



VA SHIELD

Presentation to Research Advisory Committee on Gulf War Veterans' Illnesses

Dr. Holly Krull and Dr. Robert A. Bonomo

September 7, 2023



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Outline

- 1) **The Challenge of Understanding Gulf War Veterans' Illnesses**
- 2) **VA SHIELD Goals, Origin, Structure and Governance**
- 3) **VA SHIELD Working Groups**
- 4) **Facilitated Research Projects**
- 5) **Biorepository Inventory**
- 6) **On the Horizon**
- 7) **Q&A**



The Challenges of Medically Unexplained Illnesses Related to Gulf War

- Chronic fatigue syndrome
- Fibromyalgia
- Functional gastrointestinal disorders
- Medically unexplained chronic multi-symptom illness
- Other undiagnosed illnesses, such as cardiovascular signs and symptoms, muscle and joint pain, and headaches
- Burn pit and other toxic exposures

PLOS PATHOGENS

PEARLS

The viral origin of myalgic encephalomyelitis/
chronic fatigue syndrome

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 **frontiers**
in Immunology

MINI REVIEW
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Epstein-Barr Virus and the Origin of Myalgic Encephalomyelitis or Chronic Fatigue Syndrome

Manuel Ruiz-Pablos^{1*}, Bruno Paiva², Rosario Montero-Mateo³, Nicolas Garcia²
and Aintzane Zabaleta^{2*}



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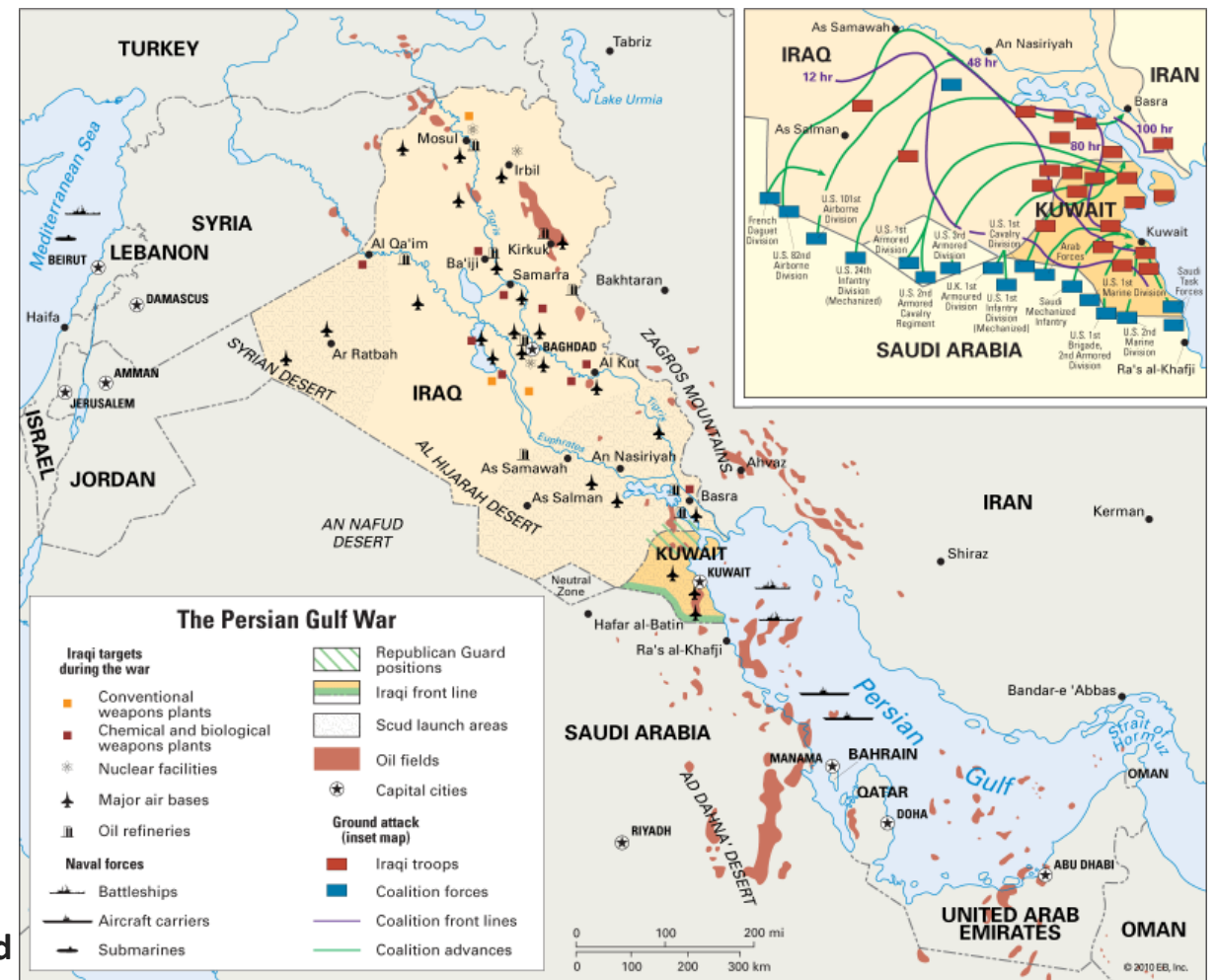
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Locations and Exposures : impact on Gulf War veterans

