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# Harmonization Study Participation Status, Logistics, Analysis Plans

Coronavirus Standards Working Group

# What should a Coronavirus Standards Working Group do?



Assure development and availability of standards, controls, interlab testing, knowledge to support successful rollout & scaling of 2019-nCoV testing



Identify and develop critical infrastructure to support...

- confidence in test results
- interoperability
- scale-up
- long-term capacity



Identify best practices that should be institutionalized

Learn what we need to so next time we have a global network in place ready to make standards.

# Harmonization Study Participation Status, Logistics, Reporting, & Analysis

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Invitations

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Sample Panel

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Labs in Study

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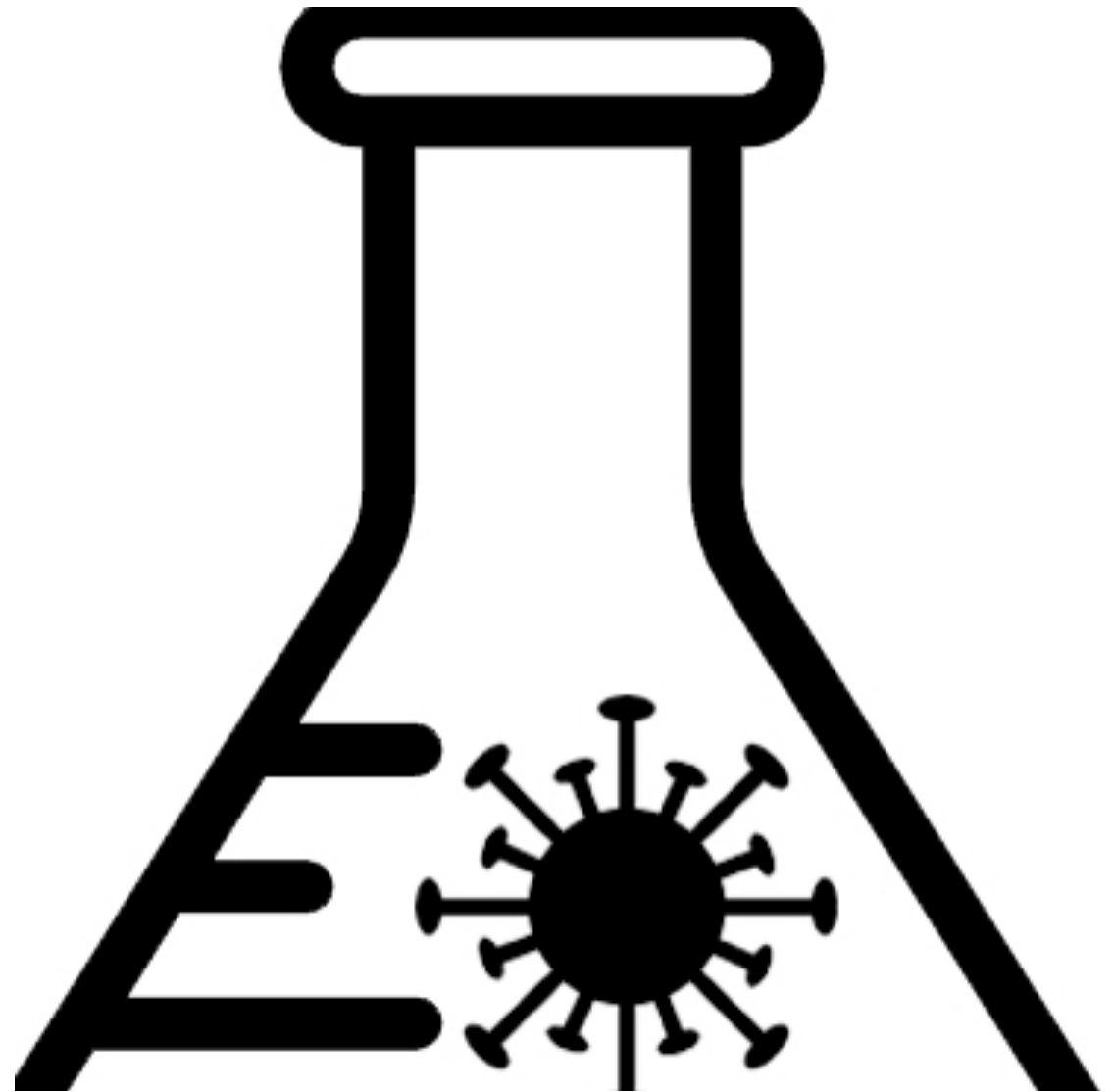
Reporting

