

# Serological Sciences Network SeroNet (SeroNet): Serology Lab Effort Updates

**Ligia Pinto, PhD**

*Director, Vaccine, Immunity and Cancer Directorate*

**Frederick National Laboratory  
Advisory Committee Meeting  
July 10, 2024**



**Frederick National Laboratory  
for Cancer Research**

# Vaccine, Immunity and Cancer Directorate (VICD): Who We Are



## Science and Technology Group

Leonard Freedman, PhD



## Vaccine, Immunity and Cancer Directorate (VICD)

Ligia Pinto, PhD, Director



## Administration and Finance

Bo Park, Director

## HPV Serology Laboratory (2001)

Troy Kemp, PhD

*NCI/BMGF-sponsored (cCRADAs: Univ. of London, PATH)*



## Cancer Immunoprevention Laboratory (CIPL) (2015)

Jason Marshall, PhD

Yurong Song, PhD

*NCI/DCP-sponsored*



## SARS-CoV-2 Serological Sciences Network Initiative (2020)

Ligia Pinto, PhD

**COVID-19 Serology Lab**, Troy Kemp, PhD

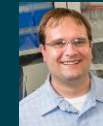
**Coordinating Center**

Nancy Roche, PhD

**Center of Excellence for Serology Development and Emergency Preparedness**

Bruce Brown, PhD

*NCI CSSI-sponsored (HHS)*



**Mission:** To provide scientific leadership and laboratory infrastructure to study **immune responses to Human Papillomavirus (HPV) and SARS-CoV-2 infection and vaccines** as well as other cancer preventive strategies in the context of clinical and pre-clinical studies



# VICD Main Efforts: What We Do

Investigate immune responses to vaccines, infections, and cancer

Develop and validate new methods for laboratory biomarkers of protection

Monitor immunity in clinical trials and pre-clinical studies

Provide evidence to inform new trials and create tools to enable decision-making and public health changes

Support for NCI Vaccine Trials and Epidemiological Studies  
NCI Costa Rica Vaccine Trials

Collaboration with the Extramural HPV Vaccine Community

cCRADAs: Moffitt Cancer Center, University of London, PATH

HPV Serology

HPV Serology International Standardization Initiative (Central Reference Lab)

Partners: BMGF, CDC, PHE, NIBSC, KI and WHO

World Health Organization (WHO) Reference Laboratory  
FDA Testing Laboratory





# The HPV Serology Laboratory – 2017 S NCI and The Bill & Melinda Gates Founda

PEARLS

The HPV Serology Laboratory leads an initiative to standardize and harmonize human papillomavirus serology assays

## Mission:

- To work in **partnership** with the **international** HPV serology community to **promote further standardization, harmonization and proficiency of HPV serology assays** to assess vaccine immunogenicity in vaccine trials through:
  - development of **qualified assay standards, critical reagents** (HPV Virus-Like Particles), **multiplex assays and guidelines**, available to the scientific community, as well as **high-throughput testing** in clinical trials

## Impact:

- Enable comparisons of data between different vaccines and studies
- Accelerate implementation of new vaccines and new vaccine recommendations



## Partners:

**Frederick National Laboratory:** Ligia Pinto, Troy Kemp  
**NCI:** Doug Lowy, John Schiller, Sean Hanlon  
**The Bill and Melinda Gates Foundation:** Peter Dull  
**CDC:** Elizabeth Unger  
**Public Health England:** Simon Beddows  
**Karolinska Institute:** Joakim Dillner  
**Biostat Consulting, LLC:** Brian Plikaytis  
**National Institutes of Biological Standards and Control (NIBSC):** Dianna Wilkinson

**Collaborators:** Academic Labs, Vaccine Industry Labs, National Institutes for Food and Drug Control (NIFDC), WHO

# Immunogenicity Testing at the FNL HPV Serology Lab: Completed and Ongoing One Dose HPV Vaccine Trials (100,000s tests)



Scientific Evaluation of One or Two Doses of the Bivalent or Nonavalent Prophylactic HPV Vaccines (ESCUDDO)

