UNDER SECRETARY OF DEFENSE
4000 DEFENSE PENTAGON
WASHINGTON, D.C. 20301-4000

PERSONNEL AND READINESS

The Honorable James M. Inhofe
Chairman
Committee on Armed Services
United States Senate
Washington, DC 20510

SEP 16 2020

Dear Mr. Chairman:

The Department's response to Senate Report 116–103, pages 239–240, accompanying S. 2474, the Department of Defense Appropriations Bill, 2020, on the Inclusion of Women and Minorities in the Congressionally Directed Medical Research Program (CDMRP) is enclosed.

The report summarizes CDMRP's processes for clinical research and clinical trials; compares CDMRP's requirements for clinical research and trial applications with the National Institutes of Health (NIH) "Policy and Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research;" and provides an overview of the CDMRP's implementation plan for its policy and guidelines, which were developed in collaboration with the NIH to ensure appropriate representation of women and minorities in its extramural research.

Thank you for your continued strong support for our Service members, civilian workforce, and families. I am sending identical letters to the other congressional defense committees.

Sincerely,

Matthew P. Donovan

Enclosure:
As stated

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PERSONNEL AND READINESS

SEP 16 2020

The Honorable Jack Reed
Ranking Member
Committee on Armed Services
United States Senate
Washington, DC 20510

Dear Senator Reed:

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PERSONNEL AND READINESS

The Honorable Adam Smith
Chairman
Committee on Armed Services
U.S. House of Representatives
Washington, DC 20515

SEP 16 2020

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PERSONNEL AND READINESS

The Honorable William M. "Mac" Thornberry
Ranking Member
Committee on Armed Services
U.S. House of Representatives
Washington, DC 20515

SEP 16 2020

Dear Representative Thornberry:

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PERSONNEL AND READINESS

The Honorable Richard C. Shelby
Chairman
Subcommittee on Defense
Committee on Appropriations
United States Senate
Washington, DC 20510

SEP 16 2020

Dear Mr. Chairman:

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PERSONNEL AND READINESS

The Honorable Richard J. Durbin
Ranking Member
Subcommittee on Defense
Committee on Appropriations
United States Senate
Washington, DC 20510

SEP 16 2020

Dear Senator Durbin:

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PERSONNEL AND READINESS

The Honorable Peter J. Visclosky
Chairman
Subcommittee on Defense
Committee on Appropriations
U.S. House of Representatives
Washington, DC 20515

SEP 16 2020

Dear Mr. Chairman:

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PERSONNEL AND READINESS

The Honorable Ken Calvert
Ranking Member
Subcommittee on Defense
Committee on Appropriations
U.S. House of Representatives
Washington, DC 20515

SEP 16 2020

Dear Representative Calvert:

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Report to Congressional Defense Committees

Inclusion of Women and Minorities in the Congressionally-Directed Medical Research Program

September 2020

In Response To: Senate Report 116–103, Pages 239–240, Accompanying S. 2474, Department of Defense Appropriations Bill, 2020

The estimated cost of this report or study for the Department of Defense (DoD) is approximately $13,000.00 for Fiscal Years 2019–2020. This includes $1,900.00 in expenses and $11,000.00 in DoD labor.

