cobas® eplex blood culture identification gram-negative (BCID-GN) panel

Package Insert

CE 2797 IVD UKCA

Rx Only

Designed for the Patient, Optimized for the Lab®

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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*$_{CTX-M}$), IMP (*bla*$_{IMP}$) , KPC (*bla*$_{KPC}$) , NDM (*bla*$_{NDM}$), OXA (*bla*$_{OXA}$) (OXA-23 and OXA-48 groups only), and VIM (*bla*$_{VIM}$).

The **cobas eplex** BCID-GN panel contains assays for the detection of genetic determinants associated with resistance to antimicrobial agents including CTX-M(*bla*$_{CTX-M}$), which is associated with resistance to extended spectrum beta-lactamase (ESBL)-mediated resistance to penicillins, cephalosporins, and monobactams, as well as OXA (*bla*$_{OXA}$) (OXA-23 and OXA-48 groups only), KPC (*bla*$_{KPC}$), and metallo-beta-lactamases IMP (*bla*$_{IMP}$), VIM (*bla*$_{VIM}$), and NDM (*bla*$_{NDM}$), 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.[1] Antimicrobial resistance is common among gram-negative organisms, and multi-drug resistance is increasingly common in many species.[2] When involved in bacteremia, the species belonging to this group have mortality rates ranging from 20% to over 90% in some populations.[3]

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

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

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.[4,5,6] *Acinetobacter baumannii* is inherently resistant to multiple antibiotics including amoxicillin-clavulanic acid, ertapenem, trimethoprim, and chloramphenicol.[7] Isolates carrying CTX-M, IMP, KPC, NDM, OXA, and VIM resistance markers have been reported.[8,9,10]

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.[11] Since *Bacteroides fragilis* is a fastidious organism, it is difficult to isolate and often overlooked.[12] *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%.[13]

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.[14] 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.[15,16,17,18,19,20]

***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.[21]

***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.[22] In one study over four years and nine hospital wards, *Enterobacter cloacae* alone represented nearly 8% of all gram-negative bloodstream infections.[23] The **cobas eplex** BCID-GN panel *Enterobacter cloacae* complex assay detects *Enterobacter asburiae, Enterobacter cloacae*, *Enterobacter cloacae* subsp. *cloacae*, *Enterobacter cloacae* subsp. d*issolvens*, *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 (*also known as *Klebsiella 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.[24] Some have been noted as intrinsically resistant to ampicillin, amoxicillin, and a number of cephalosporins.[7] Multi-drug resistant strains have also begun to circulate with strains of an epidemic clone being detected in many European hospitals.[25] 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.[26] *Escherichia coli* is classified into over 150 serotypes based on surface antigens and is the gram-negative species most frequently isolated from blood culture.[23] *Escherichia coli* strains in the gastrointestinal tract are usually commensal, however some strains can cause severe disease, and many carry genes for antibiotic resistance.[27] Resistance markers CTX-M, IMP, KPC, NDM, OXA, and VIM have all been noted in clinical isolates of *Escherichia coli*.[28,29,30,31,32,33]

Fusobacterium necrophorum, Fusobacterium nucleatum
Fusobacterium species are non-sporulating, anaerobic organisms commonly found in oropharyngeal, gastrointestinal, and urogenital tracts.[34] *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.[35]

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.[36,37] 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.[36,37] 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.[38] The genus *Klebsiella* consists of at least 11 species,[39] 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.[40] Both *Klebsiella pneumoniae* and *Klebsiella oxytoca* are generally resistant to multiple antibiotics,[41] and antibiotic susceptibility and treatment guidelines for infection are virtually identical.[41] Resistance markers

CTX-M, IMP, KPC, NDM, OXA, and VIM have all been noted in clinical isolates of both *Klebsiella oxytoca* and *Klebsiella pneumoniae*.[42,43,44,45,46,47,48,49,50,51,52,53]

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,[54] while some isolates have shown the ability to produce extended spectrum beta-lactamases (ESBLs).[55] Resistance markers CTX-M, IMP, KPC, NDM, OXA, and VIM have all been noted in clinical isolates of *Morganella morganii*.[56,57,58,59,60,61]

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.[62,63] 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.[64] 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*.[65] *Proteus* species are a common part of the human intestinal flora and can also be found as colonizers of the skin and oral mucosa.[66] They are present in soil, water, and often in seafood, and they are the most prevalent bacteria isolated from kidney stones.[65] Proteus species are a common cause of bacteremia, especially following catheter-associated urinary tract infections.[67] Resistance markers CTX-M, IMP, KPC, NDM, OXA, and VIM have all been noted in clinical isolates of *Proteus* species.[68, 69,70,71,72,73]

Proteus mirabilis

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

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.[74] 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%.[75] Resistance markers CTX-M, IMP, KPC, NDM, OXA, and VIM have all been noted in clinical isolates of *Pseudomonas aeruginosa*.[76,77,78]

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.[79,80] Mortality rates for invasive non-typhoidal *Salmonella* (iNTS) have been reported as high as 28%,[81] 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.[82] Resistance markers CTX-M, IMP, KPC, NDM, OXA, and VIM have all been noted in clinical isolates of *Salmonella* species.[83,84,85,86,87]

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.[88] In some cases, *Serratia* infection can develop into meningitis or bacteremia, where it has a mortality rate of up to 37% in some populations.[89,90] 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.[91,92,88] *Serratia* species are intrinsically resistant to several beta-lactams,[93] and resistance markers CTX-M, IMP, KPC, NDM, OXA, and VIM have all been noted in clinical isolates of *Serratia* species.[94,95,96,97,98,99] 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.[100] 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.[94,95,96,97,98,99]

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.[101] 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.[7,102] Mortality rates for bacteremia caused by *Stenotrophomonas maltophilia* range broadly between 10-60%, with underlying disease playing a large role in the mortality rate.[103] The resistance marker CTX-M has been noted in clinical isolates of *Stenotrophomonas maltophilia*.[76]

Antimicrobial Resistance Markers

***ctx*-M (*bla*$_{CTX-M}$) (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.[104]

***imp* (*bla*$_{IMP}$) (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.[105]

***kpc* (*bla*$_{KPC}$) (*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*.[105]

***ndm* (*bla*$_{NDM}$) (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.[106] Originally isolated from an Indian patient in 2008, it has now been isolated throughout the world.[107]

***oxa* (*bla*$_{OXA}$) (oxacillin-hydrolyzing beta-lactamase, OXA)**
OXA enzymes are class D beta-lactamases and confer resistance to cefpirome, cephalothin, and oxacillin.[78] There are over 500 OXA enzymes to date,[108] 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*$_{VIM}$) (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.[109]

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.[110] 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. pasteuri, 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

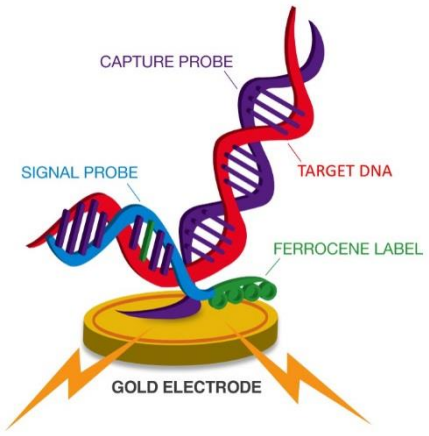
The True Sample-to-Answer Solution® **cobas eplex** instrument automates all aspects of nucleic acid testing including extraction, amplification, and detection, combining electrowetting and the eSensor® technology in a single-use cartridge. eSensor technology is based on the principles of competitive 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 **Box Contents**

Product	Material number	Components (quantity)	Storage
cobas eplex blood culture identification Gram-Negative (BCID-GN) panel	9556494001	**cobas eplex** BCID-GN panel Cartridge (12)	2–8 ˚C

Safety Data Sheets (SDS) for all reagents provided in this kit may be obtained at: https://navifyportal.roche.com/. For paper copies, please reach out to your local affiliate: https://www.roche.com/about/business/roche_worldwide.htm.

COMPOSITION OF REAGENTS

Component	Concentration (w/v)
Salting Buffer	
Guanidine hydrochloride	≤ 45%
Sodium perchlorate	≤ 14%
Binding Buffer	
PEG 8000	≤ 20%
NaH_2PO_4	≤ 1.0%
EDTA	≤ 0.1%
NaCl	≤ 5.0%
NaN_3	≤ 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_2PO_4	≤ 1.0%
EDTA	≤ 0.1%
NaCl	≤ 5.0%
NaN_3	≤ 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
$MgCl_2$	≤ 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.
- **cobas eplex** BCID-GN panel is single use only.
- 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 manufaturer 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 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 and proceed immediately to the next step.
7. Wipe the septum of the positive blood culture bottle with 70% ethanol or isopropyl alcohol (or equivalent) prior to withdrawing the sample.
8. Transfer an aliquot to a 1.5 mL RNase/DNase-free microcentrifuge tube or equivalent. Invert several times to mix and proceed immediately to the next step.
9. 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.
10. 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.
11. 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.
12. 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
PASS	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 **cobas eplex** BCID-GN panel Detection Report. Test is valid, report results.
FAIL	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 **cobas eplex** BCID-GN panel Detection Report. Test is not valid, repeat the test using a new cartridge.
N/A	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 **cobas eplex** BCID-GN panel Detection Report. Test is valid, report results.
INVALID	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 **cobas eplex** 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 **cobas eplex** 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 **cobas eplex** 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 **Table 7** for resistance marker organism associations).	All results are displayed on the **cobas eplex** 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 **cobas eplex** 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

***Proteus* Result**	***Proteus* Assay**	***Proteus mirabilis* Assay**	**Description**
Not Detected	Negative	Negative	No *Proteus* species detected
Detected	Positive	Positive	*Proteus mirabilis* detected
Detected	Positive	Negative	Unspeciated *Proteus* 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

***Serratia* Result**	***Serratia* Assay**	***Serratia marcescens* Assay**	**Description**
Not Detected	Negative	Negative	No *Serratia* species detected
Detected	Positive	Positive	*Serratia marcescens* detected
Detected	Positive	Negative	Unspeciated *Serratia* 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

Organism	**Resistance Marker**					
	CTX-M	**IMP**	**KPC**	**NDM**	**OXA**	**VIM**
Acinetobacter baumannii	X	X	X	X	X	X
Bacteroides fragilis						
Citrobacter	X	X	X	X	X	X
Cronobacter sakazakii			X			
Enterobacter cloacae complex	X	X	X	X	X	X
Enterobacter (non-*cloacae* complex)	X	X	X	X	X	X
Escherichia coli	X	X	X	X	X	X
Fusobacterium necrophorum						
Fusobacterium nucleatum						
Haemophilus influenzae						
Klebsiella oxytoca	X	X	X	X	X	X
Klebsiella pneumoniae group	X	X	X	X	X	X
Morganella morganii	X	X	X	X	X	X
Neisseria meningitidis						
Proteus	X	X	X	X	X	X
Proteus mirabilis	X	X	X	X	X	X
Pseudomonas aeruginosa	X	X	X	X	X	X
Salmonella	X	X	X	X	X	X
Serratia	X	X	X	X	X	X
Serratia marcescens	X	X	X	X	X	X
Stenotrophomonas maltophilia	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: *Enterococcus*, *Bacillus cereus* group, *Bacillus subtilis* group, *Staphylococcus,* and/or *Streptococcus*. 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 *Candida* Result	Description
Not Detected	No specified *Candida* species detected.
Detected	One or more of the following *Candida* organisms has been detected: *Candida albicans, Candida glabrata, Candida krusei,* and/or *Candida parapsilosis*. 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 x 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 >1x10^4 CFU/mL.
- *Enterobacter cowanii* was shown to cross-react with the *Enterobacter cloacae* complex assay at levels >1x10^8 CFU/mL.
- *Escherichia hermanii* was shown to cross-react with the *Enterobacter* (non-*cloacae* complex) assay at levels >1x10^6 CFU/mL, and with the *Serratia* assay at levels >1x10^7 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 unspeciated target may be masked in the case of a co-infection. For example, in the event that an unspeciated *Serratia* species is present in the same sample as *Serratia marcescens*, there is no ability to determine that the unspeciated *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 (%)
Acinetobacter baumannii	4 (1.1)	0 (0.0)	0 (0.0)	1 (2.0)	2 (1.6)	1 (0.8)	0 (0.0)
Bacteroides fragilis	11 (3.2)	0 (0.0)	0 (0.0)	2 (4.0)	4 (3.2)	2 (1.6)	3 (9.1)
Citrobacter	8 (2.3)	0 (0.0)	0 (0.0)	2 (4.0)	1 (0.8)	2 (1.6)	3 (9.1)
Cronobacter sakazakii	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Enterobacter (non-*cloacae* complex)	9 (2.6)	0 (0.0)	1 (10.0)	2 (4.0)	5 (4.0)	1 (0.8)	0 (0.0)
Enterobacter cloacae complex	23 (6.6)	3 (42.9)	1 (10.0)	6 (12.0)	5 (4.0)	8 (6.4)	0 (0.0)
Escherichia coli	132 (37.8)	2 (28.6)	2 (20.0)	16 (32.0)	41 (33.1)	55 (44.0)	16 (48.5)
Fusobacterium necrophorum	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Fusobacterium nucleatum	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Haemophilus influenzae	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 (%)
Klebsiella oxytoca	12 (3.4)	0 (0.0)	0 (0.0)	3 (6.0)	8 (6.5)	1 (0.8)	0 (0.0)
Klebsiella pneumoniae group	59 (16.9)	1 (14.3)	1 (10.0)	10 (20.0)	26 (21.0)	17 (13.6)	4 (12.1)
Morganella morganii	3 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.6)	1 (0.8)	0 (0.0)
Neisseria meningitidis	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Proteus	22 (6.3)	0 (0.0)	0 (0.0)	0 (0.0)	6 (4.8)	13 (10.4)	3 (9.1)
Proteus mirabilis	22 (6.3)	0 (0.0)	0 (0.0)	0 (0.0)	6 (4.8)	13 (10.4)	3 (9.1)
Pseudomonas aeruginosa	28 (8.0)	0 (0.0)	2 (20.0)	3 (6.0)	12 (9.7)	10 (8.0)	1 (3.0)
Salmonella	2 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	1 (0.8)	0 (0.0)
Serratia	10 (2.9)	0 (0.0)	1 (10.0)	0 (0.0)	5 (4.0)	4 (3.2)	0 (0.0)
Serratia marcescens	9 (2.6)	0 (0.0)	1 (10.0)	0 (0.0)	4 (3.2)	4 (3.2)	0 (0.0)
Stenotrophomonas maltophilia	3 (0.9)	0 (0.0)	0 (0.0)	3 (6.0)	0 (0.0)	0 (0.0)	0 (0.0)
Pan *Candida*	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 (%)
Acinetobacter baumannii	4 (1.1)	3 (3.4)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Bacteroides fragilis	11 (3.2)	2 (2.3)	3 (13.0)	3 (3.1)	2 (3.4)	1 (2.2)	0 (0.0)	0 (0.0)
Citrobacter	8 (2.3)	2 (2.3)	0 (0.0)	3 (3.1)	1 (1.7)	1 (2.2)	1 (3.6)	0 (0.0)
Cronobacter sakazakii	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Enterobacter (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)
Enterobacter cloacae 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)
Escherichia coli	132 (37.8)	30 (34.1)	8 (34.8)	37 (37.8)	25 (43.1)	17 (37.0)	12 (42.9)	3 (37.5)
Fusobacterium necrophorum	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Fusobacterium nucleatum	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Haemophilus influenzae	7 (2.0)	1 (1.1)	0 (0.0)	2 (2.0)	2 (3.4)	1 (2.2)	1 (3.6)	0 (0.0)
Klebsiella oxytoca	12 (3.4)	5 (5.7)	0 (0.0)	3 (3.1)	1 (1.7)	2 (4.3)	1 (3.6)	0 (0.0)
Klebsiella pneumoniae 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)
Morganella morganii	3 (0.9)	0 (0.0)	1 (4.3)	2 (2.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Neisseria meningitidis	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Proteus	22 (6.3)	9 (10.2)	0 (0.0)	5 (5.1)	5 (8.6)	2 (4.3)	1 (3.6)	0 (0.0)
Proteus mirabilis	22 (6.3)	9 (10.2)	0 (0.0)	5 (5.1)	5 (8.6)	2 (4.3)	1 (3.6)	0 (0.0)
Pseudomonas aeruginosa	28 (8.0)	5 (5.7)	2 (8.7)	10 (10.2)	8 (13.8)	2 (4.3)	1 (3.6)	0 (0.0)
Salmonella	2 (0.6)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.2)	0 (0.0)	0 (0.0)
Serratia	10 (2.9)	1 (1.1)	2 (8.7)	1 (1.0)	3 (5.2)	3 (6.5)	0 (0.0)	0 (0.0)
Serratia marcescens	9 (2.6)	1 (1.1)	2 (8.7)	1 (1.0)	3 (5.2)	2 (4.3)	0 (0.0)	0 (0.0)
Stenotrophomonas maltophilia	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 *Candida*	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
Acinetobacter baumannii	Standard laboratory procedures for organism ID. PCR/sequencing to confirm *Acinetobacter baumannii* or different *Acinetobacter* species not included in this panel.
Bacteroides fragilis	Standard laboratory procedures for organism ID.
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	

