Inclusion of Women, Minorities, and Individuals Across the Lifespan

ACRWH | Dawn Corbett | April 10, 2019

National Institutes of Health
Office of Extramural Research

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

CONGRESS.GOV | Legislation

H.R.34 - 21st Century Cures Act

114th Congress (2015-2016) | Get alerts

Requires:

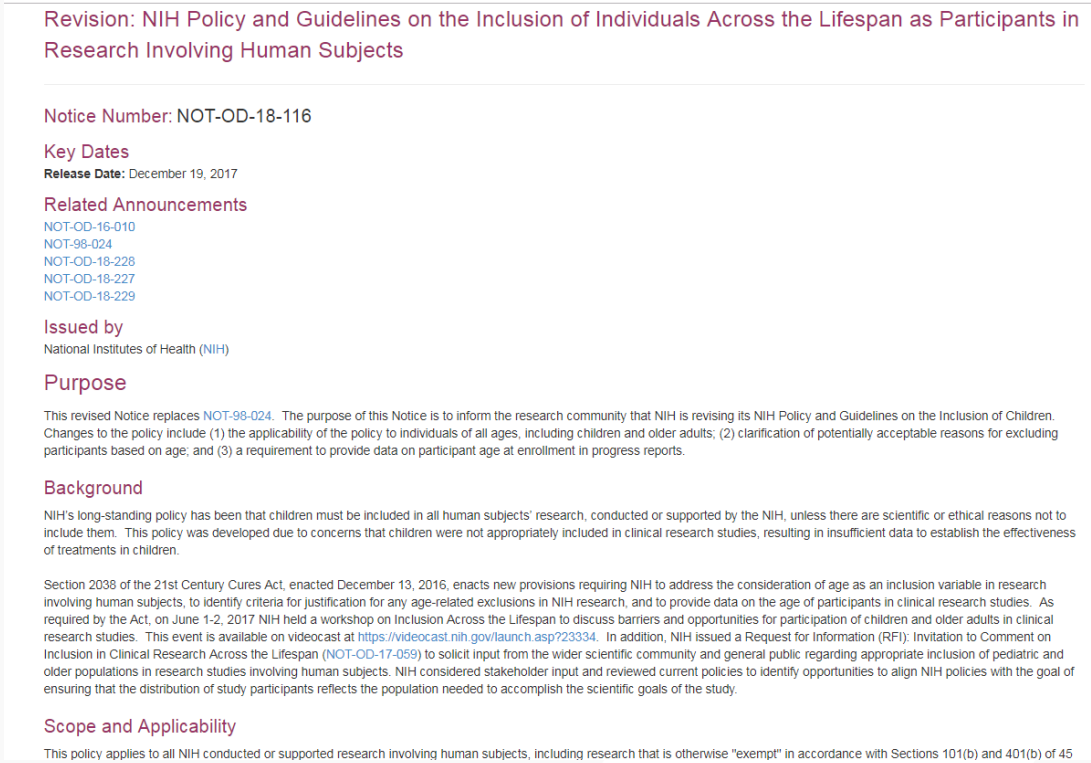
1. NIH convene a workshop on age groupings and exclusions, examine inclusion guidelines on age, and publish data on age of participants
2. NIH assemble participant inclusion data disaggregated by research area, condition, and disease categories
3. Applicable clinical trials must report results of valid analyses by sex/gender and race/ethnicity to Clinicaltrials.gov

Inclusion Across the Lifespan Workshop
June 1-2, 2017 Bethesda, MD

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



Revision: NIH Policy and Guidelines on the Inclusion of Individuals Across the Lifespan as Participants in Research Involving Human Subjects

Notice Number: NOT-OD-18-116

Key Dates

Release Date: December 19, 2017

Related Announcements

NOT-OD-16-010
NOT-98-024
NOT-OD-18-228
NOT-OD-18-227
NOT-OD-18-229

Issued by

National Institutes of Health (NIH)

Purpose

This revised Notice replaces NOT-98-024. The purpose of this Notice is to inform the research community that NIH is revising its NIH Policy and Guidelines on the Inclusion of Children. Changes to the policy include (1) the applicability of the policy to individuals of all ages, including children and older adults; (2) clarification of potentially acceptable reasons for excluding participants based on age; and (3) a requirement to provide data on participant age at enrollment in progress reports.

