

DEPARTMENT OF HEALTH AND HUMAN SERVICES

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**2013-2014 BIENNIAL ADVISORY COUNCIL REPORT
CERTIFYING COMPLIANCE WITH THE
NIH POLICY ON INCLUSION GUIDELINES**

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NATIONAL HUMAN GENOME RESEARCH INSTITUTE
2013-2014 BIENNIAL ADVISORY COUNCIL REPORT CERTIFYING
COMPLIANCE WITH INCLUSION GUIDELINES

Background and Overview

NIH mandates that women and members of minority groups and their subpopulations be included in all NIH-funded clinical research, unless a clear and compelling rationale and justification establishes, to the satisfaction of the relevant Institute/Center Director, that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. Exclusion under other circumstances may be made by the Director, NIH, upon recommendation of an Institute/Center Director based on a compelling rationale and justification. Cost is not an acceptable reason for exclusion except where the study would duplicate data from other sources. Women of childbearing potential should not routinely be excluded from participation in clinical research. The policy applies to research subjects of all ages in all NIH-funded clinical research studies.

Clinical research is defined as research with human subjects that is:

1. 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. It includes:
 - o mechanisms of human disease
 - o therapeutic interventions
 - o clinical trials
 - o development of new technologies
2. Epidemiological and behavioral studies.
3. Outcomes research and health services research.

Studies falling under 45 CFR part 46.101(b) (4) (Exemption 4) are not considered clinical research by this definition.

Not all studies involving human participants must be tracked. Most training, fellowship and career development awards do not require tracking. In addition, certain types of grants can be coded as exempt from tracking when the grant checklist is completed. Tracking data are collected in two forms: proposed or “target” data as described in an investigator’s grant application and actual or “enrollment” data based on participants actually recruited and examined in the course of the study.

Every two years, each NIH Institutional advisory council is required to review the aggregate data on the actual enrollment of participants in research supported by the Institute to ensure that the Institute: 1) is in compliance with the mandate for appropriate gender and minority inclusion; and 2) has in place adequate procedures to ensure these inclusion levels are monitored and maintained.

The following report discusses the aggregate enrollment data reported in FY2013 and FY2014 from the Extramural Research Programs (ERP) including the Divisions of Genomic Medicine, Genome Sciences, and Genomics and Society; and the Intramural Research Program (IRP) including the Division of Intramural Research. This report also describes the procedures followed by NHGRI staff to ensure appropriate gender and minority inclusion in all NHGRI research. The information contained in this report was discussed at the February 9-10, 2015, meeting of the National Advisory Council on Human Genome Research (NACHGR).

