

The Congressionally Directed Medical Research Programs' Toxic Exposures Research Program

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21 November 2024



Transforming Health Care through Innovative and Impactful Research



CDMRP
DEPARTMENT OF DEFENSE
**CONGRESSIONALLY DIRECTED
MEDICAL RESEARCH PROGRAMS**

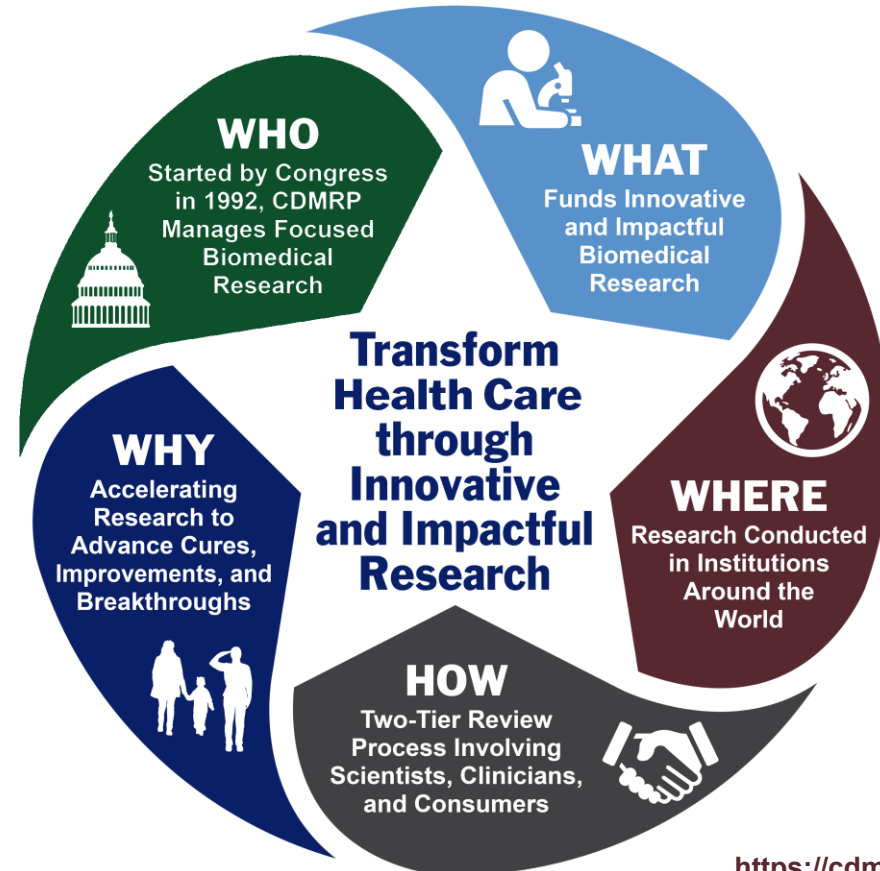
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- CDMRP Overview
- Toxic Exposures Research Program, TERP
- Gulf War Illness Research
- TERP Coordination Efforts

About CDMRP

Mission

Responsibly manage collaborative research that discovers, develops, and delivers health care solutions for Service Members, their Families, Veterans and the American public



<https://cdmrp.health.mil>

IMPACT



- Funds impactful, innovative research for specific programs added by Congress to the Defense Appropriations Bill
- Targeted research fills gaps and addresses high-priority needs
- Focused on improving health, well-being, and health care quality for those affected

STRATEGY



- Annually adapts each program's vision and investment strategy, allowing rapid response to changing needs, opportunities, and congressional intent
- Publicly announces and competes funding opportunities
- Ensures scientific excellence and programmatic relevance through the National Academy of Medicine-recommended two-tier review process

Hallmarks, cont'd

COLLABORATION



- Integrates consumers as full participants throughout program processes and as the “True North” of CDMRP
- Collaborates with other funding organizations – complementary, not duplicative

