Rapid Acceleration of Diagnostics: *RADx (Tech + ATP)*

Bruce J. Tromberg, Ph.D.
Director, National Institute of Biomedical Imaging and Bioengineering (NIBIB)

National Institute of Biomedical Imaging and Bioengineering

RADx Tech & ATP

NIH Office of the Director


Francis Collins


Rachael Fleurance


Larry Tabak


Tara Schwetz

RADx Tech – $500M
Highly competitive, rapid three-phase challenge to identify the best candidates for at-home or point-of-care tests for COVID-19

RADx Advanced Technology Platforms (RADx-ATP) – $230M
Rapid scale-up of advanced technologies to increase rapidity and enhance and validate throughput – create ultra-high throughput machines and facilities

RADx Underserved Populations (RADx-UP) – $500M
Interlinked community-based demonstration projects focused on implementation strategies to enable and enhance testing of COVID-19 in vulnerable populations

RADx Radical (RADx-Rad) – $200M
Develop and advance novel, non-traditional approaches or new applications of existing approaches for testing

April 24, 2020: $1.5B to NIH
$500 Million to NIBIB


Jill Heemskerk.


Bruce Tromberg

National Institute of Biomedical Imaging and Bioengineering (NIBIB)

The NEW ENGLAND JOURNAL of MEDICINE

Rapid Scaling Up of Covid-19 Diagnostic Testing in the United States — The NIH RADx Initiative

Bruce J. Tromberg, Ph.D., Tara A. Schwetz, Ph.D., Eliseo J. Pérez-Stable, M.D., Richard J. Hodes, M.D., Richard P. Woychik, Ph.D., Rick A. Bright, Ph.D., Rachael L. Fleurence, Ph.D., and Francis S. Collins, M.D., Ph.D.

The first reports of an unusual cluster of pneumonia cases in the city of Wuhan, China, emerged in December 2019, heralding a global pandemic. As of July 13, 2020, more than 3.3 of RADx and their goals, and we end with a review of the challenges ahead.

On April 24, 2020, Congress appropriated $1.5 billion, from the $25 billion provided in the

RADx Tech & ATP

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April 29

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BARDA

$307 M Partnership with BARDA

Tech/ATP Team Leads: Tiffani Lash, Todd Merchak, Taylor Gilliland, Kate Egan, Mike Wolfson, Doug Sheeley, Gene Civillico

NHLBI COAC: Ann Gawalt, Allison Cristman, Kristi Cooper, Shirley Ruiz-Lundgren, Roxane Burkett, Cornelius Moore, Lynn Furtaw, John Lear, Ahmed Hassan, Linda Smith, Natalie Bruning, Stacey Turner, Tara Knox