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Analysis

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Timeline



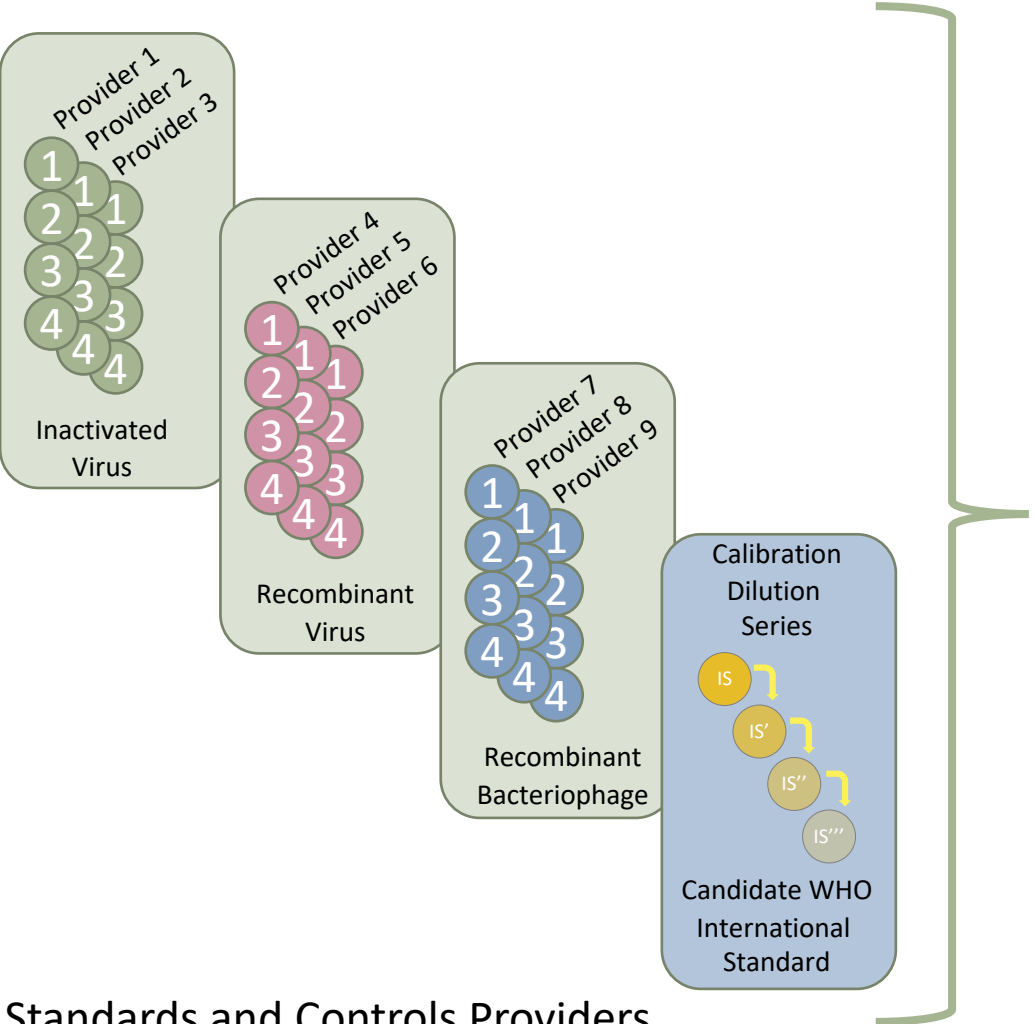
# Purpose of Harmonization Study

The CSWG “Harmonization Study” will establish the equivalence of SARS-CoV-2 RNA target concentrations across a panel of materials and calibrate those results against the candidate WHO International Standard (IS) reference sample.