Target	Comparator Method
Serratia marcescens	
Stenotrophomonas maltophilia	
Pan Gram-Positive	
Pan *Candida*	Standard laboratory procedures for organism ID. PCR/sequencing to confirm *C. parapsilosis* or identify *C. metapsilosis, C. orthopsilosis.*
CTX-M, IMP, KPC, NDM, OXA, VIM	qPCR/sequencing in samples with associated organism detected by comparator method. See **Table 7** 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 (%)**
Sex								
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)
Age								
<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 (%)
Sex											
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)
Age											
<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)
Acinetobacter baumannii	Prospective (Fresh)	0/0	---	167/167	100 (97.8-100)
	Prospective (Frozen)	4/4	100 (51.0-100)	178/178	100 (97.9-100)
	Prospective (All)	**4/4**	**100 (51.0-100)**	**345/345**	**100 (98.9-100)**
	Retrospective	15/15	100 (79.6-100)	560/561	99.8 (99.0-100)
	Prospective / Retrospective	**19/19**	**100 (83.2-100)**	**905/906[A]**	**99.9 (99.4-100)**
	Contrived	55/55	100 (93.5-100)	722/722	100 (99.5-100)
	Overall	**74/74**	**100 (95.1-100)**	**1627/1628**	**99.9 (99.7-100)**

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)
Bacteroides fragilis	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)
	Prospective (All)	**11/11**	**100 (74.1-100)**	**338/338**	**100 (98.9-100)**
	Retrospective	14/17	82.4 (59.0-93.8)	558/560	99.6 (98.7-99.9)
	Prospective / Retrospective	**25/28[A]**	**89.3 (72.8-96.3)**	**896/898[B]**	**99.8 (99.2-99.9)**
	Contrived	40/40	100 (91.2-100)	737/737	100 (99.5-100)
	Overall	**65/68**	**95.6 (87.8-98.5)**	**1633/1635**	**99.9 (99.6-100)**

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)
Citrobacter	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)
	Prospective (All)	**5/5**	**100 (56.6-100)**	**341/344**	**99.1 (97.5-99.7)**
	Retrospective	20/21	95.2 (77.3-99.2)	555/556	99.8 (99.0-100)
	Prospective / Retrospective	**25/26**	**96.2 (81.1-99.3)**	**896/900[A]**	**99.6 (98.9-99.8)**
	Contrived	43/43	100 (91.8-100)	734/734	100 (99.5-100)
	Overall	**68/69**	**98.6 (92.2-99.7)**	**1630/1634**	**99.8 (99.4-99.9)**

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)
Cronobacter sakazakii	Prospective (Fresh)	0/0	---	167/167	100 (97.8-100)
	Prospective (Frozen)	0/0	---	182/182	100 (97.9-100)
	Prospective (All)	**0/0**	**---**	**349/349**	**100 (98.9-100)**
	Retrospective	1/1	100 (20.7-100)	576/576	100 (99.3-100)
	Prospective / Retrospective	**1/1**	**100 (20.7-100)**	**925/925**	**100 (99.6-100)**
	Contrived	45/45	100 (92.1-100)	732/732	100 (99.5-100)
	Overall	**46/46**	**100 (92.3-100)**	**1657/1657**	**100 (99.8-100)**

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)
Enterobacter cloacae 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)
	Prospective (All)	**19/19**	**100 (83.2-100)**	**326/330**	**98.8 (96.9-99.5)**
	Retrospective	47/50	94.0 (83.8-97.9)	526/527	99.8 (98.9-100)
	Prospective / Retrospective	**66/69[A]**	**95.7 (88.0-98.5)**	**852/857[B]**	**99.4 (98.6-99.8)**
	Contrived	35/37[C]	94.6 (82.3-98.5)	739/740	99.9 (99.2-100)
	Overall	**101/106**	**95.3 (89.4-98.0)**	**1591/1597**	**99.6 (99.2-99.8)**

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)
Enterobacter -non-*cloacae* 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)
	Prospective (All)	**8/10**	**80.0 (49.0-94.3)**	**338/339**	**99.7 (98.3-99.9)**
	Retrospective	12/12	100 (75.8-100)	565/565	100 (99.3-100)
	Prospective / Retrospective	**20/22[A]**	**90.9 (72.2-97.5)**	**903/904[B]**	**99.9 (99.4-100)**
	Contrived	36/36	100 (90.4-100)	741/741	100 (99.5-100)
	Overall	**56/58**	**96.6 (88.3-99.0)**	**1644/1645**	**99.9 (99.7-100)**

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)
Escherichia coli	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)
	Prospective (All)	**131/133**	**98.5 (94.7-99.6)**	**215/216**	**99.5 (97.4-99.9)**
	Retrospective	132/140	94.3 (89.1-97.1)	435/437	99.5 (98.3-99.9)
	Prospective / Retrospective	**263/273**	**96.3 (93.4-98.0)**	**650/653[A]**	**99.5 (98.7-99.8)**
	Contrived	52/52	100 (93.1-100)	725/725	100 (99.5-100)
	Overall	**315/325**	**96.9 (94.4-98.3)**	**1375/1378**	**99.8 (99.4-99.9)**

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)
Fusobacterium necrophorum	Prospective (Fresh)	0/0	---	167/167	100 (97.8-100)
	Prospective (Frozen)	0/0	---	182/182	100 (97.9-100)
	Prospective (All)	**0/0**	**---**	**349/349**	**100 (98.9-100)**
	Retrospective	1/1	100 (20.7-100)	576/576	100 (99.3-100)
	Prospective / Retrospective	**1/1**	**100 (20.7-100)**	**925/925**	**100 (99.6-100)**
	Contrived	47/48	97.9 (89.1-99.6)	729/729	100 (99.5-100)
	Overall	**48/49**	**98.0 (89.3-99.6)**	**1654/1654**	**100 (99.8-100)**

Table 23: Clinical Performance for *Fusobacterium nucleatum*

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

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)
Haemophilus influenzae	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)
	Prospective (All)	**7/7**	**100 (64.6-100)**	**342/342**	**100 (98.9-100)**
	Retrospective	7/7	100 (64.6-100)	570/570	100 (99.3-100)
	Prospective / Retrospective	**14/14**	**100 (78.5-100)**	**912/912**	**100 (99.6-100)**
	Contrived	41/41	100 (91.4-100)	736/736	100 (99.5-100)
	Overall	**55/55**	**100 (93.5-100)**	**1648/1648**	**100 (99.8-100)**

Table 25: Clinical Performance for *Klebsiella oxytoca*

Target	Sample Type	Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
Klebsiella oxytoca	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)
	Prospective (All)	**11/13**	**84.6 (57.8-95.7)**	**335/336**	**99.7 (98.3-99.9)**
	Retrospective	29/34	85.3 (69.9-93.6)	541/543	99.6 (98.7-99.9)
	Prospective / Retrospective	**40/47[A]**	**85.1 (72.3-92.6)**	**876/879[B]**	**99.7 (99.0-99.9)**
	Contrived	20/20	100 (83.9-100)	757/757	100 (99.5-100)
	Overall	**60/67**	**89.6 (80.0-94.8)**	**1633/1636**	**99.8 (99.5-99.9)**

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)
Klebsiella pneumoniae 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)
	Prospective (All)	**58/61**	**95.1 (86.5-98.3)**	**287/288**	**99.7 (98.1-99.9)**
	Retrospective	106/108	98.1 (93.5-99.5)	466/469	99.4 (98.1-99.8)
	Prospective / Retrospective	**164/169[A]**	**97.0 (93.3-98.7)**	**753/757[B]**	**99.5 (98.6-99.8)**
	Contrived	72/72	100 (94.9-100)	705/705	100 (99.5-100)
	Overall	**236/241**	**97.9 (95.2-99.1)**	**1458/1462**	**99.7 (99.3-99.9)**

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)
Morganella morganii	Prospective (Fresh)	3/3	100 (43.9-100)	164/164	100 (97.7-100)
	Prospective (Frozen)	0/0	---	182/182	100 (97.9-100)
	Prospective (All)	**3/3**	**100 (43.9-100)**	**346/346**	**100 (98.9-100)**
	Retrospective	10/10	100 (72.2-100)	566/567	99.8 (99.0-100)
	Prospective / Retrospective	**13/13**	**100 (77.2-100)**	**912/913[A]**	**99.9 (99.4-100)**
	Contrived	49/49	100 (92.7-100)	728/728	100 (99.5-100)
	Overall	**62/62**	**100 (94.2-100)**	**1640/1641**	**99.9 (99.7-100)**

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)
Neisseria meningitidis	Prospective (Fresh)	0/0	---	167/167	100 (97.8-100)
	Prospective (Frozen)	0/0	---	182/182	100 (97.9-100)
	Prospective (All)	**0/0**	**---**	**349/349**	**100 (98.9-100)**
	Retrospective	0/0	---	576/577	99.8 (99.0-100)
	Prospective / Retrospective	**0/0**	**---**	**925/926[A]**	**99.9 (99.4-100)**
	Contrived	44/44	100 (92.0-100)	733/733	100 (99.5-100)
	Overall	**44/44**	**100 (92.0-100)**	**1658/1659**	**99.9(99.7-100)**

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)
Proteus	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)
	Prospective (All)	**22/23**	**95.7 (79.0-99.2)**	**326/326**	**100 (98.8-100)**
	Retrospective	54/55	98.2 (90.4-99.7)	522/522	100 (99.3-100)
	Prospective / Retrospective	**76/78**	**97.4 (91.1-99.3)**	**848/848**	**100 (99.5-100)**
	Contrived	9/9	100 (70.1-100)	768/768	100 (99.5-100)
	Overall	**85/87**	**97.7 (92.0-99.4)**	**1616/1616**	**100 (99.8-100)**

Table 30: Clinical Performance for *Proteus mirabilis*

Target	Sample Type	Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
Proteus mirabilis	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)
	Prospective (All)	**22/23**	**95.7 (79.0-99.2)**	**326/326**	**100 (98.8-100)**
	Retrospective	50/51	98.0 (89.7-99.7)	526/526	100 (99.3-100)
	Prospective / Retrospective	**72/74**	**97.3 (90.7-99.3)**	**852/852**	**100 (99.6-100)**
	Contrived	9/9	100 (70.1-100)	768/768	100 (99.5-100)
	Overall	**81/83**	**97.6 (91.6-99.3)**	**1620/1620**	**100 (99.8-100)**

Table 31: Clinical Performance for *Pseudomonas aeruginosa*

Target	Sample Type	Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
Pseudomonas aeruginosa	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)
	Prospective (All)	**27/28**	**96.4 (82.3-99.4)**	**320/321**	**99.7 (98.3-99.9)**
	Retrospective	56/60	93.3 (84.1-97.4)	514/517	99.4 (98.3-99.8)
	Prospective / Retrospective	**83/88**	**94.3 (87.4-97.5)**	**834/838[A]**	**99.5 (98.8-99.8)**
	Contrived	32/32	100 (89.3-100)	745/745	100 (99.5-100)
	Overall	**115/120**	**95.8 (90.6-98.2)**	**1579/1583**	**99.7 (99.4-99.9)**

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)
Salmonella	Prospective (Fresh)	2/2	100 (34.2-100)	165/165	100 (97.7-100)
	Prospective (Frozen)	0/0	---	182/182	100 (97.9-100)
	Prospective (All)	**2/2**	**100 (34.2-100)**	**347/347**	**100 (98.9-100)**
	Retrospective	18/19	94.7 (75.4-99.1)	558/558	100 (99.3-100)
	Prospective / Retrospective	**20/21[A]**	**95.2 (77.3-99.2)**	**905/905**	**100 (99.6-100)**
	Contrived	34/35	97.1 (85.5-99.5)	742/742	100 (99.5-100)
	Overall	**54/56**	**96.4 (87.9-99.0)**	**1647/1647**	**100 (99.8-100)**

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)
Serratia	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)
	Prospective (All)	**10/10**	**100 (72.2-100)**	**339/339**	**100 (98.9-100)**
	Retrospective	34/34	100 (89.8-100)	542/543	99.8 (99.0-100)
	Prospective / Retrospective	**44/44**	**100 (92.0-100)**	**881/882[A]**	**99.9 (99.4-100)**
	Contrived	36/36	100 (90.4-100)	741/741	100 (99.5-100)
	Overall	**80/80**	**100 (95.4-100)**	**1622/1623**	**99.9 (99.7-100)**

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)
Serratia marcescens	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)
	Prospective (All)	**9/9**	**100 (70.1-100)**	**340/340**	**100 (98.9-100)**
	Retrospective	34/34	100 (89.8-100)	542/543	99.8 (99.0-100)
	Prospective / Retrospective	**43/43**	**100 (91.8-100)**	**882/883[A]**	**99.9 (99.4-100)**
	Contrived	19/19	100 (83.2-100)	758/758	100 (99.5-100)
	Overall	**62/62**	**100 (94.2-100)**	**1640/1641**	**99.9 (99.7-100)**