**Dr. Aimee Kreimer**  
NCI

**20,000**  
girls

**12-16**  
years old

**Costa Rica**



NCT03180034



Single-Dose HPV Vaccination for the Prevention of Cervical Cancer in Young Adult Women in Costa Rica, The PRISMA ESCUDDO Trial

**Dr. Aimee Kreimer**  
NCI

**5,000**  
women

**18-30**  
years old

**Costa Rica**



NCT05237947



Non-inferiority Trial Comparing Immunogenicity from 1 Dose of Bivalent HPV Vaccine in Girls to 3 Doses of Quadrivalent Vaccine in Women (PRIMAVERA)

**Dr. Aimee Kreimer**  
NCI

**620** **9-14**  
girls years old

**620** **18-25**  
women years old

**Costa Rica**



NCT03728881



Phase IIA Trial of a Nonavalent Prophylactic HPV Vaccine to Assess Immunogenicity of a Prime and Deferred-Booster Dosing Schedule among 9-11 Year-Old Girls and Boys (NCI)

**Dr. Yi Zeng**  
**Dr. Anna-Barbara Moscicki**

**Dr. Vikrant Sahasrabudhe**  
NCI

**200**  
boys & girls

**9-11**  
years old

**USA**



NCT02568566



A Dose Reduction Immunobridging and Safety Study of Two HPV Vaccines in Tanzanian Girls (DoRIS)

**Dr. Deborah Watson-Jones**  
University of London

**900**  
girls

**9-14**  
years old

**Tanzania**



NCT02834637



Kenya Single Dose HPV Vaccine Efficacy (KEN-SHE)

**Dr. Ruanne Barnabas**  
University of Washington

**2,250**  
women

**15-20**  
years old

**Kenya**



HPV One and Two Dose Population Effectiveness (HOPE) Study (WITS RHI)

**Dr. Sinead Delany-Moretlwe**  
University of the Witwatersrand

**4,807**  
girls

**17-18**  
years old

**South Africa**



NCT03675256



A Phase 3 Randomized, Active-Comparator Controlled, Open-Label Trial to Evaluate the Immunogenicity and Safety of Alternate Two-Dose Regimens of a Bivalent Human Papillomavirus (HPV) Vaccine (Cecolin®) Compared to a Licensed Quadrivalent HPV Vaccine (Gardasil®) in Healthy 9-14 Year-Old Girls in Low and Low-Middle Income Countries (PATH)