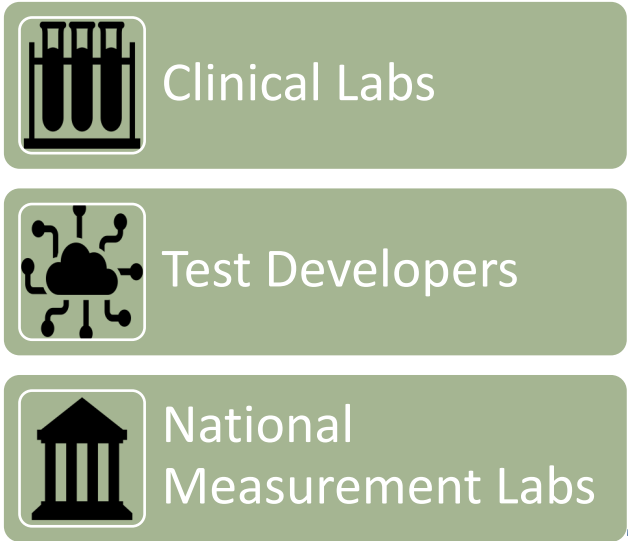
*By calibrating with the NIBSC sample intended to establish the International Unit (IU), the values on the materials included in this study can be assert traceability to the IU when it becomes available.*



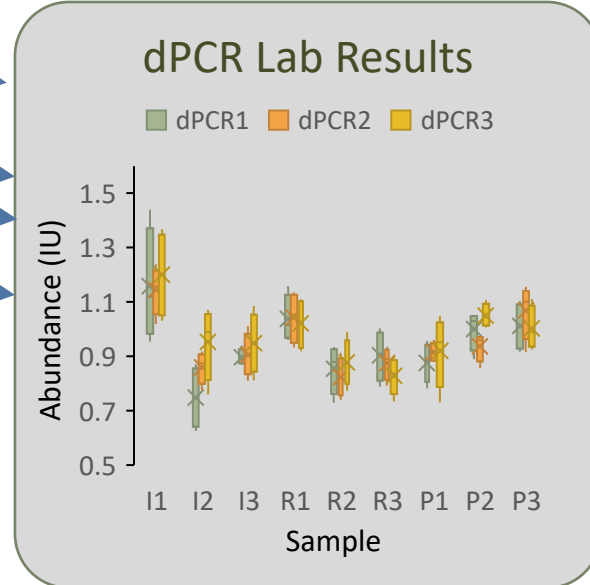
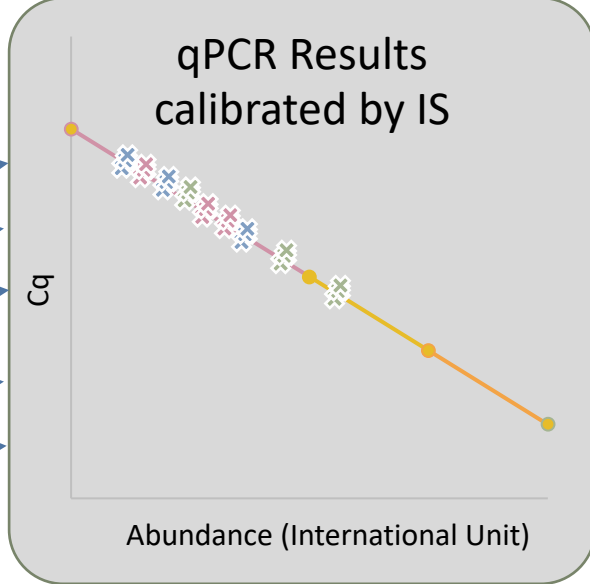
# CSWG Harmonization Study Design



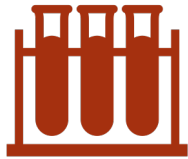
Standards and Controls Providers will contribute materials to be compared to candidate WHO International Standard (IS) with RT-qPCR and dPCR.



Labs will measure study materials calibrated with candidate IS. All results will be harmonized to the value of the IS.



# What this study is not going to do



a comparison of tests



a comparison of labs



a survey of method  
performance (LOD,  
precision, repeatability)



an evaluation of  
commutability

Who have we  
invited to  
participate in  
the study?

