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Harmonization Study Planning – Design and Recruiting

Coronavirus Standards Working Group

What should a Coronavirus Standards Working Group do?

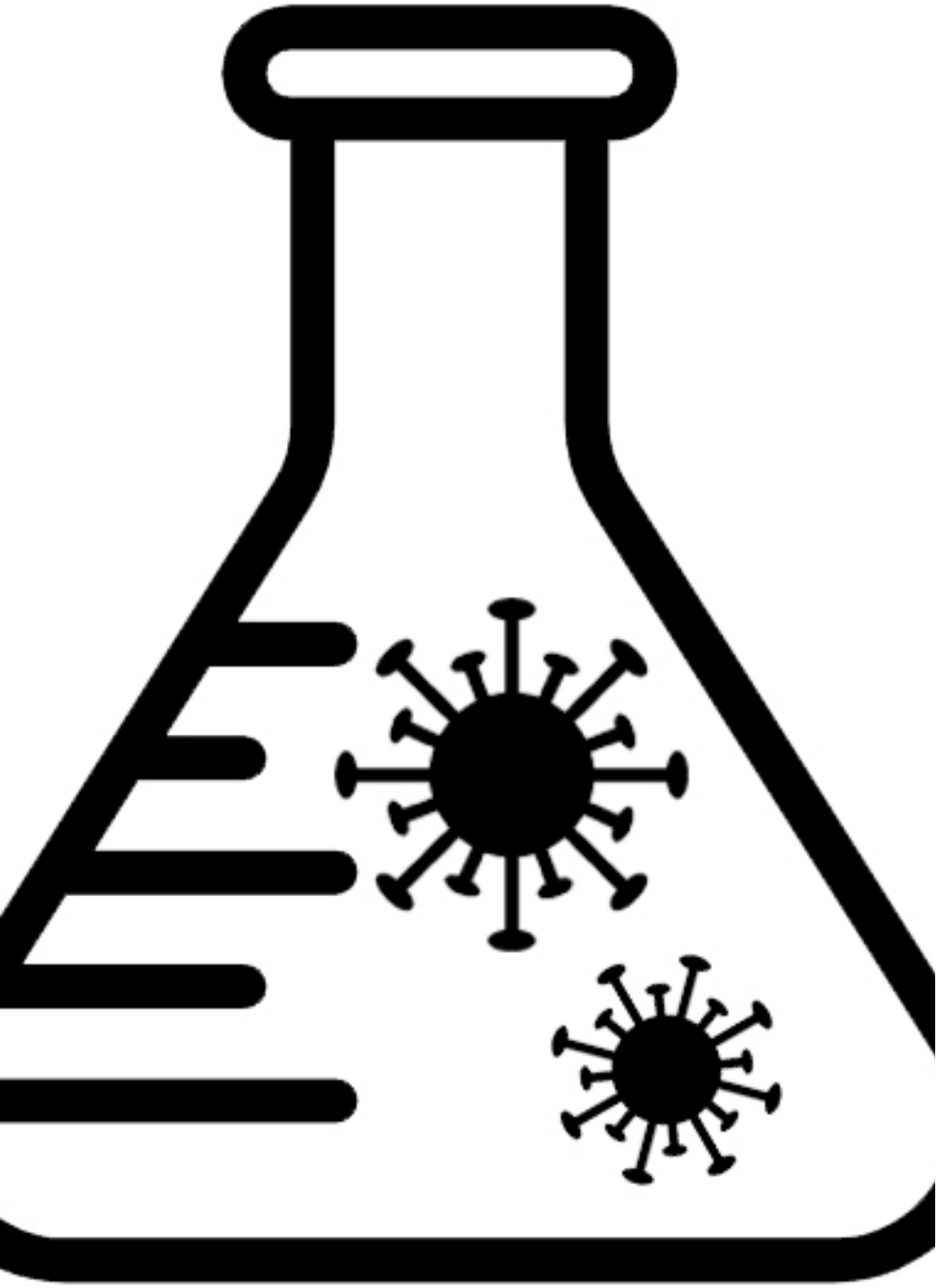
Assure development and availability of standards, controls, interlab testing, knowledge to support successful rollout & scaling of 2019-nCoV testing

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.



