invalid	The test has not successfully completed and results for this test are not valid. This may be due to an instrument or software error.	No results are displayed on the <b>cobas eplex</b> BCID-GN panel Detection Report.  Test is not valid, repeat test.

### Genus and Group Assay Result Interpretation

While many results on the **cobas eplex** BCID-GN panel are based on a single assay, the **cobas eplex** BCID-GN panel uses two assays for each of the *Proteus* and *Serratia* results.

The **cobas eplex** BCID-GN *Proteus* result is based on two assays: the species-specific *Proteus mirabilis* and the broad *Proteus* assay. The broad *Proteus* assay will detect *Proteus mirabilis*, however, its primary purpose is to detect non-*mirabilis* *Proteus* species. See **Table 5** for detailed *Proteus* target call logic.

**Table 5: *Proteus* Target Results from cobas eplex BCID-GN panel Detection Report**

<i>Proteus</i> Result	<i>Proteus</i> Assay	<i>Proteus mirabilis</i> Assay	Description
Not Detected	Negative	Negative	No <i>Proteus</i> species detected
Detected	Positive	Positive	<i>Proteus mirabilis</i> detected
Detected	Positive	Negative	Unspeciated <i>Proteus</i> detected

The **cobas eplex** BCID-GN *Serratia* result is based on two assays: the species-specific *Serratia marcescens* and the broad *Serratia* assay. The broad *Serratia* assay will detect *Serratia marcescens*, however, its primary purpose is to detect non-*marcescens* *Serratia* species. See **Table 6** for detailed *Serratia* target call logic.

**Table 6: *Serratia* Target Results from cobas eplex BCID-GN panel Detection Report**

<b>Serratia Result</b>	<b>Serratia Assay</b>	<b><i>Serratia marcescens</i> Assay</b>	<b>Description</b>
Not Detected	Negative	Negative	No <i>Serratia</i> species detected
Detected	Positive	Positive	<i>Serratia marcescens</i> detected
Detected	Positive	Negative	Unspeciated <i>Serratia</i> detected

## Resistance Marker Assay Result Interpretation

Test results for resistance markers are only reported when an associated organism assay is positive in the same sample. See **Table 7** for organisms specifically associated with the six resistance markers on the **cobas eplex** BCID-GN panel (Indicated by X on the table). If an associated organism from **Table 7** is not detected, the resistance marker will be reported as “N/A” (see **Table 4** for more information).

**Table 7: Resistance Marker Organism Associations**

<b>Organism</b>	<b>Resistance Marker</b>					
	<b>CTX-M</b>	<b>IMP</b>	<b>KPC</b>	<b>NDM</b>	<b>OXA</b>	<b>VIM</b>
<i>Acinetobacter baumannii</i>	X	X	X	X	X	X
<i>Bacteroides fragilis</i>						
<i>Citrobacter</i>	X	X	X	X	X	X
<i>Cronobacter sakazakii</i>			X			
<i>Enterobacter cloacae</i> complex	X	X	X	X	X	X
<i>Enterobacter</i> (non- <i>cloacae</i> complex)	X	X	X	X	X	X
<i>Escherichia coli</i>	X	X	X	X	X	X
<i>Fusobacterium necrophorum</i>						
<i>Fusobacterium nucleatum</i>						
<i>Haemophilus influenzae</i>						
<i>Klebsiella oxytoca</i>	X	X	X	X	X	X
<i>Klebsiella pneumoniae</i> group	X	X	X	X	X	X
<i>Morganella morganii</i>	X	X	X	X	X	X
<i>Neisseria meningitidis</i>						
<i>Proteus</i>	X	X	X	X	X	X
<i>Proteus mirabilis</i>	X	X	X	X	X	X
<i>Pseudomonas aeruginosa</i>	X	X	X	X	X	X
<i>Salmonella</i>	X	X	X	X	X	X
<i>Serratia</i>	X	X	X	X	X	X
<i>Serratia marcescens</i>	X	X	X	X	X	X
<i>Stenotrophomonas maltophilia</i>	X					

## Pan Assay Results

The **cobas eplex** BCID-GN panel Pan Gram-Positive result indicates the presence of one or more of the following gram-positive organisms: *Enterococcus*, *Bacillus cereus* group, *Bacillus subtilis* group, *Staphylococcus*, and/or *Streptococcus* as shown in **Table 8**.

**Table 8: Pan Gram-Positive Target Results from cobas eplex BCID-GN panel Detection Report**

Pan Gram-Positive Result	Description
Not Detected	No specified gram-positive organism detected.
Detected	One or more of the following gram-positive organisms has been detected: <i>Enterococcus</i> , <i>Bacillus cereus</i> group, <i>Bacillus subtilis</i> group, <i>Staphylococcus</i> , and/or <i>Streptococcus</i> . Additional testing for speciation is suggested.

The **cobas eplex** BCID-GN panel Pan *Candida* result indicates the presence of one or more of the following *Candida* species: *Candida albicans*, *Candida glabrata*, *Candida krusei*, and/or *Candida parapsilosis* as shown in **Table 9**.

**Table 9: Pan *Candida* Target Results from cobas eplex BCID-GN panel Detection Report**

Pan <i>Candida</i> Result	Description
Not Detected	No specified <i>Candida</i> species detected.
Detected	One or more of the following <i>Candida</i> organisms has been detected: <i>Candida albicans</i> , <i>Candida glabrata</i> , <i>Candida krusei</i> , and/or <i>Candida parapsilosis</i> . Additional testing for identification is recommended.

## TEST REPORTS

Several different reports are available on the **cobas eplex** system. Results are provided in a printable format and may be viewed electronically or exported for additional analysis. Reports can be customized with account specific information such as the address, logo and institutional specific footers on each report. For more information on **cobas eplex** Reports, refer to the **cobas eplex** Operator Manual.

### Detection Report

The **cobas eplex** BCID-GN panel Detection Report includes the results for each individual sample run on the **cobas eplex** system. The Summary section indicates the overall test result and lists all detected targets in that sample. The Results section includes a list of all targets on the panel with an individual result for each target. Results are reported as Detected, Not Detected, N/A (in the case of a resistance gene detected without detection of an associated organism) or Invalid (displayed as a red **X**); results for the Internal Control are reported as PASS, FAIL, INVALID, or N/A.

### External Control Report

The **cobas eplex** BCID-GN panel External Control Report is generated for an external control that has been pre-defined in the **cobas eplex** BCID-GN panel Software. For more information on defining external controls on the **cobas eplex** system, refer to the **cobas eplex** Operator Manual.

The Summary section indicates the overall result (PASS or FAIL status) and lists all detected targets for that external control. The Results section includes a list of all panel targets with the result, expected result, and PASS/FAIL status for each. Results are reported as Detected, Not Detected, N/A (in the case of a resistance gene detected without detection of an associated organism) or Invalid (displayed as a red **X**). A target is reported as PASS if the actual result matches the expected result (as defined for that control); a target is reported as FAIL if the actual result does not match the expected result. If the actual result for each target matches the expected result (all targets reported as PASS), the overall result for the

external control is reported as PASS in the Summary section. If the actual result for any target does not match the expected result, the overall result for the external control is reported as FAIL in the Summary section.

## Summary Report

The Summary Report allows the operator to use searchable criteria to create customized reports, using specified targets, dates, range of dates, sample, external control, test bay, or operator. For more information on creating Summary Reports, refer to the **cobas eplex** Operator Manual.

## LIMITATIONS OF THE PROCEDURE

- For prescription use only.
- This test is a qualitative test and does not provide a quantitative value.
- This product should not be used with blood culture media that contains charcoal.
- This product can be used only with the **cobas eplex** instrument.
- The performance of the test has been evaluated for use with human specimen material only.
- This test has not been validated for testing specimens other than positive blood cultures with presence of an organism confirmed by Gram stain.
- Decreased sensitivity has been observed for some targets in the BD BACTEC™ Lytic Anaerobic bottle type (see the **Sample Matrix Equivalency (Bottle Evaluation) study, Table 113**).
- Bacterial and fungal nucleic acids may be present in blood culture media, independent of bacterial or fungal viability. Detection of an assay target does not guarantee that the corresponding bacteria or fungi are infectious or are the causative agents for clinical symptoms.
- There is a risk of false negative values due to the presence of sequence variants in the bacterial or fungal targets of the test.
- Results from this test must be correlated with the clinical history, epidemiological data, and other data available to the clinician evaluating the patient.
- The detection of bacterial or fungal nucleic acid is dependent upon proper specimen collection, handling, transportation, storage, and preparation. Failure to observe proper procedures in any one of these steps can lead to incorrect results. There is a risk of both false positive and false negative results due to improperly collected, transported, or handled specimens.
- A result of “No Targets Detected” on the **cobas eplex** BCID-GN panel does not preclude the possibility of bacterial or fungal infection. A specimen with a result of No Targets Detected may contain an organism not targeted by the **cobas eplex** BCID-GN panel.
- Not Detected results may occur due to the presence of inhibitors, technical error, sample mix-up, or an infection caused by an organism not detected by the panel.
- Test results may be affected by concurrent antimicrobial therapy or levels of bacteria or fungi in the specimen that are below the limit of detection for the test.
- In mixed cultures, the **cobas eplex** BCID-GN panel may not identify all organisms in the specimen, depending upon the concentration of each target present.
- The results of the **cobas eplex** BCID-GN panel should not be used as the sole basis for diagnosis, treatment, or other patient management decisions.
- The BCID-GN Pan *Candida* and Pan Gram-Positive assays are designed to detect *Candida* and gram-positive microorganisms in mixed blood cultures where these microorganisms might be missed by Gram stain. Lower than expected clinical sensitivity was observed for these analytes, which was likely due to the presence of *Candida* spp. or gram-positive microorganisms in mixed cultures at concentrations below the respective limits of detection for the Pan *Candida* and Pan Gram-Positive targets.
- The effect of interfering substances has only been evaluated for those listed in this package insert. Interference due to substances other than those described in the “Interfering Substances” section can lead to erroneous results.



- For *Enterococcus saccharolyticus*, *Serratia odorifera*, and *Streptococcus thoraltensis*, 100% detection was not observed at expected bottle positivity concentrations. Decreased sensitivity may be observed for these species. See the **Analytical Reactivity (Inclusivity) Study Table 65** and the **Predicted (in silico) Reactivity section** for additional details.
- False negative results may occur for specimens containing *Fusobacterium necrophorum* because the assay's limit of detection for *F. necrophorum* can be near the concentration observed at the time of bottle positivity. See the **Limit of Detection (LoD) Study Table 64** for additional details.
- Staphylococcus simulans* was not reactive at a concentration of  $1 \times 10^8$  CFU/mL and may not be detected by the **cobas eplex BCID-GN panel**.
- Shigella* was shown to cross-react with the *Escherichia coli* assay.
- Fusobacterium periodonticum*, *canifelinum* and *simiae* cross-react with the *Fusobacterium nucleatum* assay.
- Acinetobacter anitratus* was shown to cross-react with the *Acinetobacter baumannii* assay at levels  $>1 \times 10^4$  CFU/mL.
- Enterobacter cowanii* was shown to cross-react with the *Enterobacter cloacae* complex assay at levels  $>1 \times 10^8$  CFU/mL.
- Escherichia hermannii* was shown to cross-react with the *Enterobacter* (non-*cloacae* complex) assay at levels  $>1 \times 10^6$  CFU/mL, and with the *Serratia* assay at levels  $>1 \times 10^7$  CFU/mL. The genus level and group assays included as a part of the **cobas eplex BCID-GN panel** are designed to detect a broad range of species but will not necessarily detect all species within a genus or group. For species detected by these assays, please refer to the **Analytical Reactivity (Inclusivity) Study Table 65** and the **Predicted (in silico) Reactivity section** of this package insert.
- For genus level assays, it is possible that an unspiciated target may be masked in the case of a co-infection. For example, in the event that an unspiciated *Serratia* species is present in the same sample as *Serratia marcescens*, there is no ability to determine that the unspiciated *Serratia* species is present.
- BLAST searches to support *in silico* analyses were conducted in March 2018. Therefore, new gene variants deposited into GenBank after March 2018 have not been evaluated.

## EXPECTED VALUES

A prospective, multicenter clinical study was conducted to evaluate the clinical performance of the **cobas eplex BCID-GN panel** in positive blood culture samples. A total of 349 samples were prospectively collected at 7 clinical sites in 2 phases from patients of all ages and genders. In the first phase from June 2014 through July 2016, 182 samples were prospectively collected and frozen; from June through July 2018, 167 samples were prospectively collected and tested fresh (never frozen). The expected values of individual analytes based on the **cobas eplex BCID-GN panel** results in prospective samples are summarized by age group and by site in **Tables 10** and **11** below.

**Table 10: Expected Value by Age Group (Prospective Samples)**

Target	All Ages (N=349) n (%)	Age <1 (N=7) n (%)	Age 1-17 (N=10) n (%)	Age 18-44 (N=50) n (%)	Age 45-64 (N=124) n (%)	Age 65-84 (N=125) n (%)	Age 85+ (N=33) n (%)
<i>Acinetobacter baumannii</i>	4 (1.1)	0 (0.0)	0 (0.0)	1 (2.0)	2 (1.6)	1 (0.8)	0 (0.0)
<i>Bacteroides fragilis</i>	11 (3.2)	0 (0.0)	0 (0.0)	2 (4.0)	4 (3.2)	2 (1.6)	3 (9.1)
<i>Citrobacter</i>	8 (2.3)	0 (0.0)	0 (0.0)	2 (4.0)	1 (0.8)	2 (1.6)	3 (9.1)
<i>Cronobacter sakazakii</i>	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
<i>Enterobacter</i> (non- <i>cloacae</i> complex)	9 (2.6)	0 (0.0)	1 (10.0)	2 (4.0)	5 (4.0)	1 (0.8)	0 (0.0)
<i>Enterobacter cloacae</i> complex	23 (6.6)	3 (42.9)	1 (10.0)	6 (12.0)	5 (4.0)	8 (6.4)	0 (0.0)
<i>Escherichia coli</i>	132 (37.8)	2 (28.6)	2 (20.0)	16 (32.0)	41 (33.1)	55 (44.0)	16 (48.5)
<i>Fusobacterium necrophorum</i>	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
<i>Fusobacterium nucleatum</i>	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
<i>Haemophilus influenzae</i>	7 (2.0)	0 (0.0)	0 (0.0)	3 (6.0)	1 (0.8)	1 (0.8)	2 (6.1)

Target	All Ages (N=349) n (%)	Age <1 (N=7) n (%)	Age 1-17 (N=10) n (%)	Age 18-44 (N=50) n (%)	Age 45-64 (N=124) n (%)	Age 65-84 (N=125) n (%)	Age 85+ (N=33) n (%)
<i>Klebsiella oxytoca</i>	12 (3.4)	0 (0.0)	0 (0.0)	3 (6.0)	8 (6.5)	1 (0.8)	0 (0.0)
<i>Klebsiella pneumoniae</i> group	59 (16.9)	1 (14.3)	1 (10.0)	10 (20.0)	26 (21.0)	17 (13.6)	4 (12.1)
<i>Morganella morganii</i>	3 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.6)	1 (0.8)	0 (0.0)
<i>Neisseria meningitidis</i>	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
<i>Proteus</i>	22 (6.3)	0 (0.0)	0 (0.0)	0 (0.0)	6 (4.8)	13 (10.4)	3 (9.1)
<i>Proteus mirabilis</i>	22 (6.3)	0 (0.0)	0 (0.0)	0 (0.0)	6 (4.8)	13 (10.4)	3 (9.1)
<i>Pseudomonas aeruginosa</i>	28 (8.0)	0 (0.0)	2 (20.0)	3 (6.0)	12 (9.7)	10 (8.0)	1 (3.0)
<i>Salmonella</i>	2 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	1 (0.8)	0 (0.0)
<i>Serratia</i>	10 (2.9)	0 (0.0)	1 (10.0)	0 (0.0)	5 (4.0)	4 (3.2)	0 (0.0)
<i>Serratia marcescens</i>	9 (2.6)	0 (0.0)	1 (10.0)	0 (0.0)	4 (3.2)	4 (3.2)	0 (0.0)
<i>Stenotrophomonas maltophilia</i>	3 (0.9)	0 (0.0)	0 (0.0)	3 (6.0)	0 (0.0)	0 (0.0)	0 (0.0)
Pan <i>Candida</i>	2 (0.6)	1 (14.3)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)
Pan Gram-Positive	24 (6.9)	1 (14.3)	2 (20.0)	5 (10.0)	7 (5.6)	7 (5.6)	2 (6.1)
CTX-M	24 (6.9)	0 (0.0)	0 (0.0)	2 (4.0)	7 (5.6)	12 (9.6)	3 (9.1)
IMP	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
KPC	3 (0.9)	0 (0.0)	0 (0.0)	1 (2.0)	1 (0.8)	1 (0.8)	0 (0.0)
NDM	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
OXA	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)
VIM	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Table 11: Expected Value by Collection Site (Prospective Samples)

Target	All Sites (N=349) n (%)	Site 1 (N=88) n (%)	Site 2 (N=23) n (%)	Site 3 (N=98) n (%)	Site 4 (N=58) n (%)	Site 5 (N=46) n (%)	Site 6 (N=28) n (%)	Site 7 (N=8) n (%)
<i>Acinetobacter baumannii</i>	4 (1.1)	3 (3.4)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
<i>Bacteroides fragilis</i>	11 (3.2)	2 (2.3)	3 (13.0)	3 (3.1)	2 (3.4)	1 (2.2)	0 (0.0)	0 (0.0)
<i>Citrobacter</i>	8 (2.3)	2 (2.3)	0 (0.0)	3 (3.1)	1 (1.7)	1 (2.2)	1 (3.6)	0 (0.0)
<i>Cronobacter sakazakii</i>	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
<i>Enterobacter</i> (non-cloacae complex)	9 (2.6)	2 (2.3)	0 (0.0)	4 (4.1)	0 (0.0)	1 (2.2)	2 (7.1)	0 (0.0)
<i>Enterobacter cloacae</i> complex	23 (6.6)	3 (3.4)	1 (4.3)	10 (10.2)	1 (1.7)	6 (13.0)	2 (7.1)	0 (0.0)
<i>Escherichia coli</i>	132 (37.8)	30 (34.1)	8 (34.8)	37 (37.8)	25 (43.1)	17 (37.0)	12 (42.9)	3 (37.5)
<i>Fusobacterium necrophorum</i>	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
<i>Fusobacterium nucleatum</i>	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
<i>Haemophilus influenzae</i>	7 (2.0)	1 (1.1)	0 (0.0)	2 (2.0)	2 (3.4)	1 (2.2)	1 (3.6)	0 (0.0)
<i>Klebsiella oxytoca</i>	12 (3.4)	5 (5.7)	0 (0.0)	3 (3.1)	1 (1.7)	2 (4.3)	1 (3.6)	0 (0.0)
<i>Klebsiella pneumoniae</i> group	59 (16.9)	17 (19.3)	3 (13.0)	20 (20.4)	5 (8.6)	7 (15.2)	4 (14.3)	3 (37.5)
<i>Morganella morganii</i>	3 (0.9)	0 (0.0)	1 (4.3)	2 (2.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
<i>Neisseria meningitidis</i>	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
<i>Proteus</i>	22 (6.3)	9 (10.2)	0 (0.0)	5 (5.1)	5 (8.6)	2 (4.3)	1 (3.6)	0 (0.0)
<i>Proteus mirabilis</i>	22 (6.3)	9 (10.2)	0 (0.0)	5 (5.1)	5 (8.6)	2 (4.3)	1 (3.6)	0 (0.0)
<i>Pseudomonas aeruginosa</i>	28 (8.0)	5 (5.7)	2 (8.7)	10 (10.2)	8 (13.8)	2 (4.3)	1 (3.6)	0 (0.0)
<i>Salmonella</i>	2 (0.6)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.2)	0 (0.0)	0 (0.0)
<i>Serratia</i>	10 (2.9)	1 (1.1)	2 (8.7)	1 (1.0)	3 (5.2)	3 (6.5)	0 (0.0)	0 (0.0)
<i>Serratia marcescens</i>	9 (2.6)	1 (1.1)	2 (8.7)	1 (1.0)	3 (5.2)	2 (4.3)	0 (0.0)	0 (0.0)
<i>Stenotrophomonas maltophilia</i>	3 (0.9)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	1 (3.6)	0 (0.0)
Pan <i>Candida</i>	2 (0.6)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)	1 (3.6)	0 (0.0)
Pan Gram-Positive	24 (6.9)	15 (17.0)	1 (4.3)	5 (5.1)	1 (1.7)	0 (0.0)	2 (7.1)	0 (0.0)

Target	All Sites (N=349) n (%)	Site 1 (N=88) n (%)	Site 2 (N=23) n (%)	Site 3 (N=98) n (%)	Site 4 (N=58) n (%)	Site 5 (N=46) n (%)	Site 6 (N=28) n (%)	Site 7 (N=8) n (%)
CTX-M	24 (6.9)	9 (10.2)	1 (4.3)	3 (3.1)	4 (6.9)	5 (10.9)	2 (7.1)	0 (0.0)
IMP	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
KPC	3 (0.9)	1 (1.1)	0 (0.0)	1 (1.0)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)
NDM	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
OXA	1 (0.3)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
VIM	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

## PERFORMANCE CHARACTERISTICS

### CLINICAL PERFORMANCE

Samples with final, valid **cobas eplex** BCID-GN panel test results and a valid comparator result were evaluable and included in summaries and analyses of demographics, expected values (positivity rate), and performance characteristics. Evaluable samples included 167 prospective fresh and 182 prospective frozen samples as well as 577 retrospective samples and 777 contrived samples.

### Comparator Method

The performance of the **cobas eplex** BCID-GN panel was compared to standard laboratory procedures for identification of blood culture isolates, including traditional and automated identification methods, MALDI-TOF IVD, and microbiological and biochemical techniques. Identification for samples with *Acinetobacter baumannii* or *Candida parapsilosis* identified by standard laboratory procedures was confirmed using analytically validated PCR assays followed by bi-directional sequencing. For antibiotic resistance genes, the **cobas eplex** BCID-GN panel was compared to analytically validated qPCR amplification assays followed by bi-directional sequencing in samples with an associated organism identified by culture (See **Table 7** for organism associations).

The comparator method(s) results were used to determine the Detected / Not Detected status for each target organism on the **cobas eplex** BCID-GN panel. The comparator methods for each target are summarized in **Table 12**.

**Table 12: Comparator Method(s) by cobas eplex BCID-GN panel Target**

Target	Comparator Method
<i>Acinetobacter baumannii</i>	Standard laboratory procedures for organism ID. PCR/sequencing to confirm <i>Acinetobacter baumannii</i> or different <i>Acinetobacter</i> species not included in this panel.
<i>Bacteroides fragilis</i>	Standard laboratory procedures for organism ID.
<i>Citrobacter</i>	
<i>Cronobacter sakazakii</i>	
<i>Enterobacter cloacae</i> complex	
<i>Enterobacter</i> (non-cloacae complex)	
<i>Escherichia coli</i>	
<i>Fusobacterium necrophorum</i>	
<i>Fusobacterium nucleatum</i>	
<i>Haemophilus influenzae</i>	
<i>Klebsiella oxytoca</i>	
<i>Klebsiella pneumoniae</i> group	
<i>Morganella morganii</i>	
<i>Neisseria meningitidis</i>	
<i>Proteus</i>	
<i>Proteus mirabilis</i>	
<i>Pseudomonas aeruginosa</i>	
<i>Salmonella</i>	
<i>Serratia</i>	

Target	Comparator Method
<i>Serratia marcescens</i>	
<i>Stenotrophomonas maltophilia</i>	
Pan Gram-Positive	
Pan <i>Candida</i>	Standard laboratory procedures for organism ID. PCR/sequencing to confirm <i>C. parapsilosis</i> or identify <i>C. metapsilosis</i> , <i>C. orthopsilosis</i> .
CTX-M, IMP, KPC, NDM, OXA, VIM	qPCR/sequencing in samples with associated organism detected by comparator method. See <b>Table 7</b> for organism associations.

## Demographics of Clinical Samples

Clinical performance was evaluated in positive blood culture samples prospectively and retrospectively collected. Prospective samples were collected at 7 clinical sites in 2 phases. From June 2014 through July 2016, 183 samples were prospectively collected and frozen; from June through July 2018, 171 samples were prospectively collected and tested fresh (never frozen) for a total of 354 samples across the 2 phases. One of these samples was withdrawn due to organism identification from unacceptable methods. Of the 353 prospectively-collected samples eligible for testing, 349 were evaluable. Samples with final, valid **cobas eplex** BCID-GN panel results and a valid comparator result were evaluable. Four samples were not evaluable because they did not have final, valid **cobas eplex** BCID-GN panel results and were excluded from performance evaluations. Demographic information for prospectively-collected samples is described in **Table 13**. Subjects enrolled in this study were from a diverse demographic distribution and represent the intended patient population.

To supplement the number of positives for low prevalence targets in the prospective collection, 578 samples were collected retrospectively, 577 were evaluable. One sample was not evaluable because it did not have a final, valid **cobas eplex** BCID-GN panel result and was excluded from performance evaluations. Demographic information for retrospectively-collected samples is described in **Table 14**.

**Table 13: Demographic Data for Clinical Samples by Collection Site (Prospective Collection)**

	All Sites N = 349 n (%)	Site 1 N = 88 n (%)	Site 2 N = 23 n (%)	Site 3 N = 98 n (%)	Site 4 N = 58 n (%)	Site 5 N = 46 n (%)	Site 6 N = 28 n (%)	Site 7 N = 8 n (%)
<b>Sex</b>								
Male	168 (48.1)	37 (42.0)	12 (52.2)	52 (53.1)	28 (48.3)	21 (45.7)	13 (46.4)	5 (62.5)
Female	181 (51.9)	51 (58.0)	11 (47.8)	46 (46.9)	30 (51.7)	25 (54.3)	15 (53.6)	3 (37.5)
<b>Age</b>								
<1 yr	7 (2.0)	2 (2.3)	0 (0.0)	4 (4.1)	0 (0.0)	1 (2.2)	0 (0.0)	0 (0.0)
1-17 yrs	10 (2.9)	4 (4.5)	1 (4.3)	3 (3.1)	1 (1.7)	1 (2.2)	0 (0.0)	0 (0.0)
18-44 yrs	50 (14.3)	10 (11.4)	3 (13.0)	20 (20.4)	3 (5.2)	8 (17.4)	6 (21.4)	0 (0.0)
45-64 yrs	124 (35.5)	35 (39.8)	9 (39.1)	28 (28.6)	21 (36.2)	14 (30.4)	13 (46.4)	4 (50.0)
65-84 yrs	125 (35.8)	29 (33.0)	8 (34.8)	35 (35.7)	25 (43.1)	17 (37.0)	7 (25.0)	4 (50.0)
85+ yrs	33 (9.5)	8 (9.1)	2 (8.7)	8 (8.2)	8 (13.8)	5 (10.9)	2 (7.1)	0 (0.0)

**Table 14: Demographic Data for Clinical Samples by Collection Site (Retrospective Collection)**

	All Sites N = 577 n (%)	Site 1 N = 78 n (%)	Site 2 N = 73 n (%)	Site 3 N = 31 n (%)	Site 4 N = 93 n (%)	Site 5 N = 1 n (%)	Site 6 N = 80 n (%)	Site 7 N = 67 n (%)	Site 8 N = 48 n (%)	Site 9 N = 29 n (%)	Site 10 N = 77 n (%)
<b>Sex</b>											
Male	307 (53.2)	36 (46.2)	41 (56.2)	15 (48.4)	49 (52.7)	0 (0.0)	47 (58.8)	38 (56.7)	29 (60.4)	19 (65.5)	33 (42.9)
Female	270 (46.8)	42 (53.8)	32 (43.8)	16 (51.6)	44 (47.3)	1 (100)	33 (41.3)	29 (43.3)	19 (39.6)	10 (34.5)	44 (57.1)
<b>Age</b>											
<1 yr	9 (1.6)	1 (1.3)	0 (0.0)	0 (0.0)	3 (3.2)	0 (0.0)	2 (2.5)	0 (0.0)	1 (2.1)	0 (0.0)	2 (2.6)
1-17 yrs	20 (3.5)	1 (1.3)	0 (0.0)	1 (3.2)	8 (8.6)	0 (0.0)	6 (7.5)	0 (0.0)	0 (0.0)	1 (3.4)	3 (3.9)
18-44 yrs	78 (13.5)	13 (16.7)	7 (9.6)	2 (6.5)	10 (10.8)	1 (100)	15 (18.8)	8 (11.9)	8 (16.7)	6 (20.7)	8 (10.4)
45-64 yrs	193 (33.4)	27 (34.6)	18 (24.7)	13 (41.9)	27 (29.0)	0 (0.0)	32 (40.0)	27 (40.3)	16 (33.3)	9 (31.0)	24 (31.2)
65-84 yrs	226 (39.2)	29 (37.2)	40 (54.8)	11 (35.5)	40 (43.0)	0 (0.0)	20 (25.0)	24 (35.8)	21 (43.8)	11 (37.9)	30 (39.0)
85+ yrs	49 (8.5)	7 (9.0)	8 (11.0)	4 (12.9)	5 (5.4)	0 (0.0)	5 (6.3)	6 (9.0)	2 (4.2)	2 (6.9)	10 (13.0)
Unknown	2 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (3.0)	0 (0.0)	0 (0.0)	0 (0.0)

## Clinical Performance

Sensitivity or positive percent agreement (PPA) was calculated by dividing the number of true positive (TP) results by the sum of TP and false negative (FN) results, while specificity or negative percent agreement (NPA) was calculated by dividing the number of true negative (TN) results by the sum of TN and false positive (FP) results. A TP result being defined as a sample where the detected **cobas eplex** BCID-GN panel result matched the detected comparator method result, while a TN result was one where a negative **cobas eplex** BCID-GN panel result matched a negative comparator method result. The two-sided 95% confidence interval was also calculated.

A total of 349 prospectively-collected samples (167 tested fresh and 182 tested after previously frozen) and 577 retrospectively collected samples from blood culture bottles flagged positive in a continuously monitoring blood culture system and removed from the system within 8 hours of positivity were evaluated for the **cobas eplex** BCID-GN panel targets. Specimens evaluated were determined to contain gram-negative or gram-variable organisms based on Gram stain. A total of 777 contrived samples were prepared by spiking an isolate into a blood culture bottle with human whole blood and growing until flagged positive by a continuously monitoring blood culture system. Contrived samples were removed from the system within 8 hours of positivity and stored frozen until the time of testing. PPA and NPA results are summarized by target in **Tables 15-42** below, and the strains used to contrive samples are summarized in **Table 43**.

**Table 15: Clinical Performance for *Acinetobacter baumannii***

Target	Sample Type	Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
<i>Acinetobacter baumannii</i>	Prospective (Fresh)	0/0	---	167/167	100 (97.8-100)
	Prospective (Frozen)	4/4	100 (51.0-100)	178/178	100 (97.9-100)
	<b>Prospective (All)</b>	<b>4/4</b>	<b>100 (51.0-100)</b>	<b>345/345</b>	<b>100 (98.9-100)</b>
	Retrospective	15/15	100 (79.6-100)	560/561	99.8 (99.0-100)
	<b>Prospective / Retrospective</b>	<b>19/19</b>	<b>100 (83.2-100)</b>	<b>905/906<sup>A</sup></b>	<b>99.9 (99.4-100)</b>
	Contrived	55/55	100 (93.5-100)	722/722	100 (99.5-100)
	<b>Overall</b>	<b>74/74</b>	<b>100 (95.1-100)</b>	<b>1627/1628</b>	<b>99.9 (99.7-100)</b>

CI= Confidence Interval

A. *A. baumannii* was detected in the 1/1 false positive sample using PCR/sequencing.**Table 16: Clinical Performance for *Bacteroides fragilis***

Target	Sample Type	Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
<i>Bacteroides fragilis</i>	Prospective (Fresh)	6/6	100 (61.0-100)	161/161	100 (97.7-100)
	Prospective (Frozen)	5/5	100 (56.6-100)	177/177	100 (97.9-100)
	<b>Prospective (All)</b>	<b>11/11</b>	<b>100 (74.1-100)</b>	<b>338/338</b>	<b>100 (98.9-100)</b>
	Retrospective	14/17	82.4 (59.0-93.8)	558/560	99.6 (98.7-99.9)
	<b>Prospective / Retrospective</b>	<b>25/28<sup>A</sup></b>	<b>89.3 (72.8-96.3)</b>	<b>896/898<sup>B</sup></b>	<b>99.8 (99.2-99.9)</b>
	Contrived	40/40	100 (91.2-100)	737/737	100 (99.5-100)
	<b>Overall</b>	<b>65/68</b>	<b>95.6 (87.8-98.5)</b>	<b>1633/1635</b>	<b>99.9 (99.6-100)</b>

A. *B. fragilis* was not detected in 2 false negative samples, but PCR/sequencing instead detected *B. caccae* and *B. thetaiotaomicron*, which were not identified by standard laboratory procedures.B. *B. fragilis* was detected in 2/2 false positive samples using PCR/sequencing.**Table 17: Clinical Performance for *Citrobacter***

Target	Sample Type	Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
<i>Citrobacter</i>	Prospective (Fresh)	3/3	100 (43.9-100)	163/164	99.4 (96.6-99.9)
	Prospective (Frozen)	2/2	100 (34.2-100)	178/180	98.9 (96.0-99.7)
	<b>Prospective (All)</b>	<b>5/5</b>	<b>100 (56.6-100)</b>	<b>341/344</b>	<b>99.1 (97.5-99.7)</b>
	Retrospective	20/21	95.2 (77.3-99.2)	555/556	99.8 (99.0-100)
	<b>Prospective / Retrospective</b>	<b>25/26</b>	<b>96.2 (81.1-99.3)</b>	<b>896/900<sup>A</sup></b>	<b>99.6 (98.9-99.8)</b>
	Contrived	43/43	100 (91.8-100)	734/734	100 (99.5-100)
	<b>Overall</b>	<b>68/69</b>	<b>98.6 (92.2-99.7)</b>	<b>1630/1634</b>	<b>99.8 (99.4-99.9)</b>

A. *C. braakii* (2) and *C. freundii* (2) were detected in 4/4 false positive samples using PCR/sequencing.



Table 18: Clinical Performance for *Cronobacter sakazakii*

Target	Sample Type	Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
<i>Cronobacter sakazakii</i>	Prospective (Fresh)	0/0	---	167/167	100 (97.8-100)
	Prospective (Frozen)	0/0	---	182/182	100 (97.9-100)
	<b>Prospective (All)</b>	<b>0/0</b>	<b>---</b>	<b>349/349</b>	<b>100 (98.9-100)</b>
	Retrospective	1/1	100 (20.7-100)	576/576	100 (99.3-100)
	<b>Prospective / Retrospective</b>	<b>1/1</b>	<b>100 (20.7-100)</b>	<b>925/925</b>	<b>100 (99.6-100)</b>
	Contrived	45/45	100 (92.1-100)	732/732	100 (99.5-100)
	<b>Overall</b>	<b>46/46</b>	<b>100 (92.3-100)</b>	<b>1657/1657</b>	<b>100 (99.8-100)</b>

Table 19: Clinical Performance for *Enterobacter cloacae* complex

Target	Sample Type	Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
<i>Enterobacter cloacae</i> complex	Prospective (Fresh)	12/12	100 (75.8-100)	153/155	98.7 (95.4-99.6)
	Prospective (Frozen)	7/7	100 (64.6-100)	173/175	98.9 (95.9-99.7)
	<b>Prospective (All)</b>	<b>19/19</b>	<b>100 (83.2-100)</b>	<b>326/330</b>	<b>98.8 (96.9-99.5)</b>
	Retrospective	47/50	94.0 (83.8-97.9)	526/527	99.8 (98.9-100)
	<b>Prospective / Retrospective</b>	<b>66/69<sup>A</sup></b>	<b>95.7 (88.0-98.5)</b>	<b>852/857<sup>B</sup></b>	<b>99.4 (98.6-99.8)</b>
	Contrived	35/37 <sup>C</sup>	94.6 (82.3-98.5)	739/740	99.9 (99.2-100)
	<b>Overall</b>	<b>101/106</b>	<b>95.3 (89.4-98.0)</b>	<b>1591/1597</b>	<b>99.6 (99.2-99.8)</b>

A. A species of the *E. cloacae* complex was not detected in 1 false negative sample, but PCR/sequencing and MALDI-TOF instead detected *E. coli*. Standard laboratory procedures identified *E. cloacae* only.

B. *E. cloacae* was detected in 2/5 false positive samples using PCR/sequencing.

C. *E. cloacae* complex was not detected in 2 samples containing *Enterobacter asburiae*.

Table 20: Clinical Performance for *Enterobacter* (non-*cloacae* complex)

Target	Sample Type	Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
<i>Enterobacter</i> non- <i>cloacae</i> complex	Prospective (Fresh)	3/3	100 (43.9-100)	163/164	99.4 (96.6-99.9)
	Prospective (Frozen)	5/7	71.4 (35.9-91.8)	175/175	100 (97.9-100)
	<b>Prospective (All)</b>	<b>8/10</b>	<b>80.0 (49.0-94.3)</b>	<b>338/339</b>	<b>99.7 (98.3-99.9)</b>
	Retrospective	12/12	100 (75.8-100)	565/565	100 (99.3-100)
	<b>Prospective / Retrospective</b>	<b>20/22<sup>A</sup></b>	<b>90.9 (72.2-97.5)</b>	<b>903/904<sup>B</sup></b>	<b>99.9 (99.4-100)</b>
	Contrived	36/36	100 (90.4-100)	741/741	100 (99.5-100)
	<b>Overall</b>	<b>56/58</b>	<b>96.6 (88.3-99.0)</b>	<b>1644/1645</b>	<b>99.9 (99.7-100)</b>

A. A species of the *E. non-cloacae* complex was not detected in 2 false negative samples. Standard laboratory procedures identified *E. aerogenes* and PCR/sequencing detected *E. cloacae*.