- Afghanistan (airspace not included)
- Bahrain
- Egypt (airspace not included)
- Iraq
- Israel (airspace not included)
- Jordan (airspace not included)
- Kuwait
- Neutral zone between Iraq and Saudi Arabia
- Oman
- Qatar
- Saudi Arabia
- Syria (airspace not included)
- Turkey (airspace not included)
- The United Arab Emirates (UAE)
- The waters of the Arabian Sea, Gulf of Aden, Gulf of Oman, Persian Gulf, and Red Sea



Infectious Diseases Diagnosed in Gulf War within 1 year of Separation

- Brucellosis
- *Campylobacter jejuni*
- *Coxiella burnetii* (Q fever)
- Malaria (or sooner in some cases)
- Nontyphoid *Salmonella*
- Shigella
- West Nile virus
- Maybe more?



What is VA SHIELD?



VA Science and Health Initiative to Combat Infectious and Emerging Life-Threatening Diseases (VA SHIELD) is an effort to support the VA's fourth mission, **to improve the Nation's preparedness for national emergencies and to support emergency management, public health, safety, and homeland security efforts.**



VA SHIELD is a comprehensive, secure **biorepository of specimens and associated data** related to COVID-19 and other emerging diseases. These specimens and data are/will be available to **VA investigators and others** to advance scientific understanding in support of developing diagnostic, therapeutic, and preventative strategies for use in clinical care.



VA SHIELD Origin

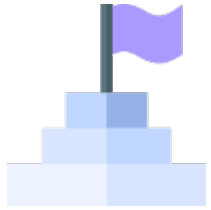
VA SHIELD was established in fall 2020 to provide the Veterans Health Administration with a comprehensive repository related to COVID-19.

- Enhance collaboration with external partners focused on COVID-19 and other emerging infectious diseases research.
- Initiated a mechanism to harmonize specimen and data collection procedures across clinical sites and to launch flexible response to dynamic disease occurrences.
- Potential to launch flexible response to dynamic disease occurrences.
- This is destined to do more....

VA SHIELD Strategy Statement



VISION: Advancing rapid detection, therapy and prevention of **emerging diseases** aimed at improving the quality and safety of health care for Veterans **(not just COVID)**.