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TABLE OF CONTENTS

PURPOSE OF REPORT

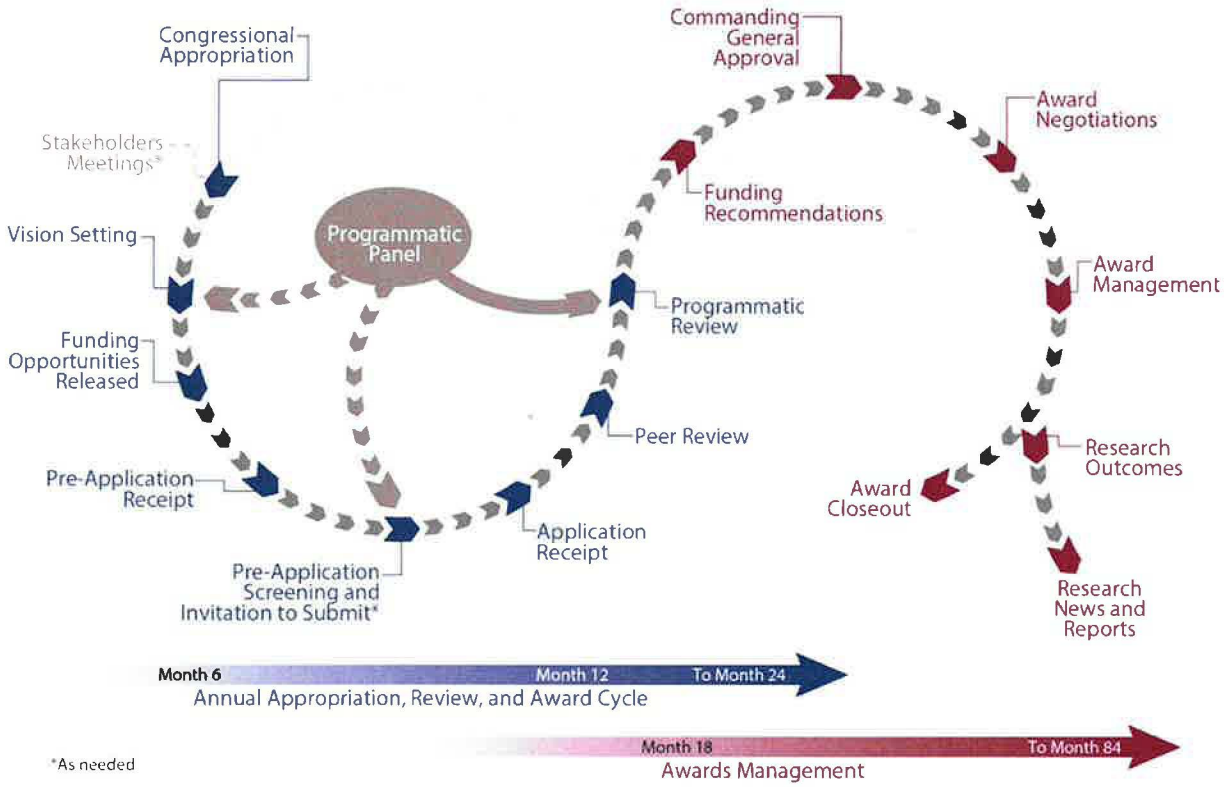
This report is in response to Senate Report 116–103, pages 239–240, to accompany S. 2474, the Department of Defense (DoD) Appropriations Bill, 2020, which requests that the DoD develop a plan to ensure the appropriate representation of women and minorities in its extramural research. The report specifies that the DoD should develop this plan in coordination with the National Institutes of Health (NIH), and include mechanisms to measure, enforce, assess the adequacy of, and improve the: (1) representation of women and minorities in each clinical trial, as well as the data on specific challenges researchers face in seeking to include women and minorities in their studies; (2) examination of biological variables, including the appropriate analysis of differential outcomes by sex, in clinical research; (3) practice of making clinical findings, subgroup analyses, and data publicly available, as appropriate and applicable; and (4) requirements (including, but not limited to, programmatic controls) and updated guidelines to ensure the appropriate representation of women in clinical research. Outcomes should also be analyzed for potential sex differences. This report summarizes existing clinical research and clinical trials processes of the Congressionally-Directed Medical Research Program (CDMRP); compares CDMRP current clinical research and trial application requirements with the "NIH Policy and Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research;" and provides an overview of its implementation plan (including goals, target dates of completion, and status) for the attached "CDMRP Policy and Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research," developed in accordance with congressional requests.

BACKGROUND

The CDMRP is a global funding organization within the DoD, managing the investment of multiple disease- and condition-specific research programs each year to support groundbreaking, high impact research that will transform healthcare for Service members, veterans, and the American public. As such, the CDMRP is the program execution and management agent for Congressional Special Interest programs, and is responsible for program planning, coordination, integration, budgeting, evaluation, administration, and reporting for each program. Since its inception in 1992, the CDMRP has been responsible for executing and managing more than $13 billion in appropriations across more than 40 programs.

