BD MAX™ Check-Points CPO

REF **278102**

For *in vitro* diagnostic use
For use with the BD MAX System

P0226(02)
2019-08

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IVD

R_X Only

Contact your local BD representative for instructions. / Свържете се с местния представител на BD за инструкзии./ Pokyny vám poskytne místní zástupce společnosti BD. / Kontakt den lokale BD repræsentant for at få instruktioner. / Die Packungsbeilage erhalten Sie bei Ihrer örtlichen BD-Vertretung. / Póngase en contacto con su representante local de BD para instrucciones. / Contacter le représentant local de BD pour les instructions. / Επικοινωνήστε με τον τοπικό αντιπρόσωπο της BD για οδηγίες. / Kasutusjuhiste suhtes kontakteeruge oma kohaliku BD esindajaga. / Ota yhteys lähimpään BD:n edustajaan ohjeiden saamiseksi. / Kontaktiraj lokalnog predstavnika BD za upute. / A használati utasítást kérje a BD helyi képviseletétől. / Rivolgersi al rappresentante BD di zona per istruzioni. / Нұсқаулар үшін жергілікті BD өкілімен хабарласыңыз. / Naudojimo instrukcijų teiraukitės vietos BD įgaliotojo atstovo. / Neem contact op met uw plaatselijke BD-vertegenwoordiger voor instructies. / Kontakt din lokale BD-representant for mer informasjon. / Aby uzyskać instrukcje użytkowania, skontaktuj się z lokalnym przedstawicielstwem BD. / Contacte o representante local da BD para instruções. / Pentru instrucţiuni, contactaţi reprezentantul local BD. / Для получения указаний обратитесь к местному представителю компании BD. / Inštrukcie získate u miestneho zástupcu spoločnosti BD. / Obratite se svom lokalnom predstavniku kompanije BD za uputstva. / Kontakta närmaste BD-representant för anvisningar. / Talimatlar için yerel BD temsilcinizle temasa geçin. / За інструкціями зверніться до місцевого представника компанії BD.

INTENDED USE

The BD MAX Check-Points CPO Assay performed on the BD MAX System is a qualitative, automated in vitro diagnostic real-time PCR test designed for the detection and differentiation of the carbapenemase genes *bla*$_{KPC}$, *bla*$_{NDM}$, *bla*$_{VIM}$/*bla*$_{IMP}$ and *bla*$_{OXA-48}$, that are associated with carbapenem non-susceptibility in Gram-negative bacteria. The assay does not distinguish between the *bla*$_{VIM}$ and *bla*$_{IMP}$ genes.

The BD MAX Check-Points CPO Assay is intended as an aid to infection control in the detection of carbapenem-non-susceptible bacteria that colonize patients in healthcare settings. The BD MAX Check-Points CPO Assay is not intended to guide or monitor treatment for carbapenem-non-susceptible bacterial infections. A negative BD MAX Check-Points CPO Assay result does not preclude the presence of other resistance mechanisms.

Testing is performed on rectal swabs from patients at risk for intestinal colonisation with carbapenem non-susceptible bacteria. This test is intended for use in conjunction with clinical presentation, laboratory findings, and epidemiological information. Results of this test should not be used as the sole basis for patient management decisions. Concomitant cultures are necessary to recover organisms for epidemiological typing, antimicrobial susceptibility testing, and for further confirmatory bacterial identification.

SUMMARY AND EXPLANATION OF THE PROCEDURE

The worldwide emergence and dissemination of carbapenem-non-susceptible Gram-negative bacteria is a serious threat to public health. These organisms are associated with high mortality rates and have the potential to spread widely. The most common cause of carbapenem resistance in Gram-negative bacteria is the expression of carbapenemases. There are five major carbapenemase genes, that are most often found in human clinical specimens: KPC (*Klebsiella pneumoniae* carbapenemase), VIM (Verona integron–encoded metallo-β-lactamase), NDM (New Delhi metallo-β-lactamase), OXA-48 (Oxacillinase-48 and OXA-48 like variants), or IMP (Imipenemase).

BD MAX Check-Points CPO Assay can be performed in approximately 2.5 hours, as compared to culture methods which will take 48 hours for a negative result and up to 96 hours for a confirmed positive result. The BD MAX Check-Points CPO Assay detects the presence of carbapenemase genes in Gram-negative bacteria and includes an internal Sample Processing Control. BD MAX Check-Points CPO Assay automates the testing process and minimizes operator intervention from the time the sample is placed onto the BD MAX System until results are available.

A rectal swab is collected and transported to the laboratory. The specimen sample is homogenized and an aliquot is transferred into a BD MAX Check-Points CPO Sample Buffer Tube. The Sample Buffer Tube is placed into the BD MAX System and the following automated procedures occur: Bacterial cells lysis, DNA extraction and concentration, reagent rehydration, nucleic acid amplification and detection of the target nucleic acid sequence using real-time polymerase chain reaction (PCR). Amplified targets are detected with hydrolysis probes labeled with quenched fluorophores. The assay also includes a Sample Processing Control, that is present in the Extraction Tube and undergoes the same extraction, concentration and amplification steps to monitor for inhibitory substances, instrument or reagent failure. No operator intervention is necessary once the clinical specimen and reagent strip are loaded onto the BD MAX System. The amplification, detection and interpretation of the signals are done automatically by the BD MAX System.

PRINCIPLES OF THE PROCEDURE

Rectal swab specimens are collected from patients using ESwabs. After sampling they are transported to the laboratory in the Amies transport media of the ESwab. The ESwab is vortexed and a 50 µl aliquot is transferred to the Sample Buffer Tube using a pipette with disposable filter tip. The Sample Buffer Tube is closed with a septum cap and vortexed. Once the worklist is generated and the clinical specimen is loaded on the BD MAX system, along with a BD MAX Check-Points CPO Reagent Strip and BD MAX PCR Cartridge, the run is started and no further operator intervention is required. The BD MAX System automates sample preparation, including target organism lysis, DNA extraction and concentration, reagent rehydration, target nucleic acid sequence amplification and detection using real-time PCR. The interpretation of the signal is performed automatically by the BD MAX System. The assay also includes a Sample Processing Control that is provided in the Extraction Tube and subjected to extraction, concentration and amplification steps. The Sample Processing Control monitors for the presence of potential inhibitory substances as well as system or reagent failures.

Following enzymatic cell lysis at an elevated temperature, the released nucleic acids are captured on magnetic affinity beads. The beads, with the bound nucleic acids, are washed and the nucleic acids are eluted. Eluted DNA is neutralized and transferred to the Master Mix Tube to rehydrate the PCR reagents. After rehydration, the BD MAX System dispenses a fixed volume of PCR-ready solution into the BD MAX PCR Cartridge. Microvalves in the BD MAX PCR Cartridge are sealed by the system prior to initiating PCR to contain the amplification mixture thus preventing evaporation and contamination. The amplified DNA targets are detected using hydrolysis (TaqMan®) probes, labeled at one end with a fluorescent reporter dye (fluorophore) and at the other end with a quencher moiety. Probes labeled with different fluorophores are used to detect amplicons for the carbapenemase genes KPC, VIM, OXA-48, NDM, IMP and the Sample Processing Control in five different optical channels of the BD MAX System.

