

11 December 2020

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# Harmonization Study Plans: Experiment Design Considerations, SOPs

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



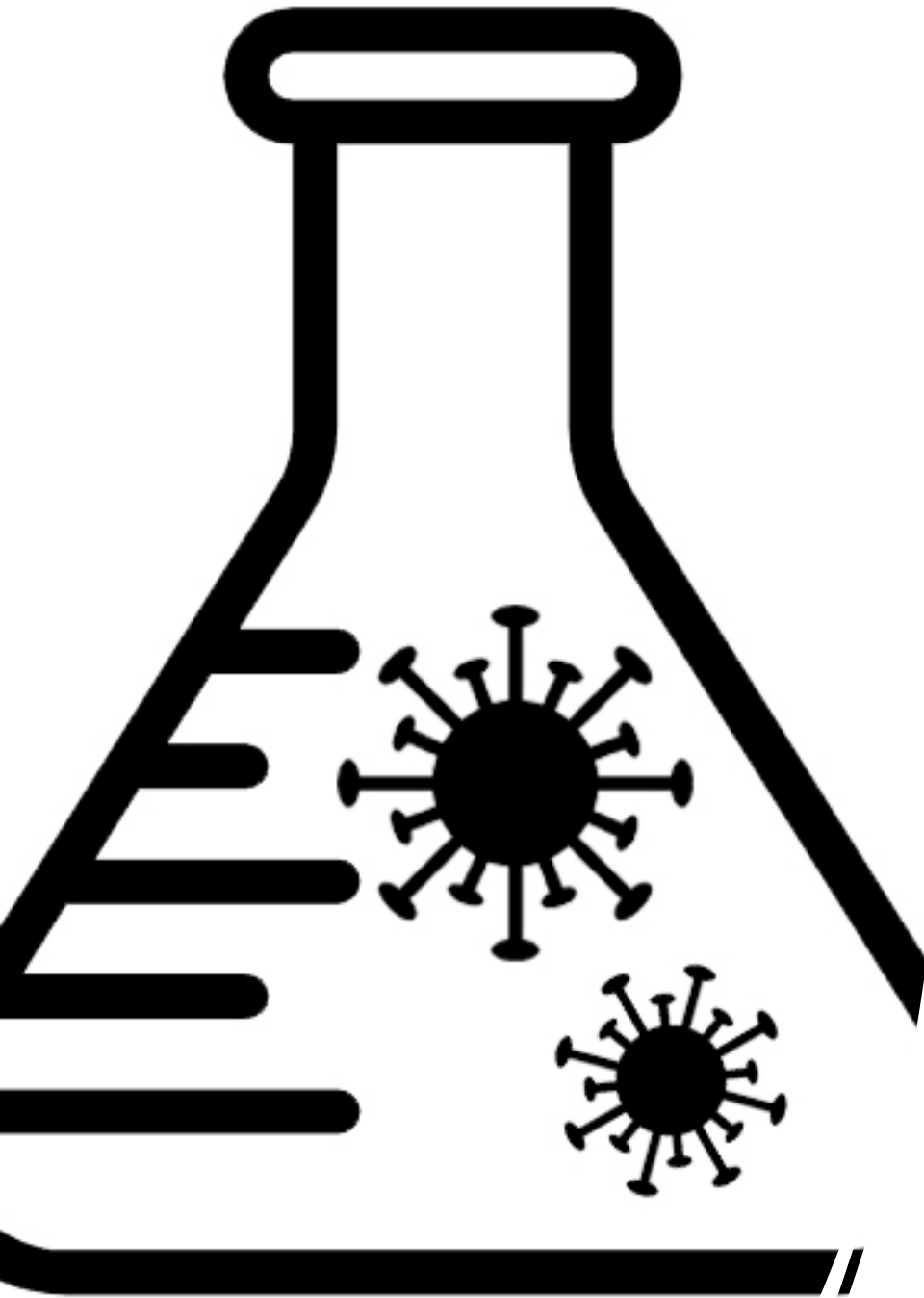
Identify and develop critical infrastructure to support...