The CDMRP uses a flexible execution cycle that is designed to tailor each program's research portfolio to the often rapidly changing knowledge gaps and discoveries within each relevant research field. The cycle follows the appropriations from cradle to grave, and includes the receipt of annual congressional appropriations, stakeholder meetings for new research programs, vision setting, release of funding opportunities soliciting research applications, preproposal screening and invitation to submit full applications, full application receipt and review, recommendation of applications for funding, and oversight of research awards (**Figure 1**).

Figure 1. CDMRP Program Cycle.



At the center of the program cycle is a two-tier review process, which is critical to ensuring that each of the CDMRP research portfolios reflects not only the most meritorious science, but also the most programmatically relevant research. This process was adopted from the recommendations set forth in 1993 by the National Academy of Medicine (NAM). Consumers, defined as patients, survivors, family members, and caretakers of those affected by each relevant disease or condition, participate at both levels of the two-tier review providing personal perspectives, passion, and a sense of urgency to the application review process. Scientifically sound applications that best meet each program's goals are recommended for funding to the Commanding General, U.S. Army Medical Research and Development Command (USAMRDC) and the Director of the Defense Health Agency Research, Development and Acquisition Directorate. Once approved, funding notifications are sent to investigators. Awards are typically in the form of one- to four-year assistance agreements, and are assigned to the CDMRP staff for full-cycle oversight of research progress and outcomes. The CDMRP ensures the integrity of the review process and provides transparency by publishing information on funded applications, programmatic panel members, ad hoc programmatic reviewers, peer review panelists, abstracts, and research accomplishments on the CDMRP website (https://cdmrp.army.mil).

Each CDMRP program is guided by a programmatic panel comprised of scientists and clinicians with renowned expertise in relevant areas of research and medicine, consumers from advocacy communities, and members of the military and other U.S. Government organizations. In response to the recommendations of the 2016 NAM report, each program has developed a

strategic plan that identifies and evaluates research foci, benchmarks for success, and investment opportunities for three to five years into the future.

Each program has a vision statement that reflects its overarching goals of ending or curing its respective disease, condition, or injury, ameliorating the consequences, and/or having a major impact on the quality of life of the survivors. On an annual basis, each programmatic panel examines its program's goals, and refines them as appropriate to reflect the current state of science and medicine. Following a comprehensive review of the program's portfolio, the present-day research and funding landscapes, and potential directions, the investment strategy for the program is developed, as well as the award mechanisms that will be offered as funding opportunities to fulfill the investment strategy.

Establishment of a program's goals, vision statement, and investment strategy leads to the development of funding opportunities that describe the intent of each award mechanism. Funding opportunities are published and advertised broadly to solicit research applications aimed at making scientific advances that have a significant impact for the individuals affected by the relevant diseases, injuries, and conditions. The CDMRP's diverse funding opportunities enable and support all stages of research, including exploring early-stage concepts, developing a foundation to understand disease biology and etiology, investigating therapeutic efficacy in disease models, advancing technological innovations, and conducting clinical trials and studies in human populations.

Federal Inclusion Policies for Clinical Research

Per Federal regulations and DoD policy (title 45, Code of Federal Regulations, part 46 and DoD Instruction 3216.02, "Protection of Human Subjects and Adherence to Ethical Standards in DoD-Conducted and -Supported Research," April 15, 2020), the USAMRDC Office of Research Protections (ORP), Human Research Protections Office (HRPO) requires that all CDMRP-funded research involving human subjects comply with *The Belmont Report*,[1] a document that outlines the basic ethical principles that should underlie all research involving human subjects. Historically, clinical research in the United States has largely been based on studies conducted in white, male populations, preventing female and minority populations from fully benefitting from clinical advances that might not have accounted for genetic and biomedical differences between sexes, races, and ethnicities. To address this disparity and improve the representation of women and minority participants in clinical research, the NIH Revitalization Act of 1993 (Public Law 103–43) was signed into law on June 10, 1993. This law directed the NIH to establish guidelines for inclusion of women and minorities in clinical research. In response, the NIH released the "NIH Policy and Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research" in 1994. This comprehensive policy, updated in 2000 and 2001, requires that all NIH-funded clinical research must include women and members of minority groups unless there is a clear and compelling justification for excluding them. Another update in November 2017

[1] The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. *The Belmont Report*. Washington, D.C.: U.S. Department of Health and Human Services, 1979.

provides additional guidelines regarding the reporting of analyses of sex/gender, racial, and ethnic differences in Phase III clinical trials.

