Sergeant First Class Heath Robinson Honoring our Promise to Address Comprehensive Toxics (PACT) Act Toxic Exposure Research Work Group Five-Year Interagency Strategic Plan

A Report by the

JOINT SUBCOMMITTEE ON ENVIRONMENT, INNOVATION, AND PUBLIC HEALTH
TOXIC EXPOSURE RESEARCH WORKING GROUP

of the

NATIONAL SCIENCE AND TECHNOLOGY COUNCIL

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About the National Science and Technology Council

The National Science and Technology Council (NSTC) is the principal means by which the Executive Branch coordinates science and technology policy across the diverse entities that make up the federal research and development (R&D) enterprise. A primary objective of the NSTC is to ensure science and technology policy decisions and programs are consistent with the President's stated goals. The NSTC prepares R&D strategies that are coordinated across federal agencies aimed at accomplishing multiple national goals. The work of the NSTC is organized under committees that oversee subcommittees and working groups focused on different aspects of science and technology. More information is available at http://www.whitehouse.gov/ostp/nstc.

About the Office of Science and Technology Policy

The Office of Science and Technology Policy (OSTP) was established by the National Science and Technology Policy, Organization, and Priorities Act of 1976 to provide the President and others within the Executive Office of the President (EOP) with advice on the scientific, engineering, and technological aspects of the economy, national security, homeland security, health, foreign relations, the environment, and the technological recovery and use of resources, among other topics. OSTP leads interagency science and technology policy coordination efforts, assists the Office of Management and Budget (OMB) with an annual review and analysis of federal research and development in budgets, and serves as a source of scientific and technological analysis and judgment for the President with respect to major policies, plans, and programs of the federal government. More information is available at http://www.whitehouse.gov/ostp.

About the Toxic Exposure Research Working Group

In August 2022, Congress passed Honoring our Promise to Address Comprehensive Toxics Act of 2022 (Public Law 117-168) or the PACT Act. The PACT Act directed the Secretary of the Department of Veterans Affairs (VA), in collaboration with specified, invited, and interested federal partners, to establish a working group (WG) with an overall charge of identifying collaborative research activities and resources and developing and guiding a collaborative five-year strategic plan on the health outcomes of toxic exposures during military service. The Toxic Exposure Research Working Group (TERWG) membership is dynamic, but generally consists of thirty-eight representatives and subject matter experts from 8 federal departments and several agencies. The TERWG is co-chaired by representatives and subject matter experts (SMEs) from the VA, Department of Defense (DOD), the Centers for Disease Control and Prevention (CDC), and White House Office of Science and Technology Policy (OSTP).

About this Document

The PACT Act directs the Secretary of the Department of Veterans Affairs (SECVA) to establish an interagency working group: 1) to identify collaborative research activities and resources available among entities represented by members of the TERWG to conduct such collaborative research activities; 2) to develop a five-year strategic plan for such entities to carry out collaborative research activities; and 3) to complete associated reporting. Through OSTP and the National Science and

Technology Council, the TERWG solicited input from member agencies about ongoing and prospective research and development efforts for toxic exposures and adverse health outcomes of veterans. The TERWG five-year interagency strategic plan provides a federal strategy for addressing the research and knowledge needs for understanding the toxic exposures of the U.S. military and the potential adverse health outcomes for veterans related to those toxic exposures.

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[1] See 17 U.S.C. §105

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Abbreviations and Acronyms

AI Artificial Intelligence

AOP Adverse Outcome Pathways

ATSDR Agency for Toxic Substances and Disease Registry

BLUF Bottom Line Up Front

CDC Centers for Disease Control and Prevention

CEQ Council on Environmental Quality

CIPHER Centralized Interactive Phenomics Resource

CM Clinical Modification

CPG Clinical Practice Guidelines

CRADA Collaborative Research, and Development Agreement

CRADO Chief Research & Development Officer

CT Clinical Terms

DAG Directed Acyclic Graph

DHA Defense Health Agency

DMDC Defense Manpower Data Center

DOC Department of Commerce

DOD Department of Defense

DOE Department of Energy

DOL Department of Labor

DOS Department of State

DUSD(I&E) Deputy Under Secretary of Defense for Installations and Environment

EHRA Electronic Health Records Acquisition

EHSS Office of Environment, Health, Safety and Security

EI&E Energy, Installations and Environment

EOP Executive Office of the President

EPA Environmental Protection Agency

FDA Food and Drug Administration

FEHRM Federal Electronic Health Record Modernization

FY Fiscal Year

GAO Government Accountability Office

HA Health Affairs

HHS Department of Health and Human Services

HOME Health Outcomes Military Exposures

ICD International Classification of Diseases

ILER Individual Longitudinal Exposure Record

JCIDS Joint Capabilities Integration and Development System

JEEP Joint Subcommittee on Environment, Innovation, and Public Health

JEM Job Exposure Matrix

JPC Joint Pathology Center

MCL Maximum Contaminant Levels

MEESC Military Environmental Exposures Sub-Council

MET Military Exposures Team

MHSC Medical and Health Services Unit

MIE Molecular Initiating Events

NAAQS National Ambient Air Quality Standards

NCEH National Center for Environmental Health

NDAA National Defense Authorization Act

NHRC Naval Health Research Center

NIEHS National Institute of Environmental Health Sciences

NIOSH National Institute for Occupational Safety & Health

NIST National Institute for Standards and Technology

NIH National Institutes of Health

NOAA National Oceanic and Atmospheric Administration

NSTC National Science and Technology Council

NTP National Toxicology Program

OMB Office of Management and Budget

OASD Office of the Assistant Secretary of Defense

ORD Office of Research & Development

OMB Office of Management and Budget

OSHA Occupational Safety and Health Administration

OSTP Office of Science and Technology Policy

PACT Promise to Address Comprehensive Toxics

PDP Presumptive Decision Process

PEL Permissible Exposure Limits

PFAS Per- and polyfluoroalkyl substances

P.L. Public Law

PPE Personal Protective Equipment

QSAR Quantitative structure-activity relationship

SDOH Social Determinants of Health

SECVA Secretary of Veterans Affairs

SEG Similar Exposure Group

SME Subject matter expert

Executive Summary

President Biden signed the Sergeant First Class Heath Robinson Honoring our Promise to Address Comprehensive Toxics Act of 2022 (hereafter referred to as "The PACT Act") to provide generations of U.S. Veterans with the care that they deserve by expanding the coverage of Department of Veterans Affairs (VA) health care and benefits for Veterans following toxic exposures.

Throughout the course of military service, troops are exposed to a variety of unique environments and hazardous situations that are not common in the civilian sector. These situations and exposures are often not fully defined, and their implications for inducing adverse acute and chronic health conditions are not fully understood. The complexity of this field comes down to the basic needs of understanding 1) sources of military exposures, 2) the dose and frequencies of toxicants that are necessary and sufficient to induce an adverse health outcome, 3) the biological adverse outcome pathways affected, and 4) identifying who may be at risk, to include genetic, sex, age, and race/ethnicity differences.

Military personnel serve in proximity to a variety of exposures through environmental and occupational pathways during deployment or in garrison. Military exposures herein are defined as exposures to chemical(s), substance(s), airborne hazards, and/or warfare agent(s) within the military environment where service members train, work, and live. Military exposures can also arise from situational circumstances, for example an accident. The military exposome[2] is defined as the totality of military exposures (environmental, occupational, and situational) encountered by an individual while serving in the armed forces (military milieu).

Notably, military personnel may not be aware of these toxic exposures nor take appropriate action to protect themselves, affecting military readiness and/or lessening quality and duration of life over time. Likewise, health care providers may not have the necessary information to provide the best care or direct them for appropriate VA claims. Taken together, transdisciplinary approaches are needed to leverage subject matter experts, technologies, data and bio repositories to enhance military exposure-informed care.

The short-term goals of this strategic plan are to identify military exposures of concern within the military milieu and catalogue diseases associated with them. In parallel, identifying the individuals who may be in contact with these toxicants and characterizing those at risk will provide an opportunity to support risk assessment with confidence. This will be accomplished by integrating exposure information from workplace and training environments, along with deployments and incidences, for risk characterization in the context of understanding health outcomes from the military exposome to support exposure-informed care[3].

[2] Exposome research is evolving, and its consideration within and across agencies is limited; therefore, this effort allows for a whole-of-government collaboration to advance exposome knowledge and application. This work is novel and isn't currently being conducted for the general population. For example, limited, if any, integrated occupational and environmental exposure information is available for individuals or cohorts, and the ability to integrate data from environmental (air, water, soil) and occupational exposures is limited.

[3] U.S. Department of Veterans Affairs, "Toxic Exposure Screenings and PACT Act Expansion of Care." https://www.va.gov/illiana-health-care/programs/toxic-exposure-screenings-and-pact-act-expansion-of-care/ (accessed July 27, 2024.

The long-term overarching goal of the TERWG is to improve Veteran health by advancing our understanding of the range of toxic military exposures and their potential adverse health effects, in order to develop treatment and prevention strategies.

This strategic plan is divided into three categories to organize and support federal agencies to study (A) the composition, substance, concentration, toxicity, and time intervals of those toxic exposures; (B) the complex relationship between exposure and adverse health outcomes that may arise from military exposure activities, environments, and situations during military service; and (C) the preventive and mitigation measures that improve quality and duration of life for all Veterans, including those at risk and underrepresented, through exposure-informed health care. This strategic plan uses research from federal research agencies and extramural research funders to support defined research to add evidence-based knowledge.

The strategic plan includes objectives with directional and infrastructure strategies to solidify a foundation to understand the adverse health effects from military toxic exposures.

The directional strategy outlines five strategic goals (Figure 1):

1. Characterize the exposome of the military milieu.
2. Prioritize and catalogue toxic exposures and associated toxicity and adverse health outcomes within the military milieu.
3. Investigate associations and interplay between priority military toxic exposures, toxicological endpoints, and adverse health outcomes.
4. Preventing and mitigating adverse health outcomes from military toxic exposures.
5. Communicate toxic exposure risk and adverse health outcomes to relevant stakeholders to enhance exposure-informed health care.

The infrastructure strategy includes an organized unit that will support processes for the implementation of the directional strategy across the federal landscape. These goals, objectives, and tasks are aligned with collaborative efforts and gaps needs identified within the expertise of the interagency TERWG.

