2 October 2020

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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…

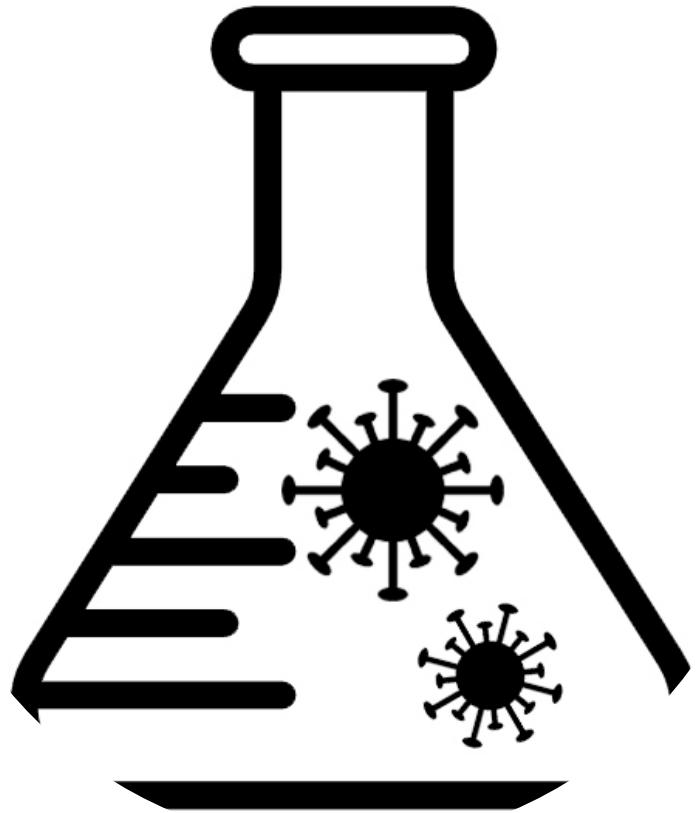
- confidence in test results
- interoperability
- scale-up
- long-term capacity

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.

2 October Agenda

- Harmonization Study
  - Fit-for-purpose Study Objectives
  - Study Design
  - What materials will we harmonize?
  - What labs will measure the materials?
  - Analysis Plans
  - Logistics & Timeline
  - Gaps



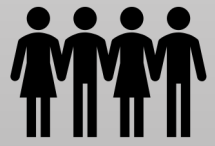
We can make the standards to make molecular testing robust, reliable, and quantitatively comparable.

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

just a few labs, NMIs

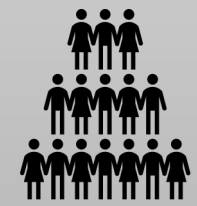
“Benchmarking Kit” for turn-key evaluation of molecular testing platforms

test developers



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

routinely measured at testing labs



Harmonization Study will yield a set of comparable calibration materials

- Study will ”value assign” ***or*** establish relative levels for two types of reference samples
  1. viral mimics & inactivated virus
  2. nucleic acids
- Need to collect materials and make “kits”
- Figure out who’s going to measure them

- Objective ***might be*** to establish consensus value assignment; this may be difficult to achieve
- Fall-back is to establish consensus relative levels

What scope of comparability is Fit for Purpose?

