PROVISIONAL AUTHORISATION OF COVID-19 DIAGNOSTIC TESTS – KEY VALIDATION REQUIREMENTS

1. Nucleic acid tests

- Analytical Sensitivity
  - Limit of Detection (LoD)
    - Probit Analysis to estimate the LoD *or*
    - Confirmation of the LoD concentration with at least 20 replicates (at least 95% of replicates must be positive)
  - Inclusivity
    - *In silico* analysis on all SARS-CoV-2 sequences published on NCBI and GISAID databases
- Analytical Specificity
  - Cross-reactivity (wet lab testing)
    - Study on other human coronaviruses (SARS-CoV, MERS-CoV, Coronavirus OC43, Coronavirus NL63, Coronavirus 229E, and Coronavirus HKU1)
    - Study on other respiratory pathogens (e.g.: Influenza A virus (H1N1-2009, H1N1, H3N2), Influenza B virus, Respiratory Syncytial Virus (RSV), Adenovirus)
  - Cross-reactivity *(in silico*)
    - BLAST analysis on the primers/probe
  - Interference (*mandatory if nucleic acid extraction is not required*)
    - Endogenous substances, including but not limited to hemoglobin, bilirubin, protein, triglyceride for blood sample types
    - Endogenous substances, including but not limited to mucin, blood for respiratory sample types
- Precision
  - Repeatability/Reproducibility (refer to CLSI EP05-A3)
- Sample matrix and nucleic acid extraction system validation
  - Analytical study on contrived specimens on the claimed specimen type *or*
  - Clinical studies on patients' samples

  Study on most challenging specimen types (e.g. sputum) could cover other matrices
- Stability studies
  - Real time or accelerated aging studies on 3 lots of reagent
  - In-use stability studies (e.g. Freeze/Thaw), if applicable, on 1 lot of reagent

  Initial establishment of shelf-life can be based on the data from experience gained with IVD reagents that can reasonably be expected to be comparable with regard to their stability characteristics. However, the claim should be subsequently verified with real time study data post approval.
- Instrument cross-validation studies
  - Verify LoD claim on the different instruments with at least 20 replicates
- Usability test (for PoCT)

2. Serology tests

- Analytical Specificity
  - Cross-reactivity
    - Studies on antibodies of other human coronaviruses (SARS-CoV, MERS-CoV, Coronavirus OC43, Coronavirus NL63, Coronavirus 229E, and Coronavirus HKU1)
    - Studies on antibodies of other respiratory pathogens (e.g.: Influenza A virus (H1N1, H3N2), Influenza B virus, Respiratory Syncytial Virus (RSV), Adenovirus)
  - Interference
    - Endogenous substances, including but not limited to hemoglobin, bilirubin, protein, triglyceride.

  Testing must be conducted on both positive and negative samples.
- Precision
  - Repeatability/Reproducibility (refer to CLSI EP05-A3)
- High dose effect
  - Studies on samples with high titre of antibodies
- Sample matrix validation
  - Analytical study on contrived specimens on the claimed specimen type
  - Clinical studies on actual patients' samples (*including finger prick whole blood specimens where applicable*)
  - If certain anticoagulants are recommended, validation study must be conducted to these anticoagulants.
- Stability studies
  - Real time or accelerated aging studies on 3 lots of reagent
  - In-use stability studies (e.g. open pouch), if applicable, on 1 lot of reagent

  Initial establishment of shelf-life can be based on the data from experience gained with IVD reagents that can reasonably be expected to be comparable with regard to their stability characteristics. However, the claim should be subsequently verified with real time study data post approval.
- Reading time and sample volume validation studies (for rapid test)
- Usability test (for PoCT)
- Clinical Studies
  - Ideally at least 50 positive and negative clinical samples.