# Question and Answers: SARSCov-2 ECHO Session April 14, 2020

| SN# | Question | Answer/ Response / Comment |
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| | | GeneXpert® System and Xpert® Xpress SARS-CoV-2* |
| **Sample management** | | |
| 1. | Can saline solution be used if no viral transport media is available? How long can we keep the sample in saline? | Guidelines for collection and alternatives are available from the CDC and FDA.<br><br>CDC: https://www.cdc.gov/coronavirus/2019-ncov/lab/guidelines-clinical-specimens.html<br><br>WHO: https://www.who.int/publications-detail/laboratory-testing-for-2019-novel-coronavirus-in-suspected-human-cases-20200117 |
| 2. | What is the appropriate storage temperature for collected samples as they are transported to the testing labs? | Nasopharyngeal, nasal, and mid-turbinate swabs and nasal wash/aspirate specimens can be stored at room temperature (15–30 °C) for up to 8 hours and refrigerated (2–8 °C) up to seven days until testing is performed on the GeneXpert Instrument Systems. |
| 3. | Why are sputum samples not tested? | This sample has not been validated by Cepheid and will be considered an off-label use. See the Xpert Xpress SARS-CoV-2 Package Insert for details. |
| 4. | Are there any rejection criteria for sample collection? | Refer to package insert and ensure sample collection, storage and cartridge preparation protocols are followed. |
| 5. | What are the most common mistakes health workers are making when collecting samples (naso, oro or nasal)? Any recommendations? What are BD/Cepheid's thoughts on self-collection by patients? | Refer to package insert and ensure sample collection, storage and cartridge preparation protocols are followed.<br><br>Proper specimen collection, storage, and transport are critical to the performance of this test. Inadequate specimen collection, improper specimen handling and/or transport may yield a false result.<br><br>Self-collected respiratory specimens for SARS-CoV-2 testing have been described in the literature. However, this sample has not been validated by Cepheid and will be |

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| | | considered an off-label use. See the Xpert Xpress SARS-CoV-2 Package Insert for details. |
| 6. | Is there any pretreatment of the sample before loading it into the cartridge? How is the viral material eluted out of the swabs before pipetting into the cartridge? | The sample is transferred into a VTM tube containing 3mL transport medium to preserve and transport respiratory virus specimens. The VTM tube is inverted 5 times before transferring the sample into the cartridge. There is no pretreatment of specimens to inactivate viruses prior to adding sample to the cartridge. |
| 7. | This virus is zoonotic, how can animals be handle for sample collection | Animal samples have not been validated by Cepheid and will be considered an off-label use. See the Xpert Xpress SARS-CoV-2 Package Insert for details. |
| 8. | For the Xpert assay, how long can you store samples before assay and at what temperature | Nasopharyngeal, nasal, and mid-turbinate swabs and nasal wash/aspirate specimens can be stored at room temperature (15–30 °C) for up to 8 hours and refrigerated (2–8 °C) up to seven days until testing is performed on the GeneXpert Instrument Systems. |
| **Reagent and consumables** | | |
| 9. | Does the open system architecture of the BD instrument allow one to use "home-made" reagents for Cov-2 detection, given the current issues with shipping and shortages of reagent kits? | N/A |

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| 10. | Can swabs eNat from Copan (the ones with inactivator ) be used with GenXpert for detection of SARS-Cov-2? Is it validated? inactivator won't interfere with the method? | This sample collection device has not been validated by Cepheid and will be considered an off-label use. See the Xpert Xpress SARS-CoV-2 Package Insert for details. |
| 11. | What kind of swabs are used - are they provided with the kit? One per test? In case we need to repeat can we use a different swab? | Sample collection devices are not included in the kit with cartridges and will have to be purchased separately. Nasopharyngeal, nasal, and mid-turbinate swabs and nasal wash/aspirate specimens can be used with the assay and are added to 3ml viral transport media (VTM).<br><br>Guidelines for collection and alternatives are available from the CDC and FDA.<br><br>Customers should refer to the CDC Interim Guidelines for Collecting, Handling, and Testing Clinical Specimens from Persons Under Investigation (PUIs) for Coronavirus Disease 2019 (COVID-19) https://www.cdc.gov/coronavirus/2019-nCoV/lab/guidelines-clinical-specimens.html and the FDA FAQs on Diagnostic Testing for SARS-CoV-2 https://www.fda.gov/medical-devices/emergency-situations-medical-devices/faqs-diagnostic-testing-sars-cov-2#whatif |
| 12. | What is your take on using RDT for diagnosis in this pandemic especially with several limitations of RDT? Also, when will your Antigen based RDT be available. Which is your preference for clinical and epidemiology purpose and not just research | N/A |

