22 May 2020

Marc Salit,
JIMB Director

SLAC National Lab and Stanford University

Coronavirus Standards Working Group

What should a Coronavirus Standards Working Group do?

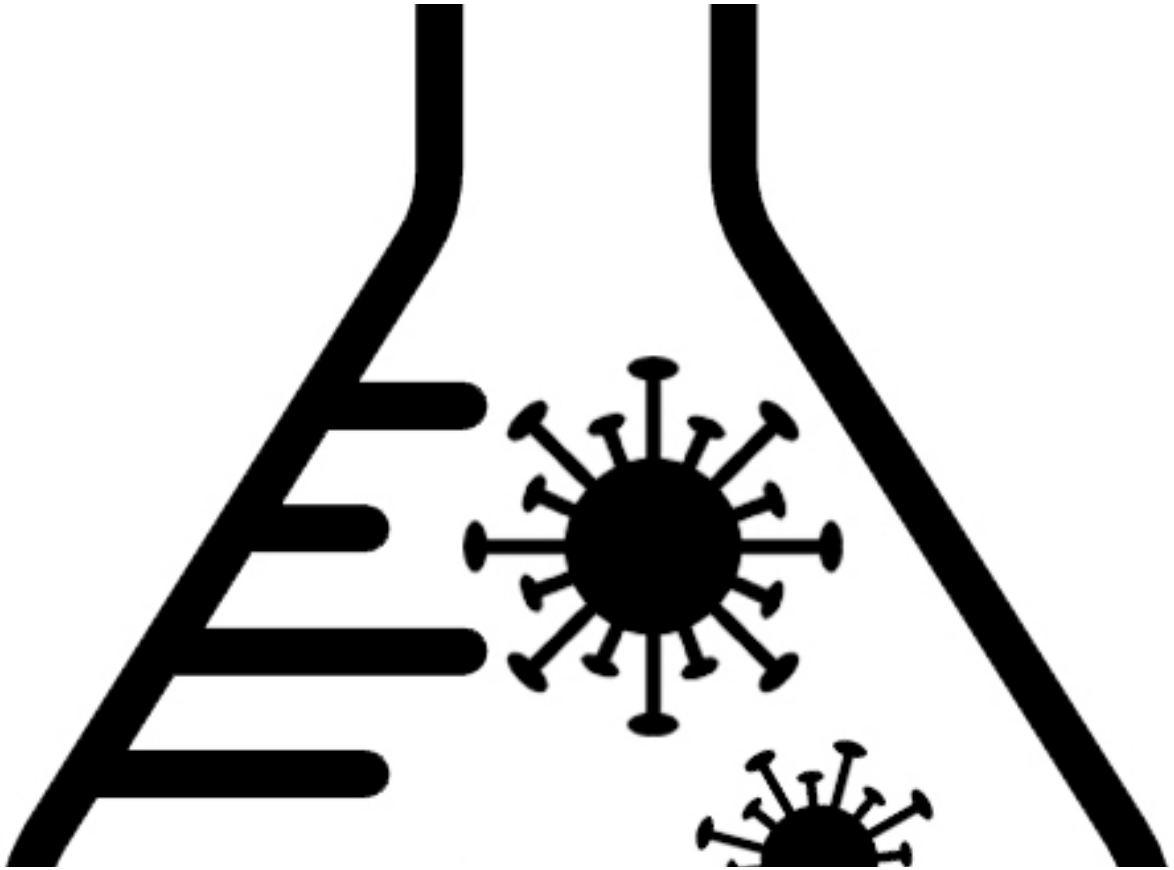
Assure development and availability of standards, controls, interlab testing, knowledge to support successful rollout & scaling of 2019-nCoV testing