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)
Stenotrophomonas maltophilia	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)
	Prospective (All)	**3/4**	**75.0 (30.1-95.4)**	**345/345**	**100 (98.9-100)**
	Retrospective	8/10	80.0 (49.0-94.3)	566/567	99.8 (99.0-100)
	Prospective / Retrospective	**11/14**	**78.6 (52.4-92.4)**	**911/912[A]**	**99.9 (99.4-100)**
	Contrived	36/36	100 (90.4-100)	741/741	100 (99.5-100)
	Overall	**47/50**	**94.0 (83.8-97.9)**	**1652/1653**	**99.9 (99.7-100)**

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)
	Prospective (All)	**22/29**	**75.9 (57.9-87.8)**	**271/271**	**100 (98.6-100)**
	Retrospective	52/56	92.9 (83.0-97.2)	483/483	100 (99.2-100)
	Prospective / Retrospective	**74/85[A]**	**87.1 (78.3-92.6)**	**754/754**	**100 (99.5-100)**
	Contrived	75/75	100 (95.1-100)	437/437	100 (99.1-100)
	Overall	**149/160**	**93.1 (88.1-96.1)**	**1191/1191**	**100 (99.7-100)**

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)
	Prospective (All)	**0/0**	**---**	**297/297**	**100 (98.7-100)**
	Retrospective	0/0	---	532/532	100 (99.3-100)
	Prospective / Retrospective	**0/0**	**---**	**829/829**	**100 (99.5-100)**
	Contrived	40/40	100 (91.2-100)	436/436	100 (99.1-100)
	Overall	**40/40**	**100 (91.2-100)**	**1265/1265**	**100 (99.7-100)**

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)
	Prospective (All)	**3/3**	**100 (43.9-100)**	**294/294**	**100 (98.7-100)**
	Retrospective	4/5	80.0 (37.6-96.4)	527/528	99.8 (98.9-100)
	Prospective / Retrospective	**7/8**	**87.5 (52.9-97.8)**	**821/822**	**99.9 (99.3-100)**
	Contrived	44/44	100 (92.0-100)	477/477	100 (99.2-100)
	Overall	**51/52**	**98.1 (89.9-99.7)**	**1298/1299**	**99.9 (99.6-100)**

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)
	Prospective (All)	**0/0**	**---**	**297/297**	**100 (98.7-100)**
	Retrospective	0/0	---	532/532	100 (99.3-100)
	Prospective / Retrospective	**0/0**	**---**	**829/829**	**100 (99.5-100)**
	Contrived	54/54	100 (93.4-100)	422/422	100 (99.1-100)
	Overall	**54/54**	**100 (93.4-100)**	**1251/1251**	**100 (99.7-100)**

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)
	Prospective (All)	**1/2**	**50.0 (9.5-90.5)**	**295/295**	**100 (98.7-100)**
	Retrospective	9/11	81.8 (52.3-94.9)	519/521	99.6 (98.6-99.9)
	Prospective / Retrospective	**10/13[A]**	**76.9 (49.7-91.8)**	**814/816**	**99.8 (99.1-99.9)**
	Contrived	37/37	100 (90.6-100)	439/439	100 (99.1-100)
	Overall	**47/50**	**94.0 (83.8-97.9)**	**1253/1255**	**99.8 (99.4-100)**

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)
	Prospective (All)	**0/0**	**---**	**297/297**	**100 (98.7-100)**
	Retrospective	0/0	---	532/532	100 (99.3-100)
	Prospective / Retrospective	**0/0**	**---**	**829/829**	**100 (99.5-100)**
	Contrived	42/42	100 (91.6-100)	434/434	100 (99.1-100)
	Overall	**42/42**	**100 (91.6-100)**	**1263/1263**	**100 (99.7-100)**

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 *Candida*	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)
	Prospective (All)	**1/1**	**100 (20.7-100)**	**347/348[A]**	**99.7 (98.4-99.9)**
	Retrospective	4/7[B]	57.1 (25.0-84.2)	569/570[C]	99.8 (99.0-100)
	Retrospective (Non-Intended Use)	99/102[D]	97.1 (91.7-99.0)	638/639[E]	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)
	Prospective (All)	**17/23[F]**	**73.9 (53.5-87.5)**	**319/326[G]**	**97.9 (95.6-99.0)**
	Retrospective	44/55[H]	80.0 (67.6-88.4)	512/522[I]	98.1 (96.5-99.0)
	Retrospective (Non-Intended Use)	567/571	99.3 (98.2-99.7)	165/170[J]	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
Acinetobacter baumannii	*Acinetobacter baumannii*	ATCC19606	2
		ATCCBAA-2093	4
		ATCCBAA-747	5
		NCIMB12457	2

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

Target	Organism	Strain	Independent Contrived Samples Tested
	***Enterobacter cloacae* complex Total**		**37**
*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
	***Enterobacter (*non-*cloacae* complex) Total**		**36**
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
	***Escherichia coli* Total**		**52**
Fusobacterium necrophorum	*Fusobacterium necrophorum* subsp. *funduliforme*	ATCC51357	24
	Fusobacterium necrophorum subsp. *necrophorum*	ATCC27852	24
	***Fusobacterium necrophorum* Total**		**48**
Fusobacterium nucleatum	*Fusobacterium nucleatum*	ATCC23726	8
		ATCC25586	20
		ATCC31647	19
	***Fusobacterium nucleatum* Total**		**47**
Haemophilus influenzae	*Haemophilus influenzae*	ATCC10211	9
		ATCC43065	6
		ATCC49144	9
		NCTC12699	9
		NCTC8468	8
	***Haemophilus influenzae* Total**		**41**
Klebsiella oxytoca	*Klebsiella oxytoca*	ATCC43086	4
		ATCC43165	4
		ATCC43863	2
		ATCC49131	4
		ATCC51817	3
		ATCC700324	3
	***Klebsiella oxytoca* Total**		**20**
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
		CDC#0080	6
	Klebsiella pneumoniae, KPC	CDC#0112	1
		CDC#0113	1
		CDC#0115	4
		CDC#0117	4
		CDC#0120	4
		CDC#0125	4
		CDC#0129	4
	Klebsiella pneumoniae, VIM	LMC_DR00015	6
		NCTC13439	5
		NCTC13440	5
	***Klebsiella pneumoniae* group Total**		**72**
Morganella morganii	*Morganella morganii*	148-200	8
		148-204	8
		148-205	8
		148-206	9
		148-209	7
	Morganella morganii, CTX-M1, NDM	CDC#0057	5
	Morganella morganii, KPC	CDC#0133	4
	***Morganella morganii* Total**		**49**
Neisseria meningitidis	*Neisseria meningitidis*	ATCC13077	9
		ATCC13090	8
		ATCC13102	8
		ATCC13113	3
		ATCC35561	10
		NCTC10026	6
	***Neisseria meningitidis* Total**		**44**
Proteus mirabilis	*Proteus mirabilis*, KPC	CDC#0155	4
	Proteus mirabilis, NDM	CDC#0159	5
	***Proteus mirabilis* Total**		**9**
Pseudomonas aeruginosa	*Pseudomonas aeruginosa*, IMP	CDC#0092	5
		CDC#0103	8
	Pseudomonas aeruginosa, KPC	CDC#0090	1
	Pseudomonas aeruginosa, VIM	CDC#0054	5
		CDC#0100	4
		CDC#0108	4
		NCTC13437	5
	***Pseudomonas aeruginosa* Total**		**32**
Salmonella	*Salmonella* 4,5,12:I:-	FSLS5-0580	2
	Salmonella Heidelberg	ATCC8326	2
	Salmonella Infantis	ATCCBAA-1675	2
	Salmonella Javiana	ATCC10721	1
	Salmonella Montevideo	ATCC8387	8
	Salmonella Muenchen	ATCC8388	1
	Salmonella Newport	ATCC6962	6
	Salmonella Typhimurium	ATCC13311	7
	Salmonella enterica subspecies *enterica* Enteritidis (Group D1)	ATCCBAA-708	6
	***Salmonella* Total**		**35**
Serratia	*Serratia ficaria*	ATCC33105	4

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

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)
Citrobacter	**5/5**	**100 (56.6-100)**	**20/21**	**95.2 (77.3-99.2)**	**43/43**	**100 (91.8-100)**	**68/69**	**98.6 (92.2-99.7)**
Citrobacter braakii			2/3	66.7 (20.8-93.9)	8/8	100 (67.6-100)	10/11	90.9 (62.3-98.4)
Citrobacter freundii	4/4	100 (51.0-100)	13/13	100 (77.2-100)	27/27	100 (87.5-100)	44/44	100 (92.0-100)
Citrobacter koseri	1/1	100 (20.7-100)	4/4	100 (51.0-100)	4/4	100 (51.0-100)	9/9	100 (70.1-100)
Citrobacter youngae			1/1	100 (20.7-100)	4/4	100 (51.0-100)	5/5	100 (56.6-100)
***Enterobacter* (non-*cloacae* complex)**	**8/10**	**80.0 (49.0-94.3)**	**12/12**	**100 (75.8-100)**	**36/36**	**100 (90.4-100)**	**56/58**	**96.6 (88.3-99.0)**
Enterobacter aerogenes	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)
Enterobacter amnigenus					10/10	100 (72.2-100)	10/10	100 (72.2-100)
Enterobacter gergoviae	1/1	100 (20.7-100)					1/1	100 (20.7-100)
***Enterobacter cloacae* complex**	**19/19**	**100 (83.2-100)**	**47/50**	**94.0 (83.8-97.9)**	**35/37**	**94.6 (82.3-98.5)**	**101/106**	**95.3 (89.4-98.0)**
Enterobacter asburiae					6/8	75.0 (40.9-92.9)	6/8	75.0 (40.9-92.9)
Enterobacter cloacae	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)
Enterobacter hormaechei			1/1	100 (20.7-100)	1/1	100 (20.7-100)	2/2	100 (34.2-100)
Proteus	**22/23**	**95.7 (79.0-99.2)**	**54/55**	**98.2 (90.4-99.7)**	**9/9**	**100 (70.1-100)**	**85/87**	**97.7 (92.0-99.4)**
Proteus mirabilis	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)
Proteus vulgaris			5/5	100 (56.6-100)			5/5	100 (56.6-100)
Salmonella	**2/2**	**100 (34.2-100)**	**18/19**	**94.7 (75.4-99.1)**	**34/35**	**97.1 (85.5-99.5)**	**54/56**	**96.4 (87.9-99.0)**
Salmonella	2/2	100 (34.2-100)	15/15	100 (79.6-100)			17/17	100 (81.6-100)
Salmonella 4,5,12:i:-					2/2	100 (34.2-100)	2/2	100 (34.2-100)
Salmonella Heidelberg					2/2	100 (34.2-100)	2/2	100 (34.2-100)
Salmonella Infantis					2/2	100 (34.2-100)	2/2	100 (34.2-100)
Salmonella Javiana					1/1	100 (20.7-100)	1/1	100 (20.7-100)
Salmonella Montevideo					7/8	87.5 (52.9-97.8)	7/8	87.5 (52.9-97.8)
Salmonella Muenchen					1/1	100 (20.7-100)	1/1	100 (20.7-100)
Salmonella Newport					6/6	100 (61.0-100)	6/6	100 (61.0-100)
Salmonella Typhimurium					7/7	100 (64.6-100)	7/7	100 (64.6-100)
Salmonella choleraesuis subsp. *arizonae*			0/1	0.0 (0.0-79.3)			0/1	0.0 (0.0-79.3)
Salmonella enterica subsp. *enterica* Enteritidis (Group D1)					6/6	100 (61.0-100)	6/6	100 (61.0-100)
Salmonella enterica subsp. *enterica* serovar Typhimurium			1/1	100 (20.7-100)			1/1	100 (20.7-100)
Salmonella Typhi			2/2	100 (34.2-100)			2/2	100 (34.2-100)
Serratia	**10/10**	**100 (72.2-100)**	**34/34**	**100 (89.8-100)**	**36/36**	**100 (90.4-100)**	**80/80**	**100 (95.4-100)**
Serratia ficaria					4/4	100 (51.0-100)	4/4	100 (51.0-100)
Serratia grimesii					3/3	100 (43.9-100)	3/3	100 (43.9-100)
Serratia liquefaciens	1/1	100 (20.7-100)					1/1	100 (20.7-100)
Serratia marcescens	9/9	100 (70.1-100)	34/34	100 (89.8-100)	19/19	100 (83.2-100)	62/62	100 (94.2-100)
Serratia plymuthica					3/3	100 (43.9-100)	3/3	100 (43.9-100)
Serratia rubidaea					7/7	100 (64.6-100)	7/7	100 (64.6-100)
Pan *Candida*	**1/1**	**100 (20.7-100)**	**4/7**	**57.1 (25.0-84.2)**	**N/A**	**N/A**	**5/8**	**62.5 (30.6-86.3)**
Candida albicans	1/1	100 (20.7-100)	2/4	50.0 (15.0-85.0)			3/5	60.0 (23.1-88.2)
Candida glabrata			1/2	50.0 (9.5-90.5)			1/2	50.0 (9.5-90.5)
Candida krusei			1/1	100 (20.7-100)			1/1	100 (20.7-100)
Candida parapsilosis								
Pan Gram-Positive	**17/23**	**73.9 (53.5-87.5)**	44/55	**80.0 (67.6-88.4)**	**N/A**	**N/A**	**61/78**	**78.2 (67.8-85.9)**
Bacillus (unspeciated)	1/4	25.0 (4.6-69.9)					1/4	25.0 (4.6-69.9)
Enterococcus (unspeciated)			0/1	0.0 (0.0-79.3)			0/1	0.0 (0.0-79.3)
Enterococcus casseliflavus			0/1	0.0 (0.0-79.3)			0/1	0.0 (0.0-79.3)
Enterococcus faecalis	5/7	71.4 (35.9-91.8)	18/20	90.0 (69.9-97.2)			23/27	85.2 (67.5-94.1)
Enterococcus faecium	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)
Staphylococcus (unspeciated)	3/3	100 (43.9-100)	4/6	66.7 (30.0-90.3)			7/9	77.8 (45.3-93.7)
Staphylococcus aureus	2/2	100 (34.2-100)	5/6	83.3 (43.6-97.0)			7/8	87.5 (52.9-97.8)
Staphylococcus cohnii	1/1	100 (20.7-100)					1/1	100 (20.7-100)
Staphylococcus epidermidis	1/1	100 (20.7-100)	2/3	66.7 (20.8-93.9)			3/4	75.0 (30.1-95.4)
Staphylococcus haemolyticus	2/2	100 (34.2-100)					2/2	100 (34.2-100)
Staphylococcus hominis	1/1	100 (20.7-100)	3/3	100 (43.9-100)			4/4	100 (51.0-100)
Streptococcus	0/1	0.0 (0.0-79.3)					0/1	0.0 (0.0-79.3)
Streptococcus - viridans group	1/1	100 (20.7-100)	0/1	0.0 (0.0-79.3)			1/2	50.0 (9.5-90.5)
Streptococcus anginosus group	1/1	100 (20.7-100)	4/5	80.0 (37.6-96.4)			5/6	83.3 (43.6-97.0)
Streptococcus infantarius			1/1	100 (20.7-100)			1/1	100 (20.7-100)
Streptococcus mitis group			1/1	100 (20.7-100)			1/1	100 (20.7-100)
Streptococcus oralis			1/1	100 (20.7-100)			1/1	100 (20.7-100)
Streptococcus pneumoniae			1/1	100 (20.7-100)			1/1	100 (20.7-100)
Streptococcus salivarius			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)
Pan *Candida*	99/102	97.1 (91.7-99.0)
Candida albicans	47/48	97.9 (89.1-99.6)
Candida glabrata	37/38	97.4 (86.5-99.5)
Candida krusei	3/3	100 (43.9-100)
Candida parapsilosis	15/16	93.8 (71.7-98.9)
Pan Gram-Positive	567/571	99.3 (98.2-99.7)
Bacillus (unspeciated)	4/4	100 (51.0-100)
Bacillus cereus	4/5	80.0 (37.6-96.4)
Bacillus cereus group - not anthracis	1/1	100 (20.7-100)
Enterococcus	1/1	100 (20.7-100)
Enterococcus faecalis	34/34	100 (89.8-100)
Enterococcus faecium	14/14	100 (78.5-100)
Coagulase-negative *Staphylococci* (CoNS)	14/14	100 (78.5-100)
Staphylococcus (unspeciated)	86/86	100 (95.7-100)
Staphylococcus aureus	173/174	99.4 (96.8-99.9)
Staphylococcus auricularis	3/3	100 (43.9-100)