- Sample Providers
  - Inactivated Virus
    - Instand
    - Microbiologics
    - Thermo Fisher Scientific
    - **NIBSC**
    - FDA (T1)
    - Zeptomatrix
  - Recombinant Virus
    - LGC Seracare
    - NIBSC
    - Exact Diagnostics
    - Zeptomatrix
  - Recombinant Bacteriophage/other
    - Assuragen
    - Imperial College
- Labs
  - National Measurement Labs
    - NIST, USA
    - NML, UK
    - NIB, Slovenia
  - Test Developers
    - Bio-Rad
    - Thermo Fisher Scientific
    - Roche
    - Cepheid
  - Clinical Labs
    - MUSC
    - Mayo Clinic
    - Stanford
    - Broad Institute/MassCPR
    - Western
    - Labcorp
    - Biogazelle
    - Los Alamos National Laboratory

| Provider          | Material Description                 | Class of Material         | Full Genome? | Provider Confirmed | Material Received | Comments                             |
|-------------------|--------------------------------------|---------------------------|--------------|--------------------|-------------------|--------------------------------------|
| Assuragen         | Pseudo-Viral Particles               | Armored RNA               |              | TRUE               | 11 Nov 2020       | in JIMB Freezer                      |
| Instand           | Lyophilized cell lysate              | Inactivated Virus         | TRUE         | TRUE               |                   | awaiting CDC import clearance        |
| Zeptomatrix       | x 0.5 mL of NATtrol™ SARS-CoV-2      | Inactivated Virus         | TRUE         |                    |                   |                                      |
| Microbiologics    | Lyophilized cell pellet              | Inactivated Virus         | TRUE         | TRUE               | 19 Nov 2020       | in JIMB Freezer                      |
| NIBSC             | Lyophilized Viral Isolate            | Inactivated Virus         | TRUE         | TRUE               |                   | Candidate WHO international standard |
| Thermo Fisher     | Lyophilized cell lysate              | Inactivated Virus         | TRUE         | TRUE               | 17 Nov 2020       | in JIMB Freezer                      |
| Imperial College  | Packaged encapsulated RNA            | Packaged encapsulated RNA |              |                    |                   |                                      |
| Exact Diagnostics | synthetic RNA transcripts            | Recombinant Bacteriophage |              |                    |                   |                                      |
| LGC SeraCare      | Non-SARS viral particles in solution | Recombinant Virus         | TRUE         | TRUE               | 17 Nov 2020       | in JIMB Freezer                      |

What are the samples in our study panel?



| Lab                 | Type                           | Location                   | Tech  | Confirmed |
|---------------------|--------------------------------|----------------------------|-------|-----------|
| Biogazele           | Clinical Labs                  | Belgium                    |       | TRUE      |
| Labcorp             | Clinical Labs                  | Burlington, North Carolina |       | TRUE      |
| Los Alamos          | Clinical Labs                  | Los Alamos, NM             | qPCR  | TRUE      |
| MassCPR Diagnostics | Clinical Labs                  | Boston, MA                 |       | TRUE      |
| Mayo                | Clinical Labs                  | Rochester, MN              | qPCR  | TRUE      |
| MUSC                | Clinical Labs                  | Charleston, SC             | qPCR  | TRUE      |
| Quest               | Clinical Labs                  | Seacaucus, NJ              |       |           |
| Stanford Medicine   | Clinical Labs                  | Stanford, CA               |       | TRUE      |
| Western             | Clinical Labs                  | Los Angeles, CA            | qPCR  | TRUE      |
| NIB                 | National Measurement Institute | Ljubljana, Slovenia        | ddPCR | TRUE      |
| NIST                | National Measurement Institute | Gaithersburg, MD, USA      | ddPCR | TRUE      |
| NML                 | National Measurement Institute | Teddington, UK             | ddPCR | TRUE      |
| Abbott              | Test Developers                |                            | qPCR  |           |
| Bio Rad             | Test Developers                | Pleasanton, California     | dPCR  | TRUE      |
| Cephied             | Test Developers                | Sunnyvale, CA              |       |           |
| Roche               | Test Developers                |                            | qPCR  |           |
| Thermo              | Test Developers                |                            | qPCR  |           |

Who are  
the labs in  
our study?