Background

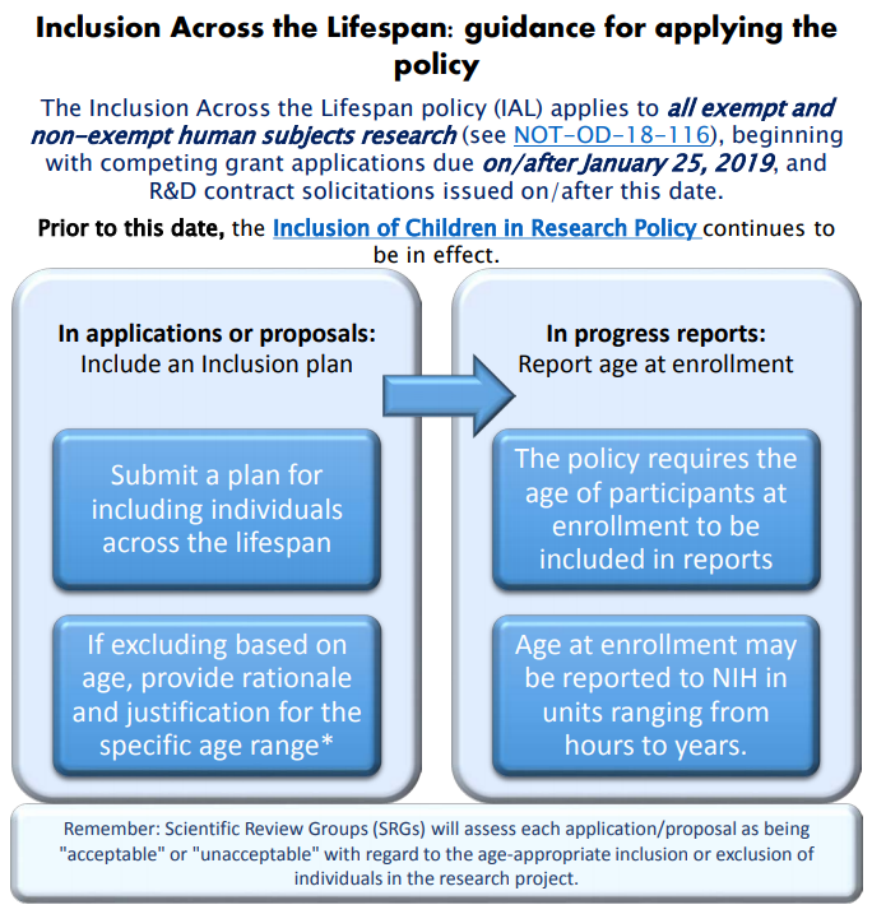
NIH's long-standing policy has been that children must be included in all human subjects' research, conducted or supported by the NIH, unless there are scientific or ethical reasons not to include them. This policy was developed due to concerns that children were not appropriately included in clinical research studies, resulting in insufficient data to establish the effectiveness of treatments in children.

Section 2038 of the 21st Century Cures Act, enacted December 13, 2016, enacts new provisions requiring NIH to address the consideration of age as an inclusion variable in research involving human subjects, to identify criteria for justification for any age-related exclusions in NIH research, and to provide data on the age of participants in clinical research studies. As required by the Act, on June 1-2, 2017 NIH held a workshop on Inclusion Across the Lifespan to discuss barriers and opportunities for participation of children and older adults in clinical research studies. This event is available on videocast at https://videocast.nih.gov/launch.asp?23334. In addition, NIH issued a Request for Information (RFI): Invitation to Comment on Inclusion in Clinical Research Across the Lifespan (NOT-OD-17-059) to solicit input from the wider scientific community and general public regarding appropriate inclusion of pediatric and older populations in research studies involving human subjects. NIH considered stakeholder input and reviewed current policies to identify opportunities to align NIH policies with the goal of ensuring that the distribution of study participants reflects the population needed to accomplish the scientific goals of the study.

Scope and Applicability

This policy applies to all NIH conducted or supported research involving human subjects, including research that is otherwise "exempt" in accordance with Sections 101(b) and 401(b) of 45

Inclusion Across the Lifespan: overview of recipient requirements



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

Amendment: NIH Policy and Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research

Notice Number: NOT-OD-18-014

Key Dates

Release Date: November 28, 2017

Related Announcements

NOT-OD-02-001
NOT-OD-01-053
NOT-OD-16-149

Issued by

National Institutes of Health (NIH)

Purpose

This Notice amends NOT-OD-02-001. The purpose of this Notice is to inform the research community that NIH is amending its NIH Policy and Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research to include a requirement that recipients conducting applicable NIH-defined Phase III clinical trials ensure results of valid analyses by sex/gender, race, and/or ethnicity are submitted to Clinicaltrials.gov. All other aspects of the NIH Policy and Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research remain unchanged.

Background

The NIH Revitalization Act of 1993, PL 103-43 (Public Health Service Act sec. 492B, 42 U.S.C. sec. 289a-2), signed into law on June 10, 1993, directed the NIH to establish guidelines for inclusion of women and minorities in clinical research The statute requires NIH to ensure that clinical trials are carried out in a manner sufficient to provide for a valid analysis of whether the variables being studied affect women or members of minority groups differently than other trial participants. See the NIH Policy and Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research for more information.

