



Sex/Gender and Minority Inclusion in NIH Clinical Research



What Investigators Need to Know!

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Overview

- Review and Rationale of Policy
- Policy Updates
 - Definition of Clinical Research
 - OMB Standards and Population Tracking
 - NIH-Defined Phase III Trials: Analyses
- Implementation
 - Applicants
 - Reviewers
 - NIH program and grant managers
- Progress and Trends
- Resources and Getting Help

NIH Policy on Inclusion of Women & Minorities in Clinical Research

Why does NIH have this policy?

- Mandated by Congress, 1993 PL 103-43
- Ethical principal of justice and importance of balancing research burdens and benefits

Public Law PL 103-43

- Women and Minorities **must** be included in all clinical research studies.
- Women and Minorities **must** be included in Phase III clinical trials & the trial must be designed to permit valid analysis.
- Cost is **NOT** allowed as an acceptable reason for exclusion.
- NIH must support outreach efforts to recruit & retain women, minorities, and their subpopulations in clinical studies.

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NIH Policy on Inclusion

- NIH Policy and Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research – (Amended October, 2001)
- http://grants.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm

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Updates to Inclusion Policy

- NIH Definition of Clinical Research
- Revised OMB Standards for Data on Ethnicity and Race
- Further Clarification about NIH-Defined Phase III Clinical Trials



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NIH Definition of Clinical Research

(1a) Patient-oriented research.

Research conducted with human subjects (or on material of human origin 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.

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NIH Definition of Clinical Research (continued)

- (1b) Patient-oriented research includes:
- (a) mechanisms of human disease, (b) therapeutic interventions, (c) clinical trials, and (d) development of new technologies;
 - (2) Epidemiologic and behavioral studies; and
 - (3) Outcomes and health services research.

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OMB Directive 15:

Racial/Ethnic Standards for Federal Statistics & Administrative Reporting

- Collect data by self-report*
 - What is your ethnicity?
 - What is your race? (option to select more than one race)

*Investigator, not subject, completes tables

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OMB Directive 15

- Ethnic Categories
 - Hispanic or Latino
 - Not Hispanic or Latino
- Racial Categories
 - American Indian or Alaska Native
 - Asian
 - Black or African American
 - Native Hawaiian or Other Pacific Islander
 - White
 - More than one race

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NIH-Defined Phase III Clinical Trials

- Evidence must be reviewed to show whether clinically important sex/gender and race/ethnicity differences in intervention effect are expected
- Plans for valid analysis must be included in the design
- Results of analyses must be reported to NIH

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NIH-Defined Phase III Clinical Trials: Requirements

- If prior studies support **significant differences*** between subgroups, a plan to conduct **valid analyses to detect significant differences** between sex/gender and/or racial/ethnic subgroups is required.
- If prior studies support **no** significant differences between subgroups, representation as subject selection criterion is not required; inclusion and analyses are encouraged.

**Significant difference = a difference of clinical or public health importance based on substantial scientific data. Not the same as statistically significant difference.*

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NIH-Defined Phase III Clinical Trials: Requirements

- If prior studies **neither support nor negate** significant differences in intervention effect between subgroups, a plan to conduct **valid analyses*** of the intervention effect in sex/gender and/or racial/ethnic subgroups is required.

*For the purpose of this policy, Valid Analysis means an unbiased assessment that does not require high statistical power and should be conducted for both large and small studies.

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Implementation: Applicants

- Instructions in SF424(R&R)/PHS 398
 - Best source of information for investigators - <http://grants.nih.gov/grants/forms.htm>
 - Create section on Human Subjects Research
 - Inclusion of Women
 - Inclusion of Minorities
 - **Application will be returned without review if this section is omitted**



Implementation: Applicants

- Instructions in SF424(R&R)/PHS 398 (cont'd)
 - Inclusion of Women and Minorities Sections **must** include:
 - Subject selection criteria and rationale
 - Rationale for exclusions
 - Enrollment dates (start and end)
 - Outreach plans for recruitment
 - Table showing proposed composition

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Implementation: Applicants

- Instructions in SF424(R&R)/PHS 398 (cont'd)
 - NIH-Defined Phase III Clinical Trials
 - Evidence must be reviewed to show whether clinically important sex/gender and race/ethnicity differences in intervention effect are expected
 - Plans for valid analysis must be included in the design

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Implementation: Applicants

- Annual Progress Reports must include cumulative enrollment (reported in the enrollment tables).
- Annual Progress Report for Phase III Clinical Trials must include:
 - Enrollment tables
 - Narrative statement about progress in data analyses for sex/gender and ethnicity/racial effects.

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Implementation: Reviewers

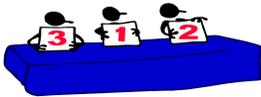
- Reviewers evaluate inclusion plans
http://grants.nih.gov/grants/peer/hs_review_inst.pdf
- Unacceptable plans **must** be reflected in the priority score



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Implementation: Reviewers

- For Phase III Clinical Trials:
 - Reviewers evaluate inclusion **AND** analysis plans.
 - <http://cms.csr.nih.gov/ResourcesforApplicants/PolicyProcedureReview+Guidelines/Guidelines+for+Review+of+Specific+Applications/>
 - http://grants.nih.gov/grants/peer/hs_review_inst.pdf
 - Unacceptable plans **must** be reflected in the priority score.



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Implementation: NIH Managers



Applications with unacceptable plans **cannot** be funded – **must** revise plans!

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Inclusion Enrollment Report Table
This report form should NOT be used for data collection from study participants.

Study Title: _____ Protocol Number: _____
 Total Enrollment: _____ Grant Number: _____

PART A. TOTAL ENROLLMENT REPORT: Number of Subjects Enrolled to Date (Cumulative)
by Ethnicity and Race

Ethnic Category	Enrollment			Total
	Female	Male	Unknown or Not Reported	
Hispanic or Latino				
Not Hispanic or Latino				
Unknown (Individuals not reporting ethnicity)				
Ethnic Category: Total of All Subjects*				
Racial Categories				
American Indian/Alaska Native				
Asian				
Native Hawaiian or Other Pacific Islander				
Black or African American				
White				
More than one race				
Unknown or not reported				
Racial Categories: Total of All Subjects*				
PART B. HISPANIC ENROLLMENT REPORT: Number of Hispanics or Latinos Enrolled to Date (Cumulative)				
Racial Categories	Female	Male	Unknown or Not Reported	Total
American Indian or Alaska Native				
Asian				
Native Hawaiian or Other Pacific Islander				
Black or African American				
White				
More Than One Race				
Unknown or not reported				
Racial Categories: Total of Hispanics or Latinos*				

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Progress and Trends

- The number of clinical studies and total and minority enrollment have increased significantly over 12 years.
- More Females have been reported than males, although the F/M ratio is relatively constant.
- The vast majority are domestic studies.
- Domestic minority enrollment has been ~25% of total domestic enrollment.

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Summary/Conclusions

- NIH has made substantial progress in including women & minorities in clinical research.
- Need to analyze trial data for sex/gender and ethnic/racial differences
- Primary aim of policy is to collect scientific information leading to changes in standard of care.

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Resources and Getting Help

- PHS 398 Instructions
<http://grants.nih.gov/grants/funding/phs398/phs398.html>
- PHS 2590 Instructions
<http://grants.nih.gov/grants/funding/2590/2590.htm>

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Resources and Getting Help

- Inclusion of Women and Minorities – Implementation Page

http://grants.nih.gov/grants/funding/women_min/women_min.htm

- CONTACT IC PROGRAM STAFF!