**Dr. Niranjana Bhat**  
PATH

**1,025**  
girls

**9-14**  
years old

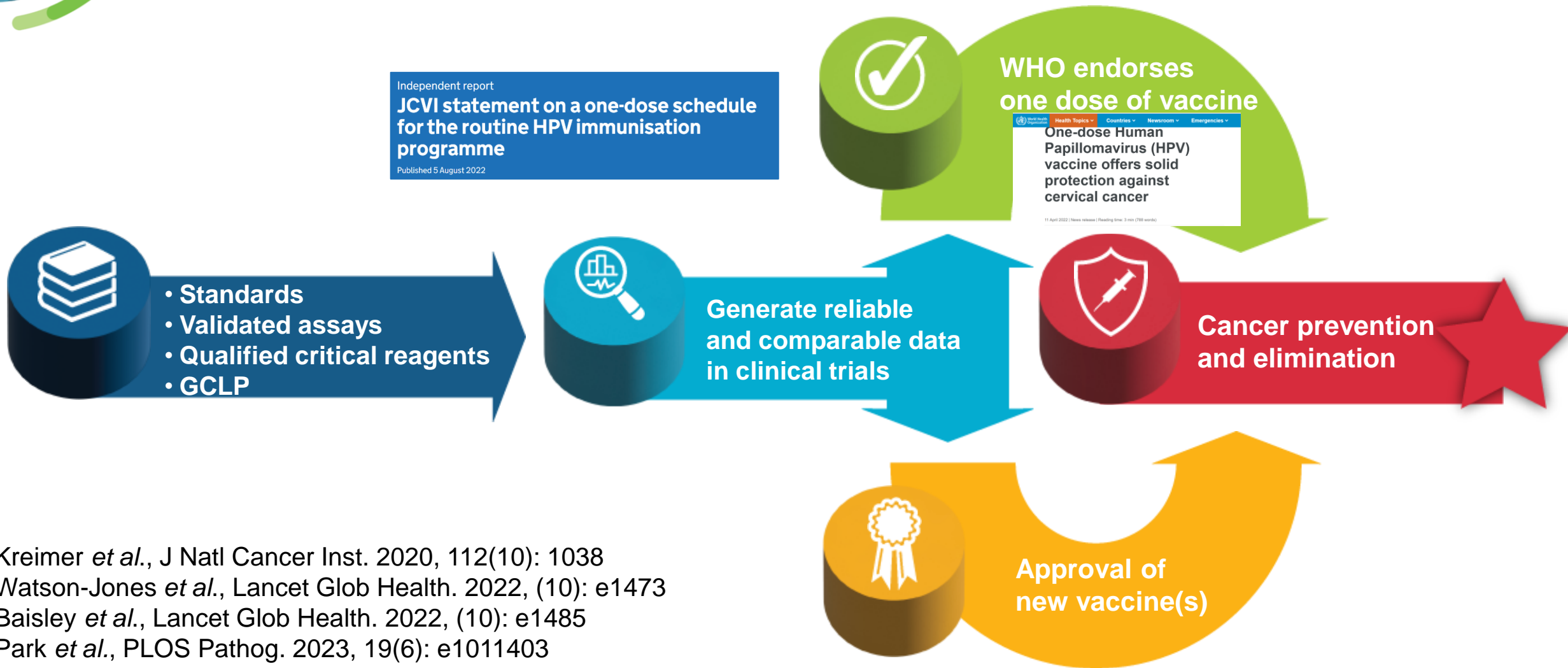
**Ghana and Bangladesh**



NCT04508309



# HPV Serology Standardization: Contributions to inform public health decisions



Kreimer *et al.*, J Natl Cancer Inst. 2020, 112(10): 1038  
Watson-Jones *et al.*, Lancet Glob Health. 2022, (10): e1473  
Baisley *et al.*, Lancet Glob Health. 2022, (10): e1485  
Park *et al.*, PLOS Pathog. 2023, 19(6): e1011403  
Zen *et al.*, Pediatrics. 2023,152(1): e2022060301  
Miller *et al.*, J Immunol Methods. 2023, 523: 113585

# From HPV to COVID-19: HPV Serology Laboratory was well positioned to respond to the COVID-19 pandemic in March 2020

## Initial Serology Lab involvement with SARS-CoV-2 serology

- HPV serology lab quickly pivoted to SARS-CoV-2 serology at the request of NCI (end of March 2020)
  - Expertise in HPV serology, immunology and production of standards in collaboration with NIBSC and WHO
- FDA asked us to help evaluate quality of emerging commercial serology devices submitted to FDA
  - Large collaborative effort involving NIAID, CDC, BARDA, NCI-designated cancer centers