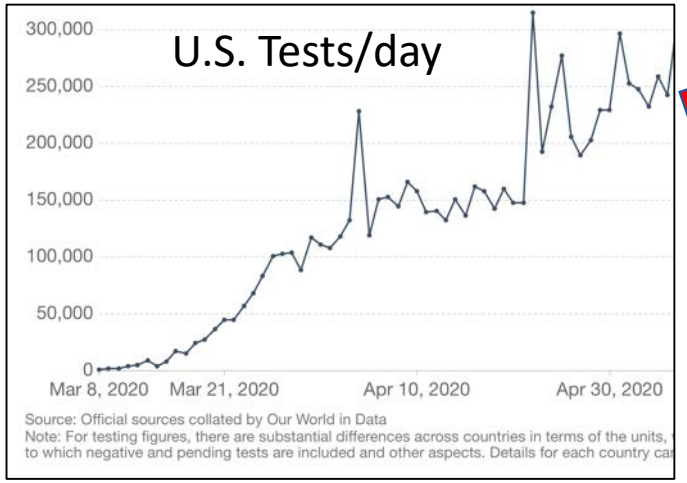
OASH FDA CMS CDC

RADx Tech & ATP Goals

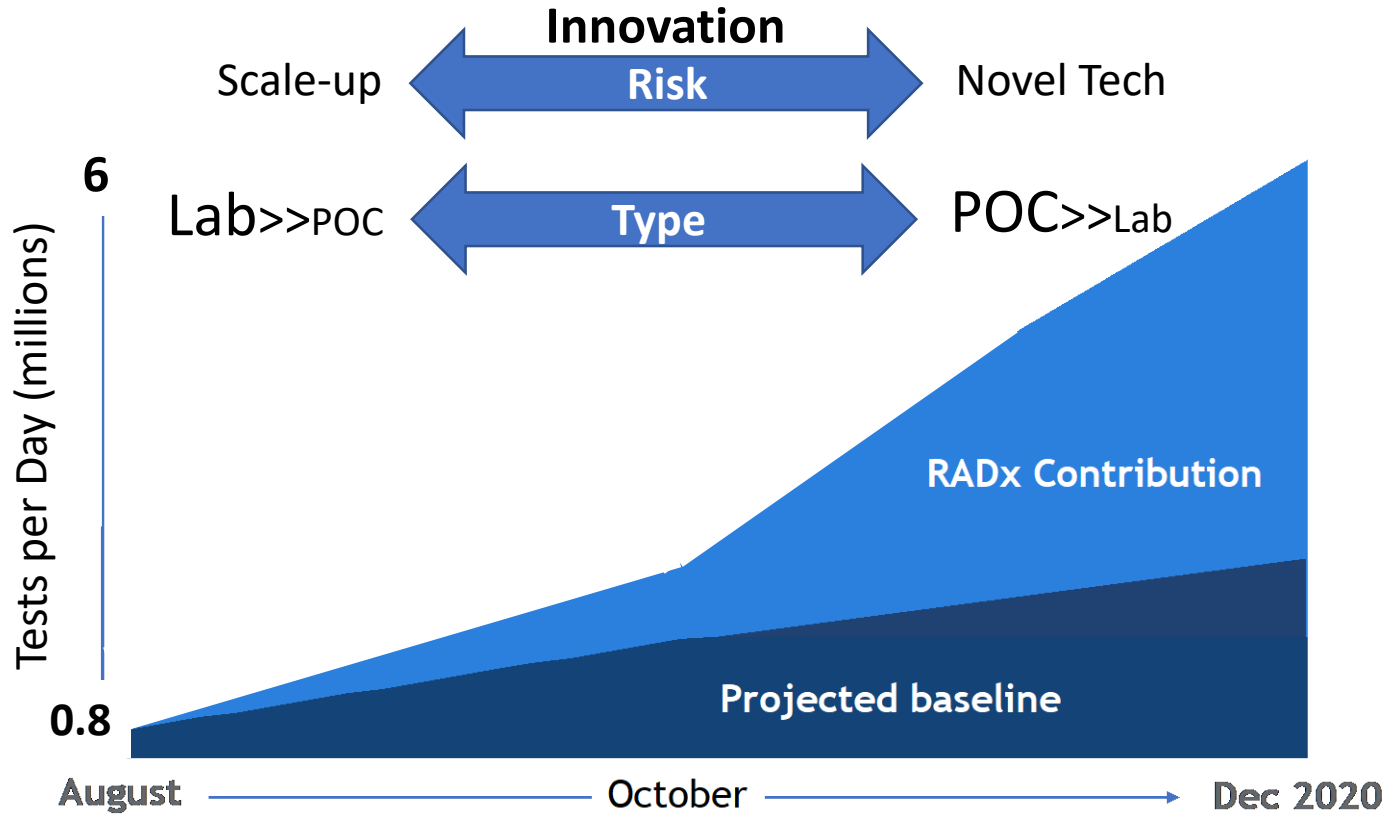
1) Expand COVID-19 Testing Technologies: *Number, Type and Access*
2) Optimize Performance: *Technologic and Operational; Match Community Needs*

