

RAD<sub>x</sub>RAD  
DCC  
D<sub>x</sub> Core  
Monthly All Hands



**Rapid Acceleration  
of Diagnostics (RADx)**

Agenda  
April 12, 2021

RADx-rad All  
Hands Meeting

Meeting is being  
recorded



Updates from the core



Variant Deep Dive with Dr.  
Carlin

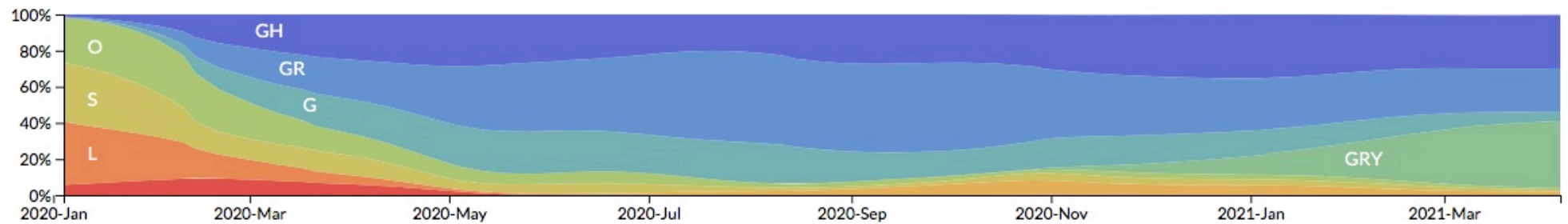


Questions



# SARS-CoV-2 changes in clade frequency

Frequencies (colored by GISAID Clade )



Data updated 2021-04-09 • [DOWNLOAD DATA](#) • Auspice v2.25.1



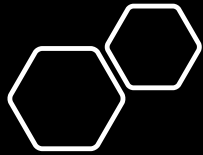
Powered by Nextstrain (Hadfield et al *Bioinformatics*)



# SARS-CoV-2 production for VQA panels

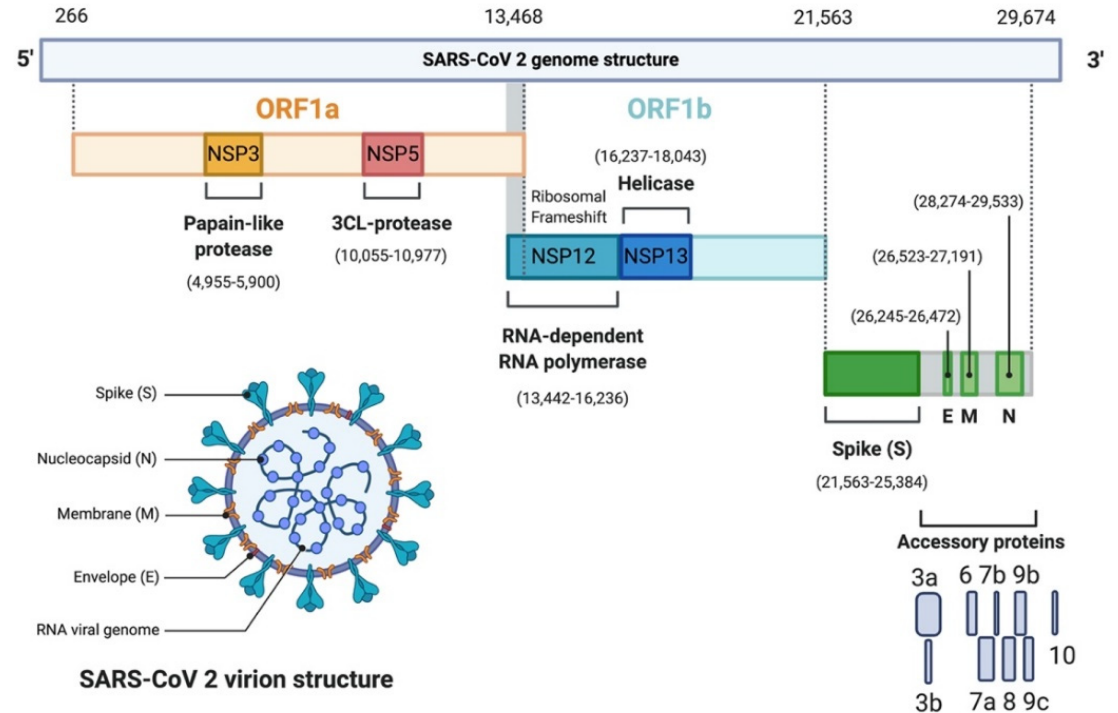
## Methods of SARS-CoV-2 variant acquisition:

- Laboratory isolated strains (clinical samples, repositories)
  - Strain must be accessible – Time
  - Each variant production is independent (non-interchangeable) – Time
  - Isolation via multiple passages often selects for mutations – Accuracy
- Recombinant viral production
  - Any strain can be built regardless of accessibility
  - New variant production can be built on interchangeable parts
  - Recombinant strains will require less passages and growth conditions optimized