Strategies for Ensuring Compliance

Extramural Research Programs

- The ERP conducts an annual review of NHGRI's inclusion efforts and provides data to the NIH Office of Research on Women's Health. During the FY2013 and FY2014 reporting period, Dr. Rongling Li, Program Director, Division of Genomic Medicine, oversaw the process and provided leadership. She was assisted in this task by Ms. Joy Boyer, Ms. Christine Chang, Dr. Bettie Graham, and Ms. Jacqueline Odgis.
- The Extramural Research Program Directors document enrollment targets and progress on enrollment of human participants. If the information is missing or incomplete, the Program Director contacts the Principal Investigator and notifies her/him of the need to provide the necessary documentation. After ensuring that the data in the target/enrollment form are correct, the document is given to the extramural staff members who input the information into the Population Tracking Database. The extramural assistant, Ms. Jacqueline Odgis, reviews, approves, and signs off on the data in the database. A document providing detailed guidance on the roles and responsibilities of Program Directors in implementing the inclusion process is provided in the Appendix. All NHGRI extramural program staff members are provided with these guidelines and a presentation and discussion of the guidelines is provided at regularly scheduled staff meetings as needed.
- Scientific Review Officers (SROs) read all applications and proposals and note if clinical research is being proposed, and if the application is in compliance with the NIH policy on the Inclusion of Women and Minorities.
- SROs send "NIH Instructions to Reviewers for Evaluating Research Involving Human Subjects in Grant and Cooperative Agreement Applications" (http://grants.nih.gov/grants/peer/hs_review_inst.pdf) to scientists/clinicians/scholars that serve as peer reviewers on Scientific Review Panels to ensure that they are up to date on all human subject policy issues when evaluating applications.
- The Scientific Review Panels evaluate each application dealing with human participants during the initial review to determine if it is in compliance with the Inclusion Policy. The evaluation results are noted on the Summary Statement. The reviewers are instructed to include compliance with the inclusion policy when assigning an impact score.
- SROs document the gender and minority codes in summary statements.
- In cases where the Scientific Review Panel determines that a study is not in compliance or the applicant has not addressed the requirements in the application, a code is placed in the system that bars funding. If an award is to be made, the bar must be lifted, and documentation for the grounds on which the bar was lifted must be included in the official grant file. In general, the Grants Management Specialist will detect the bar and refer the issue to the Program Director. The Program Director must justify the lifting of the bar. This usually entails contacting the applicant institution and receiving additional information for inclusion in the official file. It is the responsibility of the Program Director to work with the applicant and her/his institution to comply with the NIH regulations. A document providing guidance is included in the appendix.
- Once the Program Director is assured that all the concerns have been addressed adequately, the Grants Management Specialist can request that the bar be lifted so that the award can be made.

- The non-competing renewal application (Type 5) is reviewed to determine how well the recruitment is going. If a Program Director determines that the recruitment is behind schedule, s/he will contact the grantee to determine what measures can be taken to ensure that the recruitment goals are met within the specified time.
- NHGRI arranges for staff to participate in NIH-wide and institute training sessions on population tracking.

Intramural Research Program

- The "Standards for Clinical Research within the NIH Intramural Program" found at <http://www.cc.nih.gov/ccc/clinicalresearch/index.html> states: "All clinical PIs are required to take an overview training course, or equivalent, on the roles and responsibilities of clinical investigators". The Clinical Center web site <http://www.cc.nih.gov/researchers/training.html> describes the general and degree training programs in clinical research that are available. The "Introduction to the Principles and Practice of Clinical Research" is part of the core curriculum in clinical research training, and is required of all principal investigators before they can submit a protocol for review by an NIH Institutional Review Board. All new clinical fellows are oriented as to the clinical research training programs that are available shortly after they arrive at NIH.
- In addition, as established in Standard Operating Procedures Chapter 25, Training Requirements for the NIH Human Research Protection Program [HRPP] (http://ohsr.od.nih.gov/ohsr/public/SOP_25_v3_2-26-14_508.pdf), "[a]ll Intramural Research Program (IRP) scientists are required to complete training in order to assure that they understand when research activities involve human subjects research and what is required when they conduct this type of research." All investigators and non-investigator research staff for the FY2013-FY2014 protocols covered in this report were required to complete the training requirements established in SOP 25.
- The Intramural scientists who are conducting clinical studies with human subjects submit their research protocols to the Intramural Institutional Review Board (IRB) for review. Only protocols that ensure the health and safety of human participants and that meet the NIH standards for appropriate inclusion of women and racial/ethnic minorities are approved. Specifically, investigators submit to the IRB a detailed description of their recruitment strategy for each protocol, including efforts to include under-represented minorities. In addition, investigators project their targeted/planned enrollment, with anticipated numbers of participants in gender, racial, and ethnic categories. Continuing review applications that include ongoing gender and minority enrollment forms are reviewed by the IRB at least annually to ensure ongoing compliance. Enrollment data are submitted annually to the Clinical Center Office of Protocol Services (OPS) for inclusion in their central database. NHGRI receives this data on a biennial basis for reporting purposes.
- Dr. Sara Hull, Chair, NHGRI Institutional Review Board coordinates with OPS on behalf of the NHGRI Division of Intramural Research for the receipt and review of these data in preparation of biennial reports.