Target Species Detected by Comparator Method	Retrospective (Non-Intended Use) Samples	
	Sensitivity/PPA	
	TP/TP+FN	% (95% CI)
Staphylococcus capitis	7/7	100 (64.6-100)
Staphylococcus cohnii	1/1	100 (20.7-100)
Staphylococcus epidermidis	86/87	98.9 (93.8-99.8)
Staphylococcus haemolyticus	6/6	100 (61.0-100)
Staphylococcus hominis	19/19	100 (83.2-100)
Staphylococcus hominis ssp *hominis*	21/21	100 (84.5-100)
Staphylococcus intermedius	1/1	100 (20.7-100)
Staphylococcus lugdunensis	1/1	100 (20.7-100)
Staphylococcus saccharolyticus	1/1	100 (20.7-100)
Staphylococcus saprophyticus	1/1	100 (20.7-100)
Staphylococcus sciuri	1/1	100 (20.7-100)
Staphylococcus simulans	2/2	100 (34.2-100)
Staphylococcus warneri	4/4	100 (51.0-100)
Alpha Hemolytic *Streptococcus*	1/1	100 (20.7-100)
Beta Hemolytic *Streptococci*, Group G	1/1	100 (20.7-100)
Gamma Hemolytic *Streptococcus*	1/1	100 (20.7-100)
Streptococcus (unspeciated)	9/9	100 (70.1-100)
Streptococcus - viridans group	17/17	100 (81.6-100)
Streptococcus agalactiae	21/21	100 (84.5-100)
Streptococcus anginosus	2/2	100 (34.2-100)
Streptococcus bovis	2/2	100 (34.2-100)
Streptococcus constellatus ssp *constellatus*	1/1	100 (20.7-100)
Streptococcus dysgalactiae (Group G)	4/4	100 (51.0-100)
Streptococcus gordonii	1/1	100 (20.7-100)
Streptococcus intermedius	1/1	100 (20.7-100)
Streptococcus mitis	11/12	91.7 (64.6-98.5)
Streptococcus mitis group	2/2	100 (34.2-100)
Streptococcus pneumoniae	22/22	100 (85.1-100)
Streptococcus pyogenes	9/9	100 (70.1-100)
Streptococcus salivarius	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)
Acinetobacter baumannii	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)
	Combined	**0/0**	**---**	**74/74**	**100 (95.1-100)**
Citrobacter	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)
	Combined	**7/7**	**100 (64.6-100)**	**62/62**	**100 (94.2-100)**
Enterobacter (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)
	Combined	**0/0**	**---**	**58/58**	**100 (93.8-100)**
Enterobacter cloacae 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)
	Combined	**22/22**	**100 (85.1-100)**	**84/84**	**100 (95.6-100)**
Escherichia coli	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)
	Combined	**73/77**	**94.8 (87.4-98.0)**	**248/248**	**100 (98.5-100)**
Klebsiella oxytoca	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)
	Combined	**0/1**	**0.0 (0.0-79.3)**	**66/66**	**100 (94.5-100)**
Klebsiella pneumoniae 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)
	Combined	**39/40**	**97.5 (87.1-99.6)**	**201/201**	**100 (98.1-100)**
Morganella morganii	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)
	Combined	**5/5**	**100 (56.6-100)**	**57/57**	**100 (93.7-100)**
Proteus	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)
	Combined	**4/8**	**50.0 (21.5-78.5)**	**79/79**	**100 (95.4-100)**
Proteus mirabilis	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)
	Combined	**4/8**	**50.0 (21.5-78.5)**	**75/75**	**100 (95.1-100)**
Pseudomonas aeruginosa	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)
	Combined	**0/1**	**0.0 (0.0-79.3)**	**119/119**	**100 (96.9-100)**

Species Detected by Comparator Method		Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
Salmonella	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)
	Combined	**1/1**	**100 (20.7-100)**	**55/55**	**100 (93.5-100)**
Serratia	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)
	Combined	**0/0**	**---**	**80/80**	**100 (95.4-100)**
Serratia marcescens	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)
	Combined	**0/0**	**---**	**62/62**	**100 (94.2-100)**
Stenotrophomonas maltophilia	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)
	Combined	**0/0**	**---**	**50/50**	**100 (92.9-100)**

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

	Comparator Method			
BCID-GN	**Org+/ARG+**	**Org+/ARG-**	**Org-**	**Total**
Org+/ARG+	74	0	2	76
Org+/ARG-	8[A]	741	2	751
Org-	3[B]	13	83	99
Total	**85**	**754**	**87**	**926**

% 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)
Acinetobacter baumannii	0/0	---	74/74	100 (95.1-100)
Citrobacter	0/0	---	69/69	100 (94.7-100)
Enterobacter (non-*cloacae* complex)	5/5	100 (56.6-100)	53/53	100 (93.2-100)
Enterobacter cloacae complex	0/0	---	106/106	100 (96.5-100)
Escherichia coli	7/7	100 (64.6-100)	318/318	100 (98.8-100)
Klebsiella oxytoca	0/0	---	67/67	100 (94.6-100)
Klebsiella pneumoniae group	14/14	100 (78.5-100)	227/227	100 (98.3-100)
Morganella morganii	0/0	---	62/62	100 (94.2-100)
Proteus	0/0	---	87/87	100 (95.8-100)
Proteus mirabilis	0/0	---	83/83	100 (95.6-100)
Pseudomonas aeruginosa	13/13	100 (77.2-100)	107/107	100 (96.5-100)
Salmonella	0/0	---	56/56	100 (93.6-100)
Serratia	1/1	100 (20.7-100)	79/79	100 (95.4-100)
Serratia marcescens	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

	Comparator Method			
BCID-GN	**Org+/ARG+**	**Org+/ARG-**	**Org-**	**Total**
Org+/ARG+	0	0	0	0
Org+/ARG-	0	812	4	816
Org-	0	17	93	110
Total	**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)

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)
Acinetobacter baumannii	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)
	Combined	**0/0**	**---**	**74/74**	**100 (95.1-100)**
Citrobacter	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)
	Combined	**4/4**	**100 (51.0-100)**	**65/65**	**100 (94.4-100)**
Cronobacter sakazakii	Prospective	---	---	---	---
	Retrospective	0/0	---	1/1	100 (20.7-100)
	Contrived	0/0	---	45/45	100 (92.1-100)
	Combined	**0/0**	**---**	**46/46**	**100 (92.3-100)**
Enterobacter (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)
	Combined	**0/0**	**---**	**58/58**	**100 (93.8-100)**
Enterobacter cloacae 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)
	Combined	**3/4**	**75.0 (30.1-95.4)**	**102/102**	**100 (96.4-100)**
Escherichia coli	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)
	Combined	**7/7**	**100 (64.6-100)**	**318/318**	**100 (98.8-100)**
Klebsiella oxytoca	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)
	Combined	**0/0**	**---**	**67/67**	**100 (94.6-100)**
Klebsiella pneumoniae 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)
	Combined	**28/28**	**100 (87.9-100)**	**212/213**	**99.5 (97.4-99.9)**
Morganella morganii	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)
	Combined	**4/4**	**100 (51.0-100)**	**58/58**	**100 (93.8-100)**
Proteus	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)
	Combined	**4/4**	**100 (51.0-100)**	**83/83**	**100 (95.6-100)**
Proteus mirabilis	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)
	Combined	**4/4**	**100 (51.0-100)**	**79/79**	**100 (95.4-100)**
Pseudomonas aeruginosa	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)
	Combined	**1/1**	**100 (20.7-100)**	**119/119**	**100 (96.9-100)**
Salmonella	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)
	Combined	**0/0**	**---**	**56/56**	**100 (93.6-100)**
Serratia	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)
	Retrospective	0/0	---	34/34	100 (89.8-100)
	Contrived	0/0	---	36/36	100 (90.4-100)
	Combined	**0/0**	**---**	**80/80**	**100 (95.4-100)**
Serratia marcescens	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)
	Combined	**0/0**	**---**	**62/62**	**100 (94.2-100)**

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

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

% 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)
Acinetobacter baumannii	5/5	100 (56.6-100)	69/69	100 (94.7-100)
Citrobacter	0/0	---	69/69	100 (94.7-100)
Enterobacter (non-*cloacae* complex)	0/0	---	58/58	100 (93.8-100)
Enterobacter cloacae complex	13/13	100 (77.2-100)	93/93	100 (96.0-100)
Escherichia coli	23/23	100 (85.7-100)	302/302	100 (98.7-100)
Klebsiella oxytoca	0/0	---	67/67	100 (94.6-100)
Klebsiella pneumoniae group	3/3	100 (43.9-100)	238/238	100 (98.4-100)
Morganella morganii	5/5	100 (56.6-100)	57/57	100 (93.7-100)
Proteus	5/5	100 (56.6-100)	82/82	100 (95.5-100)
Proteus mirabilis	5/5	100 (56.6-100)	78/78	100 (95.3-100)
Pseudomonas aeruginosa	0/0	---	120/120	100 (96.9-100)
Salmonella	0/0	---	56/56	100 (93.6-100)
Serratia	0/0	---	80/80	100 (95.4-100)
Serratia marcescens	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

	Comparator Method			
BCID-GN	**Org+/ARG+**	**Org+/ARG-**	**Org-**	**Total**
Org+/ARG+	0	0	0	0
Org+/ARG-	0	812	4	816
Org-	0	17	93	110
Total	**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)

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)**
Acinetobacter baumannii	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)
	Combined	**21/21**	**100 (84.5-100)**	**53/53**	**100 (93.2-100)**
Citrobacter	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)
	Combined	**0/0**	**---**	**69/69**	**100 (94.7-100)**
Enterobacter (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)
	Combined	**12/12**	**100 (75.8-100)**	**46/46**	**100 (92.3-100)**
Enterobacter cloacae 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)
	Combined	**0/0**	**---**	**106/106**	**100 (96.5-100)**
Escherichia coli	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)
	Combined	**1/3**	**33.3 (6.1-79.2)**	**322/322**	**100 (98.8-100)**
Klebsiella oxytoca	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)
	Combined	**0/0**	**---**	**67/67**	**100 (94.6-100)**
Klebsiella pneumoniae 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)
	Combined	**12/13**	**92.3 (66.7-98.6)**	**228/228**	**100 (98.3-100)**
Morganella morganii	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)
	Combined	**0/0**	**---**	**62/62**	**100 (94.2-100)**
Proteus	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)
	Combined	**1/1**	**100 (20.7-100)**	**85/86**	**98.8 (93.7-99.8)**
Proteus mirabilis	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)
	Combined	**0/0**	**---**	**82/83**	**98.8 (93.5-99.8)**
Pseudomonas aeruginosa	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)
	Combined	**0/0**	**---**	**119/120**	**99.2 (95.4-99.9)**
Salmonella	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)
	Combined	**0/0**	**---**	**56/56**	**100 (93.6-100)**
Serratia	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)
	Combined	**0/0**	**---**	**80/80**	**100 (95.4-100)**
Serratia marcescens	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)
	Combined	**0/0**	**---**	**62/62**	**100 (94.2-100)**

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

	Comparator Method			
BCID-GN	**Org+/ARG+**	**Org+/ARG-**	**Org-**	**Total**
Org+/ARG+	10	2	0	12
Org+/ARG-	2[A]	798	4	804
Org-	1[B]	16	93	110
Total	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)**
Acinetobacter baumannii	0/0	---	74/74	100 (95.1-100)
Citrobacter	0/0	---	69/69	100 (94.7-100)
Enterobacter (non-*cloacae* complex)	0/0	---	58/58	100 (93.8-100)
Enterobacter cloacae complex	6/6	100 (61.0-100)	100/100	100 (96.3-100)
Escherichia coli	2/2	100 (34.2-100)	323/323	100 (98.8-100)
Klebsiella oxytoca	0/0	---	67/67	100 (94.6-100)
Klebsiella pneumoniae group	16/16	100 (80.6-100)	225/225	100 (98.3-100)
Morganella morganii	0/0	---	62/62	100 (94.2-100)
Proteus	0/0	---	87/87	100 (95.8-100)
Proteus mirabilis	0/0	---	83/83	100 (95.6-100)
Pseudomonas aeruginosa	18/18	100 (82.4-100)	102/102	100 (96.4-100)
Salmonella	0/0	---	56/56	100 (93.6-100)
Serratia	0/0	---	80/80	100 (95.4-100)
Serratia marcescens	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