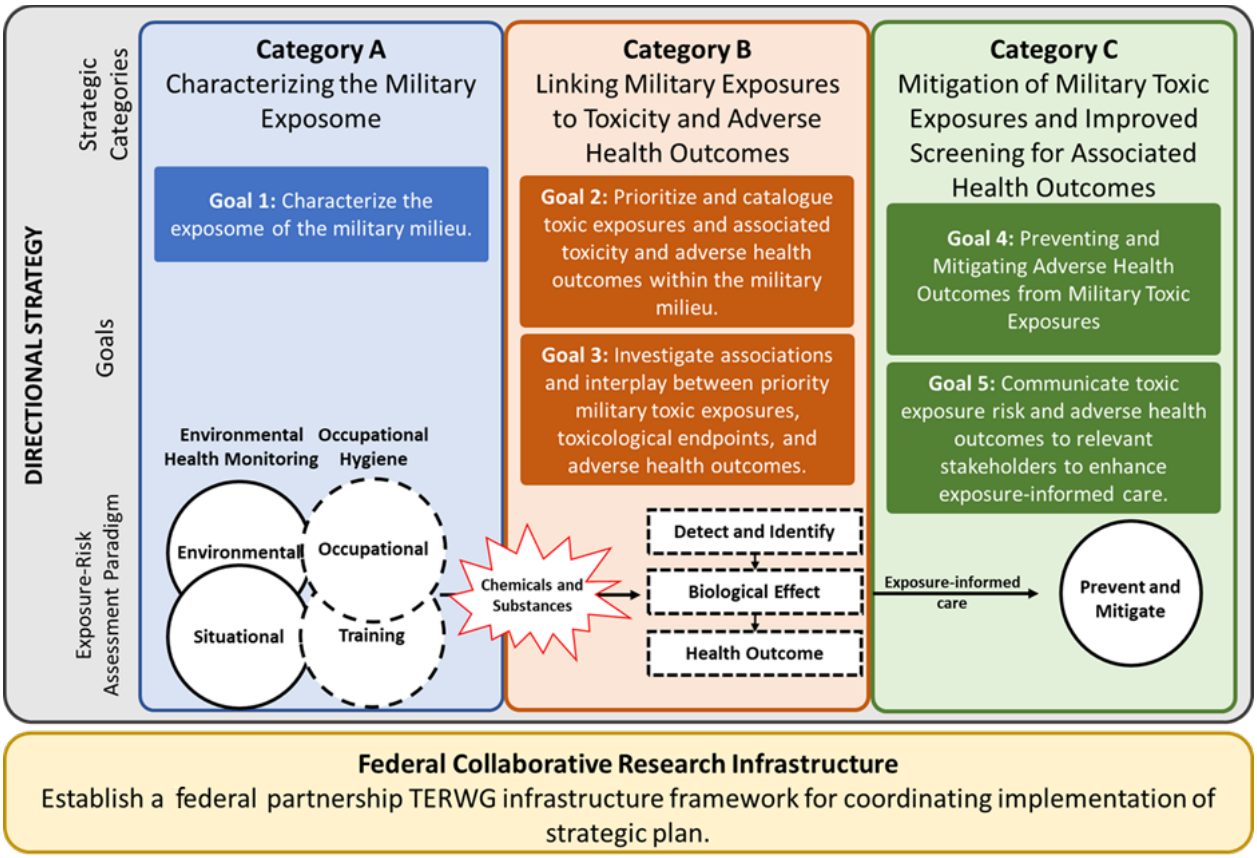

Figure 1. Visual diagram of the strategic plan layout

Strategic Plan Implementation

The TERWG directional strategy outlined herein encompasses a federal government-wide, strategic plan with meaningful, specific, measurable, and attainable goals, interagency operational tasks, and mission-aligned collaborative research opportunities to understand the health consequences of military toxic exposures. However, the feasibility and achievability to conduct this plan, as written, remains ambitious without more available time and needed resources.

To define a five-year feasible and achievable scope for the strategic plan, the TERWG will conduct oversight of priorities and accomplishments, in part, through our ongoing partnership with the NSTC Joint Subcommittee on Environment, Innovation, and Public Health (JEEP) and, in part, through the infrastructure unit via TERWG subgroups. Within this capacity, and as time and resources allow, TERWG subgroups should be formed with mission-aligned scope and collaborative-aligned interest. Coordination of TERWG subgroups under the JEEP or infrastructure unit will include development of charters and establishment of interagency co-chairs and members, administrative support, technical writers, and other resources as deemed critical for execution.

Appendix A outlines a more detailed implementation strategy with articulated measures of success.

Introduction

Understanding the connection between military toxic exposures and the subsequent adverse health outcomes has long been, and remains, a concern for U.S. service members, Veterans, their families, and the nation. In August 2022, Congress passed, and President Biden enacted, the PACT Act. This comprehensive legislation expands access to health care and benefits for Veterans exposed to toxic substances during their military service. As part of the PACT Act, Congress and the Biden-Harris Administration called upon the federal government to come together to develop a unified, federal strategy for identifying, and providing solutions, for toxic exposure-related illnesses in Veterans.

> *Military exposures are defined as chemical(s), substance(s), and/or physical and biological warfare agents within the military environment where service members train, work, and live.*

Elucidating health outcomes arising from military toxic exposures is complex and requires a whole-of-government approach with unified goals of **1)** cataloging trusted capabilities and resources that are available across federal departments and agencies, **2)** identifying processes by which these capabilities can be readily shared or leveraged to support transdisciplinary research with inclusion of genetic, sex, age, and race/ethnicity differences in adverse health outcomes (prevalence and severity) due to military toxic exposures, and **3)** translation of research into improved health care practice and benefits determinations.

Evidence-based decision making is foundational for informing health care and policy at every level; therefore, widespread federal partnerships will provide diverse expertise and perspectives to produce quality evidence and strengthen recommendations. Advancing this work is a high-priority effort for VA to provide more timely services and benefits to all eligible service members and Veterans.

Under the PACT Act, VA established the interagency Toxic Exposure Research Working Group (TERWG) aimed at developing a 5-year strategic plan to coordinate collaborative research activities on the health consequences of toxic exposures experienced during active military service. The strategic plan aims to advance efforts to improve health care for Veterans who have been exposed during military service and are experiencing health and related consequences as a result. The TERWG serves as a nexus for agencies to come together to establish collaborative efforts.

Scope of the Report

This interagency strategic plan presents short- and long-term objectives and tasks that are intended to meet the goals. Implementation may be under the purview of the TERWG or other coordinating body, but the research enterprise that will support the implementation will be shared among all participating agencies. The tasks presented include operational, administrative, and mission-aligned research goals that can be accomplished through federal and external subject matter expertise and both intramural and extramural research. Research is an ongoing and evolving endeavor, and some research-based advancements from our current knowledge are anticipated within the 5-year scope of this strategic plan; however, research advancements are expected to continue beyond the current timeline. The short-term research accomplishments described in this 5-year strategic plan will serve as a foundation for long-term achievements that may require additional time and resources for success. Thus, the current strategic plan identifies opportunities for research that will address existing knowledge gaps, and additional gaps are expected to be identified during execution of the strategic plan. Operational task subgroups and collaborative research opportunities subgroups will provide the necessary available resources to conduct the collaborative research activities when activated. In

addition, the TERWG and agency leadership will convene to discuss further financial resources, if needed, for conducting additional collaborative research activities.

Background

Military Historical Situational Exposures. Historical military exposures refer to instances where military personnel have been exposed to various hazardous substances, chemicals, environmental contaminants, or airborne hazards during their service. These exposures may have occurred during training exercises, combat operations, workplace activities, or while stationed at military installations and highlight the importance of assessing and mitigating health risks associated with military service, providing appropriate health care and support to affected Veterans, and conducting research to better understand the long-term health effects of military exposures. Efforts to address historical military exposures may include health screening and surveillance programs, preventive medicine initiatives, disability compensation and benefits, outreach and educational initiatives, enhanced support for existing biorepositories (e.g., serum, formalin-fixed paraffin-embedded tissue, urine) and establishment of novel biorepositories (e.g., dried blood spots, fresh frozen tissue, etc.), and environmental remediation efforts at contaminated military sites.[4] Historical examples of situational, environmental, and occupational exposures include:

Agent Orange – an herbicide and defoliant consisting of 2,4-dichlorophenoxyacetic acid (2,4-D) and 2,4,5-trichlorophenoxyacetic acid (2,4,5-T), as well as trace levels of the dioxin 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), which has been linked to cancer, hypertension, and other adverse health outcomes among military personnel.

Gulf War Exposures – during the 1990-91 Gulf War, military personnel were exposed to a variety of environmental hazards, including oil well fires, depleted uranium munitions, chemical warfare agents, pesticides, and other toxic substances. Gulf War Veterans have reported a range of health problems, often referred to as Gulf War Illness, including chronic fatigue, cognitive dysfunction, musculoskeletal pain, gastrointestinal issues, and respiratory problems.

Burn Pit Exposures – military personnel deployed to Iraq, Afghanistan, and other conflict zones have been exposed to toxic emissions from burn pits used to dispose of waste, including trash, hazardous materials, and medical waste. Inhalation of burn pit smoke has been associated with respiratory disorders, asthma, lung disease, various types of cancers, and other health problems among Veterans.

Asbestos Exposure – military personnel have been exposed to asbestos-containing materials used in ships, aircraft, buildings, and other infrastructure components. Asbestos exposure can cause lung cancer, mesothelioma, and other asbestos-related diseases, with latency periods of several decades between exposure and disease onset.

Radiation Exposure – military personnel involved in nuclear testing, cleanup operations, or nuclear accidents may have been exposed to ionizing radiation while nuclear submariners may be continuously exposed to low levels of external ionizing radiation. Notably, military aviators are exposed to cosmic radiation. Radiation exposure can increase the risk of cancer, genetic mutations, and other long-term health effects.

[4] U.S. Department of Veterans Affairs, "Military Exposures." https://www.publichealth.va.gov/exposures/ (accessed July 27, 2024.

Chemical Weapons Exposures – military personnel may have been exposed to chemical warfare agents, such as nerve agents, blister agents, and choking agents, during conflicts or training exercises. Exposure to chemical weapons can cause acute toxicity, respiratory distress, neurological damage, and other severe health effects.

Occupational Exposures – military personnel may encounter occupational exposures to various hazardous substances, such as solvents, fuels, heavy metals, pesticides, and industrial chemicals, depending on their military occupational specialties and job duties.

MILITARY EXPOSOME. The human exposome model refers to the totality of external exposures an individual encounters over their lifetime, as well as how those exposures impact internal biological responses, giving rise to the whole health phenotype of that individual. Notably, external exposures within this exposome model are dynamic and include an extensive range of chemical and non-chemical factors, such as: radiation, infectious agents, chemical contaminants, environmental pollutants, lifestyle factors, occupational interventions, psychological stress, social/economical stress, mental stress, and other social determinants of health (SDOH).

The military experience can add a pronounced level of complexity to the civilian exposome model by introducing unique stressors and a variety of exposure sources, including the environments where service members train, work, and live, as well as situational (accidental) exposures. Military toxic exposures are defined herein as chemicals, substances, airborne hazards, and/or physical and biological warfare agents within the military environment. The aim of the exposome concept is to understand how individuals' entire exposure history contributes to their health. It is important to recognize that military exposures may impact individual biological responses or vulnerability to subsequent civilian exposures (environmental and lifestyle) after their transition from military service. Likewise, civilian exposures that occur prior to military service may impact biological responses to military exposures. Additionally, military personnel suffer from military and non-military stressors, and research should be included to evaluate the role of these factors in adverse health outcomes within the background of military toxic exposures. Characterizing the exposures encountered within the military milieu (entrance to- and exit from- military service) is necessary for understanding the interplay and contributions between military life and civilian life on the whole health phenotype.

Military exposures encountered in the military milieu by a person serving in the armed forces makes up the individual military exposome (**Figure 2**). Current understanding of the role of total exposures during military service on an individual's biological outcomes, such as aging and health, is limited. The complexity required to elucidate the impact of every exposure, including the interactions of exposures and the role of genetics, sex, age, race/ethnicity, and psychosocial stressors on the associated biological outcomes is enormous, but it is too important to ignore or sporadically tackle. A whole of government, transdisciplinary approach, with a focused, systematic process to include meaningful, specific, measurable, and attainable goals, is the key to building the foundational knowledge needed to move this field forward.

