Inclusion of Women, Minorities, and Individuals Across the Lifespan

ACRWH | Dawn Corbett | April 10, 2019
Goals for Today

• Understand recent changes to NIH policies and procedures regarding inclusion of women, minorities, and individuals across the lifespan in NIH-funded clinical research

• Review status of Government Accountability Office recommendations related to inclusion of women and minorities

• Review FY 2016-FY 2018 data on the inclusion of women and minorities in NIH-funded clinical research

• Learn about recent changes to the Federal Policy for the Protection of Human Subjects (the Common Rule)
Timeline of NIH Inclusion Policies

1986
- NIH establishes policy encouraging researchers to include women in studies

1993
- PL103-43 requires inclusion of women and minorities in NIH clinical research

1998
- NIH issues policy requiring inclusion of children in NIH clinical research

2015
- NIH issues notice changing definition of child from individuals under 21 to under 18

2016
- 21st Century Cures Act includes new requirements for inclusion and reporting of participants based on sex/gender, race, ethnicity and age

2017
- NIH requires Phase III trials report results of sex/gender, race and ethnicity analyses in Clinicaltrials.gov

2019
- Inclusion Across the Lifespan policy requires inclusion of individuals of all ages in NIH clinical research
Requires:

1. NIH convene a workshop on age groupings and exclusions, examine inclusion guidelines on age, and publish data on age of participants
2. NIH assemble participant inclusion data disaggregated by research area, condition, and disease categories
3. Applicable clinical trials must report results of valid analyses by sex/gender and race/ethnicity to ClinicalTrials.gov
Purpose: To discuss the challenges and barriers to including children and older adults in clinical trials and to identify strategies that would produce more age-inclusive clinical trials.
Inclusion Across the Lifespan Policy

• Effective for applications submitted for due dates January 25, 2019 or later

• Requires individuals of all ages be included in NIH-funded human subjects research unless there are scientific or ethical reasons not to include them

• Requires submission of individual-level participant data in progress reports
Inclusion Across the Lifespan: overview of recipient requirements

Inclusion Across the Lifespan: guidance for applying the policy

The Inclusion Across the Lifespan policy (IAL) applies to all exempt and non-exempt human subjects research (see NOT-OD-18-116), beginning with competing grant applications due on after January 25, 2019, and R&D contract solicitations issued on after this date. Prior to this date, the Inclusion of Children in Research Policy continues to be in effect.

In applications or proposals:
- Include an Inclusion plan
- Submit a plan for including individuals across the lifespan
- If excluding based on age, provide rationale and justification for the specific age range

In progress reports:
- Report age at enrollment
- The policy requires the age of participants at enrollment to be included in reports
- Age at enrollment may be reported to NIH in units ranging from hours to years.

*Remember: Scientific Review Groups (SRGs) will assess each application/proposal as being "acceptable" or "unacceptable" with regard to the age-appropriate inclusion or exclusion of individuals in the research project."
Amended Inclusion of Women and Minorities Policy

• Effective for competing awards on or after December 13, 2017

• Requires applicable NIH defined Phase III clinical trials report results of analyses by sex/gender and race/ethnicity to Clinicaltrials.gov
October 2015

NATIONAL INSTITUTES OF HEALTH

Better Oversight Needed to Help Ensure Continued Progress Including Women in Health Research
**GAO Recommendations**

1. Make IC-level enrollment data readily available through public means  **CLOSED**

2. Examine approaches for aggregating more detailed enrollment data at the disease and condition level  **OPEN**

3. Ensure that program officers have a means of recording their monitoring of awardees plans for and progress in conducting analysis of potential sex differences  **CLOSED**

4. On a regular basis, systematically collect and analyze summary data regarding awardees’ plans for analysis of potential sex differences  **OPEN**

5. Report on this summary data and analysis in its regular report to Congress on the inclusion of women in research  **OPEN**
### Summary of Inclusion Records
**FYs 2016 - 2018**