	Comparator Method			
BCID-GN	**Org+/ARG+**	**Org+/ARG-**	**Org-**	**Total**
Org+/ARG+	0	0	0	0
Org+/ARG-	0	812	4	816
Org-	0	17	93	110
Total	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 x (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 x (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 (%)
A. baumannii	---	---	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%)
Citrobacter	---	---	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%)
Enterobacter	---	---	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%)
E. cloacae 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%)
E. coli	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%)
K. oxytoca	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%)
K. pneumoniae 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%)
M. morganii			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%)
Proteus	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%)
P. mirabilis	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%)
P. aeruginosa			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%)
Salmonella	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%)
Serratia			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%)
S. marcescens			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%)
S. maltophilia			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 CI	42/48 (87.5%) (75.3-94.1)	117/117 (100%) (96.8-100)	44/102 (43.1%) (33.9-52.8)	528/541 (97.6%) (95.9-98.6)	73/168 (43.5%) (36.2-51.0)	613/615 (99.7%) (98.8-99.9)	38/74 (51.4%) (40.2-62.4)	403/408 (98.8%) (97.2-99.5)	73/183 (39.9%) (33.1-47.1)	684/686 (99.7%) (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 x (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 x (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 (%)
A. baumannii	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%)
Citrobacter	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%)
C. sakazakii	---	---	0/0	1/1 (100%)	---	---	---	---	---	---	---	---
Enterobacter	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%)
E. cloacae 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%)
E. coli	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%)
K. oxytoca	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%)
K. pneumoniae 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%)
M. morganii	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%)
Proteus	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%)
P. mirabilis	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%)
P. aeruginosa	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%)
Salmonella	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%)
Serratia	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%)
S. marcescens	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 CI	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)[A,B]
Target 1	**Target 2**	**Target 3**	**Resistance Marker**		
A. baumannii	Pan Gram-Positive			2 (0)	
Citrobacter	*E. cloacae* complex	*K. oxytoca*		2 (2)	*Citrobacter* (2), *E. cloacae* complex (2)
Citrobacter	*K. oxytoca*	*K. pneumoniae* group		1 (1)	*Citrobacter* (1)
Citrobacter	*P. mirabilis*	Pan Gram-Positive		1 (1)	Pan Gram-Positive (1)
E. cloacae complex	*E. coli*	*K. pneumoniae* group		1 (0)	
E. cloacae complex	Pan *Candida*	Pan Gram-Positive		1 (0)	
E. cloacae complex	Pan Gram-Positive			2 (0)	
E. coli	*K. oxytoca*			2 (1)	*K. oxytoca* (1)
E. coli	*K. pneumoniae* group		CTX-M	1 (1)	*E. coli* (1)
E. coli	Pan Gram-Positive			2 (1)	Pan Gram-Positive (1)
Enterobacter	*K. pneumoniae* group			1 (1)	*Enterobacter* (1)
K. oxytoca	Pan Gram-Positive			1 (0)	
K. oxytoca	*S. marcescens*			1 (0)	
K. pneumoniae group	*P. mirabilis*			1 (0)	
K. pneumoniae group	Pan Gram-Positive			2 (0)	
K. pneumoniae group	Pan Gram-Positive		CTX-M, KPC	1 (1)	Pan Gram-Positive (1)
M. morganii	*P. mirabilis*			1 (0)	
P. aeruginosa	*P. mirabilis*	Pan Gram-Positive		1 (0)	
P. aeruginosa	Pan Gram-Positive			1 (0)	
P. mirabilis	Pan Gram-Positive			3 (2)	Pan Gram-Positive (2)
P. mirabilis	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)[A,B]
Target 1	**Target 2**	**Target 3**	**Resistance Marker**		
A. baumannii	*K. pneumoniae* group	Pan Gram-Positive	CTX-M, OXA	1 (1)	*A. baumannii* (1), *K. pneumoniae* group (1), Pan Gram-Positive (1)
A. baumannii	Pan Gram-Positive			2 (0)	
A. baumannii	Pan Gram-Positive		OXA	4 (1)	Pan Gram-Positive (1)
B. fragilis	*E. cloacae* complex	Pan Gram-Positive		1 (1)	*B. fragilis* (1)
B. fragilis	*E. coli*			2 (1)	*B. fragilis* (1)
B. fragilis	Pan Gram-Positive			1 (0)	
Citrobacter	*E. cloacae* complex			1 (1)	*E. cloacae* complex (1)
Citrobacter	*E. coli*			1 (0)	
Citrobacter	*K. oxytoca*			1 (1)	*Citrobacter* (1)
Citrobacter	*K. oxytoca*	*K. pneumoniae* group		1 (1)	*K. oxytoca* (1)
Citrobacter	*K. pneumoniae* group			1 (0)	
Citrobacter	*K. pneumoniae* group	Pan Gram-Positive	CTX-M	1 (0)	
Citrobacter	*M. morganii*	Pan Gram-Positive		1 (1)	*M. morganii* (1)
Citrobacter	Pan Gram-Positive			3 (2)	Pan Gram-Positive (2)
E. cloacae complex	*K. pneumoniae* group			1 (0)	
E. cloacae complex	*P. aeruginosa*	Pan Gram-Positive		1 (1)	*P. aeruginosa* (1)
E. cloacae complex	Pan *Candida*			1 (1)	Pan *Candida* (1)
E. cloacae complex	Pan Gram-Positive			2 (1)	Pan Gram-Positive (1)
E. coli	*K. oxytoca*			1 (0)	
E. coli	*K. oxytoca*	Pan Gram-Positive		1 (0)	
E. coli	*K. pneumoniae* group			2 (0)	
E. coli	*M. morganii*			1 (0)	
E. coli	*P. mirabilis*			3 (0)	
E. coli	*P. mirabilis*	Pan Gram-Positive		1 (0)	
E. coli	Pan Gram-Positive			8 (2)	Pan Gram-Positive (2)
E. coli	Pan Gram-Positive		CTX-M	1 (0)	
Enterobacter	Pan *Candida*			1 (0)	
Enterobacter	Pan Gram-Positive			1 (0)	
H. influenzae	*N. meningitidis*	*P. aeruginosa*		1 (1)	*N. meningitidis* (1), *P. aeruginosa* (1)
K. oxytoca	*K. pneumoniae* group			2 (1)	*K. pneumoniae* group (1)
K. oxytoca	Pan Gram-Positive			3 (2)	Pan Gram-Positive (2)
K. oxytoca	*S. marcescens*			1 (1)	*S. marcescens* (1)
K. pneumoniae group	Pan Gram-Positive			4 (1)	Pan Gram-Positive (1)
K. pneumoniae group	Pan Gram-Positive	*S. marcescens*		1 (1)	*K. pneumoniae* group (1)
K. pneumoniae group	*S. maltophilia*			1 (0)	
M. morganii	*P. aeruginosa*	Pan Gram-Positive		1 (1)	*P. aeruginosa* (1)
M. morganii	*P. mirabilis*			1 (0)	
M. morganii	Pan Gram-Positive	*Proteus*		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)[A,B]
Target 1	**Target 2**	**Target 3**	**Resistance Marker**		
P. aeruginosa	Pan Gram-Positive			1 (0)	
P. mirabilis	Pan Gram-Positive			5 (0)	
Pan *Candida*	Pan Gram-Positive			2 (0)	
Pan Gram-Positive	*S. maltophilia*			1 (0)	
Pan Gram-Positive	*S. marcescens*			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.
   i. In 1/1 false positive *A.baumannii* sample, *A. baumannii* was detected.
   ii. In 2/2 false positive *B. fragilis* samples, *B. fragilis* was detected.
   iii. In 1/1 false positive *Citrobacter* sample, *Citrobacter* was detected.
   iv. In the one false positive *E. cloacae* complex sample, PCR/sequencing was indeterminate.
   v. In 1/1 false positive K. oxytoca sample, K. oxytoca was detected.
   vi. In 3/3 false positive *K. pneumoniae* group samples, *K. pneumoniae* group was detected.
   vii. In 1/1 false positive sample, *M. morganii* was detected.
   viii. *N. meningitidis* was not detected in the 1 *N. meningitidis* false positive sample.
   ix. In 2/3 false positive *P. aeruginosa* samples, *P. aeruginosa* was detected. *P. aeruginosa* was not detected in the remaining sample.
   x. In 1/1 false positive pan *Candida* sample, Pan *Candida* was detected.
   xi. In 8/8 false positive Pan Gram-Positive samples, a Pan Gram-Positive organism was detected.
   xii. 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)[A]
Organism 1	**Organism 2**	**Organism 3**	**Organism 4**	**Resistance Marker**		
A. baumannii	*E. faecium*	*Staphylococcus*			1 (0)	
A. baumannii	*Staphylococcus*				1 (0)	
*Achromobacter xylosoxidans**	*E. cloacae*				1 (0)	
*Acinetobacter lwoffii**	*Staphylococcus hominis*				1 (0)	
*Acinetobacter pittii**	*S. aureus*				1 (0)	
*Aerococcus viridans**	*K. oxytoca*	*S. epidermidis*	*Staphylococcus cohnii*		1 (0)	
*Aerococcus viridans**	*Staphylococcus hominis*				1 (0)	
B. fragilis	*Clostridium species**				1 (0)	
Bacillus	*E. cloacae*				1 (0)	
*C. acnes**	*E. coli*				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)[A]
Organism 1	**Organism 2**	**Organism 3**	**Organism 4**	**Resistance Marker**		
C. albicans	*E. cloacae*	*E. faecalis*			1 (0)	
C. freundii	*P. mirabilis*	*Providencia stuartii**			1 (0)	
*Candida lusitaniae**	*S. liquefaciens*				1 (0)	
*Citrobacter amalonaticus**	*E. coli*				1 (0)	
E. aerogenes	*K. oxytoca*	*Leclercia adecarboxylata**			2 (2)	*E. aerogenes* (2)
E. aerogenes	*P. aeruginosa*				1 (1)	*P. aeruginosa* (1)
E. cloacae	*E. coli*	*K. pneumoniae*			1 (0)	
E. cloacae	*S. aureus*				1 (0)	
E. coli	*E. faecalis*				1 (0)	
E. coli	*K. pneumoniae*				1 (1)	*E. coli* (1)
E. coli	*P. mirabilis*	*Providencia stuartii**	*S. anginosus* group	CTX-M	1 (1)	*E. coli* (1)
E. faecalis	*K. pneumoniae*				3 (1)	*E. faecalis* (1)
E. faecalis	*M. morganii*	*P. mirabilis*			1 (1)	*E. faecalis* (1)
E. faecalis	*Providencia stuartii**				1 (0)	
*Enterobacteriaceae**	*K. pneumoniae*				1 (0)	
K. pneumoniae	*Staphylococcus haemolyticus*	Non-fermenting Gram-Negative bacilli*			1 (1)	*K. pneumoniae* (1)
*Lactococcus lactis**	*P. mirabilis*				1 (0)	
*Micrococcus luteus**	*Sphingomonas paucimobilis**				1 (0)	
P. aeruginosa	*P. mirabilis*	*Streptococcus - viridans* group			1 (0)	
P. aeruginosa	*S. maltophilia*				1 (1)	*S. maltophilia* (1)
P. aeruginosa	*Staphylococcus haemolyticus*				1 (0)	
P. mirabilis	*Staphylococcus*				1 (0)	
S. maltophilia	*Streptococcus*				1 (1)	*Streptococcus* (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)[A]
Organism 1	**Organism 2**	**Organism 3**	**Organism 4**	**Resistance Marker**		
A. baumannii	*E. faecalis*			OXA	2 (0)	
A. baumannii	*E. faecalis*	*S. aureus*			1 (0)	
A. baumannii	*E. faecium*			OXA	1 (0)	
A. baumannii	*Staphylococcus*				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)[A]
Organism 1	**Organism 2**	**Organism 3**	**Organism 4**	**Resistance Marker**		
*Acinetobacter radioresistens**	*P. vulgaris*			OXA	1 (0)	
*Aeromonas caviae**	*E. coli*	*Enterococcus casseliflavus*	*K. oxytoca*		1 (1)	*E. casseliflavus* (1)
*Aeromonas veronii**	*E. cloacae*				1 (1)	*E. cloacae* (1)
B. fragilis	*S. anginosus* group				1 (0)	
C. albicans	*E. faecalis*				1 (0)	
C. albicans	*E. faecium*	*Staphylococcus hominis*			1 (1)	*C. albicans* (1)
C. albicans	*P. aeruginosa*				1 (1)	*C. albicans* (1)
C. albicans	*S. epidermidis*				1 (0)	
C. braakii	*E. cloacae*	*K. oxytoca*			1 (1)	*C. braakii* (1), *K. oxytoca* (1)
C. braakii	*E. coli*				1 (0)	
C. braakii	*Streptococcus oralis*				1 (0)	
C. freundii	*Enterococcus*				1 (1)	*Enterococcus* (1)
C. freundii	*K. pneumoniae*				2 (0)	
C. freundii	*K. pneumoniae*	*Staphylococcus hominis*		CTX-M	1 (0)	
C. glabrata	*E. aerogenes*	*Staphylococcus*			1 (1)	*Staphylococcus* (1)
C. glabrata	*P. mirabilis*				1 (1)	*C. glabrata* (1)
C. koseri	*E. faecalis*				1 (0)	
C. krusei	*S. epidermidis*				1 (1)	*S. epidermidis* (1)
C. youngae	*K. oxytoca*				1 (1)	*K. oxytoca* (1)
*Clostridium perfringens**	*E. coli*				1 (0)	
E. aerogenes	*S. anginosus* group				1 (0)	
E. cloacae	*E. coli*				1 (1)	*E. coli* (1)
E. cloacae	*E. faecalis*				1 (1)	*E. faecalis* (1)
E. cloacae	*E. faecium*				1 (0)	
E. cloacae	*E. faecium*	*Staphylococcus hominis*			1 (0)	
E. cloacae	*K. pneumoniae*				1 (0)	
E. cloacae	*M. morganii*				1 (1)	*E. cloacae* (1)
E. cloacae	*S. anginosus* group				1 (0)	
E. cloacae	*S. maltophilia*				1 (1)	*S. maltophilia* (1)
E. coli	*E. faecalis*				2 (0)	
E. coli	*E. faecalis*			CTX-M	1 (0)	
E. coli	*E. faecalis*	*K. pneumoniae*			1 (1)	*E. coli* (1)
E. coli	*E. faecalis*	*P. mirabilis*			1 (0)	
E. coli	*E. faecium*				1 (0)	
E. coli	*E. faecium*			CTX-M	1 (1)	*E. faecium* (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)[A]
Organism 1	**Organism 2**	**Organism 3**	**Organism 4**	**Resistance Marker**		
E. coli	*K. oxytoca*	*Streptococcus infantarius*			1 (0)	
E. coli	*P. aeruginosa*				1 (1)	*P. aeruginosa* (1)
E. coli	*P. mirabilis*				1 (1)	*E. coli* (1)
E. coli	*P. mirabilis*	*P. vulgaris*	*Streptococcus - viridans* group		1 (1)	*S. viridans* group (1)
E. coli	*Propionibacteria**				1 (0)	
E. coli	*S. anginosus gp*				1 (1)	*S. anginosus* group (1)
E. coli	*S. aureus*				1 (0)	
E. coli	*S. pneumoniae*				1 (0)	
E. coli	*Staphylococcus*				1 (0)	
E. faecalis	*K. pneumoniae*				1 (1)	*K. pneumoniae* (1)
E. faecalis	*M. morganii*				1 (0)	
E. faecalis	*M. morganii*	*P. vulgaris*			1 (0)	
E. faecalis	*P. aeruginosa*	*S. aureus*			1 (1)	*P. aeruginosa* (1)
E. faecalis	*P. mirabilis*				3 (0)	
E. faecalis	*S. maltophilia*				1 (1)	*E. faecalis* (1)
E. faecalis	*S. marcescens*				1 (0)	
E. faecium	*K. pneumoniae*				1 (0)	
E. faecium	*P. aeruginosa*				1 (0)	
E. faecium	*P. mirabilis*				1 (0)	
K. oxytoca	*S. anginosus* group				1 (0)	
K. pneumoniae	*P. aeruginosa*				1 (1)	*P. aeruginosa* (1)
K. pneumoniae	*S. aureus*				2 (1)	*S. aureus* (1)
K. pneumoniae	*Staphylococcus*				1 (1)	*Staphylococcus* (1)
P. aeruginosa	*S. maltophilia*				1 (1)	*S. maltophilia* (1)
P. mirabilis	*Peptostreptococcus anaerobius**				1 (0)	
P. mirabilis	*Providencia stuartii**				2 (1)	*P. mirabilis* (1)
P. mirabilis	*Staphylococcus*				1 (0)	
*Pseudomonas putida**	*S. epidermidis*	*S. maltophilia*			1 (0)	
S. aureus	*S. marcescens*				1 (0)	
S. marcescens	*Staphylococcus*				1 (0)	
S. marcescens	*Streptococcus mitis* group	*Streptococcus salivarius*			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)
Acinetobacter baumannii	*Acinetobacter baumannii*	NCTC 13421	1×10^6
	Acinetobacter baumannii	NCTC 13304	1×10^6
Bacteroides fragilis	*Bacteroides fragilis*	ATCC 25285	1×10^5
	Bacteroides fragilis	ATCC 43860	1×10^4
Citrobacter	*Citrobacter freundii*	NCTC 9750	1×10^6
	Citrobacter koseri	ATCC 27156	1×10^6
Cronobacter sakazakii	*Cronobacter sakazakii*	ATCC 29544	1×10^5
	Cronobacter sakazakii	ATCC 29004	1×10^6
Enterobacter (non-*cloacae* complex)	*Enterobacter aerogenes*	CDC#0074	1×10^6
	Enterobacter aerogenes	CDC#0161	1×10^5
	Enterobacter amnigenus	ATCC 33072	1×10^6
Enterobacter cloacae Complex	*Enterobacter cloacae*	CDC#0154	1×10^6
	Enterobacter asburiae	ATCC 35957	1×10^6
	Enterobacter hormaechei	ATCC BAA-2082	1×10^6
Escherichia coli	*Escherichia coli*	CDC#0118	1×10^7
	Escherichia coli	NCTC 13441	1×10^6
	Escherichia coli	JHU01-D80401147	1×10^7
Fusobacterium necrophorum	*Fusobacterium necrophorum*	ATCC 51357	1×10^8

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

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

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 10^9 CFU/mL or less and fungal strains were tested at 1 x 10^6 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. murliniae*, and *C. sedlakii*. *Serratia odorifera* and *Staphylococcus simulans* were not detected at concentrations of 1 x 10^8 CFU/mL and only one of three replicates were detected at concentrations of 1 x 10^9 CFU/mL.