B. A species of the *E. non-cloacae* complex was not detected in the false positive sample using PCR/sequencing.

Table 21: Clinical Performance for *Escherichia coli*

Target	Sample Type	Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
<i>Escherichia coli</i>	Prospective (Fresh)	59/60	98.3 (91.1-99.7)	106/107	99.1 (94.9-99.8)
	Prospective (Frozen)	72/73	98.6 (92.6-99.8)	109/109	100 (96.6-100)
	<b>Prospective (All)</b>	<b>131/133</b>	<b>98.5 (94.7-99.6)</b>	<b>215/216</b>	<b>99.5 (97.4-99.9)</b>
	Retrospective	132/140	94.3 (89.1-97.1)	435/437	99.5 (98.3-99.9)
	<b>Prospective / Retrospective</b>	<b>263/273</b>	<b>96.3 (93.4-98.0)</b>	<b>650/653<sup>A</sup></b>	<b>99.5 (98.7-99.8)</b>
	Contrived	52/52	100 (93.1-100)	725/725	100 (99.5-100)
	<b>Overall</b>	<b>315/325</b>	<b>96.9 (94.4-98.3)</b>	<b>1375/1378</b>	<b>99.8 (99.4-99.9)</b>

A. *E. coli* was detected in 3/3 false positive samples using PCR/sequencing.

Table 22: Clinical Performance for *Fusobacterium necrophorum*

Target	Sample Type	Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
<i>Fusobacterium necrophorum</i>	Prospective (Fresh)	0/0	---	167/167	100 (97.8-100)
	Prospective (Frozen)	0/0	---	182/182	100 (97.9-100)
	<b>Prospective (All)</b>	<b>0/0</b>	<b>---</b>	<b>349/349</b>	<b>100 (98.9-100)</b>
	Retrospective	1/1	100 (20.7-100)	576/576	100 (99.3-100)
	<b>Prospective / Retrospective</b>	<b>1/1</b>	<b>100 (20.7-100)</b>	<b>925/925</b>	<b>100 (99.6-100)</b>
	Contrived	47/48	97.9 (89.1-99.6)	729/729	100 (99.5-100)
	<b>Overall</b>	<b>48/49</b>	<b>98.0 (89.3-99.6)</b>	<b>1654/1654</b>	<b>100 (99.8-100)</b>

Table 23: Clinical Performance for *Fusobacterium nucleatum*

Target	Sample Type	Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
<i>Fusobacterium nucleatum</i>	Prospective (Fresh)	0/0	---	167/167	100 (97.8-100)
	Prospective (Frozen)	0/0	---	182/182	100 (97.9-100)
	<b>Prospective (All)</b>	<b>0/0</b>	<b>---</b>	<b>349/349</b>	<b>100 (98.9-100)</b>
	Retrospective	5/5	100 (56.6-100)	571/572	99.8 (99.0-100)
	<b>Prospective / Retrospective</b>	<b>5/5</b>	<b>100 (56.6-100)</b>	<b>920/921<sup>A</sup></b>	<b>99.9 (99.4-100)</b>
	Contrived	47/47	100 (92.4-100)	730/730	100 (99.5-100)
	<b>Overall</b>	<b>52/52</b>	<b>100 (93.1-100)</b>	<b>1650/1651</b>	<b>99.9 (99.7-100)</b>

A. *F. nucleatum* was detected in the 1/1 false positive sample using PCR/sequencing.

Table 24: Clinical Performance for *Haemophilus influenzae*

Target	Sample Type	Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
<i>Haemophilus influenzae</i>	Prospective (Fresh)	3/3	100 (43.9-100)	164/164	100 (97.7-100)
	Prospective (Frozen)	4/4	100 (51.0-100)	178/178	100 (97.9-100)
	<b>Prospective (All)</b>	<b>7/7</b>	<b>100 (64.6-100)</b>	<b>342/342</b>	<b>100 (98.9-100)</b>
	Retrospective	7/7	100 (64.6-100)	570/570	100 (99.3-100)
	<b>Prospective / Retrospective</b>	<b>14/14</b>	<b>100 (78.5-100)</b>	<b>912/912</b>	<b>100 (99.6-100)</b>
	Contrived	41/41	100 (91.4-100)	736/736	100 (99.5-100)
	<b>Overall</b>	<b>55/55</b>	<b>100 (93.5-100)</b>	<b>1648/1648</b>	<b>100 (99.8-100)</b>

Table 25: Clinical Performance for *Klebsiella oxytoca*

Target	Sample Type	Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
<i>Klebsiella oxytoca</i>	Prospective (Fresh)	4/6	66.7 (30.0-90.3)	160/161	99.4 (96.6-99.9)
	Prospective (Frozen)	7/7	100 (64.6-100)	175/175	100 (97.9-100)
	<b>Prospective (All)</b>	<b>11/13</b>	<b>84.6 (57.8-95.7)</b>	<b>335/336</b>	<b>99.7 (98.3-99.9)</b>
	Retrospective	29/34	85.3 (69.9-93.6)	541/543	99.6 (98.7-99.9)
	<b>Prospective / Retrospective</b>	<b>40/47<sup>A</sup></b>	<b>85.1 (72.3-92.6)</b>	<b>876/879<sup>B</sup></b>	<b>99.7 (99.0-99.9)</b>
	Contrived	20/20	100 (83.9-100)	757/757	100 (99.5-100)
	<b>Overall</b>	<b>60/67</b>	<b>89.6 (80.0-94.8)</b>	<b>1633/1636</b>	<b>99.8 (99.5-99.9)</b>

A. *K. oxytoca* was not detected in 2 false negative samples using PCR/sequencing, but 16S sequencing instead detected *Raoultella ornithinolytica* and *Raoultella planticola*, which were not identified by standard laboratory procedures.

B. *K. oxytoca* was detected in 3/3 false positive samples using PCR/sequencing.

Table 26: Clinical Performance for *Klebsiella pneumoniae* group

Target	Sample Type	Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
<i>Klebsiella pneumoniae</i> group	Prospective (Fresh)	29/30	96.7 (83.3-99.4)	136/137	99.3 (96.0-99.9)
	Prospective (Frozen)	29/31	93.5 (79.3-98.2)	151/151	100 (97.5-100)
	<b>Prospective (All)</b>	<b>58/61</b>	<b>95.1 (86.5-98.3)</b>	<b>287/288</b>	<b>99.7 (98.1-99.9)</b>
	Retrospective	106/108	98.1 (93.5-99.5)	466/469	99.4 (98.1-99.8)
	<b>Prospective / Retrospective</b>	<b>164/169<sup>A</sup></b>	<b>97.0 (93.3-98.7)</b>	<b>753/757<sup>B</sup></b>	<b>99.5 (98.6-99.8)</b>
	Contrived	72/72	100 (94.9-100)	705/705	100 (99.5-100)
	<b>Overall</b>	<b>236/241</b>	<b>97.9 (95.2-99.1)</b>	<b>1458/1462</b>	<b>99.7 (99.3-99.9)</b>

A. *K. pneumoniae* was not detected in 1 false negative sample, but PCR/sequencing and MALDI-TOF instead detected *K. oxytoca*, which was not identified by standard laboratory procedures.

B. *K. pneumoniae* was detected in 4/4 false positive samples using PCR/sequencing.

Table 27: Clinical Performance for *Morganella morganii*

Target	Sample Type	Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
<i>Morganella morganii</i>	Prospective (Fresh)	3/3	100 (43.9-100)	164/164	100 (97.7-100)
	Prospective (Frozen)	0/0	---	182/182	100 (97.9-100)
	<b>Prospective (All)</b>	<b>3/3</b>	<b>100 (43.9-100)</b>	<b>346/346</b>	<b>100 (98.9-100)</b>
	Retrospective	10/10	100 (72.2-100)	566/567	99.8 (99.0-100)
	<b>Prospective / Retrospective</b>	<b>13/13</b>	<b>100 (77.2-100)</b>	<b>912/913<sup>A</sup></b>	<b>99.9 (99.4-100)</b>
	Contrived	49/49	100 (92.7-100)	728/728	100 (99.5-100)
	<b>Overall</b>	<b>62/62</b>	<b>100 (94.2-100)</b>	<b>1640/1641</b>	<b>99.9 (99.7-100)</b>

A. *M. morganii* was detected in 1/1 false positive clinical samples using PCR/sequencing.

Table 28: Clinical Performance for *Neisseria meningitidis*

Target	Sample Type	Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
<i>Neisseria meningitidis</i>	Prospective (Fresh)	0/0	---	167/167	100 (97.8-100)
	Prospective (Frozen)	0/0	---	182/182	100 (97.9-100)
	<b>Prospective (All)</b>	<b>0/0</b>	<b>---</b>	<b>349/349</b>	<b>100 (98.9-100)</b>
	Retrospective	0/0	---	576/577	99.8 (99.0-100)
	<b>Prospective / Retrospective</b>	<b>0/0</b>	<b>---</b>	<b>925/926<sup>A</sup></b>	<b>99.9 (99.4-100)</b>
	Contrived	44/44	100 (92.0-100)	733/733	100 (99.5-100)
	<b>Overall</b>	<b>44/44</b>	<b>100 (92.0-100)</b>	<b>1658/1659</b>	<b>99.9 (99.7-100)</b>

A. *N. meningitidis* was not detected in the false positive sample using PCR/sequencing.

Table 29: Clinical Performance for *Proteus*

Target	Sample Type	Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
<i>Proteus</i>	Prospective (Fresh)	7/8	87.5 (52.9-97.8)	159/159	100 (97.6-100)
	Prospective (Frozen)	15/15	100 (79.6-100)	167/167	100 (97.8-100)
	<b>Prospective (All)</b>	<b>22/23</b>	<b>95.7 (79.0-99.2)</b>	<b>326/326</b>	<b>100 (98.8-100)</b>
	Retrospective	54/55	98.2 (90.4-99.7)	522/522	100 (99.3-100)
	<b>Prospective / Retrospective</b>	<b>76/78</b>	<b>97.4 (91.1-99.3)</b>	<b>848/848</b>	<b>100 (99.5-100)</b>
	Contrived	9/9	100 (70.1-100)	768/768	100 (99.5-100)
	<b>Overall</b>	<b>85/87</b>	<b>97.7 (92.0-99.4)</b>	<b>1616/1616</b>	<b>100 (99.8-100)</b>

**Table 30: Clinical Performance for *Proteus mirabilis***

Target	Sample Type	Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
<i>Proteus mirabilis</i>	Prospective (Fresh)	7/8	87.5 (52.9-97.8)	159/159	100 (97.6-100)
	Prospective (Frozen)	15/15	100 (79.6-100)	167/167	100 (97.8-100)
	<b>Prospective (All)</b>	<b>22/23</b>	<b>95.7 (79.0-99.2)</b>	<b>326/326</b>	<b>100 (98.8-100)</b>
	Retrospective	50/51	98.0 (89.7-99.7)	526/526	100 (99.3-100)
	<b>Prospective / Retrospective</b>	<b>72/74</b>	<b>97.3 (90.7-99.3)</b>	<b>852/852</b>	<b>100 (99.6-100)</b>
	Contrived	9/9	100 (70.1-100)	768/768	100 (99.5-100)
	<b>Overall</b>	<b>81/83</b>	<b>97.6 (91.6-99.3)</b>	<b>1620/1620</b>	<b>100 (99.8-100)</b>

**Table 31: Clinical Performance for *Pseudomonas aeruginosa***

Target	Sample Type	Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
<i>Pseudomonas aeruginosa</i>	Prospective (Fresh)	10/10	100 (72.2-100)	157/157	100 (97.6-100)
	Prospective (Frozen)	17/18	94.4 (74.2-99.0)	163/164	99.4 (96.6-99.9)
	<b>Prospective (All)</b>	<b>27/28</b>	<b>96.4 (82.3-99.4)</b>	<b>320/321</b>	<b>99.7 (98.3-99.9)</b>
	Retrospective	56/60	93.3 (84.1-97.4)	514/517	99.4 (98.3-99.8)
	<b>Prospective / Retrospective</b>	<b>83/88</b>	<b>94.3 (87.4-97.5)</b>	<b>834/838<sup>A</sup></b>	<b>99.5 (98.8-99.8)</b>
	Contrived	32/32	100 (89.3-100)	745/745	100 (99.5-100)
	<b>Overall</b>	<b>115/120</b>	<b>95.8 (90.6-98.2)</b>	<b>1579/1583</b>	<b>99.7 (99.4-99.9)</b>

A. *P. aeruginosa* was detected in 2/4 false positive samples using PCR/sequencing.

**Table 32: Clinical Performance for *Salmonella***

Target	Sample Type	Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
<i>Salmonella</i>	Prospective (Fresh)	2/2	100 (34.2-100)	165/165	100 (97.7-100)
	Prospective (Frozen)	0/0	---	182/182	100 (97.9-100)
	<b>Prospective (All)</b>	<b>2/2</b>	<b>100 (34.2-100)</b>	<b>347/347</b>	<b>100 (98.9-100)</b>
	Retrospective	18/19	94.7 (75.4-99.1)	558/558	100 (99.3-100)
	<b>Prospective / Retrospective</b>	<b>20/21<sup>A</sup></b>	<b>95.2 (77.3-99.2)</b>	<b>905/905</b>	<b>100 (99.6-100)</b>
	Contrived	34/35	97.1 (85.5-99.5)	742/742	100 (99.5-100)
	<b>Overall</b>	<b>54/56</b>	<b>96.4 (87.9-99.0)</b>	<b>1647/1647</b>	<b>100 (99.8-100)</b>

A. *Salmonella* was not detected in 1 false negative sample, but PCR/sequencing instead detected *E. coli*, which was not identified by standard laboratory procedures.

Table 33: Clinical Performance for *Serratia*

Target	Sample Type	Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
<i>Serratia</i>	Prospective (Fresh)	6/6	100 (61.0-100)	161/161	100 (97.7-100)
	Prospective (Frozen)	4/4	100 (51.0-100)	178/178	100 (97.9-100)
	<b>Prospective (All)</b>	<b>10/10</b>	<b>100 (72.2-100)</b>	<b>339/339</b>	<b>100 (98.9-100)</b>
	Retrospective	34/34	100 (89.8-100)	542/543	99.8 (99.0-100)
	<b>Prospective / Retrospective</b>	<b>44/44</b>	<b>100 (92.0-100)</b>	<b>881/882<sup>A</sup></b>	<b>99.9 (99.4-100)</b>
	Contrived	36/36	100 (90.4-100)	741/741	100 (99.5-100)
	<b>Overall</b>	<b>80/80</b>	<b>100 (95.4-100)</b>	<b>1622/1623</b>	<b>99.9 (99.7-100)</b>

A. *S. marcescens* was detected in the 1/1 false positive sample using PCR/sequencing.

Table 34: Clinical Performance for *Serratia marcescens*

Target	Sample Type	Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
<i>Serratia marcescens</i>	Prospective (Fresh)	5/5	100 (56.6-100)	162/162	100 (97.7-100)
	Prospective (Frozen)	4/4	100 (51.0-100)	178/178	100 (97.9-100)
	<b>Prospective (All)</b>	<b>9/9</b>	<b>100 (70.1-100)</b>	<b>340/340</b>	<b>100 (98.9-100)</b>
	Retrospective	34/34	100 (89.8-100)	542/543	99.8 (99.0-100)
	<b>Prospective / Retrospective</b>	<b>43/43</b>	<b>100 (91.8-100)</b>	<b>882/883<sup>A</sup></b>	<b>99.9 (99.4-100)</b>
	Contrived	19/19	100 (83.2-100)	758/758	100 (99.5-100)
	<b>Overall</b>	<b>62/62</b>	<b>100 (94.2-100)</b>	<b>1640/1641</b>	<b>99.9 (99.7-100)</b>

A. *S. marcescens* was detected in the 1/1 false positive sample using PCR/sequencing.

Table 35: Clinical Performance for *Stenotrophomonas maltophilia*

Target	Sample Type	Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
<i>Stenotrophomonas maltophilia</i>	Prospective (Fresh)	2/3	66.7 (20.8-93.9)	164/164	100 (97.7-100)
	Prospective (Frozen)	1/1	100 (20.7-100)	181/181	100 (97.9-100)
	<b>Prospective (All)</b>	<b>3/4</b>	<b>75.0 (30.1-95.4)</b>	<b>345/345</b>	<b>100 (98.9-100)</b>
	Retrospective	8/10	80.0 (49.0-94.3)	566/567	99.8 (99.0-100)
	<b>Prospective / Retrospective</b>	<b>11/14</b>	<b>78.6 (52.4-92.4)</b>	<b>911/912<sup>A</sup></b>	<b>99.9 (99.4-100)</b>
	Contrived	36/36	100 (90.4-100)	741/741	100 (99.5-100)
	<b>Overall</b>	<b>47/50</b>	<b>94.0 (83.8-97.9)</b>	<b>1652/1653</b>	<b>99.9 (99.7-100)</b>

A. *S. maltophilia* was detected in the 1/1 false positive sample using PCR/sequencing.

Table 36: Clinical Performance for CTX-M

Target	Sample Type	Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
CTX-M	Prospective (Fresh)	10/13	76.9 (49.7-91.8)	127/127	100 (97.1-100)
	Prospective (Frozen)	12/16	75.0 (50.5-89.8)	144/144	100 (97.4-100)
	<b>Prospective (All)</b>	<b>22/29</b>	<b>75.9 (57.9-87.8)</b>	<b>271/271</b>	<b>100 (98.6-100)</b>
	Retrospective	52/56	92.9 (83.0-97.2)	483/483	100 (99.2-100)
	<b>Prospective / Retrospective</b>	<b>74/85<sup>A</sup></b>	<b>87.1 (78.3-92.6)</b>	<b>754/754</b>	<b>100 (99.5-100)</b>
	Contrived	75/75	100 (95.1-100)	437/437	100 (99.1-100)
	<b>Overall</b>	<b>149/160</b>	<b>93.1 (88.1-96.1)</b>	<b>1191/1191</b>	<b>100 (99.7-100)</b>

A. In 3/11 false negative samples, CTX-M signal was above the threshold for detection; however, an associated organism was not detected by the BCID-GN panel and the CTX-M target was reported as 'N/A'. Further testing of the 8/11 remaining false negative samples indicated that 7 of the 8 samples may have been contaminated during the original comparator extraction process and misidentified as having CTX-M present. Specifically, results for 7 of the 8 samples were negative for CTX-M from the following additional testing: 1) qPCR testing of 2 repeat extractions from the original sample, 2) qPCR testing of an extraction from the isolate, and 3) testing of the original sample with an FDA-cleared multiplex assay. For these 7 samples, the originally extracted sample was re-tested with qPCR and CTX-M was again detected, suggesting contamination during the original extraction process. The remaining 8th sample was positive for CTX-M from the repeat extractions, negative for CTX-M from the isolate, and negative for CTX-M when tested with an FDA-cleared multiplex assay. These inconsistent detection results suggest the 8th sample may be a true low-copy CTX-M positive sample.

Table 37: Clinical Performance for IMP

Target	Sample Type	Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
IMP	Prospective (Fresh)	0/0	---	138/138	100 (97.3-100)
	Prospective (Frozen)	0/0	---	159/159	100 (97.6-100)
	<b>Prospective (All)</b>	<b>0/0</b>	<b>---</b>	<b>297/297</b>	<b>100 (98.7-100)</b>
	Retrospective	0/0	---	532/532	100 (99.3-100)
	<b>Prospective / Retrospective</b>	<b>0/0</b>	<b>---</b>	<b>829/829</b>	<b>100 (99.5-100)</b>
	Contrived	40/40	100 (91.2-100)	436/436	100 (99.1-100)
	<b>Overall</b>	<b>40/40</b>	<b>100 (91.2-100)</b>	<b>1265/1265</b>	<b>100 (99.7-100)</b>

Table 38: Clinical Performance for KPC

Target	Sample Type	Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
KPC	Prospective (Fresh)	2/2	100 (34.2-100)	136/136	100 (97.3-100)
	Prospective (Frozen)	1/1	100 (20.7-100)	158/158	100 (97.6-100)
	<b>Prospective (All)</b>	<b>3/3</b>	<b>100 (43.9-100)</b>	<b>294/294</b>	<b>100 (98.7-100)</b>
	Retrospective	4/5	80.0 (37.6-96.4)	527/528	99.8 (98.9-100)
	<b>Prospective / Retrospective</b>	<b>7/8</b>	<b>87.5 (52.9-97.8)</b>	<b>821/822</b>	<b>99.9 (99.3-100)</b>
	Contrived	44/44	100 (92.0-100)	477/477	100 (99.2-100)
	<b>Overall</b>	<b>51/52</b>	<b>98.1 (89.9-99.7)</b>	<b>1298/1299</b>	<b>99.9 (99.6-100)</b>



Table 39: Clinical Performance for NDM

Target	Sample Type	Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
NDM	Prospective (Fresh)	0/0	---	138/138	100 (97.3-100)
	Prospective (Frozen)	0/0	---	159/159	100 (97.6-100)
	<b>Prospective (All)</b>	<b>0/0</b>	<b>---</b>	<b>297/297</b>	<b>100 (98.7-100)</b>
	Retrospective	0/0	---	532/532	100 (99.3-100)
	<b>Prospective / Retrospective</b>	<b>0/0</b>	<b>---</b>	<b>829/829</b>	<b>100 (99.5-100)</b>
	Contrived	54/54	100 (93.4-100)	422/422	100 (99.1-100)
	<b>Overall</b>	<b>54/54</b>	<b>100 (93.4-100)</b>	<b>1251/1251</b>	<b>100 (99.7-100)</b>

Table 40: Clinical Performance for OXA

Target	Sample Type	Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
OXA	Prospective (Fresh)	0/1	0.0 (0.0-79.3)	137/137	100 (97.3-100)
	Prospective (Frozen)	1/1	100 (20.7-100)	158/158	100 (97.6-100)
	<b>Prospective (All)</b>	<b>1/2</b>	<b>50.0 (9.5-90.5)</b>	<b>295/295</b>	<b>100 (98.7-100)</b>
	Retrospective	9/11	81.8 (52.3-94.9)	519/521	99.6 (98.6-99.9)
	<b>Prospective / Retrospective</b>	<b>10/13<sup>A</sup></b>	<b>76.9 (49.7-91.8)</b>	<b>814/816</b>	<b>99.8 (99.1-99.9)</b>
	Contrived	37/37	100 (90.6-100)	439/439	100 (99.1-100)
	<b>Overall</b>	<b>47/50</b>	<b>94.0 (83.8-97.9)</b>	<b>1253/1255</b>	<b>99.8 (99.4-100)</b>

A. In 1/3 false negative samples, OXA signal was above the threshold for detection; however, an associated organism was not detected by the BCID-GN panel and the OXA target was reported as 'N/A'. One additional false negative sample was tested with an FDA-cleared multiplex assay and OXA was not detected. The isolate from the remaining false negative sample tested negative for OXA-23 and OXA-48 by qPCR.

Table 41: Clinical Performance for VIM

Target	Sample Type	Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
VIM	Prospective (Fresh)	0/0	---	138/138	100 (97.3-100)
	Prospective (Frozen)	0/0	---	159/159	100 (97.6-100)
	<b>Prospective (All)</b>	<b>0/0</b>	<b>---</b>	<b>297/297</b>	<b>100 (98.7-100)</b>
	Retrospective	0/0	---	532/532	100 (99.3-100)
	<b>Prospective / Retrospective</b>	<b>0/0</b>	<b>---</b>	<b>829/829</b>	<b>100 (99.5-100)</b>
	Contrived	42/42	100 (91.6-100)	434/434	100 (99.1-100)
	<b>Overall</b>	<b>42/42</b>	<b>100 (91.6-100)</b>	<b>1263/1263</b>	<b>100 (99.7-100)</b>

## Pan Targets

In addition to the evaluable prospective and retrospective samples that contain gram-negative organisms, the clinical performance of the Pan *Candida* and Pan Gram-Positive targets was evaluated by testing an additional 741 non-intended use retrospective samples with gram-positive or fungal organisms; these are denoted as Retrospective (Non-Intended Use) samples. Results for the Pan targets are summarized in **Table 42** and results stratified by species are summarized in **Table 44**. A summary of the strains used to prepare contrived samples and the number of strains for each target is shown in **Table 43**.

**Table 42: Clinical Performance for Pan Targets**

Target	Sample Type	Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
Pan <i>Candida</i>	Prospective (Fresh)	1/1	100 (20.7-100)	165/166	99.4 (96.7-99.9)
	Prospective (Frozen)	0/0	---	182/182	100 (97.9-100)
	<b>Prospective (All)</b>	<b>1/1</b>	<b>100 (20.7-100)</b>	<b>347/348<sup>A</sup></b>	<b>99.7 (98.4-99.9)</b>
	Retrospective	4/7 <sup>B</sup>	57.1 (25.0-84.2)	569/570 <sup>C</sup>	99.8 (99.0-100)
	Retrospective (Non-Intended Use)	99/102 <sup>D</sup>	97.1 (91.7-99.0)	638/639 <sup>E</sup>	99.8 (99.1-100)
	Contrived	0/0	---	777/777	100 (99.5-100)
Pan Gram-Positive	Prospective (Fresh)	7/8	87.5 (52.9-97.8)	155/159	97.5 (93.7-99.0)
	Prospective (Frozen)	10/15	66.7 (41.7-84.8)	164/167	98.2 (94.9-99.4)
	<b>Prospective (All)</b>	<b>17/23<sup>F</sup></b>	<b>73.9 (53.5-87.5)</b>	<b>319/326<sup>G</sup></b>	<b>97.9 (95.6-99.0)</b>
	Retrospective	44/55 <sup>H</sup>	80.0 (67.6-88.4)	512/522 <sup>I</sup>	98.1 (96.5-99.0)
	Retrospective (Non-Intended Use)	567/571	99.3 (98.2-99.7)	165/170 <sup>J</sup>	97.1 (93.3-98.7)
	Contrived	0/0	---	776/777	99.9 (99.3-100)

- A. *C. glabrata* was detected in the 1/1 false positive sample using PCR/sequencing.
- B. 3 of 3 (100%) false negative results occurred in samples in mixed infections with bacterial organisms where the BCID-GN panel results were correct for the other infections in these samples.
- C. *C. albicans* was detected in the 1/1 false positive sample using PCR/sequencing.
- D. 2 of 3 (67%) false negative results occurred in samples in mixed infections with bacterial organisms where the BCID-GN panel results were correct for the other infections in these samples.
- E. *C. glabrata* was detected in the 1/1 false positive sample using PCR/sequencing.
- F. *Bacillus* (the gram-positive organism identified by standard laboratory procedures) was not detected in 2 false negative samples using PCR/sequencing, but 16S sequencing instead detected *Paenibacillus lautus* and *Paenibacillus urinalis*, which were not identified by standard laboratory procedures. 3 of the remaining 4 (75%) false negative results occurred in samples in mixed infections with bacterial organisms where the BCID-GN panel correctly detected the gram-negative organisms present.
- G. *Enterococcus* (1), *Staphylococcus* (3), or *Streptococcus* (2) were detected in 6/7 false positive samples using PCR/sequencing (testing was not performed for the remaining 1/7 false positive samples).
- H. 11 of 11 (100%) false negative results occurred in samples in mixed infections with bacterial organisms where the BCID-GN panel correctly detected the gram-negative organisms present.
- I. *Enterococcus* (2), *Staphylococcus* (1), or *Streptococcus* (5) were detected in 8/10 false positive samples using PCR/sequencing (testing was not performed for the remaining 2/10 false positive samples).
- J. *Bacillus* (1) or *Streptococcus* (1) were detected in 2/5 false positive samples using PCR/sequencing (testing was not performed for the remaining 3/5 false positive samples).

**Table 43: Contrived Sample Summary**

Target	Organism	Strain	Independent Contrived Samples Tested
<i>Acinetobacter baumannii</i>	<i>Acinetobacter baumannii</i>	ATCC19606	2
		ATCCBAA-2093	4
		ATCCBAA-747	5
		NCIMB12457	2

Target	Organism	Strain	Independent Contrived Samples Tested
	<i>Acinetobacter baumannii</i> , NDM <i>Acinetobacter baumannii</i> , OXA-23 <b><i>Acinetobacter baumannii</i> Total</b>	NCTC13302	3
		NCTC13303	4
		NCTC13423	17
		CDC#0033	5
		ATCCBAA-1605	5
		NCTC13304	5
		NCTC13305	3
			<b>55</b>
<i>Bacteroides fragilis</i>	<i>Bacteroides fragilis</i> <b><i>Bacteroides fragilis</i> Total</b>	ATCC23745	8
		ATCC25285	8
		ATCC43860	8
		ATCC700786	8
		NCTC9343	8
			<b>40</b>
<i>Citrobacter</i>	<i>Citrobacter braakii</i>	ATCC43162	4
		ATCC51113	4
	<i>Citrobacter freundii</i>	ATCC43864	4
		ATCC8090	4
		NCTC8581	4
		NCTC9750	5
	<i>Citrobacter freundii</i> , CTX-M	JMI2047	6
	<i>Citrobacter freundii</i> , KPC	CDC#0116	4
	<i>Citrobacter koseri</i>	ATCC27156	4
	<i>Citrobacter youngae</i>	ATCC29935	4
	<b><i>Citrobacter</i> Total</b>		<b>43</b>
<i>Cronobacter sakazakii</i>	<i>Cronobacter sakazakii</i> <b><i>Cronobacter sakazakii</i> Total</b>	ATCC12868	2
		ATCC29004	2
		ATCC29544	4
		ATCCBAA-894	3
		FSLF6-0023	4
		FSLF6-0028	4
		FSLF6-0029	4
		FSLF6-0034	3
		FSLF6-0035	3
		FSLF6-0043	4
		FSLF6-0049	3
		FSLF6-0050	4
		FSLF6-0051	5
			<b>45</b>
<i>Enterobacter cloacae</i> complex	<i>Enterobacter asburiae</i>	ATCC35953	2
		ATCC35955	1
		ATCC35956	4
		ATCC35957	1
	<i>Enterobacter cloacae</i> , CTX-M	CDC#0038	4
		NCTC13464	3
	<i>Enterobacter cloacae</i> , CTX-M, KPC	CDC#0163	2
	<i>Enterobacter cloacae</i> , CTX-M, NDM	CDC#0038	1
		JMI53571	12
	<i>Enterobacter cloacae</i> , VIM	CDC#0154	6
	<i>Enterobacter hormaechei</i> , KPC	ATCCBAA-2082	1

Target	Organism	Strain	Independent Contrived Samples Tested
	<b>Enterobacter cloacae complex Total</b>		<b>37</b>
Enterobacter (non-cloacae complex)	Enterobacter aerogenes	ATCC13048	3
		ATCC29010	3
		ATCC51697	3
	Enterobacter aerogenes, IMP	CDC#0161	5
	Enterobacter aerogenes, OXA-48	CDC#0074	12
	Enterobacter amnigenus	ATCC33072	3
		ATCC33731	3
		ATCC51816	4
	<b>Enterobacter (non-cloacae complex) Total</b>		<b>36</b>
Escherichia coli	Escherichia coli, CTX-M	CDC#0086	3
		NCTC13452	3
		NCTC13461	6
		NCTC13463	2
	Escherichia coli, CTX-M, NDM	CDC#0137	6
		CDC#0151	2
	Escherichia coli, IMP	NCTC13476	7
	Escherichia coli, KPC	ATCCBAA-2340	2
		CDC#0114	4
	Escherichia coli, NDM	CDC#0118	6
		CDC#0150	5
		CDC#0151	4
	Escherichia coli, VIM	JMI32465	2
	<b>Escherichia coli Total</b>		<b>52</b>
Fusobacterium necrophorum	Fusobacterium necrophorum subsp. funduliforme	ATCC51357	24
	Fusobacterium necrophorum subsp. necrophorum	ATCC27852	24
	<b>Fusobacterium necrophorum Total</b>		<b>48</b>
Fusobacterium nucleatum	Fusobacterium nucleatum	ATCC23726	8
		ATCC25586	20
		ATCC31647	19
	<b>Fusobacterium nucleatum Total</b>		<b>47</b>
Haemophilus influenzae	Haemophilus influenzae	ATCC10211	9
		ATCC43065	6
		ATCC49144	9
		NCTC12699	9
		NCTC8468	8
	<b>Haemophilus influenzae Total</b>		<b>41</b>
Klebsiella oxytoca	Klebsiella oxytoca	ATCC43086	4
		ATCC43165	4
		ATCC43863	2
		ATCC49131	4
		ATCC51817	3
		ATCC700324	3
	<b>Klebsiella oxytoca Total</b>		<b>20</b>
Klebsiella pneumoniae group	Klebsiella pneumoniae, CTX-M	NCTC13465	5
	Klebsiella pneumoniae, CTX-M, NDM	ATCCBAA-2146	3
	Klebsiella pneumoniae, CTX-M, OXA	CDC#0140	12
	Klebsiella pneumoniae, IMP	CDC#0034	8

Target	Organism	Strain	Independent Contrived Samples Tested
	<i>Klebsiella pneumoniae</i> , KPC	CDC#0080	6
		CDC#0112	1
		CDC#0113	1
		CDC#0115	4
		CDC#0117	4
		CDC#0120	4
		CDC#0125	4
		CDC#0129	4
	<i>Klebsiella pneumoniae</i> , VIM	LMC_DR00015	6
		NCTC13439	5
		NCTC13440	5
<b><i>Klebsiella pneumoniae</i> group Total</b>		<b>72</b>	
<i>Morganella morganii</i>	<i>Morganella morganii</i>	148-200	8
		148-204	8
		148-205	8
		148-206	9
		148-209	7
	<i>Morganella morganii</i> , CTX-M1, NDM	CDC#0057	5
	<i>Morganella morganii</i> , KPC	CDC#0133	4
	<b><i>Morganella morganii</i> Total</b>		<b>49</b>
<i>Neisseria meningitidis</i>	<i>Neisseria meningitidis</i>	ATCC13077	9
		ATCC13090	8
		ATCC13102	8
		ATCC13113	3
		ATCC35561	10
		NCTC10026	6
	<b><i>Neisseria meningitidis</i> Total</b>		<b>44</b>
<i>Proteus mirabilis</i>	<i>Proteus mirabilis</i> , KPC	CDC#0155	4
	<i>Proteus mirabilis</i> , NDM	CDC#0159	5
	<b><i>Proteus mirabilis</i> Total</b>		<b>9</b>
<i>Pseudomonas aeruginosa</i>	<i>Pseudomonas aeruginosa</i> , IMP	CDC#0092	5
		CDC#0103	8
	<i>Pseudomonas aeruginosa</i> , KPC	CDC#0090	1
	<i>Pseudomonas aeruginosa</i> , VIM	CDC#0054	5
		CDC#0100	4
		CDC#0108	4
		NCTC13437	5
		<b><i>Pseudomonas aeruginosa</i> Total</b>	
<i>Salmonella</i>	<i>Salmonella</i> 4,5,12:I:-	FSL5-0580	2
	<i>Salmonella</i> Heidelberg	ATCC8326	2
	<i>Salmonella</i> Infantis	ATCCBAA-1675	2
	<i>Salmonella</i> Javiana	ATCC10721	1
	<i>Salmonella</i> Montevideo	ATCC8387	8
	<i>Salmonella</i> Muenchen	ATCC8388	1
	<i>Salmonella</i> Newport	ATCC6962	6
	<i>Salmonella</i> Typhimurium	ATCC13311	7
	<i>Salmonella enterica</i> subspecies <i>enterica</i> Enteritidis (Group D1)	ATCCBAA-708	6
	<b><i>Salmonella</i> Total</b>		<b>35</b>
	<i>Serratia</i>	<i>Serratia ficaria</i>	ATCC33105

Target	Organism	Strain	Independent Contrived Samples Tested
	<i>Serratia grimesii</i>	ATCC14460	3
	<i>Serratia plymuthica</i>	ATCC53858	3
	<i>Serratia rubidaea</i>	ATCC27593	4
		ATCC29025	3
	<b>Serratia Total</b>		<b>17</b>
<i>Serratia marcescens</i>	<i>Serratia marcescens</i>	ATCC13880	2
		ATCC14041	3
		ATCC14756	3
		ATCC43861	4
		ATCC43862	3
		ATCC8100	3
	<i>Serratia marcescens</i> , IMP	LMC-DR23105	1
	<b>Serratia marcescens Total</b>		<b>19</b>
<i>Stenotrophomonas maltophilia</i>	<i>Stenotrophomonas maltophilia</i>	148-201	7
		148-222	6
		148-223	7
		148-224	8
		148-225	8
	<b>Stenotrophomonas maltophilia Total</b>		<b>36</b>

## Genus and Group Assay Species Stratification

The **cobas eplex** BCID-GN panel reports genus or group level results for *Citrobacter*, *Enterobacter cloacae* complex, *Enterobacter non-cloacae* complex, *Proteus*, *Salmonella*, *Serratia*, Pan *Candida*, and Pan Gram-Positive targets. Sensitivity/PPA of these genus and group level targets for species as determined by comparator methods for all evaluable samples tested are summarized in **Table 44** and for the Pan targets for non-intended use samples in **Table 45**.