The VIM and IMP genes are combined in one optical channel of the BD MAX system, all other genes have a separate optical channel. When the probes are in their native state, the fluorescence of the fluorophore is quenched due to its proximity to the quencher. However, in the presence of target DNA, the probes hybridize to their complementary sequences and are hydrolyzed by the 5'-3' exonuclease activity of the DNA polymerase as it synthesizes the nascent strand along the DNA template. As a result, the fluorophores are separated from the quencher molecules and fluorescence is emitted. The BD MAX System monitors these signals at each cycle and interprets the data at the end of the program to report the final results.

Contents	Quantity
BD MAX Check-Points CPO Master Mix (F6) *Dried PCR Master Mix containing Sample Processing Control and carbapenemase gene-specific primers and TaqMan probes.*	24 tests (2 x 12 tubes)
BD MAX Check-Points CPO Reagent Strips *Unitized reagent strip containing all the liquid reagents and disposables pipette tips necessary for DNA Extraction.*	24 tests
BD MAX Check-Points CPO Extraction Tubes (A8) *Dried pellet containing DNA magnetic affinity beads, protease reagents and Sample Processing Control.*	24 tests (2 x 12 tubes)
BD MAX Check-Points CPO Sample Buffer Tubes	24 tests
Septum caps	25

EQUIPMENT AND MATERIALS REQUIRED BUT NOT PROVIDED

- BD MAX System (BD, Cat. No. 441916)
- BD MAX PCR Cartridges (BD, Cat. No. 437519)
- Vortex Mixer
- Pipettes & disposable (filter-) tips for a volume of 50 µL
- Lab coat and powderless disposable gloves
- Sampling Devices: Copan ESwab, (Copan, Cat. No. 480CE) or BD ESwab (BD, Cat No. 220245)

Suggested Media for Cultivation of Control Isolates (see Quality Control Section): **Columbia Agar with 5% Sheep Blood** (e.g., BD™ Columbia Agar with 5% Sheep Blood, BD, Cat. No. 254005).

WARNINGS AND PRECAUTIONS

- The BD MAX Check-Points CPO Assay is for *in vitro* diagnostic use.
- This product can only be used on the BD MAX System.
- Do not use the kit if the label that seals the outer box is broken.
- Do not use reagents if the protective pouches are open or broken upon arrival.
- Close protective pouches of reagents promptly with the zip seal after each use. Remove any excess air in the pouches prior to sealing.
- Check reagent strips for proper liquid fills (ensure that the liquids are at the bottom of the tubes) (see Figure 1).
- Check reagent strips to ensure that all pipette tips are present (see Figure 1).
- Do not remove desiccant from reagent pouches.
- Do not use reagents if desiccant is not present or is broken inside reagent pouches.
- Do not use reagents if the foil has been broken or damaged.
- Do not mix reagents from different pouches and/or kits and/or lots.
- Do not interchange or reuse caps, as contamination may occur and compromise test results.
- Proceed with caution when using chemical solutions as Master Mix and Extraction Tube barcode readability may be altered.
- Do not use expired reagents and/or materials.
- Good laboratory technique is essential to the proper performance of this assay. Due to the high analytical sensitivity of this test, extreme care should be taken to preserve the purity of all materials and reagents.
- To avoid contamination by amplicons, do not break apart the BD MAX PCR Cartridges after use. The seals of the BD MAX PCR Cartridges are designed to prevent contamination.
- Performing the BD MAX Check-Points CPO Assay outside the recommended time ranges can produce invalid results. Assays not performed within the specified time ranges should be repeated with a new specimen.
- Additional controls may be tested according to guidelines or requirements of local, state, provincial and/or federal regulations or accrediting organizations.
- In cases where culture or other PCR tests are conducted in the laboratory, care must be taken to ensure that the BD MAX Check-Points CPO Assay, any additional reagents required for testing, and the BD MAX System are not contaminated. Avoid microbial and deoxyribonuclease (DNase) contamination of reagents at all times. Gloves must be changed before manipulating reagents and cartridges.
- Always handle specimens as if they are infectious and in accordance with safe laboratory procedures such as those described in the CLSI Document M29[1] and in Biosafety in Microbiological and Biomedical Laboratories.[2]
- Wear protective clothing and disposable gloves while handling all reagents.
- Wash hands thoroughly after performing the test.
- Do not smoke, drink, chew or eat in areas where specimens or kit reagents are being handled.
- Dispose of unused reagents and waste in accordance with local, state, provincial and/or federal regulations.
- Consult the BD MAX System User's Manual[3] for additional warnings, precautions and procedures.

STORAGE AND STABILITY

Specimen Stability

Collected specimens should be kept between 2 °C and 25 °C during transport. Protect against exposure to excessive heat. Specimens can be stored for up to 48 hours (2 days) at 2–25 °C before testing.

BD MAX Check-Points CPO Assay reagents and components are stable at 2–25 °C through the stated expiration date. Do not use expired components.

Kit Components Storage

BD MAX Check-Points CPO Master Mix Tubes and BD MAX Check-Points CPO Extraction Tubes are provided in sealed pouches. To protect product from humidity, immediately re-seal after opening. Master Mix tubes and Extraction Tubes are stable for up to 14 days at 2–25 °C after initial opening and re-sealing of the pouch.

INSTRUCTIONS FOR USE

Specimen Collection/Transport

In order to obtain an adequate specimen, the instructions for use from the Sampling Device manufacturer must be followed closely. Label the specimen collection tube (containing the rectal swab in liquid Amies medium) and transport to the laboratory according to institutional standard operating procedures (Refer to the Storage and Stability section).

Specimen Preparation

Note: One (1) Sample Buffer Tube, and one (1) Septum Cap are required for each specimen and each External Control to be tested.

1. Label a bar-coded BD MAX Sample Buffer Tube (clear cap) with the appropriate specimen identification. Do not obscure, write or label over the 2D-barcode.
2. Vortex the rectal swab specimen in liquid Amies transport medium at low speed for 5 seconds.
3. Remove the clear cap from the Sample Buffer Tube and pipette 50 µl of the liquid Amies transport medium into the Sample Buffer Tube.
4. Recap the inoculated Sample Buffer Tube using a Septum Cap and vortex at low speed for 10 seconds.
5. Place the Sample Buffer Tube in a suitable rack.
6. Prepare any additional specimens by repeating steps 1 through 5 for the remaining specimens, ensuring gloves are clean prior to handling additional specimens.
7. Proceed to BD MAX System Operation section to perform testing of the BD MAX Check-Points CPO Assay on the BD MAX System.