Test Settings

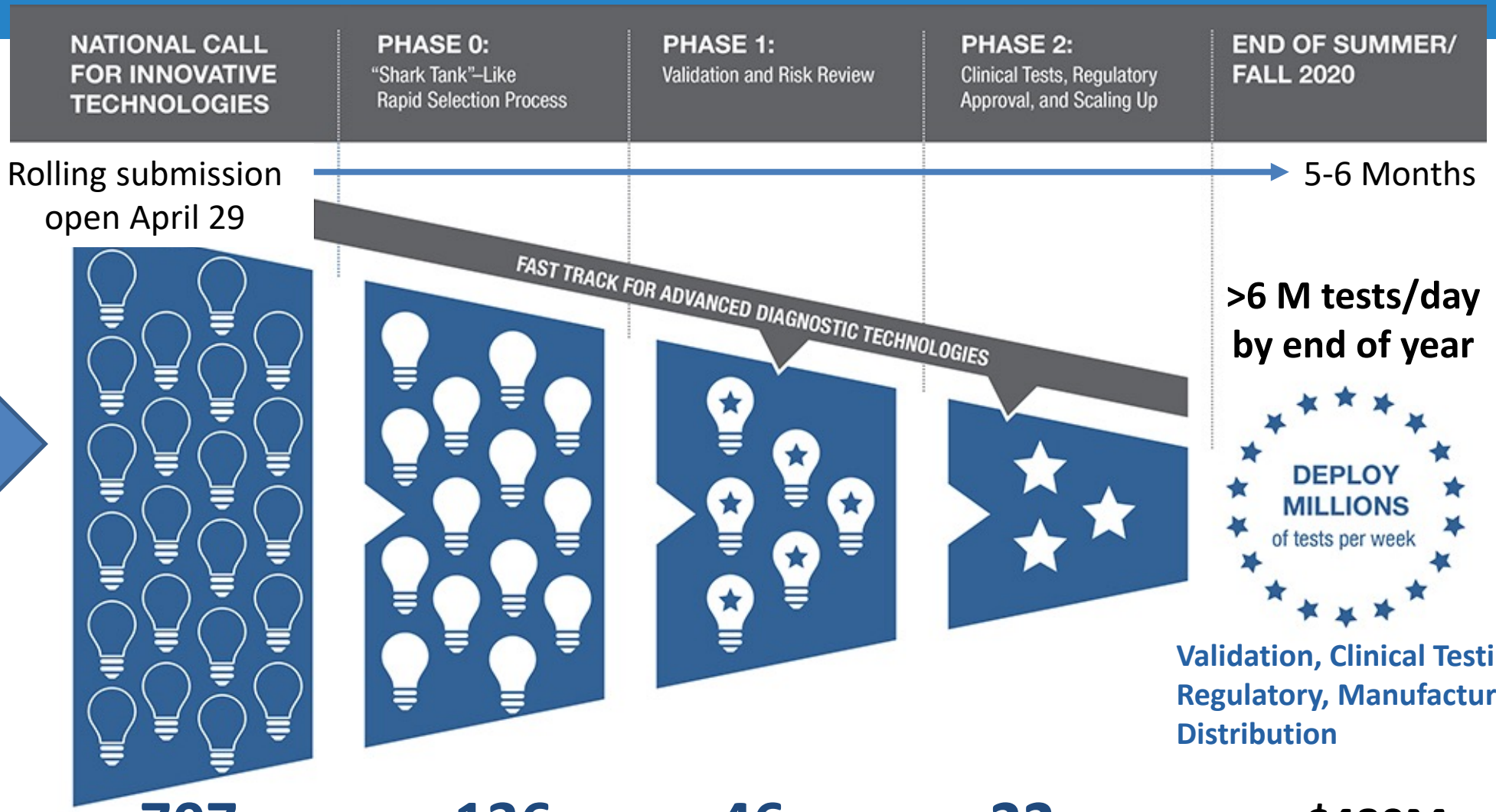
- Home-based
- Point of Care (POC)
- Laboratory (CLIA, research)