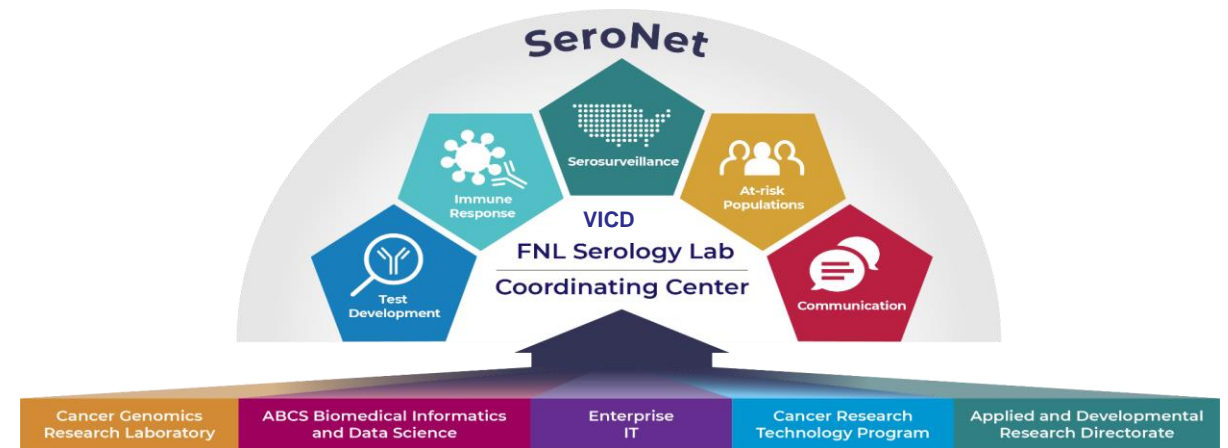


Pinto *et al.*, Microbiology Spectrum 2022;10(1):e0156421

<https://open.fda.gov/apis/device/covid19serology>

## Congressional funding for serology research

- Funding allowed NCI to support a wide range of SARS-CoV-2 serology activities, including the establishment of the Serological Sciences Network



From HPV to COVID-19 and beyond: leveraging the power of serology and standards

Hempel *et al.*, Lancet Microbe 2023; S2666-5247

# FNL Serology Laboratory Response to the COVID-19 Pandemic: Key contributions (Drs. Troy Kemp and Nancy Roche)

- Key role in **the independent evaluation program** for SARS-CoV-2 serology tests by FDA
  - Evaluated **> 115 commercial tests**
- Produced and distributed the **U.S. serology standard and validation panels** (> 185 requests)
- **Implemented and validated assays**
  - SARS-CoV-2 Spike and Nucleocapsid ELISA for different isotypes (IgM, IgG)
  - Luminex-based assay with 18 CoV Antigens, including VOC and common coronaviruses
  - Avidity for Spike IgG
  - Neutralization assays
- Investigated the immune response (**Ab levels and avidity**) to currently licensed vaccines (> 80,000 tests)
- Key role in establishing SeroNet and SeroNet Data Coordinating Center
  - **Management of Capacity Building Centers (CBC)** subcontracts (specimens and data)
  - **Data curation of SeroNet publications**, for public access, in ImmPort (413 publications)
- Established the NCI/FNL **Clinical and Translational Serology Task Force (CTTF)**

Pinto *et al.*, Microbiology Spectrum 2022,10(1):e0156421  
Kemp *et al.*, J Clin Microbiol . 2022, 60(11):e0099522  
Roy *et al.*, Microbiol Spectr. 2023, 11(2): e0389822  
Hickey *et al.*, Hum Vaccin Immunother. 2023, 19(2):2215677  
who-manual-secondary-standards-for-antibodiesv30012022.pdf  
Hempel *et al.* Lancet Microbe 2023, S2666-5247(23)00287-2  
Hempel *et al.* Lancet Microbe 2024, 5, e301-e305  
Bullock *et al.* Vaccines 2024,12, 516