BD MAX System Operation

Note: Refer to the BD MAX System User's Manual[3] for detailed instructions (Operation section).
NOTE: One (1) Master Mix, one (1) Extraction Tube and one (1) Unitized Reagent Strip are required for each specimen and each External Control to be tested. Set aside the required number of materials from their protective pouches or boxes. To store opened Master Mix or Extraction Tube pouches, remove excess air and close using the zip seal.

1. Power on the BD MAX System (if not already done) and log in by entering <user name> and <password>.
2. Gloves must be changed before manipulating reagents and cartridges.
3. Remove the required number of Unitized Reagent Strips from the BD MAX Check-Points CPO kit. Gently tap each strip onto a hard surface to ensure that all liquids are at the bottom of the tubes.
4. Remove the required number of Extraction Tube(s) and Master Mix Tube(s) from their protective pouches. Remove excess air, and close pouches with the zip seal.
5. For each specimen to be tested, place one (1) Unitized Reagent Strip into the BD MAX System Rack, starting with Position 1 of Rack A.
6. Snap one (1) Extraction Tube (white foil) into each Unitized Reagent Strip in Position 1 as shown in Figure 1.
7. Snap one (1) Master Mix Tube (green foil) into each Unitized Reagent Strip in Position 2 as shown in Figure 1.

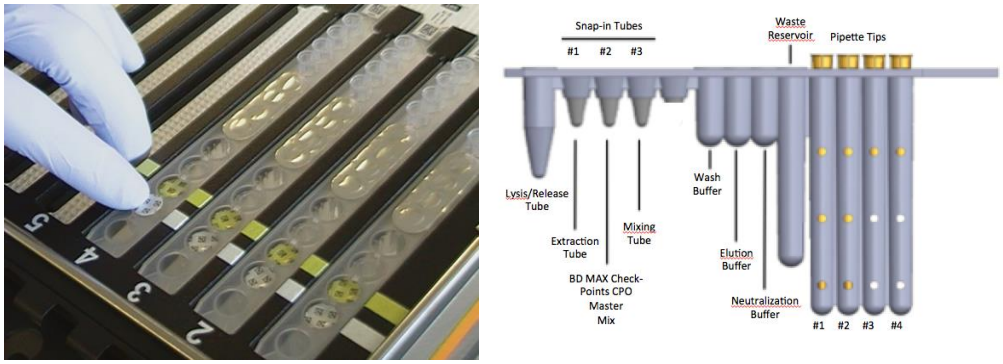

Figure 1: Snap BD MAX Check-Points CPO Extraction tubes and BD MAX Check-Points CPO Master Mix tubes into Unitized Reagent Strips

8. Click on the Run icon and enter the kit lot number for the BD MAX Check-Points CPO Assay (for lot traceability) by either scanning the barcode with the scanner or by manual entry.
   NOTE: Repeat step 8 each time a new kit lot is used.
9. Navigate to the Worklist. Using the pull-down menu, select **<BD MAX CPO 62>**.
10. Enter the Sample Buffer Tube ID, Patient ID and Accession Number (if applicable) into the Worklist, either by scanning the barcode with the scanner or by manual entry.
11. Select the appropriate kit lot number (found on the outer box) from the pull-down menu.
12. Repeat steps 9 to 11 for all remaining Sample Buffer Tubes.
13. Place the Sample Buffer Tubes in the BD MAX System Rack(s) corresponding to the Unitized Reagent Strips assembled in steps 5 to 7.
14. Place the required number of BD MAX PCR Cartridge(s) into the BD MAX™ System (see Figure 2).
    - Each cartridge accommodates up to 24 samples.
    - The BD MAX System will automatically select the position and row on the BD MAX PCR Cartridge for each run.
    - PCR Cartridges are used on a per-run AND rack basis.
    - BD MAX PCR Cartridges may be used multiple times until all lanes have been utilized, select Run Wizard under the Worklist tab for lane assignments.
    - Consult the BD MAX System User's Manual[3] for more details (1 cartridge per rack).

Figure 2: Load BD MAX PCR Cartridges

15. Load rack(s) onto the BD MAX System (Figure 3).
16. Close the BD MAX System lid and click **<Start>** to begin processing.

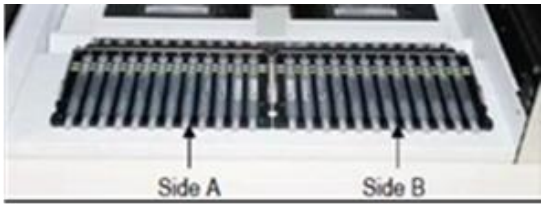

Figure 3: Load Rack(s) into the BD MAX System

17. At the end of the run, check results immediately or store Sample Buffer Tubes at 2-25 °C for a maximum of 48 h until the results are checked.

NOTE: If a septum cap was damaged during the run, replace it with a new one before storing the sample.
NOTE: When an Indeterminate (IND), Unresolved (UNR), or Incomplete (INC) result is obtained, or when an External Control failure occurs, a repeat test from the prepared Sample Buffer Tube must be performed (see "Repeat Test Procedure"). If an External Control fails, repeat testing of all specimens using freshly prepared External Controls (see "Quality Control").

QUALITY CONTROL

Quality control procedures monitor the performance of the assay. Laboratories must establish the number, type and frequency of testing control materials according to guidelines or requirements of local, provincial, state and/or federal regulations or accreditation organizations in order to monitor the entire analytical process. For general QC guidance, the user may wish to refer to CLSI MM03 and EP12.[4, 5]

1. External Positive and Negative Controls are not used by the BD MAX System software for the purpose of sample test result interpretation. External Controls are treated as if they were patient specimens. (Refer to Table 2 for the interpretation of External Control assay results.)
2. One (1) External Positive Control and one (1) External Negative Control should be run at least daily until adequate process validation is achieved on the BD MAX System in each laboratory setting. Reduced frequency of control testing should be in accordance with applicable regulations.
3. The External Positive Control is intended to monitor for substantial reagent failure. The External Negative Control is used to detect reagent or environmental contamination (or carry-over) by target nucleic acids.
4. Various types of external controls are recommended to allow the user to select the most appropriate for their laboratory quality control program.
    a. External Negative Control: Previously characterized specimens known to be negative or commercially available control material such as the *E. coli* ATCC 25922 Gram-negative control strain not carrying any of the BD MAX Check-Points CPO target carbapenemase genes. Check-Points recommends that the External Negative Control is prepared prior to the External Positive Control.
    b. External Positive Control: commercially available control materials that carry one or more of the BD MAX Check-Points CPO target carbapenemase genes are recommended such as NCTC Gram-negative control strains listed below (Refer to Table 1).