United States Government Accountability Office

GAO

Report to Congressional Requesters

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

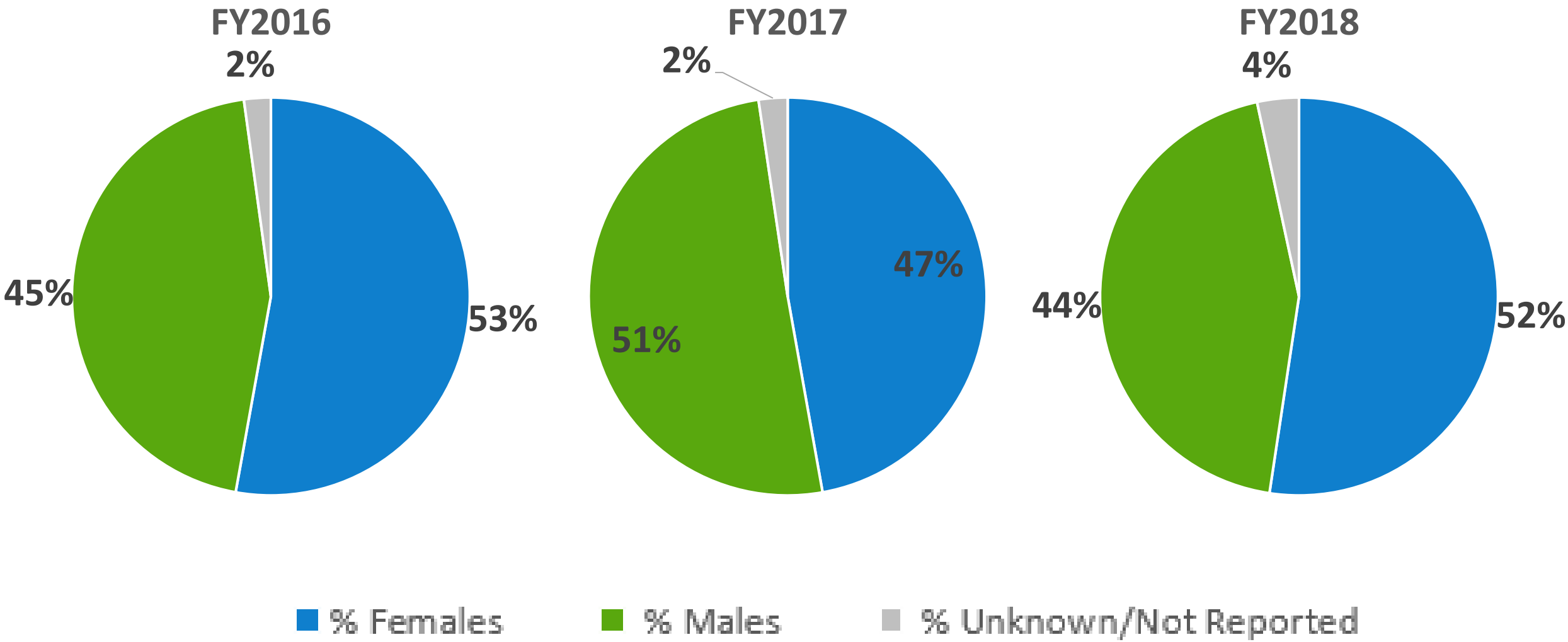
Table 2-1. Total Inclusion Data Records (IERs) for NIH-Defined Extramural and Intramural Clinical Research

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

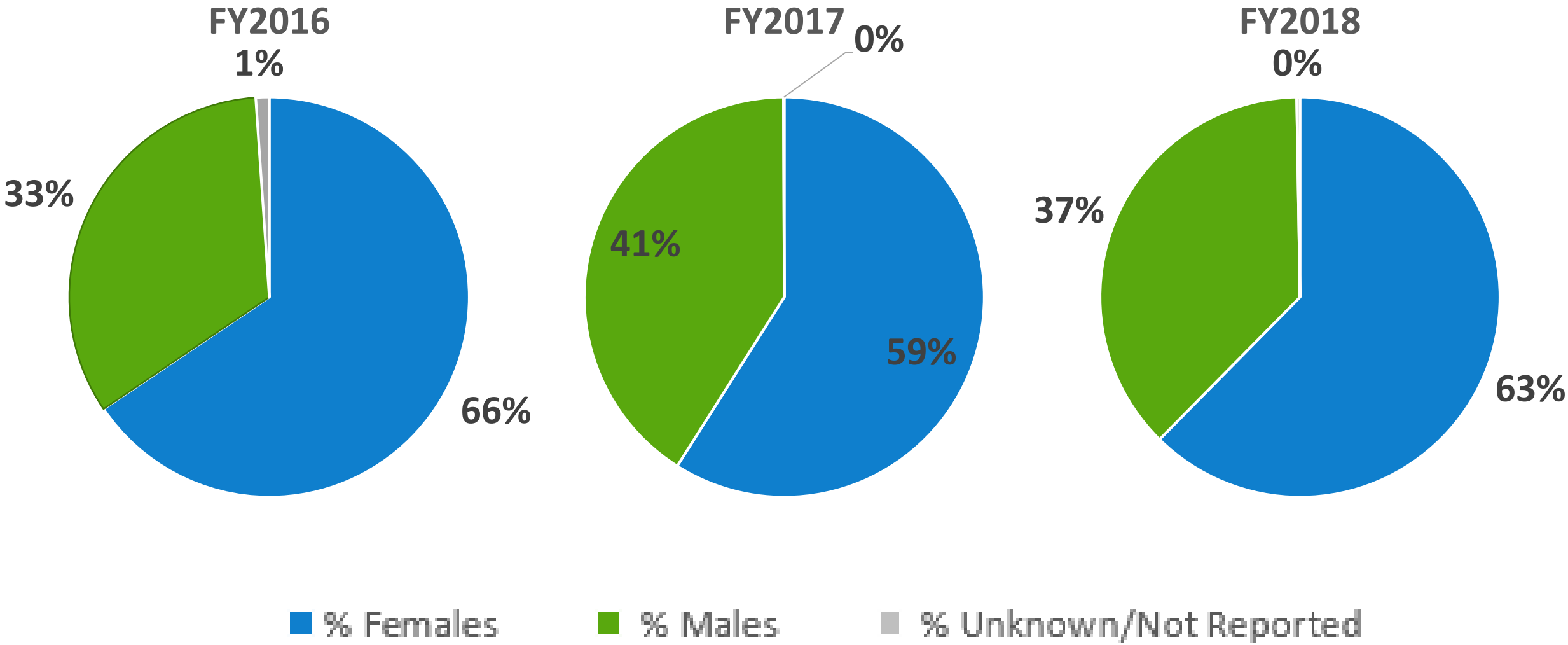
Table 2-2. Total Inclusion Data Records (IERs) for NIH-Defined Extramural and Intramural Phase III Trials