- 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 Materials, Participants, Timeline, Next Steps for Reporting, & Analysis

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Update on Lab Meeting



Experiment Design



SOP Development



More info on Materials in Study



Labs & Tests



Timeline

# Purpose of Harmonization Study

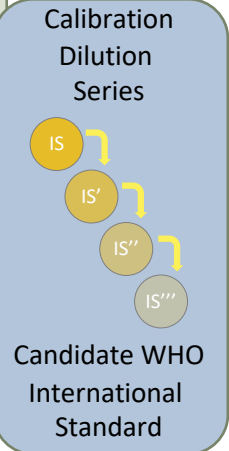
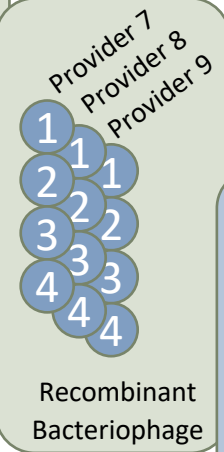
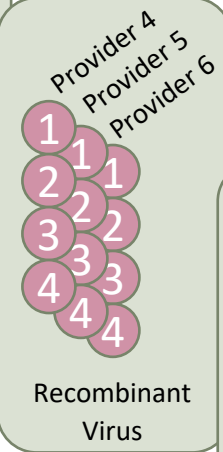
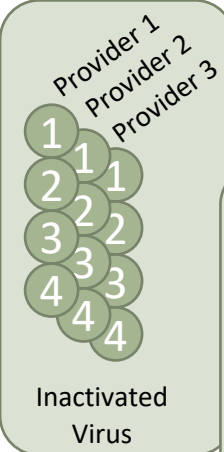
The CSWG “Harmonization Study” will establish the equivalence of SARS-CoV-2 RNA target concentrations across a panel of materials and calibrate those results against the WHO International Standard (IS) reference sample.

*By calibrating with the WHO International Standard (IS) the values on the materials included in this study can be assigned in the International Unit for SARS-CoV-2.*

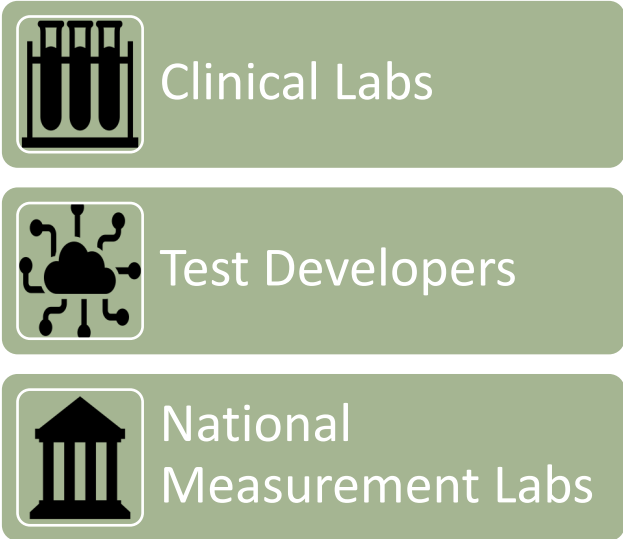
A decorative graphic on the right side of the slide. It features a large orange five-pointed star in the center. Inside the star, the text "News from the WHO..." is written in white. Surrounding the star are various geometric shapes: a purple circle at the top right, a maroon circle at the bottom, a maroon semi-circle to the right of the star, a gold-outlined square at the top, and several green dashed lines scattered around the bottom and right. A gold-outlined square is also visible at the bottom right.

News from  
the WHO...