Table 65: Analytical Reactivity (Inclusivity)

Organism	Strain
Acinetobacter baumannii	
Acinetobacter baumannii	CDC#0052
	NCTC 13302
	NCTC 13303
	NCTC 13305
	NCTC 13420
	NCTC 13422
	NCTC 13423
Acinetobacter baumannii (NDM-1)	CDC#0033
Acinetobacter baumannii (OXA-23)	ATCC BAA-1605
	CDC#0045
	CDC#0056
	NCTC 13301
	NCTC 13424
Acinetobacter spp. (IMP only)	JMI4084[A]
Bacteroides fragilis	
Bacteroides fragilis	ATCC 23745
	ATCC 700786
	NCTC 9343
Citrobacter	
Citrobacter braakii	ATCC 43162
	ATCC 51113
Citrobacter freundii	ATCC 6879
	ATCC 8090
Citrobacter freundii (CTX)	JMI2047
Citrobacter freundii (KPC-2)	CDC#0116
Citrobacter koseri	ATCC 25409
	ATCC 27028
	ATCC 29225
	ATCC 29936
Citrobacter species (CTX-15, NDM-1)	CDC #0157
Citrobacter werkmanii	ATCC 51114
Citrobacter youngae	ATCC 29935
Cronobacter sakazakii	
Cronobacter sakazakii	ATCC 12868
	ATCC BAA-894
	FSL F6-0023
***Enterobacter* (non-cloacae complex)**	
Enterobacter aerogenes	ATCC 13048
	ATCC 29010
	ATCC 51697
Enterobacter amnigenus	ATCC 33731
	ATCC 51816[B]

Organism	Strain
Enterobacter gergoviae	ATCC 33028
	ATCC 33426
***Enterobacter cloacae* complex**	
Enterobacter asburiae	ATCC 35954
	ATCC 35955
	ATCC 35956
Enterobacter cloacae (CTX-15)	CDC#0038
Enterobacter cloacae (CTX-9)	NCTC 13464
Enterobacter cloacae (CTX-15, KPC-2)	CDC#0163
Enterobacter cloacae (CTX, NDM)	JMI53571
Enterobacter cloacae subsp. *cloacae*	ATCC 23355
	ATCC 35030
Enterobacter cloacae subsp. *dissolvens*	ATCC 23373
Enterobacter hormaechei	ATCC 700323
Enterobacter hormaechei subsp. *hormaechei*	ATCC 49162
Enterobacter hormaechei subsp. *oharae*	ATCC 49163
Enterobacter hormaechei subsp. *steigerwaltii*	CIP108489T
Enterobacter ludwigii	DSM-16688
Escherichia coli	
Escherichia coli	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
	ATCC 14169
Escherichia coli (CTX-14)	CDC#0086
Escherichia coli (CTX-15)	ATCC BAA-2326
	NCTC 13353
	NCTC 13400
	NCTC 13450
	NCTC 13451
Escherichia coli (CTX-3)	NCTC 13452
Escherichia coli (CTX-1)	NCTC 13461
Escherichia coli (CTX-2)	NCTC 13462
Escherichia coli (CTX-8)	NCTC 13463
Escherichia coli (CTX-15, NDM-6)	CDC#0137
Escherichia coli (CTX-15, NDM-7)	CDC#0162
Escherichia coli (IMP)	NCTC 13476
Escherichia coli (KPC)	ATCC BAA-2340
Escherichia coli (NDM-5)	CDC#0150
Escherichia coli (OXA)	LMC_DR00012
Escherichia coli (VIM)	JMI32465
Fusobacterium necrophorum	
Fusobacterium necrophorum subsp. *necrophorum*	ATCC 25286
	NCTC 10575
	NCTC 10577
Fusobacterium nucleatum	
Fusobacterium nucleatum subsp. *nucleatum*	ATCC 31647
Fusobacterium nucleatum subsp. *fusiforme*	ATCC 51190
Fusobacterium nucleatum subsp. *vincentii*	ATCC 49256
Haemophilus influenzae	
Haemophilus influenzae	ATCC 33930
	ATCC 43065
	ATCC 43163
	NCTC 11931
	NCTC 12699
	NCTC 8143
Haemophilus influenzae Type b	ATCC 10211
Haemophilus influenzae Type c	ATCC 9007
Haemophilus influenzae Type d	ATCC 9332
Haemophilus influenzae Type e	NCTC 8472
Haemophilus influenzae Type f	ATCC 9833
Klebsiella oxytoca	
Klebsiella oxytoca	ATCC 43086
	ATCC 43863
	ATCC 49131
	ATCC 700324
	ATCC 51817
Klebsiella oxytoca (KPC-3)	CDC#0147
Klebsiella pneumoniae group	
Klebsiella pneumoniae (CTX-15)	CDC#0109
Klebsiella pneumoniae (CTX-25)	NCTC 13465
Klebsiella pneumoniae (CTX, KPC)	IMH-C2261309
Klebsiella pneumoniae (CTX, NDM-1)	NCTC 13443
Klebsiella pneumoniae (CTX-15; NDM-1; OXA-232)	CDC#0153
Klebsiella pneumoniae (CTX-15, OXA-232)	CDC#0075
	CDC#0066
Klebsiella pneumoniae (CTX-15, OXA-181)	CDC#0039
	CDC#0140
	CDC#0141

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

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

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

Organism	Strain
Pan *Candida*	
Candida albicans	ATCC 24433
	ATCC 90028
Candida glabrata	ATCC 2001
	ATCC 66032
Candida krusei	ATCC 14243
	ATCC 32196
	ATCC 34135[G]
Candida parapsilosis	ATCC 22019
	ATCC 58895
	ATCC 90018[H]

A. Non-target species used to evaluate resistance marker.
B. 5/6 replicates detected at 2.0 x 10^8 CFU/mL.
C. 5/6 replicates detected at 4.5 x 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 x 10^8 CFU/mL.
F. Strain may have reduced sensitivity and was not 100% detected at concentrations <4 x 10^8 CFU/mL.
G. In initial testing, 1/6 replicates was detected at 1x 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 x 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 ≥95% of target sequences		
*Citrobacter koseri**	*Citrobacter intermedius*	
Detection Predicted for 85%-94% of target sequences		
*Citrobacter freundii**	*Citrobacter braakii**	
Detection Predicted for <85.0% of target sequences		
*Citrobacter werkmanii** (66.7%)	*Citrobacter youngae** (50.0%)	
Detection Not Predicted		
Citrobacter europaeus	*Citrobacter gillenii*	*Citrobacter amalonaticus*[A]
Citrobacter farmeri	*Citrobacter sedlakii*	*Citrobacter murliniae*

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

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

Detection Predicted for ≥95% of target sequences		
*Enterobacter aerogenes**	*Enterobacter gergoviae**	
Detection Predicted for 85%-94% of target sequences		
None Identified		
Detection Predicted for <85.0% of target sequences		
*Enterobacter amnigenus** (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		
*Klebsiella pneumoniae**	*Klebsiella quasipneumoniae**	*Klebsiella variicola**
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		
*Proteus mirabilis**	*Proteus penneri**	*Proteus vulgaris**
*Proteus hauseri**	*Proteus cibarius*	
Detection Predicted for 85%-94% of target sequences		
None Identified		
Detection Predicted for <85.0% of target sequences		
None Identified		
Detection Not Predicted		
Proteus myxofaciens		

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

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

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

Detection Predicted for ≥95% of target sequences		
Streptococcus caballi	*Streptococcus lactarius*	*Streptococcus pseudopneumoniae*
Streptococcus constellatus	*Streptococcus loxodontisalivarius*	*Streptococcus pseudoporcinus*
Streptococcus criceti	*Streptococcus luteciae*	*Strepotococcus pyogenes*
Streptococcus cristatus	*Streptococcus lutetiensis*	*Streptococcus rifensis*
Streptococcus danieliae	*Streptococcus macedonicus*	*Streptococcus rubneri*
Streptococcus dentasini	*Streptococcus marimammalium*	*Streptococcus salivarius**
Streptococcus dentisani	*Streptococcus massiliensis*	*Streptococcus saliviloxodontae*
Streptococcus didelphis	*Streptococcus mitis**	*Streptococcus sanguinis*
Streptococcus difficilis	*Streptococcus moroccensis*	*Streptococcus seminale*
Streptococcus dysgalactiae subsp. *dysgalactiae*	*Streptococcus oligofermentans*	*Streptococcus sinensis*
Streptococcus dysgalactiae subsp. *equisimilis*	*Streptococcus oralis**	*Streptococcus suis*
*Streptococcus dysgalactiae**	*Streptococcus oricebi*	*Streptococcus thermophilus*
*Streptococcus equi**	*Streptococcus orisratti*	*Streptococcus thoraltensis**
Streptococcus equinus	*Streptococcus panodentis*	*Streptococcus tigurinus*
Streptococcus fryi	*Streptococcus parasanguinis**	*Streptococcus troglodytae*
*Streptococcus gallolyticus**	*Streptococcus parasuis*	*Streptococcus troglodytidis*
*Streptococcus gordonii**	*Streptococcus parauberis*	*Streptococcus urinalis*
Streptococcus himalayensis	*Streptococcus pasteuri*	*Streptococcus ursoris*
Streptococcus hongkongensis	*Streptococcus pasteurianus*	*Streptococcus vestibularis*
Streptococcus hyointestinalis	*Streptococcus peroris*	*Streptococcus waiu*
Detection Predicted for 85%-94% of target sequences		
*Bacillus cereus**	*Enterococcus hirae**	*Staphylococcus saccharolyticus*
*Enterococcus casseliflavus**	*Staphylococcus arlettae*	*Streptococcus bovis*
Enterococcus cecorum	*Staphylococcus condimenti*	*Streptococcus uberis*
Enterococcus gallinarum	*Staphylococcus intermedius*	
Detection Predicted for <85.0% of target sequences		
Bacillus mojavensis (77.8%)	*Bacillus sonorensis* (83.3%)	*Streptococcus halichoeri* (66.7%)
Streptococcus ratti (75.0%)		
Detection Not Predicted		
Bacillus pseudomycoides	*Enterococcus sulfureus*	*Streptococcus hyovaginalis*
Enterococcus aquimarinus	*Enterococcus termitis*	*Streptococcus ictaluri*
Enterococcus asini	*Enterococcus ureasiticus*	*Streptococcus iniae*
Enterococcus caccae	*Enterococcus ureilyticus*	*Streptococcus lactis*
Enterococcus camelliae	*Enterococcus villorum*	*Streptococcus macacae*
Enterococcus canintestini	*Staphylococcus caseolyticus*	*Streptococcus marmotae*

Detection Predicted for ≥95% of target sequences		
Enterococcus canis	*Streptococcus acidominimus*	*Streptococcus merionis*
Enterococcus columbae	*Streptococcus azizii*	*Streptococcus milleri*
Enterococcus devriesei	*Streptococcus cameli*	*Streptococcus minor*
Enterococcus haemoperoxidus	*Streptococcus canis*	*Streptococcus oriloxodontae*
Enterococcus hawaiiensis	*Streptococcus castoreus*	*Streptococcus orisasini*
Enterococcus hermanniensis	*Streptococcus cremoris*	*Streptococcus orisuis*
Enterococcus italicus	*Streptococcus criae*	*Streptococcus ovis*
Enterococcus mundtii	*Streptococcus cuniculi*	*Streptococcus pharyngis*
Enterococcus pallens	*Streptococcus dentapri*	*Streptococcus pluranimalium*
Enterococcus pernyi	*Streptococcus dentiloxodontae*	*Streptococcus plurextorum*
Enterococcus phoeniculicola	*Streptococcus dentirousetti*	*Streptococcus plutanimalium*
Enterococcus plantarum	*Streptococcus devriesei*	*Streptococcus porci*
Enterococcus quebecensis	*Streptococcus downei*	*Streptococcus rupicaprae*
Enterococcus ratti	*Streptococcus entericus*	*Streptococcus sobrinus*
Enterococcus rivorum	*Streptococcus ferus*	*Streptococcus tangierensis*
Enterococcus rotai	*Streptococcus gallinaceus*	
Enterococcus silesiacus	*Streptococcus henryi*	

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

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

Target	Associated Organism	Variant Detected
Stenotrophomonas maltophilia	*Stenotrophomonas maltophilia*	CTX-M-15

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

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

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

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

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

Target	Associated Organism	Variant Detected
Klebsiella pneumoniae Group	*Klebsiella pneumoniae*	CTX-M-63
Morganella morganii	*Morganella morganii*	CTX-M-63
Salmonella	*Salmonella enterica*	CTX-M-8