    For the preparation of External Control suspension, it is recommended that isolates be re-suspended in a saline solution to a turbidity of 0.5 McFarland and perform serial dilutions with saline solution to obtain the final dilution presented in Table 1. The final dilution should be made in negative rectal swab matrix to best mimic a real clinical specimen. Inoculate 50 µL of the external control specimen to the corresponding Sample Buffer Tube. Process and test as a sample (refer to the Specimen Preparation and BD MAX System operation sections).
5. All External Controls should yield the expected results (positive for External Positive Control, negative for External Negative Control) and no failed external controls (Unresolved or Indeterminate results).
6. An External Negative Control that yields a positive test result is indicative of a sample handling and/or contamination problem. Review the sample handling technique to avoid mix-up and/or contamination. An External Positive Control that yields a negative result is indicative of a sample handling/preparation problem. Review the sample handling/preparation technique.
7. An External Control that yields an Unresolved, Indeterminate or Incomplete test result is indicative of a reagent or a BD MAX System failure. Check the BD MAX System monitor for any error messages. Refer to the System Error Summary section of the BD MAX System User's Manual[3] for interpretation of warning and error codes. If the problem persists, use reagents from an unopened pouch or use a new BD MAX Check-Points CPO Kit.

Table 1: Commercially Available Strains for External Positive and Negative Control

Target Gene	External Control Strain	Final Dilution from 0.5 McFarland
KPC	*Klebsiella pneumoniae* (NCTC-13438)	1/1,000
VIM	*Pseudomonas aeruginosa* (NCTC-13437)	1/5,000
IMP	*Escherichia coli* (NCTC 13476)	1/7,000
OXA-48	*Klebsiella pneumoniae* (NCTC-13442)	1/10,000
NDM	*Klebsiella pneumoniae* (NCTC-13443)	1/400
Negative Control	*Escherichia coli* (ATCC 25922)	1/10

8. Each BD MAX Check-Points CPO Extraction Tube contains a Sample Processing Control which is a plasmid containing a synthetic target DNA sequence. The Sample Processing Control monitors the efficiency of DNA capture, washing and elution during the sample processing steps, as well as the efficiency of DNA amplification and detection during PCR analysis. If the Sample Processing Control result fails to meet the acceptance criteria, the result of the sample will be reported as Unresolved; however, any positive (POS) assay results will be reported and no targets will be called NEG. An Unresolved result is indicative of sample-associated inhibition or reagent failure.

RESULTS INTERPRETATION

Results are available on the **<Results>** tab in the **<Results>** window on the BD MAX System monitor. The BD MAX System software automatically interprets test results. Results are reported for each of the analytes and for the Sample Processing Control. A test result may be called NEG (Negative), POS (Positive) or UNR (Unresolved) based on the amplification status of the target and of the Sample Processing Control. IND (Indeterminate) or INC (Incomplete) results are due to BD MAX System failure.

Table 2: BD MAX Check-Points CPO Assay Result Interpretation

Assay Result Reported	Interpretation of Result
KPC POS	KPC gene detected
KPC NEG	No KPC gene detected
VIM and or IMP POS	VIM and/or IMP gene detected
VIM and or IMP NEG	No VIM or IMP gene detected
OXA POS	OXA-48 gene detected
OXA NEG	No OXA-48 gene detected
NDM POS	NDM gene detected
NDM NEG	No NDM gene detected
UNR	Unresolved – inhibitory sample or reagent failure; no Sample Processing Control amplification
IND	Indeterminate due to BD MAX System failure (with Warning or Error Codes*)
INC	Incomplete run (with Warning or Error Codes*)

* Refer to "Troubleshooting" section of the BD MAX System User's Manual[3] for interpretation of warning and error codes.

REPEAT TEST PROCEDURE

NOTE: Sufficient volume is available for one repeat test from the Sample Buffer Tube. For Sample Buffer Tubes stored at 2-25 °C, retesting must be performed within 48 hours following the initial Sample Buffer Tube inoculation with the specimen.

NOTE: New specimens may be tested in the same run with repeat samples.

Unresolved Result

Unresolved results may be obtained in the event that sample-associated inhibition or reagent failure prevents proper target or Sample Processing Control amplification. If the Sample Processing Control does not amplify, the sample will be reported as UNR; however, any positive (POS) assay results will be reported. Sample(s) can be repeated from their corresponding Sample Buffer Tube(s) within the timeframe defined above. Vortex and restart from the BD MAX System Operation section. Alternatively, sample(s) can be repeated using the remaining rectal swab specimen with a new Sample Buffer Tube within the timeframes defined above. Restart from the Specimen Preparation section.

Indeterminate Result

Indeterminate results may be obtained in the event that a System failure occurs. Sample(s) can be repeated from their corresponding Sample Buffer Tube(s) within the timeframe defined above. Vortex and restart from the BD MAX System Operation section. Alternatively, sample(s) can be repeated using the remaining rectal swab specimen with a new Sample Buffer Tube within the timeframes defined above. Restart from the Specimen Preparation section. For the interpretation of warning or error code messages, refer to the BD MAX System User's Manual[3] (Troubleshooting section).

Incomplete Result

Incomplete results may be obtained in the event that the Specimen Preparation or the PCR failed to complete. Sample(s) can be repeated from their corresponding Sample Buffer Tube(s) within the timeframe defined above. Vortex and restart from the BD MAX System Operation section. Alternatively, sample(s) can be repeated using the remaining rectal swab specimen with a new Sample Buffer Tube within the timeframes defined above. Restart from the Specimen Preparation

section. For the interpretation of warning or error code messages, refer to the BD MAX System User's Manual[3] (Troubleshooting section).

External Control Failure

External Controls should yield expected results when tested. If samples have to be repeated due to an incorrect External Control result, they should be repeated along with freshly prepared External Controls within the allowed timeframes defined above.

CULTURING OF SPECIMENS

Culture and identification of organisms from positive specimens should be performed per laboratory procedures.