**Table 44: Species Detected in Genus and Group Assays by Comparator Methods**

Target Species Detected by Comparator Method	Prospective Samples		Retrospective Samples		Contrived Samples		Combined Samples	
	Sensitivity/PPA		Sensitivity/PPA		Sensitivity/PPA		Sensitivity/PPA	
	TP/TP+FN	% (95% CI)	TP/TP+FN	% (95% CI)	TP/TP+FN	% (95% CI)	TP/TP+FN	% (95% CI)
<b><i>Citrobacter</i></b>	<b>5/5</b>	<b>100 (56.6-100)</b>	<b>20/21</b>	<b>95.2 (77.3-99.2)</b>	<b>43/43</b>	<b>100 (91.8-100)</b>	<b>68/69</b>	<b>98.6 (92.2-99.7)</b>
<i>Citrobacter braakii</i>			2/3	66.7 (20.8-93.9)	8/8	100 (67.6-100)	10/11	90.9 (62.3-98.4)
<i>Citrobacter freundii</i>	4/4	100 (51.0-100)	13/13	100 (77.2-100)	27/27	100 (87.5-100)	44/44	100 (92.0-100)
<i>Citrobacter koseri</i>	1/1	100 (20.7-100)	4/4	100 (51.0-100)	4/4	100 (51.0-100)	9/9	100 (70.1-100)
<i>Citrobacter youngae</i>			1/1	100 (20.7-100)	4/4	100 (51.0-100)	5/5	100 (56.6-100)
<b><i>Enterobacter</i> (non-cloacae complex)</b>	<b>8/10</b>	<b>80.0 (49.0-94.3)</b>	<b>12/12</b>	<b>100 (75.8-100)</b>	<b>36/36</b>	<b>100 (90.4-100)</b>	<b>56/58</b>	<b>96.6 (88.3-99.0)</b>
<i>Enterobacter aerogenes</i>	7/9	77.8 (45.3-93.7)	12/12	100 (75.8-100)	26/26	100 (87.1-100)	45/47	95.7 (85.8-98.8)
<i>Enterobacter amnigenus</i>					10/10	100 (72.2-100)	10/10	100 (72.2-100)
<i>Enterobacter gergoviae</i>	1/1	100 (20.7-100)					1/1	100 (20.7-100)
<b><i>Enterobacter cloacae</i> complex</b>	<b>19/19</b>	<b>100 (83.2-100)</b>	<b>47/50</b>	<b>94.0 (83.8-97.9)</b>	<b>35/37</b>	<b>94.6 (82.3-98.5)</b>	<b>101/106</b>	<b>95.3 (89.4-98.0)</b>
<i>Enterobacter asburiae</i>					6/8	75.0 (40.9-92.9)	6/8	75.0 (40.9-92.9)
<i>Enterobacter cloacae</i>	19/19	100 (83.2-100)	46/49	93.9 (83.5-97.9)	28/28	100 (87.9-100)	93/96	96.9 (91.2-98.9)

Target Species Detected by Comparator Method	Prospective Samples		Retrospective Samples		Contrived Samples		Combined Samples	
	Sensitivity/PPA		Sensitivity/PPA		Sensitivity/PPA		Sensitivity/PPA	
	TP/TP+FN	% (95% CI)	TP/TP+FN	% (95% CI)	TP/TP+FN	% (95% CI)	TP/TP+FN	% (95% CI)
<i>Enterobacter hormaechei</i>			1/1	100 (20.7-100)	1/1	100 (20.7-100)	2/2	100 (34.2-100)
<b>Proteus</b>	<b>22/23</b>	<b>95.7 (79.0-99.2)</b>	<b>54/55</b>	<b>98.2 (90.4-99.7)</b>	<b>9/9</b>	<b>100 (70.1-100)</b>	<b>85/87</b>	<b>97.7 (92.0-99.4)</b>
<i>Proteus mirabilis</i>	22/23	95.7 (79.0-99.2)	50/51	98.0 (89.7-99.7)	9/9	100 (70.1-100)	81/83	97.6 (91.6-99.3)
<i>Proteus vulgaris</i>			5/5	100 (56.6-100)			5/5	100 (56.6-100)
<b>Salmonella</b>	<b>2/2</b>	<b>100 (34.2-100)</b>	<b>18/19</b>	<b>94.7 (75.4-99.1)</b>	<b>34/35</b>	<b>97.1 (85.5-99.5)</b>	<b>54/56</b>	<b>96.4 (87.9-99.0)</b>
<i>Salmonella</i>	2/2	100 (34.2-100)	15/15	100 (79.6-100)			17/17	100 (81.6-100)
<i>Salmonella</i> 4,5,12:i:-					2/2	100 (34.2-100)	2/2	100 (34.2-100)
<i>Salmonella</i> Heidelberg					2/2	100 (34.2-100)	2/2	100 (34.2-100)
<i>Salmonella</i> Infantis					2/2	100 (34.2-100)	2/2	100 (34.2-100)
<i>Salmonella</i> Javiana					1/1	100 (20.7-100)	1/1	100 (20.7-100)
<i>Salmonella</i> Montevideo					7/8	87.5 (52.9-97.8)	7/8	87.5 (52.9-97.8)
<i>Salmonella</i> Muenchen					1/1	100 (20.7-100)	1/1	100 (20.7-100)
<i>Salmonella</i> Newport					6/6	100 (61.0-100)	6/6	100 (61.0-100)
<i>Salmonella</i> Typhimurium					7/7	100 (64.6-100)	7/7	100 (64.6-100)
<i>Salmonella choleraesuis</i> subsp. <i>arizonae</i>			0/1	0.0 (0.0-79.3)			0/1	0.0 (0.0-79.3)
<i>Salmonella enterica</i> subsp. <i>enterica</i> Enteritidis (Group D1)					6/6	100 (61.0-100)	6/6	100 (61.0-100)
<i>Salmonella enterica</i> subsp. <i>enterica</i> serovar Typhimurium			1/1	100 (20.7-100)			1/1	100 (20.7-100)
<i>Salmonella</i> Typhi			2/2	100 (34.2-100)			2/2	100 (34.2-100)
<b>Serratia</b>	<b>10/10</b>	<b>100 (72.2-100)</b>	<b>34/34</b>	<b>100 (89.8-100)</b>	<b>36/36</b>	<b>100 (90.4-100)</b>	<b>80/80</b>	<b>100 (95.4-100)</b>
<i>Serratia ficaria</i>					4/4	100 (51.0-100)	4/4	100 (51.0-100)
<i>Serratia grimesii</i>					3/3	100 (43.9-100)	3/3	100 (43.9-100)
<i>Serratia liquefaciens</i>	1/1	100 (20.7-100)					1/1	100 (20.7-100)
<i>Serratia marcescens</i>	9/9	100 (70.1-100)	34/34	100 (89.8-100)	19/19	100 (83.2-100)	62/62	100 (94.2-100)
<i>Serratia plymuthica</i>					3/3	100 (43.9-100)	3/3	100 (43.9-100)
<i>Serratia rubidaea</i>					7/7	100 (64.6-100)	7/7	100 (64.6-100)
<b>Pan Candida</b>	<b>1/1</b>	<b>100 (20.7-100)</b>	<b>4/7</b>	<b>57.1 (25.0-84.2)</b>	<b>N/A</b>	<b>N/A</b>	<b>5/8</b>	<b>62.5 (30.6-86.3)</b>
<i>Candida albicans</i>	1/1	100 (20.7-100)	2/4	50.0 (15.0-85.0)			3/5	60.0 (23.1-88.2)
<i>Candida glabrata</i>			1/2	50.0 (9.5-90.5)			1/2	50.0 (9.5-90.5)
<i>Candida krusei</i>			1/1	100 (20.7-100)			1/1	100 (20.7-100)
<i>Candida parapsilosis</i>								
<b>Pan Gram-Positive</b>	<b>17/23</b>	<b>73.9 (53.5-87.5)</b>	<b>44/55</b>	<b>80.0 (67.6-88.4)</b>	<b>N/A</b>	<b>N/A</b>	<b>61/78</b>	<b>78.2 (67.8-85.9)</b>
<i>Bacillus</i> (unspeciated)	1/4	25.0 (4.6-69.9)					1/4	25.0 (4.6-69.9)
<i>Enterococcus</i> (unspeciated)			0/1	0.0 (0.0-79.3)			0/1	0.0 (0.0-79.3)
<i>Enterococcus casseliflavus</i>			0/1	0.0 (0.0-79.3)			0/1	0.0 (0.0-79.3)
<i>Enterococcus faecalis</i>	5/7	71.4 (35.9-91.8)	18/20	90.0 (69.9-97.2)			23/27	85.2 (67.5-94.1)
<i>Enterococcus faecium</i>	1/1	100 (20.7-100)	8/9	88.9 (56.5-98.0)			9/10	90.0 (59.6-98.2)

Target Species Detected by Comparator Method	Prospective Samples		Retrospective Samples		Contrived Samples		Combined Samples	
	Sensitivity/PPA		Sensitivity/PPA		Sensitivity/PPA		Sensitivity/PPA	
	TP/TP+FN	% (95% CI)	TP/TP+FN	% (95% CI)	TP/TP+FN	% (95% CI)	TP/TP+FN	% (95% CI)
<i>Staphylococcus</i> (unspeciated)	3/3	100 (43.9-100)	4/6	66.7 (30.0-90.3)			7/9	77.8 (45.3-93.7)
<i>Staphylococcus aureus</i>	2/2	100 (34.2-100)	5/6	83.3 (43.6-97.0)			7/8	87.5 (52.9-97.8)
<i>Staphylococcus cohnii</i>	1/1	100 (20.7-100)					1/1	100 (20.7-100)
<i>Staphylococcus epidermidis</i>	1/1	100 (20.7-100)	2/3	66.7 (20.8-93.9)			3/4	75.0 (30.1-95.4)
<i>Staphylococcus haemolyticus</i>	2/2	100 (34.2-100)					2/2	100 (34.2-100)
<i>Staphylococcus hominis</i>	1/1	100 (20.7-100)	3/3	100 (43.9-100)			4/4	100 (51.0-100)
<i>Streptococcus</i>	0/1	0.0 (0.0-79.3)					0/1	0.0 (0.0-79.3)
<i>Streptococcus</i> - viridans group	1/1	100 (20.7-100)	0/1	0.0 (0.0-79.3)			1/2	50.0 (9.5-90.5)
<i>Streptococcus anginosus</i> group	1/1	100 (20.7-100)	4/5	80.0 (37.6-96.4)			5/6	83.3 (43.6-97.0)
<i>Streptococcus infantarius</i>			1/1	100 (20.7-100)			1/1	100 (20.7-100)
<i>Streptococcus mitis</i> group			1/1	100 (20.7-100)			1/1	100 (20.7-100)
<i>Streptococcus oralis</i>			1/1	100 (20.7-100)			1/1	100 (20.7-100)
<i>Streptococcus pneumoniae</i>			1/1	100 (20.7-100)			1/1	100 (20.7-100)
<i>Streptococcus salivarius</i>			1/1	100 (20.7-100)			1/1	100 (20.7-100)

**Table 45: Species Detected in Pan Assays by Comparator Methods for Samples in Retrospective (Non-Intended Use) Samples with Gram-Positive or Fungal Organisms**

Target Species Detected by Comparator Method	Retrospective (Non-Intended Use) Samples	
	Sensitivity/PPA	
	TP/TP+FN	% (95% CI)
<b>Pan Candida</b>	99/102	97.1 (91.7-99.0)
<i>Candida albicans</i>	47/48	97.9 (89.1-99.6)
<i>Candida glabrata</i>	37/38	97.4 (86.5-99.5)
<i>Candida krusei</i>	3/3	100 (43.9-100)
<i>Candida parapsilosis</i>	15/16	93.8 (71.7-98.9)
<b>Pan Gram-Positive</b>	567/571	99.3 (98.2-99.7)
<i>Bacillus</i> (unspeciated)	4/4	100 (51.0-100)
<i>Bacillus cereus</i>	4/5	80.0 (37.6-96.4)
<i>Bacillus cereus</i> group - not anthracis	1/1	100 (20.7-100)
<i>Enterococcus</i>	1/1	100 (20.7-100)
<i>Enterococcus faecalis</i>	34/34	100 (89.8-100)
<i>Enterococcus faecium</i>	14/14	100 (78.5-100)
Coagulase-negative <i>Staphylococci</i> (CoNS)	14/14	100 (78.5-100)
<i>Staphylococcus</i> (unspeciated)	86/86	100 (95.7-100)
<i>Staphylococcus aureus</i>	173/174	99.4 (96.8-99.9)
<i>Staphylococcus auricularis</i>	3/3	100 (43.9-100)



Target Species Detected by Comparator Method	Retrospective (Non-Intended Use) Samples	
	Sensitivity/PPA	
	TP/TP+FN	% (95% CI)
<i>Staphylococcus capitis</i>	7/7	100 (64.6-100)
<i>Staphylococcus cohnii</i>	1/1	100 (20.7-100)
<i>Staphylococcus epidermidis</i>	86/87	98.9 (93.8-99.8)
<i>Staphylococcus haemolyticus</i>	6/6	100 (61.0-100)
<i>Staphylococcus hominis</i>	19/19	100 (83.2-100)
<i>Staphylococcus hominis</i> ssp <i>hominis</i>	21/21	100 (84.5-100)
<i>Staphylococcus intermedius</i>	1/1	100 (20.7-100)
<i>Staphylococcus lugdunensis</i>	1/1	100 (20.7-100)
<i>Staphylococcus saccharolyticus</i>	1/1	100 (20.7-100)
<i>Staphylococcus saprophyticus</i>	1/1	100 (20.7-100)
<i>Staphylococcus sciuri</i>	1/1	100 (20.7-100)
<i>Staphylococcus simulans</i>	2/2	100 (34.2-100)
<i>Staphylococcus warneri</i>	4/4	100 (51.0-100)
Alpha Hemolytic <i>Streptococcus</i>	1/1	100 (20.7-100)
Beta Hemolytic <i>Streptococci</i> , Group G	1/1	100 (20.7-100)
Gamma Hemolytic <i>Streptococcus</i>	1/1	100 (20.7-100)
<i>Streptococcus</i> (unspeciated)	9/9	100 (70.1-100)
<i>Streptococcus</i> - <i>viridans</i> group	17/17	100 (81.6-100)
<i>Streptococcus agalactiae</i>	21/21	100 (84.5-100)
<i>Streptococcus anginosus</i>	2/2	100 (34.2-100)
<i>Streptococcus bovis</i>	2/2	100 (34.2-100)
<i>Streptococcus constellatus</i> ssp <i>constellatus</i>	1/1	100 (20.7-100)
<i>Streptococcus dysgalactiae</i> (Group G)	4/4	100 (51.0-100)
<i>Streptococcus gordonii</i>	1/1	100 (20.7-100)
<i>Streptococcus intermedius</i>	1/1	100 (20.7-100)
<i>Streptococcus mitis</i>	11/12	91.7 (64.6-98.5)
<i>Streptococcus mitis</i> group	2/2	100 (34.2-100)
<i>Streptococcus pneumoniae</i>	22/22	100 (85.1-100)
<i>Streptococcus pyogenes</i>	9/9	100 (70.1-100)
<i>Streptococcus salivarius</i>	2/2	100 (34.2-100)

## Resistance Gene Assay Species Stratification

Test results for resistance genes are only reported when an associated organism assay is positive in the same sample. (See **Table 7** for organisms specifically associated with the six resistance markers on the **cobas eplex BCID-GN** panel).

### CTX-M

The PPA and NPA of the BCID-GN panel CTX-M target stratified by the organism identified by comparator methods for prospective, retrospective, and contrived samples are shown in **Tables 46**.

**Table 46: Clinical Performance of CTX-M Target in Samples with Associated Organisms Detected by Comparator Methods**

Species Detected by Comparator Method		Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
<i>Acinetobacter baumannii</i>	Prospective	0/0	---	4/4	100 (51.0-100)
	Retrospective	0/0	---	15/15	100 (79.6-100)
	Contrived	0/0	---	55/55	100 (93.5-100)
	<b>Combined</b>	<b>0/0</b>	<b>---</b>	<b>74/74</b>	<b>100 (95.1-100)</b>
<i>Citrobacter</i>	Prospective	0/0	---	5/5	100 (56.6-100)
	Retrospective	1/1	100 (20.7-100)	20/20	100 (83.9-100)
	Contrived	6/6	100 (61.0-100)	37/37	100 (90.6-100)
	<b>Combined</b>	<b>7/7</b>	<b>100 (64.6-100)</b>	<b>62/62</b>	<b>100 (94.2-100)</b>
<i>Enterobacter</i> (non-cloacae complex)	Prospective	0/0	---	10/10	100 (72.2-100)
	Retrospective	0/0	---	12/12	100 (75.8-100)
	Contrived	0/0	---	36/36	100 (90.4-100)
	<b>Combined</b>	<b>0/0</b>	<b>---</b>	<b>58/58</b>	<b>100 (93.8-100)</b>
<i>Enterobacter cloacae</i> complex	Prospective	0/0	---	19/19	100 (83.2-100)
	Retrospective	0/0	---	50/50	100 (92.9-100)
	Contrived	22/22	100 (85.1-100)	15/15	100 (79.6-100)
	<b>Combined</b>	<b>22/22</b>	<b>100 (85.1-100)</b>	<b>84/84</b>	<b>100 (95.6-100)</b>
<i>Escherichia coli</i>	Prospective	16/18	88.9 (67.2-96.9)	115/115	100 (96.8-100)
	Retrospective	35/37	94.6 (82.3-98.5)	103/103	100 (96.4-100)
	Contrived	22/22	100 (85.1-100)	30/30	100 (88.6-100)
	<b>Combined</b>	<b>73/77</b>	<b>94.8 (87.4-98.0)</b>	<b>248/248</b>	<b>100 (98.5-100)</b>
<i>Klebsiella oxytoca</i>	Prospective	0/1	0.0 (0.0-79.3)	12/12	100 (75.8-100)
	Retrospective	0/0	---	34/34	100 (89.8-100)
	Contrived	0/0	---	20/20	100 (83.9-100)
	<b>Combined</b>	<b>0/1</b>	<b>0.0 (0.0-79.3)</b>	<b>66/66</b>	<b>100 (94.5-100)</b>
<i>Klebsiella pneumoniae</i> group	Prospective	5/5	100 (56.6-100)	56/56	100 (93.6-100)
	Retrospective	14/15	93.3 (70.2-98.8)	93/93	100 (96.0-100)
	Contrived	20/20	100 (83.9-100)	52/52	100 (93.1-100)
	<b>Combined</b>	<b>39/40</b>	<b>97.5 (87.1-99.6)</b>	<b>201/201</b>	<b>100 (98.1-100)</b>
<i>Morganella morganii</i>	Prospective	0/0	---	3/3	100 (43.9-100)
	Retrospective	0/0	---	10/10	100 (72.2-100)
	Contrived	5/5	100 (56.6-100)	44/44	100 (92.0-100)
	<b>Combined</b>	<b>5/5</b>	<b>100 (56.6-100)</b>	<b>57/57</b>	<b>100 (93.7-100)</b>
<i>Proteus</i>	Prospective	2/5	40.0 (11.8-76.9)	18/18	100 (82.4-100)
	Retrospective	2/3	66.7 (20.8-93.9)	52/52	100 (93.1-100)
	Contrived	0/0	---	9/9	100 (70.1-100)
	<b>Combined</b>	<b>4/8</b>	<b>50.0 (21.5-78.5)</b>	<b>79/79</b>	<b>100 (95.4-100)</b>
<i>Proteus mirabilis</i>	Prospective	2/5	40.0 (11.8-76.9)	18/18	100 (82.4-100)
	Retrospective	2/3	66.7 (20.8-93.9)	48/48	100 (92.6-100)
	Contrived	0/0	---	9/9	100 (70.1-100)
	<b>Combined</b>	<b>4/8</b>	<b>50.0 (21.5-78.5)</b>	<b>75/75</b>	<b>100 (95.1-100)</b>
<i>Pseudomonas aeruginosa</i>	Prospective	0/1	0.0 (0.0-79.3)	27/27	100 (87.5-100)
	Retrospective	0/0	---	60/60	100 (94.0-100)
	Contrived	0/0	---	32/32	100 (89.3-100)
	<b>Combined</b>	<b>0/1</b>	<b>0.0 (0.0-79.3)</b>	<b>119/119</b>	<b>100 (96.9-100)</b>

Species Detected by Comparator Method		Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
<i>Salmonella</i>	Prospective	0/0	---	2/2	100 (34.2-100)
	Retrospective	1/1	100 (20.7-100)	18/18	100 (82.4-100)
	Contrived	0/0	---	35/35	100 (90.1-100)
	<b>Combined</b>	<b>1/1</b>	<b>100 (20.7-100)</b>	<b>55/55</b>	<b>100 (93.5-100)</b>
<i>Serratia</i>	Prospective	0/0	---	10/10	100 (72.2-100)
	Retrospective	0/0	---	34/34	100 (89.8-100)
	Contrived	0/0	---	36/36	100 (90.4-100)
	<b>Combined</b>	<b>0/0</b>	<b>---</b>	<b>80/80</b>	<b>100 (95.4-100)</b>
<i>Serratia marcescens</i>	Prospective	0/0	---	9/9	100 (70.1-100)
	Retrospective	0/0	---	34/34	100 (89.8-100)
	Contrived	0/0	---	19/19	100 (83.2-100)
	<b>Combined</b>	<b>0/0</b>	<b>---</b>	<b>62/62</b>	<b>100 (94.2-100)</b>
<i>Stenotrophomonas maltophilia</i>	Prospective	0/0	---	4/4	100 (51.0-100)
	Retrospective	0/0	---	10/10	100 (72.2-100)
	Contrived	0/0	---	36/36	100 (90.4-100)
	<b>Combined</b>	<b>0/0</b>	<b>---</b>	<b>50/50</b>	<b>100 (92.9-100)</b>

A comparison of CTX-M identified by comparator methods versus the **cobas eplex** BCID-GN panel results are shown in **Table 47** for prospective and retrospective samples.

**Table 47: Distribution of CTX-M in Clinical Samples**

BCID-GN	Comparator Method			
	Org+/ARG+	Org+/ARG-	Org-	Total
Org+/ARG+	74	0	2	76
Org+/ARG-	8 <sup>A</sup>	741	2	751
Org-	3 <sup>B</sup>	13	83	99
<b>Total</b>	<b>85</b>	<b>754</b>	<b>87</b>	<b>926</b>

% Agreement (95% CI) for Org+/ARG+: 74/85=87.1% (78.3-92.6)

% Agreement (95% CI) for Org+/ARG-: 741/754=98.3% (97.1-99.0)

% Agreement (95% CI) for Org-: 83/87=95.4% (88.8-98.2)

A. Further testing of these 8 false negative samples indicated that 7 of the 8 samples may have been contaminated during the original extraction process and misidentified as having CTX-M present. Specifically, results for 7 of the 8 samples were negative for CTX-M from the following additional testing: 1) qPCR testing of 2 repeat extractions from the original sample, 2) qPCR testing of an extraction from the isolate, and 3) testing of the original sample with an FDA-cleared multiplex assay. For these 7 samples, the originally extracted sample was re-tested with qPCR and CTX-M was again detected, suggesting contamination during the original extraction process. The remaining 8th sample was positive for CTX-M from the repeat extractions, negative for CTX-M from the isolate, and negative for CTX-M when tested with an FDA-cleared multiplex assay. These inconsistent detection results suggest the 8th sample may be a true low-copy CTX-M positive sample.

B. For these 3 samples, CTX-M signal was above the threshold for detection; however, an associated organism was not detected by the **cobas eplex** BCID-GN panel and the CTX-M target was reported as 'N/A'.

## IMP

The PPA and NPA of the BCID-GN panel IMP target stratified by the contrived organism are shown below in **Table 48**. No prospective or retrospective samples were found to contain IMP.

**Table 48: Clinical Performance of IMP Target in Contrived Samples**

Species Detected by Comparator Method	Sensitivity/PPA		Specificity/NPA	
	TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
<i>Acinetobacter baumannii</i>	0/0	---	74/74	100 (95.1-100)
<i>Citrobacter</i>	0/0	---	69/69	100 (94.7-100)
<i>Enterobacter</i> (non-cloacae complex)	5/5	100 (56.6-100)	53/53	100 (93.2-100)
<i>Enterobacter cloacae</i> complex	0/0	---	106/106	100 (96.5-100)
<i>Escherichia coli</i>	7/7	100 (64.6-100)	318/318	100 (98.8-100)
<i>Klebsiella oxytoca</i>	0/0	---	67/67	100 (94.6-100)
<i>Klebsiella pneumoniae</i> group	14/14	100 (78.5-100)	227/227	100 (98.3-100)
<i>Morganella morganii</i>	0/0	---	62/62	100 (94.2-100)
<i>Proteus</i>	0/0	---	87/87	100 (95.8-100)
<i>Proteus mirabilis</i>	0/0	---	83/83	100 (95.6-100)
<i>Pseudomonas aeruginosa</i>	13/13	100 (77.2-100)	107/107	100 (96.5-100)
<i>Salmonella</i>	0/0	---	56/56	100 (93.6-100)
<i>Serratia</i>	1/1	100 (20.7-100)	79/79	100 (95.4-100)
<i>Serratia marcescens</i>	1/1	100 (20.7-100)	61/61	100 (94.1-100)

A comparison of IMP identified by comparator methods versus the **cobas eplex** BCID-GN panel results are shown in **Table 49** for prospective and retrospective samples.

**Table 49: Distribution of IMP in Clinical Samples**

BCID-GN	Comparator Method			
	Org+/ARG+	Org+/ARG-	Org-	Total
Org+/ARG+	0	0	0	0
Org+/ARG-	0	812	4	816
Org-	0	17	93	110
<b>Total</b>	<b>0</b>	<b>829</b>	<b>97</b>	<b>926</b>

% Agreement (95% CI) for Org+/ARG+: 0/0= N/A

% Agreement (95% CI) for Org+/ARG-: 812/829=97.9% (96.7-98.7)

% Agreement (95% CI) for Org-: 93/97=95.9% (89.9-98.4)

## KPC

The PPA and NPA of the BCID-GN panel KPC target stratified by the organism identified by comparator methods for prospective, retrospective, and contrived samples are shown in **Table 50**.

**Table 50: Clinical Performance of KPC Target in Samples with Associated Organisms Detected by Comparator Methods**

Species Detected by Comparator Method		Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
<i>Acinetobacter baumannii</i>	Prospective	0/0	---	4/4	100 (51.0-100)
	Retrospective	0/0	---	15/15	100 (79.6-100)
	Contrived	0/0	---	55/55	100 (93.5-100)
	<b>Combined</b>	<b>0/0</b>	<b>---</b>	<b>74/74</b>	<b>100 (95.1-100)</b>
<i>Citrobacter</i>	Prospective	0/0	---	5/5	100 (56.6-100)
	Retrospective	0/0	---	21/21	100 (84.5-100)
	Contrived	4/4	100 (51.0-100)	39/39	100 (91.0-100)

Species Detected by Comparator Method		Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
	<b>Combined</b>	<b>4/4</b>	<b>100 (51.0-100)</b>	<b>65/65</b>	<b>100 (94.4-100)</b>
<i>Cronobacter sakazakii</i>	Prospective	---	---	---	---
	Retrospective	0/0	---	1/1	100 (20.7-100)
	Contrived	0/0	---	45/45	100 (92.1-100)
	<b>Combined</b>	<b>0/0</b>	<b>---</b>	<b>46/46</b>	<b>100 (92.3-100)</b>
<i>Enterobacter (non-cloacae complex)</i>	Prospective	0/0	---	10/10	100 (72.2-100)
	Retrospective	0/0	---	12/12	100 (75.8-100)
	Contrived	0/0	---	36/36	100 (90.4-100)
	<b>Combined</b>	<b>0/0</b>	<b>---</b>	<b>58/58</b>	<b>100 (93.8-100)</b>
<i>Enterobacter cloacae</i> complex	Prospective	0/0	---	19/19	100 (83.2-100)
	Retrospective	0/1	0.0 (0.0-79.3)	49/49	100 (92.7-100)
	Contrived	3/3	100 (43.9-100)	34/34	100 (89.8-100)
	<b>Combined</b>	<b>3/4</b>	<b>75.0 (30.1-95.4)</b>	<b>102/102</b>	<b>100 (96.4-100)</b>
<i>Escherichia coli</i>	Prospective	1/1	100 (20.7-100)	132/132	100 (97.2-100)
	Retrospective	0/0	---	140/140	100 (97.3-100)
	Contrived	6/6	100 (61.0-100)	46/46	100 (92.3-100)
	<b>Combined</b>	<b>7/7</b>	<b>100 (64.6-100)</b>	<b>318/318</b>	<b>100 (98.8-100)</b>
<i>Klebsiella oxytoca</i>	Prospective	0/0	---	13/13	100 (77.2-100)
	Retrospective	0/0	---	34/34	100 (89.8-100)
	Contrived	0/0	---	20/20	100 (83.9-100)
	<b>Combined</b>	<b>0/0</b>	<b>---</b>	<b>67/67</b>	<b>100 (94.6-100)</b>
<i>Klebsiella pneumoniae</i> group	Prospective	2/2	100 (34.2-100)	59/59	100 (93.9-100)
	Retrospective	4/4	100 (51.0-100)	103/104	99.0 (94.8-99.8)
	Contrived	22/22	100 (85.1-100)	50/50	100 (92.9-100)
	<b>Combined</b>	<b>28/28</b>	<b>100 (87.9-100)</b>	<b>212/213</b>	<b>99.5 (97.4-99.9)</b>
<i>Morganella morganii</i>	Prospective	0/0	---	3/3	100 (43.9-100)
	Retrospective	0/0	---	10/10	100 (72.2-100)
	Contrived	4/4	100 (51.0-100)	45/45	100 (92.1-100)
	<b>Combined</b>	<b>4/4</b>	<b>100 (51.0-100)</b>	<b>58/58</b>	<b>100 (93.8-100)</b>
<i>Proteus</i>	Prospective	0/0	---	23/23	100 (85.7-100)
	Retrospective	0/0	---	55/55	100 (93.5-100)
	Contrived	4/4	100 (51.0-100)	5/5	100 (56.6-100)
	<b>Combined</b>	<b>4/4</b>	<b>100 (51.0-100)</b>	<b>83/83</b>	<b>100 (95.6-100)</b>
<i>Proteus mirabilis</i>	Prospective	0/0	---	23/23	100 (85.7-100)
	Retrospective	0/0	---	51/51	100 (93.0-100)
	Contrived	4/4	100 (51.0-100)	5/5	100 (56.6-100)
	<b>Combined</b>	<b>4/4</b>	<b>100 (51.0-100)</b>	<b>79/79</b>	<b>100 (95.4-100)</b>
<i>Pseudomonas aeruginosa</i>	Prospective	0/0	---	28/28	100 (87.9-100)
	Retrospective	0/0	---	60/60	100 (94.0-100)
	Contrived	1/1	100 (20.7-100)	31/31	100 (89.0-100)
	<b>Combined</b>	<b>1/1</b>	<b>100 (20.7-100)</b>	<b>119/119</b>	<b>100 (96.9-100)</b>
<i>Salmonella</i>	Prospective	0/0	---	2/2	100 (34.2-100)
	Retrospective	0/0	---	19/19	100 (83.2-100)
	Contrived	0/0	---	35/35	100 (90.1-100)
	<b>Combined</b>	<b>0/0</b>	<b>---</b>	<b>56/56</b>	<b>100 (93.6-100)</b>
<i>Serratia</i>	Prospective	0/0	---	10/10	100 (72.2-100)

Species Detected by Comparator Method		Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
<i>Serratia marcescens</i>	Retrospective	0/0	---	34/34	100 (89.8-100)
	Contrived	0/0	---	36/36	100 (90.4-100)
	<b>Combined</b>	<b>0/0</b>	<b>---</b>	<b>80/80</b>	<b>100 (95.4-100)</b>
	Prospective	0/0	---	9/9	100 (70.1-100)
<i>Serratia marcescens</i>	Retrospective	0/0	---	34/34	100 (89.8-100)
	Contrived	0/0	---	19/19	100 (83.2-100)
	<b>Combined</b>	<b>0/0</b>	<b>---</b>	<b>62/62</b>	<b>100 (94.2-100)</b>
	Prospective	0/0	---	9/9	100 (70.1-100)

A comparison of KPC identified by comparator methods versus the **cobas eplex** BCID-GN panel results are shown in **Table 51** for prospective and retrospective samples.

**Table 51: Distribution of KPC in Clinical Samples**

BCID-GN	Comparator Method			Total
	Org+/ARG+	Org+/ARG-	Org-	
Org+/ARG+	7	1	0	8
Org+/ARG-	1	804	4	809
Org-	0	17	92	109
<b>Total</b>	<b>8</b>	<b>822</b>	<b>96</b>	<b>926</b>

% Agreement (95% CI) for Org+/ARG+: 7/8=87.5% (52.9-97.8)

% Agreement (95% CI) for Org+/ARG-: 804/822=97.8% (96.6-98.6)

% Agreement (95% CI) for Org-: 92/96=95.8% (89.8-98.4)

## NDM

The PPA and NPA of the BCID-GN panel NDM target stratified by the contrived organism are shown below in **Table 52**. No prospective or retrospective samples were found to contain NDM.

**Table 52: Clinical Performance of NDM Target in Contrived Samples by Organism**

Species Detected by Comparator Method		Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
<i>Acinetobacter baumannii</i>		5/5	100 (56.6-100)	69/69	100 (94.7-100)
<i>Citrobacter</i>		0/0	---	69/69	100 (94.7-100)
<i>Enterobacter</i> (non-cloacae complex)		0/0	---	58/58	100 (93.8-100)
<i>Enterobacter cloacae</i> complex		13/13	100 (77.2-100)	93/93	100 (96.0-100)
<i>Escherichia coli</i>		23/23	100 (85.7-100)	302/302	100 (98.7-100)
<i>Klebsiella oxytoca</i>		0/0	---	67/67	100 (94.6-100)
<i>Klebsiella pneumoniae</i> group		3/3	100 (43.9-100)	238/238	100 (98.4-100)
<i>Morganella morganii</i>		5/5	100 (56.6-100)	57/57	100 (93.7-100)
<i>Proteus</i>		5/5	100 (56.6-100)	82/82	100 (95.5-100)
<i>Proteus mirabilis</i>		5/5	100 (56.6-100)	78/78	100 (95.3-100)
<i>Pseudomonas aeruginosa</i>		0/0	---	120/120	100 (96.9-100)
<i>Salmonella</i>		0/0	---	56/56	100 (93.6-100)
<i>Serratia</i>		0/0	---	80/80	100 (95.4-100)
<i>Serratia marcescens</i>		0/0	---	62/62	100 (94.2-100)

A comparison of NDM identified by comparator methods versus the **cobas eplex** BCID-GN panel results are shown in **Table 53** for prospective and retrospective samples.

**Table 53: Distribution of NDM in Clinical Samples**

BCID-GN	Comparator Method			Total
	Org+/ARG+	Org+/ARG-	Org-	
Org+/ARG+	0	0	0	0
Org+/ARG-	0	812	4	816
Org-	0	17	93	110
<b>Total</b>	<b>0</b>	<b>829</b>	<b>97</b>	<b>926</b>

% Agreement (95% CI) for Org+/ARG+: 0/0= N/A

% Agreement (95% CI) for Org+/ARG-: 812/829=97.9% (96.7-98.7)

% Agreement (95% CI) for Org-: 93/97=95.9% (89.9-98.4)

## OXA

The PPA and NPA of the BCID-GN panel OXA target stratified by target identified by comparator methods for prospective, retrospective, and contrived samples are shown in **Table 54**.

**Table 54: Clinical Performance of OXA Target in Samples with Associated Organisms Detected by Comparator Methods**

Species Detected by Comparator Method		Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
<i>Acinetobacter baumannii</i>	Prospective	1/1	100 (20.7-100)	3/3	100 (43.9-100)
	Retrospective	7/7	100 (64.6-100)	8/8	100 (67.6-100)
	Contrived	13/13	100 (77.2-100)	42/42	100 (91.6-100)
	<b>Combined</b>	<b>21/21</b>	<b>100 (84.5-100)</b>	<b>53/53</b>	<b>100 (93.2-100)</b>
<i>Citrobacter</i>	Prospective	0/0	---	5/5	100 (56.6-100)
	Retrospective	0/0	---	21/21	100 (84.5-100)
	Contrived	0/0	---	43/43	100 (91.8-100)
	<b>Combined</b>	<b>0/0</b>	<b>---</b>	<b>69/69</b>	<b>100 (94.7-100)</b>
<i>Enterobacter</i> (non-cloacae complex)	Prospective	0/0	---	10/10	100 (72.2-100)
	Retrospective	0/0	---	12/12	100 (75.8-100)
	Contrived	12/12	100 (75.8-100)	24/24	100 (86.2-100)
	<b>Combined</b>	<b>12/12</b>	<b>100 (75.8-100)</b>	<b>46/46</b>	<b>100 (92.3-100)</b>
<i>Enterobacter cloacae</i> complex	Prospective	0/0	---	19/19	100 (83.2-100)
	Retrospective	0/0	---	50/50	100 (92.9-100)
	Contrived	0/0	---	37/37	100 (90.6-100)
	<b>Combined</b>	<b>0/0</b>	<b>---</b>	<b>106/106</b>	<b>100 (96.5-100)</b>
<i>Escherichia coli</i>	Prospective	0/1	0.0 (0.0-79.3)	132/132	100 (97.2-100)
	Retrospective	1/2	50.0 (9.5-90.5)	138/138	100 (97.3-100)
	Contrived	0/0	---	52/52	100 (93.1-100)
	<b>Combined</b>	<b>1/3</b>	<b>33.3 (6.1-79.2)</b>	<b>322/322</b>	<b>100 (98.8-100)</b>
<i>Klebsiella oxytoca</i>	Prospective	0/0	---	13/13	100 (77.2-100)
	Retrospective	0/0	---	34/34	100 (89.8-100)
	Contrived	0/0	---	20/20	100 (83.9-100)
	<b>Combined</b>	<b>0/0</b>	<b>---</b>	<b>67/67</b>	<b>100 (94.6-100)</b>
<i>Klebsiella pneumoniae</i> group	Prospective	0/0	---	61/61	100 (94.1-100)
	Retrospective	0/1	0.0 (0.0-79.3)	107/107	100 (96.5-100)

Species Detected by Comparator Method		Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
	Contrived	12/12	100 (75.8-100)	60/60	100 (94.0-100)
	<b>Combined</b>	<b>12/13</b>	<b>92.3 (66.7-98.6)</b>	<b>228/228</b>	<b>100 (98.3-100)</b>
<i>Morganella morganii</i>	Prospective	0/0	---	3/3	100 (43.9-100)
	Retrospective	0/0	---	10/10	100 (72.2-100)
	Contrived	0/0	---	49/49	100 (92.7-100)
	<b>Combined</b>	<b>0/0</b>	<b>---</b>	<b>62/62</b>	<b>100 (94.2-100)</b>
<i>Proteus</i>	Prospective	0/0	---	23/23	100 (85.7-100)
	Retrospective	1/1	100 (20.7-100)	53/54	98.1 (90.2-99.7)
	Contrived	0/0	---	9/9	100 (70.1-100)
	<b>Combined</b>	<b>1/1</b>	<b>100 (20.7-100)</b>	<b>85/86</b>	<b>98.8 (93.7-99.8)</b>
<i>Proteus mirabilis</i>	Prospective	0/0	---	23/23	100 (85.7-100)
	Retrospective	0/0	---	50/51	98.0 (89.7-99.7)
	Contrived	0/0	---	9/9	100 (70.1-100)
	<b>Combined</b>	<b>0/0</b>	<b>---</b>	<b>82/83</b>	<b>98.8 (93.5-99.8)</b>
<i>Pseudomonas aeruginosa</i>	Prospective	0/0	---	28/28	100 (87.9-100)
	Retrospective	0/0	---	59/60	98.3 (91.1-99.7)
	Contrived	0/0	---	32/32	100 (89.3-100)
	<b>Combined</b>	<b>0/0</b>	<b>---</b>	<b>119/120</b>	<b>99.2 (95.4-99.9)</b>
<i>Salmonella</i>	Prospective	0/0	---	2/2	100 (34.2-100)
	Retrospective	0/0	---	19/19	100 (83.2-100)
	Contrived	0/0	---	35/35	100 (90.1-100)
	<b>Combined</b>	<b>0/0</b>	<b>---</b>	<b>56/56</b>	<b>100 (93.6-100)</b>
<i>Serratia</i>	Prospective	0/0	---	10/10	100 (72.2-100)
	Retrospective	0/0	---	34/34	100 (89.8-100)
	Contrived	0/0	---	36/36	100 (90.4-100)
	<b>Combined</b>	<b>0/0</b>	<b>---</b>	<b>80/80</b>	<b>100 (95.4-100)</b>
<i>Serratia marcescens</i>	Prospective	0/0	---	9/9	100 (70.1-100)
	Retrospective	0/0	---	34/34	100 (89.8-100)
	Contrived	0/0	---	19/19	100 (83.2-100)
	<b>Combined</b>	<b>0/0</b>	<b>---</b>	<b>62/62</b>	<b>100 (94.2-100)</b>

A comparison of OXA identified by comparator methods versus the **cobas eplex** BCID-GN panel results are shown in **Table 55** for prospective and retrospective samples.