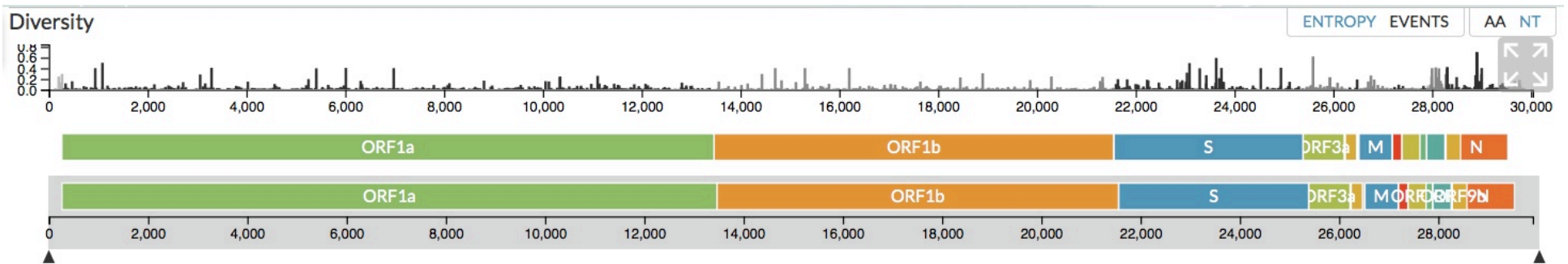


# SARS-CoV-2 30kb (+)ssRNA genome

- *Pathogens* 2020, 9(5), 331; <https://doi.org/10.3390/pathogens9050331>



# SARS-CoV-2 mutations occur throughout the genome



B.1.1.7



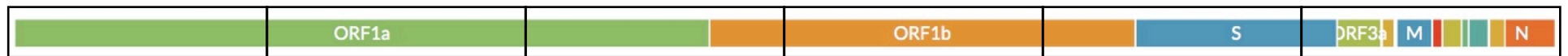
P.1



<https://outbreak.info//situation-reports>

GISAID Nextstrain

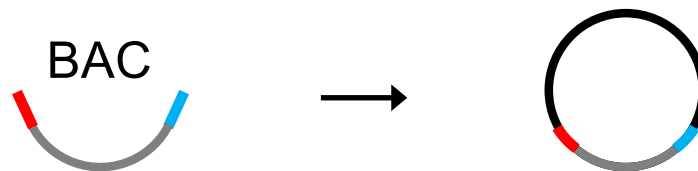
# Recombinant SARS-CoV-2 stage 2 assembly