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

Target	Associated Organism	Variant Detected
Citrobacter	*Citrobacter freundii*	CTX-M-14
		CTX-M-65
Enterobacter non-*cloacae* Complex	*Enterobacter aerogenes*	CTX-M-9
Enterobacter cloacae Complex	*Enterobacter cloacae*	CTX-M-9*
		CTX-M-13
		CTX-M-14
		CTX-M-64
		CTX-M-125
Escherichia coli	*Escherichia coli*	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
Klebsiella pneumoniae Group	*Klebsiella pneumoniae*	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
		CTX-M-65
		CTX-M-81
		CTX-M-99
		CTX-M-104
		CTX-M-147
		CTX-M-159
		CTX-M-201
Proteus mirabilis/*Proteus*	*Proteus mirabilis*	CTX-M-13
		CTX-M-14
		CTX-M-24
		CTX-M-65
		CTX-M-90
Salmonella	*Salmonella enterica*	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
Serratia	*Serratia liquefaciens*	CTX-M-14

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

Target	Associated Organism	Variant Detected
Escherichia coli	*Escherichia coli*	CTX-M-25
		CTX-M-39
		CTX-M-94
		CTX-M-100
Klebsiella pneumoniae Group	*Klebsiella pneumoniae*[A]*	CTX-M-26
	Proteus mirabilis	CTX-M-41
Proteus mirabilis/*Proteus*		CTX-M-89
		CTX-M-91
		CTX-M-160
Salmonella	*Salmonella enterica*	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
Acinetobacter baumannii	*Acinetobacter baumannii*	IMP-1
		IMP-2
		IMP-4
		IMP-5
		IMP-8
		IMP-10
		IMP-11
		IMP-14
		IMP-19
		IMP-55
		IMP-61
Citrobacter	*Citrobacter freundii*	IMP-1
		IMP-4
		IMP-8
		IMP-23
		IMP-38
Enterobacter non-*cloacae* Complex	*Enterobacter aerogenes*	IMP-4
Enterobacter cloacae Complex	*Enterobacter cloacae*	IMP-1
		IMP-4
		IMP-8
		IMP-11
		IMP-26
		IMP-34
		IMP-60
Enterobacter cloacae Complex	*Enterobacter hormaechei*	IMP-13
		IMP-14
Escherichia coli	*Escherichia coli*	IMP-1
		IMP-4
		IMP-6
		IMP-8
		IMP-14
		IMP-30
		IMP-52
		IMP-59
		IMP-66
Klebsiella oxytoca	*Klebsiella oxytoca*	IMP-1
		IMP-4
		IMP-8
		IMP-28
		IMP-34
Klebsiella pneumoniae Group	*Klebsiella pneumoniae*	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
Proteus mirabilis/*Proteus*	*Proteus mirabilis*	IMP-1
		IMP-27
		IMP-64
Pseudomonas aeruginosa	*Pseudomonas aeruginosa*	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
		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
Salmonella	*Salmonella enterica*	IMP-4
Serratia marcescens/*Serratia*	*Serratia marcescens*	IMP-1
		IMP-2
		IMP-6
		IMP-8
		IMP-24
Stenotrophomonas maltophilia	*Stenotrophomonas maltophilia*	IMP-25

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

Target	Associated Organism	Variant Detected
Acinetobacter baumannii	*Acinetobacter baumannii*	KPC-2
		KPC-3
		KPC-10
Citrobacter	*Citrobacter freundii*	KPC-2*
		KPC-3
		KPC-18
Enterobacter non-*cloacae* Complex	*Enterobacter aerogenes*	KPC-2
		KPC-3
Enterobacter cloacae Complex	*Enterobacter cloacae*	KPC-2*
		KPC-3
		KPC-4
		KPC-13
		KPC-18
Escherichia coli	*Escherichia coli*	KPC-2
		KPC-3
		KPC-4
		KPC-5
		KPC-9
		KPC-18
		KPC-21
		KPC-28
Klebsiella oxytoca	*Klebsiella oxytoca*	KPC-2
		KPC-3*
Klebsiella pneumoniae Group	*Klebsiella pneumoniae*	KPC-1
		KPC-2
		KPC-3*
		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
Proteus mirabilis/*Proteus*	*Proteus mirabilis*	KPC-2
		KPC-6*
Pseudomonas aeruginosa	*Pseudomonas aeruginosa*	KPC-2
		KPC-5*
Salmonella	*Salmonella enterica*	KPC-2
Serratia marcescens/*Serratia*	*Serratia marcescens*	KPC-2
		KPC-3

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

Target	Associated Organism	Variant Detected
Acinetobacter baumannii	*Acinetobacter baumannii*	VIM-1
		VIM-2
		VIM-6
		VIM-11
Citrobacter	*Citrobacter freundii*	VIM-1
		VIM-2
		VIM-4
		VIM-23
Enterobacter non-*cloacae* Complex	*Enterobacter aerogenes*	VIM-1
Enterobacter cloacae Complex	*Enterobacter cloacae*	VIM-1
		VIM-2
		VIM-4
		VIM-23
		VIM-31
		VIM-40
	Enterobacter hormaechei	VIM-1
		VIM-4
		VIM-23
	Enterobacter xiangfangensis	VIM-1
Escherichia coli	*Escherichia coli*[A]	VIM-1
		VIM-2
		VIM-19
		VIM-29
Klebsiella oxytoca	*Klebsiella oxytoca*	VIM-1
		VIM-2
		VIM-4
		VIM-32
		VIM-35
Klebsiella pneumoniae Group	*Klebsiella pneumoniae*	VIM-1*
		VIM-2
		VIM-4
		VIM-12
		VIM-19
		VIM-24
		VIM-26
		VIM-27*
		VIM-33
		VIM-34
		VIM-39
		VIM-42
		VIM-51
		VIM-52
Morganella morganii	*Morganella morganii*	VIM-4
Proteus mirabilis/*Proteus*	*Proteus mirabilis*	VIM-1
Pseudomonas aeruginosa	*Pseudomonas aeruginosa*	VIM-1
		VIM-2*
		VIM-3
		VIM-4*
		VIM-5
		VIM-6
		VIM-8
		VIM-9
		VIM-10
		VIM-11
		VIM-14
		VIM-15
		VIM-16
		VIM-17
		VIM-18
		VIM-20
		VIM-28
		VIM-30
		VIM-36
		VIM-37
		VIM-41
		VIM-43
		VIM-44
		VIM-45
		VIM-46
		VIM-48
		VIM-50
Salmonella	*Salmonella enterica*	VIM-1
Serratia marcescens/*Serratia*	*Serratia marcescens*	VIM-2
		VIM-4
		VIM-54
Stenotrophomonas maltophilia	*Stenotrophomonas maltophilia*	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
Acinetobacter baumannii	*Acinetobacter baumannii*	OXA-23*
		OXA-49
		OXA-23/OXA-104
		OXA-23/OXA-64
		OXA-23/OXA-66
		OXA-23/OXA-69
		OXA-27
		OXA-65/OXA-239
		OXA-68
		OXA-146
		OXA-165
		OXA-166
		OXA-167
		OXA-168
		OXA-169
		OXA-170
		OXA-171
		OXA-183
		OXA-225
		OXA-366
		OXA-398
		OXA-422
		OXA-423
		OXA-435
		OXA-440
		OXA-469
		OXA-481
		OXA-482
		OXA-483
		OXA-565

Target	Associated Organism	Variant Detected
Escherichia coli	*Escherichia coli*	OXA-23
Klebsiella pneumoniae Group	*Klebsiella pneumoniae*	OXA-73
Proteus mirabilis	*Proteus mirabilis*	OXA-23

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

Target	Associated Organism	Variant Detected
Acinetobacter baumannii	*Acinetobacter baumannii*	OXA-48
Citrobacter	*Citrobacter freundii*	OXA-48
		OXA-181
Enterobacter non-*cloacae Complex*	*Enterobacter aerogenes*	OXA-244
Enterobacter cloacae Complex	*Enterobacter cloacae*	OXA-48
		OXA-163
		OXA-181
	Enterobacter hormaechei	OXA-370
	Enterobacter ludwigii	OXA-48
Escherichia coli	*Escherichia coli*[A]	OXA-48
		OXA-163
		OXA-181
		OXA-204
		OXA-232
		OXA-244
		OXA-438
		OXA-439
		OXA-566
Klebsiella pneumoniae Group	*Klebsiella pneumoniae*	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
	Klebsiella variicola	OXA-181
Morganella morganii	*Morganella morganii*	OXA-181
Proteus mirabilis/*Proteus*	*Proteus mirabilis*	OXA-48
		OXA-244
Serratia marcescens/*Serratia*	*Serratia marcescens*	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
Acinetobacter baumannii	*Acinetobacter baumannii*	NDM-1*
		NDM-2
Citrobacter	*Citrobacter braakii*	NDM-4
Citrobacter	*Citrobacter freundii*	NDM-1[A]
		NDM-4
		NDM-6
		NDM-7
Enterobacter non-*cloacae* Complex	*Enterobacter aerogenes*	NDM-1
		NDM-4
		NDM-5
		NDM-7
Enterobacter cloacae Complex	*Enterobacter cloacae*[B]	NDM-1
		NDM-4
		NDM-7
	Enterobacter hormaechei	NDM-1
	Enterobacter ludwigii	NDM-1
Escherichia coli	*Escherichia coli*	NDM-1
		NDM-3
		NDM-4
		NDM-5*
		NDM-6*
		NDM-7*
		NDM-8
		NDM-11
		NDM-12
		NDM-13
		NDM-15
		NDM-16
		NDM-17
		NDM-18
		NDM-19
Klebsiella oxytoca	*Klebsiella oxytoca*	NDM-1
		NDM-4
Klebsiella pneumoniae Group	*Klebsiella pneumoniae*	NDM-1*
		NDM-4
		NDM-5
		NDM-6
		NDM-7
		NDM-10
		NDM-16
Morganella morganii	Morganella morganii	NDM-1[C]
Proteus mirabilis/*Proteus*	*Proteus mirabilis*	NDM-1
Pseudomonas aeruginosa	*Pseudomonas aeruginosa*	NDM-1
		NDM-5
Salmonella	*Salmonella enterica*	NDM-1
		NDM-5

Target	Associated Organism	Variant Detected
Serratia marcescens/Serratia	*Serratia marcescens*	NDM-1

Target	Associated Organism	Variant Detected
Stenotrophomonas maltophilia	*Stenotrophomonas maltophilia*	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	*Klebsiella pneumoniae*	3
	CTX-M-15		
	Not Specified		
IMP	IMP-31	*Pseudomonas aeruginosa*	2
	IMP-35		2
	IMP-7		1
NDM	NDM-1	*Escherichia coli*	6
		Klebsiella variicola	3
		Salmonella enterica	1
	NDM-3	*Acinetobacter baumannii*	1
	NDM-4	*Escherichia coli*	1
	NDM-9	*Cronobacter sakazakii*	1
		Escherichia coli	1
		Klebsiella pneumoniae	2
	Not specified	*Escherichia coli*	2
		Klebsiella pneumoniae	1

Resistance Marker	Variant Not Detected	Associated Organism	No. of Sequences
		Klebsiella sp	1
		Pseudomonas aeruginosa	1
VIM	VIM-1	*Pseudomonas aeruginosa*	3
		Providencia vermicola	1
	VIM-2	*Klebsiella pneumoniae*	1
	VIM-5	*Enterobacter cloacae*	2
		Klebsiella pneumoniae	3
	VIM-7	*Pseudomonas aeruginosa*	4
	VIM-13		3
	VIM-25	*Acinetobacter baumannii*	1
		Proteus mirabilis	2
	VIM-38	*Pseudomonas aeruginosa*	2
	VIM-47		2
	VIM-49		2
	Not specified		1
OXA-48	OXA-232	*Escherichia coli*	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 ~1x10^9 CFU/mL while fungi were tested in triplicate at a concentration of ~1x10^7 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 >1x10^4 CFU/mL) cross-reacts with the *Acinetobacter baumannii* assay, *Enterobacter cowanii* (at a concentration of >1x10^8 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 >1x10^6 CFU/mL) and with the *Serratia* assay (at a concentration of >1x10^7 CFU/mL), *Fusobacterium periodonticum* (at a concentration of 5x10^8 CFU/mL) and *Fusobacterium simiae* (at a concentration of 2.9x10^8 CFU/mL) cross-react with the *Fusobacterium nucleatum* assay, and *Shigella* (at a concentration of 1x10^9 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
Acinetobacter haemolyticus	ATCC 19002
Acinetobacter lwoffii	ATCC 15309
Acinetobacter junii	ATCC 17908
Acinetobacter anitratus[A]	ATCC 49139
Aeromonas hydrophila	JMI 938982
Aeromonas salmonicida	ATCC 33658
Aeromonas sobria	ATCC 35993
Bacteroides distasonis (Parabacteroides)	ATCC 8503
Bacteroides merdae	ATCC 43184
Bacteroides thetaiotaomicron	ATCC 29741
*Bacteroides vulgatus**	ATCC 8482
Bacteroides caccae	ATCC 700189
Bacteroides eggerthii	ATCC 27754
*Bacteroides ovatus**	ATCC BAA-1296
*Bacteroides ureolyticus**	ATCC 33387
Bordetella pertussis	ATCC 9797
Burkholderia cepacia	ATCC 25416
Citrobacter amalonaticus	ATCC BAA-2563
Citrobacter gillenii	ATCC 51640
Citrobacter sedlakii	ATCC 51493
Citrobacter farmeri	ATCC 51112
Citrobacter murliniae	ATCC 51642
Edwardsiella tarda	ATCC 15947
Enterobacter kobei	ATCC BAA-260
Enterobacter cancerogenus	ATCC 35315
Enterobacter cowanii[B]	DSM-18146
Escherichia albertii	DSM-17582
Escherichia fergusonii	ATCC 35469
Escherichia hermanii[C]	ATCC 33650
*Ewingella americana**	ATCC 33853
Eikenella corrodens	ATCC BAA-1152
*Fusobacterium naviforme**	ATCC 25832
Fusobacterium gonidiaformans	ATCC 25563
*Fusobacterium necrogenes**	ATCC 25556
Fusobacterium periodonticum*[D]	ATCC 33693
Fusobacterium simiae*[D]	ATCC 33568
Fusobacterium varium	ATCC 27725
*Fusobacterium russii**	ATCC 25533
Fusobacterium ulcerans	ATCC 49186
Haemophilus haemolyticus	ATCC 33390
Haemophilus parahaemolyticus	ATCC 10014
Hafnia alvei	ATCC 51815
*Kingella kingae**	ATCC 23331

Gram Negative Organism	Strain ID
Kluyvera cochleae	ATCC 51609
Legionella pneumoniae	ATCC 33823
Leclercia adecarboxylata	ATCC 700325
*Methylobacterium mesophilicum**	ATCC 29983
Neisseria gonorrhoeae	ATCC 19424
Neisseria mucosa	ATCC 19695
Neisseria sicca	ATCC 29193
Neisseria flavecens	ATCC 13115
Neisseria lactamica	ATCC 23970
Neisseria perflava	ATCC 14799
Ochrobactrum anthropi	ATCC BAA-749
Pantoea agglomerans	ATCC 14537
Pantoea ananatis	NRRL B-41502
Pasteurella aerogenes	ATCC 27883
Pasteurella multicida subsp multicide	ATCC 12945
Prevotella intermedia	ATCC 15032
*Prevotella corporis**	ATCC 33547
*Prevotella oralis**	ATCC 33269
*Prevotella nigrescens**	ATCC 33563
Providencia rettgeri	ATCC 9250
Providencia stuartii	ATCC 33672
Providencia alcalifaciens	ATCC 9886
Pseudomonas fluorescens	ATCC 13525
Pseudomonas putida	ATCC 49128
Pseudomonas alcaligenes	ATCC 14909
Ralstonia insidiosa	ATCC 49129
Ralstonia pickettii	ATCC 27511
Raoultella planticola (Klebsiella planticola)	ATCC 31900
Raoultella ornithinolytica	CDC# 0134
Raoultella terrigena (Klebsiella terrigena)	ATCC 55553
Shigella boydii[E]	ATCC 9207
Shigella sonnei[E]	ATCC 25931
Shigella flexneri[E]	ATCC 9199
Vibrio furnissii	NCTC11218
Vibrio alginolyticus	ATCC 17749
Vibrio parahaemolyticus	ATCC 17802
Yersinia enterocolitica subsp *enterocolitica*	ATCC 9610
Yersinia ruckeri	ATCC 29473
Yersinia kristensenii	ATCC 33639