RADx Launch: *~250k/day*



RADx Innovation Funnel



Applications Started

~3000

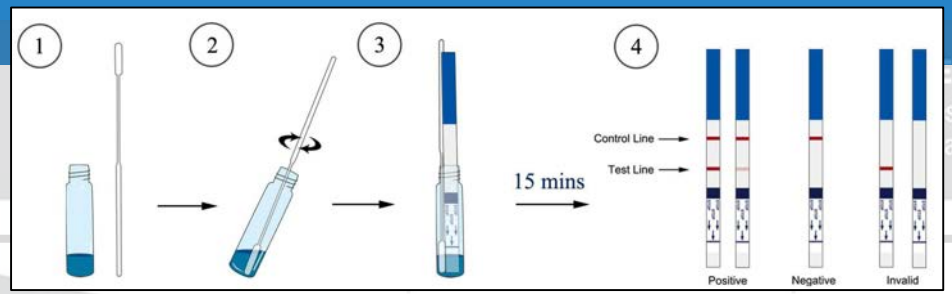
>6 M tests/day by end of year

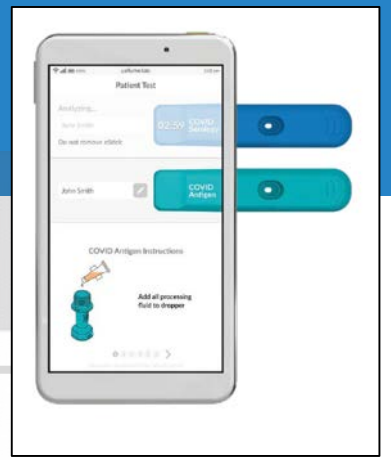
Validation, Clinical Testing, Regulatory, Manufacturing, Distribution

Projects in each Phase

707 | **136** | **46** | **22** (Tech + ATP) | **~$480M**

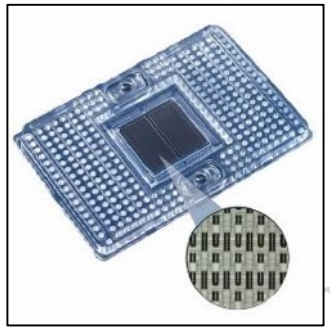
RADx Innovation Funnel

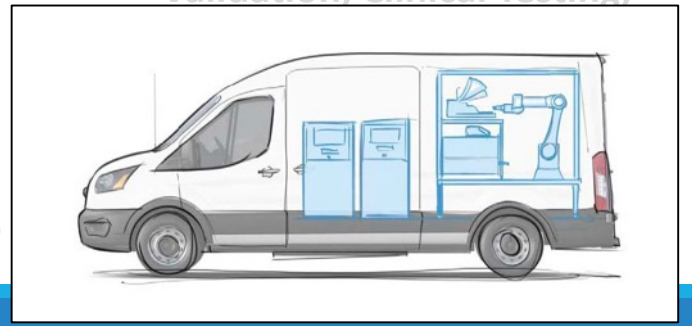




Innovation

1) Separation/concentration
2) µ-Fluidics
3) Chemistries, e.g. CRISPR, NGS
4) Labels, Reporters
5) Readout Tech
6) Miniaturization
7) Automation