Fiscal Year	Total Inclusion Records	Inclusion Records with Enrollment	US Site Inclusion Records	Non-US Site Inclusion Records	Female Only Inclusion Records	Male Only Inclusion Records
2016	574	534	413	121	66	32
2017	618	574	440	134	89	27
2018	717	648	493	155	103	30

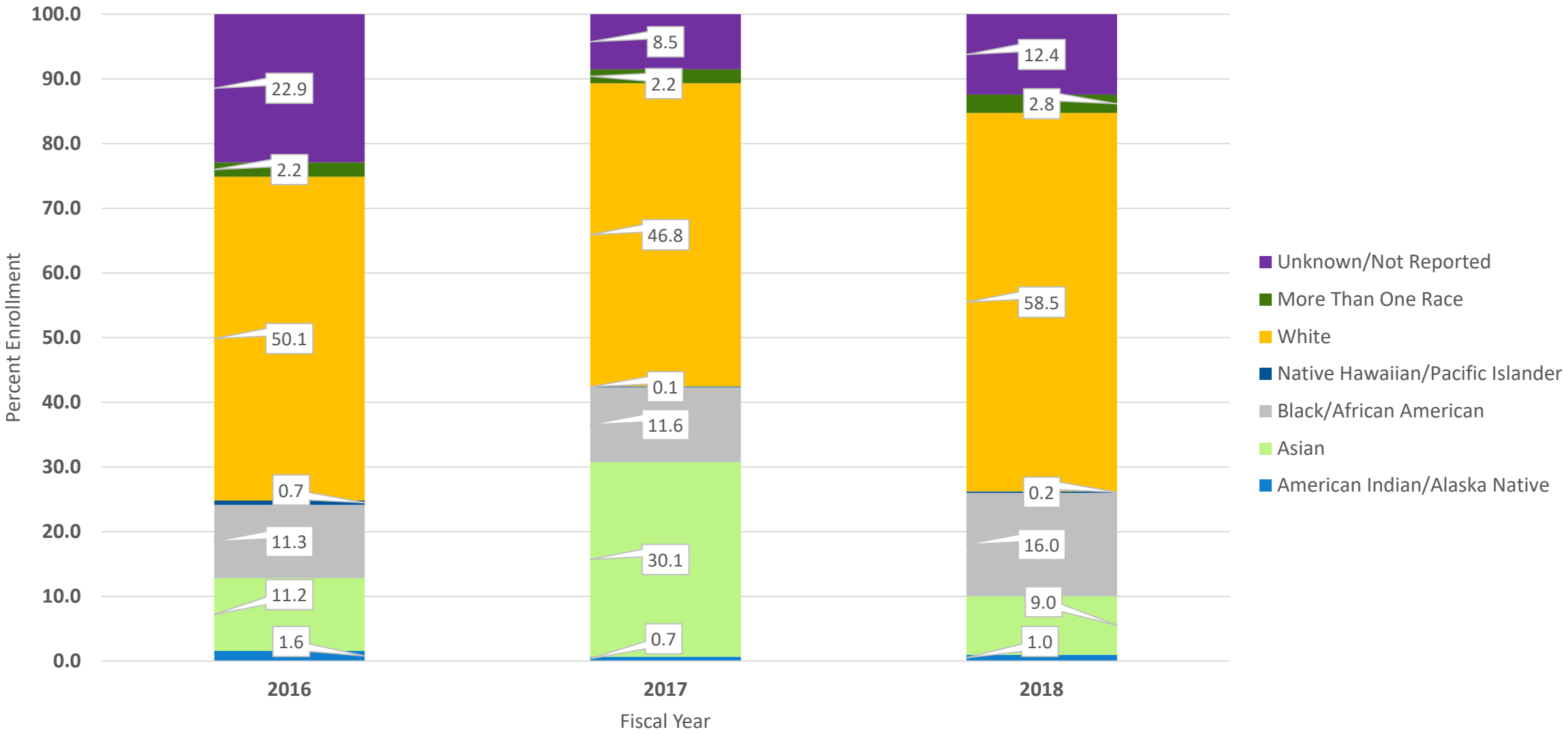
NIH Enrollment in Clinical Research by Sex/Gender FY2016 to FY2018