***This effort marked the first time the federal government evaluated tests itself to inform FDA authorizations.***

Shuren and Stenzel, N Engl J Med 2021; 384:592

<https://open.fda.gov/apis/device/covid19serology>

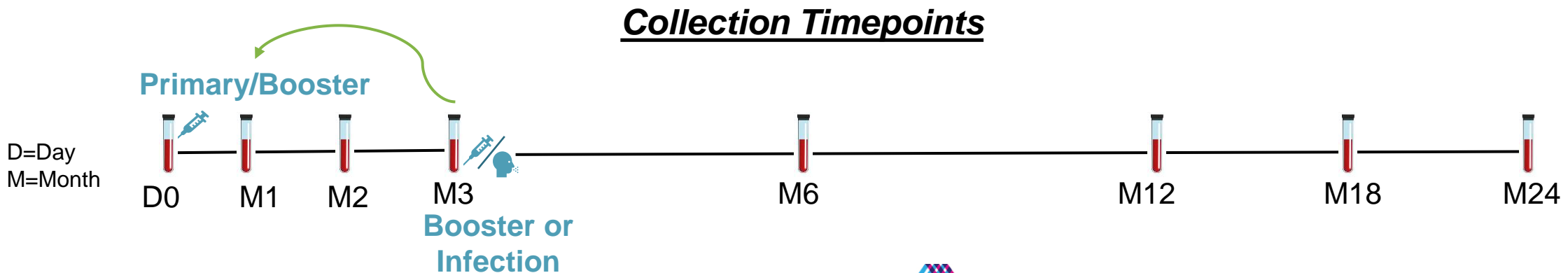




# Development of a Unique Repository of Specimens from Longitudinal Studies of Immune Responses to SARS-CoV-2 Vaccines and Infection

- **Studies harmonized across 4 CBCs (serum and PBMC collections)**
  - Same sample processing SOPs and data elements
- **Participant enrollment began in 2021**
- **Samples used by FNL Serology Laboratory and SeroNet**

Population	Enrolled Participants
Healthy	1502
Cancer	748
Autoimmune	489
Transplant Recipients	346
HIV	216



# SARS-CoV-2 Serology Activities Timeline: Power of Agility and Collaboration

*March 31, 2020 – April 15, 2020*

1

Assays materials received at FNL  
Started serology assay evaluation program with FDA

2

*April 8, 2020*

Implementation of ELISA at FNL

Mar 2020

Apr 2020

May 2020

Jun 2020

Jul 2020

Aug 2020

Sep 2020

Oct 2020

Nov 2020

Dec 2020

Jan 2021

3

*April 21, 2020*

Generation of first NCI/FDA evaluation panel

4

*April 24, 2020*

Paycheck Protection Program and Health Care Enhancement Act Passed

5

*June 5–6, 2020*

RFA/RFP published

6

*Late September 2020*

Grants and contracts awarded

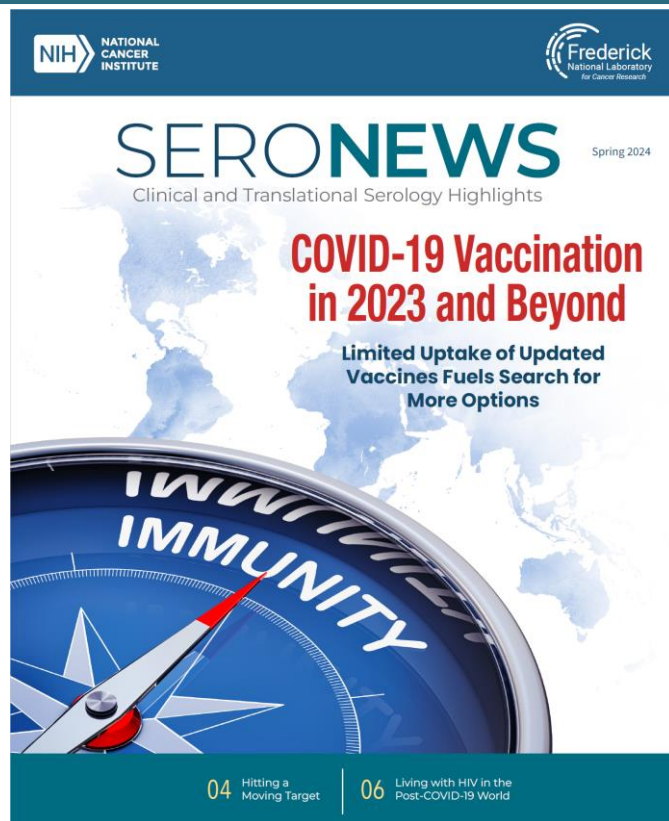
*December 2020 – January 2021*

U.S. SARS-CoV-2 Standard Available  
Assay Validation Panel Production  
Clinical and Translation Task Force