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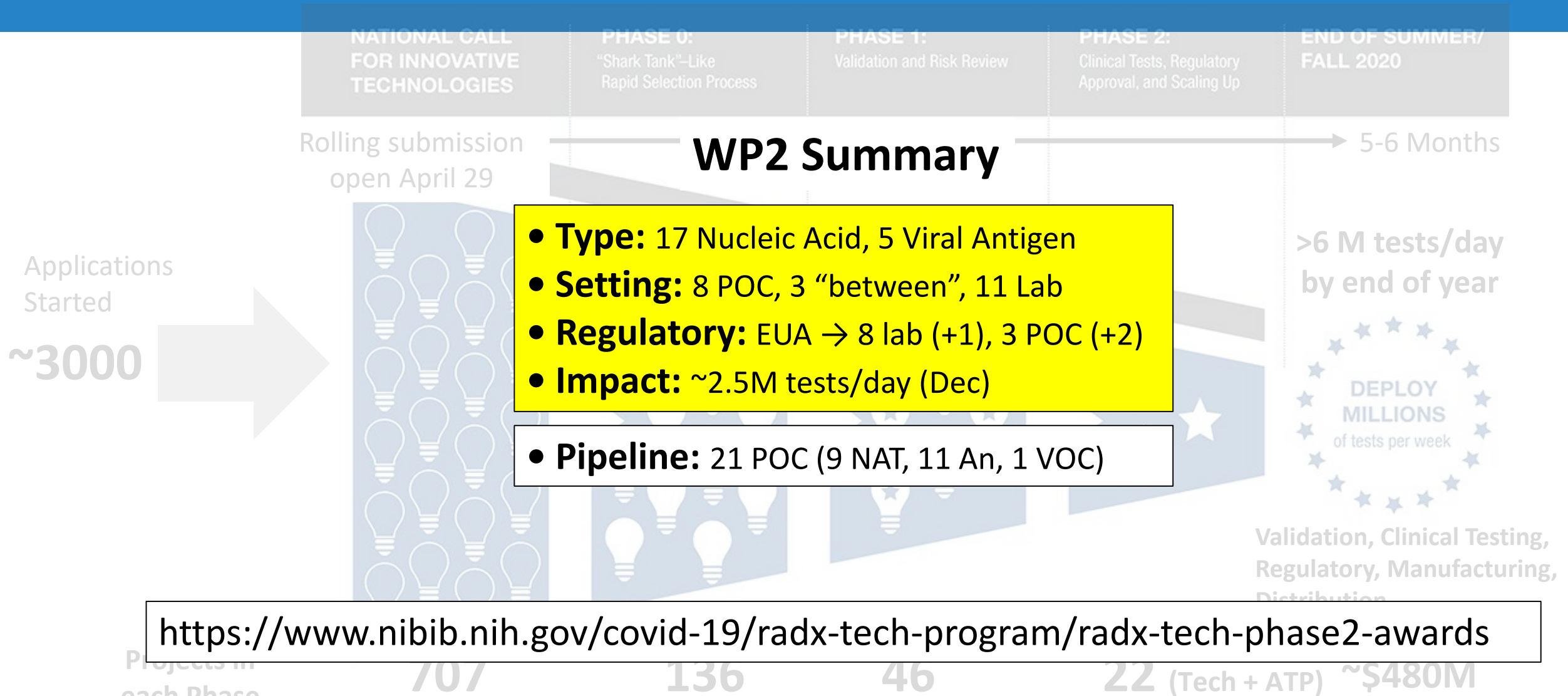


WP2 Summary

- **Type:** 17 Nucleic Acid, 5 Viral Antigen
- **Setting:** 8 POC, 3 "between", 11 Lab
- **Regulatory:** EUA → 8 lab (+1), 3 POC (+2)
- **Impact:** ~2.5M tests/day (Dec)

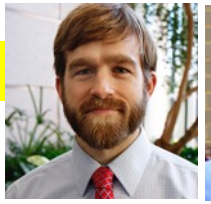
- **Pipeline:** 21 POC (9 NAT, 11 An, 1 VOC)

https://www.nibib.nih.gov/covid-19/radx-tech-program/radx-tech-phase2-awards

Point-of-Care Technologies Research Network (POCTRN)

NIBIB National Network: *5-6 years for new POC technologies*

Established 2007, Expanded 2020: >1000 RADx experts & contributors


Todd Merchak


Tiffany Lash

https://www.poctrn.org

VENTUREWELL™ idea to impact

GaTech/Emory
- ✓Engineering
- ✓Design/Prototype
- ✓Clinical Validation
- ✓Biobank samples
- ✓In-Home Validation

Johns Hopkins
- ✓Public Health/STD
- ✓Global Health
- ✓Clinical Validation
- ✓Biobank samples
- ✓Validation in LMICs

CIMIT/MGH
- ✓Coordinating Center
- ✓Collaboration/Management Platform
- ✓Business/Commercialization

Northwestern
- ✓HIV/AIDS
- ✓Engineering
- ✓Global Health
- ✓Clinical Validation
- ✓Validation in LMICs

UMass
- ✓Heart, lung, blood
- ✓Engineering
- ✓Clinical Validation
- ✓Biobank samples
- ✓Clinical Trials
- ✓Business/Commercialization

C BIO M C3i

Project Tech:

1) Review
2) Funding
3) Expertise
4) Testing

Validation Core

15 projects complete, 11 ongoing, >1500 participants

Clinical Studies Core

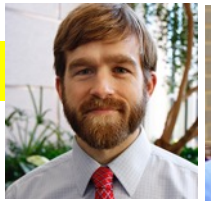
Standard Trial Design, Digital Health Platform, Single IRB, Center Network