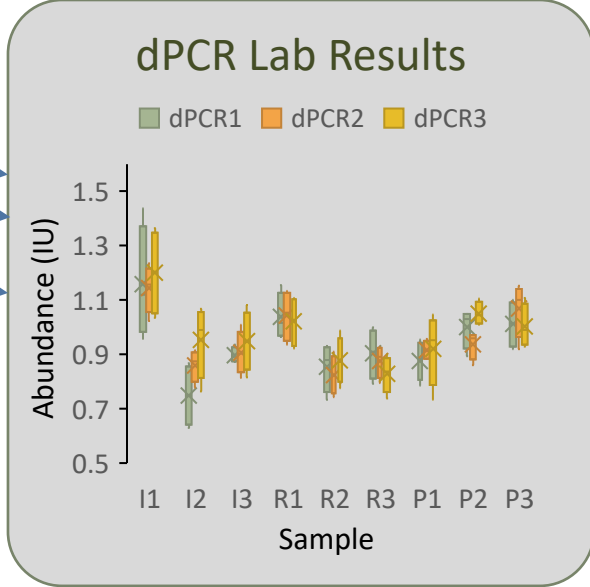
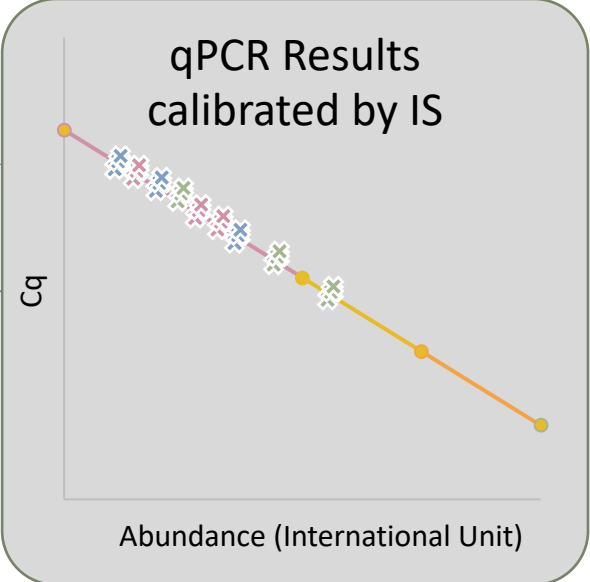
# CSWG Harmonization Study Design