Synthesize ~24 short DNA fragments

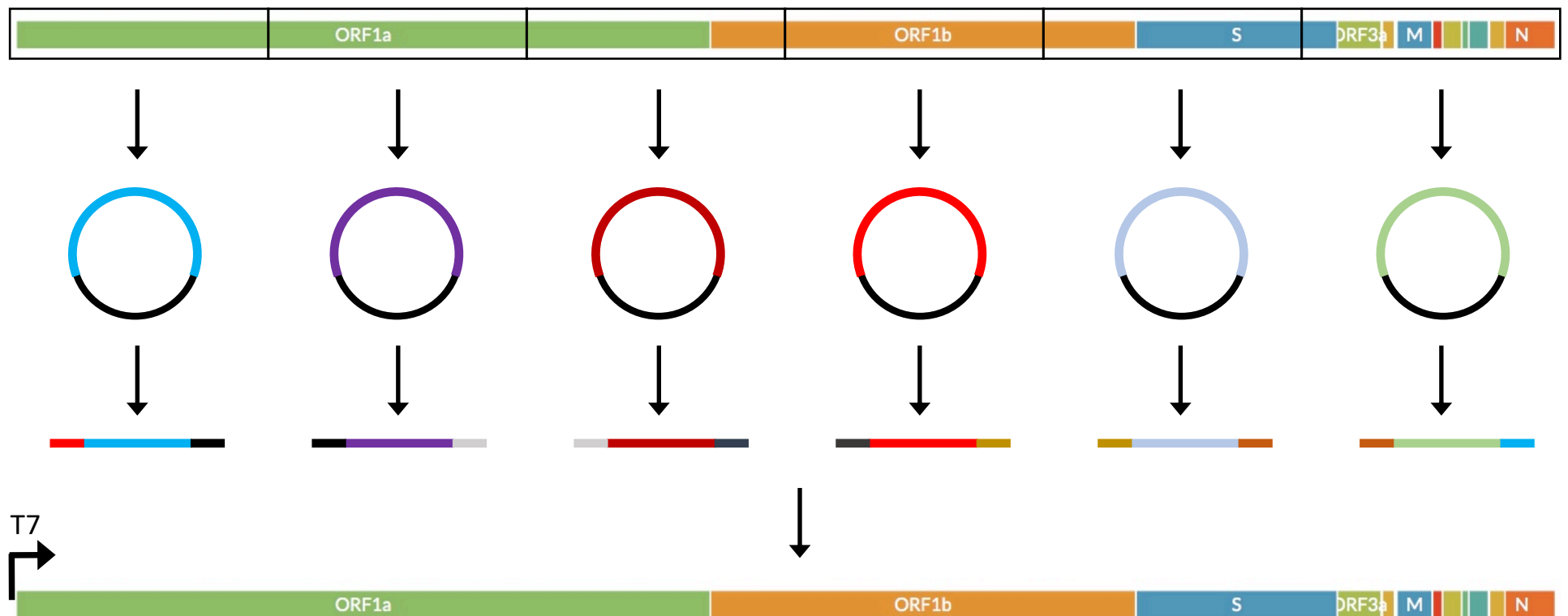


Individually clone &  
assemble into 6  
stage 2 vectors

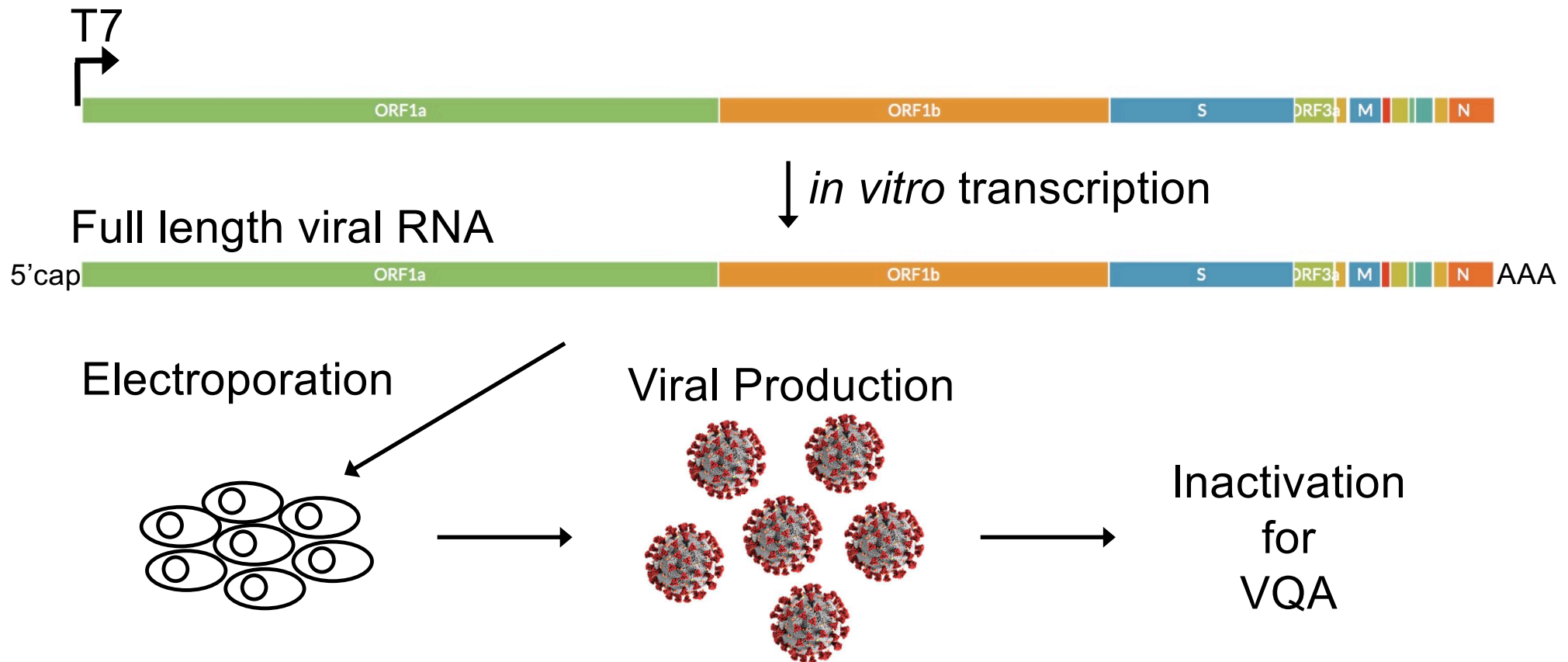




# Stage 2 vector assembly into full length viral DNA



# SARS-CoV-2 DNA to RNA to Virus production



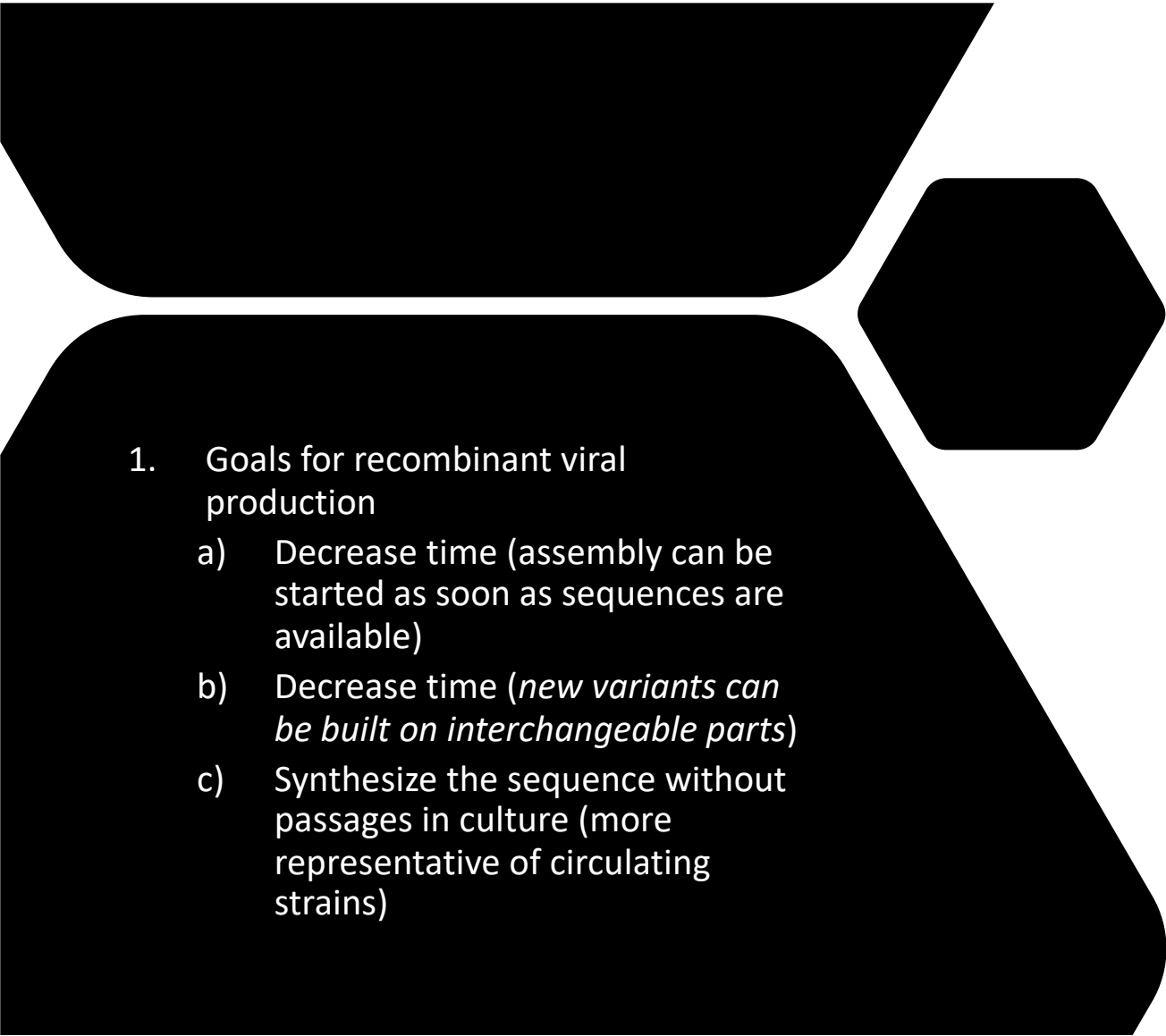
# VQA panel progress

## Laboratory isolated SARS-CoV-2 strains

- Ready now
  - WA1 (S clade)
- Viral production in progress
  - B.1.1.7 (20B/501Y.V1, 20I/501Y.V1, VOC-202012/01, UK variant)
  - B.1.351 (20H/501Y.V2, South African variant)
