13 November 2020

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SLAC National Lab
Stanford University

Harmonization Study Update, What about Vaccine Assays?

Coronavirus Standards Working Group

What should a Coronavirus Standards Working Group do?

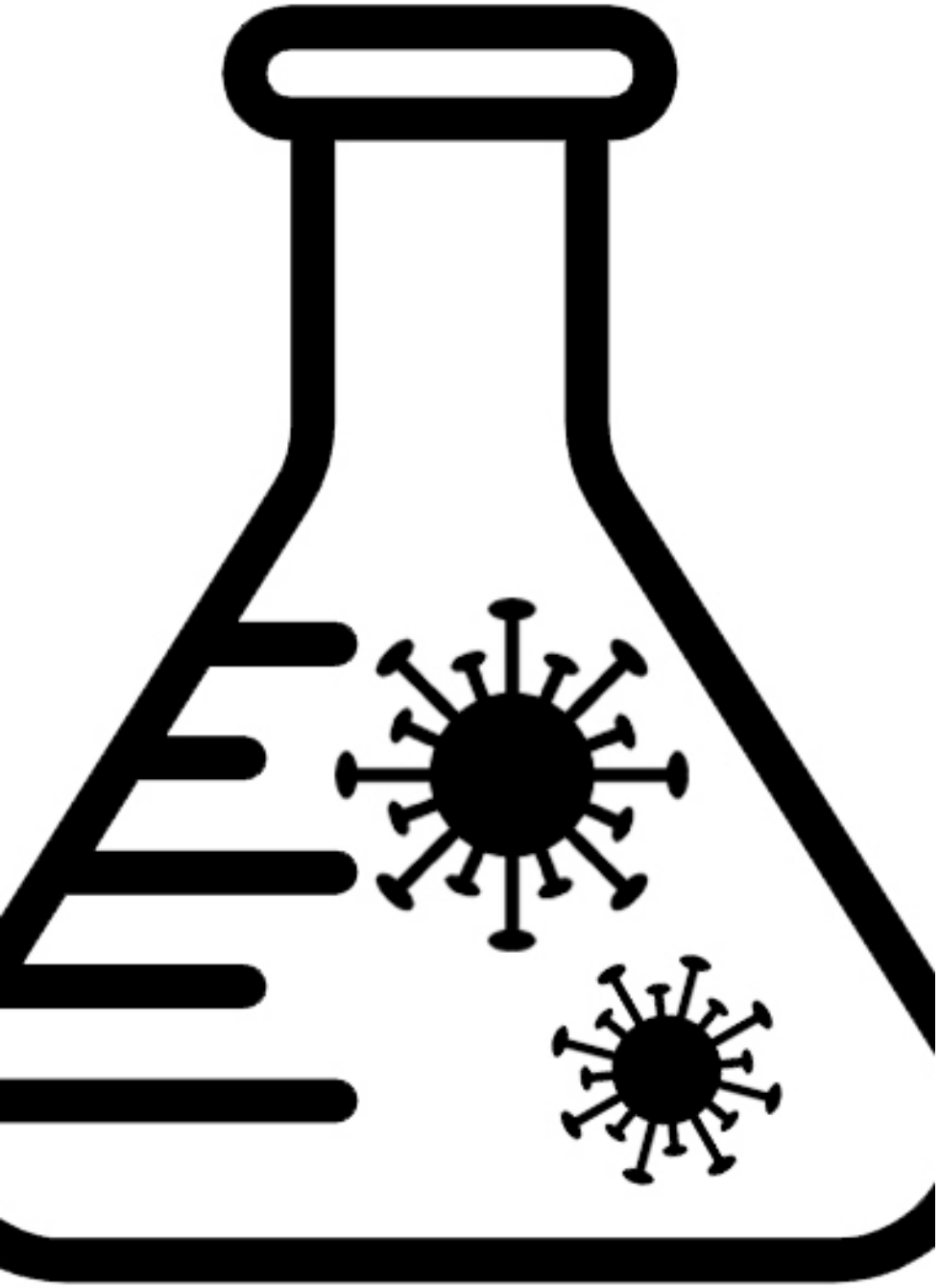
Assure development and availability of standards, controls, interlab testing, knowledge to support successful rollout & scaling of 2019-nCoV testing

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.