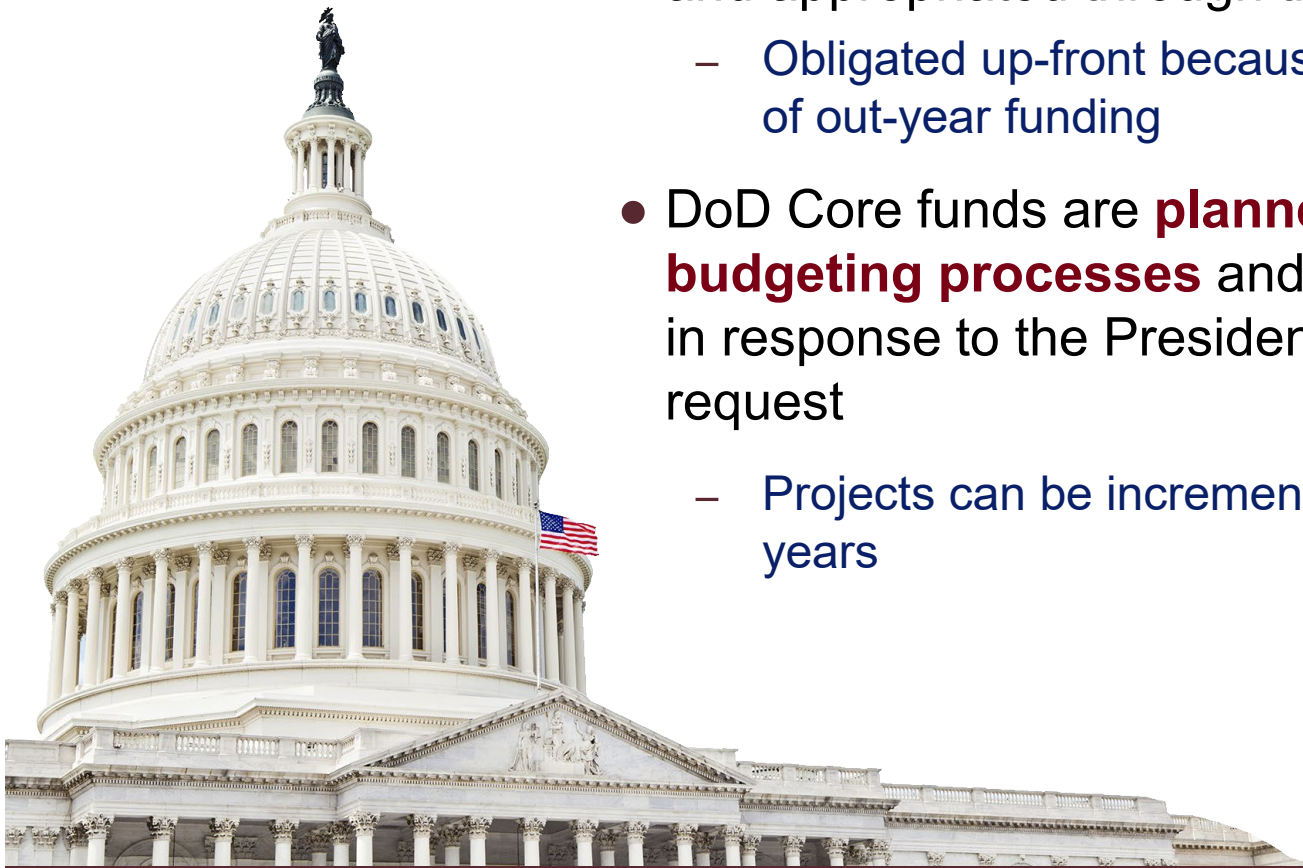
STEWARDSHIP



- Obligates funds up front; limited out-year budget commitments
- Maximizes funding available for research through low management costs and efficient processes
- Maintains transparency and accountability

Congressional Special Interest (CSI) versus DOD Core funding

- CDMRP's CSI funds are **directed by Congress** and appropriated through the DoD budget
 - Obligated up-front because there is no guarantee of out-year funding
- DoD Core funds are **planned through specific budgeting processes** and appropriated yearly in response to the President's DoD budget request
 - Projects can be incrementally funded in out-years

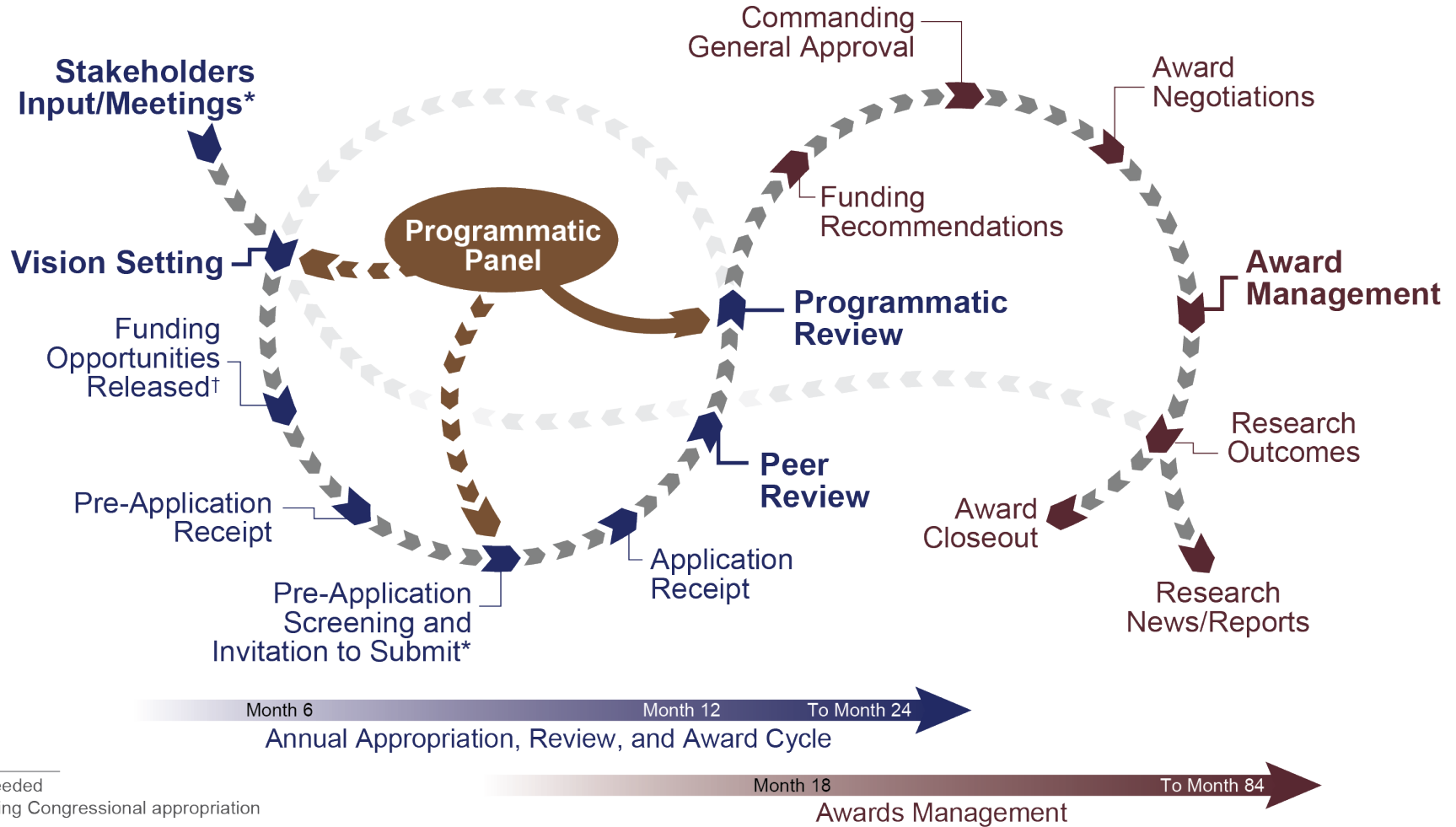


CDMRP FY24 Appropriations



Research Program	FY24 \$M	Research Program	FY24 \$M
Alcohol and Substance Use Disorders	\$4.0	Neurofibromatosis	\$25.0
Amyotrophic Lateral Sclerosis	\$40.0	Ovarian Cancer	\$45.0
Arthritis (<i>New for FY24</i>)	\$10.0	Pancreatic Cancer	\$15.0
Autism	\$15.0	Parkinson's	\$16.0
Bone Marrow Failure	\$7.5	Peer Reviewed Alzheimer's	\$15.0
Breast Cancer	\$150.0	Peer Reviewed Cancer (18 Topics)	\$130.0
Combat Readiness Medical	\$5.0	Peer Reviewed Medical (42 Topics)	\$370.0
Duchenne Muscular Dystrophy	\$10.0	Peer Reviewed Orthopaedic	\$30.0
Epilepsy	\$12.0	Prostate Cancer	\$110.0
Glioblastoma (<i>New for FY24</i>)	\$10.0	Rare Cancers	\$17.5
Hearing Restoration	\$5.0	Reconstructive Transplant	\$12.0
Joint Warfighter Medical	\$20.0	Spinal Cord Injury	\$40.0
Kidney Cancer	\$50.0	Tick-Borne Disease	\$7.0
Lung Cancer	\$25.0	Toxic Exposures	\$30.0
Lupus	\$10.0	Traumatic Brain Injury and Psychological Health	\$175.0
Melanoma	\$40.0	Tuberous Sclerosis Complex	\$8.0
Military Burn	\$10.0	Vision	\$20.0
Multiple Sclerosis	\$20.0	TOTAL = \$1.509B	