- Obtaining isolates
  - B.1.427 and B.1.429 (CA VUI1, CAL.20C)
  - P.1 (B.1.1.28.1, 20J/501Y.V3)
  - *B.1.526 (.1 .2) ?*

## Recombinant viral production

- P.1 in progress

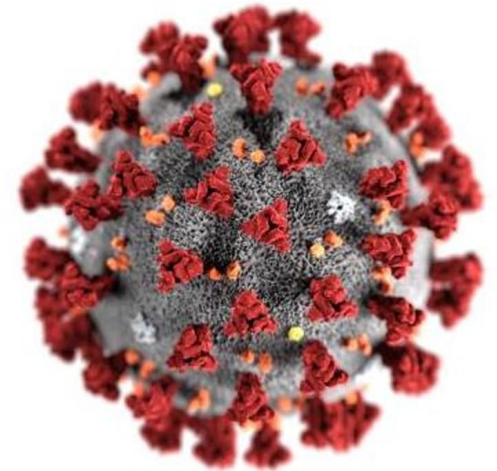
- 
1. Goals for recombinant viral production
    - a) Decrease time (assembly can be started as soon as sequences are available)
    - b) Decrease time (*new variants can be built on interchangeable parts*)
    - c) Synthesize the sequence without passages in culture (more representative of circulating strains)