Identify and develop critical infrastructure to support…

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

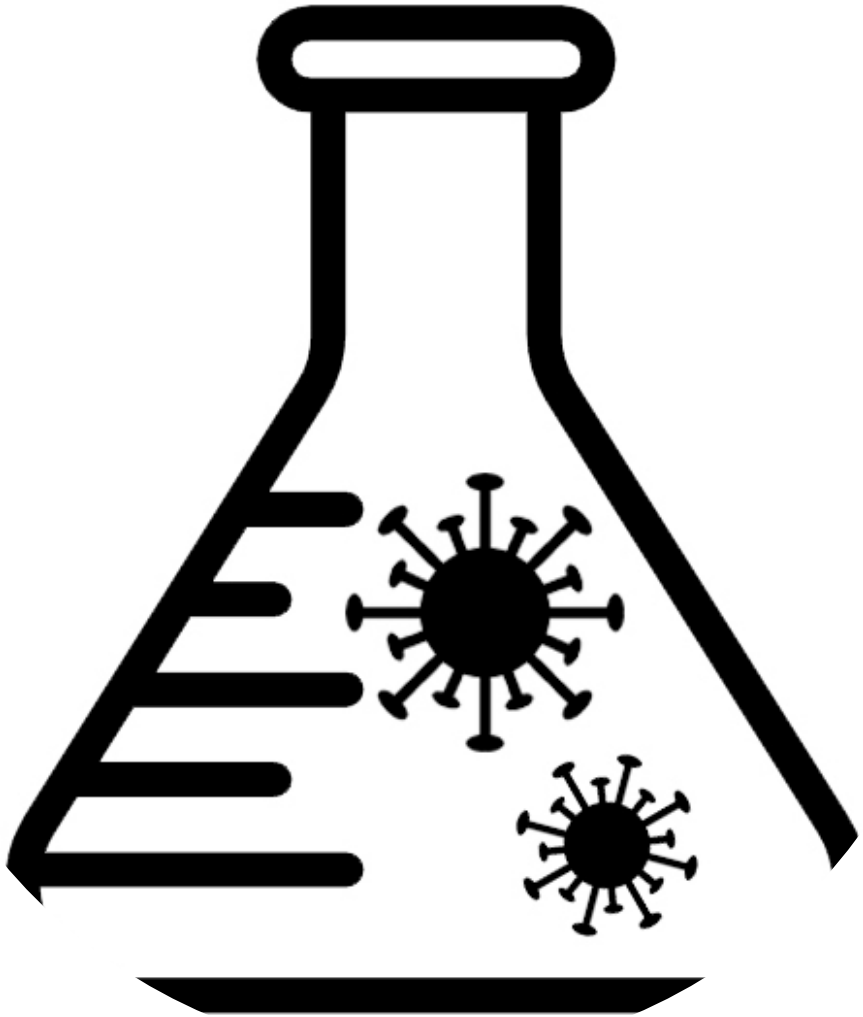
Identify best practices that should be institutionalized

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



22 May Agenda

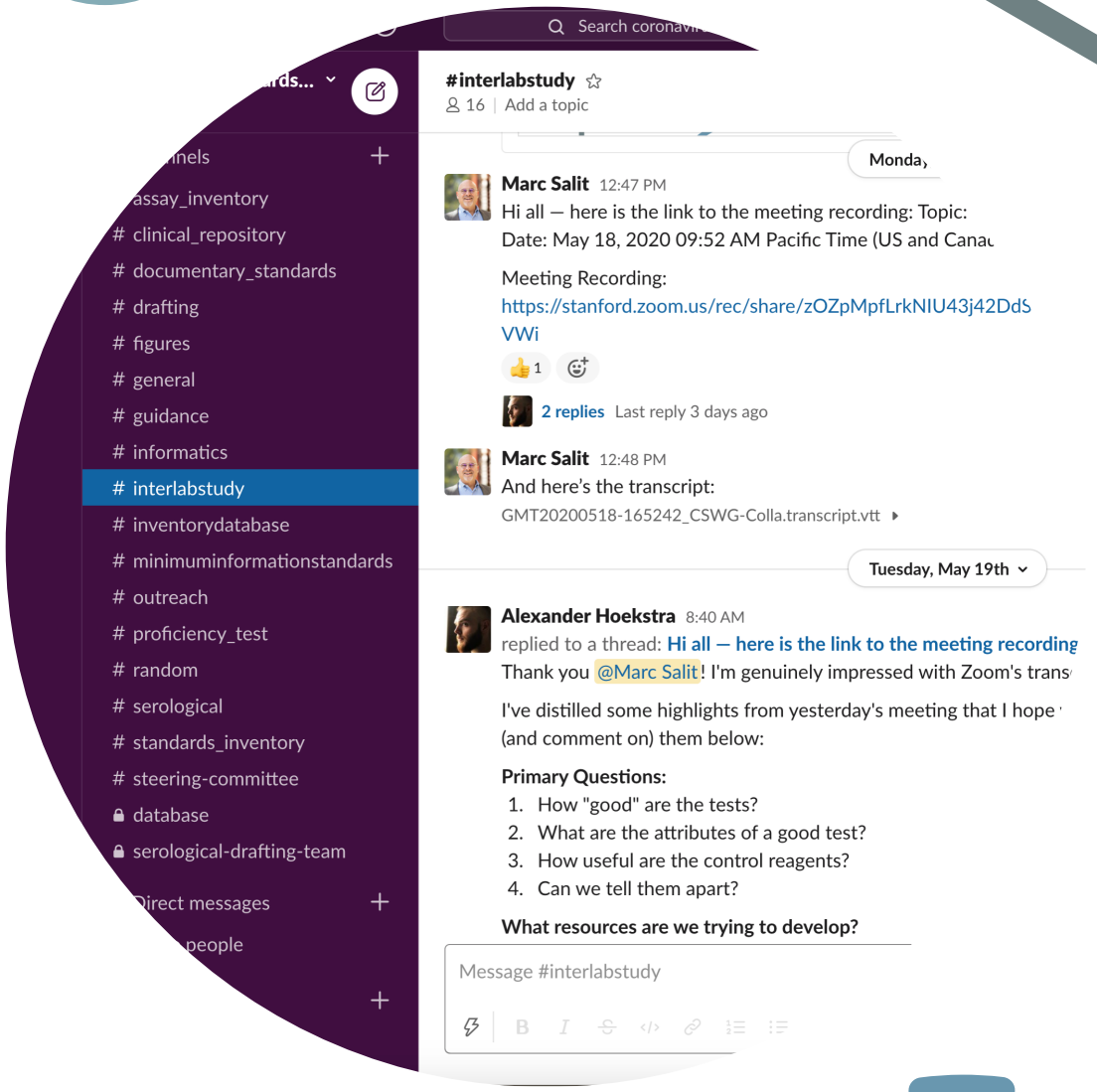
- Clare Morris, NIBSC Development of WHO International Standards
- Conversations on Interlab Study Proposal
  - Marc Salit
  - Alex Hoekstra