#### Table 2-1. Total Inclusion Data Records (IERs) for NIH-Defined Extramural and Intramural Clinical Research

<table>
<thead>
<tr>
<th>Fiscal Year</th>
<th>Total Inclusion Records</th>
<th>Inclusion Records with Enrollment</th>
<th>US Site Inclusion Records</th>
<th>Non-US Site Inclusion Records</th>
<th>Female Only Inclusion Records</th>
<th>Male Only Inclusion Records</th>
</tr>
</thead>
<tbody>
<tr>
<td>2016</td>
<td>13,069</td>
<td>11,804</td>
<td>10,741</td>
<td>1,063</td>
<td>1,279</td>
<td>628</td>
</tr>
<tr>
<td>2017</td>
<td>14,580</td>
<td>12,932</td>
<td>11,792</td>
<td>1,140</td>
<td>1,419</td>
<td>686</td>
</tr>
<tr>
<td>2018</td>
<td>16,209</td>
<td>13,827</td>
<td>12,428</td>
<td>1,399</td>
<td>1,601</td>
<td>763</td>
</tr>
</tbody>
</table>

#### Table 2-2. Total Inclusion Data Records (IERs) for NIH-Defined Extramural and Intramural Phase III Trials

<table>
<thead>
<tr>
<th>Fiscal Year</th>
<th>Total Inclusion Records</th>
<th>Inclusion Records with Enrollment</th>
<th>US Site Inclusion Records</th>
<th>Non-US Site Inclusion Records</th>
<th>Female Only Inclusion Records</th>
<th>Male Only Inclusion Records</th>
</tr>
</thead>
<tbody>
<tr>
<td>2016</td>
<td>574</td>
<td>534</td>
<td>413</td>
<td>121</td>
<td>66</td>
<td>32</td>
</tr>
<tr>
<td>2017</td>
<td>618</td>
<td>574</td>
<td>440</td>
<td>134</td>
<td>89</td>
<td>27</td>
</tr>
<tr>
<td>2018</td>
<td>717</td>
<td>648</td>
<td>493</td>
<td>155</td>
<td>103</td>
<td>30</td>
</tr>
</tbody>
</table>
NIH Enrollment in Clinical Research by Sex/Gender
FY2016 to FY2018

FY2016
- 45% Females
- 53% Males
- 2% Unknown/Not Reported

FY2017
- 51% Females
- 47% Males
- 2% Unknown/Not Reported

FY2018
- 44% Females
- 52% Males
- 4% Unknown/Not Reported
NIH-Defined Phase 3 Enrollment by Sex/Gender FY2016 to FY2018

- **FY2016**
  - 33% % Females
  - 66% % Males
  - 1% % Unknown/Not Reported

- **FY2017**
  - 41% % Females
  - 59% % Males
  - 0% % Unknown/Not Reported

- **FY2018**
  - 37% % Females
  - 63% % Males
  - 0% % Unknown/Not Reported
NIH Total: NIH-Defined Phase 3 Enrollment by Race
FY2016 - FY2018

<table>
<thead>
<tr>
<th>Fiscal Year</th>
<th>White</th>
<th>Black/African American</th>
<th>Asian</th>
<th>Native Hawaiian/Pacific Islander</th>
<th>American Indian/Alaska Native</th>
<th>More Than One Race</th>
<th>Unknown/Not Reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>2016</td>
<td>0.1</td>
<td>36.3</td>
<td>6.6</td>
<td>48.7</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>2017</td>
<td>0.5</td>
<td>29.2</td>
<td>14.7</td>
<td>49.7</td>
<td>0.1</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>2018</td>
<td>7.3</td>
<td>64.6</td>
<td>19.1</td>
<td>0.2</td>
<td>0.6</td>
<td>0.0</td>
<td>0.0</td>
</tr>
</tbody>
</table>
NIH Enrollment in Clinical Research by Ethnicity
FY 2016 - FY 2018

FY 2016:
- 68% Not Hispanic
- 20% Hispanic
- 12% Unknown/Not Reported

FY 2017:
- 84% Not Hispanic
- 7% Hispanic
- 9% Unknown/Not Reported

FY 2018:
- 78% Not Hispanic
- 9% Hispanic
- 13% Unknown/Not Reported
NIH Total: NIH-Defined Phase III Enrollment by Ethnicity FY2016 - FY2018

- **FY 2016**
  - Not Hispanic: 91%
  - Hispanic: 9%
  - Unknown/Not Reported: 0%

- **FY 2017**
  - Not Hispanic: 87%
  - Hispanic: 6%
  - Unknown/Not Reported: 7%

- **FY 2018**
  - Not Hispanic: 85%
  - Hispanic: 12%
  - Unknown/Not Reported: 3%
What is the Common Rule?