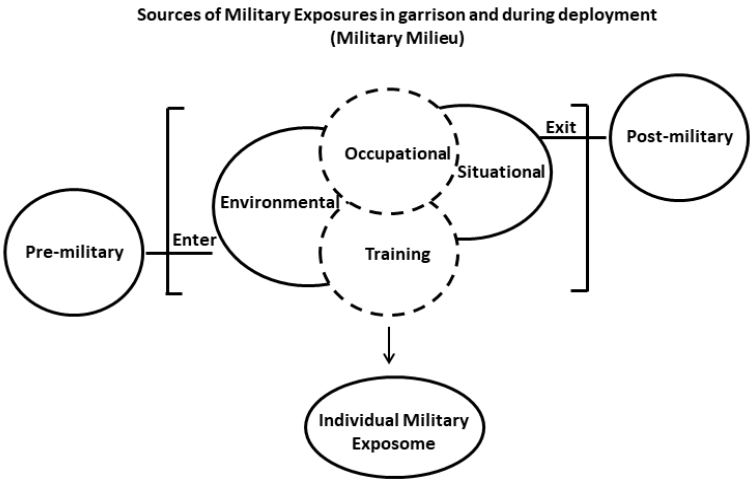

Figure 2. The Military Exposome. Exposures experienced between the entrance to- and exit from- military service make up the individual military exposome. Major sources of military exposures, both in garrison and during deployment, can be narrowed down to four broad categories: 1) environmental, 2) situational, 3) occupational, and 4) training.

Focused Gaps

Military environmental and industrial hygiene contaminants are commonly monitored by the DoD using sample testing of nearby media such as air, water, and soil whereas situational exposures are commonly evaluated retrospectively using statistical models. These approaches are necessary but not sufficient for identifying all possible military exposures that can mediate a probable adverse health outcome. Applying, or developing, emerging personal exposure technologies in the form of wearables or biosensors would be a complementary action to capture exposures.

Epidemiological and surveillance approaches only inform after a health concern has emerged, which can take years to identify and limits appropriate care. Lack of exposure data at the individual level is a major gap for predicting risk of adverse acute and/or delayed diseases that may arise under sufficient toxic conditions. Efforts in understanding foundational military exposures arising from work and training exercises where service members spend the majority of their time should be factored into the environmental and situational model in order to recognize the full spectrum of risk for adverse health outcomes driven by toxic exposures.

Military exposures may become toxic under sufficient conditions; however, penetrance of that toxicant into the human body at a concentration to elicit a biological response is needed to drive onset of subsequent symptoms or disease. Moreover, diversity, genetics, and outside factors can also play a role in sensitivity and susceptibility of penetrance and onset of disease. Therefore, characterizing biomarkers as a proxy for penetrance, measurement of a biological response in blood or tissue, and identifying populations at risk is an important need for risk assessment and exposure-informed care.

Although due diligence is focused on understanding the toxicity of chemicals, substances, airborne hazards, and warfare agents to prevent or circumvent their effects toward troops, concerns remain, and adverse health outcomes occur. Much focus is often on evaluation of exposures incurred during

deployment however, anecdotal evidence suggests that some military personnel who never deployed or were not located in areas with reported toxic exposures nonetheless demonstrate potential service-related chronic adverse health concerns, suggesting additional characterization of the individual military exposome is required.

Directional Strategy

INTRODUCTION TO DIRECTIONAL STRATEGY

The TERWG directional strategy includes five goals with mission-aligned interagency objectives. To conduct these objectives, interagency operational tasks and mission-aligned collaborative research opportunities are suggested. These goals can be realized through intra- and inter- agency coordination and contribution, giving rise to a foundational knowledge base in which continuing research can flourish and expand our understanding of adverse health effects from military toxic exposures.

Category A: Characterizing the Military Exposome

Bottom Line Up Front

The major sources of military exposures, both in garrison and during deployment, can be narrowed down to four broad categories: 1) environmental, 2) situational, 3) occupational, and 4) training. Although a systematic deep dive of each category is necessary to characterize the totality of the military exposome, the TERWG has identified occupational and training exposure characterization as a foundational need and predominant major gap in the context of characterizing the individual military exposome and is therefore critical to understanding health outcomes from military toxic exposures. Moreover, consideration and integration of industrial hygiene and environmental health monitoring will provide key insights into which military exposures are captured and which are not.

Background and Significance

Military personnel transition from civilian life to the military typically as young adults (18-24 years old) and back to civilian life within 10 years. Approximately 17% of military members retire with at least 20-cumulative years of service.

The primary exposure pathways include inhalation, ingestion, and dermal absorption. The risk and consequences of toxicants can most accurately be applied when the exposure is known and how much of the toxicant (concentration), how often the exposure occurred (frequency), and how long (duration) a person or population encountered that exposure. Monitoring, measuring, and documenting sporadic environmental and situational military exposures also informs service member readiness. Historical military exposures have not been well-documented or -characterized, which significantly limits understanding of the health consequences of military toxic exposures. Morbidity and mortality surveillance and epidemiological longitudinal studies are one approach to predict trends and identify disease. These studies have contributed to our understanding of etiology, initiation, and progression of disease across all areas of research through enhances in technology, digital data, collections of specimens linked to medical diagnoses, and subject matter expertise across federal agencies. Coordinated activities on mission-aligned, exposure-induced toxicity can readily expand growth in this much needed area of complex research. Taken together, rigorous characterization and detection of current exposures via environmental health- and industrial hygiene- monitoring and surveys will provide insights into the

role of military toxic exposures on health outcomes. The additional use and integration of wearable devices during occupational and training duties will increase understanding of exposures at the individual level, with the goal of estimating past and predicting future risk.

GOAL 1: Characterize the exposome of the military milieu.

Military exposures can arise from various independent sources during service tenure including deployment, in garrison, military occupational specialty, or events that are situational (accidental). Characterizing the exposome of the military milieu requires an understanding of all exposures at the individual level between the entrance into military service to exit from military service. This characterization requires systematic evaluation of exposures associated with military activities and environment, methods used for detecting and identifying exposures across all relevant exposure routes, and development of new capabilities through technology for reproducible, accurate and reliable measurement sets. To develop new technological capabilities, it is first necessary to understand the current state-of-science, define knowledge gaps, and support focused research. Characterization of the exposome for the civilian population is in its infancy, whereas characterization of the military exposome has not yet been initiated or is very limited. This is a timely area of investigation, and as this field expands, it will allow parallel lessons learned, identify best practices for protocol development, and define common data elements.

Objective 1.1: Evaluate and enhance current environmental health- and industrial hygiene-monitoring of the military milieu.

Rationale. The U.S. military actively engages in environmental health and industrial hygiene monitoring. Conventionally, exposure monitoring is a targeted procedure and is therefore limited to a finite list of contaminants and procedure-specific exposure routes. There is a significant need to review and understand the existing policies, procedures, and standard practices for identifying, quantifying, and monitoring chemical and substance exposures. By tabulating and indexing this information into a database containing monitoring policies and procedures, targeted contaminants of concern, and exposure information, the consistent data structure could be used to inform military service and Veteran health surveillance data and data management systems. The federal government has broad expertise in developing and implementing environmental and occupational exposure monitoring policies and procedures within and beyond the military milieu, which will be critical to providing a thorough review of occupational and environmental health and industrial hygiene monitoring.

Interagency operational tasks: Policies and procedures for environmental health- and industrial hygiene- monitoring should be reviewed to define gaps that may miss novel contaminants and/or exposure routes or lead to the development of standardized sampling, analysis, and data reporting. A thorough review of existing practice would lead to the identification and cataloging of key chemicals and substances that are monitored and identify trends in compounds that exceed exposure limits within the monitoring outputs across the military.

Collaborative research opportunities: Opportunities for interagency-coordinated research include:

- Development of novel technologies or validation of existing technologies for environmental health monitoring or industrial hygiene capabilities.

Objective 1.2: Understand existing practices and capabilities to identify military exposures at the individual level.

Rationale. Environmental health monitoring identifies chemicals or substances in environmental samples that may cause toxicity based on estimates of an individual's proximity to the source and duration of exposure. However, the detection of individual exposures can also be performed by the analysis of the exposed person's biological materials (e.g., blood, serum, or urine) using targeted or non-targeted methods to identify and quantify contaminant exposures to determine internal doses. These samples may also be stably maintained in biorepositories for future analysis, enabling the identification of contaminants for which exposure was not assessed in real-time. Studies, such as human biomonitoring, enable researchers and medical providers to identify chemical indicators of toxic exposures in specific populations. These findings may extend to other sub-populations, although extrapolation of findings can be limited due to the study design or scope, such as a specific population demographic that does not represent a broader or different demographic. To create trusted sources of data, the current capabilities to detect and quantify individual exposure biomarkers must be understood.

Interagency operational tasks: Current practices and capabilities for assessing military exposures at the individual level should be evaluated. Sharing trusted protocols and biospecimens to the broader research community will advance evidence-based knowledge for identification of military exposures and support surveillance studies while informing health data management systems.

Collaborative research opportunities: Opportunities for interagency-coordinated research include:

- Perform exposure assessment analysis of banked biospecimens to validate methods and protocols using military pathological coded biospecimens.
- Development/application of novel technologies or validation of existing technologies for individual monitoring capabilities.

Objective 1.3: Review and assess novel technologies for environmental, occupational, and training exposure identification determination.

Rationale. With the advent of new instruments and techniques, novel technologies are being developed that miniaturize sampling and analytical devices, expand the range of contaminants that can be measured in environmental and biological samples and decrease the detection limits for exposure biomarkers associated with chemicals and substances of interest. This can include technologies to monitor real-time measurement of chemicals, substances, and agents and/or physiological outputs. In addition, minimally invasive biospecimen collection (e.g., dried blood spots, cheek swipe) and the use of personal exposure samplers (e.g., wearable devices, skin wipes) enable researchers, environmental health experts and industrial hygienists to efficiently collect biospecimens and data at the site of suspected exposure and/or at the individual level for rapid assessment of exposure events. There is a vast amount of completed and ongoing research regarding the development of new wearable technologies, but how they address the needs for military toxic exposures is unclear. Finally, non-targeted analysis of environmental samples and biospecimens can be used to identify unknown contaminants of emerging concern.

Interagency operational tasks: Performing a literature and technical review of wearable technologies and minimally invasive biospecimen collection instruments could establish new or improved techniques to capture previously unknown (or difficult to assess) exposures. Additional

validation of the technologies could provide an increased level of confidence in the measured results. Finally, a review of the logistical hurdles required for deployment of these technologies would streamline the transition of these technologies from the laboratory to the battlefield. The outcome of this task would be the inclusion of minimally invasive biospecimen collection as part of the biomonitoring scheme, including active exposure assessment and biospecimen banking for retrospective analysis. Sharing information on trusted technologies, methods, and biospecimens to the broader research community will advance evidence-based knowledge for identification of military exposures within the environment and about physiological data in individuals during training or work-related duties, while informing health data management systems.

Collaborative research opportunities: Research is needed to further understand the utility and usage of these technologies to quantify exposure biomarkers, while deployment of these technologies may require policy changes and resources. Collaborative research opportunities include:

- Expansion, development, and validation of non-targeted, threat-agnostic analytical approaches that increase the list of chemicals, substances and agents that could be studied for risk assessment.
- Implementation of these technologies for the generation of trusted data.
- Expansion, development, testing, and validation of wearable technologies and other non-invasive or minimally invasive sampling methods.
- Development of novel technologies for individual monitoring capabilities.

