

8 January 2021

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Harmonization Study Experiment Design and SOP

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 Experiment Design, SOP, Reporting, Timeline



Design



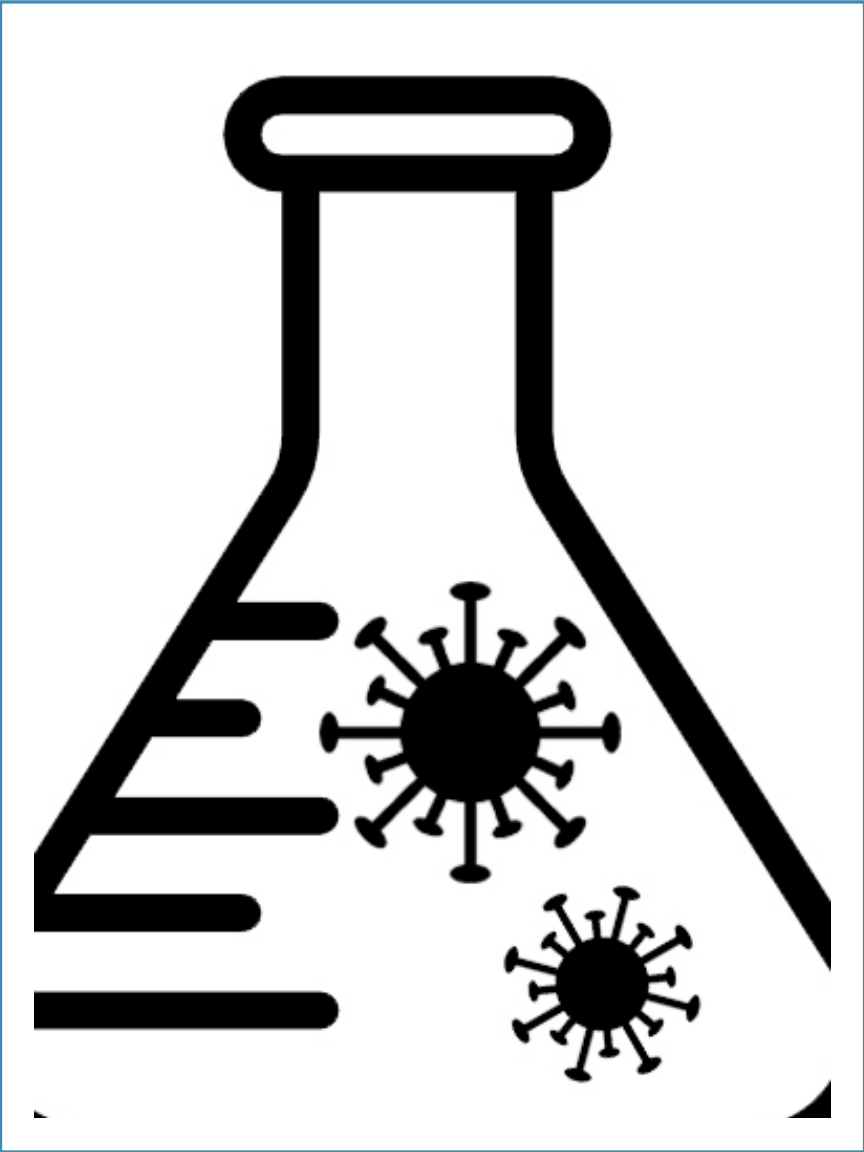
Draft SOP



Reporting



Timeline



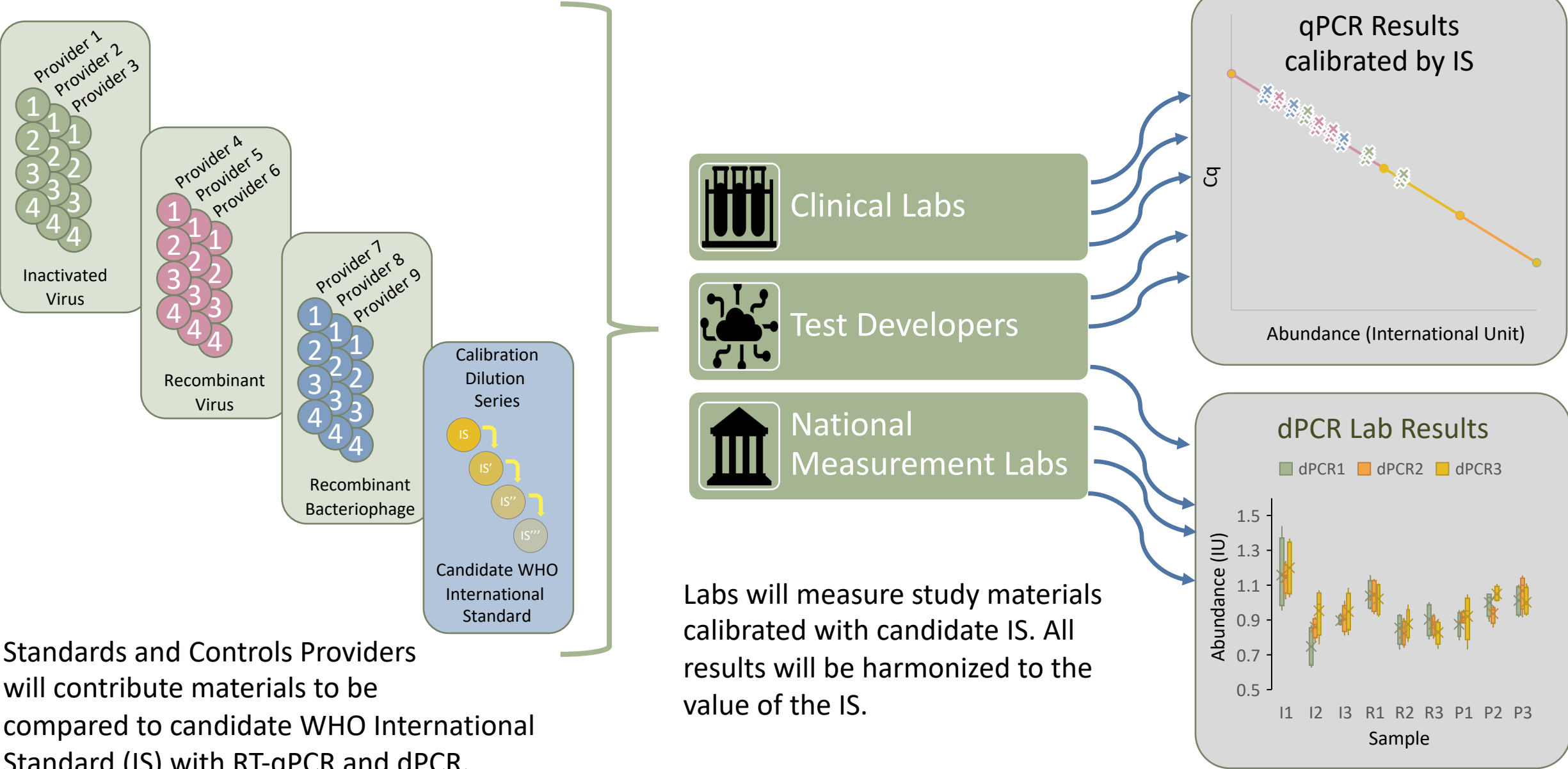
Purpose of Harmonization Study

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.