LIMITATIONS OF THE PROCEDURE

- This product can only be used on the BD MAX System.
- Erroneous results may occur from improper sample collection, handling, storage, technical error, sample mix-up, or because the number of organisms in the sample is below the analytical sensitivity of the test.
- If the BD MAX Check-Points CPO result is IND, INC, or UNR (for one or more targets) then the test should be repeated.
- A BD MAX Check-Points CPO positive result does not necessarily indicate the presence of viable organisms
- *In silico* analysis combined with inclusivity analysis predict that the following carbapenemase variants are detected:
    - KPC: 2-37
    - VIM: 1-6, 8-52, 54, 56-60
    - OXA-48 like: 48, 162, 163, 181, 204, 232, 244, 245, 370, 405, 438-439, 484, 505, 517, 519, 566
    - NDM: 1-24
    - IMP: 1-4, 6-8, 10, 19-20, 23-26, 30, 34, 38, 40, 42-43, 51-52, 55, 59-61, 66, 70, 73, 76-80
- The BD MAX CPO Check-Points Assay is not a sub-typing tool and does not report variants of the *bla*$_{IMP}$, *bla*$_{VIM}$, *bla*$_{NDM}$, *bla*$_{KPC}$, or *bla*$_{OXA-48}$ genes.
- The *in silico* analyses used to predict variants detected by the assay were based on a comparison of target gene sequences available in the BLDB database[6] to the BD MAX Check-Points CPO Assay primer/probe and amplicon sequences for each gene target. *In silico* analyses using CLUSTALW were performed in 2017-2018. *In silico* analysis of new variant gene sequences deposited into the database after 2018 for the five target genes have not been performed.
- Mutations or polymorphisms in primer or probe binding regions may affect detection of current, new, or unknown *bla*$_{IMP}$, *bla*$_{VIM}$, *bla*$_{NDM}$, *bla*$_{KPC}$, or *bla*$_{OXA-48}$ variants, resulting in a false negatve result.
- VIM and IMP are detected in the same channel and thus not differentiated.
- As with all PCR-based *in vitro* diagnostic tests, extremely low levels of target below the analytical sensitivity of the assay may be detected, but results may not be reproducible.
- False negative results may occur due to loss of nucleic acid from inadequate collection, transport or storage of specimens, or due to inadequate bacterial cell lysis. The Sample Processing Control has been added to the test to aid in the identification of specimens that contain inhibitors to PCR amplification. The Sample Processing Control does not indicate if nucleic acid has been lost due to inadequate collection, transport or storage of specimens, or whether bacterial cells have been inadequately lysed.
- Excessive or heavily soiled specimens may lead to unresolved results (UNR) due to inhibition.
- As with all *in vitro* diagnostic tests, positive and negative predictive values are highly dependent on prevalence. BD MAX Check-Points CPO performance may vary depending on the prevalence and population tested.
- The sample buffer tube has not been designed to support organism viability. If culture is necessary, it must be performed from the original specimen.
- This test is a qualitative test and does not provide quantitative values nor indicate the quantity of organisms present.
- The performance of the BD MAX Check-Points CPO Assay has not been evaluated with rectal swab speciments from pediatric patients.
- The detection of *bla*$_{IMP}$, *bla*$_{VIM}$, *bla*$_{NDM}$, *bla*$_{KPC}$, and/or *bla*$_{OXA-48}$ from rectal swab specimens may be from organisms other than *Enterobacteriaceae*, *Pseudomonas aeruginosa*, and *Acinetobacter baumannii*.
- The performance of the BD MAX Check-Points CPO Assay with susceptible isolates containing *bla*$_{IMP}$, *bla*$_{VIM}$, *bla*$_{NDM}$, *bla*$_{KPC}$, and/or *bla*$_{OXA-48}$ gene sequences has not been fully evaluated.

PERFORMANCE CHARACTERISTICS

Clinical performance characteristics of the BD MAX Check-Points CPO Assay were determined in a multi-site investigational study and a study involving contrived specimens. The investigational study involved a total of five (5) geographically diverse clinical centers where rectal swab specimens were collected as part of routine patient care, enrolled into the trial, and tested with the BD MAX Check-Points CPO Assay. Specimens were obtained from patients at risk for intestinal colonization with carbapenem non-susceptible bacteria. The reference method was a bacterial culture for recovery of non-susceptible isolates from the rectal swab specimens followed by detection of antibiotic resistance genes by PCR and sequencing. The bacterial culture comprised both direct plating on chromID Carba and chromID OXA48 as well as over-night enrichment in MacConkey broth followed by plating on MacConkey agar with a 10 ug meropenem disc. For contrived specimens, well-characterized strains were spiked into unique negative rectal swab matrix near the LoD and analyzed by BD MAX Check-Points CPO. In addition, the strains were analyzed by PCR and sequencing.

A total of 1486 prospective specimens and 166 contrived specimens were enrolled in the clinical evaluation. 13 prospective specimens were non-reportable resulting in 1473 prospective specimens for performance evaluation.Tables 3

through 6 describe the performance characteristics of the BD MAX Check-Points CPO Assay that were observed during the clinical trial.

Non-Reportable Rate

Of all specimens evaluated, 1.9% (28/1486) and 0% (0/166) were initially reported as Unresolved, Incomplete or Indeterminate for the prospective and contrived specimens, respectively. Following a valid repeat test of 17 of 28 specimens (11 were not repeated), 0.1% (2/1475) and 0% remained Unresolved for the prospective and contrived specimens, respectively.

Performance Results with KPC producing organisms

The clinical performance for KPC in the prospective study and contrived study is summarized in the Table 3 below.

Table 3. KPC – Overall Performance

KPC		Prospective						Contrived	
		MacConkey PCR/Sequencing		chromID PCR/Sequencing		MacConkey + chromID PCR/Sequencing		PCR/Sequencing	
		POS	NEG	POS	NEG	POS	NEG	POS	NEG
BD MAX Check-Points CPO	POS	23	10	28	5	30	3	30	0
	NEG	3	1437	1	1439	4	1436	0	136
Sensitivity/PPA (95% CI)		88.5 % (71.0-96.0%)		96.6 % (82.8-99.4%)		88.2 % (73.4-95.3%)		100 % (88.6-100%)	
Specificity/NPA (95% CI)		99.3 % (98.7 – 99.6)		99.7 % (99.2 – 99.9)		99.8 % (99.4 – 99.9)		100 % (97.3 – 100)	

Performance Results with VIM and IMP producing organisms

The clinical performance for VIM/IMP in the prospective study and contrived study is summarized in the Table 4 below.

Table 4. VIM/IMP – Overall Performance

VIM/IMP		Prospective						Contrived	
		MacConkey PCR/Sequencing		chromID PCR/Sequencing		MacConkey + chromID PCR/Sequencing		PCR/Sequencing	
		POS	NEG	POS	NEG	POS	NEG	POS	NEG
BD MAX Check-Points CPO	POS	5	12	4	13	6	11	50	0
	NEG	0	1456	2	1454	2	1454	2	114
Sensitivity/PPA (95% CI)		100 % (56.6-100%)		66.7 % (30.0-90.3%)		75.0 % (40.9-92.9%)		96.2 % (87.0-98.9%)	
Specificity/NPA (95% CI)		99.2 % (98.6 – 99.5)		99.1 % (98.5 – 99.5)		99.2 % (98.7 – 99.6)		100 % (96.7 – 100)	

Performance Results with OXA48 producing organisms

The clinical performance for OXA-48 in the prospective study and contrived study is summarized in the Table 5 below.

Table 5. OXA48 – Overall Performance

OXA-48		Prospective						Contrived	
		MacConkey PCR/Sequencing		chromID PCR/Sequencing		MacConkey + chromID PCR/Sequencing		PCR/Sequencing	
		POS	NEG	POS	NEG	POS	NEG	POS	NEG
BD MAX Check-Points CPO	POS	20	20	25	15	25	15	30	0
	NEG	1	1432	0	1433	1	1432	0	136
Sensitivity/PPA (95% CI)		95.2 % (77.3-99.2%)		100 % (86.7-100%)		96.2 % (81.1-99.3%)		100 % (88.6-100%)	
Specificity/NPA (95% CI)		98.6 % (97.9 – 99.1)		99.0 % (98.3 – 99.4)		99.0 % (98.3 – 99.4)		100 % (97.3 – 100)	

Performance Results with NDM producing organisms

The clinical performance for NDM in the prospective study and contrived study is summarized in the Table 6 below.