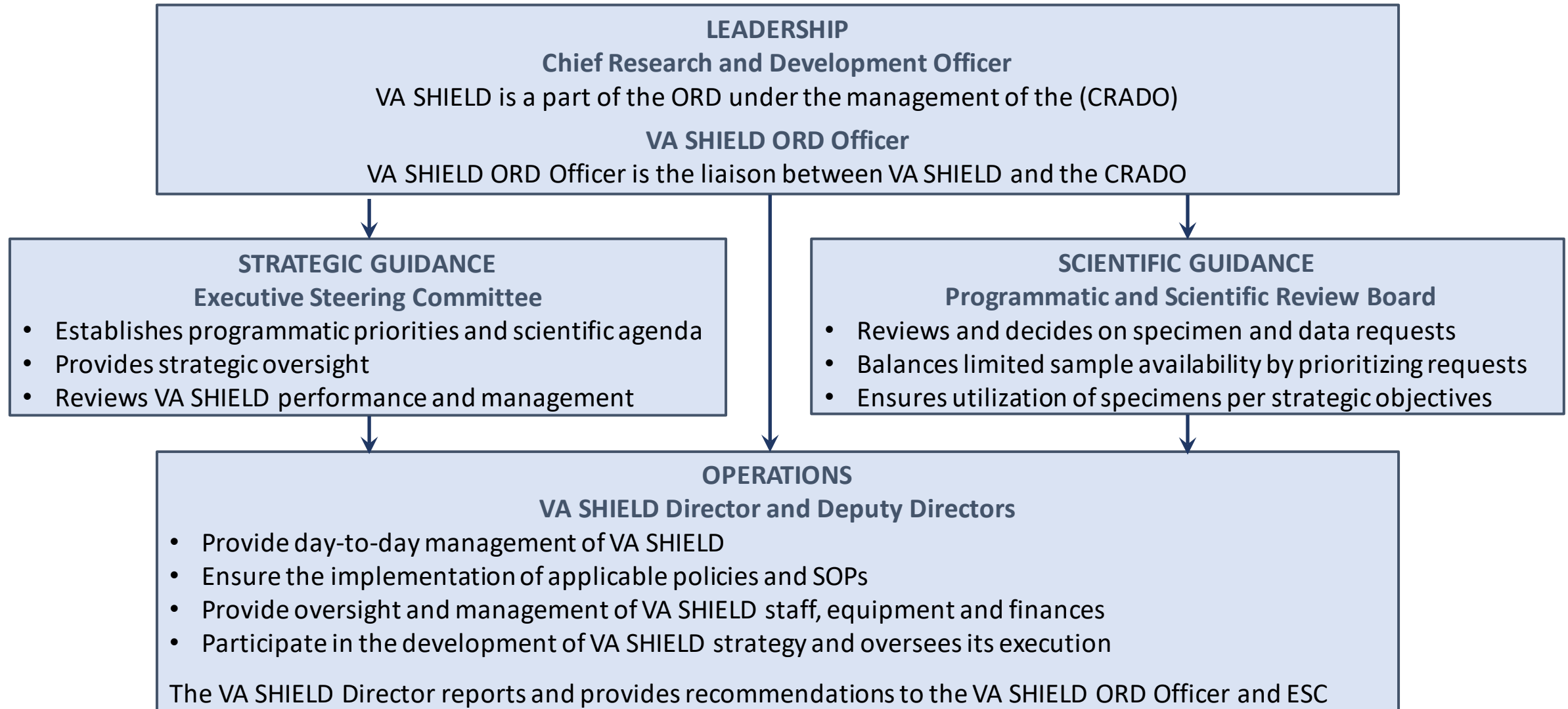
MISSION: VA SHIELD provides researchers and clinicians with high-quality biosamples and comprehensive associated medical and sample data to accelerate the **discovery-to-therapy pipeline**.



PURPOSE: Create a comprehensive infectious disease (and other clinical syndromes) repository of specimens and associated data available to advance research, improve diagnostic and therapeutic capabilities, and develop strategies for **immediate deployment in VA's clinical environments**.