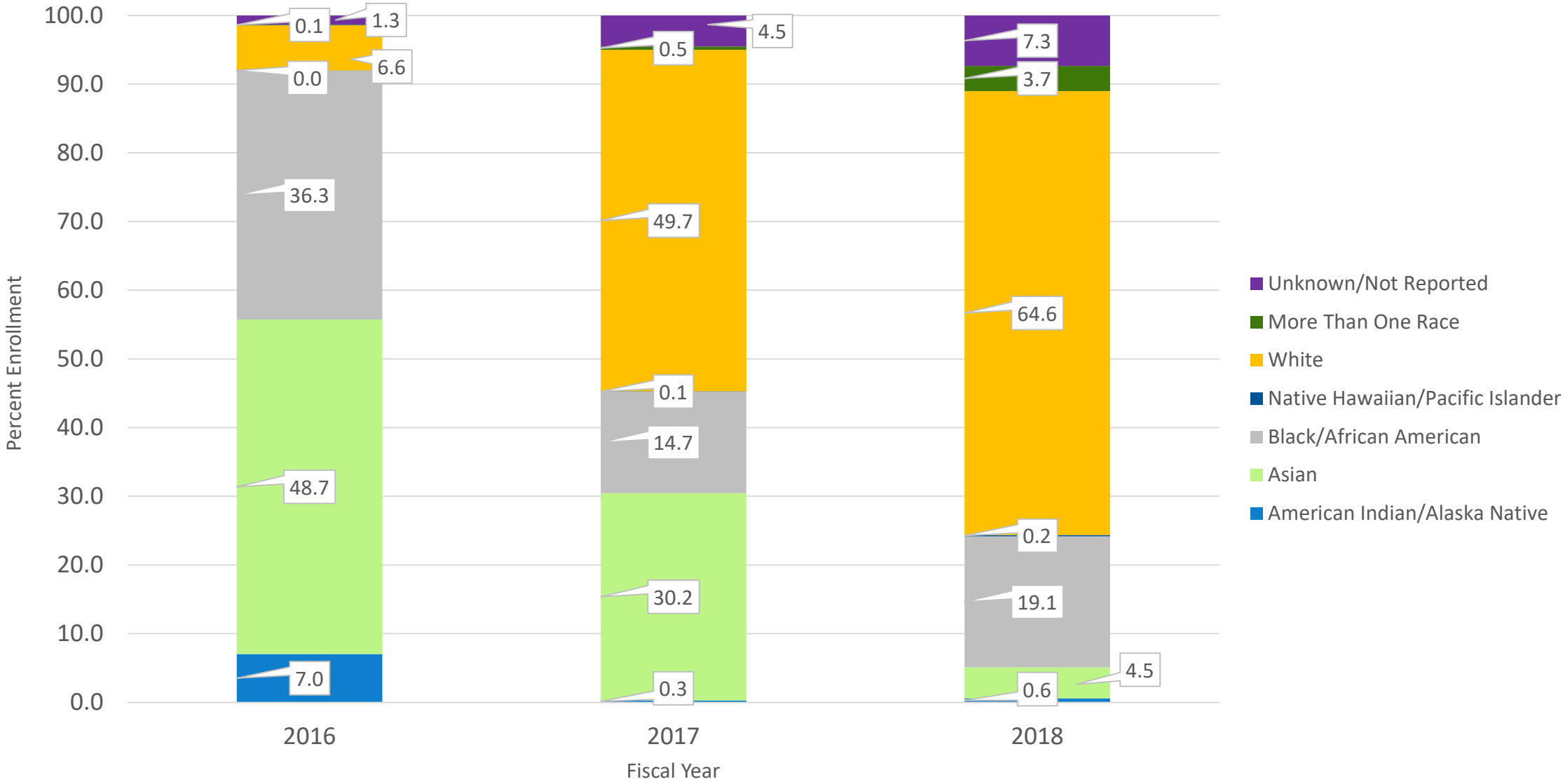
NIH-Defined Phase 3 Enrollment by Sex/Gender FY2016 to FY2018