Finalizing our Harmonization Study

Study design

Protocols

Samples

Labs

Reporting

Analysis

Logistics

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.

Teams: Samples, Labs, Reporting, Analysis Plan

Samples Team

- develop sample panel

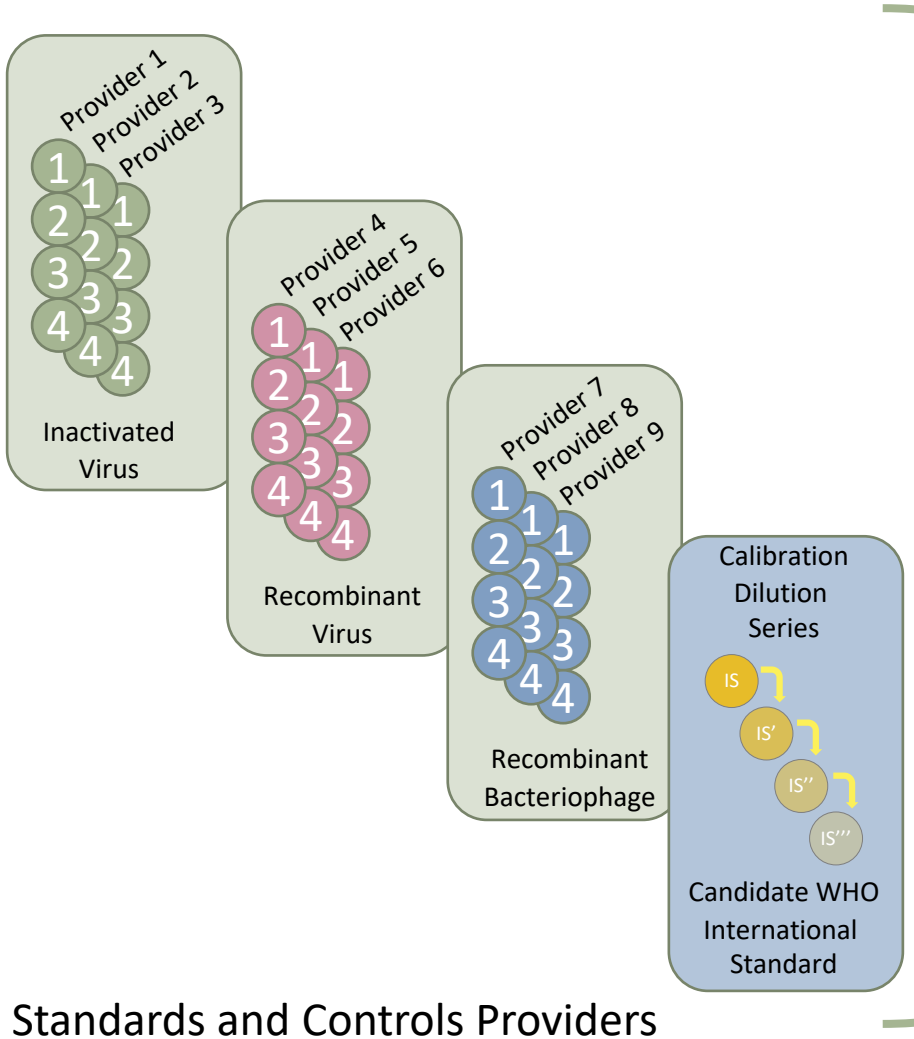
Labs Team

- assemble & coordinate labs

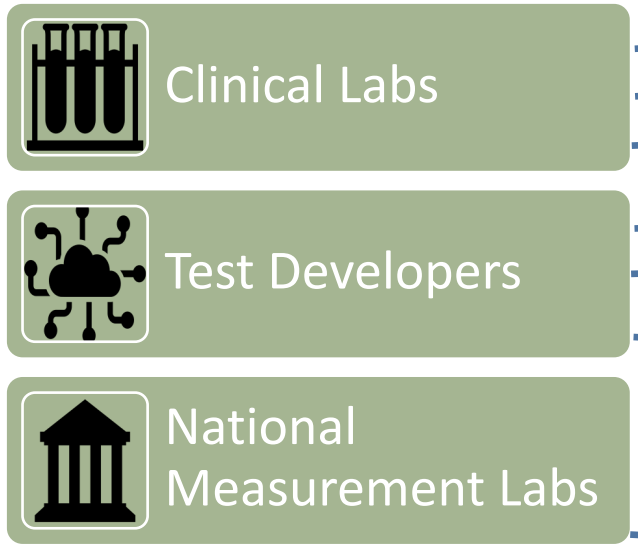
Design, Analysis & Reporting Team

- design experiment
- compose analysis plan
- draft reporting template
  - MIQE, digital MIQE

