Defense Health Agency

Congressionally Directed Medical Research Programs
Directive

March 24, 2025

DHA R&D CDMRP

SUBJECT: The Congressionally Directed Medical Research Programs Directive on Inclusion of Women and Minorities as Subjects in Clinical Research

References: See Enclosure 1.

1. PURPOSE. This Congressionally Directed Medical Research Programs (CDMRP) directive, based on the authority of References (a) and (b), establishes requirements for the inclusion of women and minorities as subjects in clinical research.

2. APPLICABILITY. This directive applies to all applications for CDMRP-supported clinical research. All awards made prior to October 1, 2020 and studies utilizing human biospecimens or datasets that cannot be linked to a specific individual, sex, ethnicity, or race (typically classified as exempt from Institutional Review Board [IRB] review) are exempt from this requirement.

3. IMPLEMENTATION. CDMRP requires women and individuals from minority groups be included in all CDMRP-funded clinical research studies, unless there is a clear, justifiable rationale it is inappropriate with respect to the health of the subjects or the purpose of the research. The inclusion of women and individuals from minority groups and their subpopulations must be addressed across the lifespan of CDMRP-funded research. This requirement extends to all clinical research, including interventional clinical trials, observational clinical studies, and studies involving human biospecimens or datasets. Inclusion on the basis of sex, race, and ethnicity should be guided by the disease and scientific aims of the study. See Enclosure 3 for requirements to implement this policy into CDMRP-funded research.

4. CANCELED DOCUMENTS. This directive replaces the "CDMRP Policy and Guidelines on Inclusion of Women and Minorities as Subjects in Clinical Research" signed July 7, 2020.

5. RESPONSIBILITIES. See Enclosure 2.

6. PROCEDURES. See Enclosure 3.

7. INFORMATION COLLECTION. Planned and cumulative (actual) enrollment data distributed on the basis of sex, race, and ethnicity is reported using the Public Health Service Inclusion Enrollment Report (PHS IER), OMB No. 0925-0770. The PHS IER is a fillable PDF form, which can be found at https://ebrap.org/eBRAP/public/Program.htm under "Resources and Reference Material."

8. PROPONENT AND WAIVERS. The proponent of this directive is the Director, CDMRP. When applicants are unable to comply with this directive, the applicant's rationale will be evaluated by the peer review panel.

9. RELEASABILITY. Cleared for public release. This directive is available on the Internet from the CDMRP website at: https://cdmrp.health.mil/ and is also available on the Electronic Biomedical Research Application Portal at: https://ebrap.org/eBRAP/public/Program.htm.

10. EFFECTIVE DATE. This directive is effective upon signature.

11. FORMS. PHS IER Form, OMB No. 0925-0770. Available at https://ebrap.org/eBRAP/public/Program.htm under "Resources and Reference Material."

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Enclosures
1. References
2. Responsibilities
3. Procedures

Appendix:
1. Additional Resources

Glossary

ENCLOSURE 1

REFERENCES

(a) Senate Report 115-290 (S. 3159), 2019.
(b) H.R. 6157 - Department of Defense and Labor, Health and Human Services, and Education Appropriations Act, 2019 and Continuing Appropriations Act, 2019.
(c) Health and Human Services Policy for Protection of Human Subjects, Code of Federal Regulations, Title 45, Part 46, 2018.
(d) Federal Policy for the Protection of Human Subjects, Subpart A - 'Common Rule,' 2018.
(e) The Belmont Report, Ethical Principles and Guidelines for the Protection of Human Subjects of Research, 1979.
(f) CDMRP Funding Process. Available at https://cdmrp.health.mil/about/fundingprocess.
(g) Public Health Service Inclusion Enrollment Report, OMB No. 0925-0770. Available at https://ebrap.org/eBRAP/public/Program.htm under "Resources and Reference Material."
(h) 21st Century Cures Act, PL 114-255, 2016.
(i) NIH Policy and Guidelines on The Inclusion of Women and Minorities as Subjects in Clinical Research at https://grants.nih.gov/policy/inclusion/women-and-minorities/guidelines.htm.

ENCLOSURE 2

RESPONSIBILITIES

1. DIRECTOR, CDMRP. The Director, CDMRP will ensure compliance and implementation of this CDMRP directive.

2. PRINCIPAL INVESTIGATORS (PI) AND ORGANIZATIONS. PIs and organizations will provide the required information on inclusion of women and minorities and their subpopulations in clinical research projects, and any required justifications for exceptions to the policy.

3. ORGANIZATIONAL INSTITUTIONAL REVIEW BOARDS (IRB). IRBs will address ethical issues pertaining to clinical research. As the IRBs implement the Common Rule, they must ensure the equitable selection of subjects in accordance with References (c) and (d).