Considerations for Collaborative Study Comparing Tests and Materials

Coronavirus Standards Working Group

18 May 2020



Links to Transcript and Video Reccording, and Alex's Summary of Monday Meeting in Slack

I wish for us to develop a set of principles that would let us decide what to do.

What questions are we asking?

how ”good” are the tests?

what are the attributes of a good test?

how useful are the control reagents?

can we tell them apart?

What resources are we trying to develop?

a benchmarking strategy

a set of benchmarking reagents

a list of characteristics of “good” tests

a list of characteristics of a useful reagent

There are 61 authorized molecular tests and about 50 different control materials for them.

Our group could lead a collaborative, multi-lab study to assess performance

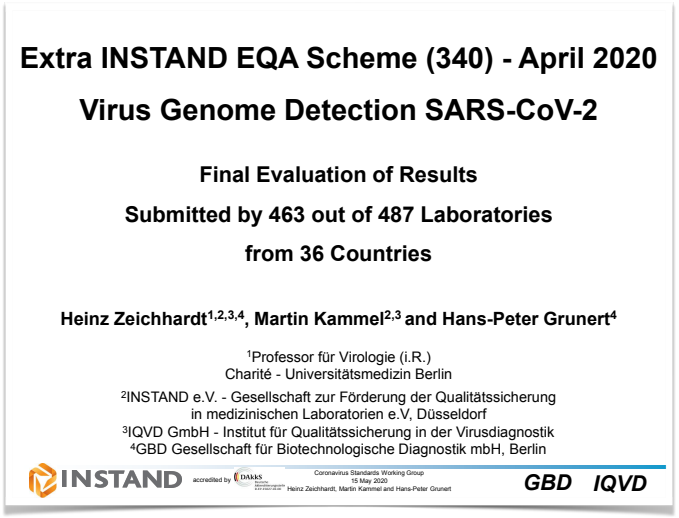
Demonstrate methods to evaluate tests

Establish utility of control materials

Demonstrate performance of tests

Compare values and utility of control materials

Other evaluations are ongoing and underway



Extra INSTAND EQA Scheme (340) - April 2020

Virus Genome Detection SARS-CoV-2

Final Evaluation of Results

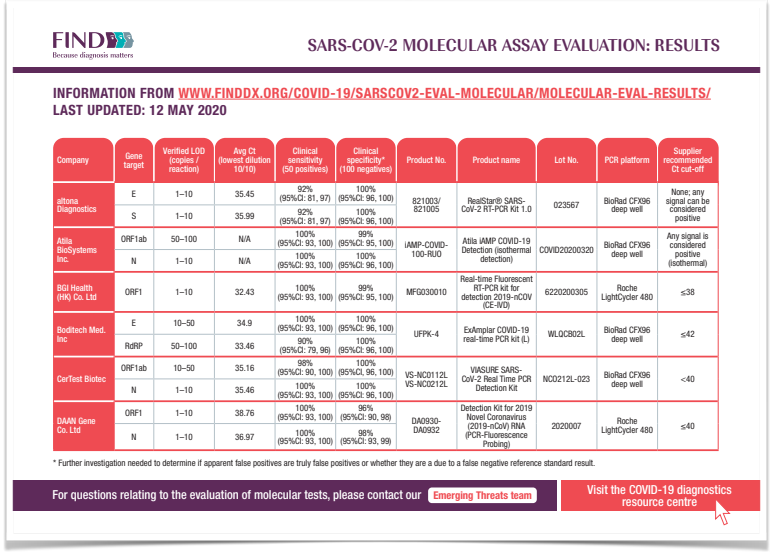
Submitted by 463 out of 487 Laboratories

from 36 Countries

Heinz Zeichhardt[1,2,3,4], Martin Kammel[2,3] and Hans-Peter Grunert[4]

[1]Professor für Virologie (i.R.)
Charité - Universitätsmedizin Berlin
[2]INSTAND e.V. - Gesellschaft zur Förderung der Qualitätssicherung in medizinischen Laboratorien e.V, Düsseldorf
[3]IQVD GmbH - Institut für Qualitätssicherung in der Virusdiagnostik
[4]GBD Gesellschaft für Biotechnologische Diagnostik mbH, Berlin

INSTAND accredited by DAkkS — Coronavirus Standards Working Group 15 May 2020 — Heinz Zeichhardt, Martin Kammel and Hans-Peter Grunert — GBD IQVD



FIND — Because diagnosis matters