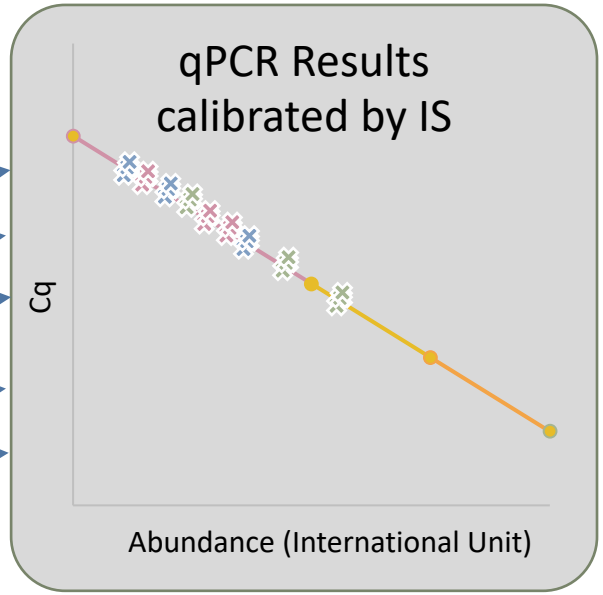
CSWG Harmonization Study Design

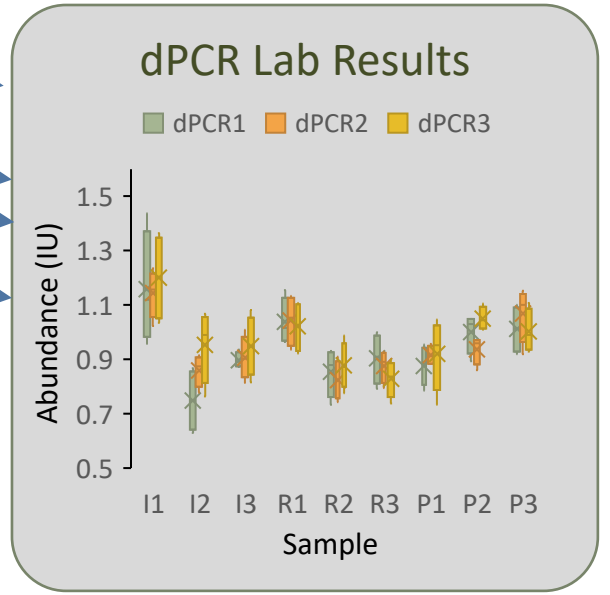


Standards and Controls Providers will contribute materials to be compared to candidate WHO International Standard (IS) with RT-qPCR and dPCR.



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





Open design and protocol questions

- How to address results from labs who are performing “Yes/No” qualitative tests
- Replication design to assess variability of lab measurements
  - do the 4 different samples cover this sufficiently?
- Do we include “No-template” controls
  - how do these fit in the replication design?
- Dilution scheme to get samples in range for lab’s method
- Other questions?

Samples Team: Recruiting Plan

Need 64 identical samples at a single high nominal concentrations that can be diluted by the testing laboratory,

16 negative controls diluted in the same VTM

Samples to include 3 suppliers each of…

- Inactivated, cultured SARS-CoV-2 virus
- Recombinant virus
- Recombinant bacteriophage (‘armored’ RNA)