CSWG Harmonization Study Design



What this study is not going to do



a comparison of tests



a comparison of labs

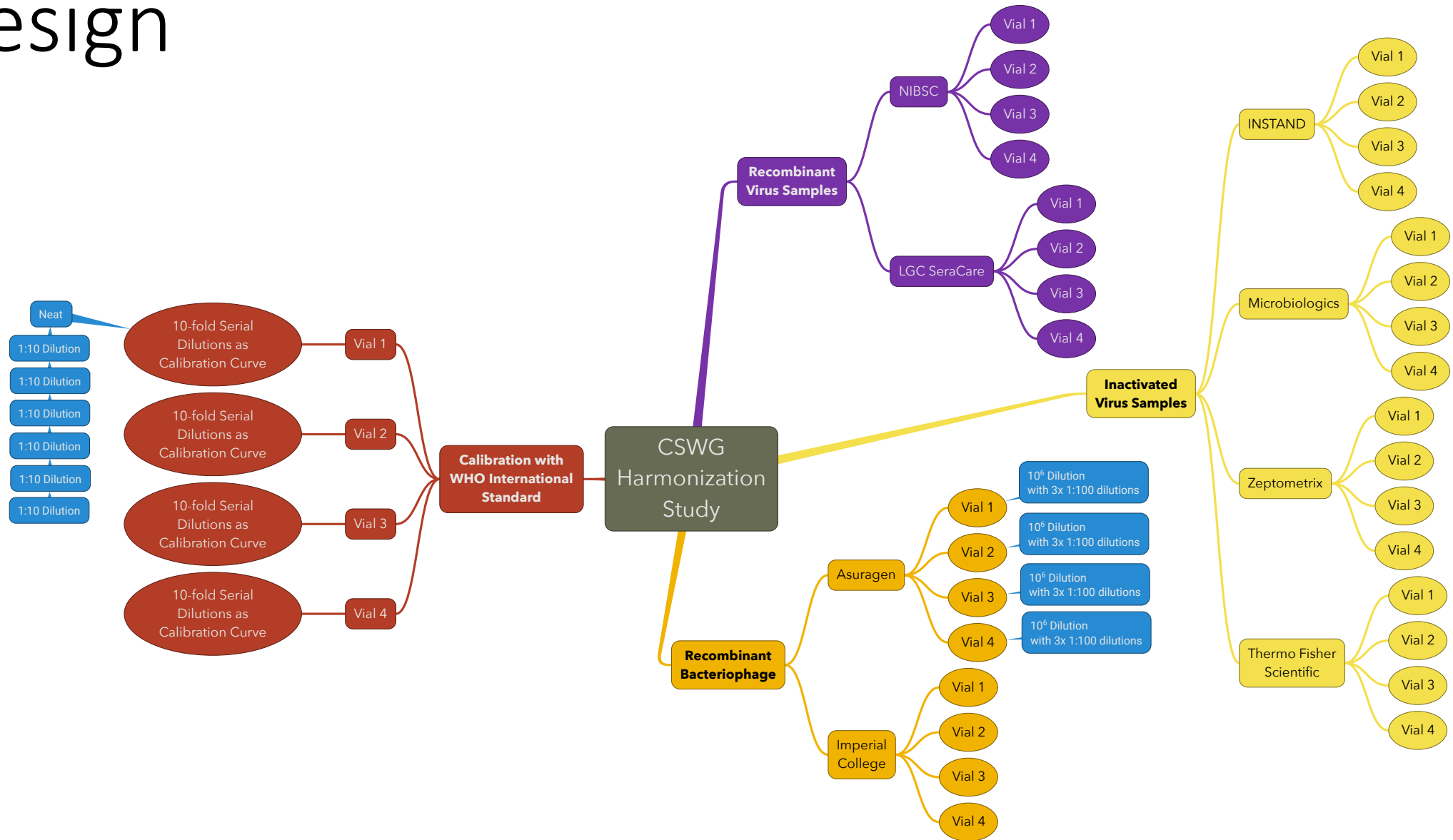


a survey of method performance (LOD, precision, repeatability)