Absolute and Relative level value assignment

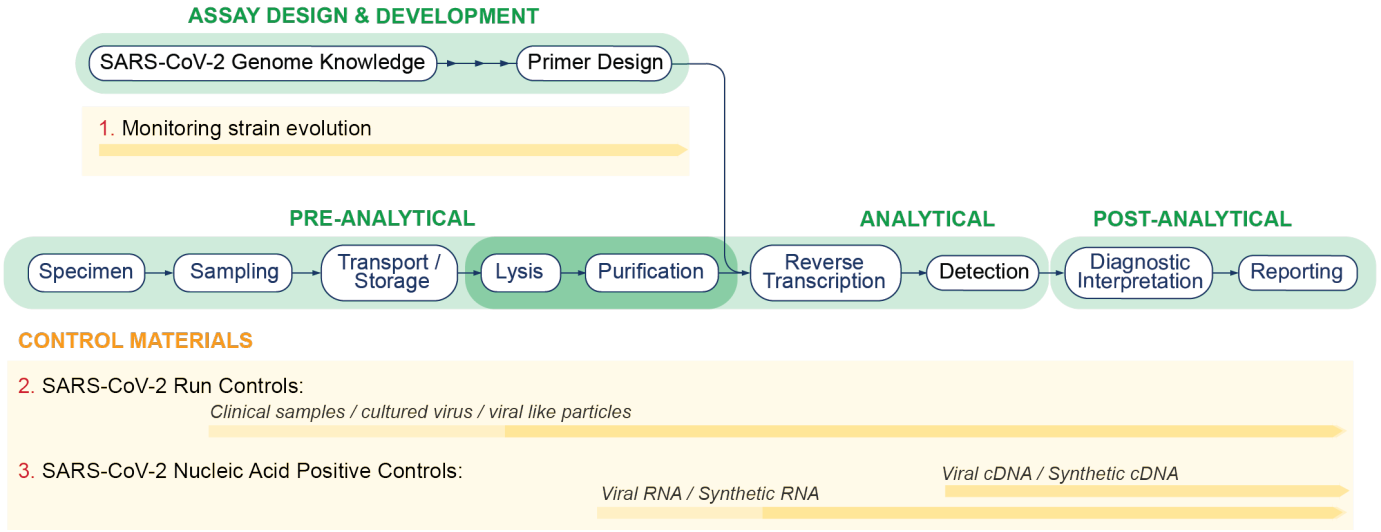
Absolute value assignment permits comparison to any material that has an absolute assignment

deliberate and enduring

Relative value assignment permits comparison only within our set of study materials

rapid and fit for purpose

can “bridge” to these materials later



Molecular Testing is a Measurement Process

Standards and controls work in different parts of the process

Our study will look at materials 2 & 3

Harmonization Kit Design – Two Types of Materials

- Viral particles and surrogates that must be extracted prior to NAAT (Type 2)
  - useful to evaluate and calibrate entire test process
  - more comprehensive knowledge and accuracy of test
  - fewer materials available (3?)
  - not routine for all metrology labs; development required
    - partnerships possible

- Nucleic acid standards (Type 3)
  - useful to evaluate and calibrate NAAT part of the test process
    - RNA includes RT step, DNA doesn't
  - broader portfolio of materials
  - compatible with metrology labs, but more limited utility in clinical settings

Candidate materials we know about…

We would like to include your standards!

- Inactivated Virus
  - INSTAND
  - FDA
- Viral Surrogates
  - SeraCare
  - NIBSC
  - Asuragen
  - Imperial College
- Nucleic Acid
  - NIST
  - Twist Bioscience