Update on our Harmonization Study

Study design

Protocols

Samples

Labs

Reporting & Analysis

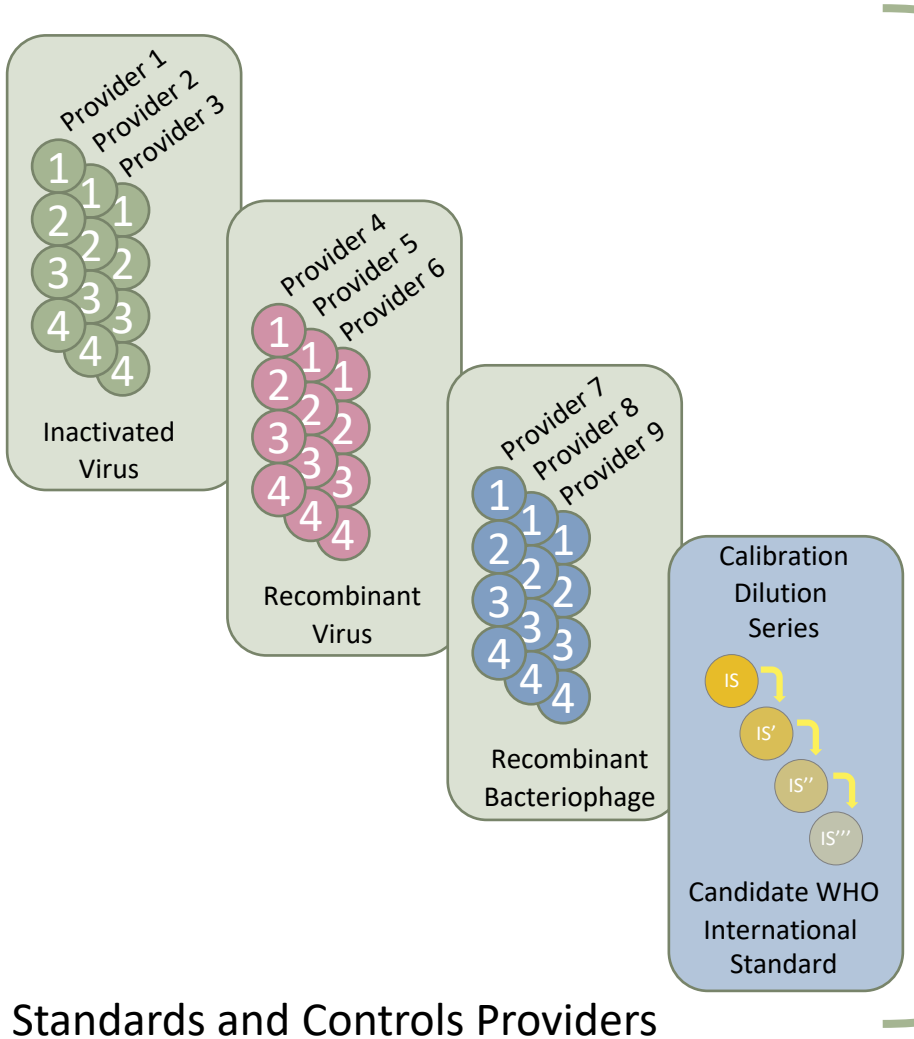
Timeline

Purpose of Harmonization Study

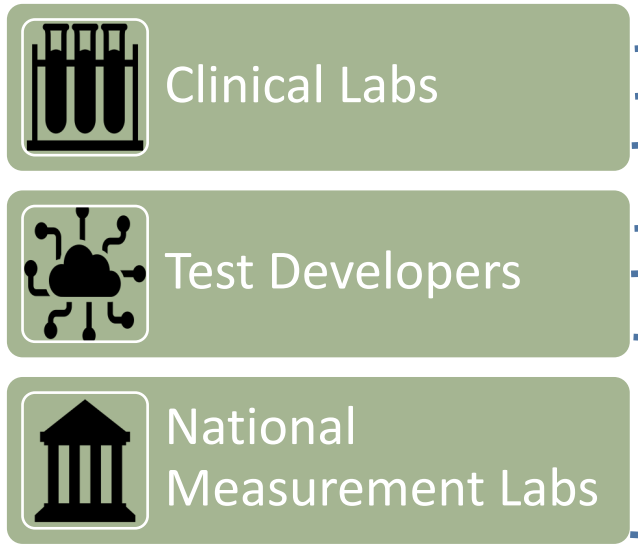
The CSWG “Harmonization Study” will establish the equivalence of SARS-CoV-2 RNA target concentrations across a panel of materials and calibrate those results against the candidate WHO International Standard (IS) reference sample.

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.

