cobas® eplex blood culture identification fungal pathogen (BCID-FP) panel

Package Insert

CE 2797 IVD UKCA

Rx Only

Designed For the Patient, Optimized For the Lab

P/N: 09556516001

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INTENDED USE

The **cobas eplex** blood culture identification fungal pathogen (BCID-FP) panel is a qualitative nucleic acid multiplex *in vitro* diagnostic test intended for use on the **cobas eplex** instrument for simultaneous detection and identification of multiple potentially pathogenic fungal organisms in positive blood culture. The **cobas eplex** BCID-FP panel is performed directly on blood culture samples identified as positive by a continuous monitoring blood culture system and which contain fungal organism.

The following fungal organisms are identified using the **cobas eplex** BCID-FP panel: *Candida albicans, Candida auris*, *Candida dubliniensis, Candida famata, Candida glabrata, Candida guilliermondii, Candida kefyr, Candida krusei, Candida lusitaniae, Candida parapsilosis, Candida tropicalis, Cryptococcus gattii, Cryptococcus neoformans, Fusarium* and *Rhodotorula*.

The detection and identification of specific 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-FP 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-FP 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-FP panel, susceptibility testing and differentiation of mixed growth) and clinical presentation must be taken into consideration in the final diagnosis of bloodstream infection.

SUMMARY AND EXPLANATION OF TEST

The **cobas eplex** BCID-FP panel is an automated qualitative nucleic acid multiplex *in vitro* diagnostic test for simultaneous detection and identification of multiple potentially pathogenic fungal organisms in positive blood culture as summarized in **Table 1**. This test is performed on *The True Sample-to-Answer Solution* **cobas eplex** instrument.

Invasive fungal infections are an increasingly common cause of sepsis in critically ill patients and are the source of significant morbidity and mortality.[1] Of the fungi with the ability to cause severe sepsis, *Candida* species are by far the most prevalent, accounting for between 8-10% of all bloodstream infections in the US and 2-3% in Europe.[1] Sepsis caused by invasive fungi is associated with high mortality rates which vary dramatically depending on the organism and underlying factors involved.

With increasing numbers of immunocompromised persons and increased use of implanted medical devices, the opportunity for infection with opportunistic pathogens is steadily increasing. This, in combination with the fact that many fungi are part of the normal human skin, vaginal and gastrointestinal flora[1] and are commonly found in the environment, has resulted in a significant increase in fungal involvement in bloodstream infections.

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

Fungal Targets	
Candida albicans	*Candida lusitaniae*
Candida auris	*Candida parapsilosis*
Candida dubliniensis	*Candida tropicalis*
Candida famata	*Cryptococcus gattii*
Candida glabrata	*Cryptococcus neoformans*
Candida guilliermondii	*Fusarium*
Candida kefyr	*Rhodotorula*
Candida krusei	

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.[2,3] 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

Candida

At least 15 *Candida* species are known to cause human disease; however, greater than 90% of invasive disease are caused by the five most common organisms: *Candida albicans, Candida glabrata, Candida krusei, Candida parapsilosis and Candida tropicalis*.[4] Additional emerging *Candida* species have been included in the **cobas eplex** BCID-FP panel due to their high likelihood of antifungal resistance and growing prevalence, especially in immuno-compromised patients. Knowing species-specific information allows for inference of drug susceptibility, which may be used to guide treatment.[5]

Candida albicans

Candida albicans commonly exists in the human intestinal tract as well as the skin and mucous membranes without causing disease.[6] In cases where *Candida albicans* is able to enter the bloodstream, it may cause fungemia. Risk factors include previous antimicrobial treatment, insertion of intravascular access devices, the presence of wounds, surgery and chemotherapy, as well as immunodeficiency.[1] *Candida albicans*, the most common of the *Candida* species, represents nearly half of clinical *Candida* isolations.[7,8]

Candida auris

Candida auris is an emerging fungal pathogen that is often multidrug resistant and can be challenging to differentiate from other organisms using conventional laboratory methods.[9] Unlike other *Candida* species, *C. auris* can persist on surfaces and spread between patients in healthcare facilities. The mortality rate for *Candida auris* has been reported between 25 and 70%.[9]

Candida dubliniensis

Candida dubliniensis appears to occur more commonly in patients with hematologic malignancies, and fluconazole resistance has been noted in some cases.[10] This species has often been misidentified as *Candida albicans* due to their phenotypic similarities.[11]

Candida famata

Candida famata is a commensal organism commonly found in dairy products and the environment. It is often misidentified as *Candida guilliermondii* due to phenotypic similarity.[12] Risk factors for bloodstream infection include immunocompromised status and the presence of central venous catheters. Studies have noted higher levels of antimicrobial resistance in cases with previous exposure to antifungals.[13]

Candida glabrata

Candida glabrata is a hyphae-forming yeast commonly isolated from the human oral cavity, respiratory tract, genitourinary tract and gastrointestinal tract[14] and ranks as the second most common cause of candidiasis.[15] *Candida glabrata* has the ability to form biofilms[14] and is distinguished from most other *Candida* species in that it has intrinsic resistance to azoles.[7,8]

Candida guilliermondii

Candida guilliermondii is an environmental fungus and common human commensal organism that is increasingly recognized as a cause of disease in immunocompromised patients.[12] This organism has been implicated in endocarditis, chronic onychomycosis and septic arthritis, as well as disseminated candidiasis.[16] *Candida guilliermondii* is intrinsically less susceptible to azoles and echinocandins.[17,18] Due to biochemical similarities, up to 67% of clinical isolates determined as *Candida famata* may be *Candida guilliermondii.* [19]

Candida kefyr

Candida kefyr thrives in a wide variety of environments including dairy products. Though incidence rates are low, this *Candida* species is emerging as a pathogen, especially in patients with neutropenia and those with hematologic malignancies.[20]

Candida krusei

Candida krusei occurs most commonly in neutropenic patients with hematologic malignancy and additional risk factors including splenectomy and exposure to antimicrobial agents with activity against anaerobes.[21] *Candida krusei* is inherently resistant to fluconazole.[22] Mortality rates due to *Candida krusei* bloodstream infection have been reported at nearly 50%.[21]

Candida lusitaniae

Candida lusitaniae is capable of inducing pyelonephritis as well as septicemia,[23] with Amphotericin B resistance distinguishing it among *Candida* species.[24]

Candida parapsilosis

Candida parapsilosis is an emerging human pathogen which, due to its high morbidity and mortality rate, is considered as relevant as *Candida albicans*.[25] It has been implicated in adhesion to prosthetics, commonly forming biofilms. *Candida parapsilosis* has been noted as an important cause of invasive fungal infections in neonates in the United Kingdom.[26] *Candida parapsilosis* may be intrinsically less sensitive to echinocandins due to naturally occurring FKS1 mutations.[17,18]

Candida tropicalis

Candida tropicalis is an emerging fungal pathogen which, along with *Candida glabrata* and *Candida parapsilosis,* has been associated with higher mortality rates in some patient populations.[27] *Candida tropicalis* shares many pathogenic traits with *Candida albicans* and is especially virulent in neutropenic patients.[28]

Cryptococcus

Cryptococcus species are found in the soil and are commonly spread via bird droppings.[29,30] The two most important *Cryptococcus* species implicated in disease are *Cryptococcus neoformans* (including var. *grubii* and var. *neoformans*), and *Cryptococcus gattii*. Opportunistic infections due to these organisms can result in sepsis or meningitis.[31] Thirty-day mortality rates as high as 37% have been reported, with up to 13% of these patients dying before culture results became available.[32]

Fusarium

Invasive fusariosis is an aggressive infection caused by species belonging to the genus *Fusarium*.[33] Fusariosis primarily affects patients with hematologic malignancies, hematopoietic cell transplant recipients,[34] patients with juvenile idiopathic arthritis and third degree burns.[33,34] Though infections usually begin in airways, they may also enter through damaged areas of the skin.[33] In patients with chronic neutropenia, the mortality rate approaches 100%.[35]

Rhodotorula

Though there are at least 46 species in the genus *Rhodotorula, Rhodotorula glutinis* and *Rhodotorula mucilaginosa* represent the most common human pathogens.[36] *Rhodotorula* species are commonly found on the skin, in urine and feces as well as in the lungs and are often associated with cancer, immunosuppression and the use of central venous catheters. *Rhodotorula mucilaginosa* is by far the most prevalent pathogenic species and represents >80% of *Rhodotorula* infections,[37] while the relative prevalence of *Rhodotorula glutinis* has been placed at ~8%. Mortality rates of over 12% have been reported for both species.[38]

PRINCIPLES OF TECHNOLOGY

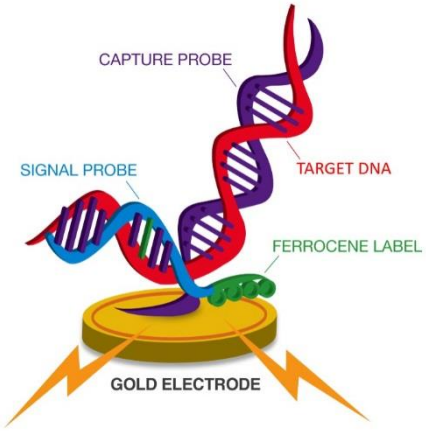
The True Sample-to-Answer Solution **cobas eplex** instrument automates all aspects of nucleic acid testing including extraction, amplification and detection, combining electrowetting and the eSensor® technology in a single-use cartridge. eSensor technology is based on the principles of competitive DNA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

Product	Item number	Components (quantity)	Storage
cobas eplex blood culture identification fungal pathogen (BCID-FP) panel	GenMark: EA005012 Roche: 9556516001	**cobas eplex** BCID-FP panel Cartridge (12)	2–8˚C

COMPOSITION OF REAGENTS

Component	Concentration (w/v)
Salting Buffer	
Guanidine hydrochloride	≤ 45%
Sodium perchlorate	≤ 14%
Binding Buffer	
PEG 8000	≤ 20%
NaH_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-FP panel kit at 2–8˚C.
- Do not use **cobas eplex** BCID-FP 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 50µL
- 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
- 1.5mL 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-FP 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 bloodstream infection.
- Do not reuse **cobas eplex** BCID-FP panel kit components.
- Do not use reagents beyond the expiration date printed on the labeling.
- Follow the procedure as described in this package insert. Read all instructions before starting the test.
- Inform your local competent authority and the manufacturer about any serious incidents which may occur when using this assay.