During the development of CDMRP's Policy and Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research, CDMRP coordinated with the NIH Inclusion Policy Officer of the Office of Extramural Programs. The Inclusion Policy Officer shared the NIH application guide instructions for completing plans on the inclusion of women and minorities in research, peer review guidelines on inclusion, Research Performance Progress Report instructions, and screenshots from the NIH system used for capturing data. CDMRP adopted existing NIH practices to the largest extent possible when developing its policy. The NIH Inclusion Policy Officer was highly supportive of the implementation plan for the new CDMRP policy on the inclusion of women and minorities, and was complimentary of the CDMRP Frequently Asked Questions (FAQ) document that accompanied the policy. This FAQ document will serve as a support tool for applicants and investigators on the public CDMRP website.

Current CDMRP Processes for Clinical Research and Clinical Trials

Some CDMRP programs specifically focus on diseases that affect women and/or minorities. The Breast Cancer and Ovarian Cancer Research Programs both offer clinical research-oriented funding opportunities that focus on female participants. The Prostate Cancer Research Program has been supporting research on the disproportionate incidence and mortality of prostate cancer in African American men since its inception in Fiscal Year (FY) 1997. Disease disparities in kidney cancer, of which there is a higher incidence in African American and Native American populations, is an area of emphasis of the Kidney Cancer Research Program's strategic plan and funding opportunities. The Peer Reviewed Medical Research Program and the Lupus Research Program solicit for and support research in diseases/conditions that disproportionately or exclusively affect women and/or minorities, including lupus, heart disease, endometriosis, rheumatoid arthritis, and Rett's syndrome.

Clinical research, including interventional clinical trials, observational clinical studies, and research on human biospecimen samples or other medical information/datasets, is important for translating healthcare solutions from the bench to the bedside. Across all programs executed or supported by CDMRP, 465 interventional clinical trials were funded over 5 years (FY 2013–FY 2017).

All clinical research and clinical trials involving the use of human subjects or biospecimens must be reviewed and approved by the USAMRDC ORP HRPO before initiating the research, as well as on an annual basis. This administrative review requirement is in addition to the standard Institutional Review Board (IRB) or Ethics Committee review required by each awardee organization.

CDMRP funding opportunity announcements require clinical research applications to outline specific components related to the proposed human subjects research, such as details of the clinical strategy, appropriate study variables/endpoints, recruitment plan or acquisition of human biospecimen samples, and inclusion/exclusion criteria. Clinical trial applications require an

intervention plan (including study procedures and a clinical monitoring plan), detailed description of human subject recruitment and safety procedures that specifically addresses the target populations, anticipated enrollment counts at each study site, any potential barriers to accrual, and a data management plan (**Figure 2**). Importantly, the human subject's recruitment and safety procedures description must include a justification related to the scientific goals of the proposed study for limiting inclusion of any group by age, ethnicity, race, and/or sex/gender. Within the inclusion/exclusion criteria for the proposed clinical trial, the inclusion of women and minorities in clinical studies must be described.

Clinical trial and clinical research applications undergo a rigorous review that evaluates against specific criteria. Guidelines are provided in each funding opportunity that instruct applicants on the information needed to support this thorough review.

Figure 2. Current CDMRP Requirements for Clinical Research and Clinical Trial Applications.