Category B: Linking Military Exposures to Toxicity and Adverse Health Outcomes

Bottom Line Up Front

Understanding adverse health effect(s) caused by military toxic exposures remains a challenge. To recognize a military exposure event as toxic, the exposure must be delivered in a concentration and duration necessary and sufficient to cause an adverse health outcome. These thresholds of toxicity must be assessed for each chemical, compound, or substance. Notably, exposure-induced adverse health outcomes may be impacted by genetics, sex, age, race/ethnicity, and psychosocial factors.

Background and Significance

Not all chemicals and substances in the air, drinking water and foods are fully absorbed, and the external exposure may differ from the internal doses. Furthermore, route of exposure may be an important determinant of the internal dose or downstream effects, especially in circumstances where an adverse effect is due to a metabolite of the toxicant. Elucidating toxicity thresholds of military toxicants and their interplay with subsequent biological targets will give rise to the identification of diagnostic, prognostic, and treatment-specific clinical biomarkers.

When assessing risk, one must consider both the exposure and the potential hazard of an adverse health outcome due to an exposure. Estimation of total exposures can be calculated using physiologically based pharmacokinetic models, which incorporate estimates of usage, exposure route, and body weight together with absorption, distribution, metabolism, and excretion rates.

Estimation of an association between an adverse health outcome and an exposure can be considered by the concentration, frequency, and duration of the exposure, which may be influenced by the

combined effects of other exposures with additive, potentiated, synergistic or antagonistic properties, plus genetics, sex, age, and race/ethnicity, as well as environmental factors (multi-stressor interactions).

Hence, leveraging diverse scientific approaches such as epidemiological and surveillance longitudinal studies, industrial hygiene, *in vivo* diagnostic and prognostic biomonitoring, laboratory animal studies, mechanistic and genetic studies, computer modeling, data linkage, and interdisciplinary collaborative research will be required.

GOAL 2: Prioritize and catalogue toxic exposures and associated toxicity and adverse health outcomes within the military milieu.

Identification of chronic adverse health effects of specific toxic exposures within the military milieu will cultivate new partnerships and collaborations, giving rise to greater scientific understanding and progress towards development of policies, procedures, replacements, and mitigation and prevention strategies, that together will sustain an improved quality and quantity of health for service members and Veterans.

There is uncertainty associated with understanding the threshold of toxicity for each toxicant and adverse outcome. Even when existing evidence is available, controlled studies done under laboratory conditions with animals are not always predictive of effects in humans, while surveillance and epidemiological studies often do not provide sufficient information on the threshold for toxicity. Thus, multidisciplinary approaches and synthesis of all data streams should be used to support the evidence linking exposures to adverse health outcomes.

Linking military exposures to toxicity and adverse health outcomes should be explored using systematic approaches, which could be more easily validated. Key elements of this goal include: 1) Development of policies and procedures for effective toxicological testing for new materiel and unknown mixtures, epidemiological research linking exposures to adverse effects (including timing of disease manifestation), policies and resources (including quality control/quality assurance, QA/QC, procedures) for exposure and effects characterization, development of faster, more accurate toxicology prediction models (e.g., QSAR), and new approach method development to support the development of adverse outcome pathways for faster toxicological characterization for human extrapolation; 2) Use of existing biorepositories to investigate past exposures and resultant biomarkers for adverse effect; and 3) Development of toxicological benchmarks for exposure that incorporate both prediction of toxic thresholds and protective margins of exposure for use in environmental and occupational risk assessment.

Objective 2.1: Define and catalogue priority chemicals, substances, and agents of military toxic exposures for research.

Rationale. According to the Toxic Substances Control Act (TSCA) Chemical Substance Inventory, there are nearly 50,000 chemical substances manufactured, processed, or imported in the United States[5] that can be sorted by chemical structure, use, physical or radiological properties, biologic activity, or other factors. However, these chemicals are not necessarily military- or civilian-specific, and not all chemical exposures cause adverse health outcomes at environmentally- or occupationally- relevant

[5] U.S. Environmental Protection Agency, "TSCA Chemical Substance Inventory." https://www.epa.gov/tsca-inventory (accessed May 21, 2024). Note: not all substances in use in the U.S. are in the TSCA chemical inventory due to exemptions.

concentrations. A systematic approach is needed to identify, sort, and prioritize chemicals and substances that may cause or mediate an adverse health outcome and to determine who is exposed to them (Figure 3). Expertise and perspectives from relevant federal stakeholders who are responsible for establishing exposure guidelines to protect public health, such as toxicologists, physicians, environmental epidemiologists, occupational/industrial hygiene specialists, and other related subject matter experts from the federal landscape, are vital for gathering and compiling a priority list of chemicals that align with occupational and training-related activities. This priority list would enable focused application of methods for specific detection, as well as determination of human toxicity, mode of action, and mechanism to support hypothesis-driven research and read-across methodology to fill data-gaps.

Prioritization of chemicals and substances can be considered based on their overall classification of disease and other risk factors, including prevalence and severity of putative health effects, the likelihood and extent of exposure, the toxic threshold of the chemical, the persistence and bioaccumulation potential, and the presence of military exposures to service members who are at increased/higher risk. Other considerations include regulatory classifications and guidelines established by governmental agencies and international agencies. The prioritized list of toxicants will be regularly monitored and reviewed to ensure it remains current and reflective for research by incorporating new scientific evidence, emerging hazards, changes in exposure patterns, and advancements in risk assessment methodologies.

Interagency operational tasks. To address the needs of the objective, a prioritization scheme will be developed to identify candidate chemicals, substances, and agents that exhibit potential toxicity and are used in the military milieu. This will include identification of chemicals of emerging concern. This prioritization scheme could be developed using predicted or known properties such as exposure route(s), concentration of toxicity, toxicological modes of action, and/or adverse health outcomes. It will be important to rely on existing and novel predictive models to prioritize military chemicals and substances that lack adequate data for toxicological research. Environmental exposures can be to complex mixtures of chemicals that may be acting synergistically or antagonistically. As part of the prioritization process for chemicals and substances, consideration should also be given on how to treat complex toxicant mixtures in the environment. Mixtures and unknown or uncommon chemicals remain a concern due to their lack of toxicity data and/or methods to capture and identify them. Identification and characterization of these toxicants would be a big step forward.

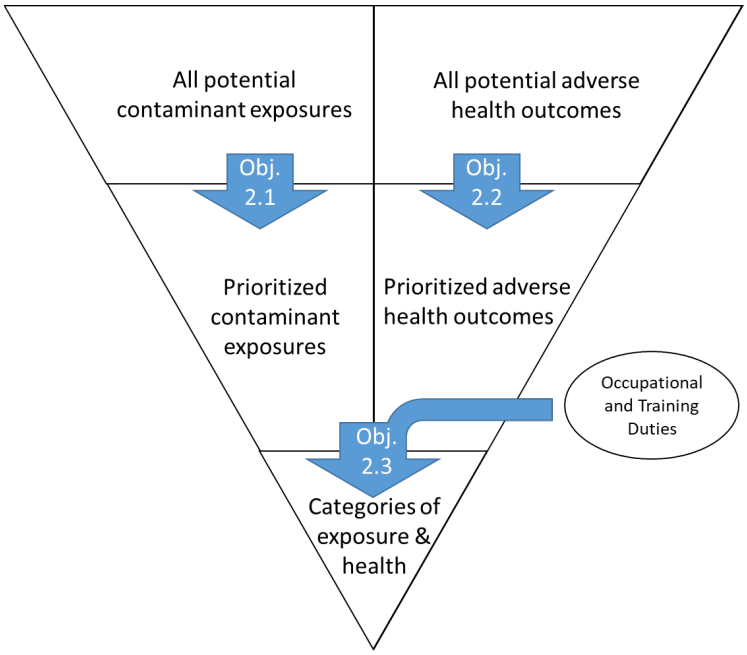

Figure 3. A prioritization scheme of all potential contaminant exposures and adverse health outcomes, aligned with training and military occupational duties and categorized with exposures & health.

Objective 2.2: Define and catalogue priority disease categories and International Classification of Diseases (ICD) diagnostic codes of military toxic exposures for research.

Rationale. The internal exposome facilitates development and progression of symptoms and chronic diseases from military exposures. Classification of diseases allows alignment for downstream methodological applications involving prevalence, severity, incidence, statistical analyses, and data science applications such as machine learning/artificial intelligence and causal inference methods, including directed acyclic graphs (DAG) and structural equation modeling, to name a few. Moreover, International Classification of Diseases (ICD) clinical modification diagnostic codes and/or the Systematized Nomenclature of Medicine Clinical Terms (SNOMED CT) can be linked to chronic adverse health outcomes. Chronic adverse health outcomes should be prioritized and aligned with priority military chemicals and substances of concern. Diagnostic ICD clinical modification codes and SNOMED CT codes should be linked, and all catalogued in a data base.

Interagency operational tasks. To achieve this objective, member agencies will first identify and classify adverse health outcomes and disease categories. Subject matter expertise from the participating agencies will be engaged to prioritize disease categories based on considerations such as disease severity, disability burden, prevention and/or mitigation methods, and quality and quantity of life. Aligning the ICD clinical modification codes and/or the SNOMED CT with priority adverse health outcomes/disease categories provides a standardized way to categorize and classify health conditions, diseases, and disorders. Transdisciplinary researchers can use these codes to accurately document and categorize the health outcomes being studied and support the collection, testing, and analysis of specimens and data and inform machine learning and common data elements. This objective will also support epidemiological studies, health services research, clinical trials and outcomes research, and health policy. Trends will be evaluated among Veterans' benefits claims, electronic health records, or health care utilization records, that align with occupation and training

duties, adverse health outcomes, and/or priority chemicals and substances and environmental exposures. Lastly, it will be important to provide recommendations to the VA Military Environmental Exposures Sub-Council (MEESC) regarding results of investigations and lessons learned related to military exposures for inclusion of potential presumptive disabilities monitoring.

Collaborative research opportunities:

- Understanding the physical properties of the chemical, substance, and agent can be used to infer biological outcomes of exposure.
- Evaluation of investigations and lessons learned from retrospective workplace and training exposures can inform future risks and mitigation approaches.
- Incorporating *in vitro*, *in vivo*, and *in silico* models into the controlled exposure testing of contaminants of concern, including complex mixtures.

Objective 2.3: Investigate exposures and effects aligned with similar exposure groups (SEGs) and training duties across the military milieu.

Rationale: SEGs or job exposure matrices (JEMs) are used to assess workplace exposures. SEGs focus on grouping individual workers based on similarities in occupational tasks and exposure profiles within a specific military occupational specialty. SEGs and training duties should be aligned and categorized with key exposures and health. Utilizing these categorical frameworks will provide opportunities to bridge adverse effects effectively using epidemiological techniques. Objective criteria such as exposure biomarker levels, frequency of exposure, and duration of exposure can be included into the SEG or JEM and linked to mode of action and reports of adverse effects evaluated using epidemiological studies and other data streams for more rigor.

Interagency operational tasks: Categorization of SEGs across all military branches would be created by their respective occupational and environmental health and industrial hygiene subject matter experts. A database containing the various key exposure and adverse health categories will be created to enable association with SEGs and training duties. Trends will be evaluated among Veterans' benefits claims, electronic health records, or health care utilization records that align with occupational and training duties, adverse health outcomes, and/or priority chemicals and substances and environmental exposures. Recommendations will be provided to the VA MEESC regarding results of investigations and lessons learned related to military exposures for inclusion of potential presumptive disabilities monitoring.