Deployment Core

Supply chain, Manufacturing, User Community, End to end solutions

National Institute of Biomedical Imaging and Bioengineering

Point-of-Care Technologies Research Network (POCTRN)




Todd Merchak Tiffany Lash

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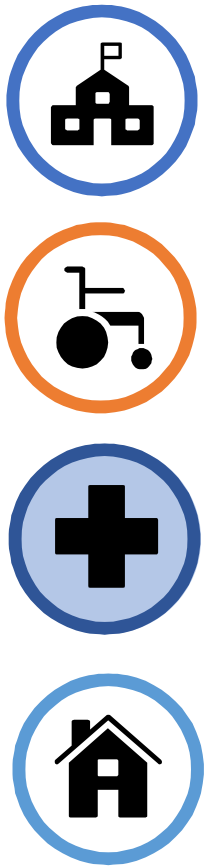
RADx UP



Duke CDCC RADx UP Coordinating Center

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C BIO M C3i

Validation Core

Clinical Studies Core

Deployment Core

National Institute of Biomedical Imaging and Bioengineering

RADx Test Validation Core (Emory-Gtech)

15 projects complete, 11 ongoing



Wilbur Lam Greg Martin. Oliver Brand

Feasibility

- Ensure positive control (provided or commercial) is positive
- Ensure negative matrix (i.e. saliva, patient sample or commercial) is negative
- Ensure negative matrix spiked with live and/or inactivated SARS-CoV-2 virus is positive

Contrived samples

- Verify the limit of detection (LOD) via live and/or inactivated SARS-CoV-2 virus by serial dilution using correct matrix
- Test non-SARS-CoV-2 coronaviruses (test specificity/cross-reactivity)
- Test different strains of SARS-CoV-2 (strain variation)

Patient samples

- Test banked patient samples (adult and pediatric) with concomitant testing on reference method to determine concordance
- Test prospective patient samples using collection sites

>1500 participants

- Calculate sensitivity, specificity, positive and negative predictive values with input from our biostatistical core

RADx Test Validation Core (Emory-Gtech)

15 projects complete, 11 ongoing

Feasibility

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NIH score range: 1 (exceptional) to 9 (poor)

ACME POCT score: 2 (88% of respondents)

RADx Test Verification Core Recommendation: Proceed to WP2

Resume and Summary of Discussion: the RADx ACME POCT convened an internal study section on July 9th, 2020 to discuss the RADx Test Verification Core's analysis of Project #2244 in which the criteria for evaluation included: LOD, Sensitivity, Specificity, Repeatability, and Usability. The testing of this COVID-19 point-of-care (POC) PCR diagnostic test comprised of 1) LOD testing at several of our sites, including our Emory BSL-3 facility, Children's Healthcare of Atlanta clinical pathology laboratory, and laboratories in

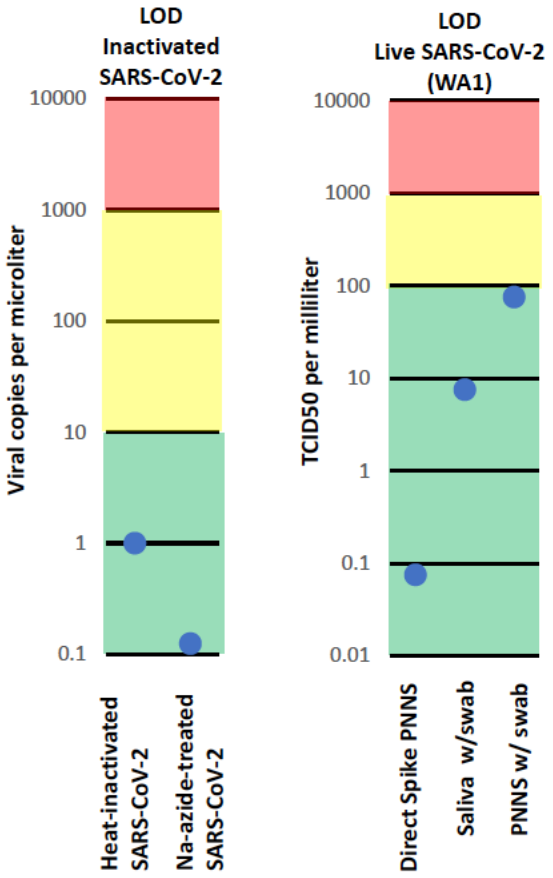
Patient samples

Test banked patient samples (adult and pediatric) wit

Test prospective patient samples using collection sites

Calculate sensitivity, specificity, positive and negative

OVERALL SUMMARY OF RESULTS ACROSS ACME POCT SITES



Specificity	
Virus Type	Lack of Cross-Reactivity?
OC43 seasonal coronavirus	✓
MERS (heat inactivated)	✓