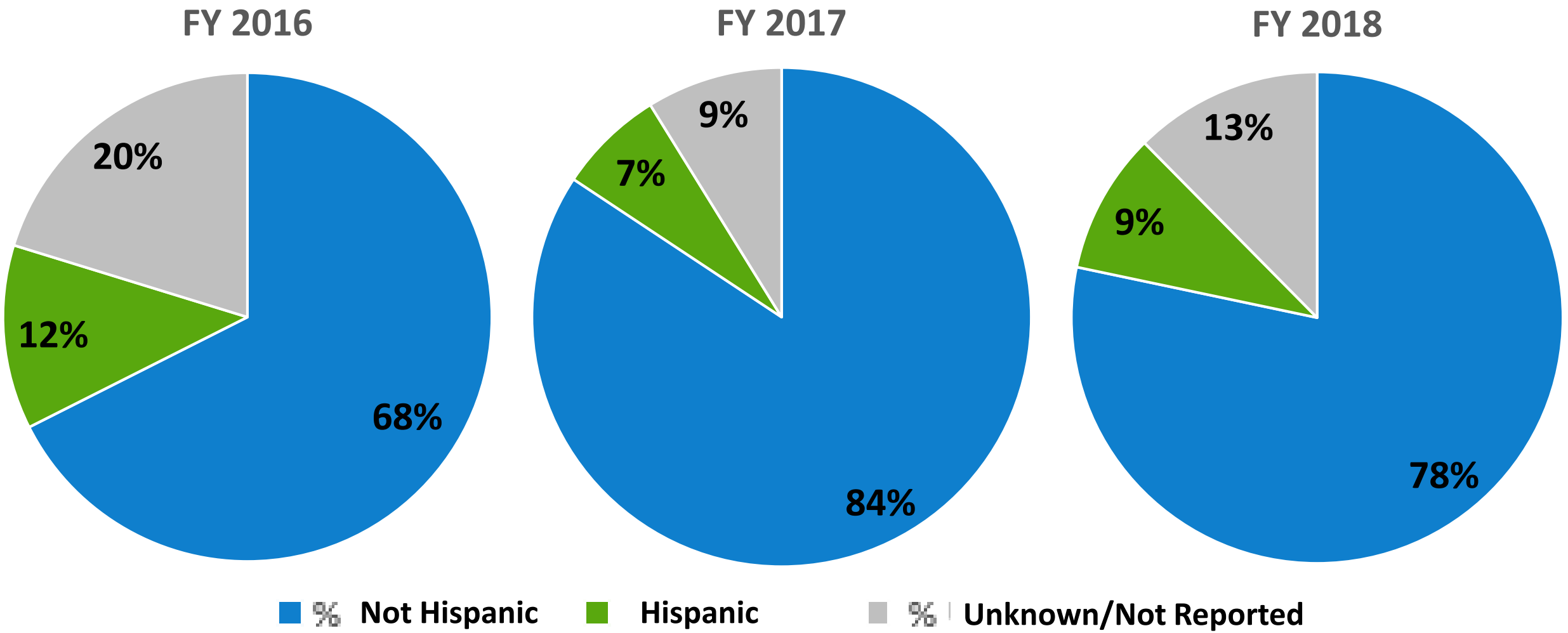
NIH Clinical Research Enrollment by Race FY2016 - FY2018



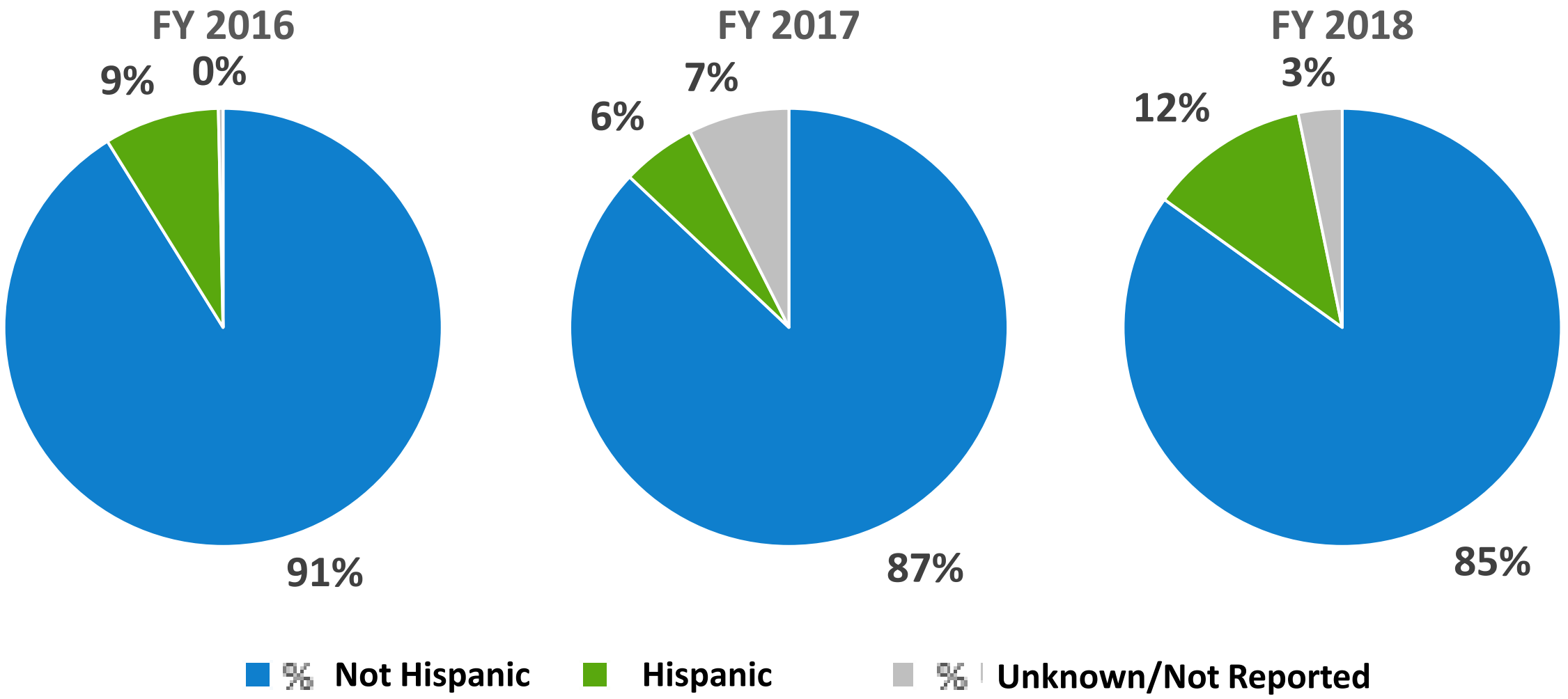
NIH Total: NIH-Defined Phase 3 Enrollment by Race FY2016 - FY2018