7



# Clinical and Translational Serology Task Force (CTTF): From Bench to Public Health



**Published 8 SeroNews issues distributed  
to >480 individuals/organizations**

**To catalyze translation of research findings into public health changes by bringing together and engaging various government organizations, academic groups, and industry partners to provide relevant tools and information related to serology testing to help decision makers manage the current and future status of the SARS-CoV-2 pandemic**

**Chairs: Ligia Pinto, PhD, Carlos Cordon-Cardo, MD, PhD  
Douglas Lowy, MD, Jim Cherry, PhD  
Editors: Sam Lopez and Heidi Hempel, PhD  
Project Manager: Marissa Blackburn**



**Organized >64 meetings and 1 Workshop (>180 speakers)**

<https://frederick.cancer.gov/initiatives/serological-sciences-network/seronews>





# Clinical and Translational Serology Task Force: Priorities and Outcomes

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- **Implement the U.S. SARS-CoV-2 standard** in serology testing to enable comparison of results between studies and vaccines
- **Assess the suitability** of available serology assays for clinical use in infected and vaccinated individuals
  - Through a **collaborative study** to compare 27 different assays from 17 different labs (Kemp *et al.*, Microbiology Spectrum 2023)
- Work closely with CDC, FDA and others **to enable development of guidelines and recommendations** for antibody testing
  - **Real World Data Infrastructure** was developed to evaluate vaccine effectiveness in immunocompromised individuals (<https://seer.cancer.gov/data-software/crwdi/>)
  - **Center of Excellence** for agile sample acquisition, as well as high quality serology and other immunological testing



# Center of Excellence for Serology Development and Emergency Preparedness (CESDEP) (Drs. Bruce Brown and Nancy Roche)

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## VISION

To leverage capabilities and the power of serology to control current and future outbreaks

## MISSION

To address critical gaps in standardization, development and validation of assays to monitor and understand immune responses to infection and vaccination to serve the public health needs of healthy individuals and people with cancer

## APPROACH

### Collaborations:

National Cancer Institute (NCI)  
Centers for Disease Control and Prevention (CDC)  
Food and Drug Administration (FDA)  
Biomedical Advanced Research and Development Authority (BARDA)  
National Institute of Allergy and Infectious Disease (NIAID)  
National Institutes for Biological Standards and Control (NIBSC)  
World Health Organization (WHO)  
Clinical centers for blood collections and testing centers (via subcontracts)  
Across FNLCR directorates

Funded by HHS in response to a proposal to address existing gaps



# Why CESDEP? To address critical gaps preventing rapid scientific response

## Critical Gaps

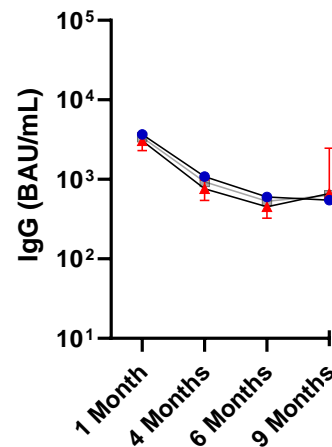
Lack of available samples for assay development