Program Cycle



*As needed
†Pending Congressional appropriation

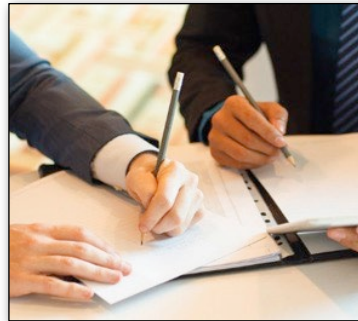
Goal of the Two-Tier Review Process

To develop funding recommendations that balance *the most meritorious science* and offer the highest promise to *fulfill the programmatic goals* set forth in the funding opportunity

Peer Review

- Criterion-based evaluation of full proposal
- Determination of “absolute” scientific merit
- **Outcome: Summary Statements**
 - No standing panels; programs recruit reviewers based on expertise needed
 - No contact between applicants, reviewers, and program staff

Partnership



Programmatic Review

- Comparison among proposals of high scientific merit
- Determination of adherence to intent, program relevance, and potential for impact
- **Outcome: Funding Recommendations**
 - No “pay line” (portfolio balance)
 - Funds obligated up front; limited out-year budget commitments (but milestones imposed)
 - No continuation funding



Additional information available at: <https://cdmrp.health.mil/about/2tierRevProcess>

Policy on Sex as a Biological Variable in Research

CDMRP expects researchers to study both males and females, across the full spectrum of basic, translational, and clinical research, unless there is a strong justification for only studying one sex

HOW DOES THIS POLICY IMPACT PROPOSED AND FUNDED RESEARCH?

Beginning with FY25 applications and awards, researchers must:

- Consider SABV in the study design and analysis plan
- Provide strong justification for proposing a single-sex study
- Report sex-based differences and/or disaggregate data

Applies to all stages of research

Basic	Translational	Clinical
Tissues Cell lines	Vertebrate animals	Humans Materials of human origin
and various types of specimens		

WHAT IS THE DIFFERENCE BETWEEN SEX AND GENDER?

Sex	Gender
<p>Defined by DNA</p> <ul style="list-style-type: none"> • Anatomy • Physiological • Genetics • Hormones 	<p>Social, cultural and psychological traits</p> <ul style="list-style-type: none"> • Identity and expression • Roles and norms

Policy and Frequently Asked Questions document available at:
<https://ebrap.org/eBRAP/public/Program.htm>

WHY IS THIS POLICY IMPORTANT?

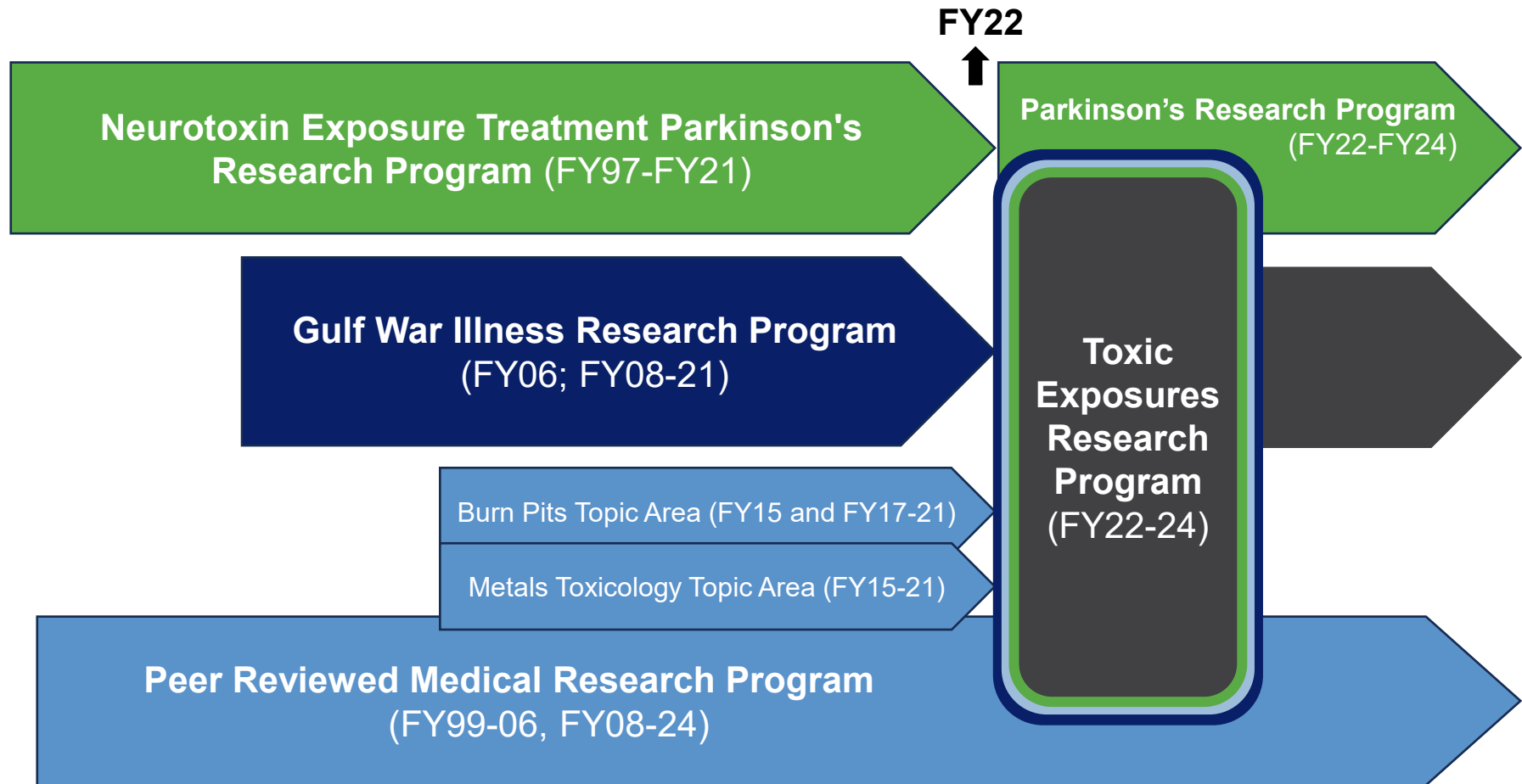
Diseases, conditions and interventions impact males and females differently. For example:

- Disease prevalence, symptoms and outcomes
- Drug efficacy and metabolism

Improves

our understanding of health and disease in both men and women

research rigor, transparency and generalizability



“Transitioning related research to a new, broader program, including neurotoxin exposure treatment research, research on Gulf War illness, exposures to burn pits, and other service-related exposures to potentially toxic chemicals and materials, will allow the research community to improve scientific understanding and pathobiology from exposure, more efficiently assess comorbidities, and speed the development of treatments, cures, and preventions.” [Consolidated Appropriations Act, 2022]

Toxic Exposures Research Program (TERP)

Vision

Prevent, minimize and mitigate the impact of military-related toxic exposures and improve the health and quality of life of those affected

Mission

Support impactful research aimed at identifying the cause and understanding the health outcomes, comorbidities, and pathological mechanisms associated with military-related toxic exposures to facilitate the prevention, diagnosis, and treatment of the visible and invisible diseases and symptoms impacting Service Members, their Families, Veterans, and the American public



Total Appropriations (FY22-24): \$90M

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<https://www.dvidshub.net/image/1025646/flurry-foam-released-travis>
<https://www.dvidshub.net/image/80303/supplying-medical-mission>
<https://www.dvidshub.net/image/6621582/chinook-refuel>

TERP Program Goals



Elucidate mechanisms of how military-related toxic exposures result in adverse effects, including but not limited to toxicities, malignancies, neurologic and respiratory disorders, cardiac complications, sleep disorders, immune system dysfunction, gastrointestinal issues, etc.



Diagnose the effects of military-related toxic exposures, understand the phenotypic, pathological and clinical outcomes associated with short-term and long-term exposures, and predict disease progression.



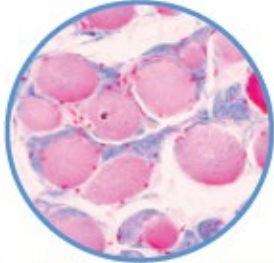
Predict and prevent military-related toxic exposures by identifying strategies that can anticipate, identify, monitor and prevent Service Members and the American public from adverse effects of exposures to toxic substances.



Develop therapeutics, treatments and strategies to minimize symptoms and disease progression associated with military-related toxic exposures.

*All program goals are of equal importance
For full language, please refer to the TERP FY24 Program Announcements*

TERP Topic Areas



Neurotoxin Exposure



Gulf War Illness and Its Treatment



Airborne Hazards and Burn Pits



Other Military Service-Related Toxic Exposures in General

Including Prophylactic Medications, Pesticides, Organophosphates, Toxic Industrial Chemicals, Materials, Metals and Minerals

All topic areas are of equal importance

TERP Overview

- **Focused on healthcare solutions for adverse health outcomes associated with military-related toxic exposures that impact pre- and post-911 Service Members and Veterans**
 - Military-related toxic exposures also impact Military Families and the American public
- **Encourage collaborative partnerships**
 - Collaboration between non-DOD/non-VA and DOD and/or VA researchers and clinicians to leverage access to existing DOD and VA resources
 - Incentives for partnerships
 - Support interdisciplinary research
- **Coordinate with the VA, NIH and other funding organizations**
- **Support research across the pipeline (basic, translational and clinical) and a diverse pool of researchers (academia, industry, DOD, VA etc.)**
 - FY22-FY23: supported 43 projects, 58 awards, - total of \$53.7M

FY24 TERP Funding Opportunities & Timeline

\$500K

Investigator-Initiated Research Award:

Supports studies that will make an important contribution toward research and/or patient care for a disease or condition associated with military-related toxic exposures.

\$800K

 for the single investigator award

\$1.6M

 for the partnering principal investigator option

Translational Research Award:

Supports translational research that will accelerate the movement of promising ideas in military-related toxic exposure research into clinical applications, including health care products, interventions, technologies, and/or clinical practice guidelines.

\$1.5M

 for the single investigator award

\$2.5M

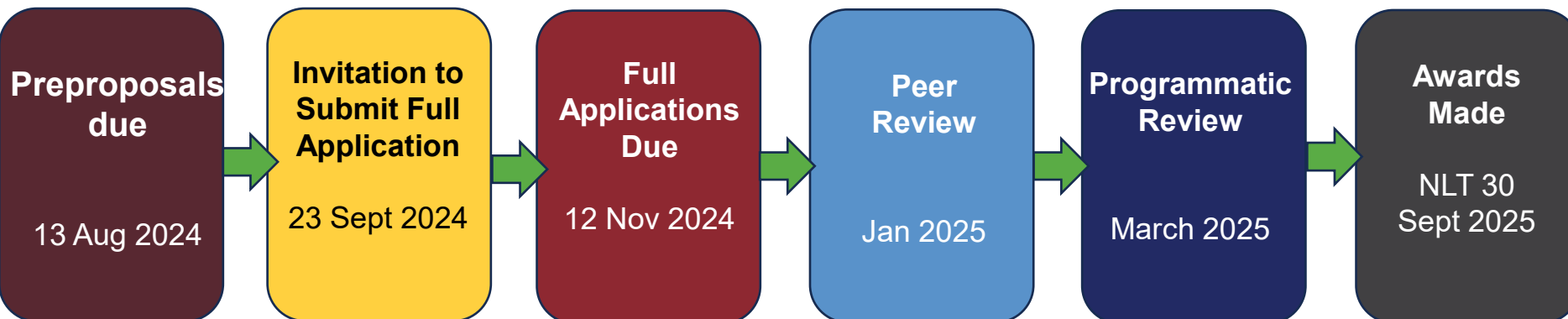
 for the partnering principal investigator option

Clinical Trial Award:

Supports the rapid implementation of clinical trials with the potential to have a significant impact on the prevention, treatment, or management of symptoms, diseases, or conditions associated with or resulting from military-related toxic exposures.