# What we'll do to get great data from our labs

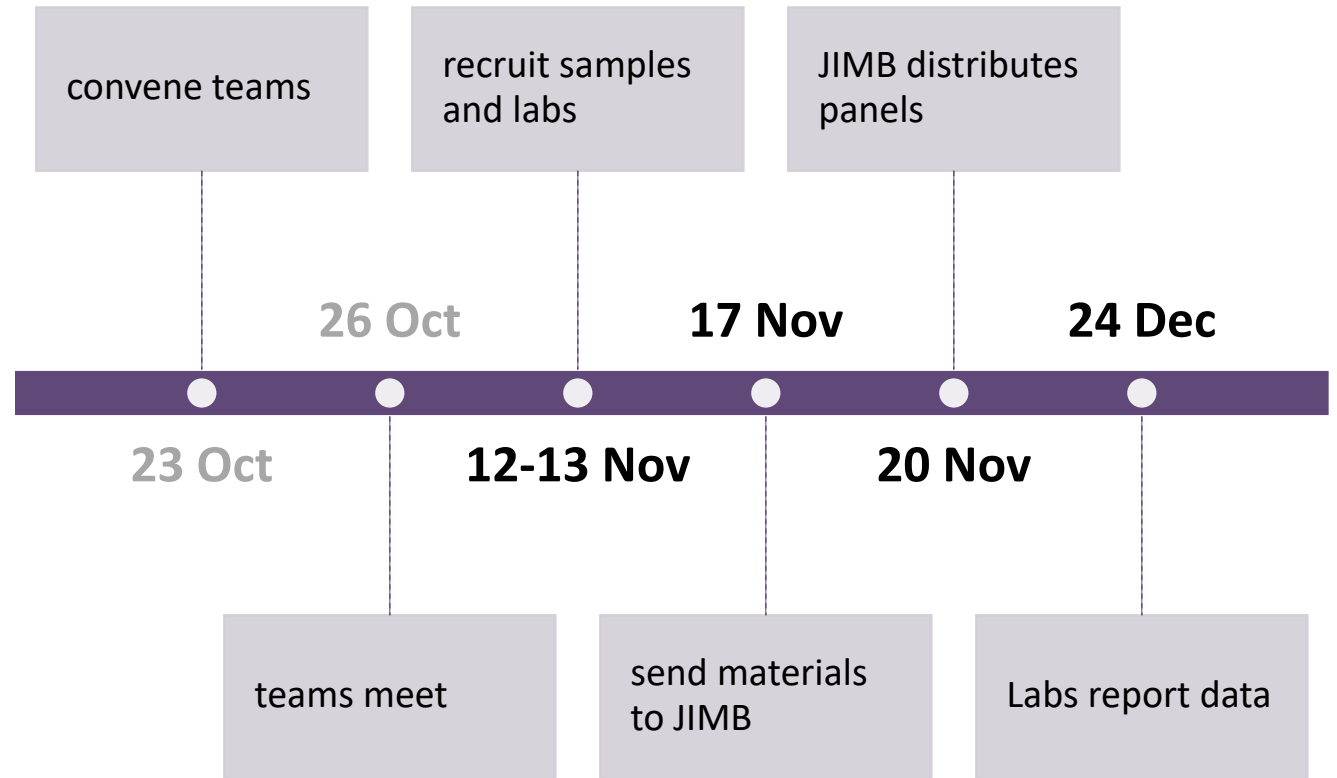
- Establish the performance of the method being used
  - do this with the calibration
  - must demonstrate utility of quantitative RT-qPCR data from tests designed for qualitative results
  - linear dynamic range?
    - Limit of Detection?
  - do this with IS dilution series?

- Jim will present on
  - design considerations
  - reporting
  - analysis

# Jim Huggett's brief overview of path for Reporting and Analysis Team

- What we'll do to get great data from our labs
  - Compare quantitative difference between Standards/QC materials and link to IU
- Submission
  - To who
  - Protocol information/MIQE table
  - Excel data report form
- What sort of data analysis can we plan to conduct?
  - TBD

# Timeline & Logistics





# Discussion

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