Safety

- Handle all specimens and waste materials as if they were capable of transmitting infectious agents in accordance with Universal Precautions. Observe safety guidelines such as those outlined in CDC/NIH *Biosafety in Microbiological and Biomedical Laboratories,* CLSI Document M29 *Protection of Laboratory Workers from Occupationally Acquired Infections*, or other appropriate guidelines.
- Follow routine laboratory safety procedures for handling of reagents (*e.g.*, do not pipette by mouth, wear appropriate protective clothing and eye protection).
- Follow your institution's safety procedures for handling biological samples.
- Dispose materials used in this test, including reagents, specimens and used vials, in accordance with all federal, state and local regulations.

- Do not stick fingers or other objects inside the **cobas eplex** instrument bays.
- Wash hands thoroughly with soap and water after handling reagents. Launder contaminated clothing prior to re-use.
- Do not puncture or pierce reagent blisters on the **cobas eplex** cartridge. Reagents may cause irritation to skin, eyes and respiratory tract. Harmful if swallowed or inhaled. Contains oxidizing liquids.
- The **cobas eplex** BCID-FP 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 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 16 months.
- Clinical specimens can be subjected to up to two freeze/thaw cycles.

PROCEDURE

PROCEDURAL NOTES

- The detection of 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 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-FP 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.
- 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.
- Once the sample is loaded onto the **cobas eplex** BCID-FP panel cartridge, the sample should be processed within 2 hours.
- 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-FP panel with 10% bleach followed by 70% ethanol or isopropyl alcohol (or equivalent).
2. Remove one **cobas eplex** BCID-FP panel cartridge pouch from kit packaging.
3. Open **cobas eplex** BCID-FP panel cartridge pouch.
4. Write the accession ID or place a barcode label with accession ID on the **cobas eplex** BCID-FP panel cartridge.
5. Invert the blood culture bottle several times to mix.
6. Allow approximately 10 seconds for the resin to settle.
7. Wipe the septum of the positive blood culture bottle with 70% ethanol or isopropyl alcohol (or equivalent) prior to withdrawing the sample.
8. Using a loading device capable of accurately delivering 50µL, aspirate 50µL of blood culture sample and load into the sample loading port of the **cobas eplex** BCID-FP panel cartridge.
   NOTE: a 1.5mL microcentrifuge tube is recommended for transfer of sample from the blood culture bottle prior to loading **cobas eplex** cartridge.
9. Close the sample loading port immediately by sliding the cap over the port and firmly pushing down on the cap to securely seal the sample delivery port.
   NOTE: Bubbles can be present when closing the cap.
10. Scan the **cobas eplex** BCID-FP panel cartridge using the barcode reader provided with the **cobas eplex** instrument.
    NOTE: If an accession ID barcode label is not used, manually enter accession ID with the on-screen keyboard.
    NOTE: The barcode scanner will read both the accession ID barcode (if placed on the cartridge by the operator) and the 2D barcode printed on the cartridge label; however, the barcode scanner will only beep once to indicate that both barcodes have been read.

11. Insert the **cobas eplex** BCID-FP 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-FP panel Reports as Internal Control with a result of PASS, FAIL, 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 BCID-FP 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 BCID-FP panel Detection Report. Test is not valid, repeat the test using a new cartridge.
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 BCID-FP 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-FP panel Detection Report

Target Result	Explanation	Action
Detected	The test was completed successfully, the target has generated signal above its defined threshold, and the Internal Control was reported as PASS.	All results are displayed on the BCID-FP panel Detection Report. Test is valid, report results.
Not Detected	The test was completed successfully, the target did not generate signal above its defined threshold, and the Internal Control was reported as PASS.	All results are displayed on the BCID-FP 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 BCID-FP panel Detection Report. Test is not valid, repeat test.

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-FP 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, or Invalid (displayed as a red **x**); results for the Internal Control are reported as PASS, FAIL, or INVALID.

External Control Report

The **cobas eplex** BCID-FP panel External Control Report is generated for an external control that has been pre-defined in the **cobas eplex** BCID-FP 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, 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.
- False results were observed for some targets using a single lot of BACT/Alert® PF Plus and BACT/Alert® FA Plus bottle types (see the **Sample Matrix Equivalency (Bottle Evaluation)** section of the package insert for additional details).
- Fungal nucleic acids may be present in blood culture, independent of viability. Detection of an assay target does not guarantee that the corresponding fungi are infectious or are the causative agents for clinical symptoms.
- The detection of 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.
- There is a risk of false negative results due to the presence of sequence variants in the fungal targets of the test.
- A result of “No Targets Detected” on the **cobas eplex** BCID-FP panel does not preclude the possibility of fungal infection. A specimen with a result of No Targets Detected may contain an organism not targeted by the **cobas eplex** BCID-FP panel.
- In mixed cultures, the **cobas eplex** BCID-FP panel may not identify all organisms in the specimen, depending upon the concentration of each target present.
- The results of the **cobas eplex** BCID-FP panel should not be used as the sole basis for diagnosis, treatment or other patient management decisions.
- 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.
- The genus level assays included as a part of the BCID-FP panel (*Fusarium*, *Rhodotorula*) are designed to detect a broad range of species but will not necessarily detect all species within a genus or group.

EXPECTED VALUES

A prospective, multicenter clinical study was conducted to evaluate the clinical performance of the **cobas eplex** BCID-FP panel in positive blood culture samples. A total of 447 positive blood culture samples were collected at 6 clinical sites in 2 phases from patients of all ages and genders. Samples were collected and frozen for future testing from May 2015 through July 2016. Samples were collected from July through August 2018 and tested fresh (never frozen). Of these 447 samples, 21 had a Gram stain result indicating fungal organism. The expected values of individual analytes based on the **cobas eplex** BCID-FP panel results in the 21 prospective samples are summarized by age group and by site in **Tables 5** and **6** below.

Table 5: Expected Value by Age Group (Prospective Samples)

Target	All Ages (N=21) n (%)	Age <1 (N=1) n (%)	Age 1-17 (N=2) n (%)	Age 18-44 (N=4) n (%)	Age 45-64 (N=11) n (%)	Age 65-84 (N=2) n (%)	Age 85+ (N=1) n (%)
Candida albicans	4 (19.0)	1 (100)	0 (0.0)	0 (0.0)	2 (18.2)	1 (50.0)	0 (0.0)
Candida auris	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Candida dubliniensis	1 (4.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (9.1)	0 (0.0)	0 (0.0)
Candida famata	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Candida glabrata	6 (28.6)	0 (0.0)	1 (50.0)	1 (25.0)	3 (27.3)	1 (50.0)	0 (0.0)
Candida guilliermondii	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Candida kefyr	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Candida krusei	2 (9.5)	0 (0.0)	0 (0.0)	0 (0.0)	2 (18.2)	0 (0.0)	0 (0.0)
Candida lusitaniae	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Candida parapsilosis	2 (9.5)	0 (0.0)	1 (50.0)	0 (0.0)	1 (9.1)	0 (0.0)	0 (0.0)
Candida tropicalis	2 (9.5)	0 (0.0)	0 (0.0)	1 (25.0)	1 (9.1)	0 (0.0)	0 (0.0)
Cryptococcus gattii	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cryptococcus neoformans	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Fusarium	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Rhodotorula	1 (4.8)	0 (0.0)	0 (0.0)	1 (25.0)	0 (0.0)	0 (0.0)	0 (0.0)

Table 6: Expected Value by Collection Site (Prospective Samples)

Target	All Sites (N=21) n (%)	Site 1 (N=1) n (%)	Site 2 (N=8) n (%)	Site 3 (N=2) n (%)	Site 4 (N=4) n (%)	Site 5 (N=4) n (%)	Site 6 (N=2) n (%)
Candida albicans	4 (19.0)	1 (100)	0 (0.0)	2 (100)	1 (25.0)	0 (0.0)	0 (0.0)
Candida auris	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Candida dubliniensis	1 (4.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (25.0)	0 (0.0)	0 (0.0)
Candida famata	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Candida glabrata	6 (28.6)	0 (0.0)	2 (25.0)	0 (0.0)	1 (25.0)	2 (50.0)	1 (50.0)
Candida guilliermondii	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Candida kefyr	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Candida krusei	2 (9.5)	0 (0.0)	2 (25.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Candida lusitaniae	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Candida parapsilosis	2 (9.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (25.0)	1 (50.0)
Candida tropicalis	2 (9.5)	0 (0.0)	2 (25.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cryptococcus gattii	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cryptococcus neoformans	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Fusarium	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Rhodotorula	1 (4.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (25.0)	0 (0.0)

PERFORMANCE CHARACTERISTICS

CLINICAL PERFORMANCE

Samples with a Gram stain result indicating fungal organism, a final, valid investigational test result, 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 11 prospective fresh and 10 prospective frozen samples as well as 120 retrospective samples and 725 contrived samples.