VA SHIELD Governance Structure



VA SHIELD Governing Documents

- **Central IRB Approved Protocol:** Establishes VA SHIELD as a biorepository, allows for the collection of remainder clinical specimens and associated data, and allows for the collection of consented specimens and associated data.
- **Standard Operating Procedures:** Sets the standards and requirements for VA SHIELD day-to-day operations.
- **Executive Steering Committee Charter:** Establishes the principles, objectives and procedures for the activities of the ESC
- **Programmatic and Scientific Review Board Charter:** Establishes the principles, objectives and procedures for the activities of the PSRB
- **Federation Kit:** Sets the procedures of adding new sites to the VA SHIELD program



VA SHIELD Operational Management

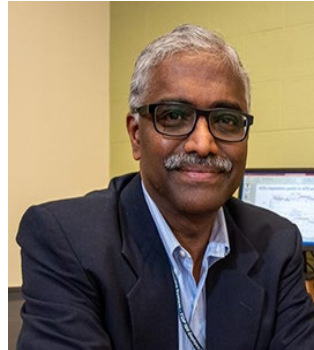
VA SHIELD ORD OFFICER AND COORDINATING CENTER:



Holly Krull, PhD
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ORD Officer



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Bonomo,
Director



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Padiernos,
Assoc. Dir.
Operations



Dr. Ian
Robey,
Assoc. Dir.
Biospecimens



Dr. Carey
Shive,
Assoc. Dir. Strategic
Research Initiatives



VA SHIELD Executive Steering Committee

VA SHIELD EXECUTIVE STEERING COMMITTEE:

- Establishes programmatic priorities and scientific agenda
- Provides strategic oversight
- Reviews VA SHIELD performance and management

COMMITTEE MEMBERS:

- | | | |
|---------------------------|---------------------------------------|------------------------|
| 1) Atkins, David | 7) Davey, Victoria | 13) Schnabl, Bernd |
| 2) Battles, Jane K. | 8) Eder, Paul | 14) Smith, Nicholas L. |
| 3) Brophy, Mary | 9) Krull, Holly (<i>ex officio</i>) | 15) Tsao, Philip S. |
| 4) Brown, Sheldon T. | 10) Marconi, Vincent | 16) Wertheim, Jason |
| 5) Cates, Jordan | 11) Moore, Helen | 17) Woods, Christopher |
| 6) Curtis, Jeffrey (Jeff) | 12) Przygodzki, Ronald | |



VA SHIELD Programmatic and Scientific Review Board

VA SHIELD PROGRAMMATIC AND SCIENTIFIC REVIEW BOARD:

- Reviews and decides on specimen and data requests
- Balances limited sample availability by prioritizing requests
- Ensures utilization of specimens per strategic objectives

COMMITTEE MEMBERS:

- 1) Diwan, Abhinav
- 2) Efird, Jimmy T.
- 3) Fawcett, Janet
- 4) Harley, John B
- 5) Hiniker, Anne E.
- 6) Mirsaeidi, Mehdi S.
- 7) Mohapatra, Shyam S



How do you put this together...VA SHIELD Infrastructure

VA SHIELD LOCATIONS IN 2023:

-  Biobanks
-  Collection Sites
-  Coordinating Center (Primary), Director
-  Coordinating Center (Secondary), Associate Director
-  VA Office of Research and Development
-  Data Hub