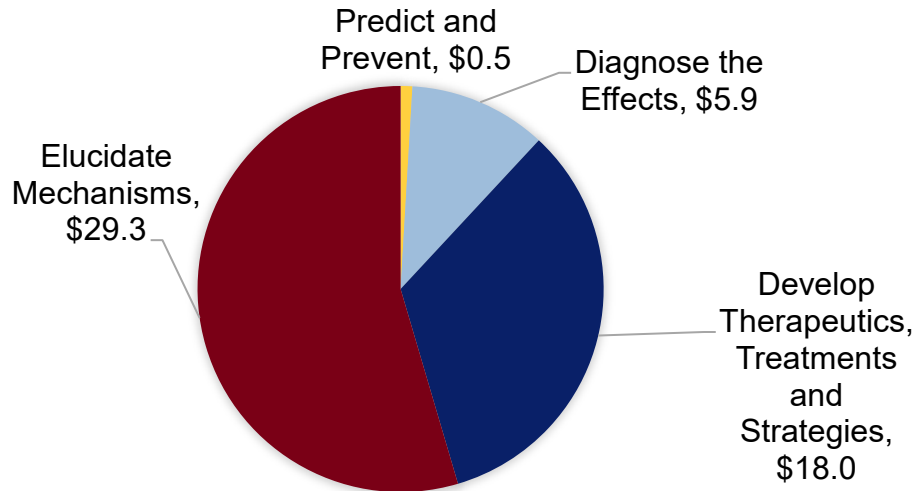
- Funding amounts refer to direct cost limits
- For full language, please refer to the TERP FY24 Program Announcements

Key Dates

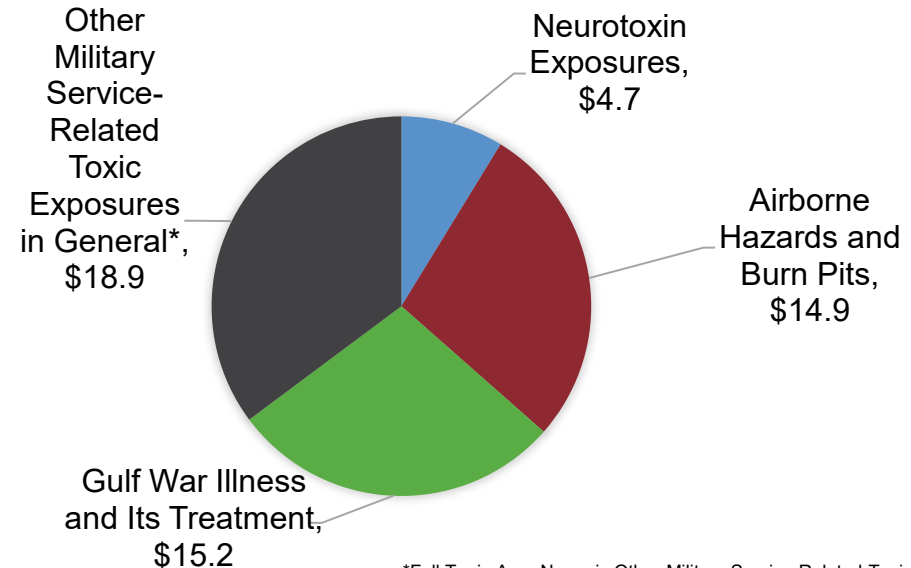


TERP FY22-FY23 Investments

TERP FY22-FY23 Investments by Primary Program Goal (\$M)



TERP FY22-FY23 Investments by Primary Topic Area (\$M)



*Full Topic Area Name is Other Military Service-Related Toxic Exposures in General, Including Prophylactic Medications, Pesticides, Organophosphates, Toxic Industrial Chemicals, Materials, Metals and Minerals

Between FY22-FY23, the TERP supported ~\$29.5M, 27 projects, that have elements focused on women's health and/or evaluate sex as a biologic variable.

TERP Portfolio Diversity

Exposures*

- Per- and polyfluoroalkyl substances
- Particulate matter 2.5
- Malaria prophylactic medication
- Sulfur dioxides +/- cigarette smoke
- Pyridostigmine Bromide and organophosphates
- Beryllium
- Trichloroethylene
- Hexavalent chromium
- Cadmium
- Jet fuel
- Burn pits
- Pesticides

Health Outcomes*

- Gulf War illness
- Cancers (testicular, lung, prostate blood)
- Deployment-Related Respiratory Disease & other respiratory conditions/diseases
- Ovarian function
- Parkinson's disease, Alzheimer's disease, neurodegeneration & cognitive dysfunction
- Liver disease
- Reproduction & developmental impacts
- Cardiac Outcomes
- Immunotoxicity

*lists are not all inclusive

TERP Metrics

- Awards: 43 projects, 58 awards*
- Total scientific investment, FY22-23: \$53.7M
- Publications: 2 as of Nov 2024
- Number of awards supporting clinical trials: 2 projects, 4 awards*

* TRA and CTA awards allow for partnering;
some projects may include multiple awards

Ongoing Gulf War Illness Projects - TERP

The TERP invested over \$15M (12 projects; 15 awards) related to GWI since its inception in FY22.

Clinical Trial to Improve Quality of Life

- Decentralized, confirmatory clinical trial that aims to confirm that **acupuncture** helps patients impacted by pain and fatigue associated with GWI*

Preclinical Treatment Pipeline

- Evaluation of **ganaxolone** to reduce GWI-induced neuronal damage and pathology*
- Intranasal **biological therapeutic** to treat broad range of symptoms associated with GWI including neuroinflammation*

Diagnostics with Potential to Lead to Therapeutic Targets

- **Non-invasive brain imaging tool** combined with blood markers and computational analysis to identify neurological changes and biomarkers in Veterans with GWI; If successful, will be able to diagnose and predict risk of neurological impairment and ultimately facilitate personalized medicine treatments.*
- Metabolic **biomarkers** of Gulf War exposures and GWI using pre- and post- deployment samples (DOD Serum Repository) from Veterans living with GWI compared to healthy controls. Veterans identified using data from the Boston Biorepository and Integrative Network, BBRAIN*

*expands upon GWIRP-funded studies

GWIRP Metrics

- Awards: 240
- Total scientific investment, FY06; FY08-FY21: \$236M
- Publications: ~300 as of Nov 2024
- Number of awards supporting clinical trials: 40

Ongoing Gulf War Illness Projects- GWIRP

The former GWIRP has 49 ongoing research projects, totaling ~\$70M

Clinical Trials

- Transcranial magnetic stimulation to treat headache and pain in those with GWI**
- CoQ10-ubiquinone to alleviate symptoms of GWI
- Consortium- (Phase Ib mifepristone/etanercept, Phase II N-Acetyl Cysteine, Phase II Bacopa)
- Nicotinamide riboside (Niagen) for restoring mitochondrial bioenergetics in GWI patients
- Oleoylethanolamide for Targeting Lipid Metabolism in GWI
- Montelukast to treat cognitive and mood dysfunction and neuroinflammation in Veterans with GWI