Collaborative research opportunities: Collaborative research opportunities that would advance understanding of specific chemicals and substances associated with occupational and training duties include:

- Studies that evaluate biological plausibility and adverse health outcomes from military exposures aligned and prioritized with SEGs and/or JEMs.
- Identification of SEGs and/or JEMs using existing retrospective military cohorts or federal data sources such as the Individual Longitudinal Exposure Record (ILER).

GOAL 3: Investigate associations and interplay between priority military toxic exposures, toxicological endpoints, and adverse health outcomes.

There is a need to work across mission-aligned federal funding agencies to coordinate transdisciplinary research that narrows the gaps of evidence linking military exposures to toxicity and adverse health outcomes. Human epidemiological studies provide the most direct relevance linking exposures to adverse outcomes, but these studies can be limited by incomplete exposure assessment and the time it takes to conduct longitudinal studies. Controlled studies done under laboratory conditions with animals allow for more precise control of exposure but are not always predictive of effects in humans. Furthermore, a mechanistic understanding of toxicokinetics, toxicodynamics, and mode of action is needed to understand cause and effect relationships and human relevance.

This work can include a better understanding of the interaction between psychosocial stress and toxic exposures and their combined impact on the toxicological endpoints. To most accurately represent the total human exposome and associated cumulative health effects in a military population, there is growing consensus that exposure science needs to holistically account for SDOH. All three evidence streams are required to assist in providing more definitive risk assessment, preventive medicine practice, countermeasures (prophylaxis), and informed health care and therapeutics. Information obtained from the tasks in this goal will assist other goals related to prevention and characterization of adverse effects (from past exposures). Hazard assessments are needed for each airborne hazard that determine whether there is sufficient evidence in humans and animals, as well as biological mechanisms between species, to support relevance and extrapolation. Information gathered from Goal 2 will help prioritize and support this effort. TERWG members will coordinate the integration of data streams for effective hazard assessment and decision-making.

Objective 3.1: Coordinate transdisciplinary research across federal partners to enhance evidence-based knowledge of military toxic exposures and adverse health outcomes.

Rationale: The exposure to toxic chemicals coincident with other exposures or stressors can affect the outcome of disease. When exposed to multiple environmental toxicants or stressors (including psychosocial stress), the exposures may act either independently, additively, or in some circumstances could be enhanced or diminished by the presence of other exposures. These interrelated exposures become exponentially more complicated when exposures to multiple substances occur. Human epidemiological, laboratory animal, and mechanistic evidence streams can inform understanding of these complex environments. Human epidemiological studies typically assess complex, real-world exposures that rely on statistical models to understand the influence of individual components, but often lack adequate exposure and dose/response information. Controlled laboratory animal studies are conducted to explore the threshold for adverse effects and to explore other biological targets of toxicity. Laboratory studies occasionally expose animals to real-world environments but most often establish causal relationships between one or a limited number of toxicants and an adverse event. Mechanistic evidence (e.g., *in vitro*, human molecular epidemiology studies, human controlled exposure, animal studies) is important to advance our interpretations of human and animal studies. Differences in genotype or past exposures (epigenetics) can modify predictions. This objective strives to explore more accurate methods to evaluate effects from mixtures to conduct risk assessment and prevent disease from exposures to multiple airborne hazards.

Collaborative research opportunities: Coordinated transdisciplinary research across the federal spectrum can build evidence-based knowledge needed to understand the mechanism and/or mode of

action, which is essential for comprehending how a substance interacts with biological systems and can inform various applications, such as drug development, toxicology, and environmental risk assessment. Classifications of specific substances can be supported by understanding biological targets, molecular mechanisms, functional effects, dose-response relationships, or toxicological implications, and can later inform therapeutic applications. Read-across surrogates could be tested for mode of action and compared. This will allow expansion of knowledge in exposure characterization. Collaborative research opportunities in this area include studies regarding the:

- Application of quantitative adverse outcome pathways (AOPs) and networks to provide a structured approach to understanding and predicting the toxicological effects of chemicals by linking molecular initiating events (MIEs) to adverse outcomes through a series of intermediate biological events, known as key events.
- Understanding of toxic molecular mechanisms to inform identification of mode of action, dose response relationships, human relevance of adverse effects identified in animals, susceptible genetic phenotypes, and risk from influence of multiple chemicals and stressors.
- Evaluation of exposure response relationships that are derived after synthesizing the various evidence streams, which include epidemiological studies, laboratory animal studies, mechanistic data and *in silico* predictions.
- Incorporation of diverse evidence streams, such as information from systems biology or epidemiological studies, to better understand the contributing effects of stress on adverse health outcomes, including reduced immunity and susceptibility to pathogens.
- Incorporation of stress biomarkers, stress questionnaires, discrimination, etc. for a comprehensive evaluation of stress and its impact on disease susceptibility.
- Development of artificial intelligence (AI), including machine-learning algorithms, modeling approaches, large-language models, and other state-of-the-art computational techniques to equitably evaluate large population sets to understand trends, make predictions of outcomes, efficiently process large quantities of data, and harmonize data originating from different sources.
- Understanding of the risks of airborne hazards, including a framework to prioritize airborne exposures of concern and chemical analyses of formalin-fixed and/or stored lung biospecimens from deployed and non-deployed servicemembers.

Objective 3.2: Integrate preserved biospecimens (e.g., serum, dried blood spots, tissues) to investigate exposure and biomarkers of effects.

Rationale. Exposure to substances in air, soil, or water is often assumed based on environmental sampling or job codes, even without direct analysis of biospecimens. Exposure reconstruction based on environmental sampling, job codes, and other factors may not accurately represent the individual exposure. Often chemicals are not evenly or consistently found in environmental media, and many substances are not efficiently absorbed into the bloodstream. Exposure estimates based on these external measures may also not consider factors such as engineering controls or personal protective equipment used by military personnel, and they also fail to incorporate the impacts of genetic, sex, age, and race/ethnicity differences or social stressors on toxicant exposure, absorption, distribution, metabolism, and excretion. Detecting specific concentrations in biospecimens (e.g., blood, sera, plasma, tissue) provides strong and useful evidence of exposure and allows toxicologists to link exposures with disease. When precise disease etiology is not known, health researchers can

investigate the same tissue to examine both biomarkers of exposure and effect, hence linking exposures more directly with disease incidence.

Collaborative research opportunities:

- Investigate novel methods of chemical and substance detection in vivo or ex vivo using biological samples collected from individuals with prioritized adverse health outcomes.
- Retrospective analysis of previously collected and analyzed samples for biomarkers of exposure and effect, leveraging on-going proof of concept studies and feasibility analysis.
- Studies to understand the link between exposure assessments and exposure biomarkers to allow for increased validity of exposure biomarkers used in population-based studies and to further align data obtained from human and animal studies.
- Epidemiological studies that examine the associations between measured environmental contaminants and observed adverse health outcomes.

Objective 3.3: Define and coordinate transdisciplinary research across mission-aligned federal funding partners to improve understanding of genetic, sex, age, and race/ethnicity differences in health outcomes due to key military toxic exposures.

Rationale. Understanding potential military toxic exposures and associated health outcomes only yields a partial picture of the impact of these exposures on our Veterans. To fully understand this impact, individual characteristics and variabilities need to be factored in. Identifying susceptible populations who may be disproportionately impacted can yield more equitable outcomes. This objective will evaluate genetic, sex, age, and race/ethnicity differences in susceptibility to adverse health outcomes (prevalence and severity) due to military toxic exposures and will develop novel methods to better assess these differential impacts to fill knowledge gaps more efficiently and effectively.

Interagency operational tasks: This task will catalogue Veteran populations that may be at greater risk, disproportionately affected, and/or disproportionately impacted by toxicant-induced adverse health outcomes. This area leans on advancing knowledge of the internal exposome or the biological impact of military exposures. Understanding specific Veteran populations who may be disproportionately impacted will allow for more holistic mitigation and prevention strategies and yield more equitable outcomes. The data streams used to support VBA, VA MEESC team, and the Presumptive Decision Process (PDP) will then be evaluated.

Collaborative research opportunities: To address the research gaps within this objective, there are opportunities for interagency-coordinated research to:

- Evaluate combined health impacts from priority military toxic exposures in at-risk and disproportionately affected Veteran populations.
- Evaluate genetic and psychosocial factors that increase risk caused by military toxic exposures.
- Utilize systems biology or computational modeling techniques to increase understanding of environmental modulators of sensitivity such as stress within those models.
- Conduct longitudinal health surveillance in populations with known exposures.

CATEGORY C: Mitigation of Military Toxic Exposures and Improved Screening for Associated Health Outcomes

Bottom Line Up Front

With the understanding that exposures to chemical(s), substance(s), airborne hazards, and/or physical and biological warfare agents within the military environment occur and may cause an adverse health outcome under sufficient conditions, attention to prevention and mitigation will support the National Security mission and lead to improved quality and quantity of life for servicemembers and Veterans. Mitigation and prevention are dependent upon knowing what exposures will occur or have occurred and what adverse health outcome to monitor for, in addition to knowing who may be at risk.

An objective approach to reducing exposure-induced adverse health effects will preserve military readiness. As understanding of causal links between military exposures and adverse health outcomes becomes clearer, particularly with respect to how the diversity of at-risk populations are unequally impacted, communication strategies to relevant stakeholders will be critical.

Background and Significance

Prevention, mitigation, and treatment can be considered as separate processes, where prevention seeks to eliminate the impact of − or susceptibility to − military exposures, and mitigation approaches seek to reduce the health impact after the military exposure(s) have occurred. Treatment can occur as a prevention (prophylactic before the exposure) or as a mitigation (post-exposure). Together, these processes will require an integrated approach to include exposure identification, health surveillance, technological advances, and development of screening and treatment protocols.

Transparent and clear communication around all the topics contained in this strategic plan facilitates better trust between federal agencies and the populations that rely on us. This critical aspect of the strategic plan will necessitate coordination both within and outside the federal government. Once data are generated, there is a necessity for collaborative communication efforts regarding the interpretation of the data.

GOAL 4: Preventing and Mitigating Adverse Health Outcomes from Military Toxic Exposures

Once military exposures have been identified and linked to health outcomes, it will be important to prevent future exposure and mitigate adverse health outcomes from ongoing exposures. To better understand prevention and mitigation in this specific and unique environment, civilian occupational practices can be evaluated for application in the military settings. Additionally, review and more consistent implementation of risk management procedures will greatly improve health care. This will include identifying current policies and/or procedures for industrial hygiene risk management, as well as understanding current gaps in these policies/procedures and providing recommendations to fill these gaps. Through better prevention and mitigation strategies and better risk management, there will be an overall improvement in exposure-informed health care.

Objective 4.1: Develop and recommend strategies to mitigate and/or prevent toxic exposures in the military environment.

Rationale. There is a need to prevent or mitigate current, ongoing exposures to protect from potential adverse health effects resulting from those exposures. To implement prevention and mitigation strategies effectively and efficiently, it is important to first understand current mitigation techniques (e.g., controls) and provide recommendations for additional/new uses based on contaminants identified in previous goals. These prevention and mitigation techniques should be specific enough to address those exposures and health outcomes identified in earlier tasks of this strategic plan but broad enough to address unknown and currently unidentified exposures. A primary focus should be on understanding the hierarchy of controls under occupational health and understand other mitigation techniques that can be gleaned from occupational and environmental health and industrial hygiene partners.