4 sites added this year



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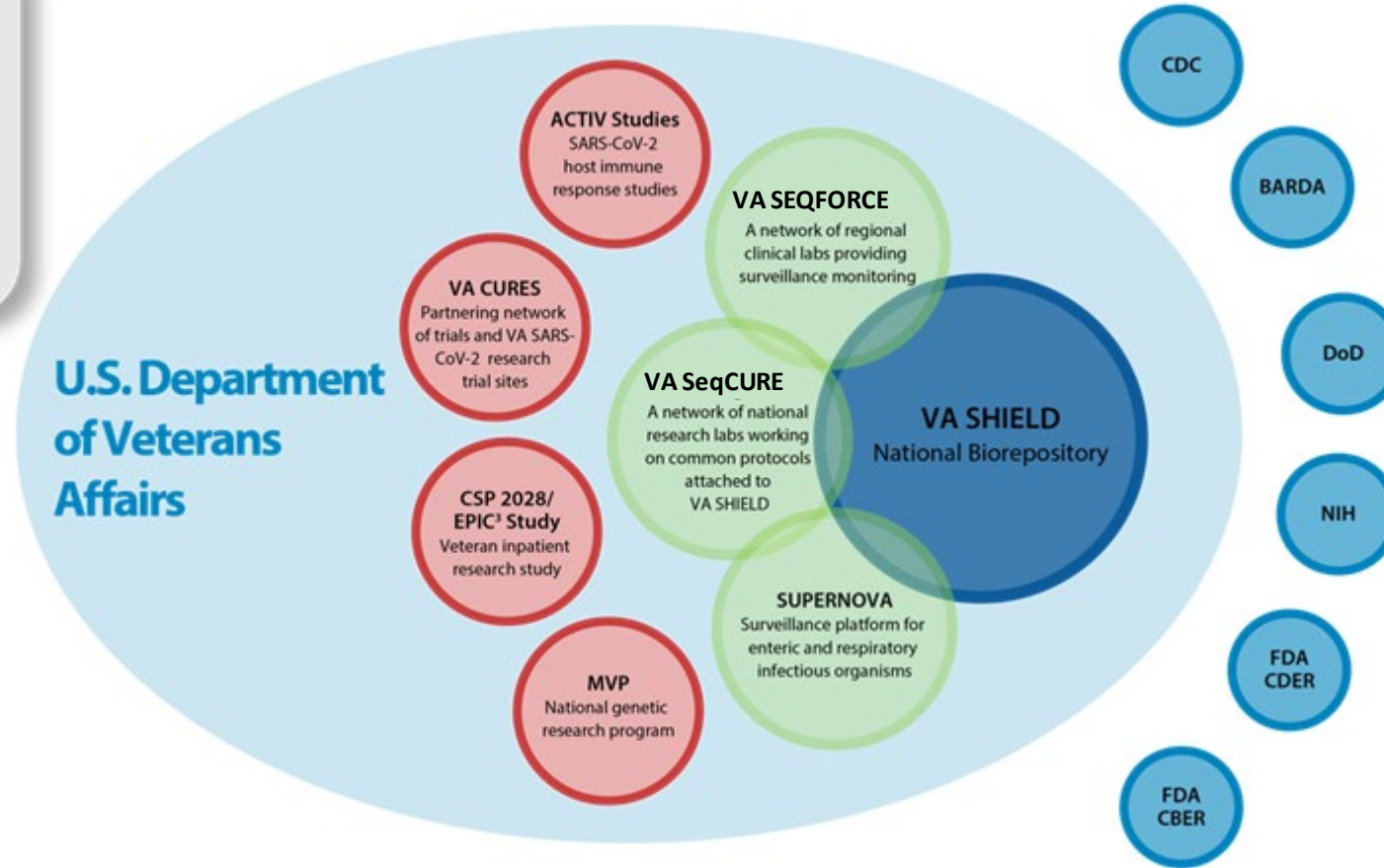


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VA SHIELD Infrastructure: relationships developing

VA SHIELD COOPERATION:

- Federal Agencies
- VA Projects not contributing specimens to VA SHIELD repository
- VA Projects contributing to VA SHIELD repository



What are all these collaborations and what do they mean?