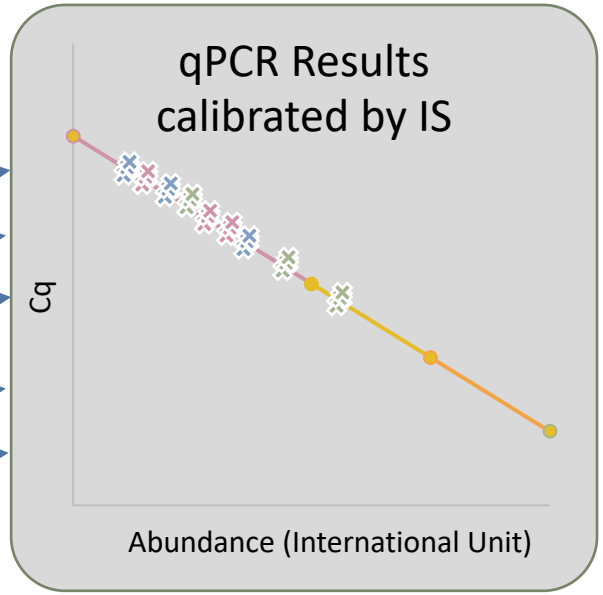
CSWG Harmonization Study Design

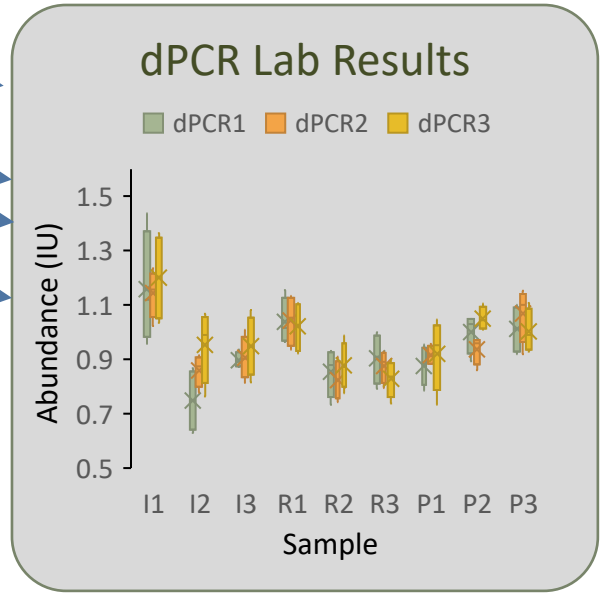


Standards and Controls Providers will contribute materials to be compared to candidate WHO International Standard (IS) with RT-qPCR and dPCR.

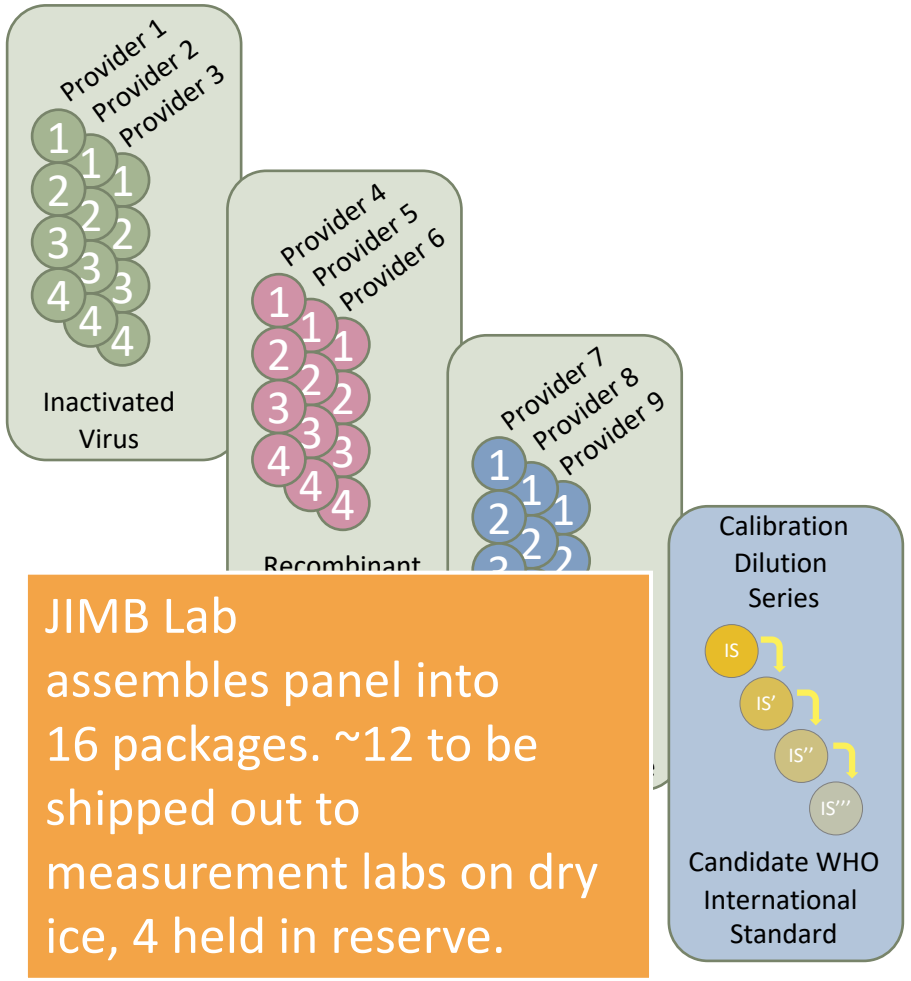


Labs will measure study materials calibrated with candidate IS. All results will be harmonized to the value of the IS.

