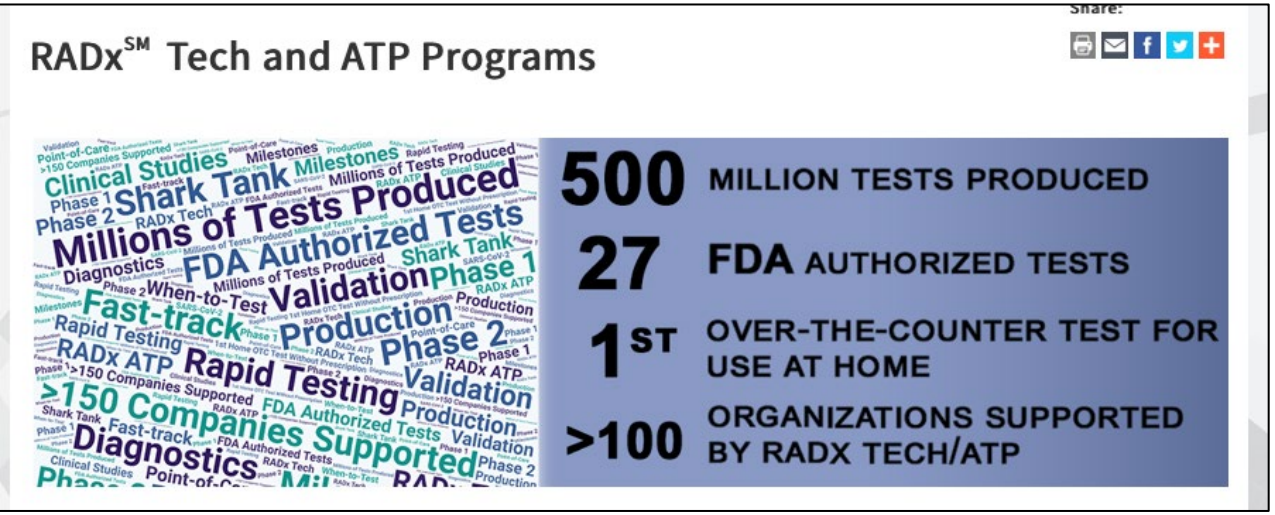
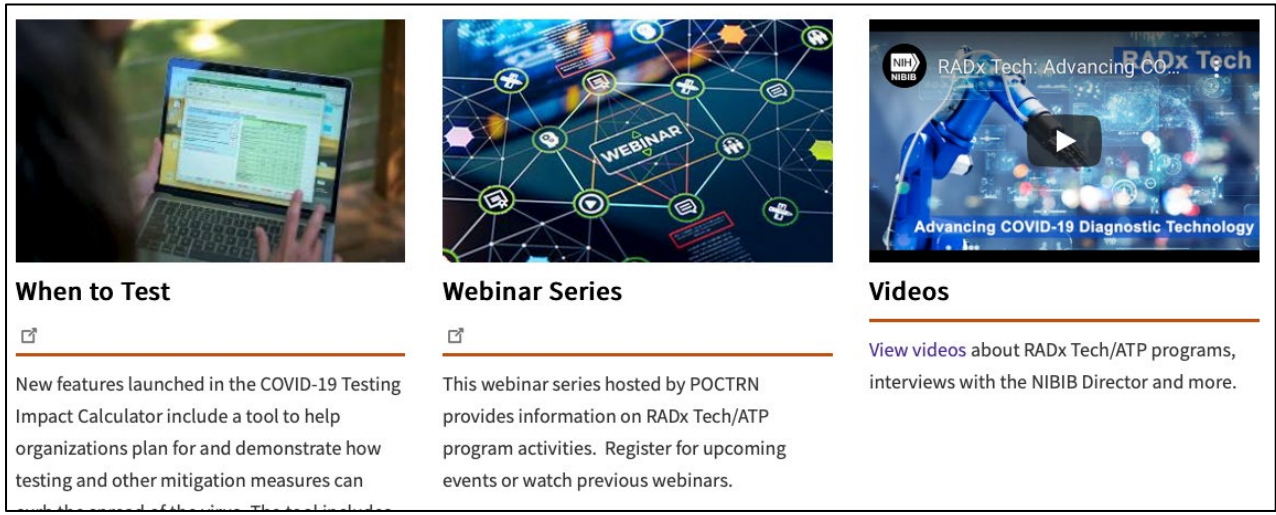
Rapid Acceleration of Diagnostics Technology (RADx Tech)

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





RADx Tech NIH Leads: Jill Heemskerk, Todd Merchak, Tiffani Lash, Mike Wolfson, Doug Sheeley, Bill Heetderks, Felicia Qashu, Tony Kirilusha, Mark Snyder, Andrew Weitz, Krishna Juluru, Taylor Gilliland, Rachael Fleurence, Matt McMahon, Jennifer Jackson, Ray MacDougall, Patty Wiley, Chris Cooper, David George

RADx: Unexpected Opportunity

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

NIH Office of the Director


Francis Collins


Rachael Fleurance


Larry Tabak


Tara Schwetz

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

April 29

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

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

>12 NIH Institutes, Centers, and Offices


Jill Heemskerk.


Bruce Tromberg

National Institute of Biomedical Imaging and Bioengineering (NIBIB)

$307 M Partnership

OASH

https://www.nih.gov/research-training/medical-research-initiatives/radx

RADx: Leverage Existing Network (POCTRN)

NIBIB Point of Care Tech Network: NHLBI, NIAID, NCCIH, FIC, OBSSR, OAR, ODP

Established 2007, Expanded 2020: >900 RADx experts & contributors
(USG, Academia, Industry, NFP)

https://www.poctrn.org


Todd Merchak


Tiffany Lash

Operations:

- Review & Fund
- Test & Validate
- Expert Guidance

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/Commer-cialization

C BIO M C3i

Validation Core

>70 projects complete, >3000 participants

Clinical Studies Core

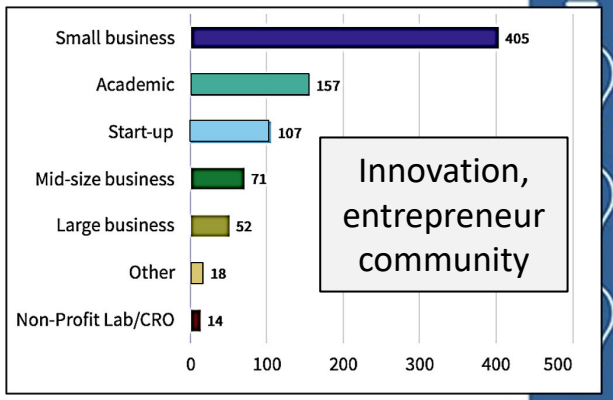
Standard Trial Design, Digital Health Platform, Single IRB, Center Network