Prospective Clinical Results

2244

	DiaSorin RT-PCR +	DiaSorin RT-PCR -
+	4	0
-	0	48

Sensitivity: 100%
Specificity: 100%

RADx Clinical Studies Core (UMass)

Mission: Evaluate RADx platforms that advance to Phase 2 in rigorous clinical studies w/ diverse populations and settings.

Laura Gibson, MD

David McManus, MD

Standard Trial Design: Master protocols, powered studies (~250 subjects), device-specific amendments, accelerate regulatory review

Eureka Digital Health Platform mobile app and website, participants enter own data

Data Safety Board and Single IRB for oversight and safety monitoring

Robust Research Center Network: POCTRN core center network for enrollment (w/Practice Based Research Network and Centers for Clinical and Translational Science assisting)

COVID-19 Test US

Clinical Study Partners

UMassMemorial Health Care

UCSF Health

Northwestern Medicine

Eureka

Participant ID & Enrollment

JOHNS HOPKINS MEDICINE

EMORY HEALTHCARE

The CTSA Trial Innovation Network

Connecting: NIH Institutes, Industry, Researchers, and Participants

Investigators at CTSA Hubs across the U.S.

Trial Innovation Centers (TICs)

Request Support and Advice for Success

Recruitment Innovation Centers (RICs)

RADx Deployment Core (CIMIT)

Bridging NIH/USG, non-profit Foundations, Academia, and Industry

Mission

Provide support for successful commercialization and deployment of COVID-19 solutions in unique communities.

- Members: 32
- Nancy Gagliano, MD, Core Lead
- Brian Walsh, Commercialization Lead
- Sreeram Ramakrishnan, Data Solutions Lead
- Susan Moreira, Deployment Lead

Nancy Gagliano, MD

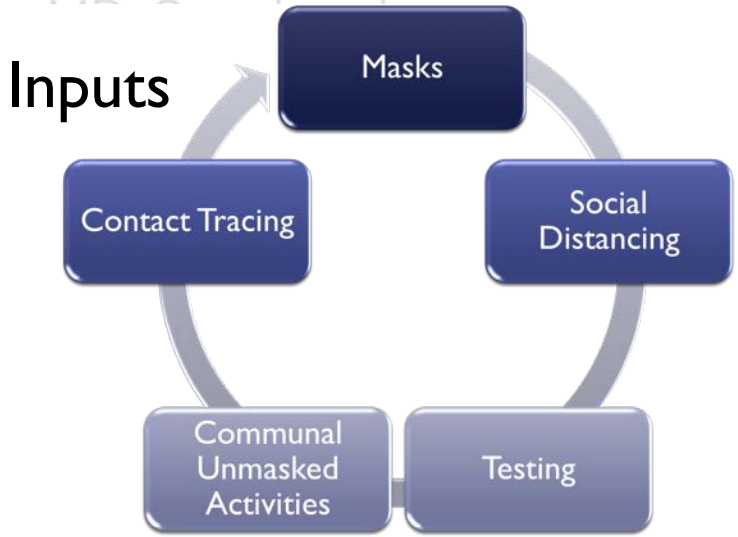
Current Highlights

- Supply Chain continues to be core challenge
- Development of Testing Model has received international recognition
- User communities need end-to-end solutions to deploy COVID testing
- Design-a-thon scheduled to develop data solutions

RADx Deployment Core (CIMIT)

Bridging NIH/USG, non-profit Foundations, Academia, and Industry

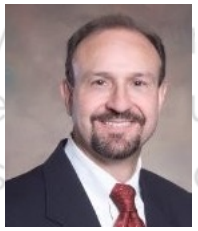
"When-to-Test" modeling tool: Match testing approaches w/needs; evaluate impact of risk reducing activities.