Discussion of Data Reported in FY2013 and FY2014

The clinical research studies funded by NHGRI tend to fall into a few basic categories: 1) qualitative studies that include a small number of research participants in focus group or structured interview settings; 2) larger phone, paper, or internet-based studies that survey the attitudes, beliefs or practices of either discrete populations (e.g. health professionals, genomic researchers, IRB chairs, individuals who have undergone genetic testing, disease/disability communities, minority communities) or the general population; and 3) studies that utilize existing or prospectively identified

cohorts for statistical analysis, prospective linkage/gene identification, or genome-wide associations. A number of the qualitative, survey, and genetic testing studies are limited to discrete target populations that may not be always racially or ethnically diverse. As a result, the demographic breakdown of NHGRI research enrollment may differ slightly from the US population, depending on the types of studies active in a given year.

In addition, ERP currently funds a study conducted by 23andMe with >580,000 participants, nearly three times the size of all other ERP funded studies combined. This study collects data differently from other studies and is not directly comparable to them. We report the data from this study separately in the ERP section, and with and without the 23andMe study participants for the combined NHGRI report. It should also be noted that NHGRI does not support any Phase III clinical trials.

Note: For the purposes of this report, a protocol is defined as a single grant or IRB-approved project. Each of the sites of an extramural multicenter project is considered to be a single protocol; hence a project like eMERGE with nine sites is counted as nine protocols.

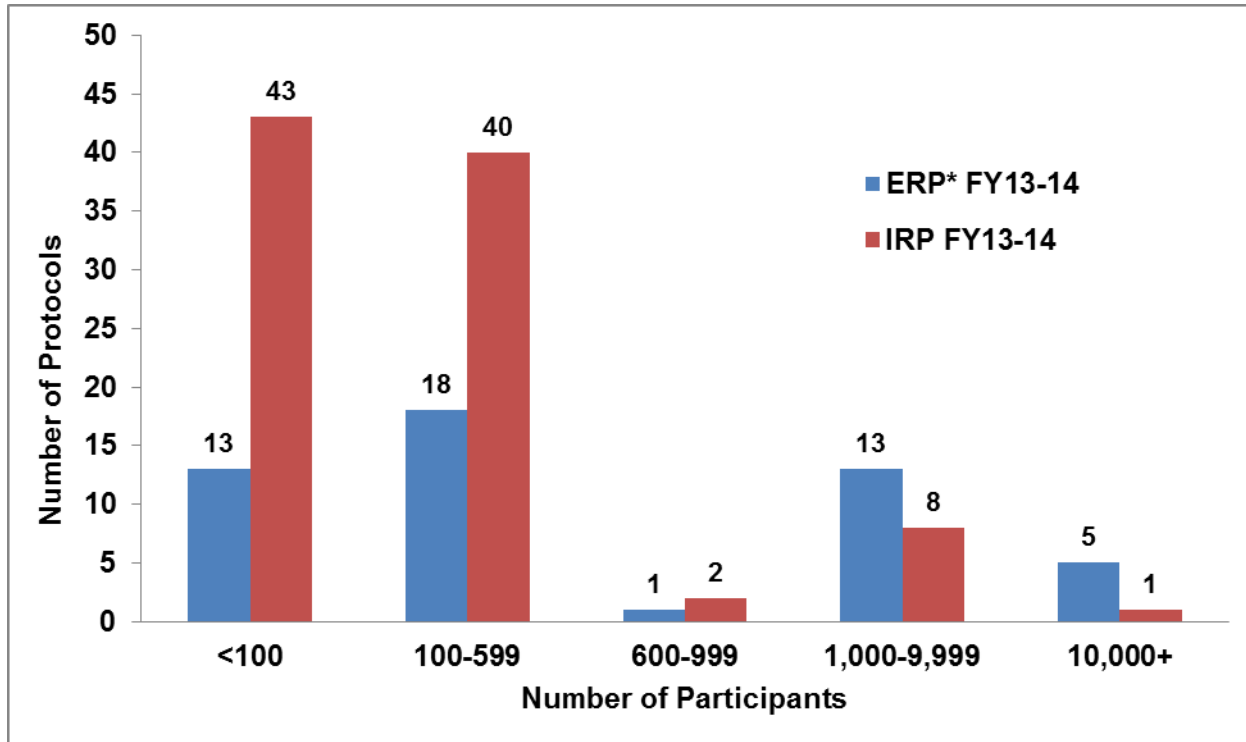
Table 1. Number of Protocols and Actual Enrollment (excluding 23andMe)