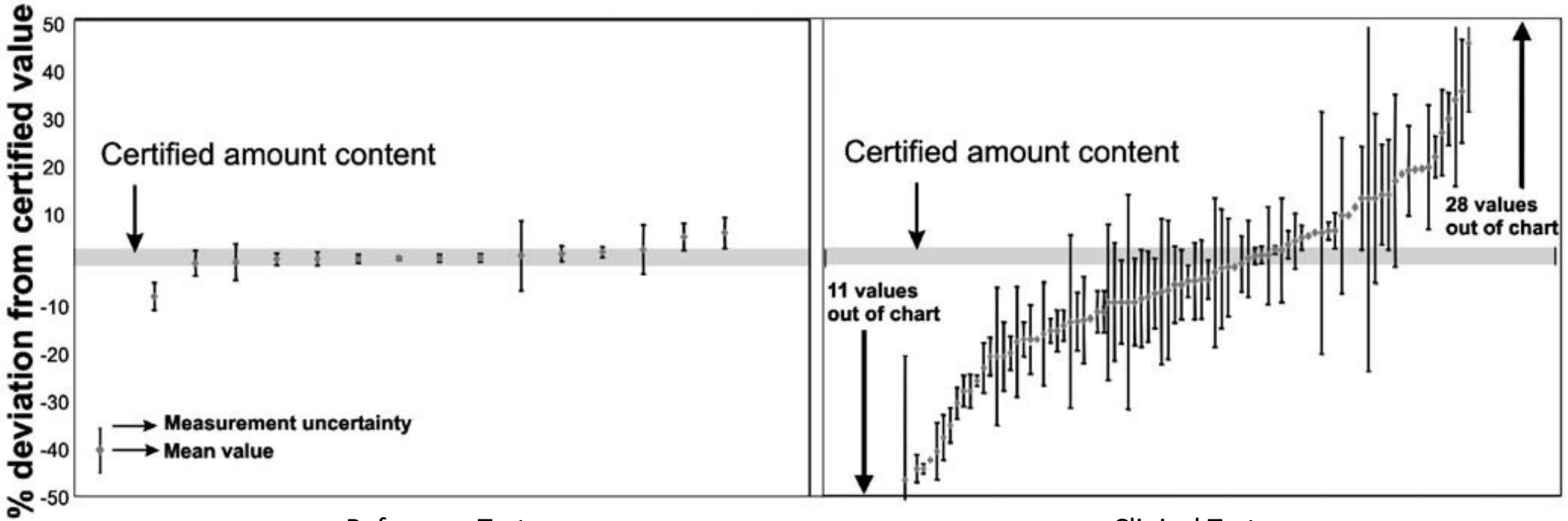
- JIMB Lab will manage logistics
  - Receive materials
  - Package into “Kits”
  - Distribute kits with proper documentation

Harmonization Study Participants

- National Measurement Labs
  - NIST (US), NML (UK), Asia-Pacific? EU?, Canada?
- Clinical Lab Partners using widely-deployed tests
  - academic or commercial testing labs
    - e.g. LANL, Mayo, MUSC, Ghent University, …
    - e.g. Quest, LabCorp, other commercial testing labs

What it may look like to have reference and clinical tests measuring the same material(s)...

- Plan to analyze results so we can assess sources of bias and variation when value assigning materials
- Data and analysis to be open and public
- Can anonymize tests, labs, participants



Reference Tests

Clinical Tests

modified from Fortunato G, Wunderli S. Evaluation of the combined measurement uncertainty in isotope dilution by MC-ICP-MS. Anal Bioanal Chem. 2003 Sep;377(1):111-6. doi: 10.1007/s00216-003-2035-6. Epub 2003 Aug 8. PMID: 12908094.

Making our results publicly available

- Intent is to make results immediately available
  - All data available as soon as validated
- Develop writing team as we develop the study
- Write draft preprint as study is underway

Logistics and Timeline

- JIMB Lab will be clearinghouse
- Commitments for materials and lab participation by 16 October
- Materials distributed 2 November
- Results received 20 November

October	28	29	30	01	**02**	03	04	Today
	05	06	07	08	09	10	11	
	12	13	14	15	**16**	17	18	Commitments
	19	20	21	22	23	24	25	
November	26	27	28	29	30	31	01	
	02	03	04	05	06	07	08	Materials distributed
	09	10	11	12	13	14	15	
	16	17	18	19	**20**	21	22	Results received
	23	24	25	26	27	28	29	

- Plan to make open Type 2 and Type 3 Kits
  - expect no more than 15 labs to measure either
  - make sufficient kits to accommodate problems and review
- Expect ~10 materials total
  - across 2 types
  - expect labs to measure in triplicate
    - a lab likely will only measure Type 2 or Type 3

Gaps

- Protocols
- Stabilty
- Homogeneity
- Refinement of design based on materials in study and participating labs
- Study of sources of variability
  - day-to-day
  - lot-to-lot
  - operator-to-operator

Discussion