Interagency operational tasks. To provide substantive and meaningful strategies to mitigate and/or prevent toxic exposures, it will be key for agencies to identify the current policies and procedures and then develop recommendations. A thorough understanding of the current practices for mitigation and prevention strategies specific to both military and civilian occupational settings can inform strategies to be implemented through this strategic plan. Mitigation or prevention strategies would use the hierarchy of controls to remove hazards or reduce risk, including the use of personal protective equipment, proper exhaust ventilation, and/or appropriate workplace training. Gaps in current mitigation strategies would be identified, and recommendations for mitigation techniques can be developed and implemented as needed. Finally, there may be toxic exposure hazards that have no current solution, and the working group could develop priorities for specific exposures that require the development of new mitigation or prevention strategies.

Objective 4.2: Evaluate and develop innovative approaches for military toxic exposures health risk management.

Rationale. In addition to prevention and mitigation strategies, there is a need to understand existing gaps in risk management policies to provide recommendations for improving exposure-informed health care and allowing for holistic evaluation of health risks. This would encompass health risks from military occupational and training exposures, as well as situational (accidental) and general environmental exposures. A holistic approach can help predict complex variations of adverse health outcomes that may arise from exposure activities, environments, and situations during military service. The interagency operational tasks under this objective will aim to understand how leveraging existing trusted resources gathered and cataloged herein on toxicants, health outcomes, and identified at-risk determinants could be merged into a useful risk assessment tool to enhance exposure-informed health care. This objective will also support multi-disciplinary research with inclusion of at-risk populations to include genetics, sex, age, and race/ethnicity differences in adverse health outcomes (prevalence and severity) due to military toxic exposures.

Interagency operational tasks. Utilizing information gathered throughout this strategic plan, the working group can compile resources from both military and civilian partners on approaches to evaluating health risks associated with toxic exposures. Through the harmonization of trusted resources, including data sources, information regarding the health risks associated with toxic exposures could be shared with health care providers for exposure-informed health care. In addition, the group could align occupational and environmental health approaches for establishing exposure limit guidance values for specific toxic exposures that enable a coherent, cross-military message regarding the hazards and potential health risks.

Collaborative research opportunities. To address the research gaps within this objective, there are opportunities for interagency-coordinated research for:

- Development of datasets and data tools to calculate health risk for exposure-informed health care by providers.
- Evaluation of at-risk and/or disproportionately affected populations for risk management considerations.
- Development of an interagency-aligned framework to generate guidance values for toxic exposures.

GOAL 5: Communicate toxic exposure risk and adverse health outcomes to relevant stakeholders to enhance exposure-informed health care.

There is a need to harmonize how federal agencies communicate toxic exposure risk and adverse health outcomes using the best-available science from trusted sources. Development of communication work products should consider uncertainties and how the information should be attuned to the intended audience. Approaches should embrace concerns and experiences of exposed Veterans and their family members and caregivers. Final products should benefit VA and community care providers to educate and elevate exposure-informed health care. Each engagement necessitates careful considerations around how to best communicate and meet those stakeholders where they are. Understanding the Veteran concerns through active listening sessions will help advance the science and make the information more relevant and usable to Veterans and their health care providers. It will also be important to communicate the risks associated with the complex interactions of toxicants, genes, social factors, and other stressors that collectively determine risk of adverse health outcomes.

Objective 5.1: Foster transparency through consistent health risk communication regarding toxic exposures and adverse health outcomes.

Rationale. Consistent guidance on transparent communication around toxic exposures and adverse health outcomes for Veterans is necessary. Understanding existing procedures and protocols for communicating occupational hazards can help inform this guidance. This allows for better alignment with partners and more consistent messaging across mission-aligned federal agencies. Additionally, this allows for identification of potential disparities in community-specific health risk communication.

Interagency operational tasks. To engage the affected communities, the working group can establish a platform that provides clear communication of toxic exposures and health risks based on the best-available science from trusted sources. There is a need for different communication and educational materials for the various stakeholder groups. These materials should be targeted and meet these audiences where they are. Moreover, sharing of these communication materials both within and outside mission-aligned federal agencies allows for more consistent messaging. Documents should include communication materials for physicians and other health care providers like those provided by ATSDR on PFAS exposure, and this communication should be coordinated using a whole-of-VA approach (e.g. VHA, VBA, Office of Communication, Equity Assurance, and Outreach, Transition and Economic Development). Academic and clinical researchers could benefit from technical documents and datasets. A platform with a formalized process for disseminating

communication documents, guidance, and templates will facilitate better transparency, avoid duplication of effort, and ultimately increased trust between the federal government and stakeholders.

I. PACT Act Section 501, TERWG collaborative research infrastructure unit

Bottom Line Up Front

Implementation of the TERWG research efforts requires a whole-of-government approach with the unified goal of 1) cataloging trusted capabilities and resources that are available across federal departments and agencies, 2) identifying processes by which these capabilities can be readily shared or leveraged to support multi-disciplinary research with inclusion of genetics, sex, age, and race/ethnicity in health outcomes, and 3) advancing knowledge through collaborative research opportunities using intra- and extra-mural funding streams. Establishing a TERWG collaborative research infrastructure unit with interagency subgroups to guide directional strategies will foster success.

Background and Significance

Throughout the process of building and shaping the interagency strategic plan, questions and discussions emerged around key needs of an infrastructure unit to enhance work products, and to support implementation and collaboration capabilities. Optimization of key administrative/operational, regulatory, and technological requirements for agencies is needed to more effectively and efficiently address the infrastructural needs that enable greater sharing of resources, data, and expertise.

This infrastructure, as described below, will allow execution of the strategic plan using best practices through communication, organization, and performance measures and by aligning objectives, tasks, outcome measures, and feasibility with TERWG subgroup teams as articulated below. It focuses on three key domains – operational, scientific, and regulatory. Altogether, these domains represent areas that are required to effectively coordinate across departments/agencies in a manner that will facilitate collaborative and systematic approaches to understanding the relationship between toxic exposures and health outcomes and finding ways to prevent, diagnose or treat associated conditions.

The strategic approach herein guides research to advance the understanding of adverse health outcomes caused by military exposures. This complex approach was developed using a federal-wide initiative involving multidisciplinary subject matter experts and decision and policy makers. Working together ensures mission-aligned commitment by all federal departments and agencies involved, and it establishes a blueprint for partnership and collaboration that is similarly critical for subsequent efficient strategic implementation.

Infrastructure Strategy: Establish a TERWG collaborative research infrastructure unit for coordinating implementation of the strategic plan.

Establishment of a TERWG collaborative research infrastructure unit will support the needs for enabling critical interagency scientific, administrative, regulatory and governance/management activities. Primary activities managed by the infrastructure unit would include research prioritization, data integration, surveying, assisting to establish new funding mechanisms, communication and dissemination, evaluation and continuous improvement, and sustainability. Scientifically, particular emphasis would be placed on central data and document management, resource planning, and

maximizing the leveraging of subject matter expertise, data, biospecimen sources, and technologies across the scientific spectrum.

There are two roles that the infrastructure unit would take on: 1) establish an organizational entity dedicated to coordinating administrative, scientific, and regulatory activities for research on toxic military exposures; and 2) develop and manage mechanisms for collaborative military toxic exposures research, including governmental and non-governmental collaborations.

Role 1: Establish an organizational entity dedicated to coordinating operational/administrative, scientific, and regulatory activities for research on toxic military exposures.

Rationale. A key building block for effective interagency and partnered research with academic and private groups is an entity that has a primary duty to handle all of the required activities involved with this work. These efforts should not be understated and would require leadership from multiple agencies to inform and guide the activities that meet respective requirements. Additionally, it would help facilitate a more systematic approach to program development in areas of toxic exposure research and infrastructure building supported by federal agencies.

Within this role, the infrastructure unit would:

- **Establish an infrastructure framework for a TERWG-guided federal partnership**, which would focus on administrative staff to support and track activities under this strategic plan. In addition, it would support the scientific directions and identified regulatory requirements proposed by the TERWG to provide a centralized hub to help align and communicate efforts.
- **Establish organizational units (referred to as "subgroups") under the context of the TERWG to support execution of the strategic plan.** It is expected that subgroups consisting of multidisciplinary subject matter experts will need to be supported by the infrastructure unit to plan, organize, and carry out particular focus areas under the strategic plan. Subgroup leadership would be charged with developing expected metrics, products, and any resource needs to achieve their objectives.

Role 2: Develop and manage mechanisms for collaborative military toxic exposures research, including governmental and non-governmental collaborations.

Rationale. Collaboration between government entities, academic institutions, and biotech companies requires much work to ensure that scope of work, dedicated resources and other legal requirements are properly addressed. Various types of mechanisms to establish collaborations, depending on whether they are federal or private entities exist including interagency agreements, collaborative research and development agreements (CRADA), material and transfer agreements, and data use agreements. Furthermore, strategies can be employed to establish an umbrella or master agreement that enables more specific project-based agreements.

Within this role, the infrastructure unit would:

- **Establish agreement models needed for governmental and non-governmental collaborations.** Coordinating multiple agencies' ability to work together in a legal and structured manner requires one or more agreements in place. Agreements would emphasize

scientific activities that may involve infrastructure or project-specific activities, as well as general access to biorepositories. Besides specific activities and prerequisite resources for conducting the scope of work, agreements should include, when appropriate, principles for sharing work products, including publications, data and bio- materials.

- **Enable better sharing of data on toxic exposures research from trusted sources.** To optimize data resources that are available, the infrastructure unit will lead efforts for inventorying, merging, and sharing key databases of curated trusted data sources. As data sources are identified, they are expected to cover a range of categories, including ones from observational research, biospecimen collection and distribution, electronic health records, and others. As activities develop, efforts may begin to focus more on activities aimed at supporting and/or guiding activities related to data collection and use of the data in VBA and VHA processes.
- **Evaluate regulatory gaps and opportunities for interagency collaboration around toxic/military exposures research, particularly around data usage/sharing.** While there may be common frameworks in human subjects' protections, privacy, and/or confidentiality in the use of data, departments and agencies may have unique considerations both internally and for any sharing across agencies.
- **Determine budgeting processes that enable departments and agencies to better leverage respective appropriations in toxic/military exposures research.** Relevant departments and agencies may have their own respective budget and appropriations processes that are aimed at supporting mission-aligned toxic exposures research. Since such activities often involve multi-year planning processes, research plans, especially ones involving interagency collaboration, should be coordinated to help ensure that funding support can be available for those areas outlined in the strategic plan. Such coordination will also help maximize taxpayer investments to avoid redundant efforts.
- **Hold state-of-the-science conferences, or similar, with federal partners to enhance knowledge gain and flow among the military toxic exposure research community.** Collaboration across all partners—both governmental and non-governmental—strengthens understanding of exposure research. Federally hosted conferences and workshops provide the opportunity to bring together experts across all fields to further the knowledge base in an efficient and effective manner.

CONCLUSION

Implementation of this strategic plan will support Veterans through advancing research using a mission-aligned, whole-of-government approach and providing SME work products that **i)** inform the government and research field by isolating and categorizing chemicals and substances in the military occupational and environmental space where Veterans work, train, and live, **ii)** advise on quality and quantity of toxicant monitoring, detecting, standards, toxicity, and biological effects within the external and internal military exposome, **iii)** use these data to inform machine learning/AI and ILER for research, **iv**) provide recommendations and communication strategies for exposure-informed health care, and **v**) support multidisciplinary activities to close research gaps and generate evidence-and implementation-based science.