Deployment Core

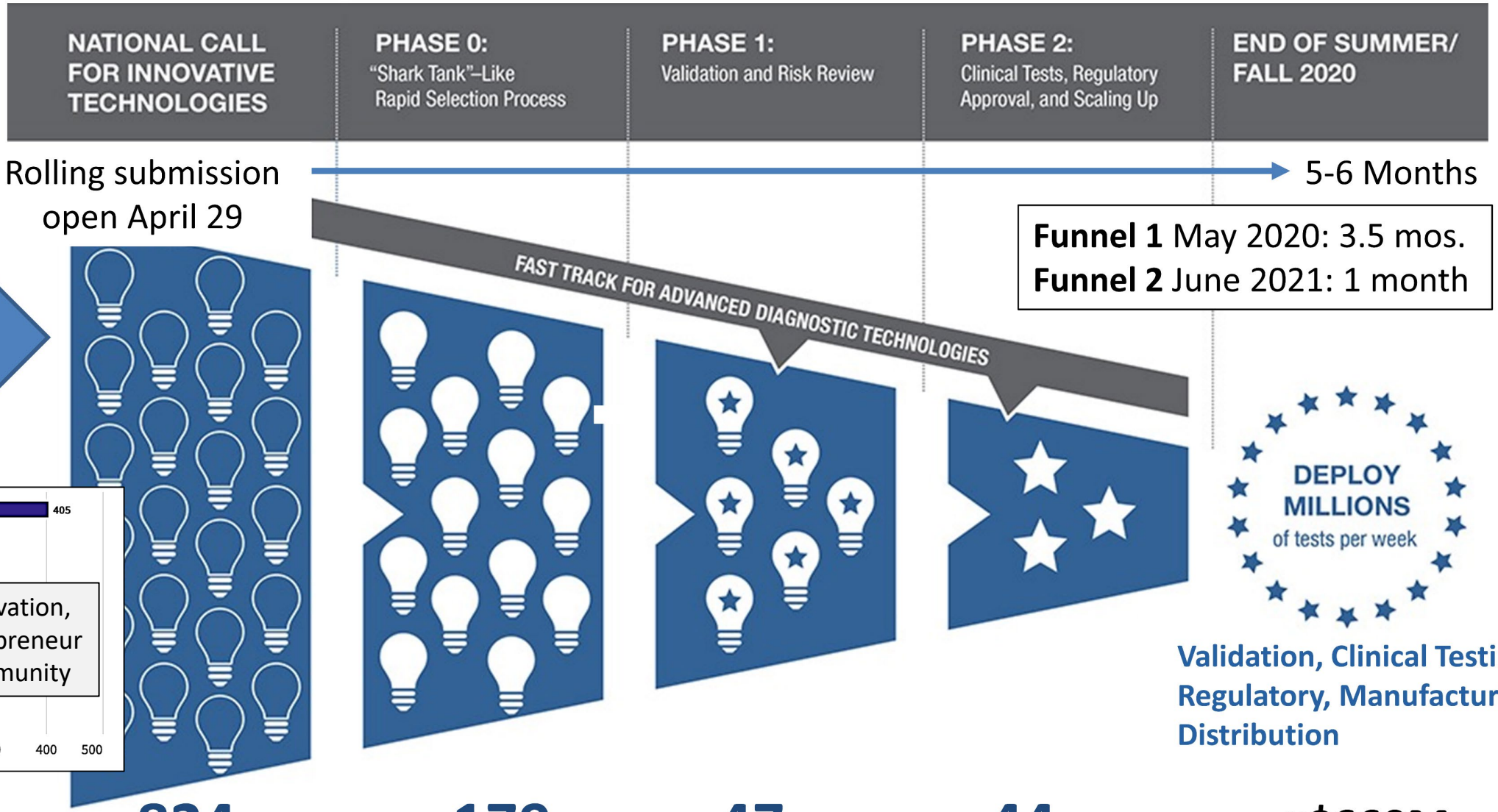
Supply chain, Manufacturing, User Community, *whentotest.org* ASU testing common Project N95

RADx Tech Process: Innovation Funnel

~3000
Applications Started



Innovation, entrepreneur community



Rolling submission open April 29

5-6 Months

Funnel 1 May 2020: 3.5 mos.
Funnel 2 June 2021: 1 month

Projects in each Phase

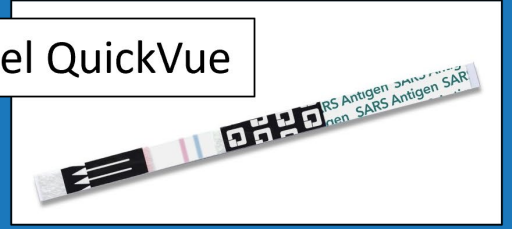
824 **179** **47** **44**

Validation, Clinical Testing, Regulatory, Manufacturing, Distribution

~$660M

Mesa BioTech

Quidel QuickVue



Quidel Sophia

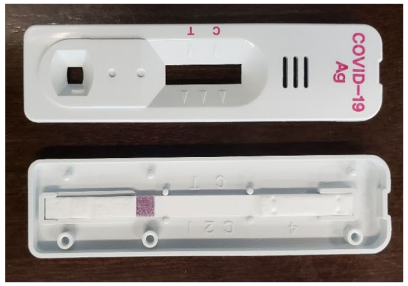
Meridian

Genbody

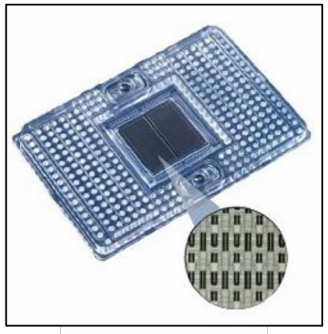
Visby Medical

Quanterix Simoa

Ellume



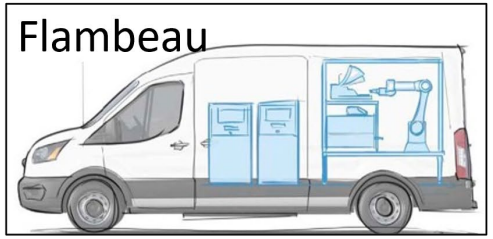
ANP



Fluidigm

Luminostics

Flambeau



Point of Care & Home	
Visby	RTPCR
Mesa	RTPCR
MicroGem	RTPCR
Talis	RT-LAMP
Ubiquitome	RTPCR
Meridian	RTPCR
GenBody	An-LFA
Quidel Sophia	An-LFA
Quidel QuickView	An-LFA
Luminostics	An-LFA
ANP	An-LFA
Ellume	An-LFA
Xtrava	An-LFA
Qorvo	An-BAW
Mologic	An-LFA
Maxim	An-LFA
Salignostics	An-LFA
ANP	An-LFA
BD Veritor	An-LFA
Princeton Biomeditech	AN-LFA
Palogen	ASIC-nanopore
Detect	RT-LAMP
Uh-Oh Labs	RT-LAMP
Lumira Dx	An-µfluidic
Anavasi	RT-LAMP
Laboratory, Tech	
Flambeau (+Saliva Direct)	PCR-mobile-lab
MatMaCorp	RTPCR-mini-lab
Fluidigm	RTPCR
Quanterix	SIMOA (An)
Minute Molecular	RTPCR
PathogenDx	RTPCR
Laboratory, Labs	
Broad Inst	RTPCR
Illumina	NGS
Helix	NGS/RTPCR
Gingko	NGS/RTPCR
Sonic Healthcare	RTPCR
PathGroup	RTPCR
Aegis	RTPCR
Octant/UCLA	NGS/RTPCR
Lab Products	
Mammoth Biosci	CRISPR
Ceres Nanosciences	Beads/Conc
Oasis	Saliva Collect
Yukon	Swabs