Comparator Method

The performance of the **cobas eplex** BCID-FP panel was compared to standard laboratory procedures, including traditional and automated culture, MALDI-TOF IVD, and microbiological and biochemical techniques. In addition, all prospective samples were tested with analytically validated PCR assays followed by bi-directional sequencing to determine the presence or absence of *Candida auris*, *Fusarium*, and *Rhodotorula*. Identification for samples with *Candida parapsilosis* identified by standard laboratory procedures was confirmed using analytically validated PCR assays followed by bi-directional sequencing.

The comparator method(s) results were used to determine the Detected / Not Detected status for each target organism on the **cobas eplex** BCID-FP panel. The comparator methods for each target are summarized in **Table 7**.

Table 7: Comparator Method(s) by cobas eplex BCID-FP panel Target

Target	Comparator Method
Candida albicans	Standard laboratory procedures for organism identification.
Candida dubliniensis	
Candida famata	
Candida glabrata	
Candida guilliermondii	
Candida kefyr	
Candida krusei	
Candida lusitaniae	
Candida tropicalis	
Cryptococcus gattii	
Cryptococcus neoformans	
Candida parapsilosis	Standard laboratory procedures for organism ID. PCR/sequencing to confirm *C. parapsilosis* or identify *C. metapsilosis, C. orthopsilosis.*
Candida auris, Fusarium, and Rhodotorula	Standard laboratory procedures for organism identification. PCR/sequencing in prospective samples.

Demographics of Clinical Samples

Clinical performance was evaluated in samples prospectively and retrospectively collected. Prospective samples were collected at 6 clinical sites, with 21 evaluable samples. Sample with final, valid, **cobas eplex** BCID-FP panel results and valid comparator results were considered evaluable. Demographic information for prospectively-collected samples is described in **Table 8.** Subjects enrolled in this study were from a diverse demographic distribution and represent the intended patient population.

To supplement the results of the prospective collection, 120 samples were collected retrospectively from a total of 9 sites, and 725 evaluable samples were contrived for organisms with low prevalence. Demographic information for retrospectively-collected samples is described in **Table 9**.

Table 8: Demographic Data for Clinical Samples by Collection Site (Prospective Collection)

	All Sites (N=21) n (%)	Site 1 (N=1) n (%)	Site 2 (N=8) n (%)	Site 3 (N=2) n (%)	Site 4 (N=4 n (%))	Site 5 (N=4) n (%)	Site 6 (N=2) n (%)
Sex, n (%)							
Male	14 (66.7)	1 (100)	7 (87.5)	1 (50.0)	3 (75.0)	1 (25.0)	1 (50.0)
Female	7 (33.3)	0 (0.0)	1 (12.5)	1 (50.0)	1 (25.0)	3 (75.0)	1 (50.0)
Age (years)							
<1 yr	1 (4.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (25.0)	0 (0.0)	0 (0.0)
1-17 yrs	2 (9.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (50.0)	0 (0.0)
18-44 yrs	4 (19.0)	0 (0.0)	2 (25.0)	0 (0.0)	1 (25.0)	1 (25.0)	0 (0.0)
45-64 yrs	11 (52.4)	1 (100)	4 (50.0)	1 (50.0)	2 (50.0)	1 (25.0)	2 (100)
65-84 yrs	2 (9.5)	0 (0.0)	1 (12.5)	1 (50.0)	0 (0.0)	0 (0.0)	0 (0.0)
85+ yrs	1 (4.8)	0 (0.0)	1 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Table 9: Demographic Data for Clinical Samples by Collection Site (Retrospective Collection)

	All Sites (N=120) n (%)	Site 1 (N=13) n (%)	Site 2 (N=14) n (%)	Site 3 (N=17) n (%)	Site 4 (N=4) n (%)	Site 5 (N=3) n (%)	Site 6 (N=13) n (%)	Site 7 (N=16) n (%)	Site 8 (N=5) n (%)	Site 9 (N=35) n (%)
Sex, n (%)										
Male	68 (56.7)	10 (76.9)	8 (57.1)	8 (47.1)	1 (25.0)	2 (66.7)	8 (61.5)	9 (56.3)	3 (60.0)	19 (54.3)
Female	52 (43.3)	3 (23.1)	6 (42.9)	9 (52.9)	3 (75.0)	1 (33.3)	5 (38.5)	7 (43.8)	2 (40.0)	16 (45.7)
Age (years)										
<1 yr	2 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (5.7)
1-17 yrs	8 (6.7)	1 (7.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	5 (38.5)	0 (0.0)	0 (0.0)	2 (5.7)
18-44 yrs	27 (22.5)	4 (30.8)	2 (14.3)	2 (11.8)	1 (25.0)	0 (0.0)	3 (23.1)	3 (18.8)	1 (20.0)	11 (31.4)
45-64 yrs	39 (32.5)	2 (15.4)	6 (42.9)	6 (35.3)	1 (25.0)	2 (66.7)	2 (15.4)	7 (43.8)	1 (20.0)	12 (34.3)
65-84 yrs	39 (32.5)	6 (46.2)	6 (42.9)	8 (47.1)	2 (50.0)	0 (0.0)	2 (15.4)	5 (31.3)	2 (40.0)	8 (22.9)
85+ yrs	5 (4.2)	0 (0.0)	0 (0.0)	1 (5.9)	0 (0.0)	1 (33.3)	1 (7.7)	1 (6.3)	1 (20.0)	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-FP panel result matched the detected comparator method result, while a TN result was one where a negative **cobas eplex** BCID-FP panel result matched a negative comparator method result. The two-sided 95% confidence interval was also calculated.

A total of 866 positive blood culture samples with a Gram stain result indicating fungal organism consisting of 11 fresh prospective, 10 frozen prospective, 120 retrospective, and 725 contrived samples were evaluated for the **cobas eplex** BCID-FP panel targets. Contrived samples were prepared by spiking an isolate into a blood culture bottle and growing until flagged positive by a continuously monitoring blood culture system. 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 10-24** below and the strains used to contrive samples are summarized in **Table 25**.

Table 10: Clinical Performance for *Candida albicans*

Target	Sample Type	Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
Candida albicans	Prospective (Fresh)	2/2	100 (34.2-100)	9/9	100 (70.1-100)
	Prospective (Frozen)	2/2	100 (34.2-100)	8/8	100 (67.6-100)
	Prospective (All)	**4/4**	**100 (51.0-100)**	**17/17**	**100 (81.6-100)**
	Retrospective	49/50	98.0 (89.5-99.6)	70/70	100 (94.8-100)
	Prospective/Retrospective	**53/54**	**98.1 (90.2-99.7)**	**87/87**	**100 (95.8-100)**
	Contrived	13/14	92.9 (68.5-98.7)	710/711	99.9 (99.2-100)
	Overall	**66/68**	**97.1 (89.9-99.2)**	**797/798**	**99.9 (99.3-100)**

CI= Confidence Interval

Table 11: Clinical Performance for *Candida auris*

Target	Sample Type	Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
Candida auris	Prospective (Fresh)	0/0	---	11/11	100 (74.1-100)
	Prospective (Frozen)	0/0	---	10/10	100 (72.2-100)
	Prospective (All)	**0/0**	**---**	**21/21**	**100 (84.5-100)**
	Retrospective	0/0	---	120/120	100 (96.9-100)
	Prospective/Retrospective	**0/0**	**---**	**141/141**	**100 (97.3-100)**
	Contrived	49/49	100 (92.7-100)	676/676	100 (99.4-100)
	Overall	**49/49**	**100 (92.7-100)**	**817/817**	**100 (99.5-100)**

Table 12: Clinical Performance for *Candida dubliniensis*

Target	Sample Type	Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
Candida dubliniensis	Prospective (Fresh)	1/1	100 (20.7-100)	10/10	100 (72.2-100)
	Prospective (Frozen)	0/0	---	10/10	100 (72.2-100)
	Prospective (All)	**1/1**	**100 (20.7-100)**	**20/20**	**100 (83.9-100)**
	Retrospective	3/3	100 (43.9-100)	117/117	100 (96.8-100)
	Prospective/Retrospective	**4/4**	**100 (51.0-100)**	**137/137**	**100 (97.3-100)**
	Contrived	48/48	100 (92.6-100)	677/677	100 (99.4-100)
	Overall	**52/52**	**100 (93.1-100)**	**814/814**	**100 (99.5-100)**

Table 13: Clinical Performance for *Candida famata*

Target	Sample Type	Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
Candida famata	Prospective (Fresh)	0/0	---	11/11	100 (74.1-100)
	Prospective (Frozen)	0/0	---	10/10	100 (72.2-100)
	Prospective (All)	**0/0**	**---**	**21/21**	**100 (84.5-100)**
	Retrospective	0/0	---	120/120	100 (96.9-100)
	Prospective/Retrospective	**0/0**	**---**	**141/141**	**100 (97.3-100)**
	Contrived	51/51	100 (93.0-100)	674/674	100 (99.4-100)
	Overall	**51/51**	**100 (93.0-100)**	**815/815**	**100 (99.5-100)**

Table 14: Clinical Performance for *Candida glabrata*

Target	Sample Type	Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
Candida glabrata	Prospective (Fresh)	4/4	100 (51.0-100)	7/7	100 (64.6-100)
	Prospective (Frozen)	2/2	100 (34.2-100)	8/8	100 (67.6-100)
	Prospective (All)	**6/6**	**100 (61.0-100)**	**15/15**	**100 (79.6-100)**
	Retrospective	37/38	97.4 (86.5-99.5)	80/82	97.6 (91.5-99.3)
	Prospective/Retrospective	**43/44**	**97.7 (88.2-99.6)**	**95/97[A]**	**97.9 (92.8-99.4)**
	Contrived	16/16	100 (80.6-100)	709/709	100 (99.5-100)
	Overall	**59/60**	**98.3 (91.1-99.7)**	**804/806**	**99.8 (99.1-99.9)**