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| 13. | What is the shelf life the cartridge considering the time of purchase and delivery? | Shelf life details will be provided with the order/quote |
| 14. | What are some of the consumables needed when using BD max system that are needed but not proprietary to BD? | N/A |
| 15. | Does the kit come with controls? | Commercially Available External Controls for Xpert® Xpress SARS-CoV-2 can be purchased from Seracare. ***Use the Order Code CEPHEID*** https://www.seracare.com/AccuPlex-SARSCoV2-Reference-Material-Kit-0505-0126/ |
| 16. | Why didn't you use the S protein | Our test targets the SARS-CoV-2 N2 and E genes. Both are conserved regions of the viral genome and have not been observed to be undergoing genetic drift. |
| 17. | What are the differences between tests manufactured for the US and those manufactured for the rest of the world. | All Xpert tests are manufactured the same. |
| **Safety consideration** | | |
| 18. | Do you recommend that the sample is added to the card in a BSL2 cabinet? Does your SARS-COV-2 PCR Test require a Bio Safety Level 2 lab to conduct the test or can it be done in a Smear Microscopy Center? What are the safety recommendations | Refer to local regulations, WHO or CDC guidelines. |

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| | for performing SARS-CoV-2 for our laboratory personnel? | |
| 19. | Testing cartridges contain GTC (GeneXpert). what is the concentration of Guanidium thiocyanate in the Xpert SARS-CoV-2 cartridge? What are the recommendations for disposal of cartridges after use? What are your plans for waste management in Africa especially in Africa? | Xpert® Xpress SARS-CoV-2 Safety Data Sheet can be accessed on the Cepheid website: https://www.cepheid.com/coronavirus<br><br>Incineration of Xpert cartridges (all types) should follow World Health Organization (WHO) recommendations. Specifically, biowaste should be burned or incinerated, preferably at temperatures above 1000°C, as detailed by WHO document "Management of Solid Health-Care Waste at Primary Health-Care Centres" available for download at: www.who.int/water_sanitation_health/medicalwaste/decisionmguiderev221105.pdf?ua=1 |
| 20. | What challenges do you foresee for rolling out of these tests in resource-limited settings? | Training and support will be provided to facilitate the roll-out |
| **Test system & procedure** | | |
| 21. | What is the throughput of the system per 8 hours work schedule keeping in mind that we need to ramp up testing in all the community settings | The test is complete in approximately 45 minutes. System throughput depends on the number of modules. |
| 22. | What are the turn-around time for both BD and Cepheid testing? | See Q21 |
| 23. | How like to hear the presenter's thoughts about the role of their diagnostics systems in the context of COVID-19 passports? These tests are | N/A |

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| | in the position to rule in with high PPV the presence of Abs in the general community? | |
| 24. | How soon can both Xpert and BD detect SARS COV-2 virus after the onset of infection?<br><br>Can Xpress SARS-COV2 be used to monitor recovery? | Generally, detection can occur immediately upon onset of symptoms since people usually have detectable virus before onset.<br><br>Presence of RNA during the convalescent phase of illness may not predict contagiousness. This usage has not been validated by Cepheid and will be considered an off-label use. |
| 25. | Is the Xpert Xpress SARS-COV2 indicated for symptomatic and/or asymptomatic patients?" | The Xpert Xpress SARS-CoV-2 test is a rapid, real-time RT-PCR test intended for the qualitative detection of nucleic acid from the SARS-CoV-2 from individuals suspected of COVID-19 by their healthcare provider. |
| 26. | Do samples have to be batched? If just three tests are run (90mins), are the other reagents wasted? 2) How many controls are in each batch | There is no need to batch Xpert tests, each module can process a test independently of the others. |
| 27. | Are they recommending local validation of testing methods prior to use? | Please see link to verification protocol if required.<br>https://www.cepheid.com/PDFs/Tests%20-%20Critical%20Infectious%20Diseases/Example-Xpert-Xpress-SARS-CoV-2-Verification-Protocol.pdf |
| 28. | Any experience using either the Cepheid or BD systems for pooled testing please? | No pooled testing has been verified. This will be considered an off-label use. See the Xpert Xpress SARS-CoV-2 Package Insert for details. |
| **Quality control** | | |