**Table 55: Distribution of OXA in Clinical Samples**

BCID-GN	Comparator Method			
	Org+/ARG+	Org+/ARG-	Org-	Total
Org+/ARG+	10	2	0	12
Org+/ARG-	2 <sup>A</sup>	798	4	804
Org-	1 <sup>B</sup>	16	93	110
<b>Total</b>	13	816	97	926

% Agreement (95% CI) for Org+/ARG+: 10/13=76.9% (49.7-91.8)

% Agreement (95% CI) for Org+/ARG-: 798/816=97.8% (96.5-98.6)

% Agreement (95% CI) for Org-: 93/97=95.9% (89.9-98.4)

A. One false negative sample was tested with an FDA-cleared multiplex assay and OXA was not detected. The isolate from the remaining false negative sample tested negative for OXA-23 and OXA-48 by qPCR.

B. For this sample, OXA signal was above the threshold for detection; however, an associated organism was not detected by the **cobas eplex** BCID-GN panel and the OXA target was reported as 'N/A'.

## VIM

The PPA and NPA of the BCID-GN panel VIM target stratified by the contrived organism are shown below in **Table 56**. No prospective or retrospective samples were found to contain VIM.

**Table 56: Clinical Performance of VIM Target in Contrived Samples by Organism**

Species Detected by Comparator Method	Sensitivity/PPA		Specificity/NPA	
	TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
<i>Acinetobacter baumannii</i>	0/0	---	74/74	100 (95.1-100)
<i>Citrobacter</i>	0/0	---	69/69	100 (94.7-100)
<i>Enterobacter</i> (non-cloacae complex)	0/0	---	58/58	100 (93.8-100)
<i>Enterobacter cloacae</i> complex	6/6	100 (61.0-100)	100/100	100 (96.3-100)
<i>Escherichia coli</i>	2/2	100 (34.2-100)	323/323	100 (98.8-100)
<i>Klebsiella oxytoca</i>	0/0	---	67/67	100 (94.6-100)
<i>Klebsiella pneumoniae</i> group	16/16	100 (80.6-100)	225/225	100 (98.3-100)
<i>Morganella morganii</i>	0/0	---	62/62	100 (94.2-100)
<i>Proteus</i>	0/0	---	87/87	100 (95.8-100)
<i>Proteus mirabilis</i>	0/0	---	83/83	100 (95.6-100)
<i>Pseudomonas aeruginosa</i>	18/18	100 (82.4-100)	102/102	100 (96.4-100)
<i>Salmonella</i>	0/0	---	56/56	100 (93.6-100)
<i>Serratia</i>	0/0	---	80/80	100 (95.4-100)
<i>Serratia marcescens</i>	0/0	---	62/62	100 (94.2-100)

A comparison of VIM identified by comparator methods versus the **cobas eplex** BCID-GN panel results are shown in **Table 57** for prospective and retrospective samples.

**Table 57: Distribution of VIM in Clinical Samples**

BCID-GN	Comparator Method			
	Org+/ARG+	Org+/ARG-	Org-	Total
Org+/ARG+	0	0	0	0
Org+/ARG-	0	812	4	816
Org-	0	17	93	110
<b>Total</b>	0	829	97	926

% Agreement (95% CI) for Org+/ARG+: 0/0= N/A

% Agreement (95% CI) for Org+/ARG-: 812/829=97.9% (96.7-98.7)

% Agreement (95% CI) for Org-: 93/97=95.9% (89.9-98.4)

## Resistance Markers and Antimicrobial Resistance Susceptibility

A supplemental comparison of the CTX-M BCID-GN panel target versus phenotypic antimicrobial susceptibility testing (AST) for extended spectrum beta-lactamase (ESBL) activity, Ceftazidime, Ceftriaxone, and Aztreonam, and a combination of the 4 results (ESBL/Combo) is provided in **Table 58** for clinical isolates with available AST results. In total, 162 isolates had ESBL confirmatory testing and 770 isolates had ESBL confirmatory testing and/or AST results for 1 or more of Ceftazidime, Ceftriaxone, or Aztreonam. A true positive (TP) result was defined where CTX-M was detected by the BCID-GN panel and the isolate was positive for the ESBL confirmatory test or resistant (R) or intermediate (I) to the specific antimicrobial. A false negative (FN) result was defined similarly when CTX-M was not detected by the BCID-GN panel. PPA was calculated as  $100 \times (TP/(TP+FN))$ . A true negative (TN) result was defined where CTX-M was not detected by the BCID-GN panel and the isolate was negative for the ESBL confirmatory test or susceptible (S) to the specific antimicrobial. A false positive (FP) result was defined similarly when CTX-M was detected by the BCID-GN panel. NPA was calculated as  $100 \times (TN/(TN+FP))$ . For the ESBL/Combo analysis, the phenotypic AST result was positive or negative based on the ESBL confirmatory test, if available. If the ESBL confirmatory test was not available, then the phenotypic AST result was positive if any of the 3 antimicrobials were resistant or intermediate, otherwise, the result was negative. Note: ESBL resistance can be due to mechanisms other than acquisition of the CTX-M resistance gene.

**Table 58: Clinical Performance of the BCID-GN panel Target CTX-M Compared to Phenotypic Antimicrobial Susceptibility Testing for ESBL, Ceftazidime, Ceftriaxone, and Aztreonam**

Associated Organism	ESBL confirmatory		Ceftazidime		Ceftriaxone		Aztreonam		ESBL/Combo	
	PPA TP/TP+FN (%)	NPA TN/TN+FP (%)	PPA TP/TP+FN (%)	NPA TN/TN+FP (%)	PPA TP/TP+FN (%)	NPA TN/TN+FP (%)	PPA TP/TP+FN (%)	NPA TN/TN+FP (%)	PPA TP/TP+FN (%)	NPA TN/TN+FP (%)
<i>A. baumannii</i>	---	---	0/10 (0.0%)	3/3 (100%)	0/11 (0.0%)	1/1 (100%)	0/3 (0.0%)	0/0	0/15 (0.0%)	2/2 (100%)
<i>Citrobacter</i>	---	---	0/2 (0.0%)	14/15 (93.3%)	0/3 (0.0%)	21/22 (95.5%)	0/1 (0.0%)	16/17 (94.1%)	0/3 (0.0%)	21/22 (95.5%)
<i>Enterobacter</i>	---	---	0/2 (0.0%)	12/12 (100%)	0/2 (0.0%)	18/18 (100%)	0/1 (0.0%)	9/9 (100%)	0/3 (0.0%)	17/17 (100%)
<i>E. cloacae</i> complex	---	---	0/10 (0.0%)	30/30 (100%)	0/17 (0.0%)	39/39 (100%)	0/5 (0.0%)	25/25 (100%)	0/18 (0.0%)	39/39 (100%)
<i>E. coli</i>	28/30 (93.3%)	82/82 (100%)	29/38 (76.3%)	159/167 (95.2%)	47/59 (79.7%)	180/181 (99.4%)	23/27 (85.2%)	118/120 (98.3%)	47/53 (88.7%)	196/197 (99.5%)
<i>K. oxytoca</i>	0/0	10/10 (100%)	0/1 (0.0%)	29/29 (100%)	0/2 (0.0%)	40/40 (100%)	0/2 (0.0%)	20/20 (100%)	0/2 (0.0%)	41/41 (100%)
<i>K. pneumoniae</i> group	7/11 (63.6%)	25/25 (100%)	13/23 (56.5%)	83/83 (100%)	17/27 (63.0%)	115/115 (100%)	10/12 (83.3%)	72/72 (100%)	17/26 (65.4%)	119/119 (100%)
<i>M. morgani</i>			0/1 (0.0%)	6/6 (100%)	0/2 (0.0%)	9/9 (100%)	0/0	4/4 (100%)	0/2 (0.0%)	9/9 (100%)
<i>Proteus</i>	3/3 (100%)	0/0	1/2 (50.0%)	46/48 (95.8%)	4/7 (57.1%)	59/59 (100%)	2/3 (66.7%)	35/36 (97.2%)	4/8 (50.0%)	59/59 (100%)
<i>P. mirabilis</i>	3/3 (100%)	0/0	1/2 (50.0%)	43/45 (95.6%)	4/5 (80.0%)	56/56 (100%)	2/3 (66.7%)	32/33 (97.0%)	4/6 (66.7%)	56/56 (100%)
<i>P. aeruginosa</i>			0/7 (0.0%)	46/46 (100%)	0/20 (0.0%)	0/0	0/9 (0.0%)	25/25 (100%)	0/32 (0.0%)	41/41 (100%)
<i>Salmonella</i>	1/1 (100%)	0/0	0/0	6/6 (100%)	1/2 (50.0%)	12/12 (100%)	1/1 (100%)	8/8 (100%)	1/2 (50.0%)	15/15 (100%)
<i>Serratia</i>			0/1 (0.0%)	25/25 (100%)	0/4 (0.0%)	32/32 (100%)	0/1 (0.0%)	20/20 (100%)	0/4 (0.0%)	34/34 (100%)
<i>S. marcescens</i>			0/1 (0.0%)	24/24 (100%)	0/4 (0.0%)	31/31 (100%)	0/1 (0.0%)	19/19 (100%)	0/4 (0.0%)	33/33 (100%)
<i>S. maltophilia</i>			0/2 (0.0%)	2/2 (100%)	0/3 (0.0%)	0/0	0/5 (0.0%)	0/0	0/5 (0.0%)	2/2 (100%)
Any Organism	42/48 (87.5%)	117/117 (100%)	44/102 (43.1%)	528/541 (97.6%)	73/168 (43.5%)	613/615 (99.7%)	38/74 (51.4%)	403/408 (98.8%)	73/183 (39.9%)	684/686 (99.7%)
CI	(75.3-94.1)	(96.8-100)	(33.9-52.8)	(95.9-98.6)	(36.2-51.0)	(98.8-99.9)	(40.2-62.4)	(97.2-99.5)	(33.1-47.1)	(98.9-99.9)

CI= confidence interval

A supplemental comparison of the 5 BCID-GN panel carbapenemase resistance gene targets (OXA, KPC, IMP, NDM, VIM) versus phenotypic antimicrobial susceptibility testing (AST) for Ertapenem, Imipenem, and Meropenem is provided in **Table 59** for clinical isolates with available AST results. In total, 731 isolates had AST results for 1 or more of Ertapenem, Imipenem, or Meropenem. A true positive (TP) result was defined where OXA, KPC, IMP, NDM and/or VIM was detected by the BCID-GN panel and the isolate was resistant (R) or intermediate (I) to Ertapenem, Imipenem, or Meropenem. A false negative (FN) result was defined similarly when OXA, KPC, IMP, NDM and/or VIM was not detected by the BCID-GN panel. PPA was calculated as  $100 \times (TP/(TP+FN))$ . A true negative (TN) result was defined where OXA, KPC, IMP, NDM and/or VIM was not detected by the BCID-GN panel and the isolate was susceptible (S) to Ertapenem, Imipenem, and Meropenem. A false positive (FP) result was defined similarly when OXA, KPC, IMP, NDM and/or VIM was detected by the BCID-GN panel. NPA was calculated as  $100 \times (TN/(TN+FP))$ . Note: Carbapenemase resistance can be due to mechanisms other than acquisition of the OXA, KPC, IMP, NDM and/or VIM resistance genes.

**Table 59: Clinical Performance of the BCID-GN panel Resistance Gene Targets Compared to Phenotypic Antimicrobial Susceptibility Testing for Ertapenem, Imipenem, and Meropenem**

Associated Organism	OXA		KPC		IMP		NDM		VIM		Any Resistance Marker	
	PPA TP/TP+FN (%)	NPA TN/TN+FP (%)	PPA TP/TP+FN (%)	NPA TN/TN+FP (%)	PPA TP/TP+FN (%)	NPA TN/TN+FP (%)	PPA TP/TP+FN (%)	NPA TN/TN+FP (%)	PPA TP/TP+FN (%)	NPA TN/TN+FP (%)	PPA TP/TP+FN (%)	NPA TN/TN+FP (%)
<i>A. baumannii</i>	8/9 (88.9%)	9/9 (100%)	0/9 (0.0%)	9/9 (100%)	0/9 (0.0%)	9/9 (100%)	0/9 (0.0%)	9/9 (100%)	0/9 (0.0%)	9/9 (100%)	8/9 (88.9%)	9/9 (100%)
<i>Citrobacter</i>	0/1 (0.0%)	22/22 (100%)	0/1 (0.0%)	22/22 (100%)	0/1 (0.0%)	22/22 (100%)	0/1 (0.0%)	22/22 (100%)	0/1 (0.0%)	22/22 (100%)	0/1 (0.0%)	22/22 (100%)
<i>C. sakazakii</i>	---	---	0/0	1/1 (100%)	---	---	---	---	---	---	---	---
<i>Enterobacter</i>	0/0	15/15 (100%)	0/0	15/15 (100%)	0/0	15/15 (100%)	0/0	15/15 (100%)	0/0	15/15 (100%)	0/0	15/15 (100%)
<i>E. cloacae</i> complex	0/1 (0.0%)	51/51 (100%)	0/1 (0.0%)	51/51 (100%)	0/1 (0.0%)	51/51 (100%)	0/1 (0.0%)	51/51 (100%)	0/1 (0.0%)	51/51 (100%)	0/1 (0.0%)	51/51 (100%)
<i>E. coli</i>	0/2 (0.0%)	247/248 (99.6%)	1/2 (50.0%)	248/248 (100%)	0/2 (0.0%)	248/248 (100%)	0/2 (0.0%)	248/248 (100%)	0/2 (0.0%)	248/248 (100%)	1/2 (50.0%)	247/248 (99.6%)
<i>K. oxytoca</i>	0/0	40/40 (100%)	0/0	40/40 (100%)	0/0	40/40 (100%)	0/0	40/40 (100%)	0/0	40/40 (100%)	0/0	40/40 (100%)
<i>K. pneumoniae</i> group	0/8 (0.0%)	136/136 (100%)	5/8 (62.5%)	135/136 (99.3%)	0/8 (0.0%)	136/136 (100%)	0/8 (0.0%)	136/136 (100%)	0/8 (0.0%)	136/136 (100%)	5/8 (62.5%)	135/136 (99.3%)
<i>M. morganii</i>	0/0	10/10 (100%)	0/0	10/10 (100%)	0/0	10/10 (100%)	0/0	10/10 (100%)	0/0	10/10 (100%)	0/0	10/10 (100%)
<i>Proteus</i>	0/0	61/62 (98.4%)	0/0	62/62 (100%)	0/0	62/62 (100%)	0/0	62/62 (100%)	0/0	62/62 (100%)	0/0	61/62 (98.4%)
<i>P. mirabilis</i>	0/0	57/57 (100%)	0/0	57/57 (100%)	0/0	57/57 (100%)	0/0	57/57 (100%)	0/0	57/57 (100%)	0/0	57/57 (100%)
<i>P. aeruginosa</i>	0/5 (0.0%)	65/66 (98.5%)	0/5 (0.0%)	66/66 (100%)	0/5 (0.0%)	66/66 (100%)	0/5 (0.0%)	66/66 (100%)	0/5 (0.0%)	66/66 (100%)	0/5 (0.0%)	65/66 (98.5%)
<i>Salmonella</i>	0/0	8/8 (100%)	0/0	8/8 (100%)	0/0	8/8 (100%)	0/0	8/8 (100%)	0/0	8/8 (100%)	0/0	8/8 (100%)
<i>Serratia</i>	0/0	38/38 (100%)	0/0	38/38 (100%)	0/0	38/38 (100%)	0/0	38/38 (100%)	0/0	38/38 (100%)	0/0	38/38 (100%)
<i>S. marcescens</i>	0/0	37/37 (100%)	0/0	37/37 (100%)	0/0	37/37 (100%)	0/0	37/37 (100%)	0/0	37/37 (100%)	0/0	37/37 (100%)
Any Organism	8/26 (30.8%) (16.5-50.0)	796/799 (99.6%) (98.9-99.9)	6/26 (23.1%) (11.0-42.1)	799/800 (99.9%) (99.3-100)	0/26 (0.0%) (0.0-12.9)	799/799 (100%) (99.5-100)	0/26 (0.0%) (0.0-12.9)	799/799 (100%) (99.5-100)	0/26 (0.0%) (0.0-12.9)	799/799 (100%) (99.5-100)	14/26 (53.8%) (35.5-71.2)	796/800 (99.5%) (98.7-99.8)

CI= confidence interval

## Co-detections in Clinical Samples

The **cobas eplex** BCID-GN panel identified a total of 103 bacterial co-detections in prospective and retrospective samples. Of the 349 prospective samples, 320 (91.7%) had single detections, 22 (6.2%) had double detections, and 7 (2.0%) had triple detections. Of the 577 retrospective samples, 503 (87.2%) had single detections, 62 (10.7%) had double detections, and 12 (2.1%) had triple detections.

**Tables 60-61** below summarize co-detections detected by the **cobas eplex** BCID-GN panel in prospective and retrospective samples.

**Table 60: Co-Detections Identified by the cobas eplex BCID-GN panel (Prospective Samples)**

Distinct Co-Detection Combinations Detected by the cobas eplex BCID-GN panel in Prospective Clinical Samples				Number of Samples (Number Discrepant)	Discrepant Organism(s) / Resistance Marker(s) <sup>A,B</sup>
Target 1	Target 2	Target 3	Resistance Marker		
<i>A. baumannii</i>	Pan Gram-Positive			2 (0)	
<i>Citrobacter</i>	<i>E. cloacae</i> complex	<i>K. oxytoca</i>		2 (2)	<i>Citrobacter</i> (2), <i>E. cloacae</i> complex (2)
<i>Citrobacter</i>	<i>K. oxytoca</i>	<i>K. pneumoniae</i> group		1 (1)	<i>Citrobacter</i> (1)
<i>Citrobacter</i>	<i>P. mirabilis</i>	Pan Gram-Positive		1 (1)	Pan Gram-Positive (1)
<i>E. cloacae</i> complex	<i>E. coli</i>	<i>K. pneumoniae</i> group		1 (0)	
<i>E. cloacae</i> complex	Pan <i>Candida</i>	Pan Gram-Positive		1 (0)	
<i>E. cloacae</i> complex	Pan Gram-Positive			2 (0)	
<i>E. coli</i>	<i>K. oxytoca</i>			2 (1)	<i>K. oxytoca</i> (1)
<i>E. coli</i>	<i>K. pneumoniae</i> group		CTX-M	1 (1)	<i>E. coli</i> (1)
<i>E. coli</i>	Pan Gram-Positive			2 (1)	Pan Gram-Positive (1)
<i>Enterobacter</i>	<i>K. pneumoniae</i> group			1 (1)	<i>Enterobacter</i> (1)
<i>K. oxytoca</i>	Pan Gram-Positive			1 (0)	
<i>K. oxytoca</i>	<i>S. marcescens</i>			1 (0)	
<i>K. pneumoniae</i> group	<i>P. mirabilis</i>			1 (0)	
<i>K. pneumoniae</i> group	Pan Gram-Positive			2 (0)	
<i>K. pneumoniae</i> group	Pan Gram-Positive		CTX-M, KPC	1 (1)	Pan Gram-Positive (1)
<i>M. morganii</i>	<i>P. mirabilis</i>			1 (0)	
<i>P. aeruginosa</i>	<i>P. mirabilis</i>	Pan Gram-Positive		1 (0)	
<i>P. aeruginosa</i>	Pan Gram-Positive			1 (0)	
<i>P. mirabilis</i>	Pan Gram-Positive			3 (2)	Pan Gram-Positive (2)
<i>P. mirabilis</i>	Pan Gram-Positive		CTX-M	1 (0)	

A. A discrepant organism or resistance marker is defined as one that was detected by the BCID-GN panel but not by the comparator method(s).

B. 12/13 false positive organisms were investigated using PCR/sequencing; the discrepant organism was detected in 11/13 and not detected in 1. One false positive Pan Gram-Positive sample was not tested.

- i. In 3/3 false positive *Citrobacter* samples, *Citrobacter* was detected.
- ii. In 2/2 false positive *E. cloacae* complex samples, *E. cloacae* complex was detected.
- iii. An *Enterobacter* species was not detected in the 1 false positive *Enterobacter* (non-*cloacae* complex) sample.
- iv. In 1/1 false positive *E. coli* sample, *E. coli* was detected.
- v. In 1/1 false positive *K. oxytoca* sample, *K. oxytoca* was detected.
- vi. In 4/4 false positive Pan Gram-Positive samples, a Pan Gram-Positive organism was detected.

**Table 61: Co-Detections Identified by the cobas eplex BCID-GN panel (Retrospective Samples)**

Distinct Co-Detection Combinations Detected by the cobas eplex BCID-GN panel in Retrospective Clinical Samples				Number Samples (Number Discrepant)	Discrepant Organism(s) / Resistance Marker(s) <sup>A,B</sup>
Target 1	Target 2	Target 3	Resistance Marker		
<i>A. baumannii</i>	<i>K. pneumoniae</i> group	Pan Gram-Positive	CTX-M, OXA	1 (1)	<i>A. baumannii</i> (1), <i>K. pneumoniae</i> group (1), Pan Gram-Positive (1)
<i>A. baumannii</i>	Pan Gram-Positive			2 (0)	
<i>A. baumannii</i>	Pan Gram-Positive		OXA	4 (1)	Pan Gram-Positive (1)
<i>B. fragilis</i>	<i>E. cloacae</i> complex	Pan Gram-Positive		1 (1)	<i>B. fragilis</i> (1)
<i>B. fragilis</i>	<i>E. coli</i>			2 (1)	<i>B. fragilis</i> (1)
<i>B. fragilis</i>	Pan Gram-Positive			1 (0)	
<i>Citrobacter</i>	<i>E. cloacae</i> complex			1 (1)	<i>E. cloacae</i> complex (1)
<i>Citrobacter</i>	<i>E. coli</i>			1 (0)	
<i>Citrobacter</i>	<i>K. oxytoca</i>			1 (1)	<i>Citrobacter</i> (1)
<i>Citrobacter</i>	<i>K. oxytoca</i>	<i>K. pneumoniae</i> group		1 (1)	<i>K. oxytoca</i> (1)
<i>Citrobacter</i>	<i>K. pneumoniae</i> group			1 (0)	
<i>Citrobacter</i>	<i>K. pneumoniae</i> group	Pan Gram-Positive	CTX-M	1 (0)	
<i>Citrobacter</i>	<i>M. morganii</i>	Pan Gram-Positive		1 (1)	<i>M. morganii</i> (1)
<i>Citrobacter</i>	Pan Gram-Positive			3 (2)	Pan Gram-Positive (2)
<i>E. cloacae</i> complex	<i>K. pneumoniae</i> group			1 (0)	
<i>E. cloacae</i> complex	<i>P. aeruginosa</i>	Pan Gram-Positive		1 (1)	<i>P. aeruginosa</i> (1)
<i>E. cloacae</i> complex	Pan <i>Candida</i>			1 (1)	Pan <i>Candida</i> (1)
<i>E. cloacae</i> complex	Pan Gram-Positive			2 (1)	Pan Gram-Positive (1)
<i>E. coli</i>	<i>K. oxytoca</i>			1 (0)	
<i>E. coli</i>	<i>K. oxytoca</i>	Pan Gram-Positive		1 (0)	
<i>E. coli</i>	<i>K. pneumoniae</i> group			2 (0)	
<i>E. coli</i>	<i>M. morganii</i>			1 (0)	
<i>E. coli</i>	<i>P. mirabilis</i>			3 (0)	
<i>E. coli</i>	<i>P. mirabilis</i>	Pan Gram-Positive		1 (0)	
<i>E. coli</i>	Pan Gram-Positive			8 (2)	Pan Gram-Positive (2)
<i>E. coli</i>	Pan Gram-Positive		CTX-M	1 (0)	
<i>Enterobacter</i>	Pan <i>Candida</i>			1 (0)	
<i>Enterobacter</i>	Pan Gram-Positive			1 (0)	
<i>H. influenzae</i>	<i>N. meningitidis</i>	<i>P. aeruginosa</i>		1 (1)	<i>N. meningitidis</i> (1), <i>P. aeruginosa</i> (1)
<i>K. oxytoca</i>	<i>K. pneumoniae</i> group			2 (1)	<i>K. pneumoniae</i> group (1)
<i>K. oxytoca</i>	Pan Gram-Positive			3 (2)	Pan Gram-Positive (2)
<i>K. oxytoca</i>	<i>S. marcescens</i>			1 (1)	<i>S. marcescens</i> (1)
<i>K. pneumoniae</i> group	Pan Gram-Positive			4 (1)	Pan Gram-Positive (1)
<i>K. pneumoniae</i> group	Pan Gram-Positive	<i>S. marcescens</i>		1 (1)	<i>K. pneumoniae</i> group (1)
<i>K. pneumoniae</i> group	<i>S. maltophilia</i>			1 (0)	
<i>M. morganii</i>	<i>P. aeruginosa</i>	Pan Gram-Positive		1 (1)	<i>P. aeruginosa</i> (1)
<i>M. morganii</i>	<i>P. mirabilis</i>			1 (0)	
<i>M. morganii</i>	Pan Gram-Positive	<i>Proteus</i>		1 (0)	

Distinct Co-Detection Combinations Detected by the cobas eplex BCID-GN panel in Retrospective Clinical Samples				Number Samples (Number Discrepant)	Discrepant Organism(s) / Resistance Marker(s) <sup>A,B</sup>
Target 1	Target 2	Target 3	Resistance Marker		
<i>P. aeruginosa</i>	Pan Gram-Positive			1 (0)	
<i>P. mirabilis</i>	Pan Gram-Positive			5 (0)	
Pan <i>Candida</i>	Pan Gram-Positive			2 (0)	
Pan Gram-Positive	<i>S. maltophilia</i>			1 (0)	
Pan Gram-Positive	<i>S. marcescens</i>			3 (0)	

- A. A discrepant organism or resistance marker is defined as one that was detected by the BCID-GN panel but not by the comparator method(s).
- B. 24/26 false positive organisms were investigated using PCR/sequencing; the discrepant organism was detected in 21/24, not detected in 2, and was indeterminate for one organism.
- In 1/1 false positive *A. baumannii* sample, *A. baumannii* was detected.
  - In 2/2 false positive *B. fragilis* samples, *B. fragilis* was detected.
  - In 1/1 false positive *Citrobacter* sample, *Citrobacter* was detected.
  - In the one false positive *E. cloacae* complex sample, PCR/sequencing was indeterminate.
  - In 1/1 false positive *K. oxytoca* sample, *K. oxytoca* was detected.
  - In 3/3 false positive *K. pneumoniae* group samples, *K. pneumoniae* group was detected.
  - In 1/1 false positive sample, *M. morganii* was detected.
  - N. meningitidis* was not detected in the 1 *N. meningitidis* false positive sample.
  - In 2/3 false positive *P. aeruginosa* samples, *P. aeruginosa* was detected. *P. aeruginosa* was not detected in the remaining sample.
  - In 1/1 false positive pan *Candida* sample, Pan *Candida* was detected.
  - In 8/8 false positive Pan Gram-Positive samples, a Pan Gram-Positive organism was detected.
  - In 1/1 false positive *S. marcescens* sample, *S. marcescens* was detected.

**Tables 62-63** below summarize co-detections identified by comparator methods in prospective and retrospective samples that differ from the co-detections represented in the previous tables that were identified by the **cobas eplex** BCID-GN panel. The following co-detections include an organism not targeted by the **cobas eplex** BCID-GN panel (i.e., off-panel organism denoted with an asterisk), an organism discrepant with the **cobas eplex** BCID-GN panel, and/or an organism with more detailed identification than provided by the **cobas eplex** BCID-GN panel (e.g., **cobas eplex** BCID-GN panel detected Pan Gram-Positive and comparator methods identified *Staphylococcus epidermidis*).

**Table 62: Co-Detections Identified by the Comparator Method(s) (Prospective Samples)**

Distinct Co-Detection Combinations Detected by the Comparator Method(s) in Prospective Clinical Samples					Number Samples (Number Discrepant)	Discrepant Organism(s) / Resistance Marker(s) <sup>A</sup>
Organism 1	Organism 2	Organism 3	Organism 4	Resistance Marker		
<i>A. baumannii</i>	<i>E. faecium</i>	<i>Staphylococcus</i>			1 (0)	
<i>A. baumannii</i>	<i>Staphylococcus</i>				1 (0)	
<i>Achromobacter xylosoxidans</i> *	<i>E. cloacae</i>				1 (0)	
<i>Acinetobacter lwoffii</i> *	<i>Staphylococcus hominis</i>				1 (0)	
<i>Acinetobacter pittii</i> *	<i>S. aureus</i>				1 (0)	
<i>Aerococcus viridans</i> *	<i>K. oxytoca</i>	<i>S. epidermidis</i>	<i>Staphylococcus cohnii</i>		1 (0)	
<i>Aerococcus viridans</i> *	<i>Staphylococcus hominis</i>				1 (0)	
<i>B. fragilis</i>	<i>Clostridium species</i> *				1 (0)	
<i>Bacillus</i>	<i>E. cloacae</i>				1 (0)	
<i>C. acnes</i> *	<i>E. coli</i>				1 (0)	



Distinct Co-Detection Combinations Detected by the Comparator Method(s) in Prospective Clinical Samples					Number Samples (Number Discrepant)	Discrepant Organism(s) / Resistance Marker(s) <sup>A</sup>
Organism 1	Organism 2	Organism 3	Organism 4	Resistance Marker		
<i>C. albicans</i>	<i>E. cloacae</i>	<i>E. faecalis</i>			1 (0)	
<i>C. freundii</i>	<i>P. mirabilis</i>	<i>Providencia stuartii</i> *			1 (0)	
<i>Candida lusitanae</i> *	<i>S. liquefaciens</i>				1 (0)	
<i>Citrobacter amalonaticus</i> *	<i>E. coli</i>				1 (0)	
<i>E. aerogenes</i>	<i>K. oxytoca</i>	<i>Leclercia adecarboxylata</i> *			2 (2)	<i>E. aerogenes</i> (2)
<i>E. aerogenes</i>	<i>P. aeruginosa</i>				1 (1)	<i>P. aeruginosa</i> (1)
<i>E. cloacae</i>	<i>E. coli</i>	<i>K. pneumoniae</i>			1 (0)	
<i>E. cloacae</i>	<i>S. aureus</i>				1 (0)	
<i>E. coli</i>	<i>E. faecalis</i>				1 (0)	
<i>E. coli</i>	<i>K. pneumoniae</i>				1 (1)	<i>E. coli</i> (1)
<i>E. coli</i>	<i>P. mirabilis</i>	<i>Providencia stuartii</i> *	<i>S. anginosus</i> group	CTX-M	1 (1)	<i>E. coli</i> (1)
<i>E. faecalis</i>	<i>K. pneumoniae</i>				3 (1)	<i>E. faecalis</i> (1)
<i>E. faecalis</i>	<i>M. morgani</i>	<i>P. mirabilis</i>			1 (1)	<i>E. faecalis</i> (1)
<i>E. faecalis</i>	<i>Providencia stuartii</i> *				1 (0)	
<i>Enterobacteriaceae</i> *	<i>K. pneumoniae</i>				1 (0)	
<i>K. pneumoniae</i>	<i>Staphylococcus haemolyticus</i>	Non-fermenting Gram-Negative bacilli*			1 (1)	<i>K. pneumoniae</i> (1)
<i>Lactococcus lactis</i> *	<i>P. mirabilis</i>				1 (0)	
<i>Micrococcus luteus</i> *	<i>Sphingomonas paucimobilis</i> *				1 (0)	
<i>P. aeruginosa</i>	<i>P. mirabilis</i>	<i>Streptococcus - viridans</i> group			1 (0)	
<i>P. aeruginosa</i>	<i>S. maltophilia</i>				1 (1)	<i>S. maltophilia</i> (1)
<i>P. aeruginosa</i>	<i>Staphylococcus haemolyticus</i>				1 (0)	
<i>P. mirabilis</i>	<i>Staphylococcus</i>				1 (0)	
<i>S. maltophilia</i>	<i>Streptococcus</i>				1 (1)	<i>Streptococcus</i> (1)

\* Indicates an off-panel organism not targeted by the BCID-GN panel.

A. A discrepant organism or resistance marker is defined as one that was detected by the comparator method(s) but not by the BCID-GN panel (excludes organisms not targeted by the BCID-GN panel).

**Table 63: Co-Detections Identified by the Comparator Method(s) (Retrospective Samples)**

Distinct Co-Detection Combinations Detected by the Comparator Method(s) in Retrospective Clinical Samples					Number Samples (Number Discrepant)	Discrepant Organism(s) / Resistance Marker(s) <sup>A</sup>
Organism 1	Organism 2	Organism 3	Organism 4	Resistance Marker		
<i>A. baumannii</i>	<i>E. faecalis</i>			OXA	2 (0)	
<i>A. baumannii</i>	<i>E. faecalis</i>	<i>S. aureus</i>			1 (0)	
<i>A. baumannii</i>	<i>E. faecium</i>			OXA	1 (0)	
<i>A. baumannii</i>	<i>Staphylococcus</i>				1 (0)	

Distinct Co-Detection Combinations Detected by the Comparator Method(s) in Retrospective Clinical Samples					Number Samples (Number Discrepant)	Discrepant Organism(s) / Resistance Marker(s) <sup>A</sup>
Organism 1	Organism 2	Organism 3	Organism 4	Resistance Marker		
<i>Acinetobacter radioresistens</i> *	<i>P. vulgaris</i>			OXA	1 (0)	
<i>Aeromonas caviae</i> *	<i>E. coli</i>	<i>Enterococcus casseliflavus</i>	<i>K. oxytoca</i>		1 (1)	<i>E. casseliflavus</i> (1)
<i>Aeromonas veronii</i> *	<i>E. cloacae</i>				1 (1)	<i>E. cloacae</i> (1)
<i>B. fragilis</i>	<i>S. anginosus</i> group				1 (0)	
<i>C. albicans</i>	<i>E. faecalis</i>				1 (0)	
<i>C. albicans</i>	<i>E. faecium</i>	<i>Staphylococcus hominis</i>			1 (1)	<i>C. albicans</i> (1)
<i>C. albicans</i>	<i>P. aeruginosa</i>				1 (1)	<i>C. albicans</i> (1)
<i>C. albicans</i>	<i>S. epidermidis</i>				1 (0)	
<i>C. braakii</i>	<i>E. cloacae</i>	<i>K. oxytoca</i>			1 (1)	<i>C. braakii</i> (1), <i>K. oxytoca</i> (1)
<i>C. braakii</i>	<i>E. coli</i>				1 (0)	
<i>C. braakii</i>	<i>Streptococcus oralis</i>				1 (0)	
<i>C. freundii</i>	<i>Enterococcus</i>				1 (1)	<i>Enterococcus</i> (1)
<i>C. freundii</i>	<i>K. pneumoniae</i>				2 (0)	
<i>C. freundii</i>	<i>K. pneumoniae</i>	<i>Staphylococcus hominis</i>		CTX-M	1 (0)	
<i>C. glabrata</i>	<i>E. aerogenes</i>	<i>Staphylococcus</i>			1 (1)	<i>Staphylococcus</i> (1)
<i>C. glabrata</i>	<i>P. mirabilis</i>				1 (1)	<i>C. glabrata</i> (1)
<i>C. koseri</i>	<i>E. faecalis</i>				1 (0)	
<i>C. krusei</i>	<i>S. epidermidis</i>				1 (1)	<i>S. epidermidis</i> (1)
<i>C. youngae</i>	<i>K. oxytoca</i>				1 (1)	<i>K. oxytoca</i> (1)
<i>Clostridium perfringens</i> *	<i>E. coli</i>				1 (0)	
<i>E. aerogenes</i>	<i>S. anginosus</i> group				1 (0)	
<i>E. cloacae</i>	<i>E. coli</i>				1 (1)	<i>E. coli</i> (1)
<i>E. cloacae</i>	<i>E. faecalis</i>				1 (1)	<i>E. faecalis</i> (1)
<i>E. cloacae</i>	<i>E. faecium</i>				1 (0)	
<i>E. cloacae</i>	<i>E. faecium</i>	<i>Staphylococcus hominis</i>			1 (0)	
<i>E. cloacae</i>	<i>K. pneumoniae</i>				1 (0)	
<i>E. cloacae</i>	<i>M. morganii</i>				1 (1)	<i>E. cloacae</i> (1)
<i>E. cloacae</i>	<i>S. anginosus</i> group				1 (0)	
<i>E. cloacae</i>	<i>S. maltophilia</i>				1 (1)	<i>S. maltophilia</i> (1)
<i>E. coli</i>	<i>E. faecalis</i>				2 (0)	
<i>E. coli</i>	<i>E. faecalis</i>			CTX-M	1 (0)	
<i>E. coli</i>	<i>E. faecalis</i>	<i>K. pneumoniae</i>			1 (1)	<i>E. coli</i> (1)
<i>E. coli</i>	<i>E. faecalis</i>	<i>P. mirabilis</i>			1 (0)	
<i>E. coli</i>	<i>E. faecium</i>				1 (0)	
<i>E. coli</i>	<i>E. faecium</i>			CTX-M	1 (1)	<i>E. faecium</i> (1)



Distinct Co-Detection Combinations Detected by the Comparator Method(s) in Retrospective Clinical Samples					Number Samples (Number Discrepant)	Discrepant Organism(s) / Resistance Marker(s) <sup>A</sup>
Organism 1	Organism 2	Organism 3	Organism 4	Resistance Marker		
<i>E. coli</i>	<i>K. oxytoca</i>	<i>Streptococcus infantarius</i>			1 (0)	
<i>E. coli</i>	<i>P. aeruginosa</i>				1 (1)	<i>P. aeruginosa</i> (1)
<i>E. coli</i>	<i>P. mirabilis</i>				1 (1)	<i>E. coli</i> (1)
<i>E. coli</i>	<i>P. mirabilis</i>	<i>P. vulgaris</i>	<i>Streptococcus - viridans</i> group		1 (1)	<i>S. viridans</i> group (1)
<i>E. coli</i>	<i>Propionibacteria</i> *				1 (0)	
<i>E. coli</i>	<i>S. anginosus</i> gp				1 (1)	<i>S. anginosus</i> group (1)
<i>E. coli</i>	<i>S. aureus</i>				1 (0)	
<i>E. coli</i>	<i>S. pneumoniae</i>				1 (0)	
<i>E. coli</i>	<i>Staphylococcus</i>				1 (0)	
<i>E. faecalis</i>	<i>K. pneumoniae</i>				1 (1)	<i>K. pneumoniae</i> (1)
<i>E. faecalis</i>	<i>M. morganii</i>				1 (0)	
<i>E. faecalis</i>	<i>M. morganii</i>	<i>P. vulgaris</i>			1 (0)	
<i>E. faecalis</i>	<i>P. aeruginosa</i>	<i>S. aureus</i>			1 (1)	<i>P. aeruginosa</i> (1)
<i>E. faecalis</i>	<i>P. mirabilis</i>				3 (0)	
<i>E. faecalis</i>	<i>S. maltophilia</i>				1 (1)	<i>E. faecalis</i> (1)
<i>E. faecalis</i>	<i>S. marcescens</i>				1 (0)	
<i>E. faecium</i>	<i>K. pneumoniae</i>				1 (0)	
<i>E. faecium</i>	<i>P. aeruginosa</i>				1 (0)	
<i>E. faecium</i>	<i>P. mirabilis</i>				1 (0)	
<i>K. oxytoca</i>	<i>S. anginosus</i> group				1 (0)	
<i>K. pneumoniae</i>	<i>P. aeruginosa</i>				1 (1)	<i>P. aeruginosa</i> (1)
<i>K. pneumoniae</i>	<i>S. aureus</i>				2 (1)	<i>S. aureus</i> (1)
<i>K. pneumoniae</i>	<i>Staphylococcus</i>				1 (1)	<i>Staphylococcus</i> (1)
<i>P. aeruginosa</i>	<i>S. maltophilia</i>				1 (1)	<i>S. maltophilia</i> (1)
<i>P. mirabilis</i>	<i>Peptostreptococcus anaerobius</i> *				1 (0)	
<i>P. mirabilis</i>	<i>Providencia stuartii</i> *				2 (1)	<i>P. mirabilis</i> (1)
<i>P. mirabilis</i>	<i>Staphylococcus</i>				1 (0)	
<i>Pseudomonas putida</i> *	<i>S. epidermidis</i>	<i>S. maltophilia</i>			1 (0)	
<i>S. aureus</i>	<i>S. marcescens</i>				1 (0)	
<i>S. marcescens</i>	<i>Staphylococcus</i>				1 (0)	
<i>S. marcescens</i>	<i>Streptococcus mitis</i> group	<i>Streptococcus salivarius</i>			1 (0)	

\* Indicates an off-panel organism not targeted by the BCID-GN panel.