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

Lab meeting agenda from 8 December 2020

# Getting to the details!



LABS IN STUDY



STUDY DESIGN



WHAT WE KNOW  
ABOUT THE  
MATERIALS



BALANCING  
PROPOSED TESTS AT  
LABS



PROTOCOL AND  
DESIGN DETAILS



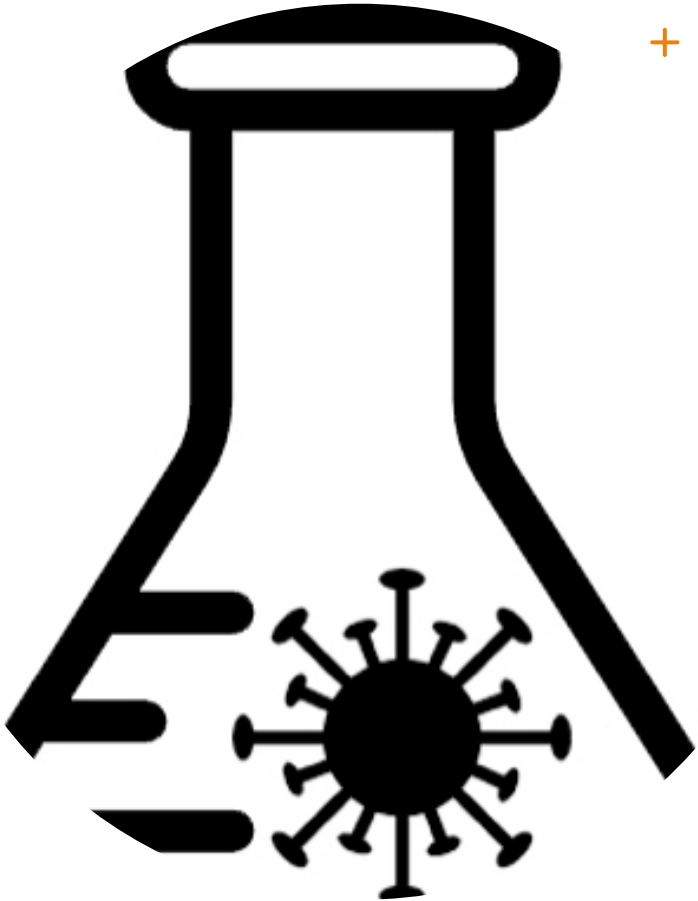
CALIBRATION



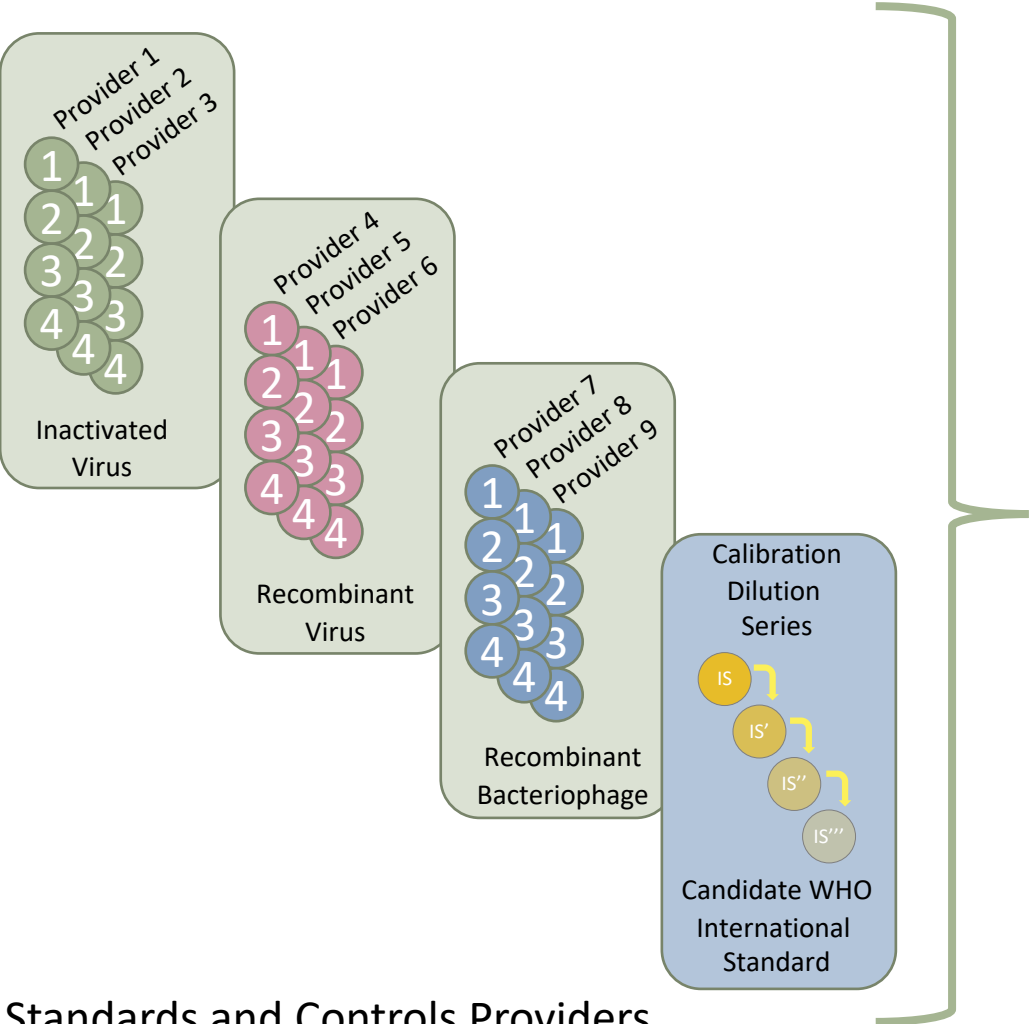
REPORTING  
PLATFORM



TIMELINE



# 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.



What are the samples in our study panel?

Provider	Material Description	Class of Material	Full Genome?	Provider Confirmation	Material Received	Comments
Instand	Lyophilized cell lysate	Inactivated Virus	TRUE	TRUE	30 Nov 2020	in JIMB Freezer
Zeptomatrix	x 0.5 mL of NATtrol™ SARS-CoV-2	Inactivated Virus	TRUE			
Thermo Fisher	Lyophilized cell lysate	Inactivated Virus	TRUE	TRUE	17 Nov 2020	in JIMB Freezer
Microbiologics	Lyophilized cell pellet	Inactivated Virus	TRUE	TRUE	19 Nov 2020	in JIMB Freezer
NIBSC	<b>Lyophilized Viral Isolate</b>	<b>Inactivated Virus</b>	<b>TRUE</b>	<b>TRUE</b>		<b>Proposed WHO international standard</b>
Assuragen	Pseudo-Viral Particles	Packaged encapsulated RNA	FALSE	TRUE	11 Nov 2020	in JIMB Freezer
Imperial College	Packaged encapsulated RNA	Packaged encapsulated RNA	FALSE	TRUE		
LGC SeraCare	Non-SARS viral particles in solution	Recombinant Virus	TRUE	TRUE	17 Nov 2020	in JIMB Freezer
NIBSC	Non-SARS viral particles in solution	Recombinant Virus	TRUE	TRUE		

What are the samples in our study panel?