Home OTC

Home OTC

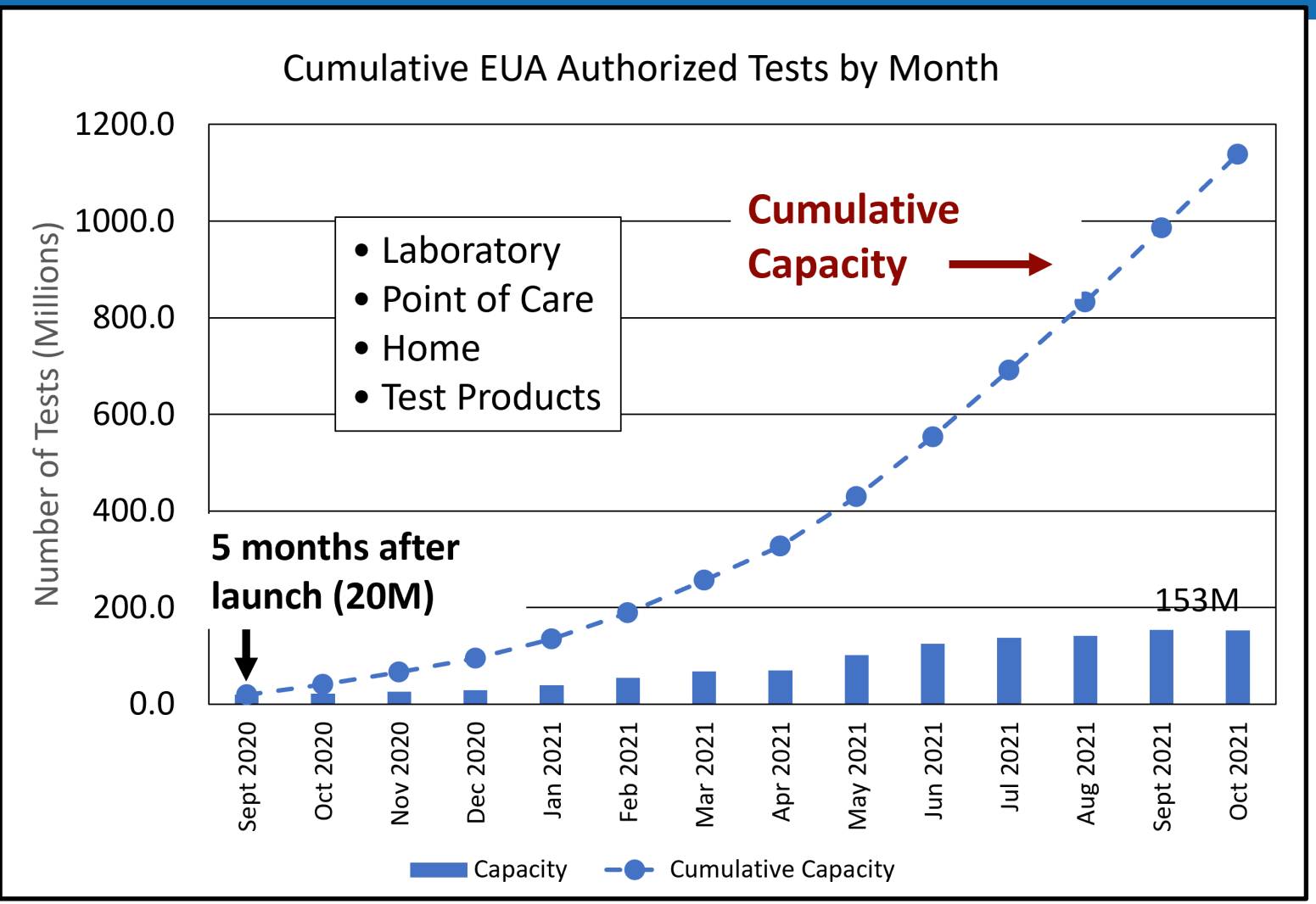
Home OTC

Home OTC

Tech

Labs

RADx Tech Impact: Capacity thru October 2021



Major Milestones

- **1.14 billion capacity thru October 2021**
- ~5.1 M tests and products/day **October 2021**
- 35 EUAs; 1st OTC EUA, 4 "at home"

~$1.1 Billion: *Special Congress Authorization* (~$600M in Phase 2)

~1.3 Billion: *Private Capital Raised*

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

Impact: *National Policy*

The Washington Post
Democracy Dies in Darkness

September 11, 2021

Health

How at-home coronavirus testing is becoming part of Biden's plan for managing the pandemic

A Pitt County Health Department worker passes out at-home coronavirus test kits April 21 in Greenville, N.C. (Melissa Sue Gerrits for The Washington Post)

By Derek Hawkins and Fenit Nirappil 395

RADx tests
SYCT program

Work (OSHA): vaccine, weekly testing
Entertainment: show negative test
School: regular testing
Procurement: $3B OTC/POC tests, DPA
Retailers: sell OTC at cost, Medicaid reimbursement
Community: distribute OTC to high SVI regions
Pharmacy: Expand free POC access

September 9. 2021

When To Test https://whentotest.org

SAY YES! COVID TEST KEEP OUR COMMUNITIES SAFE https://sayyescovidtest.org

RADx Impact: *whentotest.org*

When To Test

CALCULATOR FOR INDIVIDUALS | CALCULATOR FOR ORGANIZATIONS | RESOURCES | ABOUT | CONNECT | NEWSROOM

STOP THE SPREAD OF COVID-19

FOR INDIVIDUALS

> START CALCULATOR

Don't spread COVID-19 in your community!
The When To Test Calculator for Individuals helps you decide whether you should consider getting tested.

CIMIT® Consortia for Improving Medicine with Innovation & Technology

DataRobot

FOR ORGANIZATIONS

> START CALCULATOR

CDC guidelines provide a COVID-19 testing approach that applies to the population nationwide. The When To Test Calculator is designed to offer a more granular testing strategy for individual organizations based upon their unique mitigation strategies, level of compliance, and community prevalence.