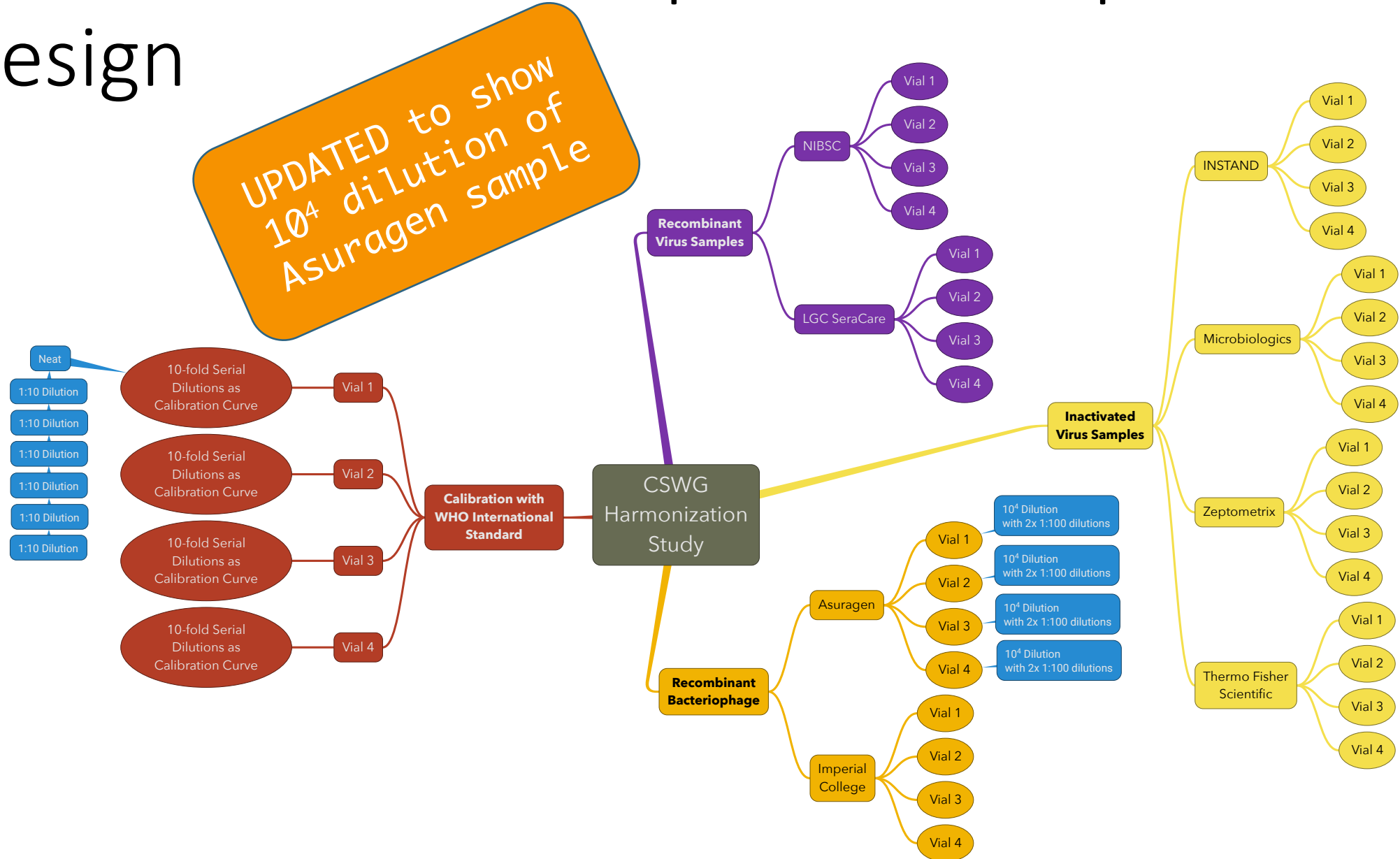


an evaluation of commutability

Calibration and Sample Panel Experiment Design

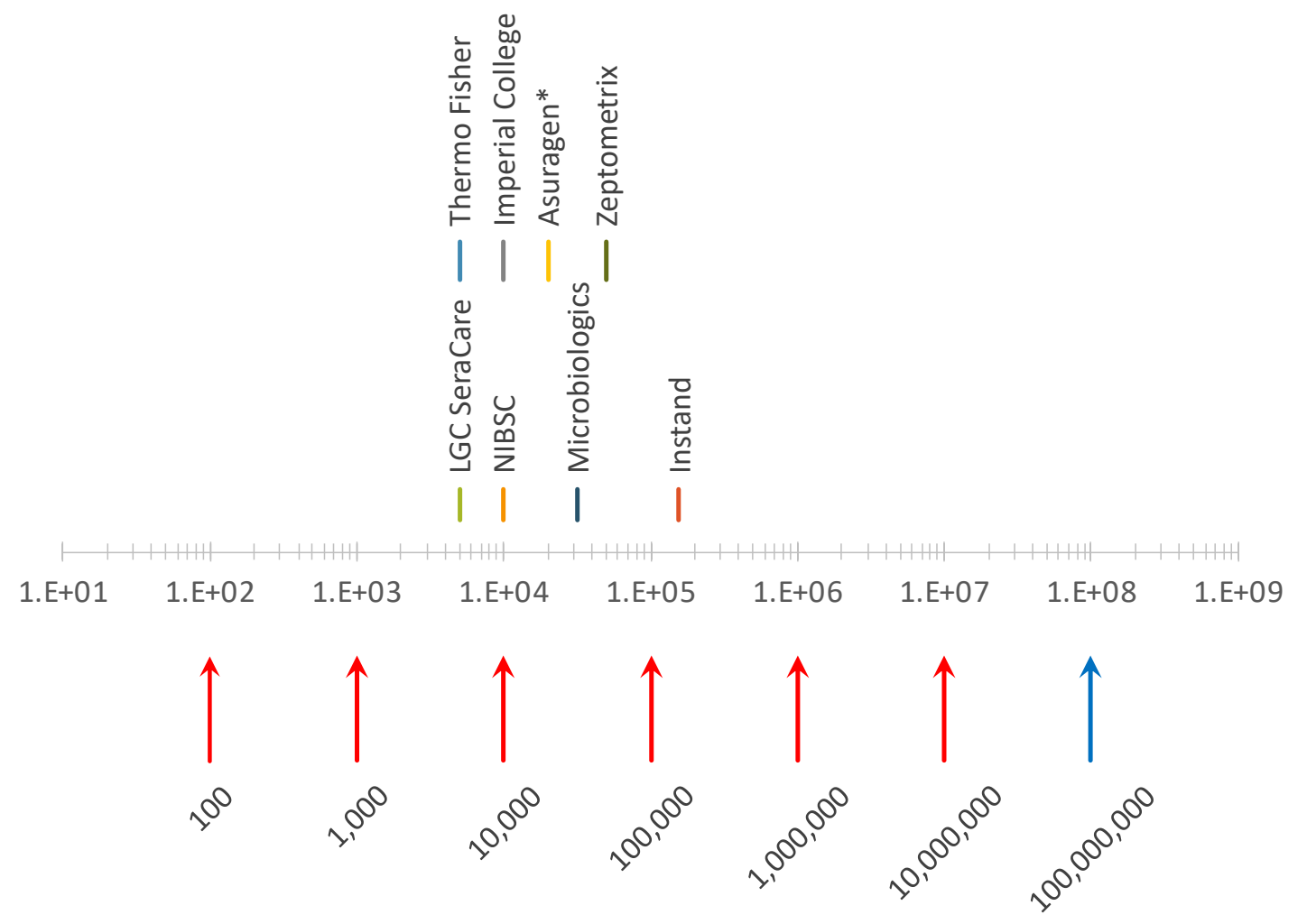


Calibration and Sample Panel Experiment Design



Calibration and Sample Levels

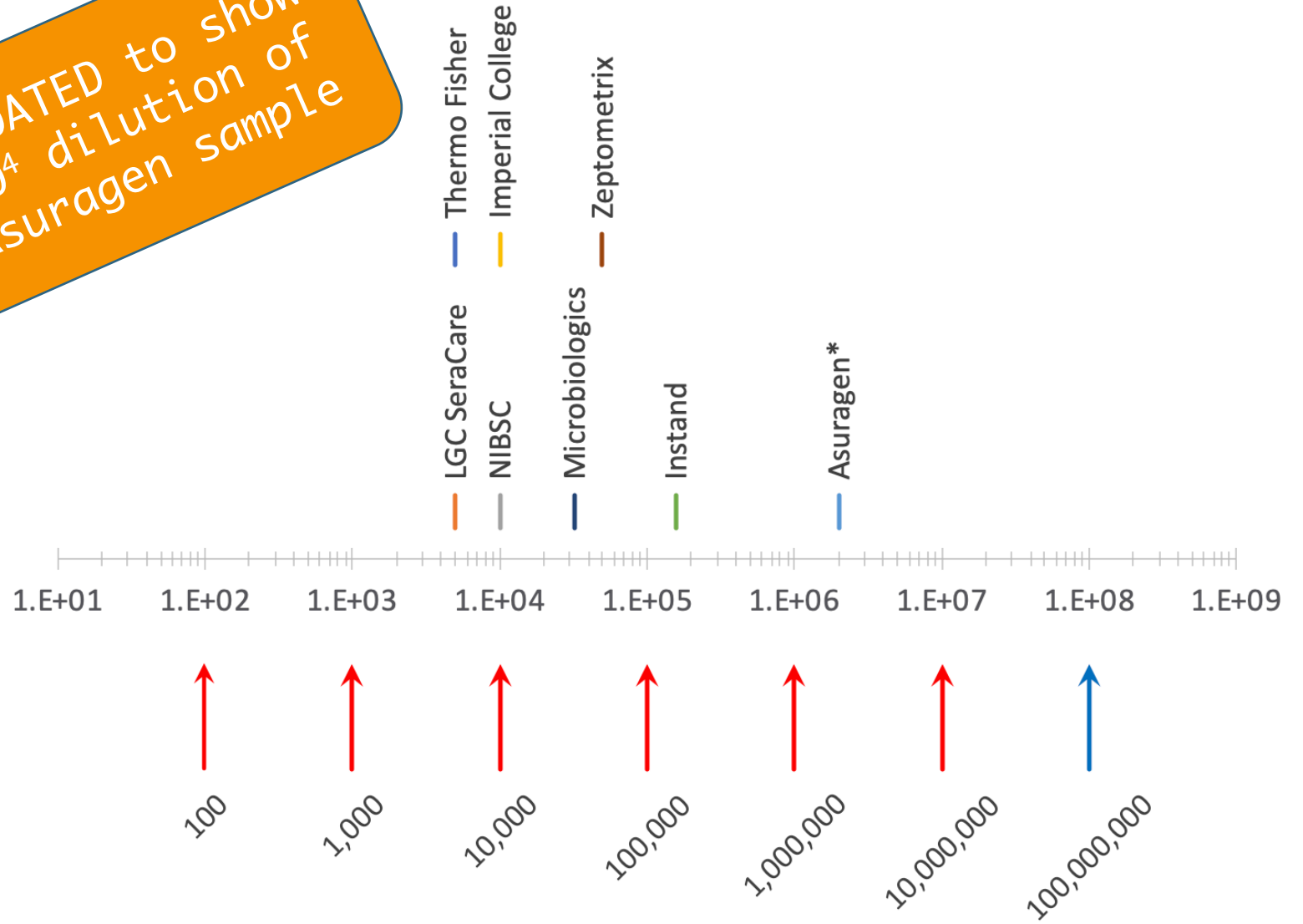
(copies/mL)



Calibration and Sample Levels

(copies/mL)

UPDATED to show
 10^4 dilution of
Asuragen sample



Structure of SOP

Intended as a recommended protocol



Nominal Levels of panel materials & Experimental Design



Supplied Reagents



Preparation of calibration curve



Preparation of sample panel



Data Entry

More on the SOP



Google Doc

<https://docs.google.com/document/d/1aEYsVD4Cvrc0AQrFXgSoCVYzMx63nFDyAzEwIYUrao/edit?usp=sharing>



Questions

dilution level of
Asuragen sample
• 10^4 or 10^6



How prescriptive
to be?