| | | ERP* | IRP | Total |
|-----------------------------|------------------------|---------|--------|---------|
| FY2013 | Number of Protocols | 32 | 85 | 117 |
| | Number of Participants | 188,372 | 60,321 | 248,693 |
| FY2014 | Number of Protocols | 40 | 92 | 131 |
| | Number of Participants | 237,448 | 64,416 | 301,864 |
| Total, FY2013-FY2014 | Number of Protocols | 50 | 94 | 144 |
| | Number of Participants | 238,273 | 64,717 | 302,990 |

*ERP data excluding 23andMe.

Table 1 shows the number of protocols and actual enrollment active during FY2013, FY2014, and the total two-year period. There were 22 extramural and 83 intramural research protocols active in both FY2013 and FY2014, so the total numbers of protocols and participants during 2013 and 2014 are not the sum of these numbers in the two individual years. For the remainder of this biennial report, we report the total numbers for the two-year period FY2013-FY2014.

Figure 1. Size of Funded Protocols



*ERP data excluding 23andMe.

Extramural Research Program

In FY2013-FY2014, 238,273 individuals were enrolled in 50 ongoing extramural research protocols, excluding 23andMe (Table 1). The sample size for these protocols ranged from 1 to 50,495; 13 protocols had a sample size less than 100, 18 protocols had a sample size of 100-599, 1 protocol has a sample size of 600-999, 13 protocols had a sample size of 1,000-9,999, and 5 protocols had a sample size equal or greater than 10,000 (Figure 1).

Table 2a presents FY2013-FY2014 actual enrollment by race, ethnicity and gender excluding 23andMe. Among the 238,273 enrolled individuals, there were 56.7% White, 20.4% Black/African American (Bl/AA), 7.3% Asian, 1.5% Hawaiian and Pacific Islanders (Haw/Pac), 3.8% American Indian/Alaska Native (AI/AN), 1.6% reported identification of more than one race, and 8.6% had no racial identification reported. Comparing the racial distribution of FY2013-FY2014 with the distribution of FY2011-FY2012, the proportion of minority participants increased for Bl/AA from 19.2% to 20.4%, and for AI/AN from 3.0% to 3.8%. The proportion of Asians (17.8% vs. 7.3%) and Haw/Pac (4.3% vs. 1.5%) decreased. The proportion of unknown race increased from 1.7% in FY2011-FY2012 to 8.6% in FY2013-FY2014. The ethnic breakdown of the Not Hispanic (Not Hisp), Hispanic/Latino (Hisp/Lat), and unknown ethnicity (Unk) participants enrolled in studies was 80.1%, 16.0% and 3.9% respectively in FY2013-FY2014 compared to 82.5%, 15.1% and 2.4% in FY2011-FY2012. There was a slight increase in Hisp/Lat and unknown ethnicity. The gender breakdown of these participants was 61.9% female, 37.6% male and 0.5% unknown gender. There was no significant difference comparing with the last report (61.2% female, 37.9% male, and 0.9% unknown in FY2011-FY2012).

The increased proportion of unknown race in FY2013-FY2014 is due to inclusion of one long-established cohort for which race and ethnicity were collected as a single variable, and two others in which persons reporting Hispanic ethnicity did not select a race. Thus, of the 8.6% unknown race, 83% (7.1% of the total participants) reported Hispanic/Latino ethnicity but did not report race and 17% (1.5% of the total) did not report either race or ethnicity.. Investigators in these studies have advised

us that persons reporting Hispanic ethnicity, particularly recent immigrants, are not familiar U.S. census categories defining race and are less likely to define themselves by these categories.