Biomarkers & Diagnostics

- Autoantibody biomarkers in plasma and saliva to diagnose the time course of sarin-induced nervous system injury
- Ocular measurements and biomarkers to diagnose and monitor GWI progression**
- P-Tau proteins as a marker for potentially more severe and neurodegenerative forms of GWI

Exploring Treatment Options

- Cannabidiol product to improve pain, insomnia, neurologic dysfunction and memory
- Regenerative epigenetic treatment for permanent reduction of neuropathology and pain and improved memory using FDA-approved histone deacetylases

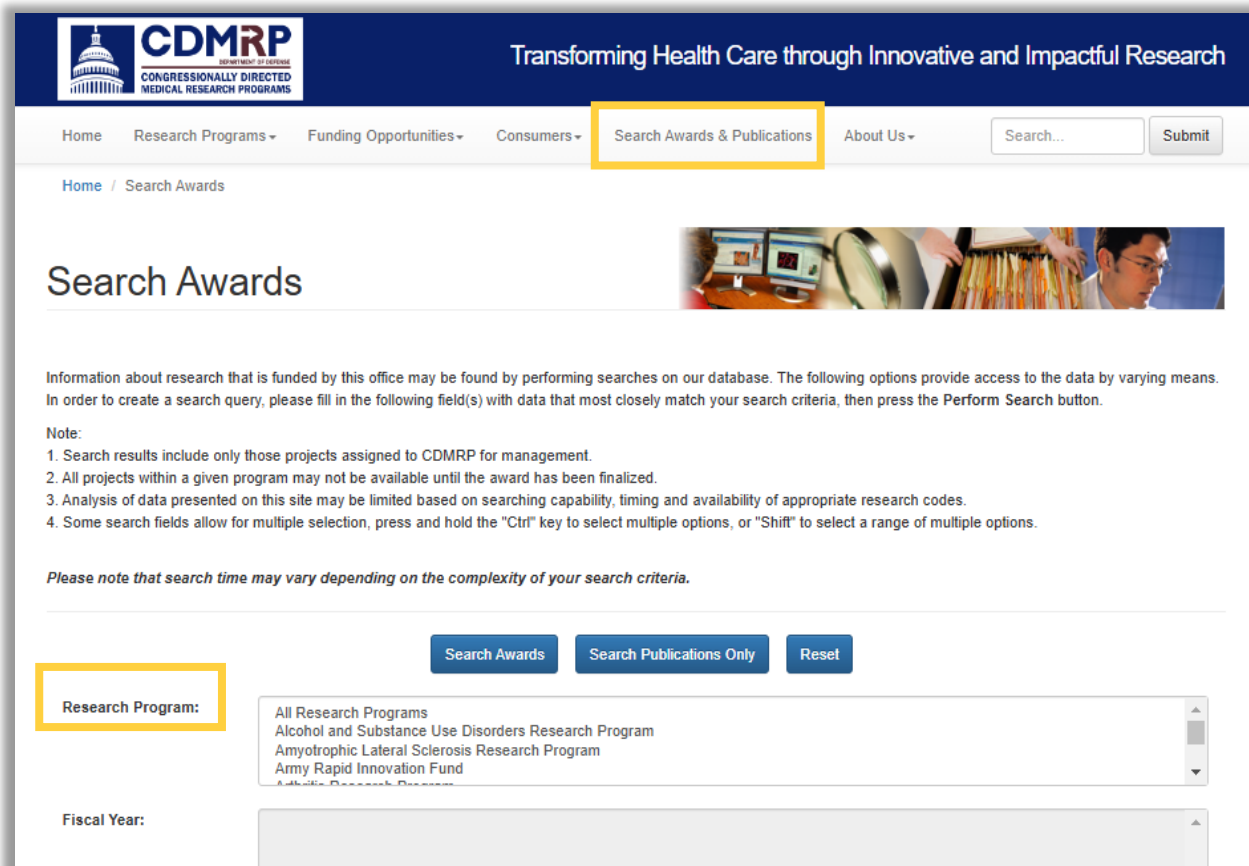
Mechanisms

- The role of gut signals and systemic inflammation, particularly in the brain and the contribution to GWI
- Impact of airborne toxic chemicals and pollutants experienced during the Gulf War on the development of GWI-associated sinonasal disease.

**relationship to VA-funded effort(s)

CDMRP Search Awards Function

- Abstracts, investigators, investments and publications can be found on the CDMRP website.
- All awards posted by the end of the fiscal year (30 Sept)



The screenshot shows the CDMRP website's search awards function. The header includes the CDMRP logo and the tagline "Transforming Health Care through Innovative and Impactful Research". The navigation menu has "Search Awards & Publications" highlighted with a yellow box. Below the navigation is a search bar with a "Submit" button. The main content area is titled "Search Awards" and features a banner image of a person looking at a computer screen. Below the banner, there is a paragraph of text explaining the search process and a "Note" section with four numbered points. A "Please note that search time may vary depending on the complexity of your search criteria." message is also present. At the bottom, there are three buttons: "Search Awards", "Search Publications Only", and "Reset". A "Research Program:" dropdown menu is highlighted with a yellow box, showing a list of research programs including "All Research Programs", "Alcohol and Substance Use Disorders Research Program", "Amyotrophic Lateral Sclerosis Research Program", and "Army Rapid Innovation Fund". A "Fiscal Year:" dropdown menu is also visible below it.

Home Research Programs ▾ Funding Opportunities ▾ Consumers ▾ **Search Awards & Publications** About Us ▾ Search... Submit

Home / Search Awards

Search Awards

Information about research that is funded by this office may be found by performing searches on our database. The following options provide access to the data by varying means. In order to create a search query, please fill in the following field(s) with data that most closely match your search criteria, then press the Perform Search button.

Note:

1. Search results include only those projects assigned to CDMRP for management.
2. All projects within a given program may not be available until the award has been finalized.
3. Analysis of data presented on this site may be limited based on searching capability, timing and availability of appropriate research codes.
4. Some search fields allow for multiple selection, press and hold the "Ctrl" key to select multiple options, or "Shift" to select a range of multiple options.

Please note that search time may vary depending on the complexity of your search criteria.