In parallel and as resources allow, federal-wide research efforts centered around the TERWG-identified collaborative research opportunities and indicated knowledge gaps will be organized and

employed using community-wide research, SME, technologies, trusted data, and specimen repositories.

The TERWG has also identified and articulated parallel topic needs within the scope of understanding health outcomes from military exposures, but outside the scope of this document:

First, gathering individual health care data in the form of diagnostic codes, laboratory data and screening data are pertinent when aligning to exposure data. This informs suspected onset and progression of disease, which provides prevalence and severity trends for research. Approximately 50% of veterans use the VHA health care system; that reflects 50% of health care information not available for case ascertainment or identification. Hence, development of a process for obtaining health care data from non-VHA users would contribute to more reliable measures for policy makers and health care staff.

Second, military personnel have expressed concerns about which toxic exposures may lead to adverse effects on their own health and whether effects from the exposures can be passed down through their descendants. Toxic exposure-induced generational health effects include male or female reproductive impairment or loss, direct gamete damage, or prenatal exposure potentially giving rise to adverse reproductive outcomes, fetal or childhood developmental defects or learning disabilities, and descendant involvement. Notably, evaluation of chemicals, substances, airborne hazards, and/or environmental factors that may result in an altered reproductive health outcome or birth defect in humans is challenging. Limitations to scientific approaches include but are not limited to: 1) small numbers of specific birth-defect cases, which are rare; 2) lack of exposure assessment at the individual level; 3) lack of a national electronic health record and birth defects database; 4) lack of long-term surveillance that tracks birth defects found later in life; and 5) barriers in approaches and methodologies to produce interpretable data. While this area of research is complex, early research suggests epigenetic processes or modifications could be a biomarker of exposure-mediated changes and a putative mechanism. Development of a National Birth Registry, and focused research on the chemicals and substances that may give rise to adverse generational phenotypes, will support effective, evidence-based research.

Third, the enactment of the PACT Act gave rise to newly presumed conditions, including specified cancers, respiratory diseases, and neurological disorders. If an individual who served in the military has a condition listed within the presumption category, the VA assumes that the service caused the condition. It will be important to incorporate knowledge gained from the successful execution of the TERWG-derived research plan and other evidence-based research derived from trusted data sources into the new presumptive process model for determination of benefits.

Fourth, with release of the Individual Longitudinal Exposure Record (ILER), a DOD and VA database that compiles declassified Defense Manpower Data Center (DMDC) records from January 2001 to the present allows physicians, benefit examiners, and governmental staff to evaluate a servicemember's proximity to potential exposures monitored geographically by environmental health or industrial hygiene using air, soil, and water. ILER use for research is in its infancy. Completion of the goals and objectives within this strategic plan will add work products to support users of ILER and strengthen ILER for research.

Fifth, the public health community recognizes that race is a social/political construct and not a fixed biological effect and recommends considering structural racism as a factor in environmental health and as a contributor to exposure and health disparities. As such, the concept of environmental justice

applies within the military context. The Department of Defense and Department of Veterans Affairs have recognized the importance of addressing environmental justice in their missions.[6, 7-8]

Sixth, the "One Health" concept recognizes that human health is intertwined with the health of animals and the shared environment. It will be important to identify research data gaps that strive to understand how environmental releases to non-human entities may affect human health. This transdisciplinary approach should consider the full life cycle of military chemicals from synthesis to disposal and also address potential impacts of soil and water contamination to the ecosystem and their subsequent effects on human health.

Taken together, parallel topic needs identified include, but are not limited to, investigation into the roles of military exposures upstream and downstream of SDOH, environmental justice, gender identity with and without hormone therapy, occupational interventions, mental health, aspects of blast exposures, SARS-CoV-2 infection, and pulse acute exposures within this purview and risk assessment workstreams.

Finally, aligning the efforts herein with other federal efforts under the EOP umbrella can leverage mutual activities, agreements in a reciprocal manner, and provide synergistic and unduplicated knowledge gained.

[6] U.S. Department of Defense, "Department of Defense Environmental Justice," July 2023. (https://www.denix.osd.mil/ej/)

[7] U.S Department of Veterans Affairs, "Energy, Environment and Fleet Program." April 2024. (https://department.va.gov/administrations-and-offices/management/asset-enterprise-management/energy-environment-and-fleet-program/#seven)

[8] U.S Department of Veterans Affairs, "Sustainability Plan," October 2022. (https://www.sustainability.gov/pdfs/va-2022-sustainability-plan.pdf)

APPENDIX A: Interagency operational tasks and mission-aligned collaborative research opportunities for the implementation of the Strategic Plan

INTRODUCTION TO APPENDIX A

This appendix elaborates on details regarding actions and deliverables that were highlighted in the TERWG strategic plan. With limited resources and timelines, execution of all possible interagency operational tasks and mission-aligned collaborative research opportunities are not feasible; however, they do reflect research activities needed to achieve foundational progress aimed at improving Veteran outcomes and health among those affected by toxic exposures.

Responsibilities and implementation include the following priorities:

- Establishing a TERWG collaborative research infrastructure unit with interagency TERWG subgroups to guide directional strategies.
- The TERWG subgroups will consist of interagency co-leads and members with multidisciplinary subject matter expertise to conduct the interagency operational tasks or collaborative research opportunity.
- TERWG subgroups will be supported by the TERWG collaborative research infrastructure unit to plan, organize, and conduct particular focus areas under the strategic plan. Subgroup leadership will be charged with developing expected metrics, work products, and a list of resource needs to achieve their objectives.
- Prioritization of interagency operational tasks and collaborative research opportunities to be initiated will be decided by the TERWG parent committee.
- The interagency operational tasks and collaborative research opportunities will be pursued concurrently and will be initiated at staggered times throughout the five years. Initiation of tasks will be determined by prioritization, sequential needs, and available resources. Completion of a chosen task or activity could last from one to five years from the year of initiation.

HOW THESE GOALS WILL BE ACCOMPLISHED

To support implementation of the five-year strategic plan, it is proposed that the TERWG would serve as the primary body for organizing and prioritizing topics and activities set forth in the strategic plan. To achieve this goal, the Co-Chairs would work with OSTP and VA leadership to establish a charge and identify any logistical requirements. Since the TERWG has already been established as a branch of the JEEP, these actions primarily serve to establish a group of agency experts representing interested parties. This effort would be completed within one year of the submission of the mission-aligned, interagency TERWG strategic plan to Congress.

As noted within this strategic plan, a collaborative infrastructure unit is proposed to support the TERWG and its subgroups to guide directional strategies with specific goals to ensure success in achieving Section 501 PACT Act goals. This infrastructure unit is proposed to be supported by VA under its research enterprise efforts led by the VHA Office of Research and Development (ORD). ORD has experience in setting up and utilizing infrastructure units with goals to achieve disease/condition-based research. VA has been allocated funding through the Toxic Exposures Fund for such purposes and would pursue organizational efforts to support a unit.

While a coordinating infrastructure unit is being established, VA would leverage existing resources, such as the Military Exposures Research Program and Gulf War Research Program staff to help with initial efforts in coordinating meetings and related administrative tasks for the TERWG. ORD would also be seeking other potential resources within VA or among other agencies, if available. An initial meeting of the TERWG for purposes of forming subgroups would be held within three months of submitting the strategic plan to Congress. Importantly, leadership of the subgroups will represent agencies that have programs within the topic areas to ensure interagency support and mission-aligned continuity.

KEY ACCOMPLISHMENTS

The strategic plan proposes a set of collaborative research activities organized as **1)** interagency operational tasks related to the development of common source work products, with emphasis on references, guidance, and standards for toxic exposure research and **2)** mission-aligned collaborative research opportunities that are focused on advancing evidence-based toxic exposure research.

Short-term elements of the strategic plan include:

- Continuation of the EOP/OSTP/JEEP TERWG partnership and use of the infrastructure.
- The establishment of a TERWG collaborative research infrastructure unit dedicated to administrative and regulatory activities to coordinate and facilitate interagency research efforts on toxic military exposures.
- Selected interagency operational tasks intended to provide a common source of information for all agencies around:
    - Policies and procedures for sample collection and analysis.
    - Trusted sources for detection of chemicals, substances, and agents in human tissue.
    - Creation of a catalogue of military exposures linked to military duties and adverse outcomes.
    - Creation of a list of ICD codes for chronic priority adverse health outcomes.
    - Development of a coordinated strategy among agencies for extramural funding of research.
    - Development of a public-facing repository for information to share results from this work.

Longer-term elements of the strategic plan (i.e., that may require more than the 5-year timeframe and/or are continual in nature) would include key mission-aligned, collaborative research opportunities, such as:

- Understanding, evaluating, and implementing methods and techniques to assess/measure exposures, including using new technologies.
- Coordinating activities around a set of areas of research to understand military exposures in the military milieu.
- Conducting specific, collaborative research activities that would be multi-year in nature.
- Validating/corroborating assessments and their relationship to health outcomes.

- Defining populations that are at risk for exposure and/or subsequent adverse health outcomes.
- Holding state-of-the-art conferences with federal partners.
- Developing and refining the framework for other determinants of health and/or factors that may affect understanding and subsequent treatment of exposed Veterans.

KEY WORK PRODUCTS

GOAL 1 ALIGNMENT

Interagency Operational Tasks - Work Products

- Develop a white paper and/or data set on current capabilities for environmental health and industrial hygiene monitoring within the military.
- Develop a white paper and/or data dictionary on current agency capabilities for detection of military exposures of individuals.
- Develop a white paper and/or recommendations on currently available and emerging technologies that enhance the military's ability to detect environmental, occupational, and training exposures.

Collaborative Research Opportunities - Work Products

Success will be defined as collaboration among agency research programs and/or extramural funding agencies to address Goal 1 research needs, including the initiation of collaborative research activities and/or the development of requests for applications (RFA) with subsequent peer-review and funding of research applications. Funded research projects will be tracked.

GOAL 2 ALIGNMENT

Interagency Operational Tasks - Work Products.

- Develop recommendations and/or a data set for identifying trusted sources of information on priority chemicals, substances, and agents of military toxic exposures.
- Develop a white paper and/or data set on methods and conclusions of creating and prioritizing disease categories for military exposures.
- Develop a white paper and/or data dictionary on methods and conclusions of categorizing SEGs across military branches, and if time allows training duties.

Collaborative Research Opportunities - Work Products

Success will be defined as collaboration among agency research programs and/or extramural funding agencies to address Goal 2 research needs, including the initiation of collaborative research activities and/or the development of requests for applications (RFA) with subsequent peer review and funding of research applications. Funded research projects will be tracked.

GOAL 3 ALIGNMENT

Interagency Operational Tasks - Work Products

- Develop a white paper and/or database on the available biospecimen repositories and associated metadata available for research.

- Develop a white paper and/or database on the impact of the internal exposome on susceptibility to toxicant-induced diseases.

Collaborative Research Opportunities - Work Products

Success will be defined as collaboration among agency research programs and/or extramural funding agencies to address Goal 3 research needs, including the initiation of collaborative research activities and/or the development of requests for applications (RFA) with subsequent peer-review and funding of research applications. Funded research projects will be tracked.