A. A discrepant organism or resistance marker is defined as one that was detected by the comparator method(s) but not by the BCID-GN panel (excludes organisms not targeted by the BCID-GN panel).

## Clinical Study cobas eplex instrument Performance

A total of 2460 samples (including prospective, retrospective, and contrived samples) were initially tested in the clinical evaluations. Of these, 23/2460 (0.9%) did not complete the run and the sample was retested. After repeat testing, all 2460 samples completed testing and 2334/2460 (94.9%, 95% CI: 93.9%-95.7%) generated valid results and 126/2460 (5.1%, 95% CI: 4.3%-6.1%) generated invalid results on the first completed attempt.

Upon repeat testing of the 126 samples with initially invalid results, 1/126 (0.8%) did not complete the run and the sample was retested. After repeat testing, all 126 samples completed testing and 114/126 (90.5%) generated valid results. Overall, after final testing, 12/2460 (0.5%, 95% CI: 0.3%-0.9%) had final, invalid results, resulting in a final validity rate of 2448/2460 (99.5%, 95% CI: 99.1%-99.7%).

## ANALYTICAL PERFORMANCE CHARACTERISTICS

### Limit of Detection (LoD)

The limit of detection (LoD), or analytical sensitivity, was identified and verified for each target on the BCID-GN panel using quantified reference strains in simulated blood culture sample matrix, which is defined as whole blood with EDTA added to a blood culture bottle in the same ratio as the manufacturer recommends and incubated for 8 hours. At least 20 replicates per target were tested for each condition. The limit of detection was defined as the lowest concentration of each target that is detected in ≥95% of tested replicates. The confirmed LoD for each **cobas eplex** BCID-GN panel organism is shown in **Table 64**.

**Table 64: LoD Results Summary**

Target	Organism	Strain	LoD Concentration (CFU/mL)
<i>Acinetobacter baumannii</i>	<i>Acinetobacter baumannii</i>	NCTC 13421	1 x 10 <sup>6</sup>
	<i>Acinetobacter baumannii</i>	NCTC 13304	1 x 10 <sup>6</sup>
<i>Bacteroides fragilis</i>	<i>Bacteroides fragilis</i>	ATCC 25285	1 x 10 <sup>5</sup>
	<i>Bacteroides fragilis</i>	ATCC 43860	1 x 10 <sup>4</sup>
<i>Citrobacter</i>	<i>Citrobacter freundii</i>	NCTC 9750	1 x 10 <sup>6</sup>
	<i>Citrobacter koseri</i>	ATCC 27156	1 x 10 <sup>6</sup>
<i>Cronobacter sakazakii</i>	<i>Cronobacter sakazakii</i>	ATCC 29544	1 x 10 <sup>5</sup>
	<i>Cronobacter sakazakii</i>	ATCC 29004	1 x 10 <sup>6</sup>
<i>Enterobacter</i> (non-cloacae complex)	<i>Enterobacter aerogenes</i>	CDC#0074	1 x 10 <sup>6</sup>
	<i>Enterobacter aerogenes</i>	CDC#0161	1 x 10 <sup>5</sup>
	<i>Enterobacter amnigenus</i>	ATCC 33072	1 x 10 <sup>6</sup>
<i>Enterobacter cloacae</i> Complex	<i>Enterobacter cloacae</i>	CDC#0154	1 x 10 <sup>6</sup>
	<i>Enterobacter asburiae</i>	ATCC 35957	1 x 10 <sup>6</sup>
	<i>Enterobacter hormaechei</i>	ATCC BAA-2082	1 x 10 <sup>6</sup>
<i>Escherichia coli</i>	<i>Escherichia coli</i>	CDC#0118	1 x 10 <sup>7</sup>
	<i>Escherichia coli</i>	NCTC 13441	1 x 10 <sup>6</sup>
	<i>Escherichia coli</i>	JHU01-D80401147	1 x 10 <sup>7</sup>
<i>Fusobacterium necrophorum</i>	<i>Fusobacterium necrophorum</i>	ATCC 51357	1 x 10 <sup>8</sup>

Target	Organism	Strain	LoD Concentration (CFU/mL)
	<i>Fusobacterium necrophorum</i>	ATCC 27852	1 x 10 <sup>7</sup>
<i>Fusobacterium nucleatum</i>	<i>Fusobacterium nucleatum</i>	ATCC 25586	1 x 10 <sup>7</sup>
	<i>Fusobacterium nucleatum</i>	ATCC 23726	1 x 10 <sup>5</sup>
<i>Haemophilus influenzae</i>	<i>Haemophilus influenzae</i>	ATCC 19418	1 x 10 <sup>5</sup>
	<i>Haemophilus influenzae</i>	ATCC 9006	1 x 10 <sup>7</sup>
	<i>Haemophilus influenzae</i>	ATCC33930	1 x 10 <sup>4</sup>
<i>Klebsiella oxytoca</i>	<i>Klebsiella oxytoca</i>	ATCC 43165	1 x 10 <sup>7</sup>
	<i>Klebsiella oxytoca</i>	ATCC 8724	1 x 10 <sup>7</sup>
<i>Klebsiella pneumoniae</i> group	<i>Klebsiella pneumoniae</i>	CDC#0160	1 x 10 <sup>6</sup>
	<i>Klebsiella pneumoniae</i>	CDC#0107	1 x 10 <sup>6</sup>
<i>Morganella morganii</i>	<i>Morganella morganii</i>	ATCC 25829	1 x 10 <sup>7</sup>
	<i>Morganella morganii</i>	CDC#0133	1 x 10 <sup>7</sup>
<i>Neisseria meningitidis</i>	<i>Neisseria meningitidis</i>	ATCC 13090	1 x 10 <sup>5</sup>
	<i>Neisseria meningitidis</i>	ATCC 13102	1 x 10 <sup>4</sup>
	<i>Neisseria meningitidis</i>	NCTC10026	1 x 10 <sup>4</sup>
<i>Proteus</i>	<i>Proteus vulgaris</i>	ATCC 6896	1 x 10 <sup>7</sup>
	<i>Proteus vulgaris</i>	ATCC 6380	1 x 10 <sup>7</sup>
<i>Proteus mirabilis</i>	<i>Proteus mirabilis</i>	CDC#0159	1 x 10 <sup>6</sup>
	<i>Proteus mirabilis</i>	ATCC 43071	1 x 10 <sup>6</sup>
<i>Pseudomonas aeruginosa</i>	<i>Pseudomonas aeruginosa</i>	CDC#0103	1 x 10 <sup>6</sup>
	<i>Pseudomonas aeruginosa</i>	NCTC 13437	1 x 10 <sup>6</sup>
	<i>Pseudomonas aeruginosa</i>	SDx071	1 x 10 <sup>5</sup>
<i>Salmonella</i>	<i>Salmonella bongori</i>	ATCC 43975	1 x 10 <sup>5</sup>
	<i>Salmonella enterica</i>	ATCC 6962	1 x 10 <sup>5</sup>
<i>Serratia</i>	<i>Serratia liquefaciens</i>	ATCC 27592	1 x 10 <sup>6</sup>
	<i>Serratia plymuthica</i>	ATCC 53858	1 x 10 <sup>7</sup>
<i>Serratia marcescens</i>	<i>Serratia marcescens</i>	ATCC 14041	1 x 10 <sup>7</sup>
	<i>Serratia marcescens</i>	ATCC 14756	1 x 10 <sup>5</sup>
<i>Stenotrophomonas maltophilia</i>	<i>Stenotrophomonas maltophilia</i>	ATCC 13637	1 x 10 <sup>6</sup>
	<i>Stenotrophomonas maltophilia</i>	ATCC 17666	1 x 10 <sup>7</sup>
Pan <i>Candida</i>	<i>Candida albicans</i>	ATCC 10231	1 x 10 <sup>6</sup>
	<i>Candida glabrata</i>	ATCC 15126	1 x 10 <sup>5</sup>
Pan Gram-Positive	<i>Enterococcus faecalis</i>	ATCC 51575	1 x 10 <sup>5</sup>
	<i>Enterococcus faecium</i>	ATCC 31282	1 x 10 <sup>7</sup>
	<i>Bacillus subtilis</i>	ATCC 21008	1 x 10 <sup>6</sup>
	<i>Staphylococcus aureus</i>	ATCC BAA-2313	1 x 10 <sup>5</sup>
	<i>Streptococcus agalactiae</i>	ATCC 13813	1 x 10 <sup>6</sup>
	<i>Streptococcus anginosus</i>	ATCC 33397	1 x 10 <sup>6</sup>
CTX-M	<i>Escherichia coli</i> (CTX-M-15)	NCTC 13441	1 x 10 <sup>4</sup>
	<i>Klebsiella pneumoniae</i> (CTX-M-2)	CDC#0107	1 x 10 <sup>5</sup>
IMP	<i>Enterobacter aerogenes</i> (IMP-4)	CDC#0161	1 x 10 <sup>6</sup>

Target	Organism	Strain	LoD Concentration (CFU/mL)
	<i>Pseudomonas aeruginosa</i> (IMP-1)	CDC#0103	1 x 10 <sup>5</sup>
KPC	<i>Enterobacter hormaechei</i> (KPC variant not known)	ATCC BAA-2082	1 x 10 <sup>6</sup>
	<i>Morganella morganii</i> (KPC-2)	CDC#0133	1 x 10 <sup>6</sup>
NDM	<i>Escherichia coli</i> (NDM-1)	CDC#0118	1 x 10 <sup>5</sup>
	<i>Proteus mirabilis</i> (NDM-1)	CDC#0159	1 x 10 <sup>5</sup>
OXA	<i>Acinetobacter baumannii</i> (OXA-23)	NCTC 13421	1 x 10 <sup>5</sup>
	<i>Acinetobacter baumannii</i> (OXA-27)	NCTC 13304	1 x 10 <sup>5</sup>
	<i>Enterobacter aerogenes</i> (OXA-48)	CDC#0074	1 x 10 <sup>6</sup>
	<i>Klebsiella pneumoniae</i> (OXA-48)	CDC#0160	1 x 10 <sup>6</sup>
VIM	<i>Enterobacter cloacae</i> (VIM-1)	CDC#0154	1 x 10 <sup>6</sup>
	<i>Pseudomonas aeruginosa</i> (VIM-10)	NCTC 13437	1 x 10 <sup>5</sup>

### Analytical Reactivity (Inclusivity)

A panel of 336 strains/isolates representing the genetic, temporal, and geographic diversity of each target on the **cobas eplex** BCID-GN panel was evaluated to demonstrate analytical reactivity. Bacteria were tested at 1 x 10<sup>9</sup> CFU/mL or less and fungal strains were tested at 1 x 10<sup>6</sup> CFU/mL. In the cases where the initial testing concentration did not result in a “Detected” result, the concentration was increased to the point where detection was observed (see footnotes for concentration of these strains). Organisms and applicable resistance markers detected by the **cobas eplex** BCID-GN panel are shown in **Table 65**. Additional strains were detected as part of the **Limit of Detection (Analytical Sensitivity)** Study and can be found in **Table 64**. *Citrobacter* strains that were tested but not detected include the following: *C. amalonaticus*, *C. farmeri*, *C. gillenii*, *C. murlinae*, and *C. sedlakii*. *Serratia odorifera* and *Staphylococcus simulans* were not detected at concentrations of 1 x 10<sup>8</sup> CFU/mL and only one of three replicates were detected at concentrations of 1 x 10<sup>9</sup> CFU/mL.

**Table 65: Analytical Reactivity (Inclusivity)**

Organism	Strain
<b><i>Acinetobacter baumannii</i></b>	
<i>Acinetobacter baumannii</i>	CDC#0052
	NCTC 13302
	NCTC 13303
	NCTC 13305
	NCTC 13420
	NCTC 13422
	NCTC 13423
<i>Acinetobacter baumannii</i> (NDM-1)	CDC#0033
<i>Acinetobacter baumannii</i> (OXA-23)	ATCC BAA-1605
	CDC#0045
	CDC#0056
	NCTC 13301
	NCTC 13424
<i>Acinetobacter</i> spp. (IMP only)	JMI4084 <sup>A</sup>
<b><i>Bacteroides fragilis</i></b>	
<i>Bacteroides fragilis</i>	ATCC 23745
	ATCC 700786
	NCTC 9343
<b><i>Citrobacter</i></b>	
<i>Citrobacter braakii</i>	ATCC 43162

Organism	Strain
	ATCC 51113
<i>Citrobacter freundii</i>	ATCC 6879
	ATCC 8090
<i>Citrobacter freundii</i> (CTX)	JMI2047
<i>Citrobacter freundii</i> (KPC-2)	CDC#0116
<i>Citrobacter koseri</i>	ATCC 25409
	ATCC 27028
	ATCC 29225
	ATCC 29936
<i>Citrobacter</i> species (CTX-15, NDM-1)	CDC #0157
<i>Citrobacter werkmanii</i>	ATCC 51114
<i>Citrobacter youngae</i>	ATCC 29935
<b><i>Cronobacter sakazakii</i></b>	
<i>Cronobacter sakazakii</i>	ATCC 12868
	ATCC BAA-894
	FSL F6-0023
<b><i>Enterobacter</i> (non-cloacae complex)</b>	
<i>Enterobacter aerogenes</i>	ATCC 13048
	ATCC 29010
	ATCC 51697
<i>Enterobacter amnigenus</i>	ATCC 33731
	ATCC 51816 <sup>B</sup>

Organism	Strain
<i>Enterobacter gergoviae</i>	ATCC 33028
	ATCC 33426
<b><i>Enterobacter cloacae</i> complex</b>	
<i>Enterobacter asburiae</i>	ATCC 35954
	ATCC 35955
	ATCC 35956
<i>Enterobacter cloacae</i> (CTX-15)	CDC#0038
<i>Enterobacter cloacae</i> (CTX-9)	NCTC 13464
<i>Enterobacter cloacae</i> (CTX-15, KPC-2)	CDC#0163
<i>Enterobacter cloacae</i> (CTX, NDM)	JMI53571
<i>Enterobacter cloacae</i> subsp. <i>cloacae</i>	ATCC 23355
	ATCC 35030
<i>Enterobacter cloacae</i> subsp. <i>dissolvens</i>	ATCC 23373
<i>Enterobacter hormaechei</i>	ATCC 700323
<i>Enterobacter hormaechei</i> subsp. <i>hormaechei</i>	ATCC 49162
<i>Enterobacter hormaechei</i> subsp. <i>oharae</i>	ATCC 49163
<i>Enterobacter hormaechei</i> subsp. <i>steigerwaltii</i>	CIP108489T
<i>Enterobacter ludwigii</i>	DSM-16688
<b><i>Escherichia coli</i></b>	
<i>Escherichia coli</i>	ATCC 14948
	ATCC 25922
	ATCC 33605
	ATCC 33876
	ATCC 35150
	ATCC 4157
	ATCC 43888
	ATCC 51446
	ATCC 51755
	ATCC 53498
	ATCC 700728
	NCIMB 8545
	NCTC 8620
	ATCC 9637
	ATCC BAA-196
	ATCC BAA-197
	ATCC BAA-198
	ATCC BAA-199
	ATCC BAA-200
	ATCC BAA-201
	ATCC BAA-202
	ATCC BAA-203
	ATCC BAA-204
	LMC_243094647
	LMC_243098776
	LMC_243098947
	LMC_243108047
	LMC_243109799
	LMC_243112411
	LMC_244006281
	LMC_244006433
	LMC_244008038
	LMC_244012579
	NCTC 13351
	NCTC 10279
	ATCC 10536
	ATCC 10538
	ATCC 10799
	ATCC 11229
	ATCC 13762

Organism	Strain
<i>Escherichia coli</i> (CTX-14)	ATCC 14169
	CDC#0086
<i>Escherichia coli</i> (CTX-15)	ATCC BAA-2326
	NCTC 13353
	NCTC 13400
	NCTC 13450
	NCTC 13451
<i>Escherichia coli</i> (CTX-3)	NCTC 13452
<i>Escherichia coli</i> (CTX-1)	NCTC 13461
<i>Escherichia coli</i> (CTX-2)	NCTC 13462
<i>Escherichia coli</i> (CTX-8)	NCTC 13463
<i>Escherichia coli</i> (CTX-15, NDM-6)	CDC#0137
<i>Escherichia coli</i> (CTX-15, NDM-7)	CDC#0162
<i>Escherichia coli</i> (IMP)	NCTC 13476
<i>Escherichia coli</i> (KPC)	ATCC BAA-2340
<i>Escherichia coli</i> (NDM-5)	CDC#0150
<i>Escherichia coli</i> (OXA)	LMC_DR00012
<i>Escherichia coli</i> (VIM)	JMI32465
<b><i>Fusobacterium necrophorum</i></b>	
<i>Fusobacterium necrophorum</i> subsp. <i>necrophorum</i>	ATCC 25286
	NCTC 10575
	NCTC 10577
<b><i>Fusobacterium nucleatum</i></b>	
<i>Fusobacterium nucleatum</i> subsp. <i>nucleatum</i>	ATCC 31647
<i>Fusobacterium nucleatum</i> subsp. <i>fusiforme</i>	ATCC 51190
<i>Fusobacterium nucleatum</i> subsp. <i>vincentii</i>	ATCC 49256
<b><i>Haemophilus influenzae</i></b>	
<i>Haemophilus influenzae</i>	ATCC 33930
	ATCC 43065
	ATCC 43163
	NCTC 11931
	NCTC 12699
	NCTC 8143
<i>Haemophilus influenzae</i> Type b	ATCC 10211
<i>Haemophilus influenzae</i> Type c	ATCC 9007
<i>Haemophilus influenzae</i> Type d	ATCC 9332
<i>Haemophilus influenzae</i> Type e	NCTC 8472
<i>Haemophilus influenzae</i> Type f	ATCC 9833
<b><i>Klebsiella oxytoca</i></b>	
<i>Klebsiella oxytoca</i>	ATCC 43086
	ATCC 43863
	ATCC 49131
	ATCC 700324
	ATCC 51817
<i>Klebsiella oxytoca</i> (KPC-3)	CDC#0147
<b><i>Klebsiella pneumoniae</i> group</b>	
<i>Klebsiella pneumoniae</i> (CTX-15)	CDC#0109
<i>Klebsiella pneumoniae</i> (CTX-25)	NCTC 13465
<i>Klebsiella pneumoniae</i> (CTX, KPC)	IMH-C2261309
<i>Klebsiella pneumoniae</i> (CTX, NDM-1)	NCTC 13443
<i>Klebsiella pneumoniae</i> (CTX-15; NDM-1; OXA-232)	CDC#0153
<i>Klebsiella pneumoniae</i> (CTX-15, OXA-232)	CDC#0075
	CDC#0066
<i>Klebsiella pneumoniae</i> (CTX-15, OXA-181)	CDC#0039
	CDC#0140
	CDC#0141

Organism	Strain
	CDC#0142
<i>Klebsiella pneumoniae</i> (IMP-4)	CDC#0034
	CDC#0080
<i>Klebsiella pneumoniae</i> (KPC-3)	CDC#0125
	CDC#0112
	CDC#0113
<i>Klebsiella pneumoniae</i> (KPC)	ATCC BAA-1705
	IMH-C2260742
	IMH-C3151729
	IMH-C4151728
	IMH-C4171868
<i>Klebsiella pneumoniae</i> (OXA-48)	NCTC 13442
<i>Klebsiella pneumoniae</i> (CTX-15; VIM-27)	CDC#0040
	CDC#0135
<i>Klebsiella pneumoniae</i> (VIM-1)	NCTC 13439
	NCTC 13440
<i>Klebsiella pneumoniae</i> subsp. <i>Ozaenae</i>	ATCC 11296
<i>Klebsiella pneumoniae</i> subsp. <i>pneumoniae</i>	ATCC 13883
	ATCC 27736
	ATCC 51503
	ATCC 51504
<i>Klebsiella quasipneumoniae</i>	ATCC 700603
<i>Klebsiella pneumoniae</i> subsp. <i>rhinoscleromatis</i>	ATCC 9436
<i>Klebsiella variicola</i>	ATCC BAA-830
<b><i>Morganella morganii</i></b>	
<i>Morganella morganii</i>	ATCC 25830
	GM148-209
<i>Morganella morganii</i> (CTX-15; NDM-1)	CDC#0057 <sup>c</sup>
<b><i>Neisseria meningitidis</i><sup>d</sup></b>	
<i>Neisseria meningitidis</i> Serotype A	ATCC 13077
<i>Neisseria meningitidis</i> Serotype B	NCTC 10026
<i>Neisseria meningitidis</i> Serotype W135	NCTC 11203
<i>Neisseria meningitidis</i> Serotype Y	ATCC 35561
<b><i>Proteus</i></b>	
<i>Proteus hauseri</i>	ATCC 13315
<i>Proteus mirabilis</i>	ATCC 33583
	ATCC BAA-663
<i>Proteus mirabilis</i> (IMP)	JMI955389
<i>Proteus mirabilis</i> (KPC-6)	CDC#0155
<i>Proteus penneri</i>	ATCC 35197
<i>Proteus vulgaris</i>	ATCC 33420
	ATCC 49132
	ATCC 8427
	NCTC 4636
<b><i>Pseudomonas aeruginosa</i></b>	
<i>Pseudomonas aeruginosa</i> (IMP-14)	CDC#0092
<i>Pseudomonas aeruginosa</i> (IMP-1)	CDC#0241
<i>Pseudomonas aeruginosa</i> (IMP)	CDC#0439
<i>Pseudomonas aeruginosa</i> (KPC-5)	CDC#0090
<i>Pseudomonas aeruginosa</i> (VIM-2)	CDC#0100
<i>Pseudomonas aeruginosa</i> (VIM-4)	CDC#0054
<b><i>Salmonella</i></b>	
<i>Salmonella enterica</i> serovar 4,[5],12:i	FSL S5-0580
<i>Salmonella enterica</i> serovar Agona	ATCC 51957
<i>Salmonella enterica</i> serovar Bareilly	ATCC 9115
<i>Salmonella enterica</i> serovar Braenderup	ATCC 700136
<i>Salmonella enterica</i> serovar Enteritidis	ATCC BAA-708
<i>Salmonella enterica</i> serovar Hadar	ATCC 51956
<i>Salmonella enterica</i> serovar Heidelberg	ATCC 8326

Organism	Strain
<i>Salmonella enterica</i> serovar Infantis	ATCC BAA-1675
<i>Salmonella enterica</i> serovar Javiana	ATCC 10721
<i>Salmonella enterica</i> serovar Montevideo	ATCC 8387
<i>Salmonella enterica</i> serovar Muenchen	ATCC 8388
<i>Salmonella enterica</i> serovar Oranienburg	ATCC 9239
<i>Salmonella enterica</i> serovar Paratyphi B	FSL S5-0447
<i>Salmonella enterica</i> serovar Saintpaul	ATCC 9712
<i>Salmonella enterica</i> serovar Thompson	ATCC 8391
<i>Salmonella enterica</i> serovar Typhi	ATCC 19430
<i>Salmonella enterica</i> subsp. <i>arizonae</i>	ATCC 13314
<i>Salmonella enterica</i> subsp. <i>diarizonae</i>	ATCC 12325
<i>Salmonella enterica</i> subsp. <i>enterica</i> serovar Typhimurium	ATCC 14028
<i>Salmonella enterica</i> subsp. <i>houtenae</i>	ATCC 29834
<i>Salmonella enterica</i> subsp. <i>indica</i>	ATCC BAA-1578
<i>Salmonella enterica</i> subsp. <i>salamae</i>	ATCC 6959
<i>Salmonella enterica</i> subsp. <i>enterica</i> serovar Mississippi	FSL A4-0633
<i>Salmonella enterica</i> subsp. <i>enterica</i> serovar Schwarzengrund	FSL S5-0458
<b><i>Serratia</i></b>	
<i>Serratia ficaria</i>	ATCC 33105
<i>Serratia fonticola</i>	ATCC 29844
<i>Serratia grimesii</i>	ATCC 14460
<i>Serratia marcescens</i>	ATCC 13880
	ATCC 43861
	ATCC 43862
<i>Serratia marcescens</i> (CTX)	JMI10244
<i>Serratia rubidaea</i>	ATCC 27593
	ATCC 29025
<b><i>Stenotrophomonas maltophilia</i></b>	
<i>Stenotrophomonas maltophilia</i>	ATCC 13636
	GM148-207
	GM148-208
<b>Pan-Gram Positive</b>	
<i>Bacillus amyloliquefaciens</i>	ATCC 23845
<i>Bacillus atrophaeus</i>	ATCC 49337
<i>Bacillus cereus</i>	ATCC 10876
<i>Bacillus licheniformis</i>	ATCC 21039
<i>Bacillus thuringiensis</i>	ATCC 35646
<i>Enterococcus avium</i>	ATCC 14025
<i>Enterococcus casseliflavus</i>	ATCC 700327
<i>Enterococcus faecalis</i>	JMI876745
<i>Enterococcus gallinarum</i>	ATCC 49573
<i>Enterococcus hirae</i>	ATCC 49479
<i>Enterococcus raffinosus</i>	ATCC 49464
<i>Enterococcus saccharolyticus</i>	ATCC 43076 <sup>E</sup>
<i>Staphylococcus capitis</i>	NRS866
<i>Staphylococcus chromogenes</i>	ATCC 43764
<i>Staphylococcus cohnii</i>	ATCC 29974
<i>Staphylococcus epidermidis</i>	ATCC 35984
<i>Staphylococcus gallinarum</i>	ATCC 700401
<i>Staphylococcus haemolyticus</i>	ATCC 29970
<i>Staphylococcus hominis</i>	ATCC 27844
<i>Staphylococcus hyicus</i>	ATCC 11249
<i>Staphylococcus lentus</i>	ATCC 700403
<i>Staphylococcus lugdunensis</i>	ATCC 49576
<i>Staphylococcus pasteurii</i>	ATCC 51128
<i>Staphylococcus vitulinus</i>	ATCC 51699
<i>Streptococcus constellatus</i>	ATCC 27513



Organism	Strain
<i>Streptococcus dysgalactiae</i>	ATCC 35666
<i>Streptococcus equi</i>	ATCC 9528
<i>Streptococcus gallolyticus</i>	ATCC 9809
<i>Streptococcus gordonii</i>	ATCC 35557
<i>Streptococcus infantis</i>	ATCC 700779
<i>Streptococcus intermedius</i>	ATCC 27335
<i>Streptococcus mitis</i>	ATCC 49456
<i>Streptococcus oralis</i>	ATCC 35037
<i>Streptococcus parasanguinis</i>	ATCC 15909
<i>Streptococcus pneumoniae</i>	ATCC 8335
<i>Streptococcus pyogenes</i>	ATCC 12344
<i>Streptococcus salivarius</i>	ATCC 7073
<i>Streptococcus thoraltensis</i>	ATCC 700865 <sup>F</sup>

Organism	Strain
<b>Pan Candida</b>	
<i>Candida albicans</i>	ATCC 24433
	ATCC 90028
<i>Candida glabrata</i>	ATCC 2001
	ATCC 66032
<i>Candida krusei</i>	ATCC 14243
	ATCC 32196
	ATCC 34135 <sup>G</sup>
<i>Candida parapsilosis</i>	ATCC 22019
	ATCC 58895
	ATCC 90018 <sup>H</sup>

A. Non-target species used to evaluate resistance marker.

B. 5/6 replicates detected at  $2.0 \times 10^8$  CFU/mL.

C. 5/6 replicates detected at  $4.5 \times 10^8$  CFU/mL.

D. Unencapsulated strains of *N. meningitidis* will not be detected

E. Strain may have reduced sensitivity and was not 100% detected at concentrations  $<1 \times 10^8$  CFU/mL.

F. Strain may have reduced sensitivity and was not 100% detected at concentrations  $<4 \times 10^8$  CFU/mL.

G. In initial testing, 1/6 replicates was detected at  $1 \times 10^6$  CFU/mL; during additional testing, 3/3 replicates detected at bottle positivity.

H. In initial testing, 2/6 replicates were detected at  $1 \times 10^6$  CFU/mL; during additional testing, 6/6 replicates detected at bottle positivity.

## Predicted (*in silico*) Reactivity for Genus and Group Assays

In addition to species-specific assays, the **cobas eplex BCID-GN** panel contains a number of broader genus or group-level assays including: *Citrobacter*, *Enterobacter cloacae* complex, *Enterobacter* (non-*cloacae* complex), *Proteus*, *Serratia*, Pan *Candida*, and Pan Gram-Positive assays. **Tables 66-73** highlight the-predicted (*in silico*) reactivity (inclusivity) for these assay targets.

**Note: the performance of the cobas eplex BCID-GN panel has not been established for all of the organisms listed in the tables below.** See the Analytical Reactivity section for data on organisms for which performance characteristics have been established (indicated with an asterisk in **Tables 66-73**). Some species were not assessed *in silico* due to lack of sequence data, though they may appear in the analytical sensitivity or specificity studies.

**Table 66: Predicted (*in silico*) Reactivity (Inclusivity) Results for *Citrobacter***

Detection Predicted for $\geq 95\%$ of target sequences		
<i>Citrobacter koseri</i> <sup>*</sup>	<i>Citrobacter intermedius</i>	
Detection Predicted for 85%-94% of target sequences		
<i>Citrobacter freundii</i> <sup>*</sup>	<i>Citrobacter braakii</i> <sup>*</sup>	
Detection Predicted for $<85.0\%$ of target sequences		
<i>Citrobacter werkmanii</i> <sup>*</sup> (66.7%)	<i>Citrobacter youngae</i> <sup>*</sup> (50.0%)	
Detection Not Predicted		
<i>Citrobacter europaeus</i>	<i>Citrobacter gillenii</i>	<i>Citrobacter amalonaticus</i> <sup>A</sup>
<i>Citrobacter farmeri</i>	<i>Citrobacter sedlakii</i>	<i>Citrobacter murlinae</i>

A. Detection predicted *in silico*, however ATCCBAA-2563 was not detected in wet testing.

**Table 67: Predicted (*in silico*) Reactivity (Inclusivity) Results for *Enterobacter cloacae* complex**

Detection Predicted for ≥95% of target sequences		
<i>Enterobacter cloacae</i> *	<i>Enterobacter asburiae</i> *	<i>Enterobacter hormaechei</i> *
<i>Enterobacter xiangfangensis</i>		
Detection Predicted for 85%-94% of target sequences		
None Identified		
Detection Predicted for <85.0% of target sequences		
<i>Enterobacter ludwigii</i> * (68.4%)	<i>Enterobacter nimipressuralis</i> (25.0%)	
Detection Not Predicted		
<i>Enterobacter kobei</i>	<i>Enterobacter cancerogenus</i>	

**Table 68: Predicted (*in silico*) Reactivity (Inclusivity) Results for *Enterobacter* (non-*cloacae* complex)**

Detection Predicted for ≥95% of target sequences		
<i>Enterobacter aerogenes</i> *	<i>Enterobacter gergoviae</i> *	
Detection Predicted for 85%-94% of target sequences		
None Identified		
Detection Predicted for <85.0% of target sequences		
<i>Enterobacter amnigenus</i> * (62.5%)		
Detection Not Predicted		
None Identified		

**Table 69: Predicted (*in silico*) Reactivity (Inclusivity) Results for *Klebsiella pneumoniae* group**

Detection Predicted for ≥95% of target sequences		
<i>Klebsiella pneumoniae</i> *	<i>Klebsiella quasipneumoniae</i> *	<i>Klebsiella variicola</i> *
Detection Predicted for 85%-94% of target sequences		
None Identified		
Detection Predicted for <85.0% of target sequences		
None Identified		
Detection Not Predicted		
None Identified		



Table 70: Predicted (*in silico*) Reactivity (Inclusivity) Results for *Proteus*

Detection Predicted for ≥95% of target sequences		
<i>Proteus mirabilis</i> *	<i>Proteus penneri</i> *	<i>Proteus vulgaris</i> *
<i>Proteus hauseri</i> *	<i>Proteus cibarius</i>	
Detection Predicted for 85%-94% of target sequences		
None Identified		
Detection Predicted for <85.0% of target sequences		
None Identified		
Detection Not Predicted		
<i>Proteus myxofaciens</i>		

Table 71: Predicted (*in silico*) Reactivity (Inclusivity) Results for *Serratia*

Detection Predicted for ≥95% of target sequences		
<i>Serratia marcescens</i> *	<i>Serratia grimesii</i> *	<i>Serratia rubidaea</i> *
<i>Serratia ficaria</i> *	<i>Serratia liquefaciens</i> *	<i>Serratia proteamaculans</i>
<i>Serratia fonticola</i> *	<i>Serratia plymuthica</i> *	
Detection Predicted for 85%-94% of target sequences		
None Identified		
Detection Predicted for <85.0% of target sequences		
<i>Serratia quinivorans</i> (33.3%)		
Detection Not Predicted		
<i>Serratia nematodiphila</i>	<i>Serratia odorifera</i> <sup>A</sup>	<i>Serratia ureilytica</i>

A. Not predicted *in silico*, however ATCC 33077 was intermittently detected in wet testing. See **Analytical Reactivity (Inclusivity) Study**.

Table 72: Predicted (*in silico*) Reactivity (Inclusivity) Results for Pan *Candida*

Detection Predicted for ≥95% of target sequences		
<i>Candida albicans</i> *	<i>Candida glabrata</i> *	<i>Candida krusei</i> *
<i>Candida parapsilosis</i> *		
Detection Predicted for 85%-94% of target sequences		
None Identified		
Detection Predicted for <85% of target sequences		
None Identified		
Detection Not Predicted		
Detection was not predicted by bioinformatic analysis for other <i>Candida</i> species for which sequence data was available.		