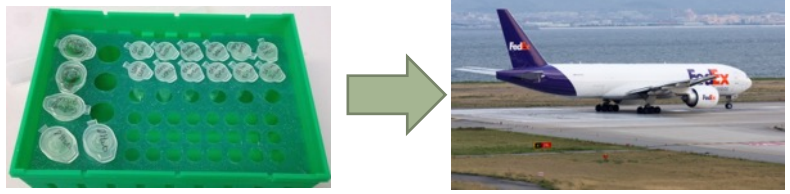




Protocols: Panel assembly, Handling, Labwork



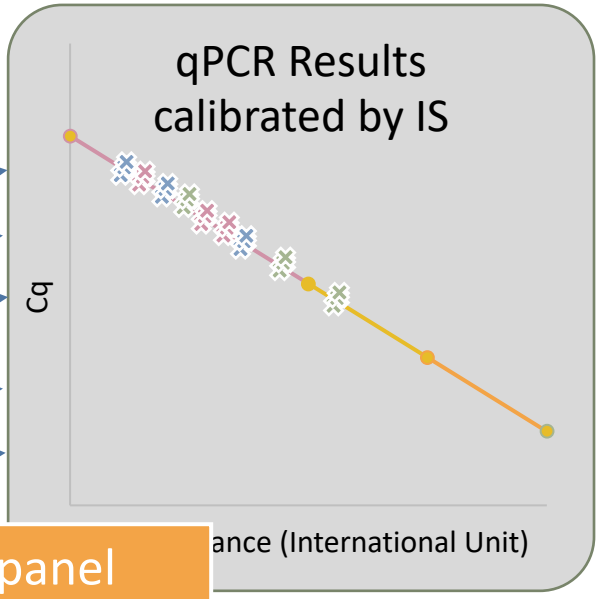
JIMB Lab assembles panel into 16 packages. ~12 to be shipped out to measurement labs on dry ice, 4 held in reserve.