CIMIT® Consortia for Improving Medicine with Innovation & Technology

IDSS MIT INSTITUTE FOR DATA, SYSTEMS, AND SOCIETY

> PROJECT N95 FIND TRUSTED TESTING SUPPLIES

> CONNECT TO TEST ASU COMPARE COVID-19 TEST BRANDS

SCHOOL LEADERS

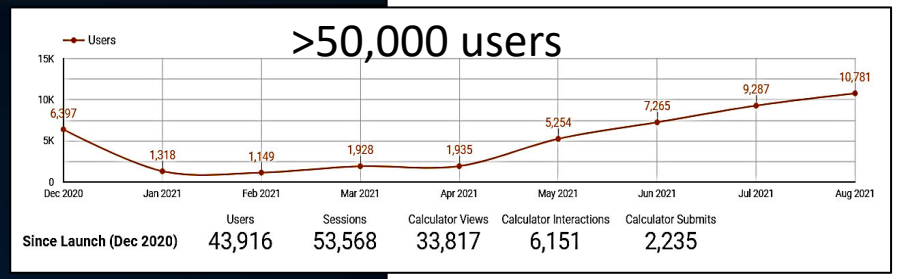
> DOWNLOAD OUR K-12 PLAYBOOK

TESTING IMPLEMENTATION

> DOWNLOAD OUR COMPREHENSIVE GUIDE

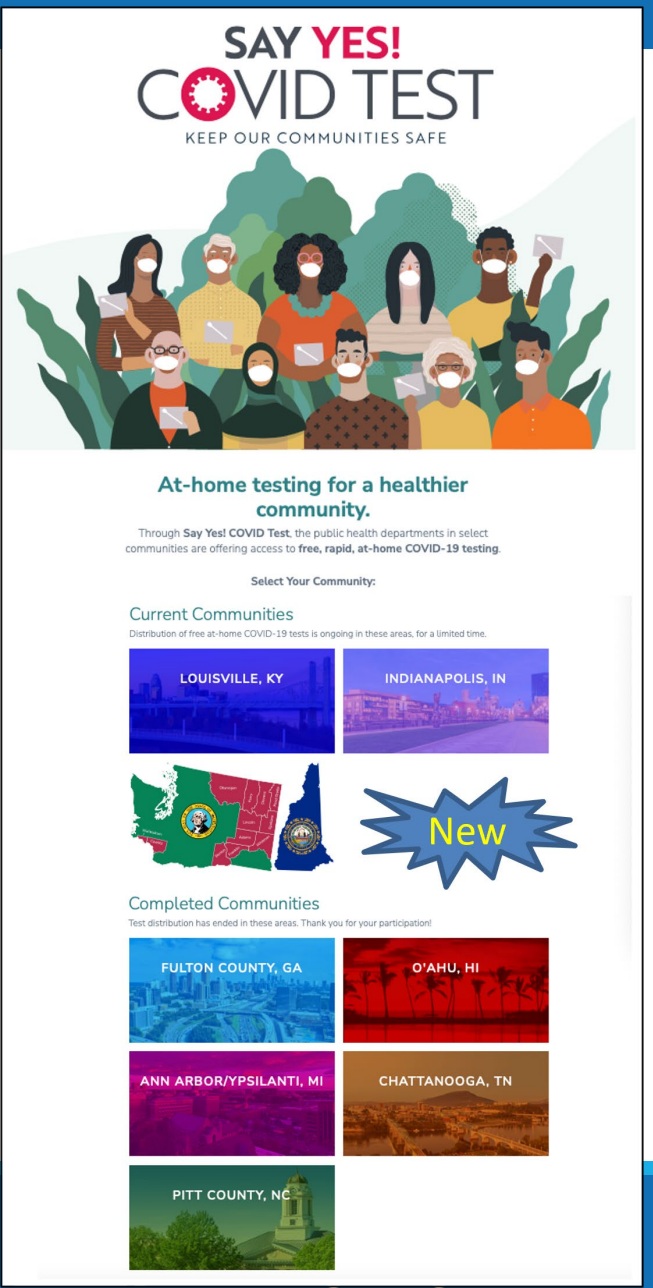
LAB POOL TESTING

> DOWNLOAD OUR LAB POOL PLAYBOOK



- **Vaccination rates**
- **R0 altered for Delta**
- **Pooling guidance**
- **K-12 playbook (CDC)**
- **Individual risk calculator**
- **Link purchase, guidance**

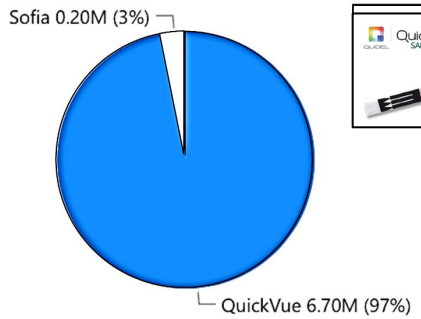
RADx Tech Impact: sayyescovidtest.org



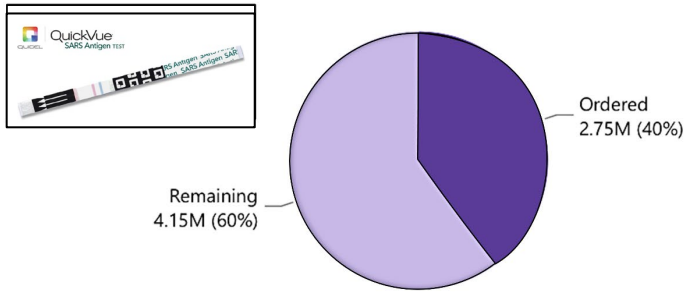
This report reflects tests purchased directly by NIH to support specified projects. Tests purchased separately by awardees are not shown.

6.9M Tests purchased	
2.7M Ordered	4.2M Remaining

Tests Purchased



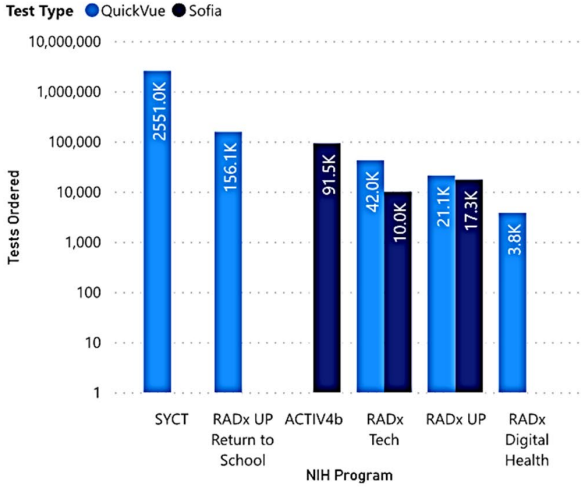
Tests ordered and remaining



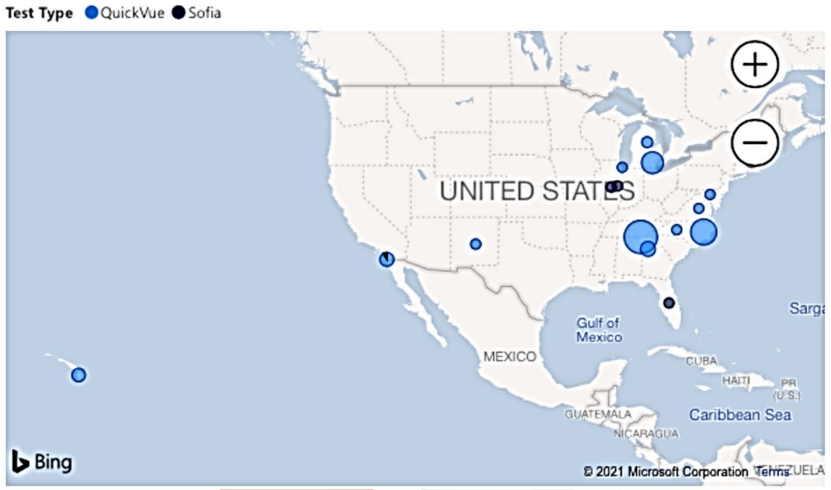
Remaining = Purchased - Ordered

Awardee
Activ Public / Private Partnership
Duke University
Johns Hopkins University
Public Health Intervention
Rush University
San Diego State University
U Massachusettes
UIUC
University of Chicago
University of Hawaii
University of New Mexico
Vibrent Health

Tests Ordered by NIH Program and Test Type



Program locations



NIH National Institutes of Health — Turning Discovery Into Health

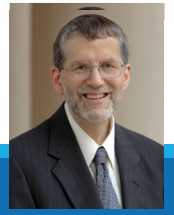
CDC Centers for Disease Control and Prevention

Duke Clinical Research Institute

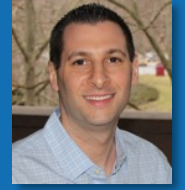
UNC School of Medicine — Center for Health Equity Research


