Sex/Gender and Minority Inclusion in NIH Clinical Research

What Investigators Need to Know!
Presenter: Miriam F. Kelty, PhD, National Institute on Aging, 2012
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 principle of justice and importance of balancing research burdens and benefits
Public Law PL 103-43
Women & Minorities **must** be included in all clinical research studies.
Women & Minorities **must** be included in Phase III clinical trials & the trial must be designed to permit valid analysis.
Cost is **NOT** allowed as a reason for exclusion.
NIH must support outreach efforts to recruit & retain women, minorities & their subpopulations in clinical studies.
Updates to Inclusion Policy 2001

NIH Definition of Clinical Research
Updated OMB Standards for Data on Ethnicity & Race
Clarified NIH-Defined Phase III Clinical Trials & Required Analyses

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.
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.

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

*Investigator, not subject, completes data tables
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
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.
NIH-Defined Phase III Clinical Trials: Requirements

If prior studies support significant differences* between subgroups, a plan for valid analyses to detect significant differences between sex/gender &/or racial/ethnic subgroups is required. If prior studies support no significant differences between subgroups, representation as subject selection criterion is not required; inclusion & 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.
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 &/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.
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 & rationale
Rationale for exclusions
Enrollment dates (start & end)
Outreach plans for recruitment
Table showing proposed composition
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
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 & racial/ethnicity/ effects.
Implementation: Reviewers

Reviewers evaluate inclusion plans

Unacceptable plans must be reflected in the summary notes & priority score
Implementation: Reviewers
For Phase III Clinical Trials:
Reviewers evaluate inclusion AND analysis plans.
Unacceptable plans must be reflected in the summary notes & priority score.
Implementation: NIH Managers
Applications with unacceptable plans cannot be funded

Applicants work with NIH program staff to revise plans so that they are acceptable to NIH
Graphic
Complying with the NIH Inclusion Policy
Principal Investigators
Review Staff and Reviewers
Program Staff
Grants Management Staff
NIH Tracking and Inclusion Committee
Congress
Public
Monitoring Compliance with the NIH Inclusion Policy
Annual Comprehensive Report: Monitoring Adherence to the NIH Policy on the Inclusion of Women and Minorities as Subjects in Clinical Research

http://orwh.od.nih.gov/inclusion/inclreports.html
Chart

NIH Extramural & Intramural Clinical Research Sex/Gender Enrollment
Reported for FY 2009
Chart

NIH Extramural & Intramural Clinical Research Sex/Gender Enrollment Reported for FY 2009
Enrollment Trend by Sex/Gender & Minority

Graphs
Progress and Trends
The number of clinical studies and total and minority enrollment have increased significantly over 15 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 varied between approximately 25% and 30%
What We Have Learned

Women’s Health Initiative (WHI):

Long-term EP hormone therapy increased heart disease, stroke, clots, breast cancer & AD. Colon cancer & fractures decreased. FDA warning that menopausal hormone therapy should not be used to prevent coronary heart disease. Knowledge led to change in practice.
What We Have Learned

Women’s Ischemia Syndrome Evaluation (WISE)

50% of enrollees with symptoms had no blockages.
Impaired microvasculature function not detectable by angiography.

Different methods necessary to diagnose cardiac ischemia in women than in men.

Most common early symptoms in women are sleep disturbance, fatigue, shortness of breath.

Sex differences in disease symptoms.
What We Have Learned
Multi-ethnic Study of Atherosclerosis
Women met LDL, SBP & aspirin adherence goals less than men
African-American & Hispanic women had higher SBP and lower aspirin use than white women
Sex & racial/ethnic differences in cardiovascular risk factor profiles
What We Have Lerned
Diabetes Prevention Program
Lifestyle changes reduce risk of diabetes in men & women & in all ethnic/racial groups
Medication intervention effective but not more effective than lifestyle changes in all groups.
Summary/Conclusions
NIH has made progress in including women & minorities in clinical research.
Need to analyze trial data for sex/gender and racial/ethnic differences.
Primary aim of policy is to collect scientific information leading to changes in standard of care.
We have gained knowledge broadly applicable to health care.
Resources and Getting Help
SF424 (R&R) Instructions
http://grants.nih.gov/grants/forms.htm

PHS 2590 Instructions
http://grants.nih.gov/grants/forms.htm
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!