Clinical Labs

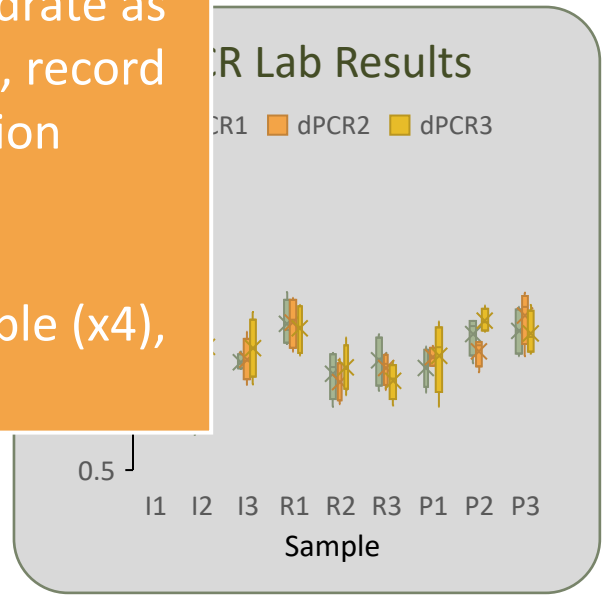
Test Developers

National Metrology Institutes

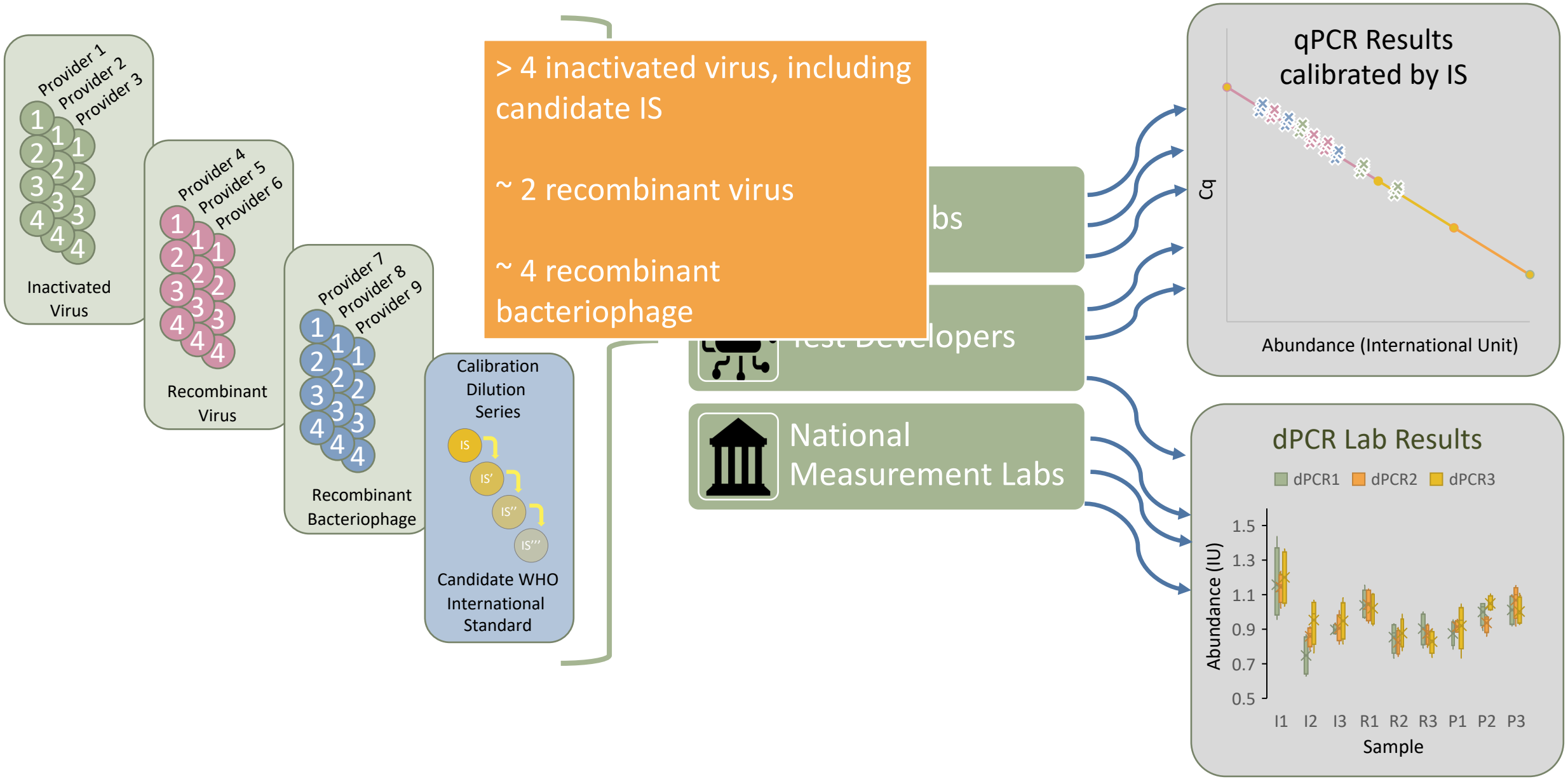


Labs will receive sample panel with COAs and IFUs, rehydrate as needed, dilute as needed, record all handling and preparation operations.