www.poctrn.org
RADx webinars, tools

	TEST OPTIONS (UNDER 'TYPICAL' CONI	
	Test 1 POC instrument-based antigen test from nasal sample	**Test 2** POC molecular test (e.g. PCR) from NP sample
Does test meet needed turnaround time	Yes	Yes
Number of people to be tested in a day	111	91
Recommended max days between tests/person	9	11
Number of instruments required	4	3
Total instrument capital cost	**$7,000**	**$30,000**
Staff required	3	3
Cost per test	$43.77	$47.03
Daily test cost	**$4,858**	**$4,280**

Anette Hosoi
MIT



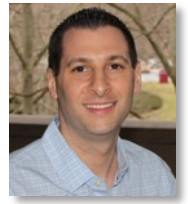
Paul Tessier,
CIMIT/MGH

RADx Digital Health Networks: *Integration*

RADx POC Test

Wearables

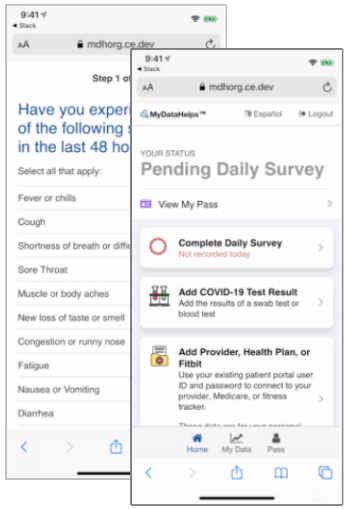
Digital Contact Tracing

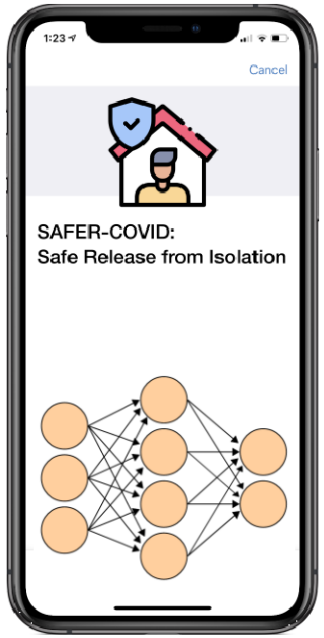


Andrew Weitz
NIBIB

Jason Levine
NCI

Symptom Surveys





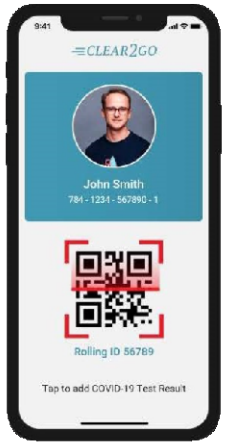
EHR & Claims

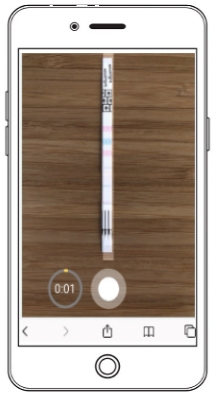
SYNC FOR SCIENCE

HL7 FHIR

Blue Button Download My Data

Proof of Health Status





Cell Phone Reader

e.g. OpenRDT (Audere)

GATES foundation

NIH National Institute of Biomedical Imaging and Bioengineering

NIH NATIONAL CANCER INSTITUTE

https://www.nibib.nih.gov/news-events/newsroom/nih-awards-contracts-develop-innovative-digital-health-technologies-covid-19

RADx Tech/ATP Summary

RADx Tech/ATP:

Accelerating innovation, Multiple platforms, Millions tests/day

Implementation Challenge:

- Standard Medical Diagnostics: *accurately detect/diagnose disease in individuals*
- **COVID Paradox: *rapidly assess, track +/- of disease in large, asymptomatic populations***
- Barriers: *Economic, cultural*

RADx Partnerships:

- Guidelines*: match & deploy tech and test protocols for range of use cases (what test/when?)*
- Evaluate: *performance, impact, efficacy; validate models*
- Inspire: *testing + DH platforms for widespread screening/surveillance*