A. Cross-reactivity seen with *Acinetobacter baumanii* at a concentration > $1x10^4$ CFU/mL.
B. Cross-reactivity seen with *Enterobacter cloacae* complex at a concentration > $1x10^8$ CFU/mL.
C. Cross-reactivity seen with *Enterobacter* (non-*cloacae* complex) at a concentration > $1x10^6$ CFU/mL and *Serratia* at a concentration of > $1x10^7$ 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
Actinomyces odontolyticus	ATCC 17929
Clostridium perfringens	ATCC 13124
Corynebacterium jeikeium	ATCC BAA-949
Corynebacterium renale	ATCC 19412
Corynebacterium ulcerans	ATCC 51799
*Corynebacterium xerosis**	ATCC 373
Corynebacterium durum	ATCC 33449
*Corynebacterium diphtheriae**	ATCC 13812
Corynebacterium pseudodiphtheriticum	ATCC 10700
*Corynebacterium striatum**	ATCC 43735
Corynebacterium urealyticum	ATCC 43044
Lactobacillus casei	ATCC 39392

Gram Positive Organisms	Strain ID
*Lactobacillus paracasei**	ATCC 25598
*Lactobacillus acidophilus**	ATCC 314
Lactobacillus crispatus	ATCC 33197
Lactobacillus rhamnosus	ATCC 39595
Lactococcus lactis	ATCC 49032
Listeria innocua	ATCC 33090
Listeria monocytogenes	ATCC 7644
Micrococcus luteus	ATCC 10240
Peptostreptococcus anaerobius	ATCC 27337
Propionibacterium acnes	ATCC 11827
Rothia mucilaginosa	ATCC 25296

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

Fungal Pathogens	Strain ID	Concentration Tested
*Aspergillus fumigatus**	ATCC 204305	2.50 x 10^6 CFU/mL
Candida orthopsilosis	ATCC 96139	1 x 10^7 CFU/mL
Candida metapsilosis	ATCC 96144	1 x 10^7 CFU/mL
Candida tropicalis	ATCC 1369	1 x 10^7 CFU/mL
Cryptococcus grubii	ATCC 208821	1 x 10^7 CFU/mL
Cryptococcus gattii	ATCC 76108	1 x 10^7 CFU/mL
Cryptococcus neoformans	ATCC 14116	1 x 10^7 CFU/mL
Geotrichum capitatum	ATCC 10663	1 x 10^7 CFU/mL
Histoplasma capsulatum	*In silico*	N/A
Penicillium marneffei	ATCC 200050	1 x 10^7 CFU/mL
Rhodotorula glutinis	ATCC 32765	1 x 10^7 CFU/mL
Rhodotorula mucilaginosa	ATCC 9449	1 x 10^7 CFU/mL
Rhodotorula minuta	ATCC 36236	1 x 10^7 CFU/mL
*Saccharomyces cervisiae**	ATCC 18824	5.55 x 10^6 CFU/mL
Trichosporon dermatis	ATCC MYA-4294	1 x 10^7 CFU/mL
Trichosporon mucoides	ATCC 90046	1 x 10^7 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 *Klebsiella oxytoca*)*[A]	JMI 954306	8 x 10^8 CFU/mL
MOX (Carried by *Aeromonas hydrophila*)	JMI 938982	1 x 10^9 CFU/mL
SME (Carried by *Serratia marcescens*)[A]	CDC #0091	1 x 10^9 CFU/mL
SHV (Carried by *Klebsiella pneumoniae)*[A]	CDC #0087	1 x 10^9 CFU/mL
TEM (Carried by *Escherichia coli*)[A]	NCTC 13351	1 x 10^9 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 (%)
Fusobacterium hwasookii	*F. nucleatum*	10	5 (50%)
Haemophilus aegyptius	*H. influenzae*	3	3 (100%)
Klebsiella michiganensis	*Klebsiella oxytoca*	40	40 (100%)
Pseudomonas denitrificans	*Pseudomonas aeruginosa*	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 (%)
Brevibacterium halotolerans	3	3 (100%)
Domibacillus indicus	1	1 (100%)
Domibacillus robiginosus	1	1 (100%)
Salinibacillus aidingensis	2	1 (50%)
Terribacillus aidingensis	1	1 (100%)
Terribacillus halophilus	2	1 (50%)
Terribacillus saccharophilus	1	1 (100%)
Planomicrobium okeanokoites	1	1 (100%)
Lactococcus chungangensis	4	4 (100%)
Lactococcus laudensis	1	1 (100%)
Lactococcus piscium	18	18 (100%)
Lactococcus plantarum	6	5 (83.8%)
Lactococcus raffinolactis	49	46 (93.9%)
Okadaella gastrococcus	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-GN 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. auerginosa*, 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			
Enterococcus faecium	ATCC BAA-2317	4.9 x 10^7 CFU/mL	3.6 x 10^7 CFU/mL
Staphylococcus aureus	NRS 483	2.8 x 10^7 CFU/mL	2.1 x 10^7 CFU/mL
Streptococcus anginosus	ATCC 33397	4.1 x 10^7 CFU/mL	4.0 x 10^8 CFU/mL
Gram-negative Organisms			
Acinetobacter baumannii	NCTC 13301	4.4 x 10^8 CFU/mL	3.8 x 10^8 CFU/mL
Bacteroides fragilis	ATCC 700786	4.7 x 10^8 CFU/mL	6.7 x 10^9 CFU/mL
Enterobacter cloacae	NCTC 13464	2.8 x 10^8 CFU/mL	7.7 x 10^8 CFU/mL
Escherichia coli	NCTC 13476	2.3 x 10^8 CFU/mL	1.5 x 10^9 CFU/mL
Fusobacterium nucleatum	ATCC 31647	6.5 x 10^7 CFU/mL	4.9 x 10^8 CFU/mL
Haemophilus influenzae	ATCC 19418	6.9 x 10^8 CFU/mL	1.2 x 10^9 CFU/mL
Klebsiella oxytoca	CDC #0147	9.3 x 10^8 CFU/mL	1.5 x 10^9 CFU/mL
Neisseria meningitidis	ATCC 13102	3.2 x 10^7 CFU/mL	2.1 x 10^8 CFU/mL
Pseudomonas aeruginosa	NCTC 13476	1.6 x 10^8 CFU/mL	8.4 x 10^8 CFU/mL
Serratia marcescens	ATCC 14041	1.2 x 10^9 CFU/mL	2.2 x 10^9 CFU/mL
Fungal Organisms			
Candida albicans	ATCC 90082	1.6 x 10^6 CFU/mL	1.4 x 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
Acinetobacter baumannii (OXA)	1 x 10^8 CFU/mL	1 x 10^9 CFU/mL
Enterobacter cloacae (CTX-M, KPC)	1 x 10^8 CFU/mL	1 x 10^9 CFU/mL
Escherichia coli (IMP)	1 x 10^8 CFU/mL	1 x 10^9 CFU/mL
Fusobacterium nucleatum	1 x 10^7 CFU/mL	1 x 10^8 CFU/mL
Haemophilus influenzae	1 x 10^8 CFU/mL	1 x 10^9 CFU/mL
Klebsiella oxytoca	1 x 10^8 CFU/mL	1 x 10^9 CFU/mL
Neisseria meningitidis	3 x 10^7 CFU/mL	3 x 10^8 CFU/mL

Organism	Bottle Positivity Concentration	Bottle Positivity +8 Hours Concentration
Pseudomonas aeruginosa (VIM)	1 x 10^8 CFU/mL	1 x 10^9 CFU/mL
Serratia marcescens	1 x 10^8 CFU/mL	1 x 10^9 CFU/mL
Candida albicans (Pan *Candida* target)	1 x 10^6 CFU/mL	1 x 10^7 CFU/mL
Staphylococcus aureus (Pan Gram-Positive target)	1 x 10^7 CFU/mL	1 x 10^8 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 *Acinetobacter baumannii*	Site	Agreement with Expected Results		
		Agreed / N	%	95% CI
Bottle Positive + 8 Hours (1x10^9 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 (1x10^8 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 *Enterobacter cloacae*	Site	Agreement with Expected Results		
		Agreed / N	%	95% CI
Bottle Positive + 8 Hours (1x10^9 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 (1x10^8 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 *Escherichia coli*	Site	Agreement with Expected Results		
		Agreed / N	%	95% CI
Bottle Positive + 8 Hours ($1x10^9$ 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 ($1x10^8$ 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 *Fusobacterium nucleatum*	Site	Agreement with Expected Results		
		Agreed / N	%	95% CI
Bottle Positive + 8 Hours ($1x10^8$ 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 ($1x10^7$ 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 *Haemophilus influenzae*	Site	Agreement with Expected Results		
		Agreed / N	%	95% CI
Bottle Positive + 8 Hours ($1x10^9$ 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 ($1x10^8$ 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 *Haemophilus influenzae*	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 *Klebsiella oxytoca*	Site	Agreement with Expected Results		
		Agreed / N	%	95% CI
Bottle Positive + 8 Hours ($1x10^9$ 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 ($1x10^8$ 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 *Neisseria meningitidis*	Site	Agreement with Expected Results		
		Agreed / N	%	95% CI
Bottle Positive + 8 Hours ($3x10^8$ 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 ($3x10^7$ 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 *Pseudomonas aeruginosa*	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 *Pseudomonas aeruginosa*	Site	Agreement with Expected Results		
		Agreed / N	%	95% CI
($1x10^9$ CFU/mL)	3	36/36	100	(90.4-100)
	All	**107/107**	**100**	**(96.5-100)**
Bottle Positive ($1x10^8$ 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 *Serratia marcescens*	Site	Agreement with Expected Results		
		Agreed / N	%	95% CI
Bottle Positive + 8 Hours ($1x10^9$ 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 ($1x10^8$ 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 *Serratia marcescens*	Site	Agreement with Expected Results		
		Agreed / N	%	95% CI
Bottle Positive + 8 Hours ($1x10^9$ 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 ($1x10^8$ 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 *Candida albicans*	Site	Agreement with Expected Results		
		Agreed / N	%	95% CI
Bottle Positive + 8 Hours ($1x10^7$ 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 ($1x10^6$ 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 *Staphylococcus aureus*	Site	Agreement with Expected Results		
		Agreed / N	%	95% CI
Bottle Positive + 8 Hours ($1x10^8$ 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 ($1x10^7$ 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 *Enterobacter cloacae* (CTX-M+, KPC+)	Site	Agreement with Expected Results		
		Agreed / N	%	95% CI
Bottle Positive + 8 Hours ($1x10^9$ 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 ($1x10^8$ 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 *Enterobacter cloacae* (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 *Escherichia coli* (IMP+)	Site	Agreement with Expected Results		
		Agreed / N	%	95% CI
Bottle Positive + 8 Hours ($1x10^9$ 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 ($1x10^8$ 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 *Enterobacter cloacae* (CTX-M+, KPC+)	Site	Agreement with Expected Results		
		Agreed / N	%	95% CI
Bottle Positive + 8 Hours ($1x10^9$ 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 ($1x10^8$ 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 *Acinetobacter baumannii* (OXA-23+)	Site	Agreement with Expected Results		
		Agreed / N	%	95% CI
Bottle Positive + 8 Hours ($1x10^9$ 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 ($1x10^8$ 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	143/143	100	(97.4-100)
	2	143/143	100	(97.4-100)
	3	144/144	100	(97.4-100)
	All	**430/430**	**100**	**(99.1-100)**

Table 110: Percent Agreement for VIM

Concentration of *Pseudomonas aeruginosa* (VIM+)	Site	Agreement with Expected Results		
		Agreed / N	%	95% CI
Bottle Positive + 8 Hours ($1x10^9$ 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 ($1x10^8$ 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	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)**

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
Acinetobacter baumanii	4 x 10^8 CFU/mL
Bacteroides fragilis	4 x 10^8 CFU/mL
Enterobacter aerogenes	2 x 10^8 CFU/mL
Enterobacter cloacae (CTX-M)	2 x 10^8 CFU/mL
Escherichia coli (OXA)	2 x 10^8 CFU/mL
Haemophilus influenzae	6 x 10^8 CFU/mL
Klebsiella oxytoca	9 x 10^8 CFU/mL
Neisseria meningitidis	3 x 10^7 CFU/mL
Pseudomonas aeruginosa (IMP)	1 x 10^8 CFU/mL
Serratia marcescens	1 x 10^9 CFU/mL
Staphylococcus aureus (Pan Gram-Positive target)	2 x 10^7 CFU/mL
Candida albicans (Pan Candida target)	1 x 10^6 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 10^5 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 **Table111**. 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 Pan *Candida*, *Enterobacter cloacae*, *Escherichia coli*, 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 x 10^9 CFU/mL each as well as *Candida krusei* (a Pan *Candida* target organism) at 1x10^7 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
Klebsiella pneumoniae	1 x 10^9 CFU/mL	9 x 10^8 CFU/mL
Escherichia coli (CTX-M+)	1 x 10^9 CFU/mL	2 x 10^8 CFU/mL
Enterobacter cloacae (VIM+)	7 x 10^8 CFU/mL	2 x 10^8 CFU/mL
Klebsiella oxytoca (KPC+)	1 x 10^9 CFU/mL	9 x 10^8 CFU/mL
Pseudomonas aeruginosa (IMP+)	8 x 10^8 CFU/mL	1 x 10^8 CFU/mL
Serratia marcescens	2 x 10^9 CFU/mL	1 x 10^9 CFU/mL
Staphylococcus aureus	1 x 10^8 CFU/mL	2 x 10^7 CFU/mL
Corynebacterium striatum[A]	2 x 10^9 CFU/mL	4 x 10^6 CFU/mL

A. Off-panel organism

Technical Support

Please refer to the **cobas eplex** user assistance manual for further information regarding the **cobas eplex** system.

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

GLOSSARY OF SYMBOLS

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

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DOCUMENT REVISION

Document Revision Information	
Doc Rev. 2.0 05/2025	Updated GenMark phone number. Replaced instances of “kit” with “box”. Removed GenMark and Roche mentions in “Item Number”. Removed “(optional)” in consumbles section. Added language to workflow to fill in gaps. Updated GCS information. Removed the “Troubleshooting” section. Removed “All rights reserved.” from the copyright statement. 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

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