4. PEER REVIEW PANELS. Peer reviewers will evaluate the following in addition to current CDMRP review practices:

   a. The proposed plan for the inclusion of women and minorities for appropriate representation or the proposed justification when representation is limited or absent.

   b. The proposed exclusion of women and minorities on the basis a requirement for inclusion is inappropriate with respect to the health of the subject.

   c. The proposed exclusion of women and minorities on the basis a requirement for inclusion is inappropriate with respect to the purpose of the research.

   d. Plans for data analysis on the basis of sex, race, and/or ethnicity in applications proposing phase 3 clinical trials, and whether or not data from prior studies strongly support significant group differences of clinical or public health importance. If so, the research plan must include plans to conduct analyses to detect significant differences in intervention effect in the relevant groups.

5. PROGRAMMATIC PANELS. Programmatic panels will consider the technical merit of the application, encompassing inclusion of women and minorities and the justification relative to the objectives of the study as evaluated by the peer reviewers in making funding recommendations.

6. CDMRP STAFF. CDMRP staff will:

   a. Provide PIs and organizational representatives with relevant resources, such as the CDMRP directive, frequently asked questions, forms, and guidance to submit with their applications and progress reports.

b. Monitor and track the inclusion of women and individuals from minority groups in funded clinical trials and clinical research projects when reviewing technical reports.

ENCLOSURE 3

PROCEDURES

1. BACKGROUND

a. In accordance with References (a) and (b), CDMRP developed a plan to ensure the appropriate representation of women and minorities in its extramural research in coordination with the NIH to account for genetic and biomedical differences between sexes, races, and ethnicities. Reference (a) specifies CDMRP must ensure research contains the following requirements:

(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.

(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.

b. Clinical research, including interventional clinical trials, observational clinical studies, and research with human biospecimen samples or other medical information/datasets, is important for translating health care solutions from the bench to the bedside.

c. All CDMRP-funded research involving new and ongoing research with human anatomical substances, human subjects, or human cadavers must be reviewed and approved by the U.S. Army Medical Research and Development Command Office of Human and Animal Research Oversight's Office of Human Research Oversight prior to research implementation. This administrative review requirement is in addition to the local IRB, Ethics Committee, or equivalent review.

d. CDMRP funding opportunity announcements included language encouraging inclusion of women and minorities in clinical trials since 2009. In accordance with Reference (e), special attention is given to inclusion of women and/or minorities in studies funded or supported by the USAMRDC. This is intended to support all populations in receiving the benefits of human subjects research, including populations historically underrepresented as participants in clinical research studies.

e. Phase 3 clinical trials include statistically significant numbers of human subjects to allow for analyses down to the sex and minority level. As opposed to earlier phases of clinical

investigation establishing safety and dosing regimens, the aim of phase 3 investigations is to provide evidence leading to a scientific basis for consideration of a change in health policy or standard of care. Therefore, requiring plans for the valid design and analysis on the basis of sex, race, and/or ethnicity and requiring entities conducting applicable clinical trials to submit results of valid analyses and outcomes by sex, race, and ethnicity in clinicaltrials.gov is appropriate only at this phase.

2. GENERAL INFORMATION

a. CDMRP requires 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 the acquisition of human biospecimen samples, and inclusion/exclusion criteria.

b. Clinical trial applications require an intervention plan (including study procedures and a clinical monitoring plan), detailed description of human subject recruitment and safety procedures specifically addressing the target populations, anticipated enrollment counts at each study site, any potential barriers to accrual, and a data management plan.

c. The human subject 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.

d. Within the inclusion/exclusion criteria for any proposed clinical study, the inclusion of women and minorities must be described and an appropriate justification must be included if women and/or minorities will be excluded.

e. Clinical trial and clinical research applications undergo a rigorous technical review evaluated against specific criteria as described in Reference (f). Guidelines provided in each funding opportunity instruct applicants on the information needed to support this thorough review.

3. CLINICAL RESEARCH APPLICATION AND AWARD REQUIREMENTS

a. In addition to CDMRP's current requirements in funding opportunity announcements for clinical trial applications, all clinical research applications must have a strategy for the inclusion of women and minorities appropriate to objectives of the study, including a description of the composition of the proposed study population in terms of sex, racial, and ethnic group, and an accompanying rationale for the selection of subjects.

b. During application submission, applicants must provide a planned enrollment table(s) with the proposed enrollment distributed on the basis of sex, race, and ethnicity in accordance with Reference (g).

c. On applications selected for funding, PIs must provide a cumulative (actual) enrollment table(s), in accordance with Reference (g), at the time of each Annual and Final

Technical Progress Report submission, to describe progress toward enrollment goals and report on challenges associated with including women and minorities in their studies.

d. Additional requirements for phase 3 clinical trials include:

(1) Consistent with References (h) and (i), a valid design and analysis on the basis of sex, race, and/or ethnicity as appropriate for the scientific goals of the study must be included in the research application.