Unblinded, nominal values provided

Provide COA and Instructions for Use

When possible, use catalog products as they would be provided to a user

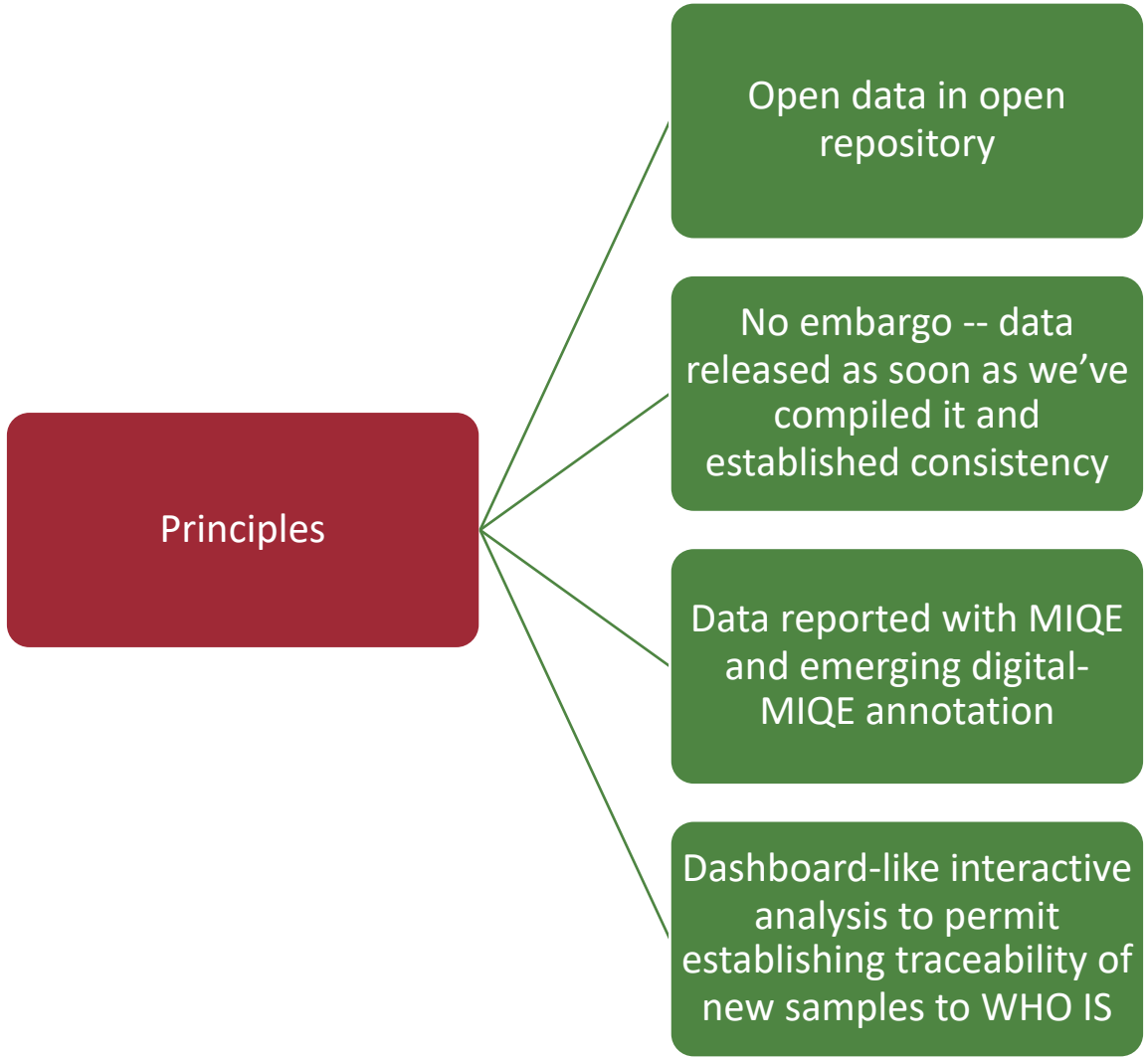
Manufacturers will send packaged materials to JIMB and JIMB will distribute to test laboratories