SARS-COV-2 MOLECULAR ASSAY EVALUATION: RESULTS

INFORMATION FROM WWW.FINDDX.ORG/COVID-19/SARSCOV2-EVAL-MOLECULAR/MOLECULAR-EVAL-RESULTS/
LAST UPDATED: 12 MAY 2020

Company	Gene target	Verified LOD (copies / reaction)	Avg Ct (lowest dilution 10/10)	Clinical sensitivity (50 positives)	Clinical specificity* (100 negatives)	Product No.	Product name	Lot No.	PCR platform	Supplier recommended Ct cut-off
altona Diagnostics	E	1–10	35.45	92% (95%CI: 81, 97)	100% (95%CI: 96, 100)	821003/ 821005	RealStar® SARS-CoV-2 RT-PCR Kit 1.0	023567	BioRad CFX96 deep well	None; any signal can be considered positive
	S	1–10	35.99	92% (95%CI: 81, 97)	100% (95%CI: 96, 100)					
Atila BioSystems Inc.	ORF1ab	50–100	N/A	100% (95%CI: 93, 100)	99% (95%CI: 95, 100)	iAMP-COVID-100-RUO	Atila iAMP COVID-19 Detection (isothermal detection)	COVID20200320	BioRad CFX96 deep well	Any signal is considered positive (isothermal)
	N	1–10	N/A	100% (95%CI: 93, 100)	100% (95%CI: 96, 100)					
BGI Health (HK) Co. Ltd	ORF1	1–10	32.43	100% (95%CI: 93, 100)	99% (95%CI: 95, 100)	MFG030010	Real-time Fluorescent RT-PCR kit for detection 2019-nCOV (CE-IVD)	6220200305	Roche LightCycler 480	≤38
Boditech Med. Inc	E	10–50	34.9	100% (95%CI: 93, 100)	100% (95%CI: 96, 100)	UFPK-4	ExAmplar COVID-19 real-time PCR kit (L)	WLQCB02L	BioRad CFX96 deep well	≤42
	RdRP	50–100	33.46	90% (95%CI: 79, 96)	100% (95%CI: 96, 100)					
CerTest Biotec	ORF1ab	10–50	35.16	98% (95%CI: 90, 100)	100% (95%CI, 96, 100)	VS-NC0112L VS-NC0212L	VIASURE SARS-CoV-2 Real Time PCR Detection Kit	NC0212L-023	BioRad CFX96 deep well	<40
	N	1–10	35.46	100% (95%CI: 93, 100)	100% (95%CI: 96, 100)					
DAAN Gene Co. Ltd	ORF1	1–10	38.76	100% (95%CI: 93, 100)	96% (95%CI: 90, 98)	DA0930-DA0932	Detection Kit for 2019 Novel Coronavirus (2019-nCoV) RNA (PCR-Fluorescence Probing)	2020007	Roche LightCycler 480	≤40
	N	1–10	36.97	100% (95%CI: 93, 100)	98% (95%CI: 93, 99)					