Lack of standards and standardized testing



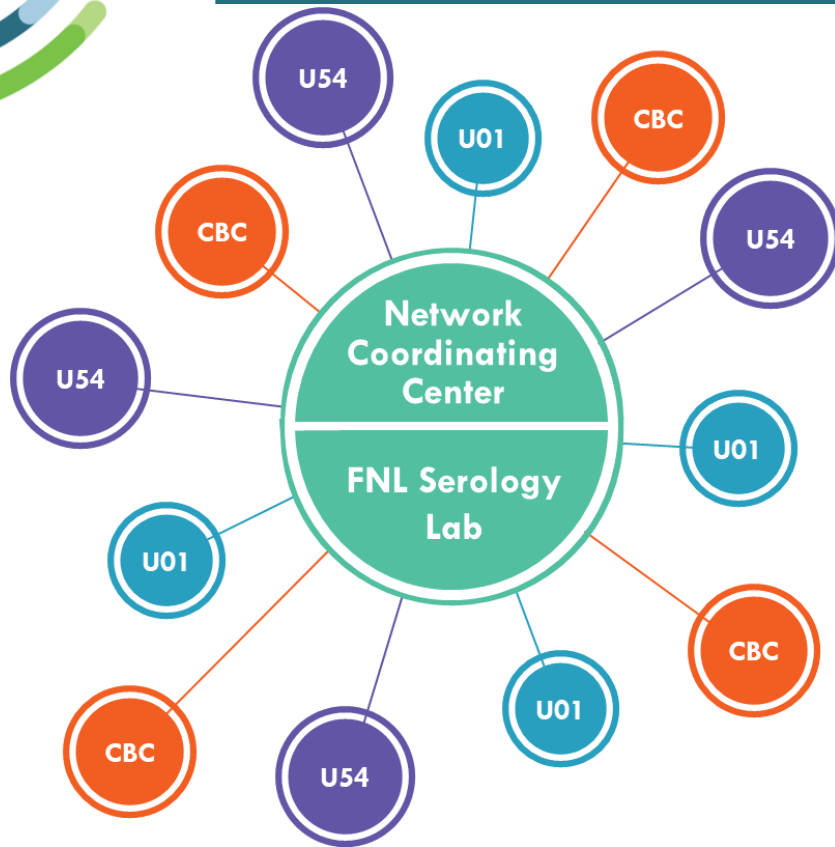
Lack of understanding of infection and vaccine-induced immune responses



## Solutions

- Build a strong network of partners (biospecimen collections and testing) and enhance internal capacity
- Develop a standardized data management infrastructure
- Make data, reference materials, specimens and procedures available to the scientific community

# Long Term Plans: Leveraging an established infrastructure for public-private partnerships for multiple uses beyond COVID-19



**FNL Serology Unit with GCLP Capabilities for Clinical Studies/Trials**

**Data, Sample, and Network Management Center Infrastructure**

## COVID-19

- **Support for COVID-related serology and immunology with existing validated technologies**
  - ◇ Vaccines/immunobridging testing and standards/validation panels
  - ◇ Study immune responses to vaccines in Cancer cohorts
  - ◇ Long COVID immunology/serology

## Emergency Preparedness

- **Standards, assays development and validation using our HPV plug and play ELISA and Luminex Technologies**
- **Infrastructure for independent assay evaluation with collaborations with FDA, CDC, and WHO/NIBSC**

## Cancer Vaccines Immunology and Standards

- **Preclinical and Clinical immunology standards and testing**
- **Network of key expertise working towards cancer vaccine development and evaluation**



# Acknowledgments

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## NCI

- Douglas Lowy
- Dinah Singer
- Juli Klemm
- Samantha Finstad
- Sean Hanlon
- Michelle Berny-Lang
- Lynne Penberthy

## Frederick National Laboratory for Cancer Research

- Troy Kemp
- Marissa Blackburn
- Bo Park and Administrative Team
- Quality Team
- Nancy Roche and SeroNet Coordinating Center Team
- Bruce Brown and CESDEP Team
- CESDEP, COVID-19, and HPV Serology Laboratory Teams
- Heidi Hempel
- Brett Smith, Brian Berkemeier and EIT Team
- Dominic Esposito and PEL Team
- Sam Lopez and SPGM Team
- Claudia Haywood and IP and Strategic Agreements Team
- Subcontracts Team
- Braulio Cabral and BACS Team

## FDA

- Brendan O’Leary
- Ribhi Shawar
- Pamela Gallagher
- Steve Gitterman

## BARDA

- Rosemary Humes

## CDC

- S. Michele Owen
- Nathalie Thornburg

## NIBSC/MHRA

- Mark Page
- Dianna Wilkinson
- Giada Mattiuzzo

## NIAID

- Jim Cherry
- Cristina Casseti

## The Bill & Melinda Gates Foundation

- Peter Dull