Table 2a. FY2013-FY2014 Extramural Research Actual Enrollment by Race, Ethnicity and Gender (excluding 23andMe)

| | | Race | | | | | | | |
|----------|---------|--------|--------|---------|-------|---------|--------|---------|--|
| | White | BI/AA | Asian | Haw/Pac | AI/AN | >1 Race | Unk | Total | |
| N | 135,005 | 48,650 | 17,471 | 3,681 | 9,079 | 3,782 | 20,605 | 238,273 | |
| % | 56.7 | 20.4 | 7.3 | 1.5 | 3.8 | 1.6 | 8.6 | 100.0 | |

| | | Ethnicity | | | | Gender | | | |
|----------|----------|-----------|-------|---------|-----------|--------|-------|---------|--|
| | Not Hisp | Hisp/Lat | Unk | Total | Female | Male | Unk | Total | |
| N | 190,867 | 38,214 | 9,192 | 238,273 | n 147,396 | 89,651 | 1,226 | 238,273 | |
| % | 80.1 | 16.0 | 3.9 | 100.0 | % 61.9 | 37.6 | 0.5 | 100.0 | |

The enrollment for the 23andMe study entitled “Development of a web-based database and research engine for genetic discovery” is presented in Table 2b. As noted, this protocol was analyzed separately from others as its enrollment is nearly three times the combined enrollment for all other ERP protocols. This online study has a high proportion of unknown race because participants have the option not to respond. Among the 583,266 enrolled individuals, there were 58.1% White, 4.9% BI/AA, 2.2% reported identification of more than one race, and 30.4% reported no racial identification. There was no reported enrollment of Haw/Pac and AI/AN participants. The ethnic breakdown of the Not Hispanic/Latino (Not Hisp) and Hispanic/Latino (Hisp/Lat) participants enrolled was 89.2% and 10.8%, respectively. Participants were assumed to be Not Hispanic/Latino unless they specifically reported otherwise, so there were no participants of unknown ethnicity reported. The gender breakdown of these participants was inferred from genetic data and was 48.6% female, 51.4% male with none unknown.

Table 2b. FY2013-FY2014 Extramural Research, 23andMe Only, Enrollment by Race, Ethnicity and Gender

| | | Race | | | | | | | |
|----------|---------|--------|--------|---------|-------|---------|---------|---------|--|
| | White | BI/AA | Asian | Haw/Pac | AI/AN | >1 Race | Unk | Total | |
| N | 338,974 | 28,511 | 25,664 | 0 | 0 | 13,007 | 177,110 | 583,266 | |
| % | 58.1 | 4.9 | 4.4 | 0.0 | 0.0 | 2.2 | 30.4 | 100.0 | |

| | | Ethnicity | | | | Gender | | | |
|----------|----------|-----------|-----|---------|---------|---------|-----|---------|--|
| | Not Hisp | Hisp /Lat | Unk | Total | Female | Male | Unk | Total | |
| N | 520,033 | 63,233 | 0 | 583,266 | 283,467 | 299,799 | 0 | 583,266 | |
| % | 89.2 | 10.8 | 0.0 | 100.0 | 48.6 | 51.4 | 0.0 | 100.0 | |

For completeness we show the ERP enrollment data including 23andMe though they are heavily skewed by the large numbers of participants in that single study (Table 2c).