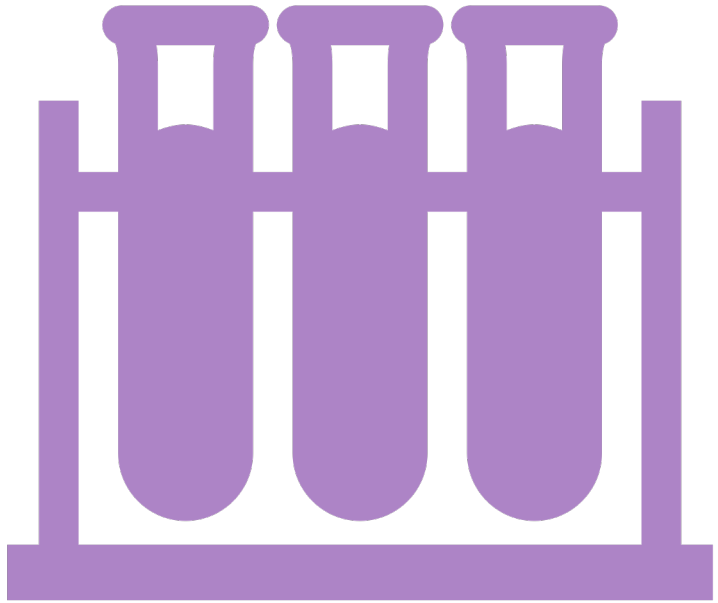
* Further investigation needed to determine if apparent false positives are truly false positives or whether they are a due to a false negative reference standard result.

For questions relating to the evaluation of molecular tests, please contact our Emerging Threats team

Visit the COVID-19 diagnostics resource centre

Scope & Conditions

- That’s a lot of tests
- The tests have multiple stages
- We have a heterogeneous set of control materials
- Some control materials are useful in some parts of some tests
- A lot of labs are busy



Current frame of Russell's Proposal

- Phase 1: Develop a panel of reference samples
  - products of multiple vendors
  - characterized in a few reference labs – "well-evaluated"

- Phase 2: Test a bunch of tests with panel
  - demonstrate utility of panel
  - demonstrate benchmark method for evaluating tests
  - gain knowledge of test performance

CSWG Phased Approach for COVID-19 Testing.

Study 1: Qualitative RNA, Study 2: Quantitative RNA, Study 3: Serology, and Study 4: Antigen testing

Phase 1 Reference Material(s) Selection: Qualitative SARS-CoV-2 Virus RNA Testing

- **Phase 1** Select Reference Samples by testing on assays available through the CSWG for qualitative RNA assays
  - Scope of Workflow being tested: Pre-analytical extraction, analytical, and post-analytical reporting,
  - Reference Samples selected by CSWG. Multiple ref. mat. assessed, select from GMP manufacturers that are part of CSWG, requires open vial stability already demonstrated to remove this variable.
    - VTM only to start. Paired saliva samples if possible.
    - Preference is that all viral genomic regions, targeted by EUA assays, are covered.
  - RNA assays for Phase 1 are selected by CSWG (e.g. dPCR, qPCR etc. and where testing is done).
  - Target viral levels that bracket lowest regions required based on clinical applications.
    - Levels informed by clinical data and reported as copies per mL
  - CSWG establishes specifications for the Phase 2 testing kit
    - Number of members and levels copies / mL
    - Blinded (preferred) or unblinded
    - Replicate testing
  - CSWG establishes a data analytics team to select appropriate statistical needs, replicates, data formats, data bases and performance analysis

Phase 2: Interlaboratory Study: Qualitative SARS-CoV-2 Virus RNA Testing

- **Phase 2** Interlab Study to Assess Analytical Sensitivity of EUA assays.
  - Kit is designed by CSWG from Phase 1
  - Kit includes vials, instructions for use, instructions for reporting results to CSWG data analytics team and contact information for project management liaison person
  - Targeting all manufacturers inclusive to assay formats and single site EUAs
  - CSWG receives, organizes and analyzes the data:
    - Performance across the sensitivity panel
    - Intra-assay accuracy and precision
    - Inter-assay comparisons of accuracy and precision
    - Other ?
  - Results are published in peer reviewed journal; data informs requirements to establish clinical sensitivity and requirements for SARS-CoV-2 RNA quant assays.

Depending on available resources, Serology Phase 1 and Phase 2 can be done in parallel

All other business

How are we doing?

Communications, planning, engagement, process, operations…

Discussion