Provider	Material Description	Class of Material	Buffer for suspension	Volume	Handling	Nominal Final Concentration
Instand	Lyophilized cell lysate	Inactivated Virus				
Zeptomatrix	x 0.5 mL of NATtrol™ SARS-CoV-2	Inactivated Virus				
Thermo Fisher	Lyophilized cell lysate	Inactivated Virus				
Microbiologics	Lyophilized cell pellet	Inactivated Virus				
NIBSC	<b>Lyophilized Viral Isolate</b>	<b>Inactivated Virus</b>				
Assuragen	Pseudo-Viral Particles	Packaged encapsulated RNA				
Imperial College	Packaged encapsulated RNA	Packaged encapsulated RNA				
LGC SeraCare	Non-SARS viral particles in solution	Recombinant Virus				
NIBSC	Non-SARS viral particles in solution	Recombinant Virus				

# Who are the labs in our study?

Labs to meet Tuesday 8 December at 1030 PST/1330 EST/1830 GMT/1930 CET

- Which tests to run at which labs?
- What are the critical protocol elements?
- What performance metrics to report?

Lab	Type	Location	Technology	Lab Confirmation
Western	Clinical Lab	Los Angeles, CA	qPCR	TRUE
MUSC	Clinical Lab	Charleston, SC	qPCR	TRUE
Mayo	Clinical Lab	Rochester, MN	qPCR	TRUE
Labcorp	Clinical Lab	Burlington, North Carolina	qPCR	TRUE
Quest	Clinical Lab	Seacaucus, NJ	qPCR	TRUE
Biogazete	Clinical Lab	Belgium	qPCR	TRUE
MassCPR Diagnostics	Clinical Lab	Boston, MA	qPCR	TRUE
Stanford Medicine	Clinical Lab	Stanford, CA	qPCR	TRUE
Los Alamos	Clinical Lab	Los Alamos, NM	qPCR	TRUE
biodesix	Clinical Lab	Boulder, CO	dPCR	TRUE
NIST	National Measurement Institute	Gaithersburg, MD, USA	dPCR	TRUE
NML	National Measurement Institute	Teddington, UK	dPCR	TRUE
NIB	National Measurement Institute	Ljubljana, Slovenia	dPCR	TRUE
Bio Rad	Test Developer	Pleasanton, California	dPCR	TRUE

Which labs will run which tests?

- Objective:  
Get a robust data set from a balanced representation of tests
- What's your favorite test?
- What's accessible and not disruptive?

Lab	Type	Location	Technology	Test
Western	Clinical Lab	Los Angeles, CA	qPCR	
MUSC	Clinical Lab	Charleston, SC	qPCR	
Mayo	Clinical Lab	Rochester, MN	qPCR	
Labcorp	Clinical Lab	Burlington, NC	qPCR	
Quest	Clinical Lab	San Juan Capistrano, CA	qPCR	
Biogazelle	Clinical Lab	Belgium	qPCR	
MassCPR Diagnostics	Clinical Lab	Boston, MA	qPCR	
Stanford Medicine	Clinical Lab	Stanford, CA	qPCR	
Los Alamos	Clinical Lab	Los Alamos, NM	qPCR	
biodesix	Clinical Lab	Boulder, CO	dPCR	
Bio Rad	Test Developer	Pleasanton, CA	dPCR	

# Protocol questions

- Replication design
- Dilution
- No-template/Negative Controls
- Sample volumes
- Do we want a reference protocol?

# Calibration

- Labs will prepare the dilution series of the IS
- Expect labs to (roughly) know their test LOD and dynamic range
- Expect replication
- Do we want a reference protocol?

# Timeline & Logistics