- HHS Regulations on Human Research Protections 45 CFR Part 46

**Subpart A – The Common Rule**

Subpart B – Pregnant women & fetuses

Subpart C – Prisoners

Subpart D – Children

Subpart E – IRB Registration
Revised Common Rule Timeline

**January 21, 2017**
Revised Common Rule published in the Federal Register

**July 19, 2018**
Implementation date; institutions allowed to use 3 burden-reducing provisions

**January 21, 2019**
Compliance date; other provisions implemented *

* Compliance date for sIRB review January 2020. NIH sIRB policy in effect for applications submitted for due dates January 25, 2018 or later.
Provisions of the Revised Common Rule

• Informed Consent
  • Changes to requirements for informed consent forms
  • Broad consent option for secondary research
  • Eliminating requirement to waive consent for some screening and recruiting activities

• IRB Review
  • Removing requirement for IRBs to review grant applications
  • Requiring use of a single IRB
  • Changes to requirements for continuing review
  • Updating and simplifying expedited review

• Definition changes
  • Human subjects
  • Research

• Expansion of categories of exempt research

NIH Implementation

• No NIH requirement for IRBs to review grant applications and contract proposals
• Posting of clinical trial consent forms
  • See https://grants.nih.gov/policy/clinical_trials/informedconsent.htm
• No NIH requirement for certain continuing reviews
  • Studies eligible for expedited review
  • Studies that have completed interventions
• Changes to exemptions
  • Forms, Instructions & Reviewer Guidance Updated
• Using single IRB review
NOT-OD-19-050: NIH Implementation of Revised Common Rule

NIH Implementation of the Final Rule on the Federal Policy for the Protection of Human Subjects (Common Rule)

Notice Number: NOT-OD-19-050

Key Dates
Release Date: January 2, 2019

Related Announcements
NOT-OD-18-341
NOT-OD-19-055

Issued by
National Institutes of Health (NIH)

Purpose
The purpose of this notice is to provide guidance to the extramural research community regarding the NIH Implementation of the Final Rule amending the Federal Policy for the Protection of Human Subjects (Common Rule). NIH, along with other Common Rule departments and agencies, published the Final Rule in the Federal Register on January 19, 2017 and subsequently amended the Final Rule to delay the general compliance date until January 21, 2019.

Several provisions in the Revised Common Rule may result in changes to NIH policies and procedures, including: 1) removal of the requirement for Institutional Review Boards (IRBs) to review grant applications and contract proposals related to research; 2) a new requirement for clinical trial informed consent documents to be posted on a public federal government website; 3) changes to categorization of research that qualify for an exemption, and 4) removal of the requirement for annual IRB reviews for certain categories of research. Additional details, including requirements and processes for adopting the new provisions, can be found in the Final Rule.

As of January 21, 2019, studies initiated on or after that date, ongoing studies that voluntarily transitioned to the Revised Common Rule, and studies that voluntarily implemented the three burden-reducing provisions during the delay period (July 19, 2016 through January 20, 2019), are expected to comply with all Revised Common Rule requirements for the remainder of the study. For these studies, the following NIH provisions will apply:

- NIH will no longer require IRB review and approval of the entire grant application or contract proposal. Instead, the IRB must review and approve the research (e.g., a research protocol) for all NIH-supported non-exempt human subjects research studies. Recipients must provide certification to NIH that the IRB has reviewed and approved the research (e.g., research protocol).
- For NIH-funded or supported clinical trials, informed consent documents must be posted on a public federal website after enrollment closes and no later than 60 days after the last study visit. More information about these requirements is available at https://grants.nih.gov/policy/clinical-trials/informed-consent.htm.
- Applications or proposals that include studies to which the Revised Common Rule applies should take note of changes to categories of research qualifying for exemption and take care to select the appropriate category. Questions and answers about changes to exemptions may be found at https://www.hhs.gov/education-and-outreach/revised-common-rule/index.htm.
- For applications submitted for due dates on or after January 25, 2019, NIH will transition from "E" (e.g., E.34) to "X" codes (e.g., X.4) to reflect categories of exempt research. Those submitting applications for due dates on or after January 25, 2019 will have the option of using the new "X" codes beginning with the NIH due date on which the application was submitted.

Removal of the Requirement for Institutional Review Board Review of NIH Grant Applications and Contract Proposals Related to Research

Notice Number: NOT-OD-19-055

Key Dates
Release Date: January 11, 2019

Related Announcements
NOT-OD-19-000
NOT-OD-19-211

Issued by
National Institutes of Health (NIH)

Purpose
The purpose of this Notice is to provide guidance to the extramural research community about the implementation of revisions to the Final Rule on the Federal policy for the Protection of Human Subjects (Common Rule). The HHS Office of Human Research Protections (OHRP) published the Final Rule in the Federal Register on January 19, 2017 and amended the Final Rule to delay implementation until January 21, 2019.