A. *C. glabrata* was detected in 2/2 false positive clinical samples using PCR/sequencing.

Table 15: Clinical Performance for *Candida guilliermondii*

Target	Sample Type	Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
Candida guilliermondii	Prospective (Fresh)	0/0	---	11/11	100 (74.1-100)
	Prospective (Frozen)	0/0	---	10/10	100 (72.2-100)
	Prospective (All)	**0/0**	**---**	**21/21**	**100 (84.5-100)**
	Retrospective	0/0	---	120/120	100 (96.9-100)
	Prospective/Retrospective	**0/0**	**---**	**141/141**	**100 (97.3-100)**
	Contrived	49/50	98.0 (89.5-99.6)	675/675	100 (99.4-100)
	Overall	**49/50**	**98.0 (89.5-99.6)**	**816/816**	**100 (99.5-100)**

Table 16: Clinical Performance for *Candida kefyr*

Target	Sample Type	Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
Candida kefyr	Prospective (Fresh)	0/0	---	11/11	100 (74.1-100)
	Prospective (Frozen)	0/0	---	10/10	100 (72.2-100)
	Prospective (All)	**0/0**	**---**	**21/21**	**100 (84.5-100)**
	Retrospective	0/0	---	120/120	100 (96.9-100)
	Prospective/Retrospective	**0/0**	**---**	**141/141**	**100 (97.3-100)**
	Contrived	51/51	100 (93.0-100)	672/674	99.7 (98.9-99.9)
	Overall	**51/51**	**100 (93.0-100)**	**813/815**	**99.8 (99.1-99.9)**

Table 17: Clinical Performance for *Candida krusei*

Target	Sample Type	Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
Candida krusei	Prospective (Fresh)	0/0	---	11/11	100 (74.1-100)
	Prospective (Frozen)	2/2	100 (34.2-100)	8/8	100 (67.6-100)
	Prospective (All)	**2/2**	**100 (34.2-100)**	**19/19**	**100 (83.2-100)**
	Retrospective	2/2	100 (34.2-100)	118/118	100 (96.8-100)
	Prospective/Retrospective	**4/4**	**100 (51.0-100)**	**137/137**	**100 (97.3-100)**
	Contrived	46/46	100 (92.3-100)	679/679	100 (99.4-100)
	Overall	**50/50**	**100 (92.9-100)**	**816/816**	**100 (99.5-100)**

Table 18: Clinical Performance for *Candida lusitaniae*

Target	Sample Type	Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
Candida lusitaniae	Prospective (Fresh)	0/0	---	11/11	100 (74.1-100)
	Prospective (Frozen)	0/0	---	10/10	100 (72.2-100)
	Prospective (All)	**0/0**	**---**	**21/21**	**100 (84.5-100)**
	Retrospective	3/4	75.0 (30.1-95.4)	116/116	100 (96.8-100)
	Prospective/Retrospective	**3/4**	**75.0 (30.1-95.4)**	**137/137**	**100 (97.3-100)**
	Contrived	45/45	100 (92.1-100)	679/680	99.9 (99.2-100)
	Overall	**48/49**	**98.0 (89.3-99.6)**	**816/817**	**99.9 (99.3-100)**

Table 19: Clinical Performance for *Candida parapsilosis*

Target	Sample Type	Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
Candida parapsilosis	Prospective (Fresh)	2/2	100 (34.2-100)	9/9	100 (70.1-100)
	Prospective (Frozen)	0/0	---	10/10	100 (72.2-100)
	Prospective (All)	**2/2**	**100 (34.2-100)**	**19/19**	**100 (83.2-100)**
	Retrospective	16/17	94.1 (73.0-99.0)	102/103	99.0 (94.7-99.8)
	Prospective/Retrospective	**18/19**	**94.7 (75.4-99.1)**	**121/122[A]**	**99.2 (95.5-99.9)**
	Contrived	41/41	100 (91.4-100)	684/684	100 (99.4-100)
	Overall	**59/60**	**98.3 (91.1-99.7)**	**805/806**	**99.9 (99.3-100)**

A. *C. parapsilosis* was detected in 1/1 false positive clinical sample using PCR/sequencing.

Table 20: Clinical Performance for *Candida tropicalis*

Target	Sample Type	Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
Candida tropicalis	Prospective (Fresh)	0/0	---	11/11	100 (74.1-100)
	Prospective (Frozen)	2/2	100 (34.2-100)	8/8	100 (67.6-100)
	Prospective (All)	**2/2**	**100 (34.2-100)**	**19/19**	**100 (83.2-100)**
	Retrospective	3/3	100 (43.9-100)	116/117	99.1 (95.3-99.8)
	Prospective/Retrospective	**5/5**	**100 (56.6-100)**	**135/136[A]**	**99.3 (96.0-99.9)**
	Contrived	45/45	100 (92.1-100)	680/680	100 (99.4-100)
	Overall	**50/50**	**100 (92.9-100)**	**815/816**	**99.9 (99.3-100)**

A. *C. tropicalis* was detected in 1/1 false positive clinical sample using PCR/sequencing.

Table 21: Clinical Performance for *Cryptococcus gattii*

Target	Sample Type	Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
Cryptococcus gattii	Prospective (Fresh)	0/0	---	11/11	100 (74.1-100)
	Prospective (Frozen)	0/0	---	10/10	100 (72.2-100)
	Prospective (All)	**0/0**	**---**	**21/21**	**100 (84.5-100)**
	Retrospective	0/0	---	120/120	100 (96.9-100)
	Prospective/Retrospective	**0/0**	**---**	**141/141**	**100 (97.3-100)**
	Contrived	50/50	100 (92.9-100)	675/675	100 (99.4-100)
	Overall	**50/50**	**100 (92.9-100)**	**816/816**	**100 (99.5-100)**

Table 22: Clinical Performance for *Cryptococcus neoformans*

Target	Sample Type	Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
Cryptococcus neoformans	Prospective (Fresh)	0/0	---	11/11	100 (74.1-100)
	Prospective (Frozen)	0/0	---	10/10	100 (72.2-100)
	Prospective (All)	**0/0**	**---**	**21/21**	**100 (84.5-100)**
	Retrospective	5/5	100 (56.6-100)	115/115	100 (96.8-100)
	Prospective/Retrospective	**5/5**	**100 (56.6-100)**	**136/136**	**100 (97.3-100)**
	Contrived	52/52	100 (93.1-100)	673/673	100 (99.4-100)
	Overall	**57/57**	**100 (93.7-100)**	**809/809**	**100 (99.5-100)**

Table 23: Clinical Performance for *Fusarium*

Target	Sample Type	Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
Fusarium	Prospective (Fresh)	0/0	---	11/11	100 (74.1-100)
	Prospective (Frozen)	0/0	---	10/10	100 (72.2-100)
	Prospective (All)	**0/0**	**---**	**21/21**	**100 (84.5-100)**
	Retrospective	0/0	---	120/120	100 (96.9-100)
	Prospective/Retrospective	**0/0**	**---**	**141/141**	**100 (97.3-100)**
	Contrived	69/70	98.6 (92.3-99.7)	655/655	100 (99.4-100)
	Overall	**69/70**	**98.6 (92.3-99.7)**	**796/796**	**100 (99.5-100)**

Table 24: Clinical Performance for *Rhodotorula*

Target	Sample Type	Sensitivity/PPA		Specificity/NPA	
		TP/TP+FN	% (95% CI)	TN/TN+FP	% (95% CI)
Rhodotorula	Prospective (Fresh)	1/1	100 (20.7-100)	10/10	100 (72.2-100)
	Prospective (Frozen)	0/0	---	10/10	100 (72.2-100)
	Prospective (All)	**1/1**	**100 (20.7-100)**	**20/20**	**100 (83.9-100)**
	Retrospective	1/1	100 (20.7-100)	119/119	100 (96.9-100)
	Prospective/Retrospective	**2/2**	**100 (34.2-100)**	**139/139**	**100 (97.3-100)**
	Contrived	48/50	96.0 (86.5-98.9)	674/675	99.9 (99.2-100)
	Overall	**50/52**	**96.2 (87.0-98.9)**	**813/814**	**99.9 (99.3-100)**

Table 25: Contrived Sample Summary

Target	Organism	Strain	Independent Contrived Samples Tested
Candida albicans	*Candida albicans*	ATCC 10231	2
		ATCC 14053	2
		ATCC 24433	2
		ATCC 90028	5
		ATCC MYA-4441	3
	Candida albicans total		14
Candida auris	*Candida auris*	ATCC 10913	1
		ATCC 12372	1
		ATCC 12766	1
		CBS 10913	3
		CBS 12372	3
		CBS 12373	2
		CBS 12766	3
		CBS 12767	3
		CBS 12768	2
		CDC#0385	5
		CDC#0386	5
		CDC#0387	5
		CDC#0388	5
		CDC#0389	5
		CDC#0390	5
	Candida auris total		49
Candida dubliniensis	*Candida dubliniensis*	ATCC MYA-577	6
		ATCC MYA-578	12
		ATCC MYA-579	12
		ATCC MYA-582	13
		NCPF3949	5
	Candida dubliniensis total		48
Candida famata	*Debaryomyces fabryi*	CBS 789	21
	Debaryomyces hansenii	CBS 1961	3
	Debaryomyces subglobosus	CBS 1796	27
	Candida famata total		51
Candida glabrata	*Candida glabrata*	128-4058	1
		128-4072	1
		ATCC 15126	2
		ATCC 15545	2
		ATCC 2001	1
		ATCC 66032	4
		ATCC 90030	2
		ATCC MYA-2950	3
	Candida glabrata total		16