Rachael Fleurence


Bill Riley

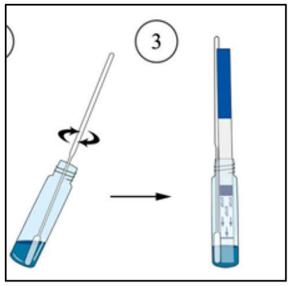

Mike Lauer

RADx Tech Impact: *Digital Health*



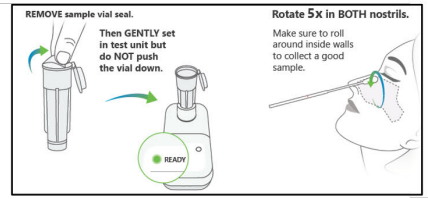

Andrew Weitz Krishna Juluru

RADx POC Test

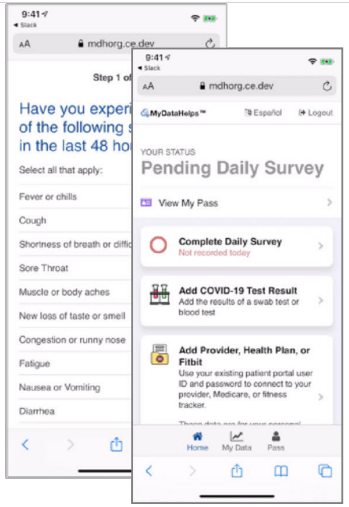


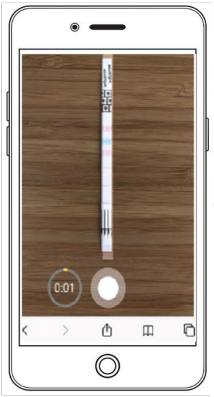
LFA

How to Use



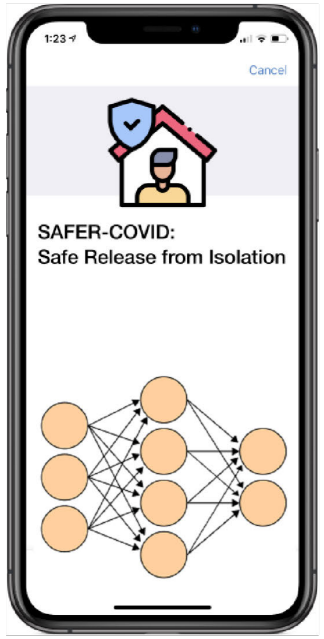
Symptom Surveys





Cell Phone Reader

careevolution HEALTHCARE TECHNOLOGY



EHR & Claims

SYNC FOR SCIENCE

HL7 FHIR

Blue Button Download My Data

Need Standards

Need Standards

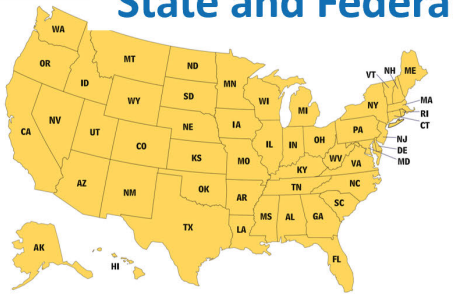
HealthIT.gov

APHL

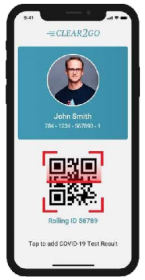
FDA

CDC Centers for Disease Control and Prevention

State and Federal



Contract Tracing



e.g. VCI

Health status

RADx Variant Task Force (est Jan 2021)

1) Impact of Variants on Test Performance (NAT, An)
2) Design tests for variant surveillance (e.g. “SNP chips”)

RADx Team

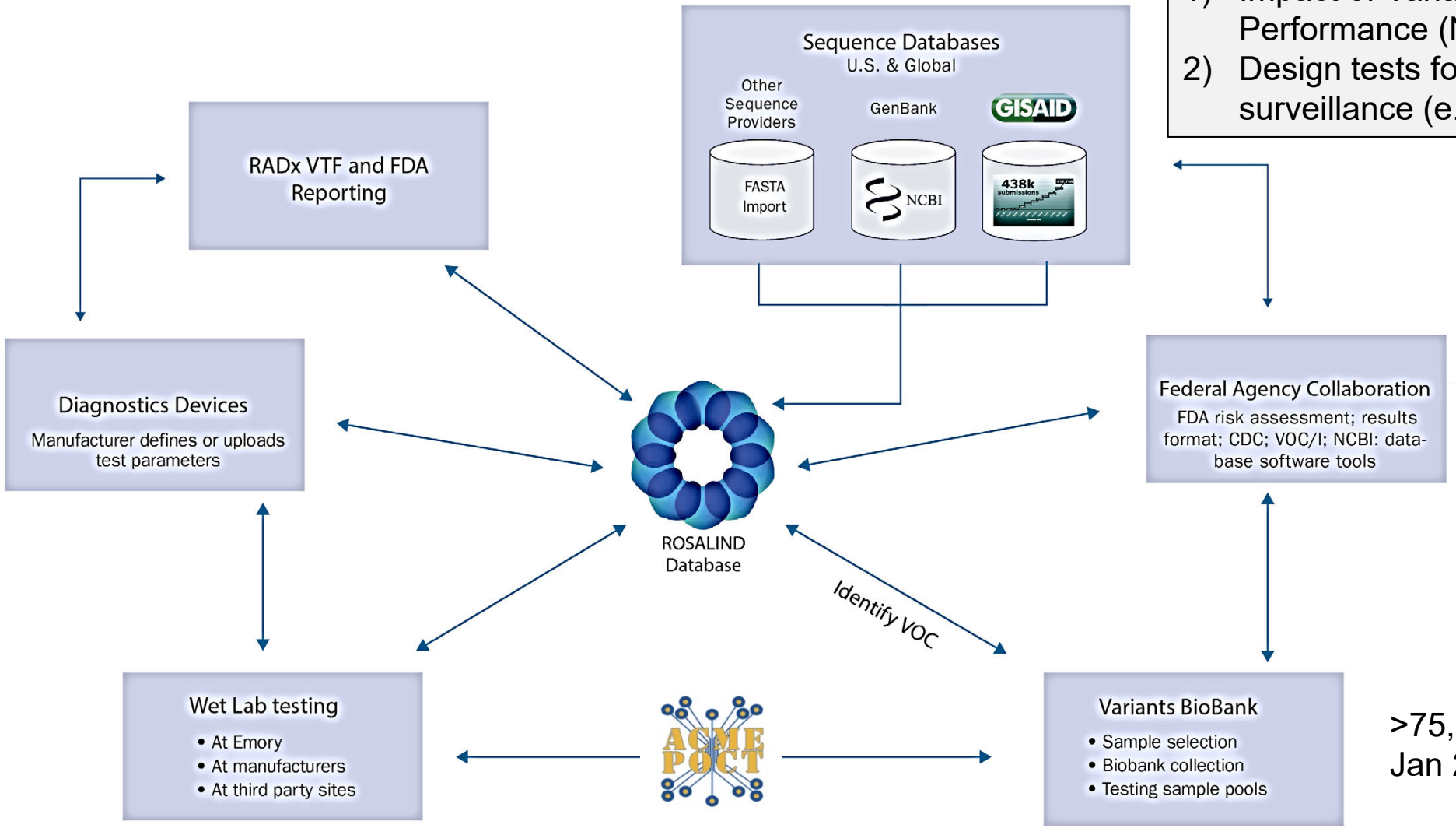
Richard Creager
Eric Lai
John Blackwood
Mia Cirrincione
Dale Gort
Emily Kennedy
D’lynne Plummer
Thomas Pribyl
Adam Samuta
Megan Shaw
Brian Walsh

Emory

Leda Bassit
Filipp Frank
Morgan Greanleaf
Wilbur Lam
Cangyuan Li
Eric Ortlund
Anuradha Rao
Raymond Schinazi
Allie Suessmith
Julie Sullivan
Thomas Vanderford

Univ of WA

Alex Greninger



NIH FDA CDC BARDA NCBI

>75,000 samples
Jan 2021-present

RADx Variant Surveillance: "SNP Chip"

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Julie Sullivan
Thomas Vanderford

Univ of WA
Alex Greninger

"Project Rosa"

ROSALIND GISAID NCBI

Helix, Thermo-Fisher, CDC

Design tests for variant surveillance (e.g. "SNP chips")

16 Markers:

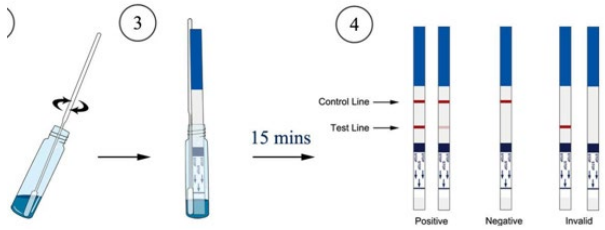
1) *Positivity of sample*
2) *Lineage (>95% sens and spec all WHO variants* ***+ Omicron****)*
3) *Mutations* of biological interest

Genotyping Validation (TaqMan, TF), 10k sample study, 4 weeks → ***Submit FDA EUA w/partner***