SOP will be a
recommendation
Where there's reason
to diverge from
recommendation, labs
are free to do so



(go to Sara and Sebastien to live-present from Google Doc)

DRAFT SOP Available Here:

<https://docs.google.com/document/d/1aEYsVD4Cvrq0AQrFXgSoCVYzMx63nFDyAzEwIYIUrao/edit?usp=sharing>

Metadata Entry Form

- Metadata describing the measurements will be in a Google Form
 - to include any lab-specific process and computationally-relevant aspects
- Intend to be MIQE/dMIQE Compliant

Google Forms

Having trouble viewing or submitting this form?

FILL OUT IN GOOGLE FORMS

Hi Marc, take a look at this google form and let me know what you think. I'll make a slide including a screenshot that I'll send to you with the finalized CDC import form slide later today.

CSWG Harmonization Study Metadata Form

This form will be filled out by each lab to provide metadata that will be used in data analysis.

Name of participating lab? *

Was an RNA extraction step used? *

- Yes
 No

If an RNA extraction step was performed, what RNA extraction platform was used?

What PCR instrument was used? *

What PCR kit was used? *

Did your lab use digital or qRT-PCR? *

- digital PCR
 qRT-PCR

What primer sequences were used?

Data Entry Form

- Values to report will depend on method
 - qPCR
 - dPCR
- Metadata will annotate this
- All data to be reported as close to 'raw' and unprocessed as possible
 - expectation is to do a single run and report all data
 - 4 replicate vials makes the experiment resilient to mishaps

	Replicate_1	Replicate_2	Replicate_3	Replicate_4
WHO-IS_neat				
WHO-IS_dilution_1				
WHO-IS_dilution_2				
WHO-IS_dilution_3				
WHO-IS_dilution_4				
WHO-IS_dilution_5				
WHO-IS_dilution_6				
Instand				
Microbiologics				
Thermo Fisher				
Zeptomatrix				
LGC SeraCare				
NIBSC				
Asuragen				
Imperial College				
Nontemplate_control				

CDC Import Permit Information

Navigate to eipp.cdc.gov

Click on 'SAMS Registration' towards the bottom right of the page

Fill out the eIPP Support Request

Once you have access to eIPP via a SAMS account, login to eIPP

Click "New Agents Form"

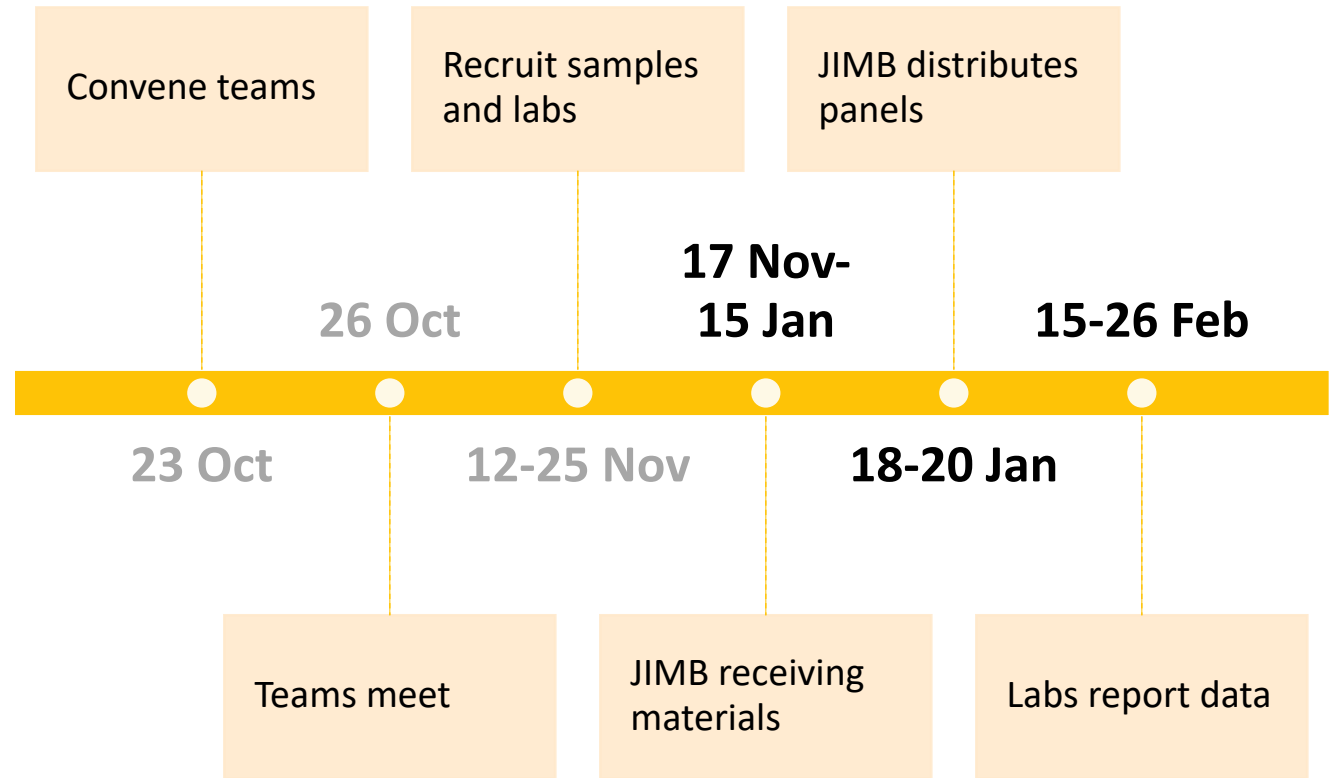
Enter the information provided in the following table