Target	Organism	Strain	Independent Contrived Samples Tested
Candida guilliermondii	*Candida guilliermondii*	ATCC 22017	13
		ATCC 6260	12
	Meyerozyma guilliermondii	ATCC 90197	10
		ATCC 90198	9
		ATCC 90199	6
	Candida guilliermondii total		50
Candida kefyr	*Candida kefyr*	ATCC 204093	4
		ATCC 2512	10
		ATCC 4135	13
		ATCC 66028	12
		ATCC 8553	12
	Candida kefyr total		51
Candida krusei	*Candida krusei*	ATCC 14243	8
		ATCC 22985	9
		ATCC 28870	9
		ATCC 32196	10
		ATCC 34135	10
	Candida krusei total		46
Candida lusitaniae	*Candida lusitaniae*	ATCC 26287	5
		ATCC 34449	10
		ATCC 42720	9
		ATCC 66035	11
		ATCC MYA-766	10
	Candida lusitaniae total		45
Candida parapsilosis	*Candida parapsilosis*	ATCC 22019	11
		ATCC 28474	5
		ATCC 28475	10
		ATCC 58895	7
		ATCC 90018	8
	Candida parapsilosis total		41
Candida tropicalis	*Candida tropicalis*	ATCC 1369	9
		ATCC 13803	12
		ATCC 201380	9
		ATCC 201381	7
		ATCC 750	8
	Candida tropicalis total		45
Cryptococcus gattii	*Cryptococcus gattii*	ATCC 14248	11
		ATCC 76108	12
		ATCC MYA-4138	10
		ATCC MYA-4560	8
		ATCC MYA-4877	9
	Cryptococcus gattii total		50

Target	Organism	Strain	Independent Contrived Samples Tested
Cryptococcus neoformans	*Cryptococcus neoformans* var. *grubii*	ATCC 14116	9
		ATCC 208821(H99)	8
		ATCC 90112	7
		NCPF8195	7
		NCPF8299	3
		NCPF8357	3
	Cryptococcus neoformans var. *neoformans* (*Filobasidiella bacillispora* Kwon-Chung, teleomorph (serotype D))	ATCC 34873	3
	Cryptococcus neoformans var. *neoformans* (serotype D)	ATCC 36556	3
		ATCC MYA-565	9
	Cryptococcus neoformans total		52
Fusarium	*Bisifusarium dimerum*	CBS 108944	3
		CBS 110317	9
		CBS 116520	3
	Fusarium moniliforme	ATCC 38159	11
	Fusarium oxysporum	CBS 116611	1
	Fusarium sacchari	ATCC 24379	10
		CBS 119828	11
	Fusarium solani	ATCC 36031	11
	Fusarium verticillioides	CBS 100312	11
	Fusarium total		70
Rhodotorula	*Rhodotorula glutinis*	ATCC 32765	3
		ATCC 32766	3
	Rhodotorula glutinis (Fresenius) Harrison	ATCC 96365	4
	Rhodotorula mucilaginosa	ATCC 66034	21
		ATCC 9449	19
	Rhodotorula total		50

Genus Assay Species Stratification

The **cobas eplex** BCID-FP panel reports genus level results for *Fusarium* and *Rhodotorula* targets. Sensitivity/PPA of these genus and group level targets for species from all clinical and contrived samples tested are summarized in **Table 26** below.

Table 26: Species Detected by Genus Assays

Target Species Detected	All Samples	
	Sensitivity/PPA	
	TP/TP+FN	% (95% CI)
Fusarium	**69/70**	**98.6 (92.3-99.7)**
Bisifusarium dimerum	14/15	93.3 (70.2-98.8)
Fusarium moniliforme	11/11	100 (74.1-100)
Fusarium oxysporum	1/1	100 (20.7-100)
Fusarium sacchari	21/21	100 (84.5-100)
Fusarium solani	11/11	100 (74.1-100)
Fusarium verticillioides	11/11	100 (74.1-100)
Rhodotorula	**50/52**	**96.2 (87.0-98.9)**
*Rhodotorula**	2/2	100 (34.2-100)
Rhodotorula glutinis	6/6	100 (61.0-100)
Rhodotorula glutinis (Fresenius) Harrison	4/4	100 (51.0-100)
Rhodotorula mucilaginosa	38/40	95.0 (83.5-98.6)

*Results are from 2 clinical samples (1 prospective, 1 retrospective). All other *Fusarium* and *Rhodotorula* samples were contrived.

Co-detections in Clinical Samples

The **cobas eplex** BCID-FP panel did not identify any fungal co-detections in prospective samples, and 6 fungal co-detections were identified in the retrospective samples. Of the 120 retrospective samples, 114 (95.0%) had single detections and 6 (5.0%) had double detections. In the 6 co-detections, 4 included 1 organism that comparator method(s) did not detect. See **Table 27** below for a summary of co-detections in retrospective samples.

Table 27: Co-Detections Identified by the cobas eplex BCID-FP panel (Retrospective Samples)

Distinct Organism Combinations Detected by the **cobas eplex** panel **in Retrospective Samples**		Number of Samples (Number Discrepant)	Discrepant Organism(s)[A,B]
Target 1	Target 2		
Candida albicans	*Candida dubliniensis*	1 (0)	
Candida albicans	*Candida parapsilosis*	1 (0)	
Candida dubliniensis	*Candida parapsilosis*	1 (1)	*C. parapsilosis* (1)
Candida dubliniensis	*Candida tropicalis*	1 (1)	*C. tropicalis* (1)
Candida glabrata	*Candida lusitaniae*	2 (2)	*C. glabrata* (2)

A. A discrepant organism is defined as one that was detected by the BCID-FP panel but not by the comparator method(s).
B. 4/4 organisms were investigated using PCR/sequencing and the discrepant organism was detected in 4/4 cases.
   i. In 1/1 sample, *C. parapsilosis* was detected.
   ii. In 1/1 sample, *C. tropicalis* was detected.
   iii. In 2/2 samples, *C. glabrata* was detected.

Summaries of additional distinct fungal co-detections detected by the comparator method in prospective and retrospective samples are provided in **Table 28** and **Table 29**. These tables include additional distinct fungal co-detections not included in the co-detections identified by the BCID-FP panel; they have 1 or more organism not detected by the BCID-FP panel or an off-panel fungal organism.

Table 28: Co-Detections Identified by the Comparator Method (Prospective Samples)

Distinct Organism Combinations Detected by the Comparator Method in Prospective Samples		Number of Samples (Number Discrepant)	Discrepant Organism(s)[A]
Target 1	Target 2		
*Candida metapsilosis**	*Trichosporon asahii**	1 (0)	

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

* Off-panel organism not targeted by the BCID-FP panel.

Table 29: Co-Detections Identified by the Comparator Method (Retrospective Samples)

Distinct Organism Combinations Detected by the Comparator Method in Retrospective Samples			Number of Samples (Number Discrepant)	Discrepant Organism(s)[A]
Target 1	Target 2	Target 3		
Candida albicans	*Candida dubliniensis*	*Candida glabrata*	1 (1)	*C. glabrata* (1)
Candida albicans	*Candida parapsilosis*		1 (1)	*C. parapsilosis* (1)

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

Clinical Study cobas eplex instrument Performance

A total of 867 samples (including prospective, retrospective, and contrived samples) were initially tested in the clinical evaluations. Of these, 7/867 (0.8%) did not complete the run and the sample was retested. After repeat testing, all 867 samples completed testing and 839/867 (96.8%, 95% CI: 95.4%-97.8%) generated valid results and 28/867 (3.2%, 95% CI: 2.2%-4.6%) generated invalid results on the first completed attempt.

Upon repeat testing of the 28 samples with initially invalid results, all completed the run and 27/28 (96.4%) generated valid results. Overall, after final testing, 1/867 (0.1%, 95% CI: 0.0%-0.7%) had final, invalid results, resulting in a final validity rate of 866/867 (99.9%, 95% CI: 99.3%-100%).

ANALYTICAL PERFORMANCE CHARACTERISTICS

Limit of Detection (Analytical Sensitivity)

The Limit of Detection (LOD), or analytical sensitivity, was identified and verified for each assay on the BCID-FP panel using at least two 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-FP panel organism is shown in **Table 30**.

Table 30: LOD Results Summary

Target	Organism	Strain	LOD Concentration (CFU/mL)
Candida albicans	*Candida albicans*	ATCC 14053	1×10^6
	Candida albicans	ATCC 24433	1×10^5
Candida auris	*Candida auris*	CBS 10913	1×10^5
	Candida auris	CBS 12766	1×10^5
Candida dubliniensis	*Candida dubliniensis*	ATCC MYA-577	1×10^4
	Candida dubliniensis	NCPF 3949	1×10^5
Candida famata	*Candida famata*	CBS 767	1×10^3
	Candida famata	CBS 766	1×10^4
Candida glabrata	*Candida glabrata*	ATCC 2001	1×10^6
	Candida glabrata	ATCC 15545	1×10^6
Candida guilliermondii	*Candida guilliermondii*	ATCC 22017	1×10^5
	Candida guilliermondii	ATCC 6260	1×10^5
Candida kefyr	*Candida kefyr*	ATCC 4135	1×10^3
	Candida kefyr	ATCC 8553	1×10^4
Candida krusei	*Candida krusei*	ATCC 22985	1×10^5
	Candida krusei	ATCC 28870	1×10^6
Candida lusitaniae	*Candida lusitaniae*	ATCC 34449	1×10^6
	Candida lusitaniae	ATCC 66035	1×10^5
Candida parapsilosis	*Candida parapsilosis*	ATCC 28474	1×10^4
	Candida parapsilosis	ATCC 28475	1×10^5
Candida tropicalis	*Candida tropicalis*	ATCC 13803	1×10^5
	Candida tropicalis	ATCC 1369	1×10^6
Cryptococcus gattii	*Cryptococcus gattii*	ATCC MYA-4877	1×10^3
	Cryptococcus gattii	ATCC MYA-4138	1×10^3
Cryptococcus neoformans	*Cryptococcus neoformans*	ATCC 208821	1×10^5
	Cryptococcus neoformans	ATCC MYA-565	1×10^5
Fusarium	*Fusarium oxysporum*	CBS 116611	1×10^6 spores/mL
	Fusarium solani	ATCC 36301	1×10^6 spores/mL
Rhodotorula	*Rhodotorula mucilaginosa*	ATCC 4058	1×10^5
	Rhodotorula glutinis	ATCC 32765	1×10^5

Analytical Reactivity (Inclusivity)

A panel of 51 strains/isolates, representing the genetic, temporal and geographic diversity of each target on the **cobas eplex** BCID-FP panel was evaluated to demonstrate analytical reactivity. Each strain was tested in triplicate at concentrations approximating bottle positivity (1×10^6 CFU/mL for *Candida* and *Rhodotorula*, 1×10^7 CFU/mL for *Cryptococcus*, and 1×10^8 spores/mL for *Fusarium*). All organisms tested were detected at bottle positive concentrations. Results of the analytical reactivity are summarized in **Table 31**. An additional 29 unique strains were detected as a part of the **Limit of Detection (Analytical Sensitivity)** study and are summarized in **Table 30**.