**Table 73: Predicted (*in silico*) Reactivity (Inclusivity) Results for Pan Gram-Positive**

Detection Predicted for ≥95% of target sequences		
<b>Bacillus</b>		
<i>Bacillus amyloliquefaciens</i> *	<i>Bacillus paralicheniformis</i>	<i>Bacillus toyonensis</i>
<i>Bacillus atrophaeus</i> *	<i>Bacillus siamensis</i>	<i>Bacillus vallismortis</i>
<i>Bacillus bombysepticus</i>	<i>Bacillus subtilis</i> *	<i>Bacillus velezensis</i>
<i>Bacillus licheniformis</i> *	<i>Bacillus tequilensis</i>	<i>Bacillus weihenstephanensis</i>
<i>Bacillus methylotrophicus</i>	<i>Bacillus thuringiensis</i> *	
<b>Enterococcus</b>		
<i>Enterococcus avium</i> *	<i>Enterococcus faecium</i> *	<i>Enterococcus raffinosus</i> *
<i>Enterococcus dispar</i>	<i>Enterococcus flavescens</i>	<i>Enterococcus saccharolyticus</i> *
<i>Enterococcus durans</i>	<i>Enterococcus malodoratus</i>	<i>Enterococcus thailandicus</i>
<i>Enterococcus faecalis</i> *	<i>Enterococcus pseudoavium</i>	
<b>Staphylococcus</b>		
<i>Staphylococcus aureus</i> *	<i>Staphylococcus haemolyticus</i> *	<i>Staphylococcus pseudintermedius</i>
<i>Staphylococcus agnetis</i>	<i>Staphylococcus hominis</i> *	<i>Staphylococcus pseudolugdunensis</i>
<i>Staphylococcus argensis</i>	<i>Staphylococcus hominis</i> subsp. <i>novobiosepticus</i>	<i>Staphylococcus pulvereri</i>
<i>Staphylococcus argenteus</i>	<i>Staphylococcus hyicus</i> *	<i>Staphylococcus rostri</i>
<i>Staphylococcus auricularis</i>	<i>Staphylococcus jettensis</i>	<i>Staphylococcus saprophyticus</i>
<i>Staphylococcus capitis</i> *	<i>Staphylococcus kloosii</i>	<i>Staphylococcus schleiferi</i>
<i>Staphylococcus caprae</i>	<i>Staphylococcus lentus</i> *	<i>Staphylococcus schweitzeri</i>
<i>Staphylococcus carnosus</i>	<i>Staphylococcus lugdunensis</i> *	<i>Staphylococcus sciuri</i>
<i>Staphylococcus chromogenes</i> *	<i>Staphylococcus lutrae</i>	<i>Staphylococcus simiae</i>
<i>Staphylococcus cohnii</i> *	<i>Staphylococcus massiliensis</i>	<i>Staphylococcus simulans</i>
<i>Staphylococcus delphini</i>	<i>Staphylococcus microti</i>	<i>Staphylococcus stepanovicii</i>
<i>Staphylococcus devriesei</i>	<i>Staphylococcus muscae</i>	<i>Staphylococcus succinus</i>
<i>Staphylococcus epidermidis</i> *	<i>Staphylococcus nepalensis</i>	<i>Staphylococcus vitulinus</i> *
<i>Staphylococcus equorum</i>	<i>Staphylococcus pasteurii</i> *	<i>Staphylococcus warneri</i>
<i>Staphylococcus felis</i>	<i>Staphylococcus petrasii</i>	<i>Staphylococcus xylosus</i>
<i>Staphylococcus fleurettii</i>	<i>Staphylococcus pettenkoferi</i>	
<i>Staphylococcus gallinarum</i> *	<i>Staphylococcus piscifermentans</i>	
<b>Streptococcus</b>		
<i>Streptococcus agalactiae</i>	<i>Streptococcus infantarius</i>	<i>Streptococcus phocae</i>
<i>Streptococcus alactolyticus</i>	<i>Streptococcus infantis</i> *	<i>Streptococcus pneumoniae</i> *
<i>Streptococcus anginosus</i>	<i>Streptococcus intermedius</i> *	<i>Streptococcus porcinus</i>
<i>Streptococcus australis</i>	<i>Streptococcus intestinalis</i>	<i>Streptococcus porcorum</i>

<i>Streptococcus caballi</i>	<i>Streptococcus lactarius</i>	<i>Streptococcus pseudopneumoniae</i>
<i>Streptococcus constellatus</i>	<i>Streptococcus loxodontisalivarius</i>	<i>Streptococcus pseudoporcinus</i>
<i>Streptococcus criceti</i>	<i>Streptococcus luteciae</i>	<i>Streptococcus pyogenes</i>
<i>Streptococcus cristatus</i>	<i>Streptococcus lutetiensis</i>	<i>Streptococcus rifensis</i>
<i>Streptococcus danieliae</i>	<i>Streptococcus macedonicus</i>	<i>Streptococcus rubneri</i>
<i>Streptococcus dentasini</i>	<i>Streptococcus marimammalium</i>	<i>Streptococcus salivarius*</i>
<i>Streptococcus dentisani</i>	<i>Streptococcus massiliensis</i>	<i>Streptococcus saliviroxodontae</i>
<i>Streptococcus didelphis</i>	<i>Streptococcus mitis*</i>	<i>Streptococcus sanguinis</i>
<i>Streptococcus difficilis</i>	<i>Streptococcus moroccensis</i>	<i>Streptococcus seminale</i>
<i>Streptococcus dysgalactiae</i> subsp. <i>dysgalactiae</i>	<i>Streptococcus oligofermentans</i>	<i>Streptococcus sinensis</i>
<i>Streptococcus dysgalactiae</i> subsp. <i>equisimilis</i>	<i>Streptococcus oralis*</i>	<i>Streptococcus suis</i>
<i>Streptococcus dysgalactiae*</i>	<i>Streptococcus oricebi</i>	<i>Streptococcus thermophilus</i>
<i>Streptococcus equi*</i>	<i>Streptococcus orisratti</i>	<i>Streptococcus thoraltensis*</i>
<i>Streptococcus equinus</i>	<i>Streptococcus panodentis</i>	<i>Streptococcus tigurinus</i>
<i>Streptococcus fryi</i>	<i>Streptococcus parasanguinis*</i>	<i>Streptococcus troglodytae</i>
<i>Streptococcus gallolyticus*</i>	<i>Streptococcus parasuis</i>	<i>Streptococcus troglodytidis</i>
<i>Streptococcus gordonii*</i>	<i>Streptococcus parauberis</i>	<i>Streptococcus urinalis</i>
<i>Streptococcus himalayensis</i>	<i>Streptococcus pasteurii</i>	<i>Streptococcus ursoris</i>
<i>Streptococcus hongkongensis</i>	<i>Streptococcus pasteurianus</i>	<i>Streptococcus vestibularis</i>
<i>Streptococcus hyointestinalis</i>	<i>Streptococcus peroris</i>	<i>Streptococcus waiu</i>
<b>Detection Predicted for 85%-94% of target sequences</b>		
<i>Bacillus cereus*</i>	<i>Enterococcus hirae*</i>	<i>Staphylococcus saccharolyticus</i>
<i>Enterococcus casseliflavus*</i>	<i>Staphylococcus arlettae</i>	<i>Streptococcus bovis</i>
<i>Enterococcus cecorum</i>	<i>Staphylococcus condimenti</i>	<i>Streptococcus uberis</i>
<i>Enterococcus gallinarum</i>	<i>Staphylococcus intermedius</i>	
<b>Detection Predicted for &lt;85.0% of target sequences</b>		
<i>Bacillus mojavensis</i> (77.8%)	<i>Bacillus sonorensis</i> (83.3%)	<i>Streptococcus halichoeri</i> (66.7%)
<i>Streptococcus rattii</i> (75.0%)		
<b>Detection Not Predicted</b>		
<i>Bacillus pseudomycoides</i>	<i>Enterococcus sulfureus</i>	<i>Streptococcus hyovaginalis</i>
<i>Enterococcus aquimarinus</i>	<i>Enterococcus termitis</i>	<i>Streptococcus ictaluri</i>
<i>Enterococcus asini</i>	<i>Enterococcus ureasiticus</i>	<i>Streptococcus iniae</i>
<i>Enterococcus caccae</i>	<i>Enterococcus ureilyticus</i>	<i>Streptococcus lactis</i>
<i>Enterococcus camelliae</i>	<i>Enterococcus villorum</i>	<i>Streptococcus macacae</i>
<i>Enterococcus canintestini</i>	<i>Staphylococcus caseolyticus</i>	<i>Streptococcus marmotae</i>
<i>Enterococcus canis</i>	<i>Streptococcus acidominimus</i>	<i>Streptococcus merionis</i>

<i>Enterococcus columbae</i>	<i>Streptococcus azizii</i>	<i>Streptococcus milleri</i>
<i>Enterococcus devriesei</i>	<i>Streptococcus cameli</i>	<i>Streptococcus minor</i>
<i>Enterococcus haemoperoxidus</i>	<i>Streptococcus canis</i>	<i>Streptococcus oriloxodontae</i>
<i>Enterococcus hawaiiensis</i>	<i>Streptococcus castoreus</i>	<i>Streptococcus orisasini</i>
<i>Enterococcus hermanniensis</i>	<i>Streptococcus cremoris</i>	<i>Streptococcus orisuis</i>
<i>Enterococcus italicus</i>	<i>Streptococcus criae</i>	<i>Streptococcus ovis</i>
<i>Enterococcus mundtii</i>	<i>Streptococcus cuniculi</i>	<i>Streptococcus pharyngis</i>
<i>Enterococcus pallens</i>	<i>Streptococcus dentapri</i>	<i>Streptococcus pluranimalium</i>
<i>Enterococcus pernyi</i>	<i>Streptococcus dentiloxodontae</i>	<i>Streptococcus plurextorum</i>
<i>Enterococcus phoeniculicola</i>	<i>Streptococcus dentirousetti</i>	<i>Streptococcus plutanimalium</i>
<i>Enterococcus plantarum</i>	<i>Streptococcus devriesei</i>	<i>Streptococcus porci</i>
<i>Enterococcus quebecensis</i>	<i>Streptococcus downei</i>	<i>Streptococcus rupicaprae</i>
<i>Enterococcus ratti</i>	<i>Streptococcus entericus</i>	<i>Streptococcus sobrinus</i>
<i>Enterococcus rivorum</i>	<i>Streptococcus ferus</i>	<i>Streptococcus tangierensis</i>
<i>Enterococcus rotai</i>	<i>Streptococcus gallinaceus</i>	
<i>Enterococcus silesiacus</i>	<i>Streptococcus henryi</i>	

### Predicted (*in silico*) Reactivity for Resistance Markers

The **cobas eplex** BCID-GN panel contains six resistance markers that were each assessed for predicted *in silico* reactivity. **Tables 74-84** highlight the-predicted (*in silico*) reactivity for CTX-M, IMP, KPC, NDM, OXA, and VIM. Strains that were tested as part of the **Analytical Reactivity (Inclusivity) Study** are marked with an asterisk in **Tables 74-84**. **It is noted that the performance of the cobas eplex BCID-GN panel has not been established for all organisms listed in Tables 74-84.** **Table 85** includes all variants that are not predicted to be detected by the BCID-GN panel by *in silico* analysis.

The CTX-M assay on the **cobas eplex** BCID-GN panel is designed to detect the following CTX-M groups: CTX-M-1, CTX-M-2, CTX-M-8, CTX-M-9, and CTX-M-25.

Table 74: Predicted (*in silico*) Reactivity (Inclusivity) Results for CTX-M-1

Target	Associated Organism	Variant Detected	Target	Associated Organism	Variant Detected
<i>Acinetobacter baumannii</i>	<i>Acinetobacter baumannii</i>	CTX-M-15			CTX-M-179
<i>Citrobacter</i>	<i>Citrobacter freundii</i>	CTX-M-3			CTX-M-180
		CTX-M-15*			CTX-M-181
		CTX-M-30			CTX-M-182
		CTX-M-55			CTX-M-184
		CTX-M-3			CTX-M-186
<i>Enterobacter</i> (non-cloacae Complex)	<i>Enterobacter aerogenes</i>	CTX-M-3	<i>Klebsiella oxytoca</i>	<i>Klebsiella oxytoca</i>	CTX-M-3
		CTX-M-15			CTX-M-15
	<i>Enterobacter gergoviae</i>	CTX-M-15			CTX-M-28
<i>Enterobacter cloacae</i> Complex	<i>Enterobacter asburiae</i>	CTX-M-15	<i>Klebsiella pneumoniae</i> group	<i>Klebsiella pneumoniae</i>	CTX-M-162
	<i>Enterobacter cloacae</i>	CTX-M-3			CTX-M-1
		CTX-M-15*			CTX-M-3
		CTX-M-22			CTX-M-10
		CTX-M-37			CTX-M-11
		CTX-M-89			CTX-M-12
		CTX-M-177			CTX-M-15*
	<i>Enterobacter hormaechei</i>	CTX-M-15			CTX-M-22
					CTX-M-28
		CTX-M-1*			CTX-M-28
		CTX-M-3*			CTX-M-32
		CTX-M-10			CTX-M-52
		CTX-M-12			CTX-M-54
		CTX-M-14*			CTX-M-55
		CTX-M-15*			CTX-M-57
		CTX-M-22			CTX-M-60
		CTX-M-23			CTX-M-62
		CTX-M-28			CTX-M-71
		CTX-M-29			CTX-M-72
		CTX-M-32			CTX-M-96
		CTX-M-33			CTX-M-155
		CTX-M-34			CTX-M-156
		CTX-M-36			CTX-M-157
		CTX-M-38			CTX-M-173
		CTX-M-42			CTX-M-176
		CTX-M-55			CTX-M-183
		CTX-M-58			CTX-M-197
		CTX-M-61			CTX-M-204
		CTX-M-65	<i>Morganella morganii</i>	<i>Morganella morganii</i>	CTX-M-3
		CTX-M-69			CTX-M-15*
		CTX-M-79			CTX-M-55
<i>Escherichia coli</i>	<i>Escherichia coli</i>	CTX-M-82	<i>Proteus mirabilis</i>	<i>Proteus mirabilis</i>	CTX-M-1
		CTX-M-101			CTX-M-3
		CTX-M-103			CTX-M-15
		CTX-M-117			CTX-M-32
		CTX-M-123			CTX-M-66
		CTX-M-127			CTX-M-116
		CTX-M-132			CTX-M-136
		CTX-M-138			CTX-M-164
		CTX-M-139			CTX-M-167
		CTX-M-142	<i>Pseudomonas aeruginosa</i>	<i>Pseudomonas aeruginosa</i>	CTX-M-15
		CTX-M-144			CTX-M-28
		CTX-M-150			CTX-M-32
		CTX-M-158	<i>Salmonella</i>	<i>Salmonella enterica</i>	CTX-M-15
		CTX-M-163			CTX-M-53
		CTX-M-166			CTX-M-55
		CTX-M-169			CTX-M-57
		CTX-M-170			CTX-M-61
		CTX-M-171			CTX-M-88
		CTX-M-172		<i>Salmonella</i> sp.	CTX-M-3
		CTX-M-174		<i>Salmonella</i> Typhimurium	CTX-M-37
		CTX-M-175	<i>Serratia</i>	<i>Serratia liquefaciens</i>	CTX-M-61
					CTX-M-22
				<i>Serratia marcescens</i>	CTX-M-3
					CTX-M-15

Target	Associated Organism	Variant Detected
<i>Serratia marcescens</i> / <i>Serratia</i>		CTX-M-55

Target	Associated Organism	Variant Detected
<i>Stenotrophomonas maltophilia</i>	<i>Stenotrophomonas maltophilia</i>	CTX-M-15

Table 75: Predicted (*in silico*) Reactivity (Inclusivity) Results for CTX-M-2

Target	Associated Organism	Variant Detected
<i>Acinetobacter baumannii</i>	<i>Acinetobacter baumannii</i>	CTX-M-2
		CTX-M-5
		CTX-M-43
		CTX-M-115
<i>Enterobacter cloacae</i> complex	<i>Enterobacter cloacae</i>	CTX-M-5
<i>Escherichia coli</i>	<i>Escherichia coli</i>	CTX-M-2*
		CTX-M-44
		CTX-M-56
		CTX-M-92
		CTX-M-97
		CTX-M-124
<i>Klebsiella pneumoniae</i> Group	<i>Klebsiella pneumoniae</i>	CTX-M-2
		CTX-M-35
		CTX-M-59
		CTX-M-141
		CTX-M-165

Target	Associated Organism	Variant Detected
		CTX-M-200
<i>Morganella morganii</i>	<i>Morganella morganii</i>	CTX-M-2
<i>Proteus mirabilis</i> / <i>Proteus</i>	<i>Proteus mirabilis</i>	CTX-M-2
		CTX-M-20
		CTX-M-171
<i>Pseudomonas aeruginosa</i>	<i>Pseudomonas aeruginosa</i>	CTX-1-2
		CTX-M-2
<i>Salmonella</i>	<i>Salmonella enterica</i>	CTX-M-2
		CTX-M-4
		CTX-M-5
		CTX-M-6
		CTX-M-7
		CTX-M-2
	<i>Salmonella</i> Typhimurium	CTX-M-4
		CTX-M-5
		CTX-M-5
		CTX-M-7

Table 76: Predicted (*in silico*) Reactivity (Inclusivity) Results for CTX-M-8

Target	Associated Organism	Variant Detected
<i>Citrobacter</i>	<i>Citrobacter amalonaticus</i>	CTX-M-8
<i>Enterobacter cloacae</i> Complex	<i>Enterobacter cloacae</i>	CTX-M-8
<i>Escherichia coli</i>	<i>Escherichia coli</i>	CTX-M-8*
		CTX-M-8

Target	Associated Organism	Variant Detected
<i>Klebsiella pneumoniae</i> Group	<i>Klebsiella pneumoniae</i>	CTX-M-63
<i>Morganella morganii</i>	<i>Morganella morganii</i>	CTX-M-63
<i>Salmonella</i>	<i>Salmonella enterica</i>	CTX-M-8

Table 77: Predicted (*in silico*) Reactivity (Inclusivity) Results for CTX-M-9

Target	Associated Organism	Variant Detected
<i>Citrobacter</i>	<i>Citrobacter freundii</i>	CTX-M-14
		CTX-M-65
<i>Enterobacter non-cloacae</i> Complex	<i>Enterobacter aerogenes</i>	CTX-M-9
<i>Enterobacter cloacae</i> Complex	<i>Enterobacter cloacae</i>	CTX-M-9*
		CTX-M-13
		CTX-M-14
		CTX-M-64
		CTX-M-125
<i>Escherichia coli</i>	<i>Escherichia coli</i>	CTX-M-1/CTX-M-65
		CTX-M-9
		CTX-M-13
		CTX-M-14
		CTX-M-14/CTX-M-15
		CTX-M-15
		CTX-M-16
		CTX-M-19
		CTX-M-21
		CTX-M-24
		CTX-M-27
		CTX-M-38

Target	Associated Organism	Variant Detected
		CTX-M-47
		CTX-M-51
		CTX-M-64
		CTX-M-65
		CTX-M-67
		CTX-M-73
		CTX-M-82
		CTX-M-87
		CTX-M-93
		CTX-M-97
		CTX-M-98
		CTX-M-102
		CTX-M-104
		CTX-M-105
		CTX-M-106
		CTX-M-121
		CTX-M-122
		CTX-M-126
		CTX-M-129
		CTX-M-130
		CTX-M-132
		CTX-M-134
		CTX-M-137

Target	Associated Organism	Variant Detected
		CTX-M-148
		CTX-M-161
		CTX-M-168
		CTX-M-173
		CTX-M-174
		CTX-M-176
		CTX-M-177
		CTX-M-191
		CTX-M-195
		CTX-M-196
		CTX-M-198
		CTX-M-199
<i>Klebsiella pneumoniae</i> Group	<i>Klebsiella pneumoniae</i>	CTX-M-9
		CTX-M-13
		CTX-M-14
		CTX-M-17
		CTX-M-18
		CTX-M-19
		CTX-M-24
		CTX-M-38
		CTX-M-46
		CTX-M-48
		CTX-M-49
		CTX-M-50

Target	Associated Organism	Variant Detected
		CTX-M-65
		CTX-M-81
		CTX-M-99
		CTX-M-104
		CTX-M-147
		CTX-M-159
		CTX-M-201
<i>Proteus mirabilis</i> / <i>Proteus</i>	<i>Proteus mirabilis</i>	CTX-M-13
		CTX-M-14
		CTX-M-24
		CTX-M-65
		CTX-M-90
<i>Salmonella</i>	<i>Salmonella enterica</i>	CTX-M-9
		CTX-M-14
		CTX-M-25
		CTX-M-27
		CTX-M-65
		CTX-M-83
		CTX-M-84
		CTX-M-85
		CTX-M-86
		CTX-M-143
<i>Serratia</i>	<i>Serratia liquefaciens</i>	CTX-M-14

Table 78: Predicted (*in silico*) Reactivity (Inclusivity) Results for CTX-M-25

Target	Associated Organism	Variant Detected
<i>Escherichia coli</i>	<i>Escherichia coli</i>	CTX-M-25
		CTX-M-39
		CTX-M-94
		CTX-M-100
<i>Klebsiella pneumoniae</i> Group	<i>Klebsiella pneumoniae</i> <sup>A*</sup>	CTX-M-26
	<i>Proteus mirabilis</i>	CTX-M-41

Target	Associated Organism	Variant Detected
<i>Proteus mirabilis</i> / <i>Proteus</i>		CTX-M-89
		CTX-M-91
		CTX-M-160
<i>Salmonella</i>	<i>Salmonella enterica</i>	CTX-M-25

A. CTX-M-25 detected in Analytical Reactivity (Inclusivity) study.

Table 79: Predicted (*in silico*) Reactivity (Inclusivity) Results for IMP

Target	Associated Organism	Variant Detected
<i>Acinetobacter baumannii</i>	<i>Acinetobacter baumannii</i>	IMP-1
		IMP-2
		IMP-4
		IMP-5
		IMP-8
		IMP-10
		IMP-11
		IMP-14
		IMP-19
		IMP-55
		IMP-61
<i>Citrobacter</i>	<i>Citrobacter freundii</i>	IMP-1
		IMP-4
		IMP-8
		IMP-23
		IMP-38
<i>Enterobacter non-cloacae</i> Complex	<i>Enterobacter aerogenes</i>	IMP-4
<i>Enterobacter cloacae</i> Complex	<i>Enterobacter cloacae</i>	IMP-1
		IMP-4
		IMP-8
		IMP-11

Target	Associated Organism	Variant Detected
		IMP-26
		IMP-34
		IMP-60
<i>Enterobacter cloacae</i> Complex	<i>Enterobacter hormaechei</i>	IMP-13
		IMP-14
<i>Escherichia coli</i>	<i>Escherichia coli</i>	IMP-1
		IMP-4
		IMP-6
		IMP-8
		IMP-14
		IMP-30
		IMP-52
		IMP-59
		IMP-66
<i>Klebsiella oxytoca</i>	<i>Klebsiella oxytoca</i>	IMP-1
		IMP-4
		IMP-8
		IMP-28
<i>Klebsiella pneumoniae</i> Group	<i>Klebsiella pneumoniae</i>	IMP-34
		IMP-1
		IMP-4*
		IMP-6

Target	Associated Organism	Variant Detected
		IMP-8
		IMP-10
		IMP-13
		IMP-19
		IMP-26
		IMP-32
		IMP-38
<i>Proteus mirabilis</i> / <i>Proteus</i>	<i>Proteus mirabilis</i>	IMP-1
		IMP-27
		IMP-64
<i>Pseudomonas aeruginosa</i>	<i>Pseudomonas aeruginosa</i>	IMP-1*
		IMP-2
		IMP-4
		IMP-6
		IMP-7
		IMP-9
		IMP-10
		IMP-11
		IMP-13
		IMP-14*
		IMP-15
		IMP-16
		IMP-17
		IMP-18
		IMP-19
		IMP-20
		IMP-21
		IMP-22

Target	Associated Organism	Variant Detected
		IMP-25
		IMP-26
		IMP-29
		IMP-30
		IMP-33
		IMP-34
		IMP-37
		IMP-40
		IMP-41
		IMP-43
		IMP-44
		IMP-45
		IMP-48
		IMP-49
		IMP-51
		IMP-53
		IMP-54
		IMP-56
		IMP-62
		IMP-63
<i>Salmonella</i>	<i>Salmonella enterica</i>	IMP-4
<i>Serratia marcescens</i> / <i>Serratia</i>	<i>Serratia marcescens</i>	IMP-1
		IMP-2
		IMP-6
		IMP-8
		IMP-24
<i>Stenotrophomonas maltophilia</i>	<i>Stenotrophomonas maltophilia</i>	IMP-25

Table 80: Predicted (*in silico*) Reactivity (Inclusivity) Results for KPC

Target	Associated Organism	Variant Detected
<i>Acinetobacter baumannii</i>	<i>Acinetobacter baumannii</i>	KPC-2
		KPC-3
		KPC-10
<i>Citrobacter</i>	<i>Citrobacter freundii</i>	KPC-2*
		KPC-3
		KPC-18
<i>Enterobacter non-cloacae</i> Complex	<i>Enterobacter aerogenes</i>	KPC-2
		KPC-3
		KPC-2*
<i>Enterobacter cloacae</i> Complex	<i>Enterobacter cloacae</i>	KPC-3
		KPC-4
		KPC-13
		KPC-18
		KPC-2
<i>Escherichia coli</i>	<i>Escherichia coli</i>	KPC-3
		KPC-4
		KPC-5
		KPC-9
		KPC-18
		KPC-21
		KPC-28
<i>Klebsiella oxytoca</i>	<i>Klebsiella oxytoca</i>	KPC-2
		KPC-3*
<i>Klebsiella pneumoniae</i> Group	<i>Klebsiella pneumoniae</i>	KPC-1
		KPC-2
		KPC-3*

Target	Associated Organism	Variant Detected
		KPC-4
		KPC-5
		KPC-6
		KPC-7
		KPC-8
		KPC-11
		KPC-12
		KPC-14
		KPC-15
		KPC-16
		KPC-17
		KPC-19
		KPC-22
		KPC-24
		KPC-25
		KPC-26
		KPC-27
		KPC-30
<i>Proteus mirabilis</i> / <i>Proteus</i>	<i>Proteus mirabilis</i>	KPC-2
		KPC-6*
<i>Pseudomonas aeruginosa</i>	<i>Pseudomonas aeruginosa</i>	KPC-2
		KPC-5*
<i>Salmonella</i>	<i>Salmonella enterica</i>	KPC-2
<i>Serratia marcescens</i> / <i>Serratia</i>	<i>Serratia marcescens</i>	KPC-2
		KPC-3



Table 81: Predicted (*in silico*) Reactivity (Inclusivity) Results for VIM

Target	Associated Organism	Variant Detected	Target	Associated Organism	Variant Detected
<i>Acinetobacter baumannii</i>	<i>Acinetobacter baumannii</i>	VIM-1			VIM-39
		VIM-2			VIM-42
		VIM-6			VIM-51
		VIM-11			VIM-52
<i>Citrobacter</i>	<i>Citrobacter freundii</i>	VIM-1	<i>Morganella morganii</i>	<i>Morganella morganii</i>	VIM-4
		VIM-2	<i>Proteus mirabilis/Proteus</i>	<i>Proteus mirabilis</i>	VIM-1
		VIM-4			
		VIM-23	<i>Pseudomonas aeruginosa</i>	<i>Pseudomonas aeruginosa</i>	VIM-1
<i>Enterobacter non-cloacae</i> Complex	<i>Enterobacter aerogenes</i>	VIM-1			VIM-2*
		VIM-1			VIM-3
<i>Enterobacter cloacae</i> Complex	<i>Enterobacter cloacae</i>	VIM-2			VIM-4*
		VIM-4			VIM-5
		VIM-23			VIM-6
		VIM-31			VIM-8
		VIM-40			VIM-9
		VIM-1			VIM-10
	<i>Enterobacter hormaechei</i>	VIM-4			VIM-11
		VIM-4			VIM-14
		VIM-23			VIM-15
	<i>Enterobacter xiangfangensis</i>	VIM-1			VIM-16
<i>Escherichia coli</i>	<i>Escherichia coli</i> <sup>A</sup>	VIM-1			VIM-17
		VIM-2			VIM-18
		VIM-19			VIM-20
		VIM-29			VIM-28
<i>Klebsiella oxytoca</i>	<i>Klebsiella oxytoca</i>	VIM-1			VIM-30
		VIM-2			VIM-36
		VIM-4			VIM-37
		VIM-32			VIM-41
		VIM-35			VIM-43
<i>Klebsiella pneumoniae</i> Group	<i>Klebsiella pneumoniae</i>	VIM-1*			VIM-44
		VIM-2			VIM-45
		VIM-4			VIM-46
		VIM-12			VIM-48
		VIM-19			VIM-50
		VIM-24	<i>Salmonella</i>	<i>Salmonella enterica</i>	VIM-1
		VIM-26	<i>Serratia marcescens/Serratia</i>	<i>Serratia marcescens</i>	VIM-2
		VIM-27*			VIM-4
		VIM-33			VIM-54
		VIM-34	<i>Stenotrophomonas maltophilia</i>	<i>Stenotrophomonas maltophilia</i>	VIM-2

A. Unspecified VIM variant detected in **Analytical Reactivity (Inclusivity)** study.

Table 82: Predicted (*in silico*) Reactivity (Inclusivity) Results for OXA-23

Target	Associated Organism	Variant Detected	Target	Associated Organism	Variant Detected
<i>Acinetobacter baumannii</i>	<i>Acinetobacter baumannii</i>	OXA-23*			OXA-170
		OXA-49			OXA-171
		OXA-23/OXA-104			OXA-183
		OXA-23/OXA-64			OXA-225
		OXA-23/OXA-66			OXA-366
		OXA-23/OXA-69			OXA-398
		OXA-27			OXA-422
		OXA-65/OXA-239			OXA-423
		OXA-68			OXA-435
		OXA-146			OXA-440
		OXA-165			OXA-469
		OXA-166			OXA-481
		OXA-167			OXA-482
		OXA-168			OXA-483
		OXA-169			OXA-565

Target	Associated Organism	Variant Detected
<i>Escherichia coli</i>	<i>Escherichia coli</i>	OXA-23
<i>Klebsiella pneumoniae</i> Group	<i>Klebsiella pneumoniae</i>	OXA-73

Target	Associated Organism	Variant Detected
<i>Proteus mirabilis</i>	<i>Proteus mirabilis</i>	OXA-23

Table 83: Predicted (*in silico*) Reactivity (Inclusivity) Results for OXA-48

Target	Associated Organism	Variant Detected
<i>Acinetobacter baumannii</i>	<i>Acinetobacter baumannii</i>	OXA-48
<i>Citrobacter</i>	<i>Citrobacter freundii</i>	OXA-48
		OXA-181
<i>Enterobacter non-cloacae</i> Complex	<i>Enterobacter aerogenes</i>	OXA-244
<i>Enterobacter cloacae</i> Complex	<i>Enterobacter cloacae</i>	OXA-48
		OXA-163
		OXA-181
	<i>Enterobacter hormaechei</i>	OXA-370
	<i>Enterobacter ludwigii</i>	OXA-48
<i>Escherichia coli</i>	<i>Escherichia coli</i> <sup>A</sup>	OXA-48
		OXA-163
		OXA-181
		OXA-204
		OXA-232
		OXA-244
		OXA-438
		OXA-439
		OXA-566

Target	Associated Organism	Variant Detected
<i>Klebsiella pneumoniae</i> Group	<i>Klebsiella pneumoniae</i>	OXA-1/OXA-48
		OXA-48*
		OXA-10
		OXA-162
		OXA-181*
		OXA-204
		OXA-232*
		OXA-244
		OXA-245
		OXA-247
		OXA-484
		OXA-505
		OXA-517
		OXA-519
	<i>Klebsiella variicola</i>	OXA-181
<i>Morganella morganii</i>	<i>Morganella morganii</i>	OXA-181
<i>Proteus mirabilis/Proteus</i>	<i>Proteus mirabilis</i>	OXA-48
		OXA-244
<i>Serratia marcescens/Serratia</i>	<i>Serratia marcescens</i>	OXA-48
		OXA-405

A. Unspecified OXA variant detected in the Analytical Reactivity (Inclusivity) study.

Table 84: Predicted (*in silico*) Reactivity (Inclusivity) Results for NDM

Target	Associated Organism	Variant Detected
<i>Acinetobacter baumannii</i>	<i>Acinetobacter baumannii</i>	NDM-1*
		NDM-2
<i>Citrobacter</i>	<i>Citrobacter braakii</i>	NDM-4
<i>Citrobacter</i>	<i>Citrobacter freundii</i>	NDM-1 <sup>A</sup>
		NDM-4
		NDM-6
		NDM-7
<i>Enterobacter non-cloacae</i> Complex	<i>Enterobacter aerogenes</i>	NDM-1
		NDM-4
		NDM-5
<i>Enterobacter cloacae</i> Complex	<i>Enterobacter cloacae</i> <sup>B</sup>	NDM-7
		NDM-1
		NDM-4
	<i>Enterobacter hormaechei</i>	NDM-7
		NDM-1
<i>Escherichia coli</i>	<i>Escherichia coli</i>	NDM-1
		NDM-3
		NDM-4
		NDM-5*
		NDM-6*
		NDM-7*
		NDM-8

Target	Associated Organism	Variant Detected
		NDM-11
		NDM-12
		NDM-13
		NDM-15
		NDM-16
		NDM-17
		NDM-18
		NDM-19
		NDM-1
<i>Klebsiella oxytoca</i>	<i>Klebsiella oxytoca</i>	NDM-4
<i>Klebsiella pneumoniae</i> Group	<i>Klebsiella pneumoniae</i>	NDM-1*
		NDM-4
		NDM-5
		NDM-6
		NDM-7
		NDM-10
		NDM-16
<i>Morganella morganii</i>	<i>Morganella morganii</i>	NDM-1 <sup>C</sup>
<i>Proteus mirabilis/Proteus</i>	<i>Proteus mirabilis</i>	NDM-1
<i>Pseudomonas aeruginosa</i>	<i>Pseudomonas aeruginosa</i>	NDM-1
		NDM-5
<i>Salmonella</i>	<i>Salmonella enterica</i>	NDM-1
		NDM-5

Target	Associated Organism	Variant Detected
<i>Serratia marcescens</i> /Serratia	<i>Serratia marcescens</i>	NDM-1

Target	Associated Organism	Variant Detected
<i>Stenotrophomonas maltophilia</i>	<i>Stenotrophomonas maltophilia</i>	NDM-1

- A. Detected in a *Citrobacter* species in the **Analytical Reactivity (Inclusivity)** study.  
 B. Unspecified NDM variant detected in the **Analytical Reactivity (Inclusivity)** study.  
 C. NDM-1 was detected in *Morganella morganii* in the **Analytical Reactivity (Inclusivity)** study but no sequences were available for *in silico* analysis.

**Table 85: Predicted (*in silico*) Reactivity (Inclusivity) Results for Variants Not Detected**

Resistance Marker	Variant Not Detected	Associated Organism	No. of Sequences
CTX-M-1	CTX-M-80	<i>Klebsiella pneumoniae</i>	3
	CTX-M-15		
	Not Specified		
IMP	IMP-31	<i>Pseudomonas aeruginosa</i>	2
	IMP-35		2
	IMP-7		1
NDM	NDM-1	<i>Escherichia coli</i>	6
		<i>Klebsiella varicola</i>	3
		<i>Salmonella enterica</i>	1
	NDM-3	<i>Acinetobacter baumannii</i>	1
	NDM-4	<i>Escherichia coli</i>	1
	NDM-9	<i>Cronobacter sakazakii</i>	1
		<i>Escherichia coli</i>	1
		<i>Klebsiella pneumoniae</i>	2
	Not specified	<i>Escherichia coli</i>	2
		<i>Klebsiella pneumoniae</i>	1

Resistance Marker	Variant Not Detected	Associated Organism	No. of Sequences
VIM		<i>Klebsiella</i> sp	1
		<i>Pseudomonas aeruginosa</i>	1
		<i>Pseudomonas aeruginosa</i>	3
	VIM-1	<i>Providencia vermicola</i>	1
	VIM-2	<i>Klebsiella pneumoniae</i>	1
	VIM-5	<i>Enterobacter cloacae</i>	2
		<i>Klebsiella pneumoniae</i>	3
	VIM-7	<i>Pseudomonas aeruginosa</i>	4
	VIM-13	<i>Pseudomonas aeruginosa</i>	3
	VIM-25	<i>Acinetobacter baumannii</i>	1
		<i>Proteus mirabilis</i>	2
	VIM-38	<i>Pseudomonas aeruginosa</i>	2
	VIM-47		2
	VIM-49		2
	Not specified		1
OXA-48	OXA-232	<i>Escherichia coli</i>	1

## Analytical Specificity (Cross-Reactivity and Exclusivity)

Cross-reactivity of on-panel and off-panel analytes was evaluated with the BCID-GN panel. Bacterial targets were tested in triplicate at a concentration of  $\sim 1 \times 10^9$  CFU/mL while fungi were tested in triplicate at a concentration of  $\sim 1 \times 10^7$  CFU/mL. If the target concentration could not be reached, the organism was diluted 2-fold from stock for use (indicated with an asterisk in **Tables 86-89**).

No cross reactivity was observed for any of the on-panel organisms. The following off-panel organisms showed cross reactivity: *Acinetobacter anitratus* (at a concentration of  $> 1 \times 10^4$  CFU/mL) cross-reacts with the *Acinetobacter baumannii* assay, *Enterobacter cowanii* (at a concentration of  $> 1 \times 10^8$  CFU/mL) cross-reacts with the *Enterobacter cloacae* complex assay, *Escherichia hermanii* cross-reacts with the *Enterobacter* (non-*cloacae* complex) assay (at a concentration of  $> 1 \times 10^6$  CFU/mL) and with the *Serratia* assay (at a concentration of  $> 1 \times 10^7$  CFU/mL), *Fusobacterium periodonticum* (at a concentration of  $5 \times 10^8$  CFU/mL) and *Fusobacterium simiae* (at a concentration of  $2.9 \times 10^8$  CFU/mL) cross-react with the *Fusobacterium nucleatum* assay, and *Shigella* (at a concentration of  $1 \times 10^9$  CFU/mL) cross-reacts with the *Escherichia coli* assay (off-panel organisms showing cross-reactivity are **bolded** in the tables below).

See **Table 65** for a summary of the on-panel strains tested and **Tables 86-89** for a summary of off-panel strains tested.

Additional *in silico* analysis was performed to identify any off-panel gram-negative and gram-positive organisms that may cross-react with the BCID-GN panel (**Tables 90-91**).

**Note:** the performance of the cobas eplex BCID-GN panel has not been established for organisms evaluated by *in silico* analysis alone.