"SNP Chip" Advantages

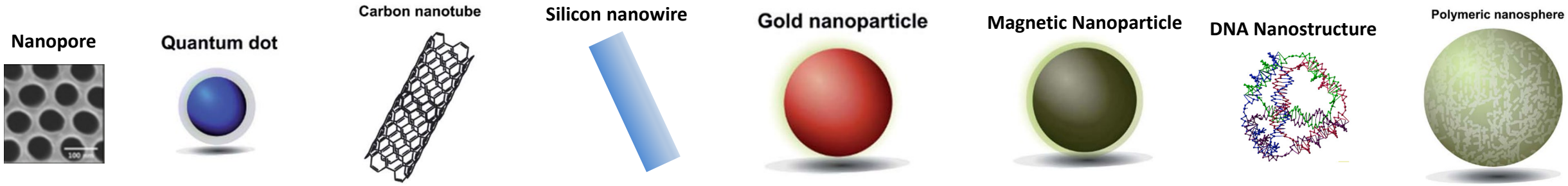
Speed: no reflex, "real time" 1000s/day vs NGS ~4 weeks
Cost: CapX and price/test << NGS
Access: Adaptable to most labs: >50% vs 5% current NGS
Modify: New variant integration ~4-6 weeks

RADx Tech Future Directions

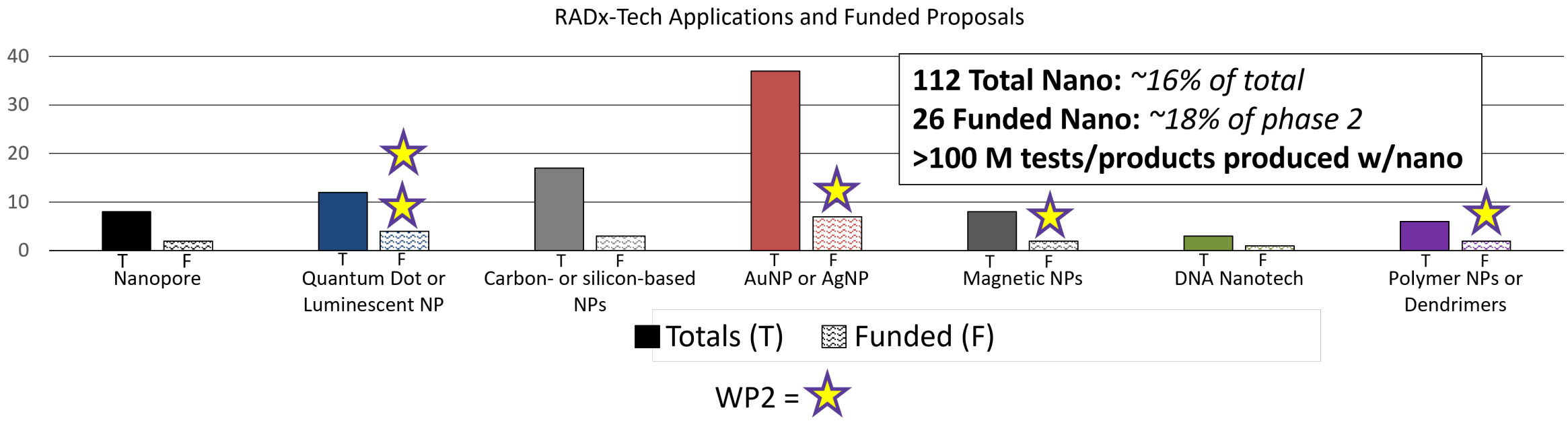
	Lab RTPCR	POC RTPCR	POC An (LFA/reader)		POC An (LFA/visual)
					
	ABL 7500	Mesa BioTech	Quidel Sophia	Ellume	Dipstick LFA
Cost	$$$$	$$$	$$	$$	$
Speed	Hours	~30 min	<15 min	→	→
Sens/Spec	>90/95	>90/95	>90/95	→	→
LOD	$<10^3$ Cp/mL	$<10^3$ Cp/mL	$<10^6$ Cp/mL	→	→

Tech to Bridge the Gap?

New Tech: *Nano in RADx*

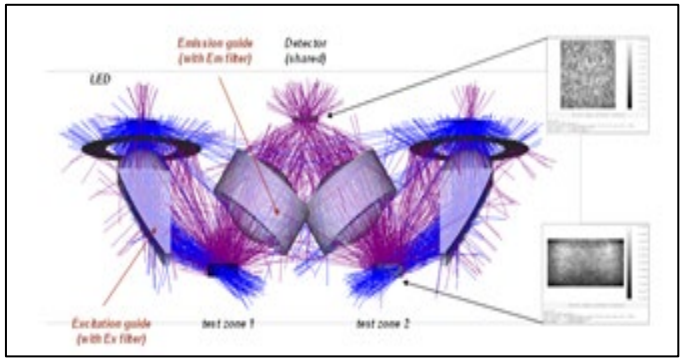


Images from Chudasama et al., *Chemical Science* 2016, Lim et al., *Nanoscale* 2015, Wikipedia