Labs Team: Recruiting Plan

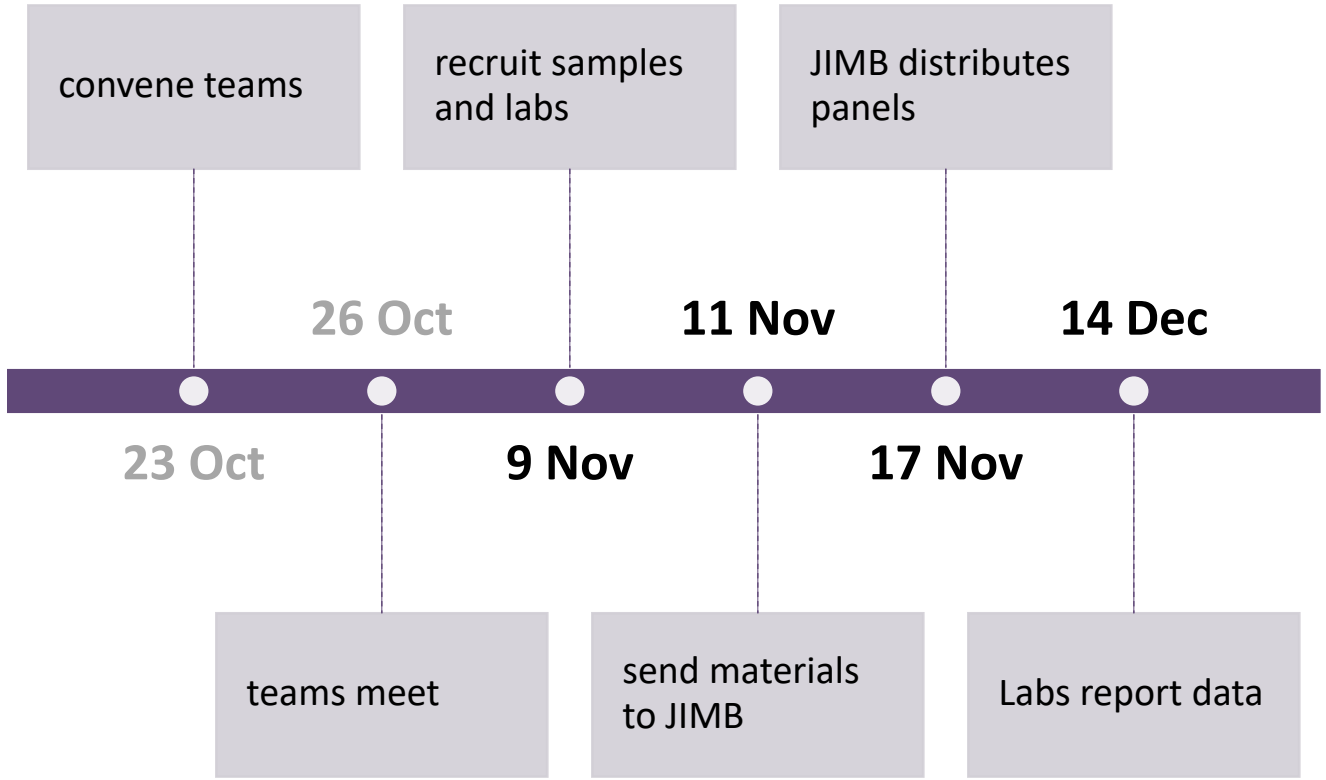
- Lab will receive 4 tubes each of about 10 samples
  - full-process materials in VTM
- Samples clearly labeled
  - nominal abundance of viral RNA
  - “Certificate of Analysis” and “Instructions for Use”
- Lab will report results for each tube
  - reporting tool will be provided
  - results and a MIQE-compliant annotation & protocol
- Recruiting
  - Test Developers
  - Clinical Labs
  - National Measurement Labs

Logistics -- David Catoe

Team formed for Design, Analysis, and Reporting



Timeline


convene teams
recruit samples and labs
JIMB distributes panels
26 Oct
11 Nov
14 Dec
23 Oct
9 Nov
17 Nov
teams meet
send materials to JIMB
Labs report data

Discussion

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

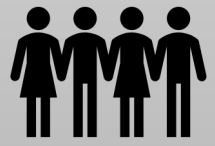
We can make the standards to make molecular testing robust, reliable, and quantitatively comparable.

‘Harmonization Kit” to establish comparability of a set of standards to put molecular testing results on a common scale

just a few labs, NMIs

“Benchmarking Kit” for turn-key evaluation of molecular testing platforms

test developers



“Validation Kit” for blinded validation with a dashboard to form a “smart-grid” for testing

routinely measured at testing labs