## Off-panel Exclusivity

**Table 86: Off-panel Gram-Negative Organisms Assessed for Cross-reactivity with the cobas eplex BCID-GN panel (Exclusivity)**

Gram Negative Organism	Strain ID	Gram Negative Organism	Strain ID
<i>Acinetobacter haemolyticus</i>	ATCC 19002	<i>Kluyvera cochleae</i>	ATCC 51609
<i>Acinetobacter lwoffii</i>	ATCC 15309	<i>Legionella pneumoniae</i>	ATCC 33823
<i>Acinetobacter junii</i>	ATCC 17908	<i>Leclercia adecarboxylata</i>	ATCC 700325
<b><i>Acinetobacter anitratus</i><sup>A</sup></b>	ATCC 49139	<i>Methylobacterium mesophilicum</i> <sup>*</sup>	ATCC 29983
<i>Aeromonas hydrophila</i>	JMI 938982	<i>Neisseria gonorrhoeae</i>	ATCC 19424
<i>Aeromonas salmonicida</i>	ATCC 33658	<i>Neisseria mucosa</i>	ATCC 19695
<i>Aeromonas sobria</i>	ATCC 35993	<i>Neisseria sicca</i>	ATCC 29193
<i>Bacteroides distasonis</i> ( <i>Parabacteroides</i> )	ATCC 8503	<i>Neisseria flavescens</i>	ATCC 13115
<i>Bacteroides merdae</i>	ATCC 43184	<i>Neisseria lactamica</i>	ATCC 23970
<i>Bacteroides thetaiotaomicron</i>	ATCC 29741	<i>Neisseria perflava</i>	ATCC 14799
<i>Bacteroides vulgatus</i> <sup>*</sup>	ATCC 8482	<i>Ochrobactrum anthropi</i>	ATCC BAA-749
<i>Bacteroides caccae</i>	ATCC 700189	<i>Pantoea agglomerans</i>	ATCC 14537
<i>Bacteroides eggerthii</i>	ATCC 27754	<i>Pantoea ananatis</i>	NRRL B-41502
<i>Bacteroides ovatus</i> <sup>*</sup>	ATCC BAA-1296	<i>Pasteurella aerogenes</i>	ATCC 27883
<i>Bacteroides ureolyticus</i> <sup>*</sup>	ATCC 33387	<i>Pasteurella multocida subsp multocida</i>	ATCC 12945
<i>Bordetella pertussis</i>	ATCC 9797	<i>Prevotella intermedia</i>	ATCC 15032
<i>Burkholderia cepacia</i>	ATCC 25416	<i>Prevotella corporis</i> <sup>*</sup>	ATCC 33547
<i>Citrobacter amalonaticus</i>	ATCC BAA-2563	<i>Prevotella oralis</i> <sup>*</sup>	ATCC 33269
<i>Citrobacter gillenii</i>	ATCC 51640	<i>Prevotella nigrescens</i> <sup>*</sup>	ATCC 33563
<i>Citrobacter sedlakii</i>	ATCC 51493	<i>Providencia rettgeri</i>	ATCC 9250
<i>Citrobacter farmeri</i>	ATCC 51112	<i>Providencia stuartii</i>	ATCC 33672
<i>Citrobacter murlinae</i>	ATCC 51642	<i>Providencia alcalifaciens</i>	ATCC 9886
<i>Edwardsiella tarda</i>	ATCC 15947	<i>Pseudomonas fluorescens</i>	ATCC 13525
<i>Enterobacter kobei</i>	ATCC BAA-260	<i>Pseudomonas putida</i>	ATCC 49128
<i>Enterobacter cancerogenus</i>	ATCC 35315	<i>Pseudomonas alcaligenes</i>	ATCC 14909
<b><i>Enterobacter cowanii</i><sup>B</sup></b>	DSM-18146	<i>Ralstonia insidiosa</i>	ATCC 49129
<i>Escherichia albertii</i>	DSM-17582	<i>Ralstonia pickettii</i>	ATCC 27511
<i>Escherichia fergusonii</i>	ATCC 35469	<i>Raoultella planticola</i> ( <i>Klebsiella planticola</i> )	ATCC 31900
<b><i>Escherichia hermannii</i><sup>C</sup></b>	ATCC 33650	<i>Raoultella ornithinolytica</i>	CDC# 0134
<i>Ewingella americana</i> <sup>*</sup>	ATCC 33853	<i>Raoultella terrigena</i> ( <i>Klebsiella terrigena</i> )	ATCC 55553
<i>Eikenella corrodens</i>	ATCC BAA-1152	<b><i>Shigella boydii</i><sup>E</sup></b>	ATCC 9207
<i>Fusobacterium naviforme</i> <sup>*</sup>	ATCC 25832	<b><i>Shigella sonnei</i><sup>E</sup></b>	ATCC 25931
<i>Fusobacterium gonidiaformans</i>	ATCC 25563	<b><i>Shigella flexneri</i><sup>E</sup></b>	ATCC 9199
<i>Fusobacterium necrogenes</i> <sup>*</sup>	ATCC 25556	<i>Vibrio furnissii</i>	NCTC11218
<b><i>Fusobacterium periodonticum</i><sup>D</sup></b>	ATCC 33693	<i>Vibrio alginolyticus</i>	ATCC 17749
<b><i>Fusobacterium simiae</i><sup>D</sup></b>	ATCC 33568	<i>Vibrio parahaemolyticus</i>	ATCC 17802
<i>Fusobacterium varium</i>	ATCC 27725	<i>Yersinia enterocolitica subsp enterocolitica</i>	ATCC 9610
<i>Fusobacterium russii</i> <sup>*</sup>	ATCC 25533	<i>Yersinia ruckeri</i>	ATCC 29473
<i>Fusobacterium ulcerans</i>	ATCC 49186	<i>Yersinia kristensenii</i>	ATCC 33639
<i>Haemophilus haemolyticus</i>	ATCC 33390		
<i>Haemophilus parahaemolyticus</i>	ATCC 10014		
<i>Hafnia alvei</i>	ATCC 51815		
<i>Kingella kingae</i> <sup>*</sup>	ATCC 23331		

- A. Cross-reactivity seen with *Acinetobacter baumannii* at a concentration > 1x10<sup>4</sup> CFU/mL.
- B. Cross-reactivity seen with *Enterobacter cloacae* complex at a concentration > 1x10<sup>8</sup> CFU/mL.
- C. Cross-reactivity seen with *Enterobacter* (non-*cloacae* complex) at a concentration > 1x10<sup>6</sup> CFU/mL and *Serratia* at a concentration of > 1x10<sup>7</sup> CFU/mL.
- D. Cross-reactivity seen with the *Fusobacterium nucleatum* assay.
- E. Cross-reactivity seen with the *Escherichia coli* assay.

**Table 87: Off-panel Gram-Positive Organisms Assessed for Cross-reactivity with the cobas eplex BCID-GN panel (Exclusivity)**

Gram Positive Organisms	Strain ID	Gram Positive Organisms	Strain ID
<i>Actinomyces odontolyticus</i>	ATCC 17929	<i>Lactobacillus paracasei</i> *	ATCC 25598
<i>Clostridium perfringens</i>	ATCC 13124	<i>Lactobacillus acidophilus</i> *	ATCC 314
<i>Corynebacterium jeikeium</i>	ATCC BAA-949	<i>Lactobacillus crispatus</i>	ATCC 33197
<i>Corynebacterium renale</i>	ATCC 19412	<i>Lactobacillus rhamnosus</i>	ATCC 39595
<i>Corynebacterium ulcerans</i>	ATCC 51799	<i>Lactococcus lactis</i>	ATCC 49032
<i>Corynebacterium xerosis</i> *	ATCC 373	<i>Listeria innocua</i>	ATCC 33090
<i>Corynebacterium durum</i>	ATCC 33449	<i>Listeria monocytogenes</i>	ATCC 7644
<i>Corynebacterium diphtheriae</i> *	ATCC 13812	<i>Micrococcus luteus</i>	ATCC 10240
<i>Corynebacterium pseudodiphtheriticum</i>	ATCC 10700	<i>Peptostreptococcus anaerobius</i>	ATCC 27337
<i>Corynebacterium striatum</i> *	ATCC 43735	<i>Propionibacterium acnes</i>	ATCC 11827
<i>Corynebacterium urealyticum</i>	ATCC 43044	<i>Rothia mucilaginosa</i>	ATCC 25296
<i>Lactobacillus casei</i>	ATCC 39392		

**Table 88: Off-panel Fungal Organisms Assessed for Cross-reactivity with the cobas eplex BCID-GN panel (Exclusivity)**

Fungal Pathogens	Strain ID	Concentration Tested
<i>Aspergillus fumigatus</i> *	ATCC 204305	2.50 x 10 <sup>6</sup> CFU/mL
<i>Candida orthopsilosis</i>	ATCC 96139	1 x 10 <sup>7</sup> CFU/mL
<i>Candida metapsilosis</i>	ATCC 96144	1 x 10 <sup>7</sup> CFU/mL
<i>Candida tropicalis</i>	ATCC 1369	1 x 10 <sup>7</sup> CFU/mL
<i>Cryptococcus grubii</i>	ATCC 208821	1 x 10 <sup>7</sup> CFU/mL
<i>Cryptococcus gattii</i>	ATCC 76108	1 x 10 <sup>7</sup> CFU/mL
<i>Cryptococcus neoformans</i>	ATCC 14116	1 x 10 <sup>7</sup> CFU/mL
<i>Geotrichum capitatum</i>	ATCC 10663	1 x 10 <sup>7</sup> CFU/mL
<i>Histoplasma capsulatum</i>	<i>In silico</i>	N/A
<i>Penicillium marneffeii</i>	ATCC 200050	1 x 10 <sup>7</sup> CFU/mL
<i>Rhodotorula glutinis</i>	ATCC 32765	1 x 10 <sup>7</sup> CFU/mL
<i>Rhodotorula mucilaginosa</i>	ATCC 9449	1 x 10 <sup>7</sup> CFU/mL
<i>Rhodotorula minuta</i>	ATCC 36236	1 x 10 <sup>7</sup> CFU/mL
<i>Saccharomyces cerevisiae</i> *	ATCC 18824	5.55 x 10 <sup>6</sup> CFU/mL
<i>Trichosporon dermatitis</i>	ATCC MYA-4294	1 x 10 <sup>7</sup> CFU/mL
<i>Trichosporon mucoides</i>	ATCC 90046	1 x 10 <sup>7</sup> CFU/mL

**Table 89: Off-panel Resistance Genes Assessed for Cross-reactivity with the cobas eplex BCID-GN panel (Exclusivity)**

Antimicrobial Resistance Genes	Strain ID	Concentration Tested
FOX (Carried by <i>Klebsiella oxytoca</i> )* <sup>A</sup>	JMI 954306	8 x 10 <sup>8</sup> CFU/mL
MOX (Carried by <i>Aeromonas hydrophila</i> )	JMI 938982	1 x 10 <sup>9</sup> CFU/mL
SME (Carried by <i>Serratia marcescens</i> ) <sup>A</sup>	CDC #0091	1 x 10 <sup>9</sup> CFU/mL
SHV (Carried by <i>Klebsiella pneumoniae</i> ) <sup>A</sup>	CDC #0087	1 x 10 <sup>9</sup> CFU/mL
TEM (Carried by <i>Escherichia coli</i> ) <sup>A</sup>	NCTC 13351	1 x 10 <sup>9</sup> CFU/mL

A. The on-panel organism associated with the resistance gene was detected by the BCID-GN panel as expected

**Table 90: Off-panel Gram-Negative Organisms Assessed for Cross-Reactivity with the cobas eplex BCID-GN panel based on *In Silico* Analysis**

Cross-reactive Organism	cobas eplex BCID-GN Target	No. of Sequences	Predicted Cross-Reactive Sequences* n (%)
<i>Fusobacterium hwasookii</i>	<i>F. nucleatum</i>	10	5 (50%)
<i>Haemophilus aegyptius</i>	<i>H. influenzae</i>	3	3 (100%)
<i>Klebsiella michiganensis</i>	<i>Klebsiella oxytoca</i>	40	40 (100%)
<i>Pseudomonas denitrificans</i>	<i>Pseudomonas aeruginosa</i>	17	16 (94.1%)

**Table 91: Off-panel Gram-Positive Organisms Assessed for Cross-Reactivity with the Pan Gram-Positive Assay based on *In Silico* Analysis**

Organism	Number of Sequences	Predicted Cross-Reactive Sequences n (%)
<i>Brevibacterium halotolerans</i>	3	3 (100%)
<i>Domibacillus indicus</i>	1	1 (100%)
<i>Domibacillus robiginosus</i>	1	1 (100%)
<i>Salinibacillus aidingensis</i>	2	1 (50%)
<i>Terribacillus aidingensis</i>	1	1 (100%)
<i>Terribacillus halophilus</i>	2	1 (50%)
<i>Terribacillus saccharophilus</i>	1	1 (100%)
<i>Planomicrobium okeanokoites</i>	1	1 (100%)
<i>Lactococcus chungangensis</i>	4	4 (100%)
<i>Lactococcus laudensis</i>	1	1 (100%)
<i>Lactococcus piscium</i>	18	18 (100%)
<i>Lactococcus plantarum</i>	6	5 (83.8%)
<i>Lactococcus raffinolactis</i>	49	46 (93.9%)
<i>Okadaella gastrococcus</i>	4	4 (100%)

## Bottle Positivity

Several representative bacterial and fungal organisms were spiked into blood culture bottles along with the manufacturer's recommended volume of human whole blood and grown to positivity in a commercially-available continuously monitoring blood culture system. Bottles were removed from the incubator within two hours of being identified as positive as well as eight hours after bottle positivity. At least two independent positive blood culture replicates and three blood replicates were quantified for each organism on culture plates. Organisms tested and approximate bottle positivity concentrations are summarized in **Table 92**. Concentrations shown below represent approximate levels that may be observed in a clinical setting. All estimated bottle positivity concentrations are equivalent or greater than the established Limit of Detection (LoD) for each of the assays of the **cobas eplex** BCID-GP panel. The following bottle types were used for the Bottle Positivity Study: BD BACTEC Plus Aerobic/F blood culture bottle (*E. faecium*, *S. aureus*, *S. anginosus*, *A. baumannii*, *E. cloacae*, *E. coli*, *H. influenzae*, *K. oxytoca*, *N. meningitidis*, *P. aeruginosa*, and *S. marcescens*), and BD BACTEC Lytic/10 Anaerobic/F (*B. fragilis* and *F. nucleatum*).



Table 92: Bottle Positivity Concentrations

Organism	Strain ID	Mean Bottle Positivity Concentration	Mean Bottle Positivity +8 hours Concentration
Gram-positive Organisms			
<i>Enterococcus faecium</i>	ATCC BAA-2317	$4.9 \times 10^7$ CFU/mL	$3.6 \times 10^7$ CFU/mL
<i>Staphylococcus aureus</i>	NRS 483	$2.8 \times 10^7$ CFU/mL	$2.1 \times 10^7$ CFU/mL
<i>Streptococcus anginosus</i>	ATCC 33397	$4.1 \times 10^7$ CFU/mL	$4.0 \times 10^8$ CFU/mL
Gram-negative Organisms			
<i>Acinetobacter baumannii</i>	NCTC 13301	$4.4 \times 10^8$ CFU/mL	$3.8 \times 10^8$ CFU/mL
<i>Bacteroides fragilis</i>	ATCC 700786	$4.7 \times 10^8$ CFU/mL	$6.7 \times 10^9$ CFU/mL
<i>Enterobacter cloacae</i>	NCTC 13464	$2.8 \times 10^8$ CFU/mL	$7.7 \times 10^8$ CFU/mL
<i>Escherichia coli</i>	NCTC 13476	$2.3 \times 10^8$ CFU/mL	$1.5 \times 10^9$ CFU/mL
<i>Fusobacterium nucleatum</i>	ATCC 31647	$6.5 \times 10^7$ CFU/mL	$4.9 \times 10^8$ CFU/mL
<i>Haemophilus influenzae</i>	ATCC 19418	$6.9 \times 10^8$ CFU/mL	$1.2 \times 10^9$ CFU/mL
<i>Klebsiella oxytoca</i>	CDC #0147	$9.3 \times 10^8$ CFU/mL	$1.5 \times 10^9$ CFU/mL
<i>Neisseria meningitidis</i>	ATCC 13102	$3.2 \times 10^7$ CFU/mL	$2.1 \times 10^8$ CFU/mL
<i>Pseudomonas aeruginosa</i>	NCTC 13476	$1.6 \times 10^8$ CFU/mL	$8.4 \times 10^8$ CFU/mL
<i>Serratia marcescens</i>	ATCC 14041	$1.2 \times 10^9$ CFU/mL	$2.2 \times 10^9$ CFU/mL
Fungal Organisms			
<i>Candida albicans</i>	ATCC 90082	$1.6 \times 10^6$ CFU/mL	$1.4 \times 10^6$ CFU/mL

## Reproducibility

Three positive mixes including 11 on-panel organisms and 5 antibiotic resistance genes representing 17 targets at two concentrations and one negative mix including an off-panel organism were tested. The positive mixes were prepared by spiking cultured isolates into negative sample matrix in BD BACTEC Standard/10 Aerobic/F blood culture bottles at concentrations reflecting those observed at time of bottle positivity and one log higher to mimic concentrations observed at the time of bottle positivity plus 8 hours. The negative mix contained *Cutibacterium granulosum* grown in BD BACTEC Lytic/10 Anaerobic/F blood culture bottles to bottle positivity and bottle positivity plus eight hours, which is expected to yield a negative result. Bottle concentrations used in this study are summarized in **Table 93**. Each of the three positive mixes at two concentrations and the one negative mix were tested a minimum of 108 times. Testing occurred at three sites, with two operators testing the mixes over six days using three cartridge lots. For the negative mix, agreement with the expected negative result was 100% for all targets in the cobas eplex BCID-GN panel.

Table 93: Bottle Positivity Concentrations

Organism	Bottle Positivity Concentration	Bottle Positivity +8 Hours Concentration
<i>Acinetobacter baumannii</i> (OXA)	$1 \times 10^8$ CFU/mL	$1 \times 10^9$ CFU/mL
<i>Enterobacter cloacae</i> (CTX-M, KPC)	$1 \times 10^8$ CFU/mL	$1 \times 10^9$ CFU/mL
<i>Escherichia coli</i> (IMP)	$1 \times 10^8$ CFU/mL	$1 \times 10^9$ CFU/mL
<i>Fusobacterium nucleatum</i>	$1 \times 10^7$ CFU/mL	$1 \times 10^8$ CFU/mL
<i>Haemophilus influenzae</i>	$1 \times 10^8$ CFU/mL	$1 \times 10^9$ CFU/mL
<i>Klebsiella oxytoca</i>	$1 \times 10^8$ CFU/mL	$1 \times 10^9$ CFU/mL
<i>Neisseria meningitidis</i>	$3 \times 10^7$ CFU/mL	$3 \times 10^8$ CFU/mL

Organism	Bottle Positivity Concentration	Bottle Positivity +8 Hours Concentration
<i>Pseudomonas aeruginosa</i> (VIM)	1 x 10 <sup>8</sup> CFU/mL	1 x 10 <sup>9</sup> CFU/mL
<i>Serratia marcescens</i>	1 x 10 <sup>8</sup> CFU/mL	1 x 10 <sup>9</sup> CFU/mL
<i>Candida albicans</i> (Pan <i>Candida</i> target)	1 x 10 <sup>6</sup> CFU/mL	1 x 10 <sup>7</sup> CFU/mL
<i>Staphylococcus aureus</i> (Pan Gram-Positive target)	1 x 10 <sup>7</sup> CFU/mL	1 x 10 <sup>8</sup> CFU/mL

The percent agreement of each target with the expected result is summarized in **Tables 94-110**. The **cobas eplex** BCID-GN assay demonstrates a high level of agreement (≥98%) with the expected results.

**Table 94: Percent Agreement for *Acinetobacter baumannii***

Concentration of <i>Acinetobacter baumannii</i>	Site	Agreement with Expected Results		
		Agreed / N	%	95% CI
Bottle Positive + 8 Hours (1x10 <sup>9</sup> CFU/mL)	1	36/36	100	(90.4-100)
	2	36/36	100	(90.4-100)
	3	36/36	100	(90.4-100)
	All	108/108	100	(96.6-100)
Bottle Positive (1x10 <sup>8</sup> CFU/mL)	1	36/36	100	(90.4-100)
	2	36/36	100	(90.4-100)
	3	36/36	100	(90.4-100)
	All	108/108	100	(96.6-100)
Negative	1	179/179	100	(97.9-100)
	2	178/179	99.4	(96.9-99.9)
	3	180/180	100	(97.9-100)
	All	537/538	99.8	(99.0-100)

CI=Confidence Interval

**Table 95: Percent Agreement for *Enterobacter cloacae* complex**

Concentration of <i>Enterobacter cloacae</i>	Site	Agreement with Expected Results		
		Agreed / N	%	95% CI
Bottle Positive + 8 Hours (1x10 <sup>9</sup> CFU/mL)	1	36/36	100	(90.4-100)
	2	36/36	100	(90.4-100)
	3	36/36	100	(90.4-100)
	All	108/108	100	(96.6-100)
Bottle Positive (1x10 <sup>8</sup> CFU/mL)	1	35/35	100	(90.1-100)
	2	36/36	100	(90.4-100)
	3	36/36	100	(90.4-100)
	All	107/107	100	(96.5-100)
Negative	1	180/180	100	(97.9-100)
	2	179/179	100	(97.9-100)
	3	180/180	100	(97.9-100)
	All	539/539	100	(99.3-100)



**Table 96: Percent Agreement for *Escherichia coli***

Concentration of <i>Escherichia coli</i>	Site	Agreement with Expected Results		
		Agreed / N	%	95% CI
Bottle Positive + 8 Hours (1x10 <sup>9</sup> CFU/mL)	1	36/36	100	(90.4-100)
	2	36/36	100	(90.4-100)
	3	36/36	100	(90.4-100)
	All	108/108	100	(96.6-100)
Bottle Positive (1x10 <sup>8</sup> CFU/mL)	1	36/36	100	(90.4-100)
	2	35/35	100	(90.1-100)
	3	36/36	100	(90.4-100)
	All	107/107*	100	(96.5-100)
Negative	1	179/179	100	(97.9-100)
	2	180/180	100	(97.9-100)
	3	180/180	100	(97.9-100)
	All	539/539	100	(99.3-100)

\* Two samples had a false positive *Bacteroides fragilis* result.**Table 97: Percent Agreement for *Fusobacterium nucleatum***

Concentration of <i>Fusobacterium nucleatum</i>	Site	Agreement with Expected Results		
		Agreed / N	%	95% CI
Bottle Positive + 8 Hours (1x10 <sup>8</sup> CFU/mL)	1	36/36	100	(90.4-100)
	2	35/35	100	(90.1-100)
	3	36/36	100	(90.4-100)
	All	107/107	100	(96.5-100)
Bottle Positive (1x10 <sup>7</sup> CFU/mL)	1	36/36	100	(90.4-100)
	2	36/36	100	(90.4-100)
	3	36/36	100	(90.4-100)
	All	108/108*	100	(96.6-100)
Negative	1	179/179	100	(97.9-100)
	2	180/180	100	(97.9-100)
	3	180/180	100	(97.9-100)
	All	539/539	100	(99.3-100)

\* One sample had a false positive *Fusobacterium necrophorum* result.**Table 98: Percent Agreement for *Haemophilus influenzae***

Concentration of <i>Haemophilus influenzae</i>	Site	Agreement with Expected Results		
		Agreed / N	%	95% CI
Bottle Positive + 8 Hours (1x10 <sup>9</sup> CFU/mL)	1	36/36	100	(90.4-100)
	2	36/36	100	(90.4-100)
	3	36/36	100	(90.4-100)
	All	108/108	100	(96.6-100)
Bottle Positive (1x10 <sup>8</sup> CFU/mL)	1	36/36	100	(90.4-100)
	2	36/36	100	(90.4-100)
	3	36/36	100	(90.4-100)
	All	108/108	100	(96.6-100)

Concentration of <i>Haemophilus influenzae</i>	Site	Agreement with Expected Results		
		Agreed / N	%	95% CI
Negative	1	179/179	100	(97.9-100)
	2	179/179	100	(97.9-100)
	3	180/180	100	(97.9-100)
	All	538/538	100	(99.3-100)

Table 99: Percent Agreement for *Klebsiella oxytoca*

Concentration of <i>Klebsiella oxytoca</i>	Site	Agreement with Expected Results		
		Agreed / N	%	95% CI
Bottle Positive + 8 Hours (1x10 <sup>9</sup> CFU/mL)	1	36/36	100	(90.4-100)
	2	36/36	100	(90.4-100)
	3	36/36	100	(90.4-100)
	All	108/108	100	(96.6-100)
Bottle Positive (1x10 <sup>8</sup> CFU/mL)	1	36/36	100	(90.4-100)
	2	36/36	100	(90.4-100)
	3	36/36	100	(90.4-100)
	All	108/108	100	(96.6-100)
Negative	1	179/179	100	(97.9-100)
	2	179/179	100	(97.9-100)
	3	180/180	100	(97.9-100)
	All	538/538	100	(99.3-100)

Table 100: Percent Agreement for *Neisseria meningitidis*

Concentration of <i>Neisseria meningitidis</i>	Site	Agreement with Expected Results		
		Agreed / N	%	95% CI
Bottle Positive + 8 Hours (3x10 <sup>8</sup> CFU/mL)	1	35/35	100	(90.1-100)
	2	36/36	100	(90.4-100)
	3	36/36	100	(90.4-100)
	All	107/107	100	(96.5-100)
Bottle Positive (3x10 <sup>7</sup> CFU/mL)	1	36/36	100	(90.4-100)
	2	36/36	100	(90.4-100)
	3	36/36	100	(90.4-100)
	All	108/108	100	(96.6-100)
Negative	1	180/180	100	(97.9-100)
	2	179/179	100	(97.9-100)
	3	180/180	100	(97.9-100)
	All	539/539	100	(99.3-100)

Table 101: Percent Agreement for *Pseudomonas aeruginosa*

Concentration of <i>Pseudomonas aeruginosa</i>	Site	Agreement with Expected Results		
		Agreed / N	%	95% CI
Bottle Positive + 8 Hours	1	36/36	100	(90.4-100)
	2	35/35	100	(90.1-100)

Concentration of <i>Pseudomonas aeruginosa</i>	Site	Agreement with Expected Results		
		Agreed / N	%	95% CI
(1x10 <sup>9</sup> CFU/mL)	3	36/36	100	(90.4-100)
	All	107/107	100	(96.5-100)
Bottle Positive (1x10 <sup>8</sup> CFU/mL)	1	36/36	100	(90.4-100)
	2	36/36	100	(90.4-100)
	3	36/36	100	(90.4-100)
	All	108/108	100	(96.6-100)
Negative	1	179/179	100	(97.9-100)
	2	180/180	100	(97.9-100)
	3	180/180	100	(97.9-100)
	All	539/539	100	(99.3-100)

Table 102: Percent Agreement for *Serratia*

Concentration of <i>Serratia marcescens</i>	Site	Agreement with Expected Results		
		Agreed / N	%	95% CI
Bottle Positive + 8 Hours (1x10 <sup>9</sup> CFU/mL)	1	35/35	100	(90.1-100)
	2	36/36	100	(90.4-100)
	3	36/36	100	(90.4-100)
	All	107/107	100	(96.5-100)
Bottle Positive (1x10 <sup>8</sup> CFU/mL)	1	36/36	100	(90.4-100)
	2	36/36	100	(90.4-100)
	3	36/36	100	(90.4-100)
	All	108/108	100	(96.6-100)
Negative	1	180/180	100	(97.9-100)
	2	179/179	100	(97.9-100)
	3	180/180	100	(97.9-100)
	All	539/539	100	(99.3-100)

Table 103: Percent Agreement for *Serratia marcescens*

Concentration of <i>Serratia marcescens</i>	Site	Agreement with Expected Results		
		Agreed / N	%	95% CI
Bottle Positive + 8 Hours (1x10 <sup>9</sup> CFU/mL)	1	35/35	100	(90.1-100)
	2	36/36	100	(90.4-100)
	3	36/36	100	(90.4-100)
	All	107/107	100	(96.5-100)
Bottle Positive (1x10 <sup>8</sup> CFU/mL)	1	36/36	100	(90.4-100)
	2	36/36	100	(90.4-100)
	3	36/36	100	(90.4-100)
	All	108/108	100	(96.6-100)
Negative	1	180/180	100	(97.9-100)
	2	179/179	100	(97.9-100)
	3	180/180	100	(97.9-100)
	All	539/539	100	(99.3-100)

**Table 104: Percent Agreement for Pan *Candida***

Concentration of <i>Candida albicans</i>	Site	Agreement with Expected Results		
		Agreed / N	%	95% CI
Bottle Positive + 8 Hours (1x10 <sup>7</sup> CFU/mL)	1	35/35	100	(90.1-100)
	2	36/36	100	(90.4-100)
	3	36/36	100	(90.4-100)
	All	107/107	100	(96.5-100)
Bottle Positive (1x10 <sup>6</sup> CFU/mL)	1	35/36	97.2	(85.8-99.5)
	2	36/36	100	(90.4-100)
	3	36/36	100	(90.4-100)
	All	107/108	99.1	(94.9-99.8)
Negative	1	180/180	100	(97.9-100)
	2	179/179	100	(97.9-100)
	3	180/180	100	(97.9-100)
	All	539/539	100	(99.3-100)

**Table 105: Percent Agreement for Pan Gram-Positive**

Concentration of <i>Staphylococcus aureus</i>	Site	Agreement with Expected Results		
		Agreed / N	%	95% CI
Bottle Positive + 8 Hours (1x10 <sup>8</sup> CFU/mL)	1	36/36	100	(90.4-100)
	2	36/36	100	(90.4-100)
	3	36/36	100	(90.4-100)
	All	108/108	100	(96.6-100)
Bottle Positive (1x10 <sup>7</sup> CFU/mL)	1	34/36	94.4	(81.9-98.5)
	2	35/35	100	(90.1-100)
	3	36/36	100	(90.4-100)
	All	105/107	98.1	(93.4-99.5)
Negative	1	179/179	100	(97.9-100)
	2	179/180	99.4	(96.9-99.9)
	3	180/180	100	(97.9-100)
	All	538/539	99.8	(99.0-100)

**Table 106: Percent Agreement for CTX-M**

Concentration of <i>Enterobacter cloacae</i> (CTX-M+, KPC+)	Site	Agreement with Expected Results		
		Agreed / N	%	95% CI
Bottle Positive + 8 Hours (1x10 <sup>9</sup> CFU/mL)	1	36/36	100	(90.4-100)
	2	36/36	100	(90.4-100)
	3	36/36	100	(90.4-100)
	All	108/108	100	(96.6-100)
Bottle Positive (1x10 <sup>8</sup> CFU/mL)	1	35/35	100	(90.1-100)
	2	36/36	100	(90.4-100)
	3	36/36	100	(90.4-100)
	All	107/107	100	(96.5-100)

Concentration of <i>Enterobacter cloacae</i> (CTX-M+, KPC+)	Site	Agreement with Expected Results		
		Agreed / N	%	95% CI
Negative	1	144/144	100	(97.4-100)
	2	143/143	100	(97.4-100)
	3	144/144	100	(97.4-100)
	All	431/431	100	(99.1-100)

Table 107: Percent Agreement for IMP

Concentration of <i>Escherichia coli</i> (IMP+)	Site	Agreement with Expected Results		
		Agreed / N	%	95% CI
Bottle Positive + 8 Hours (1x10 <sup>9</sup> CFU/mL)	1	36/36	100	(90.4-100)
	2	35/36	97.2	(85.8-99.5)
	3	36/36	100	(90.4-100)
	All	107/108	99.1	(94.9-99.8)
Bottle Positive (1x10 <sup>8</sup> CFU/mL)	1	36/36	100	(90.4-100)
	2	35/35	100	(90.1-100)
	3	35/36	97.2	(85.8-99.5)
	All	106/107	99.1	(94.9-99.8)
Negative	1	143/143	100	(97.4-100)
	2	144/144	100	(97.4-100)
	3	144/144	100	(97.4-100)
	All	431/431	100	(99.1-100)

Table 108: Percent Agreement for KPC

Concentration of <i>Enterobacter cloacae</i> (CTX-M+, KPC+)	Site	Agreement with Expected Results		
		Agreed / N	%	95% CI
Bottle Positive + 8 Hours (1x10 <sup>9</sup> CFU/mL)	1	36/36	100	(90.4-100)
	2	36/36	100	(90.4-100)
	3	36/36	100	(90.4-100)
	All	108/108	100	(96.6-100)
Bottle Positive (1x10 <sup>8</sup> CFU/mL)	1	35/35	100	(90.16-100)
	2	36/36	100	(90.4-100)
	3	36/36	100	(90.4-100)
	All	107/107	100	(96.5-100)
Negative	1	144/144	100	(97.4-100)
	2	143/143	100	(97.4-100)
	3	144/144	100	(97.4-100)
	All	431/431	100	(99.1-100)

**Table 109: Percent Agreement for OXA**

Concentration of <i>Acinetobacter baumannii</i> (OXA-23+)	Site	Agreement with Expected Results		
		Agreed / N	%	95% CI
Bottle Positive + 8 Hours (1x10 <sup>9</sup> CFU/mL)	1	36/36	100	(90.4-100)
	2	36/36	100	(90.4-100)
	3	36/36	100	(90.4-100)
	<b>All</b>	<b>108/108</b>	<b>100</b>	<b>(96.6-100)</b>
Bottle Positive (1x10 <sup>8</sup> CFU/mL)	1	36/36	100	(90.4-100)
	2	36/36	100	(90.4-100)
	3	36/36	100	(90.4-100)
	<b>All</b>	<b>108/108</b>	<b>100</b>	<b>(96.6-100)</b>
Negative	1	143/143	100	(97.4-100)
	2	143/143	100	(97.4-100)
	3	144/144	100	(97.4-100)
	<b>All</b>	<b>430/430</b>	<b>100</b>	<b>(99.1-100)</b>

**Table 110: Percent Agreement for VIM**

Concentration of <i>Pseudomonas aeruginosa</i> (VIM+)	Site	Agreement with Expected Results		
		Agreed / N	%	95% CI
Bottle Positive + 8 Hours (1x10 <sup>9</sup> CFU/mL)	1	36/36	100	(90.4-100)
	2	35/35	100	(90.1-100)
	3	36/36	100	(90.4-100)
	<b>All</b>	<b>107/107</b>	<b>100</b>	<b>(96.5-100)</b>
Bottle Positive (1x10 <sup>8</sup> CFU/mL)	1	36/36	100	(90.4-100)
	2	36/36	100	(90.4-100)
	3	36/36	100	(90.4-100)
	<b>All</b>	<b>108/108</b>	<b>100</b>	<b>(96.6-100)</b>
Negative	1	143/143	100	(97.4-100)
	2	144/144	100	(97.4-100)
	3	144/144	100	(97.4-100)
	<b>All</b>	<b>431/431</b>	<b>100</b>	<b>(99.1-100)</b>

### Interfering Substances and Sample Matrix Equivalency (Bottle Evaluation)

Three organism mixes consisting of 12 on-panel organisms representing 16 targets and negative blood matrix were used to assess potentially interfering substances and bottle types for interference. The concentration of each organism tested is summarized in **Table 111**.

**Table 111: Organism Concentrations for Interfering Substance and Bottle Equivalency Evaluations**

Organism	Concentration
<i>Acinetobacter baumannii</i>	4 x 10 <sup>8</sup> CFU/mL
<i>Bacteroides fragilis</i>	4 x 10 <sup>8</sup> CFU/mL
<i>Enterobacter aerogenes</i>	2 x 10 <sup>8</sup> CFU/mL
<i>Enterobacter cloacae</i> (CTX-M)	2 x 10 <sup>8</sup> CFU/mL
<i>Escherichia coli</i> (OXA)	2 x 10 <sup>8</sup> CFU/mL
<i>Haemophilus influenzae</i>	6 x 10 <sup>8</sup> CFU/mL
<i>Klebsiella oxytoca</i>	9 x 10 <sup>8</sup> CFU/mL
<i>Neisseria meningitidis</i>	3 x 10 <sup>7</sup> CFU/mL
<i>Pseudomonas aeruginosa</i> (IMP)	1 x 10 <sup>8</sup> CFU/mL
<i>Serratia marcescens</i>	1 x 10 <sup>9</sup> CFU/mL
<i>Staphylococcus aureus</i> (Pan Gram-Positive target)	2 x 10 <sup>7</sup> CFU/mL
<i>Candida albicans</i> (Pan Candida target)	1 x 10 <sup>6</sup> CFU/mL

### Interfering Substances

Eighteen substances were used to assess the **cobas eplex** BCID-GN panel for potential interference. The organisms in **Table 111** were spiked into negative blood matrix and tested in triplicate with and without each potentially interfering substance. Negative blood matrix was tested to control for potential positive interference. Potentially interfering substances are summarized in **Table 112**. None of the eighteen substances commonly found in blood culture specimens or as medications commonly used to treat skin or bloodstream infections were found to inhibit the **cobas eplex** BCID-GN panel at clinically relevant concentrations. The effect of interfering substances has only been evaluated for the substances listed in **Table 112**. Interference due to substances other than those described in this section can lead to erroneous results.

**Table 112: Potentially Interfering Substances: Substance List**

Endogenous Substances	Testing Concentration
Bilirubin	60 µg/mL
Hemoglobin	0.6 g/L
Human Genomic DNA	6 x 10 <sup>5</sup> copies/mL
Triglycerides	1000 mg/dL
γ-globulin	0.85 g/dL
Exogenous Substances	Testing Concentration
Amoxicillin/Clavulanate	3.5 µg/mL
Amphotericin B	2 µg/mL
Caspofungin	4.5 µg/mL
Ceftriaxone	0.23 mg/mL
Ciprofloxacin	3 mg/L
Fluconazole	25 mg/L
Flucytosine	90 µg/mL
Gentamicin sulfate	3 µg/mL



Heparin	0.9 U/mL
Imipenem	83 µg/mL
Sodium Polyanethol Sulfonate	0.25% w/v
Tetracycline	5 mg/L
Vancomycin	30 mg/L

### Sample Matrix Equivalency (Bottle Evaluation)

Thirteen bottle types were tested for interference with each of the organisms listed in **Table 111**. Five replicates of each organism were tested in each of two bottle lots. Negative blood matrix was run as a negative control. Twelve bottle types tested showed no interference for any of the targets tested. One of three lots of the BACTEC™ Lytic Anaerobic bottles tested showed reduced sensitivity for some targets. A summary of the bottle types assessed and the study outcomes is found in **Table 113**.