VA SHIELD -Announcement to the ID Community

VA SHIELD LINKS:

VA SHIELD public webpage

www.research.va.gov/programs/shield/about.cfm

VA SHIELD manuscript

<https://academic.oup.com/ofid/article/9/12/ofac641/6895720?login=true>

Open Forum Infectious Diseases

MAJOR ARTICLE



The US Department of Veterans Affairs Science and Health Initiative to Combat Infectious and Emerging Life-Threatening Diseases (VA SHIELD): A Biorepository Addressing National Health Threats

John B. Harley,¹ Saiju Pyarajan,² Elizabeth S. Partan,² Lauren Epstein,³ Jason A. Wertheim,⁴ Abhinav Diwan,⁵ Christopher W. Woods,⁶ Victoria Davey,⁷ Sharlene Blair,¹ Dennis H. Clark,¹ Kenneth M. Kaufman,¹ Shagufta Khan,¹ Iouri Chepelev,¹ Alexander Devine,⁸ Perry Cameron,⁹ Monica F. McCann,¹⁰ Mary Cloud B. Ammons,^{11,12} Devin D. Bolz,¹¹ Jane K. Battles,⁷ Jeffrey L. Curtis,¹³ Mark Holodniy,¹⁴ Vincent C. Marconi,^{3,15} Charles D. Searles,³ David O. Beenhouwer,¹⁶ Sheldon T. Brown,¹⁷ Jonathan P. Moorman,^{18,19} Zhi Q. Yao,^{18,19} Maria C. Rodriguez-Barradas,^{20,21} Shyam Mohapatra,²² Osmara Y. Molina De Rodriguez,⁴ Emerson B. Padiernos,¹¹ Eric R. McIndoo,^{11,12} Emily Price,^{11,12} Hailey M. Burgoyne,^{11,12} Ian Robey,⁴ Dawn C. Schwenke,⁴ Carey L. Shive,²³ Ronald M. Przygodzki,⁷ Rachel B. Ramoni,⁷ Holly K. Krull,^{7,a} and Robert A. Bonomo^{23,24,a}

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HOW CAN VA SHIELD WORK WITH RESEARCH ADVISORY COMMITTEE ON GULF WAR VETERANS' ILLNESS?



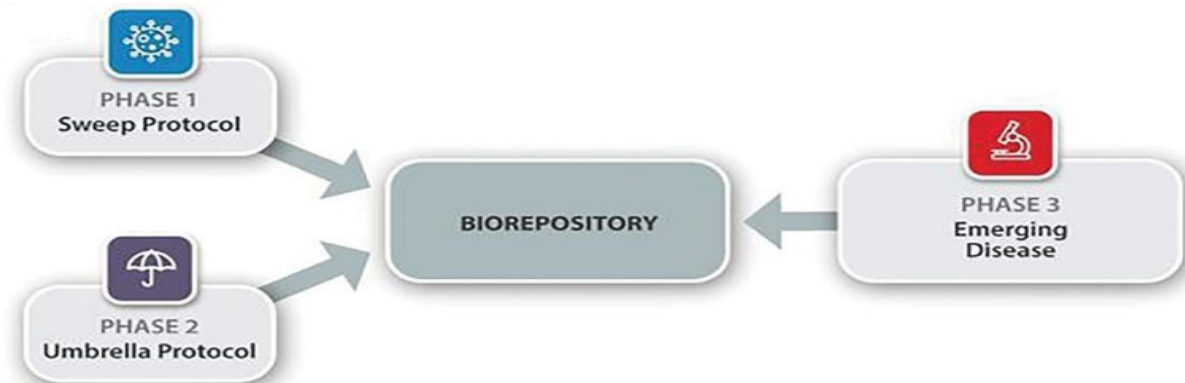
Helping Gulf War Veterans

1. As Gulf War Veterans seek medical attention in designated clinics and with specialty trained providers, VA SHIELD has protocols in place (Sweep and Umbrella) to assist the collection of biospecimens that can be used for research

Phase 1 VA–**Sweep Protocol** is underway to assemble remnant samples from severe acute respiratory syndrome coronavirus 2 affected Veterans and controls

Phase 2 was implemented in 2023 with the VA SHIELD “**Umbrella**” amendment to collect prospective samples from Veterans based on criteria that **IS** finalized. This protocol allows us to recontact the patient for follow up samples