Table 31: Analytical Reactivity (Inclusivity) Results

Target	Organism	Strain
Candida albicans	*Candida albicans*	ATCC 10231
	Candida albicans	ATCC 90028
	Candida albicans	ATCC MYA-4441
Candida auris	*Candida auris*	CDC#385
	Candida auris	CDC#386
	Candida auris	CDC#387
	Candida auris	CDC#388
	Candida auris	CDC#389
	Candida auris	CDC#390
	Candida auris	CBS 12766
Candida dubliniensis	*Candida dubliniensis*	ATCC MYA-578
	Candida dubliniensis	ATCC MYA-579
	Candida dubliniensis	ATCC MYA-582
Candida famata	*Candida famata*	ATCC 20850
	Candida famata	CBA 1961
	Candida famata	CBS 789
Candida glabrata	*Candida glabrata*	ATCC 15126
	Candida glabrata	ATCC 66032
	Candida glabrata	ATCC MYA-2950
Candida guilliermondii	*Candida guilliermondii*	ATCC 90197
	Candida guilliermondii	ATCC 90198
	Candida guilliermondii	ATCC 90199
Candida kefyr	*Candida kefyr*	ATCC 204093
	Candida kefyr	ATCC 2512
	Candida kefyr	ATCC 66028
Candida krusei	*Candida krusei*	ATCC 14243
	Candida krusei	ATCC 32196
	Candida krusei	ATCC 34135
Candida lusitaniae	*Candida lusitaniae*	ATCC 42720
	Candida lusitaniae	ATCC MYA-766
	Candida lusitaniae	Z010
Candida parapsilosis	*Candida parapsilosis*	ATCC 22019
	Candida parapsilosis	ATCC 58895
	Candida parapsilosis	ATCC 90018
Candida tropicalis	*Candida tropicalis*	ATCC 201380
	Candida tropicalis	ATCC 201381
	Candida tropicalis	ATCC 750
Cryptococcus gattii	*Cryptococcus gattii*	ATCC 14248
	Cryptococcus gattii	ATCC 4560
	Cryptococcus gattii	ATCC 76108

Target	Organism	Strain
Cryptococcus neoformans	*Cryptococcus neoformans*	ATCC 14116
	Cryptococcus neoformans	ATCC 90112
	Cryptococcus neoformans	NCPF 8299
Fusarium	*Bisifusarium dimerum*	CBS 110317
	Fusarium moniliforme	ATCC 38159
	Fusarium proliferatum	CBS 131570
	Fusarium sacchari	CBS 119828
	Fusarium verticillioides	CBS 100312
Rhodotorula	*Rhodotorula glutinis*	ATCC 96365
	Rhodotorula mucilaginosa	ATCC 66034
	Rhodotorula mucilaginosa	ATCC 9449

Predicted (*in silico*) Reactivity for Genus Assays

Note: the performance of the cobas eplex BCID-FP panel has not been established for all of the organisms listed in the tables below. See the Analytical Reactivity (Inclusivity) and Limit of Detection (Analytical Sensitivity) sections of the package insert for data on organisms for which performance characteristics have been established (indicated with an asterisk in Tables 32 and 33). Some species were not assessed *in silico* due to lack of sequence data, though they may appear in the analytical sensitivity or specificity studies.

In addition to species-specific assays, the **cobas eplex** BCID-FP panel contains two broader genus-level assays: *Fusarium* and *Rhodotorula.* **Table 32** and **Table 33** highlight the predicted (*in silico*) reactivity (inclusivity) for these assay targets.

Table 32: Predicted (*in silico*) Reactivity (Inclusivity) Results for *Fusarium*

Detection Predicted for ≥95% of target sequences		
Fusarium acaciae-mearnsii	*Fusarium cortaderiae*	*Fusarium musae*
Fusarium acuminatum	*Fusarium culmorum*	*Fusarium napiforme*
Fusarium acutatum	*Fusarium denticulatum*	*Fusarium nisikadoi*
Fusarium aethiopicum	*Bisifusarium dimerum**	*Fusarium nygamai*
Fusarium ananatum	*Fusarium dlaminii*	*Fusarium oxysporum**
Fusarium andiyazi	*Fusarium equiseti*	*Fusarium palustre*
Fusarium anthophilum	*Fusarium falciforme*	*Fusarium phyllophilum*
Fusarium armeniacum	*Fusarium foetens*	*Fusarium poae*
Fusarium asiaticum	*Fusarium fujikuroi*	*Fusarium polyphialidicum*
Fusarium austroamericanum	*Fusarium gaditjirri*	*Fusarium proliferatum**
Fusarium avenaceum	*Fusarium globosum*	*Fusarium pseudoanthophilum*
Fusarium aywerte	*Fusarium graminearum*	*Fusarium pseudocircinatum*
Fusarium bactridioides	*Fusarium guttiforme*	*Fusarium pseudograminearum*
Fusarium begoniae	*Fusarium hostae*	*Fusarium pseudonygamai*
Fusarium beomiforme	*Fusarium incarnatum*	*Fusarium ramigenum*
Fusarium boothii	*Fusarium inflexum*	*Fusarium sacchari**

Fusarium brachygibbosum	*Fusarium konzum*	*Fusarium secorum*
Fusarium brasilicum	*Fusarium lacertarum*	*Fusarium sinensis*
Fusarium brevicatenulatum	*Fusarium lactis*	*Fusarium solani**
Fusarium bulbicola	*Fusarium langsethiae*	*Fusarium sporotrichioides*
Fusarium bullatum	*Fusarium lichenicola (Cylindrocarpon lichenicola)*	*Fusarium sterilihyphosum*
Fusarium camptoceras	*Fusarium louisianense*	*Fusarium subglutinans*
Fusarium cerealis	*Fusarium lunulosporum*	*Fusarium temperatum*
Fusarium circinatum	*Fusarium mangiferae*	*Fusarium thapsinum*
Fusarium commune	*Fusarium meridionale*	*Fusarium udum*
Fusarium concentricum	*Fusarium mesoamericanum*	*Fusarium verticillioides**
Fusarium concolor	*Fusarium mexicanum*	
Detection Predicted for 85%-94% of target sequences		
Fusarium torulosum		
Detection Predicted for <85% of target sequences		
Fusarium chlamydosporum (66.7%)	*Fusarium lateritium* (50.0%)	*Fusarium nelsonii* (16.7%)
Fusarium coeruleum (50.0%)	*Fusarium longipes* (25.0%)	*Fusarium xylarioides* (81.8%)
Detection Not Predicted		
Fusarium kyushuense	*Fusarium sambucinum*	*Fusarium venenatum*
Fusarium miscanthi	*Fusarium stilboides*	
Fusarium redolens	*Fusarium succisae*	

Table 33: Predicted (*in silico*) Reactivity (Inclusivity) Results for *Rhodotorula*

Detection Predicted for ≥95% of target sequences		
Rhodotorula araucariae	*Rhodotorula graminis*	*Rhodotorula taiwanensis*
*Rhodotorula glutinis**	*Rhodotorula mucilaginosa**	
Detection Predicted for 85%-94% of target sequences		
None Identified		
Detection Predicted for <85% of target sequences		
None Identified		
Detection Not Predicted		
Rhodotorula acheniorum	*Rhodotorula fragariae*	*Rhodotorula marina*
Rhodotorula acuta	*Rhodotorula fujisanensis*	*Rhodotorula minuta*
Rhodotorula armeniaca	*Rhodotorula hinnulea*	*Rhodotorula muscorum*
Rhodotorula aurantiaca	*Rhodotorula hordea*	*Rhodotorula nothofagi*
Rhodotorula auriculariae	*Rhodotorula hylophila*	*Rhodotorula philyla*
Rhodotorula bacarum	*Rhodotorula ingeniosa*	*Rhodotorula phylloplana*
Rhodotorula bogoriensis	*Rhodotorula javanica*	*Rhodotorula pilati*
Rhodotorula buffonii	*Rhodotorula lactosa*	*Rhodotorula pustula*
Rhodotorula ferulica	*Rhodotorula lignophila*	*Rhodotorula sonckii*

Analytical Specificity (Cross-Reactivity and Exclusivity)

Cross-reactivity of on-panel and off-panel analytes was evaluated with the BCID-FP panel. On-panel organisms were tested in triplicate at concentrations approximating bottle positivity (see **Analytical Reactivity (Inclusivity)** section of the package insert for additional details). Off-panel organisms were tested at concentrations of ≥1x10^9 CFU/mL for bacteria and ≥1x10^7 CFU/mL or spores/mL for fungi unless otherwise noted in **Table 34**. If the target concentration could not be reached, the organism was diluted 2-fold from stock for use.