	CDMRP Clinical Research	CDMRP Clinical Trial	Included in NIH Policy
Regulatory Strategy			
IRB/Ethics Committee approval	X	X	X
HRPO approval	X	X	
Project Narrative			
Research Strategy describing study population and detailed plan for recruitment.	X	X	X
Describe the methods that will be used to recruit.		X	X
Describe the study population, and define each arm/study group of the proposed trial.		X	X
Human Subjects/Samples Acquisition			
Describe the study population (e.g., age ranges, gender, ethnic groups, and pertinent demographics).	X	X	X
Describe criteria for inclusion/exclusion.	X	X	X
Describe methods used for recruitment/accrual.	X	X	X
Describe how subject to group assignments will be conducted (e.g., randomization, block randomization, stratified randomization, age matched controls, alternating group, or other procedures).	X	X	X
List the inclusion/exclusion criteria and provide detailed justification for exclusions.	X	X	X
Inclusion of women and minorities in study consistent with *The Belmont Report* and Congressional legislation, special attention is given to inclusion of women/minorities. Justification must be included if women and/or minorities will be excluded from the study.	X	X	X
Provide justification related to the scientific goals of the proposed study for limiting inclusion of any group.		X	X
Peer Review			
How well the inclusion, exclusion and randomization criteria meet the needs of the proposed clinical effort.	X	X	X
How well the sample population represents the targeted patient population that might benefit from the research outcome.	X	X	X

Sources: CDMRP Program Announcements and "NIH Policy and Guidelines on the Inclusion of Women and Minorities."

Implementation Plan for the CDMRP Policy and Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research

Incremental implementation of the CDMRP policy was planned in FY 2019 and executed in FY 2020 (**Table 1**). The CDMRP policy requires administrative and technological developments to include: development of standard operating procedures (SOPs), new data collection instruments, modifications to the existing receipt and data management systems, and training of CDMRP staff. Policy implementation will be completed by the end of FY 2020.

Table 1. Implementation Plan for CDMRP's Policy and Guidelines.

Goal	Target Date of Completion	Status
Develop and release new policy and guidelines with an anticipated implementation date.	March 2020	**Completed**
Develop Frequently Asked Questions for Principal Investigators.	March 2020	**Completed**
Modify the Public Health Service (PHS) Cumulative Enrollment Report, Office of Management and Budget (OMB) No. 0925-0001/0002 to enable automated data extraction.	March 2020	**Completed**
Develop instructions for completing the forms, to include the PHS Cumulative Enrollment Report, OMB No. 0925-0001/0002, for submission with the research applications and the technical progress reports.	March 2020	**Completed**
Augment program announcements by incorporating the requirement for submitting application components consistent with the policy.	September 2020	**Pending**: incremental implementation of the attached policy is planned. This policy will be incorporated into CDMRP funding opportunity announcements beginning in FY 2021. At that time, a program announcement that confirms CDMRP met the goals can be forwarded. All awards made prior to October 1,

		2020, are exempt from this requirement.
Augment program announcements by incorporating peer review criteria for reviewers to evaluate the required points of the section on the inclusion of women and minorities in the proposed research.	September 2020	**Pending**: incremental implementation of the attached policy is planned. This policy will be incorporated into CDMRP funding opportunity announcements beginning in FY 2021. At that time, a program announcement that confirms CDMRP met the goals can be forwarded. All awards made prior to October 1, 2020 are exempt from this requirement.
Develop and initiate the use of guidelines for peer reviewers in their evaluation of each application's proposed strategy for inclusion of women and minorities, including how to factor in the quality of the strategy as it relates to the scientific goals and objectives of the study when determining the technical merit of the application. In addition, for Phase III clinical trials, peer reviewers will be required to evaluate plans for the analysis of group differences on the basis of sex/gender, race, and/or ethnicity.	September 2020	**Completed**
Develop SOPs for CDMRP staff.	September 2020	**Completed**

SUMMARY

In response to Senate Report 116–103, pages 239–240, the CDMRP developed and released policy and guidelines in March 2020 pertaining to the inclusion of women and minorities as subjects in CDMRP-funded clinical research. This policy is modeled after the "NIH Policy and Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research." In concert with development and implementation of this policy, the CDMRP is pursuing multiple efforts outlined in this report to ensure the appropriate representation of women and minorities in its extramural research.