Phase 3 prepares the system for next emerging diseases that warrant a VA SHIELD response, which is underway and will become more effective upon implementation of Phase 2



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Helping Gulf War Veterans

2. Good stewardship of Veteran biospecimens and associated data are of utmost importance to VA SHIELD.

- **Established robust governance structure Coordinating Center, ESC, PSRB, and Working Groups**

3. Biospecimens and associated data within VA SHIELD may be used for approved research projects. Specimen and data requests may be submitted to the Programmatic and Scientific Review Board (PSRB) of VA SHIELD to be evaluated for scientific merit, feasibility, and its impact on the biorepository.

- **Both existing and established programs of research may take advantage of this opportunity**
- **VA and non-VA investigators working in collaboration can avail themselves of this opportunity**



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4. Research is supported/funded through existing funding agencies and programs (MREP, Merit Review, NIH, ORD)

5. Most specimens have been nasal swabs of patients with COVID; other specimens include serum, plasma, and blood. We are expanding collections to include a variety of other biosamples.

6. Specific SOPs are in place to guide sites and investigators making collections and to ensure harmonization, standardization, and quality.

7. VA SHIELD has established Working groups to facilitate research of the following: host response to infectious diseases, epidemiology and sequencing, long Covid, cardiometabolic disease, antibiotic resistant bacteria , vector-born illnesses, cancer biomarkers, *Candida auris*, and Influenza/RSV.

- Many of these conditions directly impact on Gulf War Veterans



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8. The VA SHIELD has a robust laboratory and information management system that allows specimens to be tracked and monitored from collection, shipment, storage, use, and destruction.

9. Our C-DACS Core manages our LIMS System and supports research by facilitating linking de-identified data and biospecimens through an honest broker system. At the time of collection basic data is collected including basic demographics, medications, and other health related data . The C-DACS team can work with approved investigators to link specimens with EHRM Data.

- **Data is maintained behind secure firewalls, on secure servers**



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Research Projects on the “Horizon”

- Cross-disciplinary Platforms and Programs
- Supporting Merit/DoD/NIH grants
- CSP Trials
- Further AMR- *Candida auris*, *Mycobacteria*, *Pseudomonas*
- Pathology slides and collections/surgical samples
- VA CURES-1, -2....
- Precision Oncology
- NeuroCovid
- Bio-surveillance
- Legacy Collections/NASEM
- Pharmacogenomics



Ongoing and Future Collections



Ongoing and Future Collections

- **Air Force Health Study**
- **Warren Collection**
- **Military Exposures Research Program (MERP)**



Air Force Health Study Collection and Warren Collection

Ranch Hand Study (Vietnam War)

91,000 samples

Samples include serum, blood, and adipose tissues.

Data currently at NAS

Warren Collection (Korean War)

40,000 samples (+/-)

Serum samples only

No data available



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Military Exposures Research Program (MERP)

MERP MISSION:

The VA Military Exposures Research Program seeks to advance military exposure assessments and to understand the effects of military exposures on Veterans' health outcomes to inform care and policy.

- **Military exposures** are defined as toxic agents, singly or in combination, incurred through military service (Deployment, Occupation, or Garrison).
- **Exposure assessment** refers to identifying and quantifying toxic agent(s) to which a Veteran was exposed during military service.

VA SHIELD HAS BEEN APPROACHED BY MERP TO FACILITATE THE INTEGRATION / STORAGE OF MERP SPECIMENS WITH VA SHIELD



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Why should we care ?

- **VA SHIELD presents an opportunity to use one of the world's largest health care systems to facilitate research that meets the health care needs of Veterans and others**
 - **A dynamic biorepository of biospecimens and associated data**
- **Collaborations with various government agencies and the private sector will accelerate transformation of clinical observations into therapeutic advances**
- **Each clinician will be able to participate!**



Thank you

Thoughts?
Suggestions?
Questions?