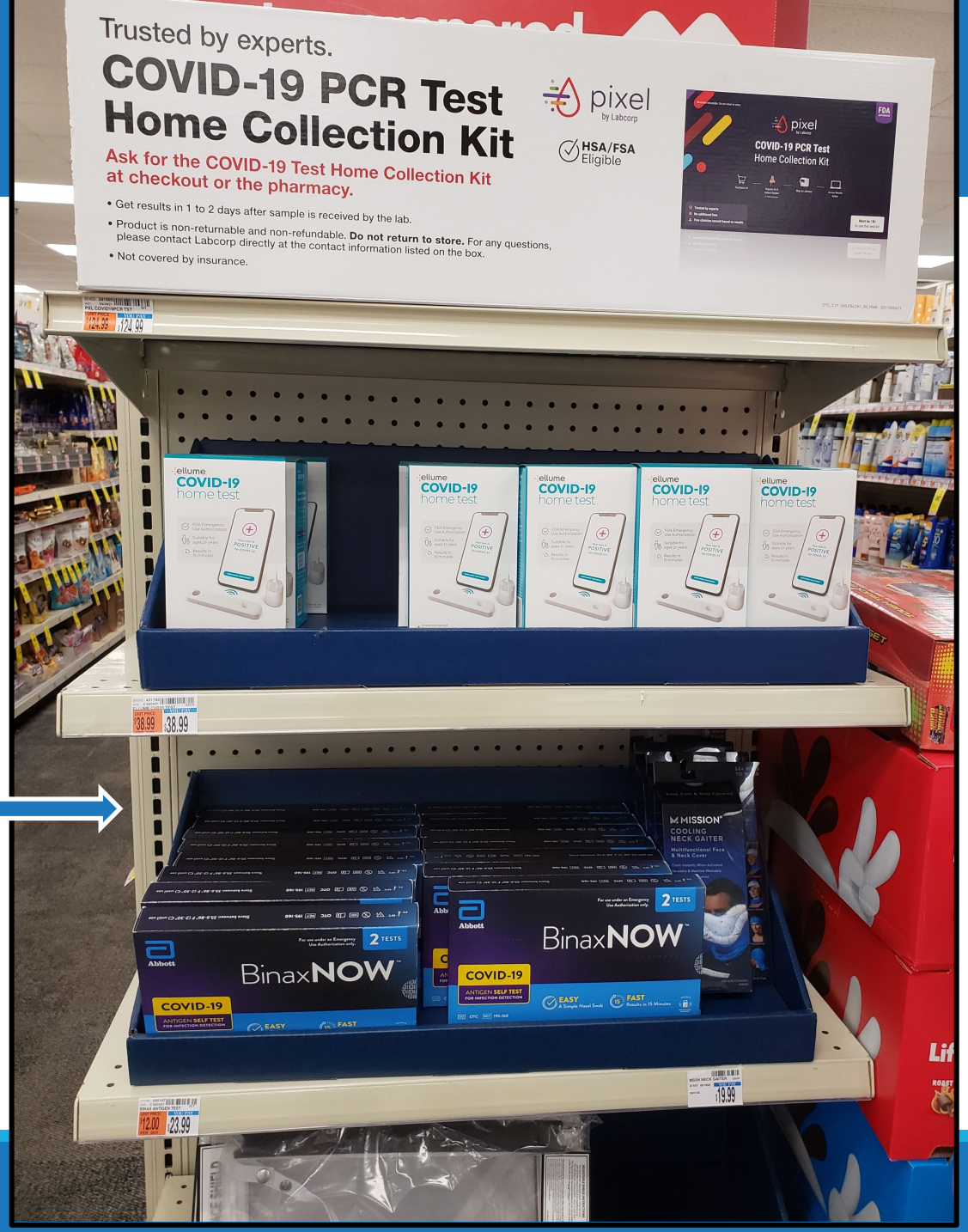


NanoScience in RADx

ellume

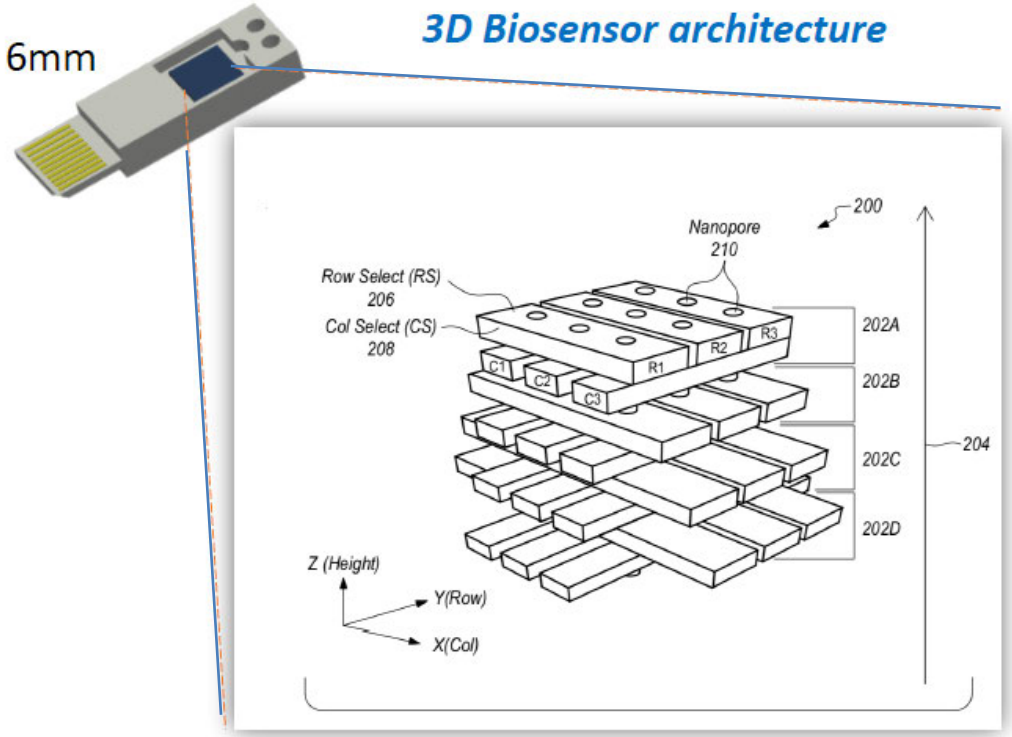


Quantum Dots on the shelves at CVS!



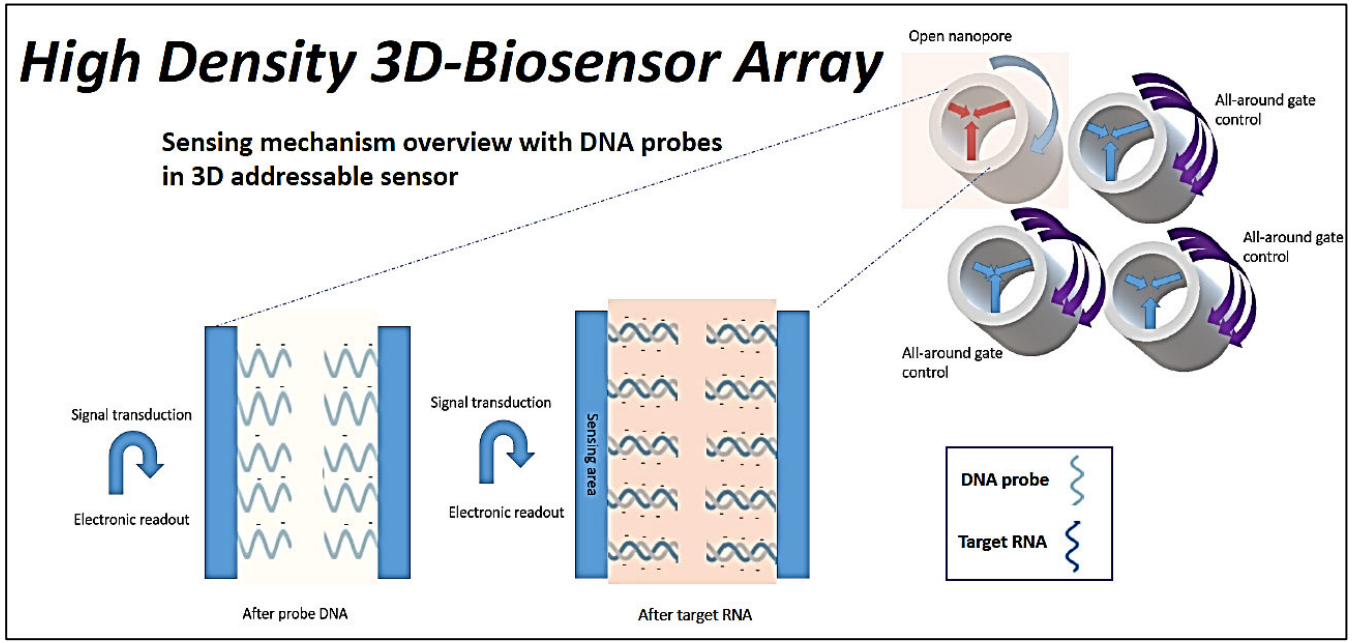
Pre-Commercial: *Palogen*

3D Nano-electronic Biosensor



3D Flash Memory (V-NAND)

DNA Probes, Parallel Nucleic Acid Detection



Ongoing Challenges

1) Reporting infrastructure

POLITICO

Inside America's Covid-reporting breakdown

Crashing computers, 3-week delays tracking infections, lab results delivered by snail mail: State officials detail a vast failure to identify hotspots quickly enough to prevent outbreaks

By ERIN BANCO
08/15/2021 07:00 AM EDT

Illustrations by Glenn Harvey

There were too many cases to count.

Covid-19 was spreading rapidly throughout the United States, as cold winter weather began to drive people indoors, but the Centers for Disease Control and Prevention was flying blind: The state agencies that it relied on

2) Insufficient screening, surveillance

Nearly 5 out of 6 coronavirus cases were undetected in pandemic's early months

LA Times, June 25, 2021

Months into the pandemic, the U.S. had six times as many cases as reported, an N.I.H. study finds.