NIH Enrollment in Clinical Research by Ethnicity FY2016 - FY2018



NIH Total: NIH-Defined Phase III Enrollment by Ethnicity FY2016 - FY2018



What is the Common Rule?

- HHS Regulations on Human Research Protections: 45 CFR Part 46

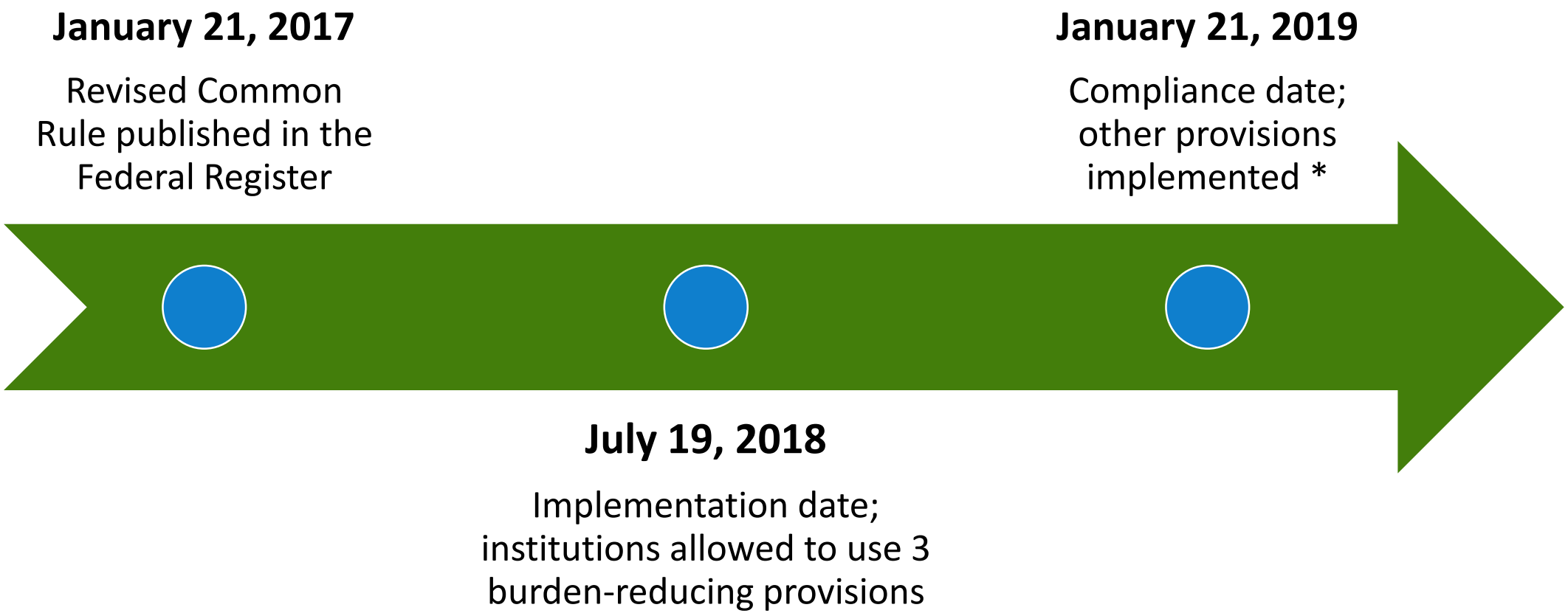
Subpart A – ***The Common Rule***

Subpart B – Pregnant women & fetuses

Subpart C – Prisoners

Subpart D – Children

Subpart E – IRB Registration



* 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

More info at https://www.hhs.gov/ohrp/education-and-outreach/revised-common-rule/index.html

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-18-211
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). HHS, 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 categories 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, 2018 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 recruitment 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/informedconsent.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/ohrp/education-and-outreach/revised-common-rule/revised-common-rule-q-and-a/index.html#exemptions.
- For applications submitted for due dates on or after January 25, 2019, NIH will transition from "E" (e.g. E4) to "X" codes (e.g. X4) to reflect categories of exempt research. Those submitting applications for due dates on or after January 25, 2019 will have the option of selecting exemption 7 or 8, if applicable. Applicants may see these changes in applications

NOT-OD-19-055: Removal of Requirement for IRB Review of Application/Proposal

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-19-050
NOT-OD-18-211

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) 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.