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| 29. | Does the system incorporate controls and if so how many? | On-board internal controls for each sample are<br>• Probe Check Control (PCC)<br>• Sample Processing Control (SPC)<br>See the Xpert Xpress SARS-CoV-2 Package Insert for details regarding these controls |
| 30. | How can we ensure and maintain the quality of tests in emergency situation? What are the recommendations for local validation of testing methods prior to use? | Please see link to verification protocol if required.<br>https://www.cepheid.com/PDFs/Tests%20-%20Critical%20Infectious%20Diseases/Example-Xpert-Xpress-SARS-CoV-2-Verification-Protocol.pdf |
| **Result interpretation and reporting** | | |
| 31. | Does this Gene Xpert model data transmission technology without having to print or keep paper models. And has it already been FDA approved? | Results from the GeneXpert can be transferred automatically without the need to print. The GeneXpert Dx can be configured to connect to a Laboratory Information System (LIS) host computer. |
| 32. | Do your testing platforms support remote test request and return of results to support paperless system between lab and clinic/ surveillance teams | See Q31 |
| 33. | If the Xpert Xpress SARS-COV-2 yields a result negative for N2 Target but positive for the E Target which is considered a Presumptive Positive, how many times can the test be repeated for confirmatory results? | A retest is advised for a non-determinate result (INVALID, NO RESULT, or ERROR) or a PRESUMPTIVE POS result, using a new cartridge. For samples with a repeated presumptive positive result, additional confirmatory testing may be conducted, if it is necessary to differentiate between SARS-CoV-2 and SARS-CoV-1 or other Sarbecovirus currently unknown to infect humans, for epidemiological purposes or clinical management. |

<table>
<tr><td>34.</td><td>How do you interpret the results if N1 is positive and N2 is Negative or vice versa?</td><td>Xpert Xpress SARS-CoV-2 result interpretation: Please see the package insert for more details.
<table>
<tr><th>Result Text</th><th>N2</th><th>E</th><th>SPC</th></tr>
<tr><td>SARS-CoV-2 POSITIVE</td><td>+</td><td>+/-</td><td>+/-</td></tr>
<tr><td>SARS-CoV-2 PRESUMPTIVE POS</td><td>-</td><td>+</td><td>+/-</td></tr>
<tr><td>SARS-CoV-2 NEGATIVE</td><td>-</td><td>-</td><td>+</td></tr>
<tr><td>INVALID</td><td>-</td><td>-</td><td>-</td></tr>
</table></td></tr>
<tr><td>35.</td><td>What can lead to presumptive positive turning to true positive from the sample?</td><td>A sample with a low virus titer near the limit of detection can produce variable results solely due to sampling variability. A sample with a presumptive positive result should be retested using another cartridge or another confirmatory test. To yield the best results the cartridge preparation as indicated by Cepheid must be followed without missing any steps e.g. inverting the sample tube 5 times before transferring the sample to the cartridge to avoid the sample settling at the bottom of the tube.</td></tr>
<tr><td>36.</td><td>Is it true that GeneXpert transmits results directly to Cepheid, conflicting Data Transfer regulations in our countries?</td><td>For Cepheid C360 users, test data may be transmitted to cloud servers in accordance with data transfer agreements and applicable privacy laws. Customers can choose whether test information is sent to the cloud database.</td></tr>
<tr><td colspan="3">Specificity, sensitivity and detection limit</td></tr>
<tr><td>37.</td><td>What is the limit of viral detection for the test?</td><td>Analytical Sensitivity:<br>The claimed LoD for the assay with AccuPlex SARS-CoV-2 Reference Material with is 250 copies/mL<br>The claimed LoD for the assay using Live SARS-CoV-2 Virus is 0.0100 PFU/mL<br>See the Xpert Xpress SARS-CoV-2 Package Insert for details</td></tr>
<tr><td>38.</td><td>What is the sensitivity and Specificity for the IgM/IgG in the first week of infection?</td><td>N/A</td></tr>
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| 39. | What is Sensitivity and Specificity of the Serology Testing? Are there going to be Testing algorithm for PCR and Serology testing? | N/A |
| 40. | What is the sensitivity and specificity for GeneXpert related to COVID-19 | **See Q37 for Analytical sensitivity**<br>7 Microorganisms from the same genetic family and 32 high priority organisms were analyzed *in silico* for possible cross-reactions. No potential unintended cross reactivity with these organisms is expected based on the *in silico* analysis. E primers and probes are not specific for SARS-CoV-2 and will detect Human and Bat SARS-coronavirus.<br>***See the Xpert Xpress SARS-CoV-2 Package Insert for details***<br><br>Clinical sensitivity and specificity were not assessed. We determined agreement with expected results using contrived specimens. |
| **Procurement and supply** | | |
| 41. | Given the global interest in Xpert Cov2 ASSAY, what is the production capacity for the Xpert Cov2 cartridges? | Production is ongoing and ramping up to meet demand. Information on capacity is confidential. |
| 42. | What is the timing and volume availability of the Covid cartridges in Africa (where will supply be manufactured? subject to export restrictions?) | Cartridges are available for Africa from our manufacturing plants in Europe and the US. |
| 43. | Is it true that the cartridges cannot be | Several African countries have already received Xpert Xpress SARS-CoV-2 tests. |

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| | available for use in Africa until May? Or is there any way to FastTrack procurement? | |
| **Cross cutting questions** | | |
| 44. | BD: how many platforms do we have in Africa? | N/A |

*For use under U.S. FDA Emergency Use Authorization (EUA) only. CE-IVD pending regulatory approval.