This Notice specifically focuses on the removal of the requirement for Institutional Review Boards (IRB) to review grant applications and contract proposals related to research. The revised Common Rule states the following at 45 CFR 46.103(d):

Certification is required when the research is supported by a Federal department or agency and not otherwise waived under 101(i) or exempted under 104. For such research, institutions shall certify that each proposed research study covered by the assurance and this section has been reviewed and approved by the IRB. Such certification must be submitted as prescribed by the Federal department or agency component supporting the research. Under no condition shall research covered by this section be initiated prior to receipt of the certification that the research has been reviewed and approved by the IRB.

POLICY REQUIREMENT:

Effective January 21, 2019, NIH will no longer require IRB review of the entire grant application or contract proposal. However, grantees and offerors will be required to certify to NIH that an IRB has reviewed and approved all NIH-supported non-exempt human subjects research (i.e., protocols) and further provide NIH with the date of final IRB approval. The only change to NIH policy is that IRB review is no longer required for NIH grant applications and contract proposals. The certification and IRB date requirements align with current policy and Just-In-Time procedures.

NIH IMPLEMENTATION OF THE POLICY REQUIREMENT:

Recipients must provide NIH with a certification that all non-exempt human subjects research has been reviewed and approved by an appropriate IRB. The date of final IRB approval is the date the IRB certifies the research has been reviewed and approved. When the research is sponsored by an organization other than NIH, the certifying entity forwards the certification to NIH. The NIH received a date of certification and the date of final IRB approval.
**Exempt Human Subjects Research**

Meets the definition of human subjects research. Exempt studies involve human subjects research: research involving a living individual about whom data or biospecimens are obtained/used/studied/analyzed through interaction/intervention, or identifiable, private information is used/studied/analyzed/generated.

**Exemption 1:** conducted in an educational setting using normal educational practices*

*Cannot include any other procedures, such as collection of clinical data or biospecimens

**Exemption 2:** uses educational tests, surveys, interviews, or observations of public behavior*

*Limited IRB review may be required

**Exemption 3:** uses benign behavioral interventions

*Limited IRB review may be required

**Exemption 4:** involves the collection or study of data or specimens if publicly available or information recorded such that subjects cannot be identified

**Exemption 5:** public service program or demonstration project

**Exemption 6:** taste and food quality

**Exemption 7:** storage of identifiable information or biospecimens for secondary research use. *Broad consent is and limited IRB review are required.

**Exemption 8:** secondary research use of identifiable information or biospecimens. *Broad consent and limited IRB review are required.

For more information see the [OER website for Research Involving Human Subjects](https://www.oer.nih.gov).

Send questions/comments to [OER-HS@nih.gov](mailto:OER-HS@nih.gov).

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**NIH Requirements:**
- HS education
- Inclusion tracking for all except 4

**45 CFR 46 Requirements:**
- Limited IRB review for 7 & 8, and some study designs under 2 & 3.
- Broad consent for 7 & 8

**NEW Exemption 3:** Replaces exemption for specific types of research on public officials & candidates. Includes verbal, written or audiovisual data.

Must be brief in duration, harmless, painless, not physically invasive, unlikely to have adverse effect or be offensive and/or embarrassing to the subjects. Limited IRB review required when identifiable info is recorded.

**Exemption 5 expanded:** Includes federally supported research. Requires list of E5 projects to be published.
Use of a Single IRB


• However, NIH policy already in effect for domestic, multisite studies:
  • Published in NIH Guide and Federal Register: June 21, 2016; revised effective date
  • Effective for
    • Competing grant applications
      • Application due dates on/after January 25, 2018
    • Contract proposals
      • Solicitations issued on/after January 25, 2018
CONTACT US

WEB
Inclusion of Women and Minorities
https://grants.nih.gov/grants/funding/women_min/women_min.htm

Inclusion Across the Lifespan
https://grants.nih.gov/grants/funding/lifespan/lifespan.htm

EMAIL
inclusion@mail.nih.gov
Additional slides
Participant-Level Data

- De-identified individual-level participant data on sex/gender, race, ethnicity, and age at enrollment required in progress reports for applications submitted for due dates January 25, 2019 or later