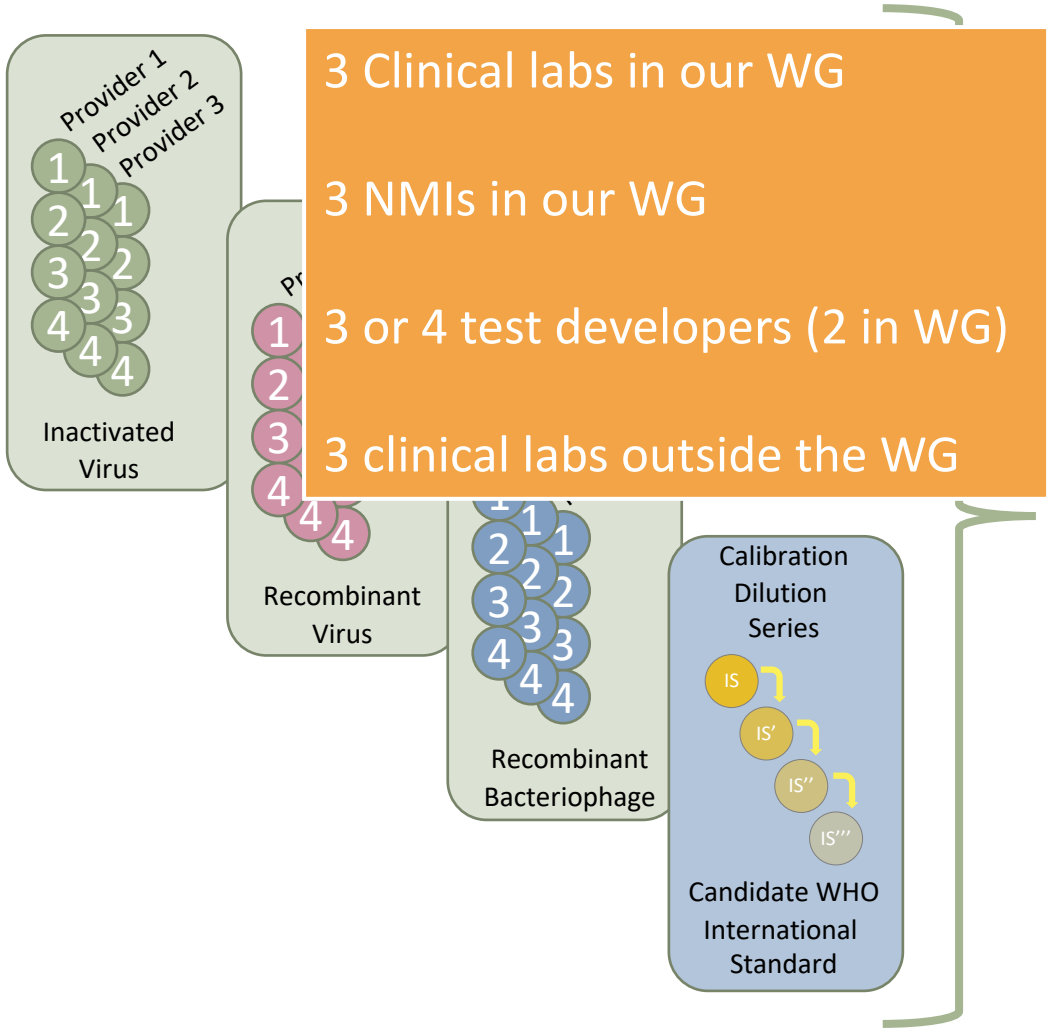
Measure each panel sample (x4), measure NTCs, report.



Samples we're hoping to include



Labs we're inviting to do measurements



3 Clinical labs in our WG

3 NMIs in our WG

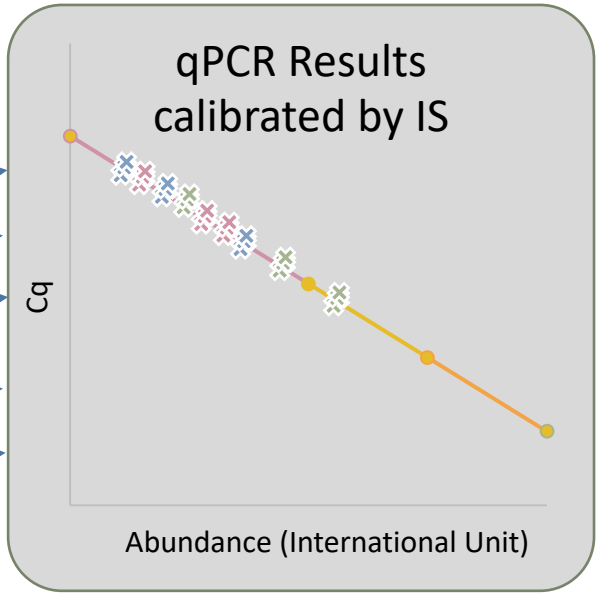
3 or 4 test developers (2 in WG)