No cross reactivity was observed for any of the organisms tested. See **Table 34** for a summary of the on-panel strains tested and **Table 35** for a summary of off-panel strains tested.

On-panel Exclusivity

Table 34: On-panel Organisms Assessed for Cross-reactivity with the cobas eplex BCID-FP panel (Exclusivity)

Organism	Strain
Candida albicans	ATCC 10231
Candida albicans	ATCC 90028
Candida albicans	ATCC MYA-4441
Candida auris	CBS 12766
Candida auris	CDC#385
Candida auris	CDC#386
Candida auris	CDC#387
Candida auris	CDC#388
Candida auris	CDC#389
Candida auris	CDC#390
Candida dubliniensis	ATCC MYA-578
Candida dubliniensis	ATCC MYA-579
Candida dubliniensis	ATCC MYA-582
Candida famata	ATCC 20850
Candida famata	CBA 1961
Candida famata	CBS 789
Candida glabrata	ATCC 15126
Candida glabrata	ATCC 66032
Candida glabrata	ATCC MYA-2950
Candida guilliermondii	ATCC 90197
Candida guilliermondii	ATCC 90198
Candida guilliermondii	ATCC 90199
Candida kefyr	ATCC 204093
Candida kefyr	ATCC 2512
Candida kefyr	ATCC 66028
Candida krusei	ATCC 14243
Candida krusei	ATCC 32196
Candida krusei	ATCC 34135
Candida lusitaniae	ATCC 42720
Candida lusitaniae	ATCC MYA-766
Candida lusitaniae	Z010
Candida parapsilosis	ATCC 22019
Candida parapsilosis	ATCC 58895
Candida parapsilosis	ATCC 90018
Candida tropicalis	ATCC 201380
Candida tropicalis	ATCC 201381
Candida tropicalis	ATCC 750
Cryptococcus gattii	ATCC 14248
Cryptococcus gattii	ATCC 4560
Cryptococcus gattii	ATCC 76108
Cryptococcus neoformans	ATCC 14116
Cryptococcus neoformans	ATCC 90112
Cryptococcus neoformans	NCPF 8299
Bisifusarium dimerum	CBS 110317
Fusarium lichenicola (Cylindrocarpon lichenicola)	ATCC 204306
Fusarium moniliforme	ATCC 38159
Fusarium proliferatum	CBS 131570
Fusarium sacchari	CBS 119828
Fusarium verticillioides	CBS 100312
Rhodotorula glutinis	ATCC 96365
Rhodotorula mucilaginosa	ATCC 66034
Rhodotorula mucilaginosa	ATCC 9449

Off-panel Exclusivity

Table 35: Off-panel Organisms Assessed for Cross-Reactivity with the cobas eplex BCID-FP panel (Exclusivity)

Organism	Strain
Acinetobacter Iwoffii	ATCC 15309
Acremonium kiliense	ATCC 4301
Aspergillus fumigatus	ATCC 204305[A]
Bacteroides fragilis	ATCC 25285
Bordetella pertussis	ATCC 9340
Candida bracarensis	CBS 10154
Candida carpophila	CBS 5256
Candida duobushaemulonii	CDC#394
Candida haemulonii	CDC#393
Candida inconspicua	ATCC 16783
Candida lambica	ATCC 24750
Candida lipolytica	ATCC 20177
Candida metapsilosis	ATCC 96144
Candida nivariensis	CBS 9984
Candida norvegensis	ATCC 22977
Candida orthopsilosis	ATCC 96139
Candida pelliculosa	ATCC 10262
Candida rugosa	CBS 96275
Candida sake	ATCC 22021
Candida utilis	ATCC 9256
Citrobacter freundii	ATCC 6879
Clostridium perfringens	ATCC 13124
Corynebacterium striatum	ATCC 7094
Enterobacter aerogenes	ATCC 29751
Enterobacter cloacae	ATCC 23373
Enterococcus faecium	ATCC 31282
Exophiala jeanselmei	ATCC 12734
Filobasidium elegans	CBS 7637
Filobasidium globisporum	CBS 7642
Klebsiella oxytoca	ATCC 43165
Kluyveromyces lactis	ATCC 10689
Kodamaea ohmeri	CDC#0396
Lactobacillus rhamnosus	ATCC 53103
Malassezia furfur	ATCC 12078
Malassezia furfur	ATCC 14521
Malassezia furfur	CBS 7710
Malassezia globosa	ATCC MYA-4612
Malassezia restricta	ATCC MYA-4611
Malassezia sympodialis	ATCC 44031
Meyerozyma caribbica (Candida fermentati)	ATCC 20296
Micrococcus luteus	ATCC 19212
Morganella morganii	ATCC 25830
Mucor velutinosus	ATCC MYA-4766
Penicillium marneffei	ATCC 200050
Proteus mirabilis	ATCC 35659
Rhodotorula minuta	ATCC 36236
Saccharomyces cerevisiae	ATCC 18824
Salmonella enterica (Typhi)	ATCC 19430
Scedosporium prolificans	ATCC 200543
Schizosaccharomyces pombe	LPY 02387
Serratia marcescens	ATCC 43861
Sporidiobolus salmonicolor	ATCC 24217
Sporothrix schenckii	ATCC 18616
Staphylococcus hominis	ATCC 27844
Staphylococcus intermedius	ATCC 29663
Staphylococcus saprophyticus	ATCC 15305
Streptococcus agalactiae	ATCC 12401
Streptococcus anginosus	ATCC 9895
Streptococcus pyogenes	ATCC 12384
Trichosporon asahii	ATCC 201110
Trichosporon asteroides	ATCC 90043
Trichosporon dermatis	ATCC 204094

A. Tested at 1 x 10^6 spores/mL

Bottle Positivity

Several representative 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 were quantified for each organism on culture plates. Organisms tested and approximate bottle positivity concentrations are summarized in **Table 36**. 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-FP panel.

Table 36: Bottle Positivity Concentrations

Organism	Strain ID	Mean Bottle Positivity Concentration	Mean Bottle Positivity +8 hours Concentration
Candida albicans	ATCC 90082	1.6 x 10^6 CFU/mL	1.4 x 10^6 CFU/mL
Cryptococcus neoformans var. grubii	ATCC 14116	1.3 x 10^7 CFU/mL	6.5 x 10^7 CFU/mL
Fusarium solani	ATCC 36031	9.6 x 10^6 spores/mL	7.7 x 10^6 spores/mL
Rhodotorula mucilaginosa	ATCC 66034	1.6 x 10^6 CFU/mL	4.2 x 10^6 CFU/mL

Reproducibility

Two positive mixes including 5 on-panel organisms at two concentrations and one negative mix including an off-panel organism were tested. Concentrations in the positive mixes reflected those observed at time of bottle positivity (BP) and time of bottle positivity plus 8 hours or one log higher than that expected at bottle positivity (BP+8) and one mix containing an off-panel organism grown to bottle positivity, which is expected to yield a negative result. Bottle concentrations used in this study are summarized in **Table 37**. Testing occurred at three sites, with two operators testing the mixes over six days using three cartridge lots.

Table 37: Bottle Positivity Concentrations

Organism	Bottle Positivity Concentration	Bottle Positivity +8 Hours Concentration
Candida albicans	1 x 10^6 CFU/mL	1 x 10^7 CFU/mL
Candida kefyr	1 x 10^6 CFU/mL	1 x 10^7 CFU/mL
Cryptococcus neoformans	1 x 10^7 CFU/mL	1 x 10^8 CFU/mL
Fusarium sacchari	6.5 x10^6 spores/mL	6.1 x10^6 spores/mL
Rhodotorula mucilaginosa	1 x 10^6 CFU/mL	1 x 10^7 CFU/mL

The percent agreement of each target with the expected result is summarized in **Tables 38-42.**

Table 38: Percent Agreement for *Candida albicans*

Concentration of *Candida albicans*	Site	Agreement with Expected Results		
		Agreed / N	%	95% CI
Bottle Positive + 8 Hours ($1x10^7$ CFU/mL)	1	34/35	97.1	(85.5-99.5)
	2	35/36	97.2	(85.8-99.5)
	3	36/36	100	(90.4-100)
	All	**105/107**	**98.1**	**(93.4-99.5)**
Bottle Positive ($1x10^6$ 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	108/108	100	(96.6-100)
	2	108/108	100	(96.6-100)
	3	108/108	100	(96.6-100)
	All	**324/324**	**100**	**(98.8-100)**

Table 39: Percent Agreement for *Candida kefyr*

Concentration of *Candida kefyr*	Site	Agreement with Expected Results		
		Agreed / N	%	95% CI
Bottle Positive + 8 Hours ($1x10^7$ 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)**
Bottle Positive ($1x10^6$ 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	107/107	100	(96.5-100)
	2	108/108	100	(96.6-100)
	3	108/108	100	(96.6-100)
	All	**323/323**	**100**	**(98.8-100)**

Table 40: Percent Agreement for *Cryptococcus neoformans*

Concentration of *Cryptococcus neoformans*	Site	Agreement with Expected Results		
		Agreed / N	%	95% CI
Bottle Positive + 8 Hours ($1x10^8$ 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)**
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	108/108	100	(96.6-100)
	2	108/108	100	(96.6-100)
	3	108/108	100	(96.6-100)
	All	**324/324**	**100**	**(98.8-100)**

