Sex/Gender and Minority Inclusion in NIH Clinical Research

What Investigators Need to Know!

Presenter: Miriam F. Kelty, PhD, National Institute on Aging, 1/2010
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 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.
NIH Policy on Inclusion

- NIH Policy and Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research – (Amended October, 2001)

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
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.
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
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 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.
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.
Implementation: Applicants

• Instructions in SF424(R&R)/PHS 398
  – 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
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 and ethnicity/racial effects.
Implementation: Reviewers

- Reviewers evaluate inclusion plans

- Unacceptable plans **must** be reflected in the summary notes and priority score
Implementation: Reviewers

• For Phase III Clinical Trials:
  – Reviewers evaluate inclusion AND analysis plans.
  – Unacceptable plans **must** be reflected in the summary notes and priority score.
Implementation: NIH Managers

Applications with unacceptable plans cannot be funded

Must revise plans so that they are acceptable to NIH
Inclusion Enrollment Report Table

This report format should NOT be used for data collection from study participants.

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

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

<table>
<thead>
<tr>
<th>Ethnic Category: Total of All Subjects*</th>
</tr>
</thead>
<tbody>
<tr>
<td>**</td>
</tr>
</tbody>
</table>

### 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

<table>
<thead>
<tr>
<th>Racial Categories: Total of All Subjects*</th>
</tr>
</thead>
</table>
| **|}

PART B. HISPANIC ENROLLMENT REPORT: Number of Hispanics or Latinos Enrolled to Date (Cumulative)

<table>
<thead>
<tr>
<th>Racial Categories: Total of Hispanics or Latinos**</th>
</tr>
</thead>
<tbody>
<tr>
<td>**</td>
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</tbody>
</table>
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
### NIH Extramural & Intramural Clinical Research: Sex/Gender Enrollment Reported for FY 2008

<table>
<thead>
<tr>
<th>3B. ENROLLMENT REPORTED</th>
<th>Total All Clinical Studies*</th>
<th>Domestic</th>
<th>Foreign</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number</td>
<td>%</td>
<td>Number</td>
</tr>
<tr>
<td>Females Enrolled</td>
<td>9,243966</td>
<td>92.1%</td>
<td>729,198</td>
</tr>
<tr>
<td>%</td>
<td>60.0%</td>
<td>60.2%</td>
<td></td>
</tr>
<tr>
<td>Males Enrolled</td>
<td>5,991,739</td>
<td>91.0%</td>
<td>540,115</td>
</tr>
<tr>
<td>%</td>
<td>38.9%</td>
<td>38.6%</td>
<td></td>
</tr>
<tr>
<td>Sex of Subjects is Unknown</td>
<td>176,650</td>
<td>95.2%</td>
<td>8,415</td>
</tr>
<tr>
<td>%</td>
<td>1.1%</td>
<td>1.2%</td>
<td></td>
</tr>
<tr>
<td>Total Subjects Enrolled</td>
<td>15,412,355</td>
<td>91.7%</td>
<td>1,277,728</td>
</tr>
<tr>
<td>%</td>
<td>100.0%</td>
<td>100.0%</td>
<td></td>
</tr>
</tbody>
</table>

1. The total "Enrollment Reported" in the NIH database in FY 2008 was 15,412,355 subjects in 11,045 protocols with enrollment.

2. Females made up 60.0% (9.2M) of the total subjects enrolled, while Males made up 38.9% (6.0M), with 1.1% unknown.

3. The total Domestic Enrollment reported was 14,134,627 (91.7%)

4. Females made up 60.2% (8.5M) of the domestic subjects enrolled, while Males made up 38.6% (5.5M), with 1.2% (.0.2M) unknown.
NIH Extramural & Intramural Clinical Research: Minority Enrollment Reported for FY 2008

<table>
<thead>
<tr>
<th></th>
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</tr>
<tr>
<td>3C. Minority Enrollment Reported</td>
<td>4,386,636</td>
<td>80.3%</td>
<td>864,945</td>
</tr>
</tbody>
</table>

1. Minorities made up 28.5% (4.4M) of total subjects enrolled.

2. Minorities made up 24.9% (3.5M) of the Domestic Minority Enrollment and 67.7% (.86M) of the Foreign Minority Enrollment.

3. The Total Minority Enrollment was made up of 80.3% Domestic and 19.7% Foreign enrollment.
Enrollment by Sex/Gender and Total Minority
FY 1995 – 2008

Sex/Gender Enrollment by Year Reported

Total Minority Enrollment Reported by Year
Progress and Trends

• The number of clinical studies and total and minority enrollment have increased significantly over 14 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 24.1% and 28.9% of total domestic enrollment
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.
Resources and Getting Help

• PHS 398 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!