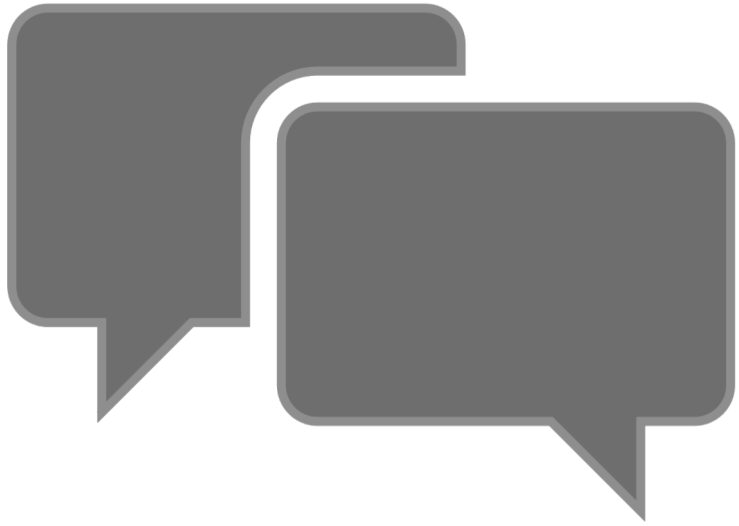
CDC Import Permit
Information for
INSTAND Standard.

This material will be
“imported” from JIMB
to domestic labs

Section A	Address	Receiver name, address and contact information
Section B	Sender	David Catoe
	Organization	Joint Initiative for Metrology in Biology
	Address:	3165 Porter Drive, Palo Alto, CA 94304
Section C	Shipment Information:	Commercial Carrier, One shipment
Section D	Use:	Research
	Detailed Description of Intended Use:	The Coronavirus Standards Working Group hosted by the Joint Initiative for Metrology in Biology at Stanford University's SLAC National Laboratory is working with the international community to conduct a standards harmonization study which will establish measurement traceability between commonly used standards in SARS-CoV-2 research including the World Health Organization International Standard.
Infectious Biological Agents:	Scientific Name:	SARS-CoV-2
	Strain:	Strain Not Applicable
	Location Info:	This is where it will be stored at the receiver's facility
Section E	Source Material:	Infected or suspected infected human
	Description of Materials	Laboratory derived isolate/culture
	Detailed Description of Material:	heat inactivated, lyophilized cell lysate
Section F	Biosafety Measures:	This may vary according to each lab's regulations, treat as BSL2
Section G	Final Destination?	Redistribution not permitted

Timeline & Logistics





Discussion