Table 6. NDM – Overall Performance

NDM		Prospective						Contrived	
		MacConkey PCR/Sequencing		chromID PCR/Sequencing		MacConkey + chromID PCR/Sequencing		PCR/Sequencing	
		POS	NEG	POS	NEG	POS	NEG	POS	NEG
BD MAX Check-Points CPO	POS	1	1	1	1	1	1	30	0
	NEG	0	1471	0	1471	0	1471	0	136
Sensitivity/PPA (95% CI)		100 % (20.7-100%)		100 % (20.7-100%)		100 % (20.7-100%)		100 % (88.6-100%)	
Specificity/NPA (95% CI)		99.9 % (99.6 – 100)		99.9 % (99.6 – 100)		99.9 % (99.6 – 100)		100 % (97.3 – 100)	

Analytical Inclusivity

A variety of BD MAX Check-Points CPO target organisms and carbapenemase gene variants were included in this study. Strain selection criteria included prevalence and clinical importance. Ninety-three (93) strains were tested, including strains from public collections and well-characterized clinical isolates.

Inclusivity testing included 16 different species and 17 KPC strains representing 2 variants, 17 VIM strains representing 7 variants, 18 IMP strains representing 7 variants, 20 OXA48-type strains representing 7 variants, 17 NDM strains representing 4 variants and 4 strains containing two carbapenemase target genes. The strains were tested in triplicate at 3x LoD (Limit of Detection). The BD MAX Check-Points CPO correctly identified 90 of the 93 strains tested upon initial testing. Three strains, an *Enterobacter cloacae* with IMP-34, a *Pseudomonas aeruginosa* with IMP-4 and a *Klebsiella pneumoniae* with NDM-1 were detected when re-tested at 10x LoD.

Table 7: BD MAX Check-Points CPO Inclusivity Results versus *in silico* Prediction

Target	Inclusivity Results			*in silico* Prediction
	No. of strains	Variants detected	Variants not detected	
KPC	17	KPC-2, 3	-	KPC-2-37
VIM	19	VIM-1, 2, 4, 19, 26, 27, 31	-	VIM-1-6, 8-52, 54, 56-60
IMP	20	IMP-1, 3, 4, 7, 8, 26, 34	-	IMP-1-4, 6-8, 10, 19, 20, 23-26, 30, 34, 38, 40, 42-43, 51, 52, 55, 59-61, 66, 70, 73, 76-80
OXA-48	22	OXA-48, 162, 163, 181, 204, 232, 244	-	OXA-48, 162, 163, 181, 204, 232, 244, 245, 370, 405, 438, 439, 484, 505, 517, 519, 566
NDM	19	NDM-1, 5, 6, 7	-	NDM-1-24

In summary, all variants tested and predicted detected by *in silico* analysis were detected by BD MAX Check-Points CPO. In addition, IMP-7 and OXA-163 not predicted detected by *in silico* analysis were detected by BD MAX Check-Points CPO. IMP-43, -51 and -73 have the same primer and probe target sequences as IMP-7 and OXA-438-439 have the same primer and probe target sequences as OXA-163 and therefore also expected detected by BD MAX Check-Points CPO Assay.

Analytical Sensitivity (Limit of Detection)

The analytical sensitivity (Limit of Detection or LoD) for the BD MAX Check-Points CPO was determined using two strains for each carbapenemase gene, i.e. 10 strains. Bacterial cell suspensions of each strain were prepared and quantified from culture prior to inclusion in this study. A total of six 2-fold serial dilutions in negative rectal matrix were prepared for all strains at test concentrations expected to comprise the LoD for each carbapenemase target gene. Replicates of 10 of each test concentration were evaluated using 3 BD MAX instruments and 3 lots of reagents and consumables to estimate the LoD. For this study, the estimated LoD was defined as the lowest concentration of target cells at which 10/10 replicates gave a positive test result. The LoD was then confirmed by testing 20 replicates for each strain at the estimated LoD. Analytical sensitivity (LoD), defined as the lowest concentration at which ≥ 95% of all replicates are expected to test positive, ranged from 144 to 4774 CFU/mL of Sample Buffer after dispensing rectal swab specimen into the Sample Buffer Tube.

Table 8: BD MAX Check-Points CPO Limit of Detection for Individual Targets

Target	Strain	Species	CFU/mL	%
KPC	CP254	*Klebsiella pneumoniae*	2005	95%
	CP365	*Klebsiella pneumoniae*	3560	100%
VIM	CP260	*Pseudomonas aeruginosa*	159	100%
	CP433	*Enterobacter cloacae*	520	95%
IMP	CP253	*Escherichia coli*	319	100%
	CP149	*Klebsiella pneumoniae*	144	95%
OXA	CP258	*Klebsiella pneumoniae*	229	95%
	CP411	*Escherichia coli*	902	95%
NDM	CP259	*Klebsiella pneumoniae*	4774	100%
	CP184	*Escherichia coli*	4492	95%

Analytical Specificity (Cross-Reactivity and Exclusivity)

The BD MAX Check-Points CPO Assay was performed on samples containing phylogenetically related species and other organisms likely to be found in rectal swab specimens. In addition, species were tested typically containing the BD MAX Check-Points CPO carbapenemase target genes, but having either no carbapenemase gene or a different carbapenemase or other antibiotic resistance gene. The bacterial cells were seeded into negative rectal swab matrix at a concentration of ~ 5 x 10^6 cells/mL. Overall, 26 organisms were tested in 3 replicates and are listed in Table 9. All organisms tested negative.

Table 9. Organisms Tested to Determine the BD MAX Check-Points CPO Specificity

Strain ID	Species	Reference	B-lactamase gene
CP-575	*Campylobacter jejuni*	CCUG-41359	None
CP-521	*Citrobacter freundii*	N/A	CTX-M9 ESBL
CP-338	*Citrobacter braakii*	N/A	GES Carbapenemase
CP-568	*Corynebacterium diphtheriae*	CCUG-37874	None
CP-484	*Enterobacter aerogenes*	N/A	None
CP-034	*Enterobacter cloacae*	N/A	CTX-M9 ESBL
CP-573	*Enterococcus casseliflavus*	CCUG-55879	None
CP-574	*Enterococcus faecalis*	CCUG-9997	None
CP-048	*Escherichia coli*	N/A	CTX-M1 ESBL
CP-576	*Helicobacter pylori*	CCUG-17874	None
CP-058	*Klebsiella oxytoca*	N/A	CTX-M9 ESBL
CP-012	*Klebsiella pneumonia*	N/A	SHV-ESBL
CP-570	*Listeria monocytogenes*	CCUG-33548	None
CP-357	*Pseudomonas aeruginosa*	N/A	PER ESBL
CP-132	*Salmonella typhimurium*	N/A	pAmpC
CP-519	*Raoultella sp.*	N/A	SHV & CTX-M9 ESBL
CP-571	*Staphylococcus aureus*	CCUG-9128	None
CP-250	*Serratia marcescens*	N/A	None
CP-009	*Stenotrophomonas maltophilia*	N/A	SHV & CTX-M9 ESBL; pAmpC
CP-284	*Acinetobacter baumannii*	N/A	OXA-23 Carbapenemase
CP-503	*Morganella morganii*	N/A	None
CP-319	*Providencia stuartii*	N/A	VEB ESBL
CP-567	*Providencia alcalifaciens*	CCUG-6325	None
CP-569	*Streptococcus agalactiae*	CCUG-29780	None
CP-052	*Proteus mirabilis*	N/A	pAmpC
CP-440	*Acinetobacter baumannii*	N/A	OXA-58 Carbapenemase