New York Times, June 24, 2021

Nearly 17M Americans May Have Went Undiagnosed With COVID Last Year: Why These Cases Matter

International Business Times, June 24, 2021

K. Sadtler et al. Sci. Transl. Med, June 22, 2021

Ongoing Challenges, continued

3) Paradigm Shift

POC, OTC >> Lab

April 2020 ~5M tests → October 2021 **~240M tests** → December 2021 **>400M tests**

Lab >> POC

Minimal POC/OTC reporting
4X increase OTC tests Sept - Dec

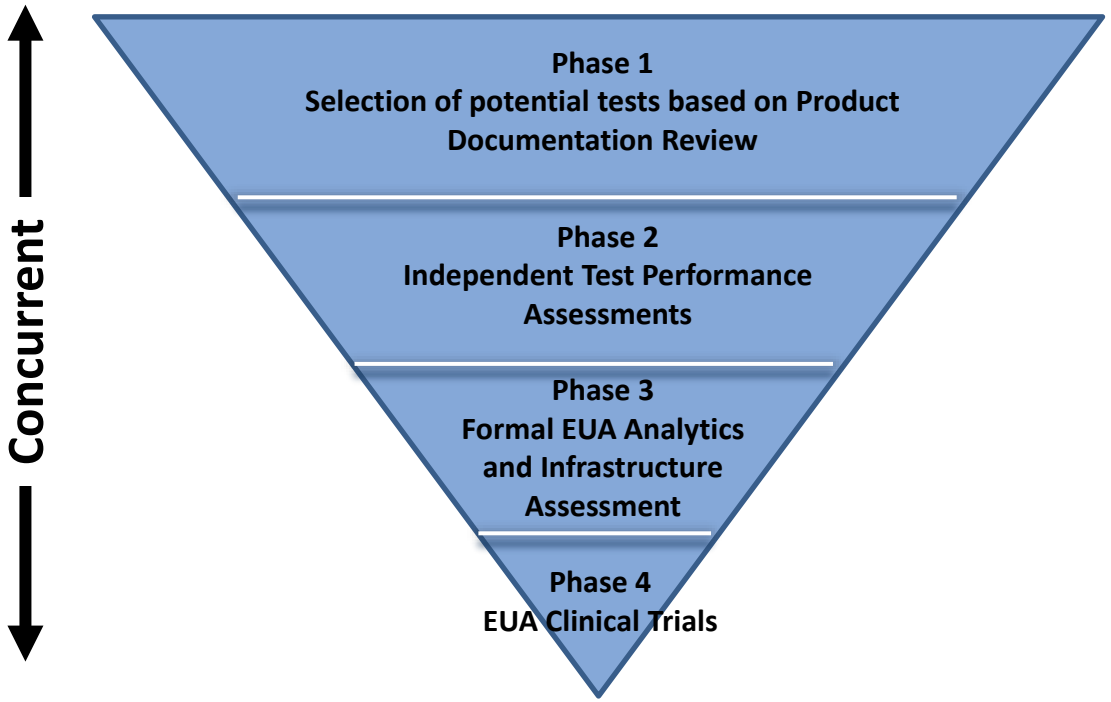
Impact: ***Guidance and policy decisions made based on lagging and incomplete test data***

Ongoing Challenges - 3

4) Cost of Rapid OTC Tests: *demand >> supply*

Independent Test Assessment Program (ITAP)

NIH-FDA: *Accelerating OTC Authorizations*



Goal

Add ~100M OTC tests/month to US in ~3 months

- Eligible companies invited to participate (Ex US and US); high volume potential
- Initial deep dive leads to detailed assessment and custom work plan
- Rapid decision to approve/reject; fund next level ITAP studies, review
- ITAP data + other info analyzed in "real time" with feedback as needed
- Completed work plan serves as EUA application for FDA review
- 10 tests in ITAP program, >250M tests/month potential

Ongoing Challenges - 4

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editorial

Radical solutions

The US RADx program has spawned a phalanx of diagnostic products to market in just 12 months. Its long-term impact on point-of-care, at-home and population testing may be even more profound.

Over the past year, the US National Institutes of Health (NIH) Rapid Acceleration of Diagnostics (RADx) program has invested hundreds of millions of dollars into the development of new

devices, loop-mediated amplification tests, paper-based diagnostics, rapid lateral flow assay (LFA) antigen tests, smartphone readers, next-generation sequencing (NGS) and machine-learning-assisted diagnostics—in a matter of months. This combination of RADx technologies, together with structural changes to healthcare during the pandemic, has the potential to radically change diagnostics, opening up the point-of-care (POC), at-home and community testing settings.

RADx was established by the NIH at the end of April 2020 as part of $1.5 billion appropriated for SARS-CoV-2 testing by US Congress in the Paycheck Protection Program and Health Care Enhancement Act. The US National Institute of Biomedical Imaging and Bioengineering established programs to build testing capacity for school and university reopening (RADx Tech and RADx ATP), galvanize innovative diagnostic and surveillance development (RADx-rad) and jump-start efforts to reach vulnerable and underserved populations (RADx-UP). By matching developers with experts from a pool of ~600 academicians, entrepreneurs and regulators, RADx aims to not only galvanize simultaneous development of assay and devices, but also parallelize performance assessment, regulatory interactions, manufacturing capacity and supply-chain logistics to compress into a single year what is typically a five-year product development cycle.

To date, RADx has awarded a total of $520 million in 27 contracts (whittled down from a starting set of 716 applications)—complementing another ~$157 million in funding from the Biomedical Advanced Research and Development Authority.

is being made available for testing, contact tracing, surveillance and containment in the coming year.

These are eye-popping numbers, especially when one considers that the entire global

investments can effect lasting change.

In certain clinical settings, RADx technology promises to change medical practice. For example, as COVID-19 becomes endemic, handheld devices developed by Mesa Biotech or Mammoth Biosciences could speed patient triage in emergency rooms, enabling rapid distinction among viruses causing respiratory infections, such as SARS-CoV-2, influenza A or B, and respiratory syncytial virus. Similarly, greater uptake of molecular tests in clinical microbiology can supersede culturing approaches carried over from the nineteenth century, returning lab results in minutes or hours rather than days.

But it is the $29.5 billion POC market (using trained personnel in physician offices and pop-up labs) and the massively under-penetrated at-home direct-to-consumer (DTC) market that seem likely to see the most change.

The RADx program is supporting numerous POC applications, including 14 PCR tests and 7 LFA antigen tests. The use of artificial intelligence for pattern recognition of test readouts and to support non-experienced technicians in areas like ultrasound will also broaden market opportunities. Similarly, Medicare reimbursement for COVID-19 testing will drive test uptake, even if private payer coverage remains variable.

Post-pandemic, increasing use of telehealth and remote care is likely to further drive diagnostics into community or home settings. In December, RADx awardee Ellume's multiplex quantum dot fluorescence test and smartphone app received Emergency Use Authorization (EUA) for home use. The

digital medicine increasingly intersects with diagnostics. Last month, another EUA was given to a Cue Health home test kit with a reusable cartridge reader and app, opening the door to repeat home testing.

more people in remote settings lacking clinical infrastructure—although the digital divide remains a concern.

A final area where RADx has targeted funding is the use of NGS platforms as an early warning system for potential outbreaks. Surveillance can be used for spot sampling of surfaces, air, urban wastewater and long-haul flight waste. The use of sample pooling is likely to prove extremely useful in opening schools and screening employees. It will also galvanize testing for SARS-CoV-2 variants circulating in the population and enable test, trace and isolate efforts during community transmission.

These trends lead to an unexpected collision of previously disparate diagnostic realms. NGS already has a foothold in clinical settings, steering therapeutic interventions via multiplexed assays for cancer, infectious agents, antimicrobial resistance genes and microbiome profiling. If the slew of funding for surveillance bears fruit outside COVID-19, the divisions between public health surveillance and individual-patient-oriented clinical diagnostics may start to blur.

Overall, RADx has both radically shifted the funding available for innovative diagnostics and greatly foreshortened product development times. But it will all be for naught if the current outmoded one-test, one-person paradigm isn't exchanged for a robust infrastructure and rational reimbursement system that actually empowers community testing and diagnostic-led medicine. For too long, we have talked the talk of precision medicine. Now is the time to walk the walk.

Call to action…

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Summary

RADx investment: ***accelerated decades of in vitro diagnostic tech for COVID***

- **Better, accessible fast tests:** Inexpensive OTC/POC; some w/ laboratory test performance
- **Multiplex tests:** COVID, flu A/B, RSV, etc. for differential Dx *(POC, lab)*
- **Fast, accurate, cost-effective surveillance:** Genotyping w/Informatics, *(lab, POC)*
- **Real Time Reporting:** Modernize, expand digital health networks and communication/reporting
- **Low Cost OTC**: Increase supply, automation, distribution channels

Future: *Leverage RADx process, tech, and networks for other pathogens, preparedness, precision medicine*