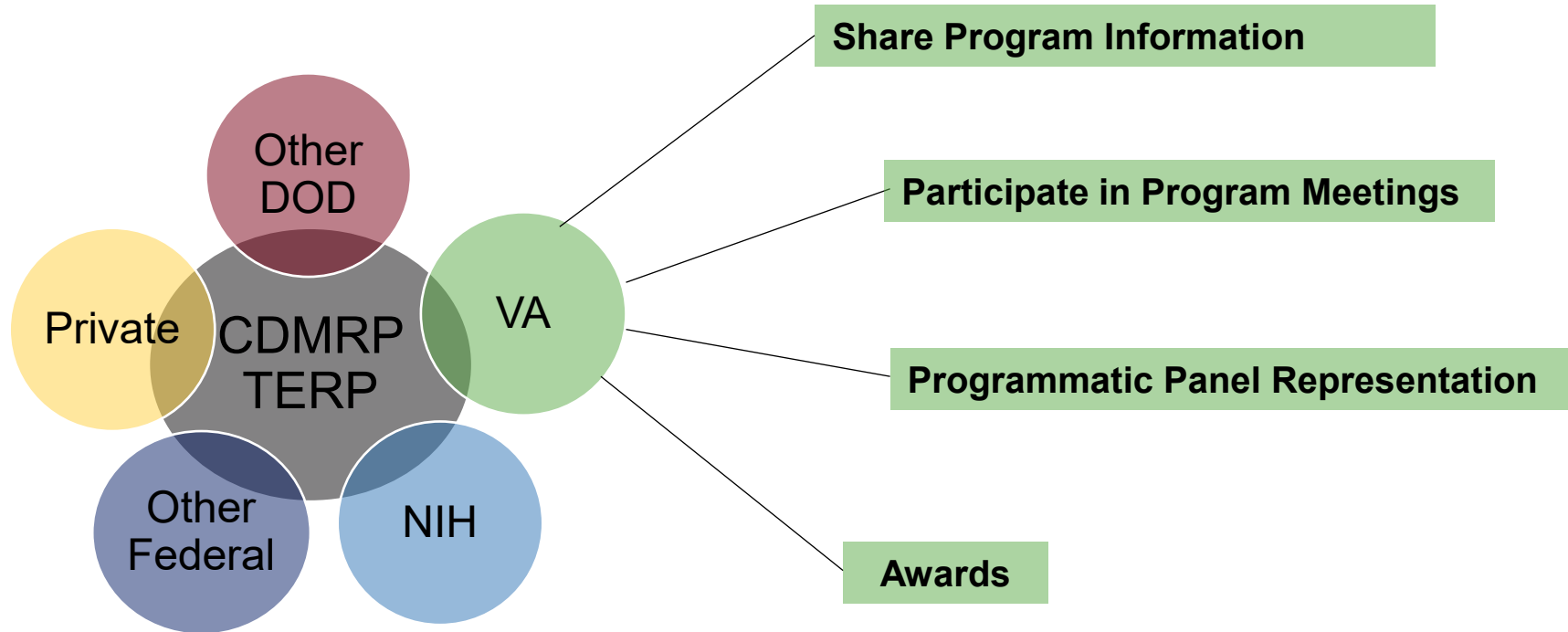
Search Awards Search Publications Only Reset

Research Program:

- All Research Programs
- Alcohol and Substance Use Disorders Research Program
- Amyotrophic Lateral Sclerosis Research Program
- Army Rapid Innovation Fund
- Autistic Research Program

Fiscal Year:

TERP Coordination with VA

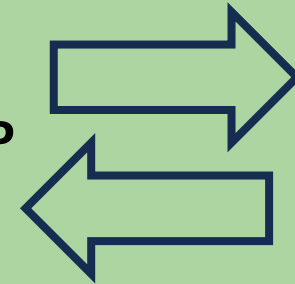


TERP Coordination with VA

Share Program Information

- Briefings and informational meetings
- Quarterly meetings with VA GW Research Program

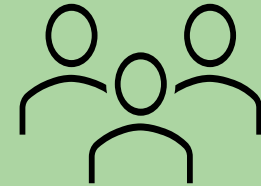
CDMRP



VA

Attend Program Meetings

- Inaugural stakeholders meeting
- Observe annual programmatic review and vision setting



Participate in Two-Tiered Review

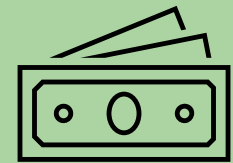
- Peer reviewers and Programmatic panel members



TERP Coordination with VA

Awards

- Some CDMRP GWIRP and TERP funded projects include VA investigators
- All applications recommended for funding are reviewed for scientific overlap prior to award and PIs are reviewed at least annually
- Application and award information is exchanged between VA and CDMRP (and NIH) via NIH's Query View Report system



Award Synergy

Awards

- TERP funded projects may advance ideas/solutions initiated by other research programs (VA, NIH, other CDMRP etc.) or address different components of a research question.
- Applicants must apply to current funding opportunities and be competitively selected through our two-tiered review process
- Examples from TERP and GWIRP:
 - **Diagnostic efforts for chronic bronchiolitis and Deployment-Related Respiratory Disease** funded by CDMRP GWIRP (FY16), VA (FY21) and CDMRP TERP (FY22)
 - **“Olfactory and cognitive decrements in 1991 Gulf War veterans with gulf war illness/chronic multisymptom illness”** funded by VA (FY19) and CDMRP GWIRP (FY20)
 - **Eye imaging as a biomarker for GWI; studies on eye pain and light sensitivity in Veterans with GWI** funded by CDMRP GWIRP (FY19) and VA (FY24)

Summary

The CDMRP TERP will:

- Manage current and any potential future appropriations according to Congressional language and intent
- Prioritize high impact research that will provide solutions for Service Members, their Families, Veterans and the American public that have been or could potentially be impacted by military-related toxic exposures
- Encourage collaborations with VA and DOD investigators
- Coordinate with VA, DOD, NIH and other federal and non-federal organizations

Questions?

For more information, please visit:



cdmrp.health.mil



CDMRP

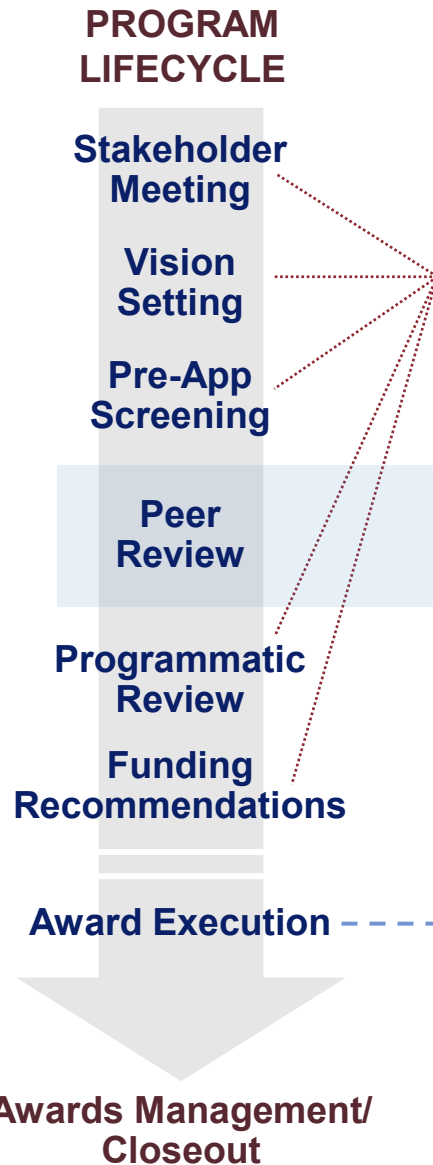
DEPARTMENT OF DEFENSE

**CONGRESSIONALLY DIRECTED
MEDICAL RESEARCH PROGRAMS**

Consumers are the “True North” and Foundation of the CDMRP

CDMRP includes consumers – patients, survivors, family members, and/or caregivers – in every aspect of the program lifecycle.

Consumers serve as full voting members on peer review and programmatic panels. Through their lived experiences with the target disease, disorder, or injury, consumers represent their respective communities and add valuable perspectives and a sense of urgency to the program mission, investment strategy, and research focus.



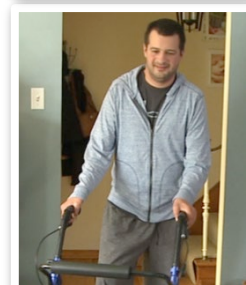
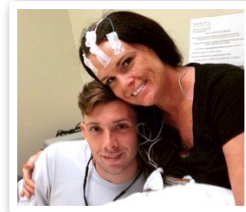
FY23 Consumer Involvement

93 consumers* assigned to Programmatic Panels as members and ad hoc reviewers representing **91** consumer advocacy organizations, Service Members, or Veterans

854 consumer reviewers** assigned to Peer Review Panels representing **334** consumer advocacy (nominating) organizations

Participate on research teams for funded projects
19 programs offered funding opportunities that incorporate consumer participation in the research project

* All unique individuals
** 734 unique individuals



Interested in Serving as a CDMRP Consumer?

Consumer Stories

Morgan Moore: Autism is part of my everyday life, *ARP Consumer Reviewer*

Mapping a Path Forward: Patient Involvement throughout ALS Therapeutic Development and Clinical Research, *ALSRP Consumer Reviewer*

Kelsey Smith: Advocacy for People with Celiac Disease Amidst Growing Popularity for a Gluten-Free Diet, *PRMRP Consumer Reviewer*

PCRP Patient Advocate Perspective – Todd Seals: A Wild Ride

Peter Fiduccia: The Importance of Polycystic Kidney Disease, *PRMRP Peer Reviewer*

Jordan Hathorn: An Impactful Way to Thank Service Members, *PRORP Peer Reviewer*

Devyn Mitchell: Staying Involved in Her Own Lupus Journey, *LRP Peer Reviewer*

Consumer Story: Carl DeSpiegelaere, *TBIPHRP Consumer Reviewer*

Consumer Involvement



"It is intellectually challenging and a big commitment. But that is part of what I like so much about serving as a Peer Reviewer: it's hard work but you come away from it feeling as if you have made a significant contribution; it is incredibly rewarding."

- Linnea Duff, *LCRP*

The Congressionally Directed Medical Research Programs (CDMRP) welcomes patients, survivors, family members, and advocates to play a pivotal role in the future of biomedical research funding. To transform healthcare for our Service members and the American public, the CDMRP looks to those who have the most experience, who understand the effects of a disease, an injury, or a condition - the individuals (consumers) living with breast cancer, orthopaedic injury, Parkinson's disease, etc. By integrating patients, survivors, family members and/or care takers into the scientific review process, the CDMRP is able to enrich the scientific review with personal perspective, passion, and a sense of urgency that ensures the human dimension is incorporated in the research focus. Over 2,000 consumers have served as Peer and Programmatic reviewers since 1995. By partnering with consumers, the CDMRP strives to find and fund collaborative research that discovers, develops, and delivers health care solutions for Service members, Veterans, and the America public.



Click on Image to View Program Booklet



About Us

[Learn More About CDMRP »](#)

[Consumer Experiences »](#)



Frequently Asked Questions

[Consumer Involvement in Peer Review: Step by Step »](#)

[View Frequently Asked Questions »](#)



Eligibility Requirements

[Consumer Reviewer Eligibility Checklist »](#)

[Program Consumer Reviewer Requirements](#)



Apply to be a Consumer Reviewer

[Consumer Nomination Application »](#)

[How You are Evaluated »](#)

TERP Consumers

For the purposes of the TERP, a consumer is a person living with a disease, injury, or condition or may be a family member or caregiver of a person impacted by a disease/injury/condition associated with military-related toxic exposures. The consumer must be an active participant in an advocacy, outreach, or support organization, or if military personnel on active duty, be approved to participate by their Commanding Officer.

Ways to Participate:

- **Review Process:** consumers included on peer and programmatic review panels
- **Research:**
 - Applicants encouraged to use relevant Veteran and/or military populations/samples/data sets in their studies (or justify how the chosen populations/samples/data sets are relevant to military-related toxic exposures and will benefit Service Members, Veterans, and/or their Families)
 - Applicants to translational and clinical trial award mechanisms are encouraged to include consumers as part of their research teams

TERP Consumers

“I am incredibly grateful to the Vietnam Veterans who welcomed me home from Desert Storm. They spoke out on our behalf when we came back with undiagnosed illnesses now understood as Gulf War Illness. I listened and learned so much from them in their struggle with the aftermath of Agent Orange and other tactical herbicide exposures. More recently, I have welcomed home a new generation of Veterans and listened to their concerns about toxic exposures, including airborne hazards, open burn pits, and other particulate matter exposures. It is my hope that the Toxic Exposures Research Program will expand the knowledge of and discover interventions for the many conditions and health concerns that Veterans experience and that the outcomes of the program will contribute to a better quality of life.”

Tech. Sgt. Vera Roddy, U.S. Air Force Retired, Veterans of Foreign Wars

“As a 23-year Veteran of combat arms and an end user of the research being funded under the CDMRP TERP, I will admit that I had some reservation of exposing myself again even if it was only mentally to the environment that all Service Members experience while serving our country. After serving on the TERP programmatic panel, I was humbled by the volume of knowledge, experience and determination that was assembled for the purpose of actually finding solutions.”

1Lt Andrew Myatt, U.S. Army Retired, Wounded Warrior Project