Recombinant  
SARS-CoV-2  
production for  
VQA panels





Thank you

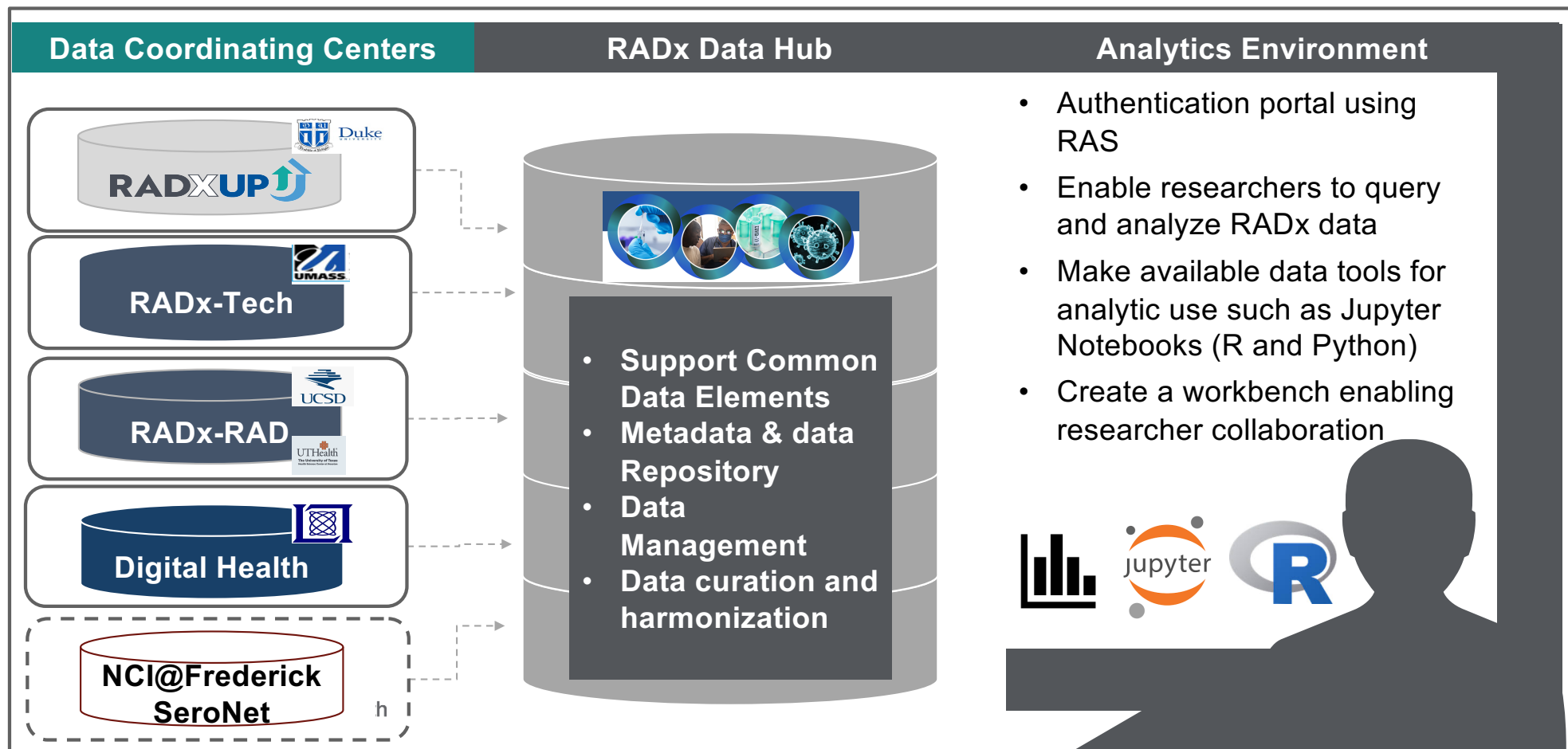


# **RADx-RAD DCC All-hands meeting**

[NIH Office of Data Science Strategy](#)






April 12th, 2021

**End Goal:** Provide researchers with a single access point to de-identified RADx and related data, algorithms, and other capabilities generated by various digital health solutions and RADx technologies.