GOAL 4 ALIGNMENT

Interagency Operational Tasks Work Products

- Develop a white paper on best practices to mitigate and prevent military exposures-induced adverse health outcomes.
- Develop a white paper on defining Veteran populations that are at-risk, disproportionately affected, and/or disproportionately impacted by adverse health outcomes related to toxic exposures.
- Develop a white paper on methods of developing a risk assessment model for military exposures with inclusions of at-risk models.

Collaborative Research Opportunities Work Products

Success will be defined as collaboration among agency research programs and/or extramural funding agencies to address Goal 4 research needs, including the initiation of collaborative research activities and/or the development of requests for applications (RFA) with subsequent peer-review and funding of research applications. Funded research projects will be tracked.

GOAL 5 ALIGNMENT

Interagency Operational Tasks - Work Products

- Develop educational materials that communicate toxic exposures and health risks to educate military personnel, Veterans, and health care providers.

Collaborative Research Opportunities Work Products

Success will be defined as collaboration among agency research programs and/or extramural funding agencies to address Goal 5 research needs, including the initiation of collaborative research activities and/or the development of requests for applications (RFA) with subsequent peer-review and funding of research applications. Funded research projects will be tracked.

KEY REPORTING FOR SUCCESS:

Each legislatively mandated annual progress report as outlined in P.L. 117-168, will include those prioritized interagency operational tasks and collaborative research opportunities that were delineated, initiated, in-progress, and completed.

APPENDIX B: TERWG Partners: Federal Agency Descriptions

ABOUT PARTNERING DEPARTMENTS AND AGENCIES

Agency for Toxic Substances and Disease Registry (ATSDR): ATSDR is an independent operating agency within the Department of Health and Human Services, the Centers for Disease Control and Prevention Director serves as ATSDR administrator. ATSDR is responsible for assessing the health impacts of exposure to hazardous substances in communities. ATSDR conducts toxicological evaluations, assesses exposure risks, and provides public health guidance to communities affected by environmental contamination.

Centers for Disease Control and Prevention (CDC): The Centers for Disease Control and Prevention is under the Department of Health and Human Services. The agency's main goal is the protection of public health and safety through the control and prevention of disease, injury, and disability in the U.S. and worldwide. The CDC focuses national attention on developing and applying disease control and prevention.

Defense Health Agency (DHA): The Defense Health Agency is a joint, integrated Combat Support Agency that enables the Army, Marines, Navy, Air Force, and Space Force medical services to provide a medically ready force and ready medical force to Combatant Commands in both peacetime and wartime. The DHA uses the principles of Ready Reliable Care to advance high reliability practices across the Military Health System by improving system operations, driving innovative solutions, and cultivating a culture of safety.

Department of Commerce (DOC): The United States Department of Commerce is an executive department of the U.S. federal government concerned with creating the conditions for economic growth and opportunity.

Department of Defense (DOD): The Department of Defense (DOD) is responsible for coordinating and supervising all agencies and functions of the government related to national security and the armed forces.

Department of Energy (DOE): The Department of Energy addresses energy, environmental, and nuclear challenges through transformative science and technology solutions. DOE is the nation’s leader in the physical sciences; advances biological, environmental, and computational sciences; and provides premier scientific instruments for the Nation's research enterprise.

Department of State (DOS): The Department of State is responsible for conducting U.S. foreign policy, representing the United States internationally, and promoting diplomatic relations with other countries and international organizations.

Department of Veterans Affairs (VA): The Department of Veterans Affairs (VA) is responsible for providing a wide range of services and benefits to military Veterans, their families, and survivors. The VA operates the nation's largest integrated health care system and offers various programs and resources to support Veterans in areas such as education, employment, housing, disability compensation, and burial benefits.

Environment, Health, Safety & Security (EHSS): EHSS is responsible for policy development and technical assistance; safety analysis; and corporate safety and security programs. The Office of

Environment, Health, Safety and Security advises DOE Senior Leadership on all matters related to environment, health, safety, and security across the complex.

Environmental Protection Agency (EPA): The Environmental Protection Agency is responsible for protecting human health and the environment by regulating pollutants and establishing exposure guidelines for various chemicals and substances. The EPA conducts risk assessments to evaluate the toxicity of chemicals and sets regulatory standards, such as Maximum Contaminant Levels (MCLs) for drinking water and National Ambient Air Quality Standards (NAAQS) for air pollutants.

EPA Office of Research and Development (EPA-ORD): The Office of Research and Development (ORD) is the scientific research arm of EPA. ORD's leading-edge research informs agency decisions and supports the emerging needs of EPA stakeholders, including the agency's state, tribal, and community partners.

Executive Office of the President (EOP): The Executive Office of the President (EOP) is a collection of agencies and offices that support the President of the United States in carrying out their constitutional duties and responsibilities. The EOP serves as the administrative arm of the President and facilitates the implementation of presidential policies and initiatives.

Federal Electronic Health Record Modernization (FEHRM): The goal of the Federal Electronic Health Record Modernization office is to implement a single, common federal electronic health record to enhance patient care and provider effectiveness, wherever health care is provided.

Health and Human Services (HHS): The goal of the U.S. Department of Health and Human Services (HHS) is to enhance the health and well-being of all Americans, by providing for effective health and human services and by fostering sound, sustained advances in the sciences underlying medicine, public health, and social services.

Health Outcomes Military Exposures (HOME): Health Outcomes Military Exposures (HOME) (formerly Post Deployment Health Services) is part of VA's Office of Patient Care Services and administers various programs related to environmental and occupational exposures of U.S. Veterans during military service. HOME is a VA-delivered core service. HOME also manages the War Related Illness and Injury Study Center, which provides clinical care, research, and education for Veterans with deployment-related health concerns.

Joint Program Committee (JPC): Joint Program Committees consist of Department of Defense and non-DOD medical and military technical experts. These experts work through coordinated efforts to translate guidance into research and development needs. They also have key responsibilities for making funding recommendations and providing program management support.

Joint Subcommittee on Environment, Innovation, and Public Health (JEEP): The Joint Subcommittee on Environment Innovation and Public Health (JEEP) is chartered under the National Science and Technology Council (NSTC) to promote federal cross-disciplinary research and development. The JEEP provides coordination and guidance to its strategy teams, including those focused on the discussion of sustainable chemistry, contaminants of emerging concerns, and per- and polyfluoroalkyl substances. On behalf of the White House, the JEEP reports to Congress on landscape and gap analysis, strategic planning, coordination of federal research, and recommendations of policy options.

Military Environmental Exposures Sub-Council (MEESC): A chartered joint VHA and VBA governing body that oversees VA's implementation of § 202 of the PACT Act, the Presumptive Decision Process,

and other issues relating to military environmental exposures. The VA MEESC is co-chaired by the Chief Consultant of HOME and the Executive Director of CS.

Military Exposures Team (MET): resides within the Veterans Benefits Administration's Compensation Service program office. The scope of the MET's work encompasses the comprehensive management of policy and procedural development related to toxic environmental exposure claims for disability compensation benefits, drawing from the broader objectives of Compensation Service. This includes qualitative analysis of claims, policy implementation, data analysis, and continuous improvement of processes and supporting training related to the administration of toxic environmental exposure benefits.

National Center for Environmental Health (NCEH): CDC's National Center for Environmental Health (NCEH) plans, directs, and coordinates a program to protect the American people from environmental hazards. We promote a healthy environment and prevent premature death, avoidable illness, and disability caused by non-infectious, non-occupational environmental and related factors.

Naval Health Research Center (NHRC): The Naval Health Research Center (NHRC) manages and executes expeditionary operational medical research, development, test and evaluation programs for the Naval Medical Research Command, Naval Medical Forces Support Command, and the Navy Bureau of Medicine and Surgery. NHRC serves as a leading research and development laboratory for the DOD.

National Institute of Environmental Health Sciences (NIEHS): The National Institute of Environmental Health Sciences (NIEHS) is part of the National Institutes of Health (NIH) within the U.S. Department of Health and Human Services. The mission of the NIEHS is to discover how the environment affects people to promote healthier lives.

National Institutes of Health (NIH): The National Institutes of Health (NIH) is the is the primary agency of the United States government responsible for biomedical and public health research. The NIH conducts its own scientific research through the NIH Intramural Research Program (IRP) and provides major biomedical research funding to non-NIH research facilities through its Extramural Research Program.

National Institute for Occupational Safety and Health (NIOSH): NIOSH is part of the Centers for Disease Control and Prevention (CDC) and is responsible for conducting research and providing recommendations to prevent work-related injuries, illnesses, and fatalities. NIOSH conducts toxicological evaluations, develops exposure limits, and publishes guidance documents to protect workers from occupational exposures.

National Institute of Standards and Technology (NIST): The National Institute of Standards and Technology is a non-regulatory agency of the United States Department of Commerce. NIST's primary mission is to promote innovation and industrial competitiveness by advancing measurement science, standards, and technology.

National Toxicology Program (NTP): The NTP is an interagency program coordinated by the Department of Health and Human Services (HHS), which includes the National Institutes of Health (NIH), CDC, and FDA. The NTP conducts toxicological research, evaluates the carcinogenicity and toxicity of chemicals, develops new tools and approaches to better predict how chemicals affect human health, and provides authoritative information on chemical hazards to the public.

Office of the Assistant Secretary of Defense for Energy, Installations, and Environment (ASD(EI&E)): The Assistant Secretary of Defense for Energy, Installations, and Environment (ASD(EI&E)), concurrently the Chief Sustainability Officer, and formerly known as the Deputy Under Secretary of Defense for Installations and Environment (DUSD(I&E)), provides management and oversight of military installations worldwide and manages environmental, safety, and occupational health programs for the Department of Defense (DOD).

Office of the Assistant Secretary of Defense for Health Affairs (OASD(HA)): The OASD(HA) is chartered under the Department of Defense (DOD) Directive 5136.01and is the principal staff element for all DOD health and force health protection policies, programs, and activities including the Integrated Disability Evaluation System.

Office of the Assistant Secretary of Defense for Readiness (ASD-R): The mission of the Assistant Secretary of Defense for Readiness is to develop DOD policies, plans, and partnerships to ensure the readiness of the Total Force to execute the National Defense Strategy.

Office of Management and Budget (OMB): The Office of Management and Budget (OMB) serves the President of the United States in overseeing the implementation of his or her vision across the Executive Branch. OMB's mission is to assist the President in meeting policy, budget, management, and regulatory objectives and to fulfill the agency's statutory responsibilities.

Office of Science and Technology Policy (OSTP): The Office of Science and Technology Policy, part of the Executive Office of the President, was established under law on May 11, 1976, with a broad mandate to advise the President on the effects of science and technology on domestic and international affairs.

Occupational Safety and Health Administration (OSHA): OSHA is part of the U.S. Department of Labor and is responsible for ensuring safe and healthful working conditions for workers. OSHA establishes Permissible Exposure Limits (PELs) for workplace chemicals based on toxicological evidence and exposure assessments to protect workers from occupational hazards.

Veterans Benefits Administration (VBA): The Veterans Benefits Administration is an agency of the U.S. Department of Veterans Affairs. It is responsible for administering the Department's programs that provide financial and other forms of assistance to Veterans, their dependents, and survivors.

Veterans Health Administration (VHA): The Veterans Health Administration (VHA) is an agency of the U.S. Department of Veterans Affairs. It is the largest integrated health care system in the United States, providing care at 1,300 health care facilities, including 170 VA Medical Centers and 1,100 outpatient sites of care of varying complexity (VHA outpatient clinics) to over 9 million Veterans enrolled in the VA health care program.