NIHs 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

Exempt Human Subjects Research

8 Exemptions

Consider

Exemption 1 addition: Cannot adversely impact student learning of required content or assessment of educators

Exemption 2 addition: NEW concept- limited IRB review for privacy/ confidentiality when identifiable info is recorded.

Exemption 4 expanded: No longer includes only existing data/specimens. Added HIPAA-regulated use as exempt.

NEW exemptions 7 and 8. Includes new concepts- broad consent and limited IRB review

1 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

2 Meets the criteria of one of the following exemptions:

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.

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

Cannot involve **prisoners**, unless includes a broader population that happens to include prisoners.

Cannot involve **children** in:
- Exemption 2 if investigators participate in the activity being observed or includes identifiable info. OR
- Exemption 3.

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.

For more information see the OER website for Research Involving Human Subjects.
Send questions/comments to OER-HS@nih.gov.

Use of a Single IRB

- Revised Common Rule requires use of a single Institutional Review Board (IRB) as of January 20, 2020.

- However, NIH policy already in effect for domestic, multi-site studies:
  - **Published in NIH Guide and Federal Register: June 21, 2016; revised effective date**
    - http://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-094.html
  - 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

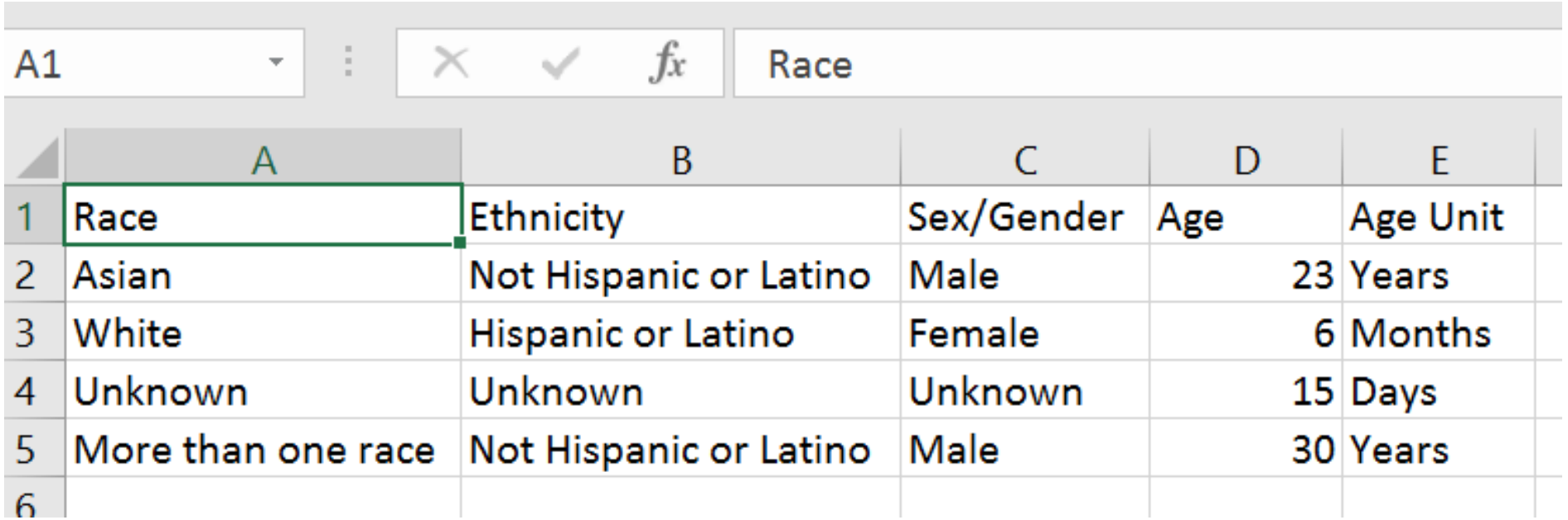
inclusion@mail.nih.gov

National Institutes of Health
Office of Extramural Research

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



	A	B	C	D	E
1	Race	Ethnicity	Sex/Gender	Age	Age Unit
2	Asian	Not Hispanic or Latino	Male	23	Years
3	White	Hispanic or Latino	Female	6	Months
4	Unknown	Unknown	Unknown	15	Days
5	More than one race	Not Hispanic or Latino	Male	30	Years
6					