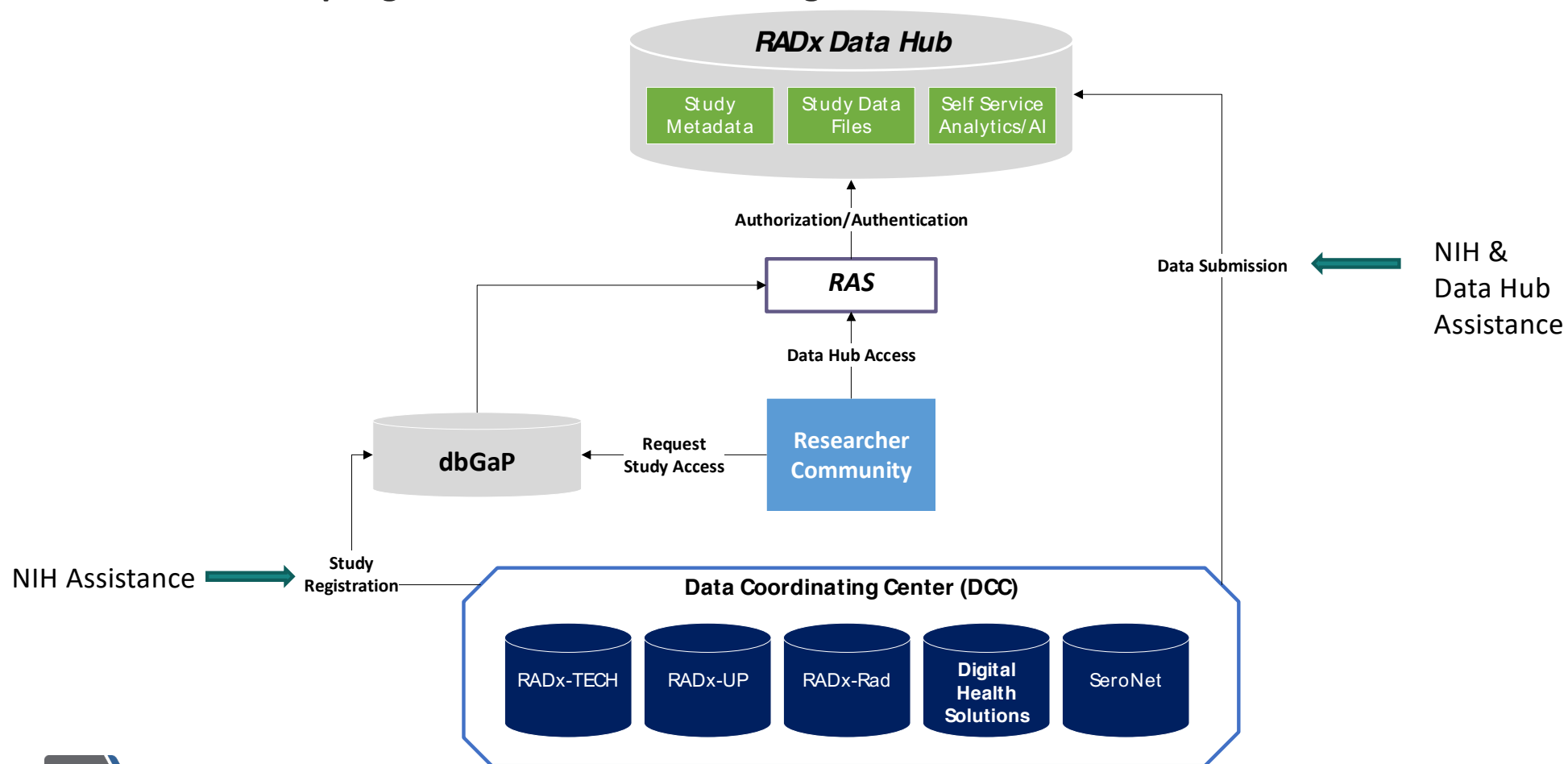
# RADx Data Hub: Purpose & Vision

Purpose of the Data Hub, CDE usage, end user, and data access control

KEY QUESTIONS	ANSWERS
 What is the purpose of the Data Hub?	➔ Adhering to NIH data FAIR principles; Solution to store, compute, and share testing data related to COVID-19 to provide researchers a single access point to find and analyze de-identified data and other capabilities generated by various programs funded by NIH.
 Who is the end user?	➔ Researcher community focusing on the conducting COVID-19 related research
 Why do PI's need to utilize the CDEs?	➔ Synchronization of the common data elements across programs enable data harmonization to support advanced analytics and machine learning
 What data access control is in place?	➔ The Data Hub is using dbGAP and RAS for data access control at the study level per researcher. Each research must request access through dbGaP to attain access to a study.
 Benefits of the RADx Data Hub	➔ <ul style="list-style-type: none"><li>• Researchers will have greater access to a wider variety of data to support their efforts.</li><li>• Researchers will be able to use a variety of tools to facilitate discovery and enable analysis of the dataset and collaboration with other researchers.</li><li>• Manual efforts to support the data ingestion process and data access management will be greatly reduced through automation.</li></ul>



## RADx Data Hub | High-level Data Context Diagram



## DCC Expectations for Data Sharing

Discussion on the expected cadence for DCC data sharing with the RADx Data Hub

Data Sharing Question: Is it feasible for **all DCCs** share project data with the Data Hub on a **regular cadence of 3 months?**




# RADx-rad DCC – Data Core

## Updates

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Hua Xu, PhD

# Information Web Portal




**RADx-rad Discoveries and Data Coordinating Center (DCC)**

Accelerating COVID-19 Diagnostic Innovation

**About RADx<sup>SM</sup> Radical**

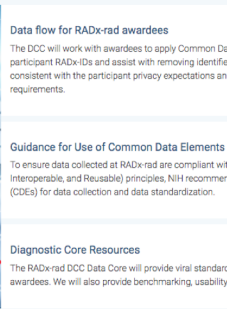
The National Institutes of Health launched the RADx<sup>SM</sup> Radical program to support innovative, non-traditional diagnostic approaches to address gaps in COVID-19 testing and surveillance. The program is expected to produce more efficient and effective ways to identify the current SARS-CoV-2 virus, which causes COVID-19, as well as its variants, and to develop tools to detect and combat emerging infectious diseases. It will also promote other ways to help diagnose and monitor COVID-19, and it will use AI and other advanced techniques to build predictive models.

**Resources**



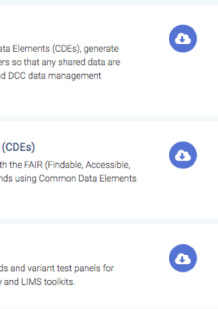
**Data flow for RADx-rad awardees**

The DCC will work with awardees to apply Common Data Elements (CDEs), generate participant RADx-IDs and assist with removing identifiers so that any shared data are consistent with the participant privacy expectations and DCC data management requirements.



**Guidance for Use of Common Data Elements (CDEs)**

To ensure data collected at RADx-rad are compliant with the FAIR (Findable, Accessible, Interoperable, and Reusable) principles, NIH recommends using Common Data Elements (CDEs) for data collection and data standardization.




**Diagnostic Core Resources**

The RADx-rad DCC Data Core will provide viral standards and variant test panels for awardees. We will also provide benchmarking, usability and LIMS toolkits.


**Resources**

**Key Resources**




**Data flow for RADx-rad awardees**

The RADx Data Hub is the ultimate destination of RADx-rad data. It is managed by the NIH. The RADx-rad DCC will ensure that data submitted to the hub will comply with standards agreed upon by the RADx program at NIH. The DCC will work with awardees to apply Common Data Elements (CDEs), generate participant RADx-IDs...




**Diagnostic Core Resources**

The RADx-rad DCC Data Core will provide viral standards and variant test panels for awardees. We will also provide benchmarking, usability and LIMS toolkits.




**Guidance for Use of Common Data Elements (CDEs)**

To ensure data collected at RADx-rad are compliant with the FAIR (Findable, Accessible, Interoperable, and Reusable) principles, NIH recommends using Common Data Elements (CDEs) for data collection and data standardization. The consistent use of CDEs within the RADx program will greatly increase the interoperability and reusability of collected data, thus enabling efficient data integration and data...



**HIPAA "Safe Harbor" Checklist From for RADx-rad**

This checklist is intended to guide RADx-rad awardees on what HIPAA-defined identifiers need to be removed before submitting data to the repository. If you have questions about a specific field, please seek guidance from your organization's IRB Chair and/or Privacy Officer.



**Minimum CDEs Required by NIH**

This resource describes the minimum common data elements (CDEs) required for awardees collecting prospective human subjects data.