(2) Evidence of whether or not clinically important sex and race or ethnicity differences are expected in the intervention effect should also be included. Considerations for existing evidence are described in more detail in Reference (i) section IIB. As described there, applicants should describe whether prior studies do or do not support the existence of significant differences, or if they neither support nor negate significant differences.

(3) Analyses of biological variables and subpopulation data must be uploaded to clinicaltrials.gov.

(4) Reporting requirements will be cited in the award terms and conditions.

(5) If final analyses of sex and race/ethnicity are not available at the time of the final technical progress report, a justification and plan ensuring completion and reporting of the analyses is required.

APPENDIX

ADDITIONAL RESOURCES

(a) CDMRP Frequently Asked Questions for Directive on Inclusion of Women and Minorities as Subjects in Clinical Research at https://ebrap.org/eBRAP/public/Program.htm.
(b) Public Health Service Inclusion Enrollment Report, OMB No. 0925-0770 at https://ebrap.org/eBRAP/public/Program.htm.
(c) NIH Application Guide Instructions for Completing Plans on the Inclusion of Women, Minorities, and Children at https://grants.nih.gov/grants/how-to-apply-application-guide/forms-e/general/g.500-phs-human-subjects-and-clinical-trials-information.htm#2.4.
(d) Food and Drug Administration Guidance for IRBs and Clinical Investigators on the Evaluation of Sex Differences in Clinical Investigations at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/evaluation-sex-differences-clinical-investigations.
(e) National Institutes of Health. Glossary of NIH Terms. Definition of clinical research is available at https://grants.nih.gov/grants/glossary.htm#ClinicalResearch.
(f) Frérot M, Lefebvre A, Aho S, Callier P, Astruc K, Aho Glélé LS. What is epidemiology? Changing definitions of epidemiology 1978-2017. PLoS One. 2018 Dec 10;13(12):e0208442.
(g) Office of Behavioral and Social Sciences Research. Definition of behavioral and social sciences research is available at https://obssr.od.nih.gov/bssr-definition.
(h) Stengel D, Neugebauer EA, Meenen NM. Outcomes research: definitions, methods and challenges in trauma and orthopaedic surgery. Trauma Surgeon. 2007 Sep;110(9):792-6.
(i) Patient Safety and Quality: An Evidence-Based Handbook for Nurses, 2008.
(j) Code of Federal Regulations. Title 45, Subtitle A, Subchapter A, Part 46 – Protection of Human Subjects. Definition of clinical trial is available at https://www.ecfr.gov/on/2018-07-19/title-45/subtitle-A/subchapter-A/part-46#46.102.
(k) National Institutes of Health. Glossary of NIH Terms. Definition of phase 3 clinical trial is available at https://grants.nih.gov/grants/glossary.htm#ClinicalTrial.
(l) Office of Management and Budget. Statistical Policy Directive 15 on Race and Ethnicity Data Standards. Minimum categories for race and ethnicity can be found at https://spd15revision.gov/content/spd15revision/en/2024-spd15/categories-definitions.html.
(m) The National Institutes of Health Revitalization Act of 1993, PL 103-43, 2017.
(n) Department Of Defense Instruction 3216.02, Protection of Human Subjects and Adherence to Ethical Standards in DoD-Conducted and Supported Research, 2020.

GLOSSARY

PART I. ABBREVIATIONS AND ACRONYMS

CDMRP	Congressionally Directed Medical Research Programs
IRB	institutional review board
PHS IER	public health service inclusion enrollment report
PI	principal investigator
R&D	research and development

PART II. DEFINITIONS

clinical research. Patient-oriented research. Research conducted with human subjects (or on material of human origins such as tissues, specimens, and cognitive phenomena) for which an investigator (or colleague) directly interacts with human subjects. Excluded from this definition are in vitro studies that utilize human tissues that cannot be linked to a living individual. Patient-oriented research includes: (a) mechanisms of human disease, (b) therapeutic interventions, (c) clinical trials, and (d) development of new technologies.

Epidemiologic and behavioral studies.

Outcomes research and health services research.

clinical trial. A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes.

phase 3 clinical trial. Study to determine efficacy of the biomedical or behavioral intervention in large groups of people (from several hundred to several thousand) by comparing the intervention to other standard or experimental interventions as well as to monitor adverse effects, and to collect information that will allow the interventions to be used safely.

racial and ethnic categories. Office of Management and Budget directive No. 15 is used to define minimum standards to maintain, collect, and present data on race and ethnicity. The standards, updated in 2024, have seven categories for data on race and ethnicity: American Indian or Alaska Native, Asian, Black or African American, Hispanic or Latino, Middle Eastern or North African, Native Hawaiian or Other Pacific Islander, and White.