Table 2c. FY2013-FY2014 Extramural Research Enrollment by Race, Ethnicity and Gender (including 23andMe)

| | Race | | | | | | | Total |
|----------|---------|--------|--------|---------|-------|---------|---------|---------|
| | White | BI/AA | Asian | Haw/Pac | AI/AN | >1 Race | Unk | |
| N | 473,979 | 77,161 | 43,135 | 3,681 | 9,079 | 16,789 | 197,715 | 821,539 |
| % | 57.7 | 9.4 | 5.3 | 0.4 | 1.1 | 2.0 | 24.1 | 100.0 |

| | Ethnicity | | | | Gender | | | |
|----------|-----------|-----------|-------|---------|---------|---------|-------|---------|
| | Not Hisp | Hisp /Lat | Unk | Total | Female | Male | Unk | Total |
| N | 710,900 | 101,447 | 9,192 | 821,539 | 430,863 | 389,450 | 1,226 | 821,539 |
| % | 86.5 | 12.3 | 1.1 | 100.0 | 52.4 | 47.4 | 0.1 | 100.0 |

Intramural Research Program

In FY2013-FY2014, there were 64,717 research participants in 94 NHGRI intramural research protocols (Table 1). The sample size for these 94 protocols ranged from 1 to 32,809; sample size was less than 100 in 43 protocols, 100-599 in 40 protocols, 600-999 in 2 protocols, 1,000-9,999 in 8 protocols, and 10,000 or greater in one protocol. (Figure 1)

The distribution of race, ethnicity and gender is shown in Table 3. Among the participants, 70.9% were White, 20.5% BI/AA, 4.4% Asian, 0.1% Haw/Pac, 0.1% AI/AN, and 0.6% identified themselves as more than one race. No racial identification was reported for approximately 3.5% of the research participants. Comparing the FY2013-FY2014 distribution to that of FY2011-FY2012, the proportion of minority participants increased for Black/African Americans from 8.2% to 20.5% and for Hawaiian/Pacific Islanders from 0.03% to 0.1%. The proportion of Asian participants enrolled decreased from FY2011-FY2012 (7.9%) to FY2013-FY2014 (4.4%). The proportion of subjects for which no racial identification was reported increased from FY2011-FY2012 (1.9%) to FY2013-FY2014 (3.5%). From FY2011-FY2012 to FY2013-FY2014, the proportion of American Indian/Alaska Natives decreased from 3.5% to 0.6%. The proportion of participants who reported identifying as more than one race remained consistent at 0.1% from FY2011-FY2012 to FY2013-2014. The ethnic breakdown of these participants was 95.4% non-Hispanic, 2.6% Hispanic, and 2.0% unknown. The gender breakdown was 43.6% female, 51.5% male and 4.9% unknown.

The missing race, ethnicity, and gender enrollment data are due to 1) participants who chose not to self-report their race, ethnicity, and/or gender in on-line surveys; and 2) one large international collaborative study for which the enrollment data by gender had not yet been received from the data coordinating center at the time of IRB submission. The principal investigator is following up with the data center and will report the updated data at the time of the next annual continuing review. This study accounted for 2,262 of the “unknowns” in the gender category. Once corrected, the proportion of unknown gender data will drop from 4.9% to approximately 1.4%.

Table 3. FY2013-FY2014 Intramural Research Actual Enrollment by Race, Ethnicity and Gender

| | Race | | | | | | | Total |
|----------|--------|--------|-------|---------|-------|---------|-------|--------|
| | White | BI/AA | Asian | Haw/Pac | AI/AN | >1 Race | Unk | |
| N | 45,854 | 13,258 | 2,822 | 34 | 94 | 403 | 2,252 | 64,717 |
| % | 70.9 | 20.5 | 4.4 | 0.1 | 0.1 | 0.6 | 3.5 | 100.0 |

| | Ethnicity | | | | Gender | | | |
|----------|-----------|----------|-------|--------|--------|--------|-------|--------|
| | Not Hisp | Hisp/Lat | Unk | Total | Female | Male | Unk | Total |
| N | 61,725 | 1,694 | 1,298 | 64,717 | 28,251 | 33,322 | 3,144 | 64,717 |
| % | 95.4 | 2.6 | 2.0 | 100.0 | 43.6 | 51.5 | 4.9 | 100.0 |

NHGRI Data Compared to 2010 US Census Data

Table 4 provides a comparison among: (1) the NHGRI actual enrollments in FY2010, FY2011-FY2012 and FY2013-FY2014, excluding and including 23andMe; and (2) the demographic breakdown from the 2010 US Census.