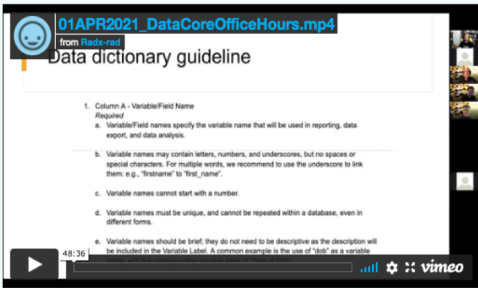
RADx<sup>SM</sup> Radical > EVENTS > Protected: DCC Weekly Office Hours: Data Core

**Protected: DCC Weekly Office Hours: Data Core**

Start Date: 2021-04-01 13:00:00 (Pacific Time)

End Date: 2021-04-01 14:00:00 (Pacific Time)

Video







01APR2021 DataCoreOfficeHours.mp4

01APR2021 DataCoreOfficeHours.mp4

Data dictionary guideline

1. Column A - Variable/Field Name  
*Required*
  - a. Variable/Field names specify the variable name that will be used in reporting, data export, and data analysis.
  - b. Variable names may contain letters, numbers, and underscores, but no spaces or special characters. For multiple words, we recommend to use the underscore to link them; e.g., "first\_name" to "first\_name".
  - c. Variable names cannot start with a number.
  - d. Variable names must be unique, and cannot be repeated within a database, even in different forms.
  - e. Variable names should be brief, they do not need to be descriptive as the description will be included in the Variable Label. A common example is the use of "id" as a variable.

Share:    

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The RADx-rad DCC is funded by NIH (U24LM013755)



# Final version of minimum CDEs approved by NIH RADx Executive Committee

Concept	Stimulus	Response
Identity	None	Project-specific identifier
Race <sup>1</sup>	What race do you identify with?	AI/AN; Asian Black or African American; Native Hawaiian or other Pacific Islander; White
Ethnicity <sup>1</sup>	What ethnicity do you identify with?	Hispanic or Latino; not Hispanic or Latino
Sex	What was your assigned sex at birth?	Male, Female, Intersex
Age	What is your age?	Age in years
Education	How many years of education have you completed?	0 - +20
Domicile	Where do you live?	Zip Code
Employment	Are you employed?	Permanent, temporary or not
Insurance Status	What kind of insurance do you have?	Private, Public, none
Disability status <sup>2</sup>	Are you deaf or do you have serious difficulty hearing?	Yes, no
	Are you blind or do you have serious difficulty seeing, even when wearing glasses?	Yes, no
	Because of a physical, mental, or emotional condition, do you have serious difficulty concentrating, remembering, or making decisions?	Yes, no
	Do you have serious difficulty walking or climbing stairs?	Yes, no
	Do you have difficulty dressing or bathing ?	Yes, no
	Because of a physical, mental, or emotional condition, do you have difficulty doing errands alone such as visiting a doctor's office or shopping?	Yes, no

Medical History	Vaping use	Yes, no
	Nicotine use	Yes, no
	Alcohol use	Yes, no
	Asthma	Yes, no
	Cancer	Yes, no
	Cardiovascular disease	Yes, no
	Chronic kidney disease	Yes, no
	Chronic lung disease	Yes, no
	Diabetes	Yes, no
	Hypertension	Yes, no
	Immunosuppressive condition	Yes, no
	Serious mental illness	Yes, no
	Sickle cell disease	Yes, no
	Pregnancy status	Currently pregnant, not
Symptoms	Cough <sup>3</sup>	Yes, no
	Fever <sup>2</sup>	Yes, no
	SoB or Difficulty breathing <sup>2</sup>	Yes, no
	Headache <sup>2</sup>	Yes, no
	Muscle ache <sup>2</sup>	Yes, no
	New Loss of taste or smell <sup>2</sup>	Yes, no
	Chills <sup>2</sup>	Yes, no
	Excessive fatigue <sup>2</sup>	Yes, no
	Nausea/vomiting <sup>2</sup>	Yes, no
	Diarrhea <sup>2</sup>	Yes, no
	Abdominal pain <sup>4</sup>	Yes, no
	Skin rash <sup>3</sup>	Yes, no
	conjunctivitis <sup>3</sup>	Yes, no
Health Status	BMI	Weight & height
	Would you say that (your) health in general is excellent, very good, good, fair or poor? <sup>5</sup>	Excellent, very good, good, fair, poor

# REDCap Codebook for minimum CDEs

Study ID		<input type="text"/>
<b>Race</b>		
What is your race? Mark one or more boxes.	<input type="checkbox"/> American Indian or Alaska Native <input type="checkbox"/> Asian <input type="checkbox"/> Black or African American <input type="checkbox"/> Native Hawaiian or Other Pacific Islander <input type="checkbox"/> White <input type="checkbox"/> Some other race	
<b>Ethnicity</b>		
Are you of Hispanic or Latino origin?	<input type="checkbox"/> Yes, of Hispanic or Latino origin <input type="checkbox"/> No, not of Hispanic or Latino origin	
<b>Age</b>		
What is your age?	<input type="text"/>	Age in years. For babies less than 1 year old, write 0 as the age
<b>Sex</b>		
What is your biological sex assigned at birth?	<input type="radio"/> Male <input type="radio"/> Female <input type="radio"/> Intersex <input type="radio"/> None of these describe me	reset
<b>Education</b>		
How many years of education have you completed?	<input type="text"/>	Years of education from 0 - 20+
<b>Domicile</b>		
Zip or Postal Code:	<input type="text"/>	5-digit zip code