N/A: Strain from in-house strain collection with no reference number available

Interfering Substances

Twenty-nine (29) biological and chemical substances that may occasionally be present in rectal swab specimens were evaluated for potential interference with the BD MAX Check-Points CPO Assay and are listed in Table 10. All substances were evaluated at a test concentration of 0.25% w/v (2.5 mg/mL) in negative rectal swab matrix. Test specimens included negative rectal swab matrix seeded with target organisms at 3x LoD (positive specimens) or not seeded (negative specimens). For each substance 6 positive and 6 negative specimens were tested. Results demonstrated no reportable interference with any of the substances tested (refer to Table 10).

Table 10. Substances not Interfering with BD MAX Check-Points CPO

Oils & fatty acids	Metal salts	Antibiotics	Painkillers
Stearic acid	Ba2SO4	Cephalexin	Naproxen
Palmitic acid	CaCO3	Ciprofloxacin	Benzocaine
Mineral Oil	Al(OH)3	Polymyxin B	Phenylephrine
Simethicone	Mg(OH)2	Bacitracin	Bismuth subsalicylate
Cholesterol		Neomycin	
Alcohols	**Histamine antagonists**	**Surfactants**	**Remaining**
Resorcinol	Famotidine	Nonoxynol-9	Hydrocortisone
Ethanol	Omeprazole	Benzalkonium chloride	Loperamide Hydrochloride
	Cimetidine		Nystatin
			Sennosides

Inter-lab reproducibility

The inter-lab reproducibility for the BD MAX Check-Points CPO Assay was determined by analyzing one strain per target spiked into negative rectal swab matrix in 2 different concentrations (1.5x LoD and 3x LoD), non-target strain spiked into negative rectal swab matrix and negative rectal swab matrix at 3 different sites by 2 operators using 1 lot during 5 days.

Table 11. Inter-lab Reproducibility Results for BD MAX Check-Points CPO

	KPC		NDM		OXA-48		VIM/IMP	
	+	-	+	-	+	-	+	-
1.5x LoD (95% CI)	**100% (60/60)** (94.0-100%)		**98.3% (59/60)** (91.1-99.7%)		**100% (60/60)** (94.0-100%)		**97.5% (117/120)** (92.9-99.1%)	
3x LoD (95% CI)	**100% (60/60)** (94.0-100%)		**100% (60/60)** (94.0-100%)		**100% (60/60)** (94.0-100%)		**99.2% (119/120)** (95.4-99.9%)	
Negatives (95% CI)		**100% (100/100)** (96.3-100%)		**100% (100/100)** (96.3-100%)		**100% (100/100)** (96.3-100%)		**100% (100/100)** (96.3-100%)

In summary, the inter-lab reproducibility ranged from 100-100%, 97.5-100% and 99.2-100% for Negatives, 1.5x LoD and 3x LoD, respectively.

Inter-lot reproducibility

The inter-lot reproducibility for the BD MAX Check-Points CPO Assay was determined by analyzing one strain per target spiked into negative rectal swab matrix in 2 different concentrations (1.5x LoD and 3x LoD), non-target strain spiked into negative rectal swab matrix and negative rectal swab matrix at 1 site by 2 operators using 3 lots during 5 days.

Table 12. Inter-lot Reproducibility Results for BD MAX Check-Points CPO

	KPC		NDM		OXA-48		VIM/IMP	
	+	-	+	-	+	-	+	-
1.5x LoD (95% CI)	**100% (60/60)** (94.0-100%)		**100% (60/60)** (94.0-100%)		**100% (60/60)** (94.0-100%)		**99.2% (119/120)** (95.4-99.9%)	
3x LoD (95% CI)	**100% (60/60)** (94.0-100%)		**100% (60/60)** (94.0-100%)		**100% (60/60)** (94.0-100%)		**100% (120/120)** (96.9-100%)	
Negatives (95% CI)		**100% (90/90)** (95.9-100%)		**100% (90/90)** (95.9-100%)		**100% (90/90)** (95.9-100%)		**100% (90/90)** (95.9-100%)

In summary, the inter-lot reproducibility ranged from 100-100%, 99.2-100% and 100-100% for Negatives, 1.5x LoD and 3x LoD, respectively.

Intra-lab reproducibility

The intra-lab reproducibility was determined by analyzing one strain per target spiked into negative rectal swab matrix in 2 different concentrations (1.5x LoD and 3x LoD), non-target strain spiked into negative rectal swab matrix and negative rectal swab matrix at 1 site by 2 operators using 1 lot during 12 days.

Table 13. Intra-lab Reproducibility Results for BD MAX Check-Points CPO

	KPC		NDM		OXA-48		VIM/IMP	
	+	-	+	-	+	-	+	-
1.5x LoD (95% CI)	**100% (48/48)** (92.6-100%)		**100% (48/48)** (92.6-100%)		**97.9% (47/48)** (89.1-99.6%)		**99.0% (95/96)** (94.3-99.8%)	
3x LoD (95% CI)	**97.9% (47/48)** (89.1-99.6%)		**100% (48/48)** (92.6-100%)		**100% (48/48)** (92.6-100%)		**100% (96/96)** (96.2-100%)	
Negatives (95% CI)		**100% (72/72)** (94.9-100%)		**100% (72/72)** (94.9-100%)		**100% (72/72)** (94.9-100%)		**100% (72/72)** (94.9-100%)

In summary, the intra-lab reproducibility ranged from 100-100%, 97.9-100% and 97.9-100% for Negatives, 1.5x LoD and 3x LoD, respectively.

Mixed Infection / Competitive interference

No interference was observed from testing of thirteen (13) specimens containing one KPC, VIM, IMP, OXA-48, or NDM target from strains with known LoD spiked at 2x LoD and one or two other target organism(s) spiked at ~1x10^6 CFU/mL into negative rectal swab matrix.

Carry-over contamination

Carry-over contamination was assessed by testing negative specimens together with positive specimens containing a high load of bacteria carrying the carbapenemase resistance genes KPC, OXA48, NDM and VIM or IMP. Positions of negative and positive specimens were alternated to maximize the possibility for carry-over contamination. Negative rectal swab matrix was used for negative specimens, and to prepare positive specimens by seeding matrix with target organisms at a concentration of 5 x 10^6 CFU/mL. No positive calls were found for a total of 166 negative specimens.