**Table 113: Sample Matrix Equivalency (Bottle Evaluation) Bottle Types**

Manufacturer	Bottle Brand	Bottle Type	Study Outcome
BD	BACTEC™	Plus Aerobic	No interference observed
BD	BACTEC	Plus Anaerobic	No interference observed
BD	BACTEC	Standard Aerobic	No interference observed
BD	BACTEC	Standard Anaerobic	No interference observed
BD	BACTEC	Peds Plus™	No interference observed
BD	BACTEC	Lytic Anaerobic	False negative results were observed for <i>Pan Candida</i> , <i>Enterobacter cloacae</i> , <i>Escherichia coli</i> , CTX-M and OXA in one of three lots*
bioMérieux	BACT/ALERT®	SA Standard Aerobic	No interference observed
bioMérieux	BACT/ALERT	SN Standard Anaerobic	No interference observed
bioMérieux	BACT/ALERT	FA Plus	No interference observed
bioMérieux	BACT/ALERT	FN Plus	No interference observed
bioMérieux	BACT/ALERT	PF Plus	No interference observed
Thermo Scientific™	VersaTREK™	REDOX™ 1 EZ Draw Aerobic	No interference observed
Thermo Scientific	VersaTREK	REDOX 2 EZ Draw Anaerobic	No interference observed

\* 2/15 replicates were false negative for *Pan Candida*; 1/15 replicates was false negative for *Enterobacter cloacae*; 1/15 replicates was false negative for *Escherichia coli* (OXA-48); 2/15 replicates were false negative for CTX-M

## Carryover and Cross-Contamination

Carryover and cross-contamination were evaluated for the **cobas eplex** BCID-GN panel within and between runs by alternating high positive and negative samples across multiple runs over 5 rounds of testing. A high-titer mix of OXA positive *Escherichia coli*, CTX-M, and KPC positive *Enterobacter cloacae*, *Salmonella enterica*, and *Enterococcus faecalis* (a Pan Gram-Positive target organism) was prepared at  $1 \times 10^9$  CFU/mL each as well as *Candida krusei* (a Pan *Candida* target organism) at  $1 \times 10^7$  CFU/mL to simulate clinically relevant high positive samples for positive testing. Negative blood culture matrix was used to represent negative samples. Over 120 runs, all valid positive runs resulted in detection of *Escherichia coli*, *Enterobacter cloacae* complex, *Salmonella*, OXA, CTX-M, KPC, Pan Gram-Positive, and Pan *Candida* and no false positives were detected in the negative runs.

## Competitive Inhibition Study

Competitive inhibition was evaluated for the **cobas eplex** BCID-GN panel by pairing eight clinically relevant organisms (including a Pan Gram-Positive assay target and an off-panel gram-positive organism) in four simulated dual infection sample mixes. Each dual infection mix was tested in combination with each of the three other mixes, such that all organisms were tested at low titer (concentrations expected at bottle positivity) while in the presence of other organisms at higher titer (concentrations expected at 8 hours beyond bottle positivity, or ~ one log higher than that expected at bottle positivity). No competitive inhibition was observed in any replicates of the twelve testing conditions. A summary of the organisms assessed and testing concentrations is found in **Table 114**.

**Table 114: Competitive Inhibition Organisms and Concentrations Tested**

Organism	High Concentration	Low Concentration
<i>Klebsiella pneumoniae</i>	$1 \times 10^9$ CFU/mL	$9 \times 10^8$ CFU/mL
<i>Escherichia coli</i> (CTX-M+)	$1 \times 10^9$ CFU/mL	$2 \times 10^8$ CFU/mL
<i>Enterobacter cloacae</i> (VIM+)	$7 \times 10^8$ CFU/mL	$2 \times 10^8$ CFU/mL
<i>Klebsiella oxytoca</i> (KPC+)	$1 \times 10^9$ CFU/mL	$9 \times 10^8$ CFU/mL
<i>Pseudomonas aeruginosa</i> (IMP+)	$8 \times 10^8$ CFU/mL	$1 \times 10^8$ CFU/mL
<i>Serratia marcescens</i>	$2 \times 10^9$ CFU/mL	$1 \times 10^9$ CFU/mL
<i>Staphylococcus aureus</i>	$1 \times 10^8$ CFU/mL	$2 \times 10^7$ CFU/mL
<i>Corynebacterium striatum</i> <sup>A</sup>	$2 \times 10^9$ CFU/mL	$4 \times 10^6$ CFU/mL

A. Off-panel organism

## TROUBLESHOOTING

Table 115: Troubleshooting Table

For a complete list of all **cobas eplex** error messages and a description of the messages, please refer to the **cobas eplex** Operator Manual.

Error	Error Messages	Description	Re-test Recommendations
Test did not start	"Cartridge failure" "The cartridge initialization test failed" "Cartridge not present" "Bay heater failure" "Unknown error" "Bay main / fluid motor failure" "Bay over pressured" "Bay temperature out of range" "The system was unable to read the cartridge" "Cartridge inserted doesn't match the serial number of the cartridge scanned" "The system is not ready to accept the cartridge" "The system was unable to enable cartridge insertion for the bay" "The system failed to prepare the cartridge for processing" "The cartridge initialization test failed" "The system rejected an attempt to process a previously used cartridge"	<p>An error that occurs during pre-flight check (initialization) of cartridge upon insertion into bay. Pre-flight or cartridge initialization occurs when the cartridge is first inserted into the bay and takes approximately 90 seconds.</p> <p>Upon completion of preflight testing or cartridge initialization, the cartridge cannot be re-used, but prior to this point, the cartridge can be re-tested.</p> <p>To verify cartridge initialization has completed, examine the cartridge label upon removal. If the <b>cobas eplex</b> BCID-GN cartridge label has been pierced, initialization started and cartridge cannot be re-tested. If the label has not been pierced, follow the recommendation as stated.</p>	<ol style="list-style-type: none"> <li>1. Remove cartridge from bay.               <ol style="list-style-type: none"> <li>a. Reset bay to clear the error</li> <li>b. Re-insert cartridge in any available bay</li> </ol> </li> <li>2. If the cartridge is not able to be initialized on the second try and again generates an error during pre-flight check, this indicates an issue with the cartridge. This cartridge should be discarded following laboratory procedures and the sample should be repeated using a new cartridge. Bay(s) should be reset to clear the errors. Please contact Roche Technical Support to alert them of the issue</li> </ol> <p>If the bay remains in an error state (flashing red) after the cartridge has been removed, then it must be reset through the Bay Configuration menu before it can be used to run cartridges.</p>
Test did not finish	"Bay heater failure" "Bay main / fluid motor failure" "Bay voltage failure" "Bay sub-system communication timeout" "Bay over pressured" "Bay auto-calibration failure" "Bay temperature out of range" "The system was unable to eject the cartridge from the bay"	<p>This type of error occurs during the run, after pre-flight checks completed and prevents the cartridge from being processed to completion.</p>	<p>Reagents have been consumed and the cartridge cannot be reused. Contact Roche Technical Support and proceed with repeat testing the sample using a new cartridge.</p> <p>If the bay remains in an error state (flashing red) after the cartridge has been removed, then it must be reset through the Bay Configuration menu before it can be used to run cartridges.</p>
Invalid		<p>This is an error that results in no valid results being generated. A test report will be generated, but all targets and internal control will be invalid.</p>	<p>Reagents have been consumed and the cartridge cannot be reused. Contact Roche Technical Support and proceed with repeat testing the sample using a new cartridge.</p>

## Technical Support (United States)

Roche Technical support is available 24 hours a day, 7 days a week to provide the highest level of customer support and satisfaction.

GenMark Diagnostics, Inc. A Member of the Roche Group  
5964 La Place Court  
Carlsbad, CA 92008 USA

In the US, please contact:













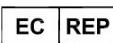



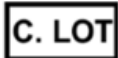






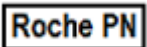
Technical support: 833.943.6627 (833.9GENMAR) or [cad.technical\\_support\\_us@roche.com](mailto:cad.technical_support_us@roche.com).

Customer service: 1-800-428-5076

## Technical Support (International)

For technical support (assistance) please reach out to your local affiliate: [https://www.roche.com/about/business/roche\\_worldwide.htm](https://www.roche.com/about/business/roche_worldwide.htm).

## GLOSSARY OF SYMBOLS

Symbol	Description	Symbol	Description
	Batch Code		Use by date YYYY-MM-DD
	Caution		Serial number
	Contains sufficient for <n> tests		Catalog number
	European Union Conformity		Biological risks
	<i>In vitro</i> diagnostic medical device		Upper limit of temperature
	Consult instructions for use		Lower limit of temperature
	Authorized representative in the European Community		Temperature range
	Manufacturer		Irritant, dermal sensitizer, acute toxicity (harmful), narcotic effects, respiratory tract irritation
	Cartridge Lot		Oxidizers
Rx Only	For prescription use only		UK Conformity Assessed
	Unique Device Identifier		Global Trade Identification Number
	Single Use		Importer
	Roche Part Number		

## REFERENCES

1. Angus, Derek C., et al. (2013) Severe Sepsis and Septic Shock. *New England Journal of Medicine*, 369(9) 840-851. DOI: 10.1056/NEJMra1208623
2. Centers for Disease Control and Prevention. Gram-negative Bacteria Infections in Healthcare Settings. Retrieved from <https://www.cdc.gov/hai/organisms/gram-negative-bacteria.html>
3. Korytny, Alexander, et al. (2016) Bloodstream infections caused by multi-drug resistant *Proteus mirabilis*: Epidemiology, risk factors and impact of multi-drug resistance. *Infectious Diseases (London)*, 48(6) 428-431. DOI: 10.3109/23744235.2015.1129551
4. Abbo, Ahron, et al. (2005) Multidrug-resistant *Acinetobacter baumannii*. *Emerging Infectious Diseases*, 11(1) 22-29. DOI: 10.3201/eid1101.04000
5. Centers for Disease Control and Prevention. *Acinetobacter* in Healthcare Settings. Retrieved from <http://www.cdc.gov/hai/organisms/acinetobacter.html>
6. Cunha, Burke A., et al. (2016) *Acinetobacter*. Retrieved from <http://emedicine.medscape.com/article/236891-overview March 15>
7. CLSI. (2013) *Performance Standards for Antimicrobial Susceptibility Testing; Twenty-Third Informational Supplement*. CLSI document M100-S23. Wayne, PA. Clinical and Laboratory Standards Institute.
8. Bonomo, Robert A., et al. (2006) Mechanisms of Multidrug Resistance in *Acinetobacter* Species and *Pseudomonas aeruginosa*. *Clinical Infectious Diseases*, 43(S2) S49-S56. DOI: 10.1086/504477
9. Boulanger, Anne, et al. (2012) NDM-1-Producing *Acinetobacter baumannii* from Algeria. *Antimicrobial Agents and Chemotherapy*, 56(4) 2214-2215. DOI: 10.1128/AAC.05653-11
10. Martinez, T., et al. (2016) Genetic environment of the KPC gene in *Acinetobacter baumannii* ST2 clone from Puerto Rico and genomic insights into its drug resistance. *Journal of Medical Microbiology*, 65(8) 784-792. DOI: 10.1099/jmm.0.000289
11. Aldridge, Kenneth E., et al. (2003) Bacteremia Due to *Bacteroides fragilis* Group: Distribution of Species, B-Lactamase Production, and Antimicrobial Susceptibility Patterns. *Antimicrobial Agents and Chemotherapy*, 47(1) 148-153. DOI: 10.1128/AAC.47.1.148-153.2003
12. Jouseimies-Simer, Hannele, et al. (2002) *Wadsworth-Ktl Anaerobic Bacteriology Manual 6th Edition*. Start Now Pr.
13. Hetch, David, W. *Bacteroides* species. Retrieved from <http://www.antimicrobe.org/b85.asp#r116>
14. Gill, MA. (1999) *Citrobacter* urinary tract infections in children. *The Pediatric Infectious Disease Journal*, 18(10) 889-92.
15. Antonelli, Alberto, et al. (2015) OXA-372, a novel carbapenem-hydrolysing class D b-lactamase from a *Citrobacter freundii* isolated from a hospital wastewater plant. *Journal of Antimicrobial Chemotherapy*, 70(10) 2749-2756. DOI: 10.1093/jac/dkv181
16. Du, Xiao-Xing, et al. (2013) Genetic characteristics of blaNDM-1-positive plasmid in *Citrobacter freundii* isolate separated from a clinical infectious patient. *Journal of Medical Microbiology* 62, 1332-1337. DOI: 10.1099/jmm.0.057091-0
17. Gaibani, Paolo, et al. (2013) Outbreak of *Citrobacter freundii* carrying VIM-1 in an Italian Hospital, identified during the carbapenemases screening actions. *International Journal of Infectious Diseases*, 17(9) e714-e717.
18. Millán, Beatriz, et al. (2011) CTX-M-14 b-lactamase-producing *Citrobacter freundii* isolated in Venezuela. Millán et al. *Annals of Clinical Microbiology and Antimicrobials*, 10:22. DOI: 10.1186/1476-0711-10-22
19. Peter, S., et al. (2014) Emergence of *Citrobacter freundii* carrying IMP-8 metallo-b-lactamase in Germany. *New Microbes and New Infections*, 2(2) 42-45. DOI: 10.1002/nmi2.36
20. Zhang, Rong, et al. (2008) High-level carbapenem resistance in a *Citrobacter freundii* clinical isolate is due to a combination of KPC-2 production and decreased porin expression. *Journal of Medical Microbiology*, 57(3) 332-337. DOI: 10.1099/jmm.0.47576-0
21. Food Safety News. CDC warns of Cronobacter in powdered milk, infant formula. Retrieved from <http://www.foodsafetynews.com/2016/04/125714/#.WG1xjX3-EhR>
22. Mezzatesta, Maria Lina, et al. (2012) Enterobacter cloacae complex: clinical impact and emerging antibiotic resistance. *Future Microbiology*. 7(7), 887-902. DOI: 10.2217/fmb.12.61
23. Trecarichi, E.M., et al. (2015) Current epidemiology and antimicrobial resistance data for bacterial bloodstream infections in patients with hematologic malignancies: an Italian multicentre prospective survey. *Clinical Microbiology and Infection*, 21(4) 337-343. DOI: 10.1016/j.cmi.2014.11.022
24. Jha, Piyush, et al. (2016) Transmission of Enterobacter aerogenes septicemia in healthcare workers. *SpringerPlus*, 5(1) 1397. DOI: 10.1186/s40064-016-3011-x
25. Davin-Regli, Anne, et al. (2015) Enterobacter aerogenes and Enterobacter cloacae; versatile bacterial pathogens confronting antibiotic treatment. *Frontiers in Microbiology*, 6:392. DOI: 10.3389/fmicb.2015.00392
26. Mayo Clinic. Diseases and Conditions E.coli. Retrieved from <http://www.mayoclinic.org/diseases-conditions/e-coli/basics/definition/con-20032105>
27. Université de Montreal. Escherichia coli Laboratory. Pathogenic E. coli. Retrieved from <http://www.ecl-lab.com/en/ecoli/index.asp>

28. Ruppé, Etienne, et al. (2009) CTX-M  $\beta$ -Lactamases in *Escherichia coli* from Community-acquired Urinary Tract Infections, Cambodia. *Emerging Infectious Diseases*, 15(5) 741-748. DOI: 10.3201/eid1505.071299
29. Oteo, Jesus, et al. (2008) Emergence of imipenem resistance in clinical *Escherichia coli* during therapy. *International Journal of Antimicrobial Agents*, 32(6) 534-537. DOI: 10.1016/j.ijantimicag.2008.06.012
30. McGuinn, Marcella, et al. (2009) *Escherichia coli* and *Klebsiella pneumoniae* Carbapenemase in Long-term Care Facility, Illinois, USA. *Emerging Infectious Diseases*, 15(6) 988-989. DOI: 10.3201/eid1506.081735
31. Rasheed, J. Kamile, et al. (2013) New Delhi Metallo- $\beta$ -Lactamase-producing Enterobacteriaceae, United States. *Emerging Infectious Diseases*, 19(6) 870-878. DOI: PMID: PMC3713825
32. Zurfluh, Katrin, et al. (2015) Emergence of *Escherichia coli* producing OXA-48  $\beta$ -Lactamase in the community in Switzerland. *Antimicrobial Resistance and Infection Control*, 4:9. DOI: 10.1186/s13756-015-0051-x
33. Scoulica, Efsthathia V., et al. (2004) Spread of blaVIM-1-producing *E.coli* in a university hospital in Greece. Genetic analysis of the integron carrying that blaVIM-1 metallo- $\beta$ -lactamase gene. *Diagnostic Microbiology & Infectious Disease*, 48(3) 167-172. DOI: 10.1016/j.diagmicrobio.2003.09.012
34. Public Health Agency of Canada. *Fusobacterium* spp. Pathogen Safety Data Sheet. Retrieved from <http://www.phac-aspc.gc.ca/lab-bio/res/psds-ftss/fusobacterium-eng.php>
35. Afra, Kevin, et al. (2013) Incidence, risk factors, and outcomes of *Fusobacterium* species bacteremia. *BMC Infectious Diseases*, 13:264. DOI: 10.1186/1471-2334-13-264
36. Centers for Disease Control and Prevention. *Haemophilus influenzae* Disease (Including Hib). Retrieved from <https://www.cdc.gov/hi-disease/clinicians.html>
37. Rubach, Matthew P., et al. (2011) Increasing Incidence of Invasive *Haemophilus influenzae* Disease in Adults, Utah, USA. *Emerging Infectious Diseases*, 17(9) 1645-1650. DOI: 10.3201/eid1709.101991
38. Paterson, David L., et al. *Klebsiella* species (*K.pneumoniae*, *K.oxytoca*, *K.ozzaenae* and *K. rhinoscleromatis*). *Infectious Disease Antimicrobial Agents*. Retrieved from <http://www.antimicrobe.org/new/b107.asp>
39. NCBI Taxonomy Browser. Retrieved from <https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=570>
40. Singh, Col Lavan, et al. (2016) *Klebsiella oxytoca*: An emerging pathogen? *Medical Journal Armed Forces India*. 72(S1) S59-S61. DOI: <http://dx.doi.org/10.1016/j.mjafi.2016.05.002>
41. Qureshi, Shahab, et al. *Klebsiella* Infections. Medscape. Retrieved from <http://emedicine.medscape.com/article/219907-overview>
42. Arnold, Ryan S., et al. (2011) Emergence of *Klebsiella pneumoniae* Carbapenemase (KPC)-Producing Bacteria. *Southern Medical Journal*, 104(1) 40–45. DOI:10.1097/SMJ.0b013e3181fd7d5a
43. Clímaco, Eduardo C., et al. (2010) CTX-M–producing *Klebsiella* spp. in a Brazilian hospital: what has changed in 6 years? *Diagnostic Microbiology & Infectious Disease*, 68(2) 186-189.
44. Conceicao, T., et al. (2005) First Isolation of blaVIM-2 in *Klebsiella oxytoca* Clinical Isolates from Portugal. *Antimicrobial Agents and Chemotherapy*, 49(1) 476. DOI: 10.1128/AAC.49.1.476.2005
45. Cuzon, Gaelle, et al. (2011) Outbreak of OXA-48-Positive Carbapenem-Resistant *Klebsiella pneumoniae* Isolates in France. *Antimicrobial Agents and Chemotherapy*, 55(5) 2420–2423. DOI: 10.1128/AAC.01452-10
46. Giakkoupi, P., et al. (2003) VIM-1 Metallo- $\beta$ -Lactamase-Producing *Klebsiella pneumoniae* Strains in Greek Hospitals. *Journal of Clinical Microbiology*, 41(8) 3893–3896. DOI: 10.1128/JCM.41.8.3893-3896
47. Hagiya, Hideharu, et al. (2015) *Klebsiella oxytoca*-producing IMP-1 Detected as the First Strain of Carbapenem-resistant Enterobacteriaceae in Our Hospital. *Internal Medicine*, 54 2939-2941. DOI: 10.2169/internalmedicine.54.4965
48. Hoenigl, Martin, et al. (2012) KPC-producing *Klebsiella oxytoca* Outbreak, Austria. *Antimicrobial Agents and Chemotherapy*, 56(4) 2158-2161. DOI:10.1128/AAC.05440-11
49. Huang, Tzu-Wen, et al. (2013) Complete Sequences of Two Plasmids in a blaNDM-1-Positive *Klebsiella oxytoca* Isolate from Taiwan. *Antimicrobial Agents and Chemotherapy*, 57(8) 4072–4076. DOI: 10.1128/AAC.02266-12
50. Wang, Guiqing, et al. (2013) CTX-M  $\beta$ -Lactamase–producing *Klebsiella pneumoniae* in Suburban New York, New York, USA. *Emerging Infectious Diseases*, 19(11) 1803-1810. DOI: 10.3201/eid1911.121470
51. Li, Jun-Jie, et al. (2016) Lactamase-1-Producing *Klebsiella pneumoniae*, Florida, USA. *Emerging Infectious Diseases*, 22(4) 1803-1810. DOI: <http://dx.doi.org/10.3201/eid2204.151176>
52. Limbago, Brandi M., et al. (2011) IMP-Producing Carbapenem-Resistant *Klebsiella pneumoniae* in the United States. *Journal of Clinical Microbiology*, 49(12) 4239–4245. DOI:10.1128/JCM.05297-11
53. Nazik, H., et al. (2014) Detection and Spread of Oxa-48-Producing *Klebsiella oxytoca* Isolates in Istanbul, Turkey. *Southeast Asian Journal of Tropical Medicine and Public Health*, 45(1) 123-129.
54. Miller, James R. *Morganella* Infections. Retrieved from <http://emedicine.medscape.com/article/222443-overview>
55. Demiray, Tayfur, et al. (2016) A severe *Morganella morganii* endophthalmitis; followed by bacteremia. *Iranian Journal of Microbiology*, 8(1) 70-72.
56. Diene, S.M., et al. (2014) CTX-M-15-producing *Morganella morganii* from Hôpital Principal de Dakar, Senegal. *New Microbes and New Infections*, 2(2) 46–49. DOI: 10.1002/nmi2.41
57. Shibata, Naohiro, et al. (2003) PCR Typing of Genetic Determinants for Metallo- $\beta$ -Lactamases and Integrases Carried by Gram-Negative Bacteria Isolated in Japan, with Focus on the Class 3 Integron. *Journal of Clinical Microbiology*, 41(12) 5407–5413. DOI: 10.1128/JCM.41.12.5407–5413.2003



58. Shi, D.-S., et al. (2012) Identification of blaKPC-2 on different plasmids of three *Morganella morganii* isolates. *European Journal of Clinical Microbiology & Infectious Diseases*, 31(5) 797-803.
59. Olaitan, Abiola Olumuyiwa, et al. (2014) Genome analysis of NDM-1 producing *Morganella morganii* clinical isolates. *Expert Review of Anti-infective Therapy*, 12(10) 1297-1305. DOI: 10.1586/14787210.2014.944504
60. Hammoudi, D., et al. (2014) Countrywide spread of OXA-48 carbapenemase in Lebanon: surveillance and genetic characterization of carbapenem-non-susceptible Enterobacteriaceae in 10 hospitals over a one-year period. *International Journal of Infectious Diseases*, 29 139–144. DOI: 10.1016/j.ijid.2014.07.017
61. Tsakris, Athanassios, et al. (2007) Characterization of In3Mor, a new integron carrying VIM-1 metallo- $\beta$ -lactamase and sat1 gene, from *Morganella morganii*. *Journal of Antimicrobial Chemotherapy*, 59(4) 739–741. DOI: 10.1093/jac/dkm020
62. Centers for Disease Control and Prevention. Meningococcal Disease (*Neisseria meningitidis*). Retrieved from <https://wwwnc.cdc.gov/travel/diseases/meningococcal-disease>
63. Centers for Disease Control and Prevention. Meningococcal Disease Causes & Transmission. Retrieved from <https://www.cdc.gov/meningococcal/about/causes-transmission.html>
64. <https://www.cdc.gov/meningitis/lab-manual/chpt10-pcr.html>
65. Drzewiecka, Dominika. (2016) Significance and Roles of *Proteus* spp. Bacteria in Natural Environments. *Microbial Ecology*, 72(4) 741–758. DOI: 10.1007/s00248-015-0720-6
66. Gonzalez, Gus, et al. *Proteus* Infections. Retrieved from <http://emedicine.medscape.com/article/226434-overview>
67. Armbruster, Chelsie E., et al. *Proteus* species. Retrieved from <http://www.antimicrobe.org/b226.asp>
68. Karapavlidou, P., et al. (2005) CTX-M-1 extended-spectrum beta-lactamase-producing *Proteus mirabilis* in Greece. *Microbial Drug Resistance*, 11(4) 351-4.
69. Dixon, Nyssa, et al. (2016) A Unique IMP-27: A Unique Metallo- $\beta$ -Lactamase Identified in Geographically Distinct Isolates of *Proteus mirabilis*. *Antimicrobial Agents Chemotherapy*, 60(10) 6418-6421. DOI: 10.1128/AAC.02945-15
70. Tibbetts, R., et al. (2008) Detection of KPC-2 in a Clinical Isolate of *Proteus mirabilis* and First Reported Description of Carbapenemase Resistance Caused by a KPC  $\beta$ -Lactamase in *P. mirabilis*. *Journal of Clinical Microbiology*, 46(9) 3080–3083.
71. Qin, Shangshang, et al. (2015) Emergence of extensively drug-resistant *Proteus mirabilis* harboring a conjugative NDM-1 plasmid and a novel *Salmonella* genomic island variant (SGI1-Z). *Antimicrobial Agents Chemotherapy*, 59(10) 6601-6604. DOI: 10.1128/AAC.00292-15
72. Chen, Liang, et al. (2015) First Report of an OXA-48-Producing Multidrug-Resistant *Proteus mirabilis* Strain from Gaza, Palestine. *Antimicrobial Agents and Chemotherapy*, 59(7) 4305-4307. DOI: 10.1128/AAC.00565-15.
73. Miriagou, V., et al. (2010) Detecting VIM-1 Production in *Proteus mirabilis* by an Imipenem-Dipicolinic Acid Double Disk Synergy Test. *Journal of Clinical Microbiology*, 48(2) 667–668.
74. Friedrich, Marcus, et al. *Pseudomonas aeruginosa* Infections. Retrieved from <http://emedicine.medscape.com/article/226748-overview>
75. McCarthy, Kate. (2015) *Pseudomonas aeruginosa*: Evolution of Antimicrobial Resistance and Implications for Therapy. *Seminars in Respiratory and Critical Care Medicine*, 36(01) 44–55. DOI: 10.1055/s-0034-1396907
76. Al Naiemi, Nashwan, et al. (2006) A CTX-M extended-spectrum  $\beta$ -Lactamase in *Pseudomonas aeruginosa* and *Stenotrophomonas maltophilia*. *Journal of Medical Microbiology*, 55(11) 1607-1608. DOI:10.1099/jmm.0.46704-0
77. Kazmierczak, Krystyna M., et al. (2016) Multiyear, Multinational Survey of the Incidence and Global Distribution of Metallo- $\beta$ -Lactamase-Producing *Enterobacteriaceae* and *Pseudomonas aeruginosa*. *Antimicrobial Agents and Chemotherapy*, 60(2) 1067-1078. DOI: 10.1128/AAC.02379-15
78. Evans, Benjamin A., et al. (2014) OXA  $\beta$ -Lactamases. *Clinical Microbiology Reviews*, 27(2) 241-263.
79. Ao, Trong T., et al. (2015) Global Burden of Invasive Nontyphoidal *Salmonella* Disease, 2010. *Emerging Infectious Diseases*, 21(6) 941-949. DOI: 10.3201/eid2106.140999
80. Gal-Mor, Ohad, et al. (2014) Same species, different diseases: how and why typhoidal and non-typhoidal *Salmonella enterica* serovars differ. *Frontiers in Microbiology*, 5:391. DOI: 10.3389/fmicb.2014.00391
81. Lan, Nguyen Phu Huong, et al. (2016) Invasive Non-typhoidal *Salmonella* Infections in Asia: Clinical Observations, Disease Outcome and Dominant Serovars from an Infectious Disease Hospital in Vietnam. *PLoS Neglected Tropical Diseases*, 10(8) e0004857. DOI: 10.1371/journal.pntd.0004857
82. Buckle, Geoffrey C., et al. (2012) Typhoid fever and paratyphoid fever: Systematic review to estimate morbidity and mortality for 2010. *Journal of Global Health*, 2(1) 010401. DOI:10.7189/jogh.02.010401
83. Sjölund-Karlsson, Maria, et al. (2011) CTX-M–producing Non-Typhi *Salmonella* spp. Isolated from Humans, United States. *Emerging Infectious Diseases*, 17(1) 97-99. DOI: 10.3201/eid1701.100511
84. Hosoda, Takuya, et al. (2015) Emergence of *Salmonella* Strain That Produces IMP-1-Type Metallo- $\beta$ -Lactamase in a Japanese Patient.
85. Jure, M.A., et al. (2014) Emergence of KPC-2-Producing *Salmonella enterica* Serotype Schwarzengrund in Argentina. *Antimicrobial Agents and Chemotherapy*, 58(10) 6335-6336. DOI: 10.1128/AAC.03322-14
86. Day, Martin R., et al. (2015) Carbapenemase-producing *Salmonella enterica* isolates in the UK. *Journal of Antimicrobial Chemotherapy*, 70(7) 2165-2167. DOI: 10.1093/jac/dkv075
87. Sotillo, Alma, et al. (2015) Emergence of VIM-1-producing *Salmonella enterica* serovar Typhimurium in a paediatric patient. *Journal of Medical Microbiology*, 64(12) 1541-1543. DOI: 10.1099/jmm.0.000170

- 
88. Herra, Celine, et al. *Serratia marcescens*. Retrieved from <http://www.antimicrobe.org/b26.asp>
  89. Anía, Basilio J, et al. *Serratia*, Overview. Retrieved from <http://emedicine.medscape.com/article/228495-overview#a5>
  90. Gastmeier, Petra. (2014) *Serratia marcescens*: an outbreak experience. *Frontiers in Microbiology*, 5:81. DOI: 10.3389/fmicb.2014.00081
  91. Heltberg, O. et al. (1993) Nosocomial epidemic of *Serratia marcescens* septicemia ascribed to contaminated blood transfusion bags. *Transfusion*, 33(3) 221-227. DOI: 10.1046/j.1537-2995.1993.33393174448.x
  92. Madani, TA, et al. (2011) *Serratia marcescens*-contaminated baby shampoo causing an outbreak among newborns at King Abdulaziz University Hospital, Jeddah, Saudi Arabia. *Journal of Hospital Infection*, 78(1) 16-19. DOI: 10.1016/j.jhin.2010.12.017
  93. Mahlen, Steven D. (2011) *Serratia* Infections: from Military Experiments to Current Practice. *Clinical Microbiology Reviews*, 24(4) 755-791. DOI: 10.1128/CMR.00017-11
  94. Batah, R., et al. (2015) Outbreak of *Serratia marcescens* Coproducing ArmA and CTX-M-15 Mediated High Levels of Resistance to Aminoglycoside and Extended-Spectrum Beta-Lactamases, Algeria. *Microbial Drug Resist.*, 21(4) 470-476. DOI: 10.1089/mdr.2014.0240
  95. Nakamura, T., et al. (2002) IMP-1 type metallo-beta-lactamase producing *Serratia marcescens* strains isolated from blood culture between 1991 to 200. *Kansenshogaku Zasshi*, 76(4) 246-53.
  96. Silva, Kesia Esther, et al. (2015) Coproduction of KPC-2 and IMP-10 in Carbapenem-Resistant *Serratia marcescens* Isolates from an Outbreak in a Brazilian Teaching Hospital. *Journal of Clinical Microbiology*, 53(7) 2324-2328. DOI: 10.1128/JCM.00727-15
  97. Gruber, Teresa M., et al. (2015) Pathogenicity of pan-drug-resistant *Serratia marcescens* harbouring blaNDM-1. *Antimicrobial Chemotherapy*, 70(4) 1026–1030. DOI: 10.1093/jac/dku482
  98. Piorel, Laurent, et al. (2012) OXA-48-like carbapenemases: the phantom menace. *Journal of Antimicrobial Chemotherapy*, 67(7) 1597-1606. DOI: 10.1093/jac/dks121
  99. Nastro, M., et al. (2013) First nosocomial outbreak of VIM-16-producing *Serratia marcescens* in Argentina. *Clinical Microbiology and Infectious Diseases*, 19(7) 617-619. DOI: 10.1111/j.1469-0691.2012.03978.x
  100. Anía, Basilio J, et al. *Serratia*, clinical. Retrieved from <http://emedicine.medscape.com/article/228495-clinical>
  101. Falagas, Matthew E., et al. (2008) Therapeutic options for *Stenotrophomonas maltophilia* infections beyond cotrimoxazole: a systematic review. *Journal of Antimicrobial Chemotherapy*, 62(5) 889–894. DOI: 10.1093/jac/dkn301
  102. Ruppé, Étienne, et al. (2015) Mechanisms of antimicrobial resistance in Gram-negative bacilli. *Annals of Intensive Care*, (2015) 5(1) 61. DOI: 10.1186/s13613-015-0061-0
  103. Pathmanathan, A., et al. (2005) Significance of positive *Stenotrophomonas maltophilia* culture in acute respiratory tract infection. *The European Respiratory Journal*, 25(5) 911–914. DOI: 10.1183/09031936.05.00096704
  104. Livermore, D.M. (2006) CTX-M: Changing the Face of ESBLs in Europe. *Journal of Antimicrobial Chemotherapy*, 59(2) 165-174.
  105. Queenan, Anne Marie, et al. (2007) Carbapenemases: The Versatile  $\beta$ -Lactamases. *Clinical Microbiology Reviews*, 20(3) 440-458. DOI: 10.1128/CMR.00001-07
  106. Zmarlicka, Monika, T., et al. (2015) Impact of New Delhi metallo-beta-lactamase on beta-lactam antibiotics. *Infection and Drug Resistance*, 2015(8) 297-309. DOI: 10.2147/IDR.S39186
  107. Nordmann, Patrice, et al. (2011) Global Spread of Carbapenemase-producing *Enterobacteriaceae*. *Emerging Infectious Diseases*, 17(10) 1791-1798. DOI: 10.3201/eid1710.110655
  108. Papp-Wallace, Krisztina M., et al. (2016) New  $\beta$ -Lactamase Inhibitors in the Clinic. *Infectious Disease Clinics of North America*, 30(2): 441–464. doi:10.1016/j.idc.2016.02.007.
  109. Makena, Anne, et al. (2015) Comparison of Verona Integron-Borne Metallo- $\beta$ -Lactamase (VIM) Variants Reveals Differences in Stability and Inhibition Profiles. *Antimicrobial Agents and Chemotherapy*, 60(3) 1377-1384. DOI: 10.1128/AAC.01768-15
  110. Samuel, Linoj P., et al. (2016) Multicenter Assessment of Gram Stain Error Rates. *Journal of Clinical Microbiology*, 54 (6) 1442-1447. DOI: 10.1128/JCM.03066-15

## DOCUMENT REVISION

Document Revision Information	
Rev. A 05/2019	Original document
Rev. B 10/2020	External control language updated; Neisseria meningitidis updated in Summary of Detected Organisms section.
Rev. C 04/2021	Specimen stability data updated
Rev. D 02/2022	GN2 inclusivity improvements and typo corrections
Rev E	Warnings and precautions, General, add language to satisfy regulatory requirements Table 112: indicate the final concentrations for y-globulin and caspofungin are reported as 0.85 g/dL and 4.5 µg/mL, respectively. Add reference to summary of safety and performance Updated EMERGO address. Added UKCA requirements. Updated technical support contact, website, Trademark, and Copyright information. Updated Glossary of Symbols.
Doc Rev. 1.0 12/2023	First publishing for Branchburg based on IFU PI1082-E. Updated branding from GenMark's ePlex® to <b>cobas® eplex</b> . Updated SDS website information in <b>Safety</b> section. Please contact your local Roche Representative if you have any questions.

The summary of safety and performance report can be found using the following link:  
<https://ec.europa.eu/tools/eudamed>

## TRADEMARKS

GenMark®, GenMark Dx®, eSensor®, **cobas® eplex**, Designed For the Patient, Optimized For the Lab® and The True Sample-to-Answer Solution® are registered trademarks of Roche.

Kimwipes™ is a trademark of Kimberly-Clark Worldwide.

BacT/Alert® is a registered trademark of bioMérieux.

BACTEC™ is a trademark of BD.

VersaTREK™ and REDOX™ are trademarks of Thermo Fisher Scientific.

## PATENT INFORMATION

**cobas eplex** blood culture identification Gram-Negative panel and/or use thereof features technology claimed in one or more of the following United States and foreign patents owned or licensed by GenMark Diagnostics Inc. or its subsidiaries, with multiple additional foreign and domestic patents pending: United States Patent Nos. 7,820,391, 8,486,247, 9,222,623, 9,410,663, 9,453,613, 9,498,778, 9,500,663, 9,598,722; 9,957,553, 10,001,476, 10,106,847, 10,273,535, 10,352,983, 10,357,774, 10,391,489, 10,495,656, 10,564,211, D881409, and D900330, and other international patents and patent applications.

Unless otherwise agreed to in writing, by using a cartridge, Recipient acknowledges that Recipient has read, accepts and agrees to be bound by and comply with the General Terms and Conditions of Sale available on Roche's website which can be amended from time to time by Roche without consent. If Recipient does not accept and agree to be bound by the General Terms and Conditions of Sale, Recipient will immediately cease any further use of the cartridge.

This product is subject to a limited license to use the product in the field of human in vitro diagnostics and research reasonably related thereto. Users are prohibited from using this product for other applications, including in the field of forensics (including human identification testing).

Effective Date: December 2023

©2023 Roche Molecular Systems, Inc. All rights reserved.

GenMark Diagnostics, Inc. A Member of the Roche Group

5964 La Place Court, Carlsbad, CA 92008

760.448.4300

<https://diagnostics.roche.com/>