Table 41: Percent Agreement for *Fusarium*

Concentration of *Fusarium sacchari*	Site	Agreement with Expected Results		
		Agreed / N	%	95% CI
Bottle Positive + 8 Hours ($6.1x10^6$ spores/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 ($6.5x10^6$ spores/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	107/107	100	(96.5-100)
	2	108/108	100	(96.6-100)
	3	108/108	100	(96.6-100)
	All	**323/323**	**100**	**(98.8-100)**

Table 42: Percent Agreement for *Rhodotorula*

Concentration of *Rhodotorula mucilaginosa*	Site	Agreement with Expected Results		
		Agreed / N	%	95% CI
Bottle Positive + 8 Hours ($1x10^7$ CFU/mL)	1	36/36	100	(90.4-100)
	2	34/36	94.4	(81.9-98.5)
	3	35/36	97.2	(85.8-99.5)
	All	**105/108**	**97.2**	**(92.1-99.1)**
Bottle Positive ($1x10^6$ CFU/mL)	1	35/36	97.2	(85.8-99.5)
	2	36/36	100	(90.4-100)
	3	35/36	97.2	(85.8-99.5)
	All	**106/108**	**98.1**	**(93.5-99.5)**
Negative	1	107/107	100	(96.5-100)
	2	108/108	100	(96.6-100)
	3	108/108	100	(96.6-100)
	All	**323/323**	**100**	**(98.8-100)**

Interfering Substances and Sample Matrix Equivalency (Bottle Evaluation)

Two organism mixes consisting of 5 on-panel organisms 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 43.**

Table 43: Interfering Substance and Bottle Equivalency Concentrations

Organism	Concentration
Candida albicans	1 x 10^6 CFU/mL
Candida kefyr	1 x 10^6 CFU/mL
Cryptococcus neoformans	1 x 10^7 CFU/mL
Fusarium sacchari	6.5 x 10^6 spores/mL
Rhodotorula mucilaginosa	1 x 10^6 CFU/mL

Interfering Substances

Eighteen substances were used to assess the **cobas eplex** BCID-FP panel for potential interference. The organisms in **Table 43** 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 44**. None of the eighteen substances commonly found in blood culture specimens or as medications commonly used to treat skin or blood infections were found to inhibit the **cobas eplex** BCID-FP panel at the clinically relevant concentrations. The effect of interfering substances has only been evaluated for the organisms listed in **Table 43**. Interference due to substances other than those described in this section can lead to erroneous results.

Table 44: 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	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 (SPS)	0.25% w/v
Tetracycline	5 mg/L
Vancomycin	30 mg/L

Sample Matrix Equivalency (Bottle Evaluation)

Fifteen bottle types were tested for interference with each of the organisms listed in **Table 43**. Five replicates of each organism were tested in each of two bottle lots. Negative blood matrix was run as a negative control. Thirteen of the bottle types tested showed no interference for any of the targets tested. One lot of the BACT/Alert® PF Plus bottle type showed lower sensitivity for *Rhodotorula* and one lot BACT/Alert® FA Plus bottle type showed lower sensitivity for *Candida albicans*. A summary of the bottle types assessed and the study outcomes is found in **Table 45**.

Table 45: 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	No interference observed
BD	BACTEC	Myco	No interference observed
bioMérieux	BACT/ALERT®	SA Standard Aerobic	No interference observed
bioMérieux	BACT/ALERT	SN Standard Anaerobic	No interference observed
bioMérieux	BACT/ALERT	FA Plus	A false negative result was observed for the *Candida albicans* target in one lot.
bioMérieux	BACT/ALERT	FN Plus	No interference observed
bioMérieux	BACT/ALERT	PF Plus	False negative results were observed for the *Rhodotorula* target in one lot.
bioMérieux	BACT/ALERT	MP Mycobacteria	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

Carryover and Cross-Contamination

Carryover and cross-contamination were evaluated for the **cobas eplex** BCID-FP panel within and between runs by alternating high positive and negative samples across multiple runs over 5 rounds of testing. *Fusarium sacchari* was grown to bottle positivity +8 hours and spiked with 1 x 10^7 CFU/mL *Candida albicans* to simulate clinically relevant high positive samples for positive testing. Negative blood culture matrix was used to represent negative samples. No false positives were detected, indicating that no carryover or cross-contamination was observed between bays or within bays with the **cobas eplex** BCID-FP panel when testing consecutively or in adjacent bays.

Competitive Inhibition Study

Competitive inhibition was evaluated for the **cobas eplex** BCID-FP panel by pairing twelve clinically relevant organisms (including 9 off-panel organisms) in thirteen simulated dual infection sample mixes. *Candida albicans* was tested at low titer (concentration 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). *Candida glabrata* and *Candida parapsilosis* were also tested at the concentration expected at bottle positivity in the presence of *Candida albicans* at a higher titer concentration. No competitive inhibition was observed in any of the sample mixes evaluated at the concentrations listed in **Table 46.**

Table 46: Competitive Inhibition Organisms and Concentrations Tested

On-panel Organisms	High Concentration	Low Concentration
Candida albicans	1 x 10^7 CFU/mL	1 x 10^6 CFU/mL
Candida glabrata	1 x 10^7 CFU/mL	1 x 10^6 CFU/mL
Candida parapsilosis	1 x 10^7 CFU/mL	1 x 10^6 CFU/mL
Off-panel Organisms	**High Concentration**	
Acinetobacter baumannii	1 x 10^9 CFU/mL	
Cutibacterium acnes	1 x 10^9 CFU/mL	
Enterococcus faecalis	1 x 10^8 CFU/mL	
Escherichia coli	1 x 10^9 CFU/mL	
Klebsiella pneumoniae	1 x 10^9 CFU/mL	
Staphylococcus aureus	1 x 10^8 CFU/mL	
Staphylococcus epidermidis	1 x 10^8 CFU/mL	
Streptococcus pneumoniae	4 x 10^8 CFU/mL	
Pseudomonas aeruginosa	4 x 10^8 CFU/mL	

TROUBLESHOOTING

Table 47: Troubleshooting Table

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

Error	Error Messages	Description	Re-test Recommendations
Test did not start	"Cartridge failure" "The cartridge initialization test failed" "Cartridge not present" "Bay heater failure" "Unknown error" "Bay main / fluid motor failure" "Bay over pressured" "Bay temperature out of range" "The system was unable to read the cartridge" "Cartridge inserted doesn't match the serial number of the cartridge scanned" "The system is not ready to accept the cartridge" "The system was unable to enable cartridge insertion for the bay" "The system failed to prepare the cartridge for processing" "The cartridge initialization test failed" "The system rejected an attempt to process a previously used cartridge"	An error that occurs during pre-flight check (initialization) of cartridge upon insertion into bay. Pre-flight or cartridge initialization occurs when the cartridge is first inserted into the bay and takes approximately 90 seconds. Upon completion of preflight testing or cartridge initialization, the cartridge cannot be re-used, but prior to this point, the cartridge can be re-tested. To verify cartridge initialization has completed, examine the cartridge label upon removal. If the **cobas eplex** BCID-FP cartridge label has been pierced, initialization started and cartridge cannot be re-tested. If the label has not been pierced, follow the recommendation as stated.	1. Remove cartridge from bay. a. Reset bay to clear the error b. Re-insert cartridge in any available bay 2. If the cartridge is not able to be initialized on the second try and again generates an error during pre-flight check, this indicates an issue with the cartridge. This cartridge should be discarded following laboratory procedures and the sample should be repeated using a new cartridge. Bay(s) should be reset to clear the errors. Please contact Technical support to alert them of the issue If the bay remains in an error state (flashing red) after the cartridge has been removed, then it must be reset through the Bay Configuration menu before it can be used to run cartridges.
Test did not finish	"Bay heater failure" "Bay main / fluid motor failure" "Bay voltage failure" "Bay sub-system communication timeout" "Bay over pressured" "Bay auto-calibration failure" "Bay temperature out of range" "The system was unable to eject the cartridge from the bay"	This type of error occurs during the run, after pre-flight checks completed and prevents the cartridge from being processed to completion.	Reagents have been consumed and the cartridge cannot be reused. Contact Roche Technical Support and proceed with repeat testing the sample using a new cartridge. If the bay remains in an error state (flashing red) after the cartridge has been removed, then it must be reset through the Bay Configuration menu before it can be used to run cartridges.
Invalid		This is an error that results in no valid results being generated. A test report will be generated, but all targets and internal control will be invalid.	Reagents have been consumed and the cartridge cannot be reused. Contact Roche Technical Support and proceed with repeat testing the sample using a new cartridge.

Technical Support (United States)

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

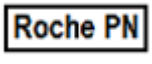
GenMark Diagnostics, Inc. A Member of the Roche Group
5964 La Place Court
Carlsbad, CA 92008 USA

In the US, please contact:
Technical support: 833.943.6627 (833.9GENMAR) or cad.technical_support_us@roche.com.
Customer service: 1-800-428-5076

Technical Support (International)

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

GLOSSARY OF SYMBOLS

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

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DOCUMENT REVISION

Document Revision Information	
Rev. A 10/2019	Original document
Rev. B 10/2020	Updated external control information and customer support contacts
Rev. C 04/2021	Specimen stability updated
Rev. D. 06/2023	IVDR Requirement Updates Warnings and precautions, General, add language to satisfy regulatory requirements Add reference to summary of safety and performance Updated Emergo address. UKCA requirement updates. Updated technical support contact, website, trademark, patent, and part number information. Updated Glossary of Symbols.
Doc Rev. 1.0 12/2023	First publishing for Branchburg based on IFU PI1076-D. Updated branding from GenMark's ePlex® to **cobas® eplex**. Updated SDS website information in **Safety** section. Updated **Trademarks** section. Please contact your local Roche Representative if you have any questions.

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

TRADEMARKS

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