REFERENCES

1.Clinical and Laboratory Standards Institute. 2005. Approved Guideline M29-A3. Protection of laboratory workers from occupationally acquired infections, 3rd ed., CLSI. Wayne, PA.

2. Centers for Disease Control and Prevention, and National Institutes of Health. Biosafety in microbiological and biomedical laboratories. Chosewood L.C. and Wilson D.E. (eds) (2009). HHS Publication number (CDC) 21-1112.

3. BD MAX System User's Manual (refer to the latest version) BD Diagnostics, Sparks, MD, USA.

4. Clinical and Laboratory Standards Institute. Molecular Diagnostic Methods for Infectious Diseases; Approved Guideline, document MM3 (Refer to the latest edition).

5. Clinical and Laboratory Standards Institute. User Protocol for Evaluation of Qualitative Test Performance; Approved Guideline.
Document EP12 (Refer to the latest edition).

6. Naas, T., Oueslati, S., Bonnin, R. A., Dabos, M. L., Zavala, A., Dortet, L., Retailleau, P. and Iorga, B. I. Beta-Lactamase DataBase (BLDB) - Structure and Function. *J. Enzyme Inhib. Med. Chem.* **2017**, *32*, 917-919.

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Temperature limitation / Температурни ограничения / Teplotní omezení / Temperaturbegrænsning / Temperaturbegrenzung / Περιορισμοί θερμοκρασίας / Limitación de temperatura / Temperatuuri piirang / Limites de température / Dozvoljena temperatura / Hőmérsékleti határ / Limiti di temperatura / Температураны шектеу /온도 제한 / Laikymo temperatūra / Temperatūras ierobežojumi / Temperatuurlimiet / Temperaturbegrensning / Ograniczenie temperatury / Limites de temperatura / Limite de temperatură / Ограничение температуры / Ohraničenie teploty / Ograničenje temperature / Temperaturgräns / Sıcaklık sınırlaması / Обмеження температури / 温度限制

LOT
Batch Code (Lot) / Код на партидата / Kód (číslo) šarže / Batch-kode (lot) / Batch-Code (Charge) / Κωδικός παρτίδας (παρτίδα) / Código de lote (lote) / Partii kood / Numéro de lot / Lot (kod) / Tétel száma (Lot) / Codice batch (lotto) / Топтама коды / 배치 코드(로트) / Partijos numeris (LOT) / Partijas kods (laidiens) / Lot nummer / Batch-kode (parti) / Kod partii (seria) / Código do lote / Cod de serie (Lot) / Код партии (лот) / Kód série (šarža) / Kod serije / Partinummer (Lot) / Parti Kodu (Lot) / Код партії / 批号（亚批


Contains sufficient for <n> tests / Съдържанието е достатъчно за <n> теста / Dostatečné množství pro <n> testů / Indeholder tilstrækkeligt til <n> tests / Ausreichend für <n> Tests / Περιέχει επαρκή ποσότητα για <n> εξετάσεις / Contenido suficiente para <n> pruebas / Külladane <n> testide jaoks / Contenu suffisant pour <n> tests / Sadržaj za <n> testova / <n> teszthez elegendő / Contenuto sufficiente per <n> test / <n> тесттері үшін жеткілікті / <n> 테스트가 충분히 포함됨 / Pakankamas kiekis atlikti <n> testų / Satur pietiekami <n> pārbaudēm / Inhoud voldoende voor “n” testen / Innholder tilstrekkelig til <n> tester / Zawiera ilość wystarczającą do <n> testów / Conteúdo suficiente para <n> testes / Conţinut suficient pentru <n> teste / Достаточно для <n> тестов(а) / Obsah vystačí na <n> testov / Sadržaj dovoljan za <n> testova / Innehåller tillräckligt för <n> analyser / <n> test için yeterli malzeme içerir / Вистачить для аналізів: <n> / 足够进行 <n> 次检测


Consult Instructions for Use / Направете справка в инструкциите за употреба / Prostudujte pokyny k použití / Se brugsanvisningen / Gebrauchsanweisung beachten / Συμβουλευτείτε τις οδηγίες χρήσης / Consultar las instrucciones de uso / Lugeda kasutusjuhendit / Consulter la notice d’emploi / Koristi upute za upotrebu / Olvassa el a használati utasítást / Consultare le istruzioni per l’uso / Пайдалану нұсқаулығымен танысып алыңыз / 사용 지침 참조 / Skaitykite naudojimo instrukcijas / Skatīt lietošanas pamācību / Raadpleeg de gebruiksaanwijzing / Se i bruksanvisningen / Zobacz instrukcja użytkowania / Consultar as instruções de utilização / Consultaţi instrucţiunile de utilizare / См. руководство по эксплуатации / Pozri Pokyny na používanie / Pogledajte uputstvo za upotrebu / Se bruksanvisningen / Kullanım Talimatları’na başvurun / Див. інструкції з використання / 请参阅使用说明


Keep dry / Пазете сухо / Skladujte v suchém prostředí / Opbevares tørt / Trocklagern / Φυλάξτε το στεγνό / Mantener seco / Hoida kuivas / Conserver au sec / Držati na suhom / Száraz helyen tartandó / Tenere all’asciutto / Құрғақ күйінде ұста / 건조 상태 유지 / Laikykite sausai / Uzglabāt sausu / Droog houden / Holdes tørt / Przechowywać w stanie suchym / Manter seco / A se feri de umezeală / Не допускать попадания влаги / Uchovávajte v suchu / Držite na suvom mestu / Förvaras torrt / Kuru bir şekilde muhafaza edin / Берегти від вологи / 请保持干燥


Perforation / Перфорация / Perforace / Perforering / Διάτρηση / Perforación / Perforatsioon / Perforacija / Perforálás / Perforazione / Тесік тесу / 절취선 / Perforacija / Perforācija / Perforatie / Perforacja / Perfuração / Perforare / Перфорация / Perforácia / Perforasyon / Перфорація / 穿孔


Keep away from light / Пазете от светлина / Nevystavujte světlu / Må ikke udsættes for lys / Vor Licht schützen / Κρατήστε το μακριά από το φως / Mantener alejado de la luz / Hoida eemal valgusest / Conserver à l'abri de la lumière / Držati dalje od svjetla / Fény nem érheti / Tenere al riparo dalla luce / Қараңғыланған жерде ұста / 빛을 피해야 함 / Laikyti atokiau nuo šilumos šaltinių / Sargāt no gaismas / Niet blootstellen aan zonlicht / Må ikke utsettes for lys / Przechowywać z dala od źródeł światła / Manter ao abrigo da luz / Feriţi de lumină / Хранить в темноте / Uchovávajte mimo dosahu svetla / Držite dalje od svetlosti / Får ej utsättas för ljus / Işıktan uzak tutun / Берегти від дії світла / 请远离光线

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Check-Points Health B.V.
Binnenhaven 5
6709 PD Wageningen
The Netherlands
info@check-points.com
www.check-points.com