Variable / Field Name	Form Name	Section Header	Field Type	Field Label	Choices, Calc	Field Note	Text Validation	Text Validation
record_id	form_1		text	Record ID				
study_id	form_1		text	Study ID				
race	form_1	Race	checkbox	What is your race?	1, American Indian or Alaska Native   2, Asian   3, Black or African American   4, Native Hawaiian or Other Pacific Islander   5, White   6, Some other race			
ethnicity	form_1	Ethnicity	checkbox	Are you of Hispanic or Latino origin?	1, Yes, of Hispanic or Latino origin   0, No, not of Hispanic or Latino origin			
age	form_1	Age	text	What is your age?		Age in years. integer		
sex	form_1	Sex	radio	What is your sex?	1, Male   2, Female   3, Intersex   4, None of these describe me			
education	form_1	Education	text	How many years of education have you completed?		Years of education integer		
zip	form_1	Domicile	text	Zip or Postal Code:		5-digit zip code		
employment	form_1	Employment	radio	Are you employed?	1, Employed in a permanent position   2, Employed in a temporary position   3, Unemployed			
insurance	form_1	Insurance Status	radio	What kind of insurance do you have?	1, Private insurance   2, Public insurance   3, None			
deaf	form_1	Disability Status	yesno	Are you deaf or do you have serious difficulty hearing?				
blind	form_1		yesno	Are you blind or do you have serious difficulty seeing, even when wearing glasses?				
memory_dis	form_1		yesno	Because of a physical, mental, or emotional condition, do you have memory problems?				
walking_climbing_dis	form_1		yesno	Do you have serious difficulty walking or climbing stairs?				
dress_bathe_dis	form_1		yesno	Do you have difficulty dressing or bathing?				
errand_dis	form_1		yesno	Because of a physical, mental, or emotional condition, do you have difficulty doing errands such as shopping, going to the doctor, or bank business?				
cancer	form_1	Medical History	yesno	Cancer				
cardiovascular_disease	form_1		yesno	Cardiovascular disease				
chronic_kidney_disease	form_1		yesno	Chronic kidney disease				
chronic_lung_disease	form_1		yesno	Chronic lung disease				
diabetes	form_1		yesno	Diabetes				
hypertension	form_1		yesno	Hypertension				
immunosuppressive_condition	form_1		yesno	Immunosuppressive condition				
serious_mental_illness	form_1		yesno	Serious mental illness				
sickle_cell_disease	form_1		yesno	Sickle cell disease				
pregnancy_status	form_1		radio	Pregnancy status	1, Currently pregnant   0, Not pregnant			
cough	form_1	Symptoms	yesno	Cough				
fever	form_1		yesno	Fever				
shortness_of_breath	form_1		yesno	Shortness of breath or difficulty breathing				
headache	form_1		yesno	Headache				
muscle_ache	form_1		yesno	Muscle ache				
new_loss_of_taste_or_smell	form_1		yesno	New loss of taste or smell				
chills	form_1		yesno	Chills				
excessive_fatigue	form_1		yesno	Excessive fatigue				

# Data Dictionary Template

Columns	Example1	Example2	Example3
Variable/Field Name	race	abdominal_pain	age
Form Name/Variable Classification	sociodemographics	condition_symptom	sociodemographics
Field Label/Variable Description	the race of the participants	if the participant is experiencing the symptom of abdominal pain	the age of the participant
Variable Question	What is your race?	Are you currently experience abdominal pain?	what is your age?
Field Type	checkbox	boolean	text
Choices, Calculations OR Slider Labels	1, American Indian or Alaska Native   2, Black or African American   3, Asian   4, Native Hawaiian or Other Pacific Islander   5, White   15, Some other race   99, Prefer not to answer	1, Yes   2, No	
Validation			integer: min 0, max 120
Field Notes			
Candidate CDEs	<a href="https://cde.nlm.nih.gov/deView?tinyId=hU6IJ3BLM">https://cde.nlm.nih.gov/deView?tinyId=hU6IJ3BLM</a>	<a href="https://cde.nlm.nih.gov/deView?tinyId=F_Vsk6QDVB">https://cde.nlm.nih.gov/deView?tinyId=F_Vsk6QDVB</a>	

Variable/Field Name	Form Name/Variable Classification	Field Label/Variable Description	Variable Question	Field Type	Choices, Calculations OR Slider Labels	Validation	Field Notes	Candidate CDEs
		▼		▼				
		▼		▼				
		▼		▼				
		▼		▼				
		▼		▼				



# Recommended CDEs for FOA Research Areas

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Peter Rose, PhD

# Activities on Data Standards for FOAs

	Automatic Detection and Tracking	Chemo- sensory Testing	Exosome Based	Multimodal Surveillance	Novel Biosensing and VOC	PreVAIL kids	SCENT	Wastewater
Minimum CDE communication								
Data Standards Kick-Off								
Data Standards Follow-up	Monthly	Ad Hoc	Monthly	Ad Hoc	Ad Hoc	Monthly	Ad Hoc	Bi-weekly
Data Dictionary Template sent out								
Study Data Dictionaries received	(1)	(1)				(3)	(1)	(4) + CDC NWSS

# Developing Recommended CDEs

## 8 FOA Groups



Send data  
dictionaries



## Data Standards Meetings

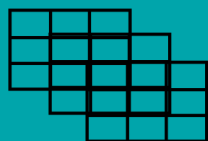


Edit shared  
data dictionary  
template



Edit, revise,  
build consensus

## DCC



Incorporate  
into template



FOA shared  
data dictionary template



Map to NIH,  
PhenX, CDC, etc.  
dictionaries





# Plans and Timelines

- Combine SCENT and VOC groups for CDE development
  - Both groups develop similar technologies
- Novel Biosensing
  - Diverse technologies, SBIR grants, data-sharing may be limited due to IP concerns
- Timeline
  - Recommended CDEs depend on data submission readiness
- Off-line work on Data Dictionary template will reduce number of meetings!