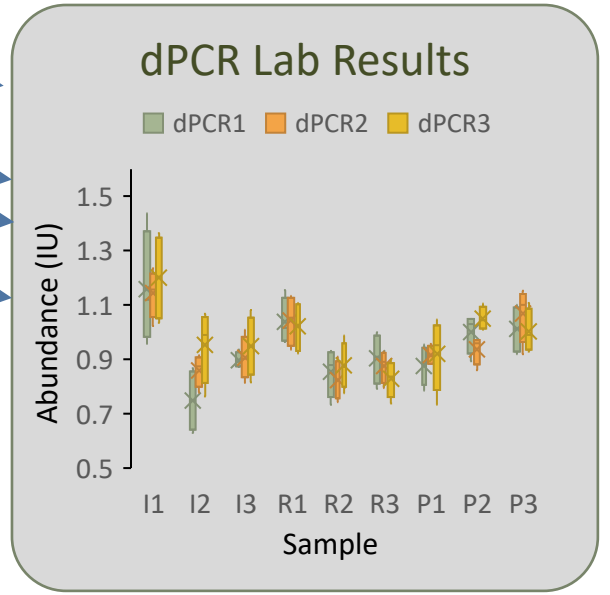
3 clinical labs outside the WG

Clinical Labs

Test Developers

National Measurement Labs



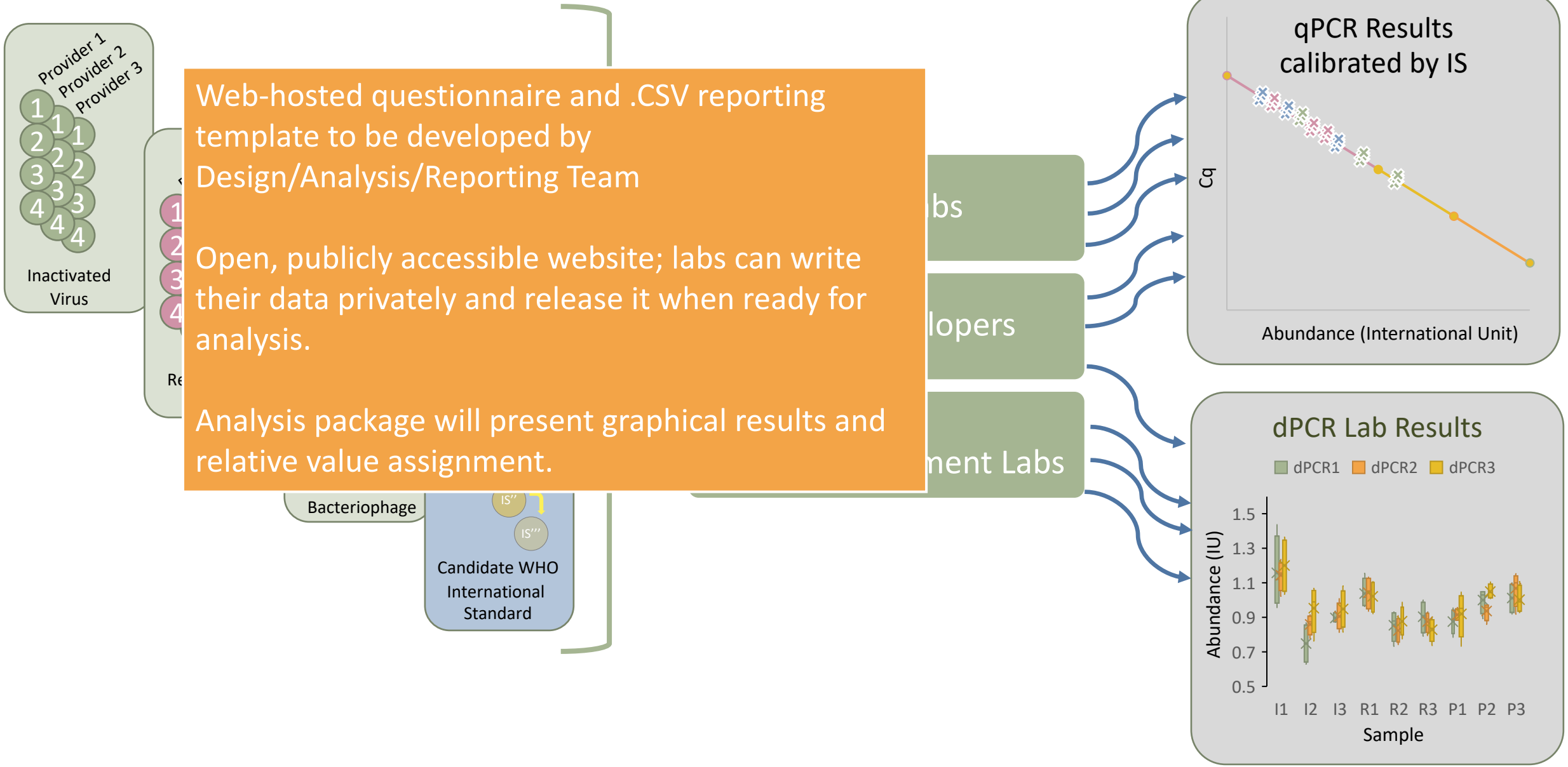


Reporting, Analysis, Open Data plans

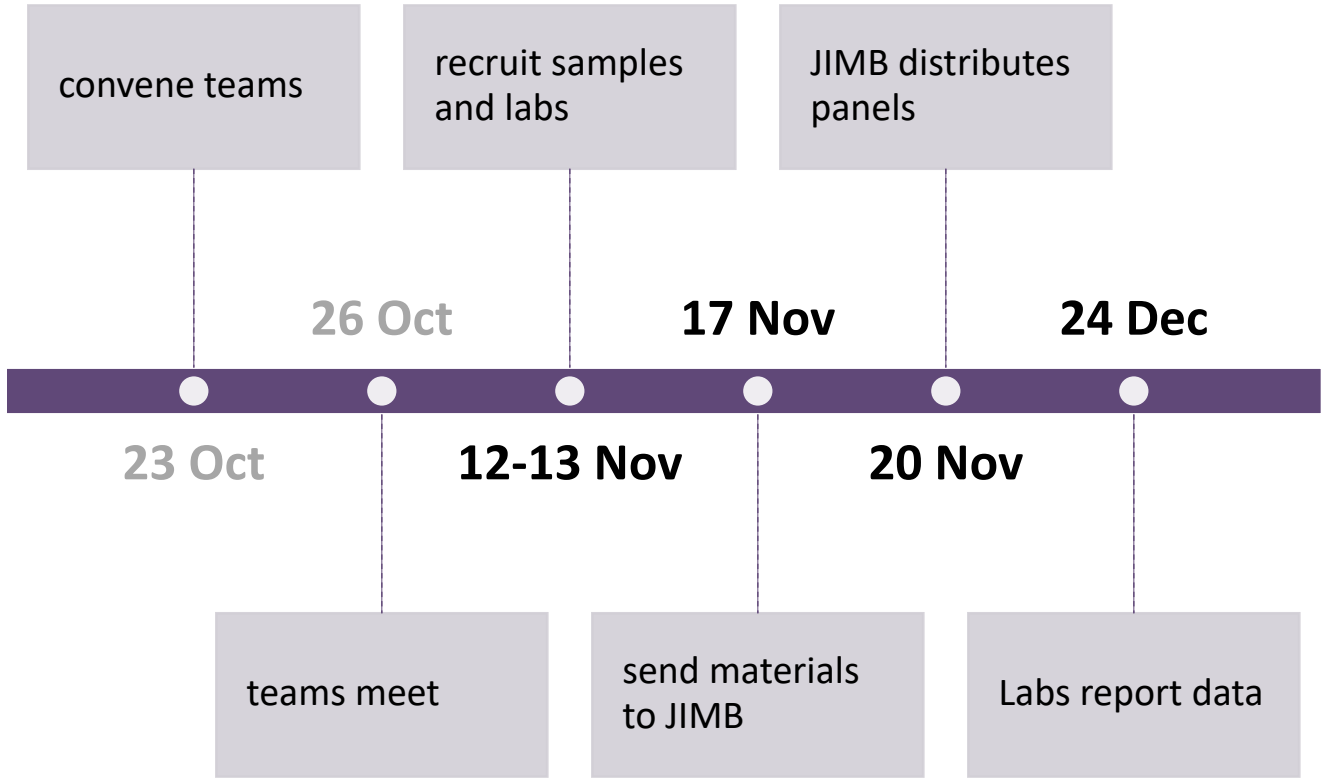
Web-hosted questionnaire and .CSV reporting template to be developed by Design/Analysis/Reporting Team

Open, publicly accessible website; labs can write their data privately and release it when ready for analysis.

Analysis package will present graphical results and relative value assignment.



Timeline & Logistics



What about Vaccine Assays?

The Covid-19 Vaccine-Development Multiverse

Confirmation of the correlation between antibody titers and protection against Covid-19 will be possible only in a large clinical efficacy study. In the meantime, the validity of the assays for measuring antibody will also need to be documented. These assays are notoriously variable because they use live virus or protein expression in cell culture with a readout that relies on an *in vitro* biologic reaction (i.e., serum antibodies binding or killing [sic] viral antigen). Optimization of the performance characteristics of these assays will be invaluable in streamlining further development and supporting bridging across varied populations and manufacturing processes.

N Engl J Med 2020; 383:1986-1988

ELISA

- Coating antigens: stabilized pre fusion full S, RBD, (NP)
- Total IgG in serum

Pseudoviral neutralization

- Viral backbone: VSV
- Safer testing alternative open to more labs (non BSL3)

Wild type neutralization

- Colorimetric microneutralization assay

ELISPOT

- Peptide pool of the whole S protein
- Cytokines: IFNy (Th1), IL-2 (Th1), IL-5 (Th2)

Assays Available Within the WHO Vaccine Network

William Dowling, Ph.D.
Co-Chair Non-clinical Vaccine Development Leader, CEPI

WHO Working Group on COVID-19 Assays
September 16, 2020

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

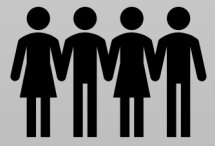
We can make the standards to make molecular testing robust, reliable, and quantitatively comparable.

‘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