Table 4. Comparison with 2010 US Census Data

| Category | 2010 NHGRI | 2011-12 NHGRI | 2013-14 NHGRI* | 2013-14 NHGRI | 2010 US Census |
|------------------------------------|----------------|----------------|----------------|----------------|--------------------|
| White (%) | 60.8 | 60.3 | 59.7 | 58.7 | 72.4 |
| Black/African American (%) | 13.4 | 17.7 | 20.4 | 10.2 | 12.6 |
| Asian (%) | 4.1 | 13.7 | 6.7 | 5.2 | 4.8 |
| Hawaiian/Pacific Islander (%) | 1.0 | 3.2 | 1.2 | 0.4 | 0.2 |
| American Indian/ Alaska Native (%) | 3.4 | 2.2 | 3.0 | 1.0 | 0.9 |
| >1 Race (%) | 1.6 | 1.2 | 1.4 | 1.9 | 2.9 |
| Unknown (%) | 15.8 | 1.7 | 7.5 | 22.6 | 6.2 |
| Not Hispanic (%) | 75.7 | 84.1 | 83.4 | 87.2 | 83.7 |
| Hispanic/Latino (%) | 8.7 | 12.1 | 13.2 | 11.6 | 16.3 |
| Unknown (%) | 15.6 | 3.8 | 3.5 | 1.2 | 0.0 |
| Female (%) | 53.4 | 57.0 | 58.0 | 51.8 | 50.8 |
| Male (%) | 34.7 | 40.1 | 40.6 | 47.7 | 49.2 |
| Unknown (%) | 11.9 | 3.0 | 1.4 | 0.5 | |
| Total | 245,563 | 375,551 | 302,990 | 886,256 | 308,745,538 |

* NHGRI data excluding 23andMe

Comparing trends across FY2010 through FY2014 and excluding 23andMe, NHGRI improved enrollment of several minority groups. Notably, Black/African American enrollment increased from 17.7% in FY2011-FY2012 to 20.4% in FY2013-FY2014, and American Indian and Alaska Native enrollment increased from 2.2% in FY2011-FY2012 to 3.0% in FY2013-FY2014. In comparison to FY2010 data and excluding 23andMe, enrollment improved for nearly all minority groups, as did enrollment of Hispanic/Latino and female participants. While the proportion of participants with unknown race decreased in FY2013-FY2014 from FY2010, it is higher than FY2011-FY2012. As noted above for Table 2a, this is due to inclusion of cohorts in which ethnicity was reported in preference to race.

The distribution of NHGRI enrolled research participants in FY2013-FY2014 was more diverse than the 2010 US Census. Comparing the FY2013-FY2014 NHGRI data (excluding the 23andMe study) with the 2010 US Census data, NHGRI studies enrolled high proportions of Black/African Americans (20.4% vs. 12.6%), Asians (6.7% vs. 4.8%), Hawaiians/Pacific Islanders (1.2% vs. 0.2%), American Indians and Alaska Natives (3.0% vs. 0.9%). This remained true, marginally, when including 23andMe. NHGRI studies also enrolled a higher proportion of female participants in FY2013-FY2014 (51.8% including and 58.0% excluding 23andMe) as compared with the 2010 US Census data (50.8%).

Summary

- NHGRI improved enrollment of minority and female participants in FY2013-FY2014 compared with previous years.
- NHGRI had a more diverse group of enrolled research participants compared with the 2010 US census.
- The high proportion of unknown race/ethnicity in the large 23andMe study significantly skewed the proportions unknown for NHGRI as a whole and are beyond the control of NHGRI and 23andMe.
- The large number of participants in existing cohorts where race and ethnicity were collected in a single item increased the proportion of unknown race in the NHGRI ERP data excluding 23andMe.

Appendix

NATIONAL HUMAN GENOME RESEARCH INSTITUTE (NHGRI) STAFF GUIDANCE FOR INCLUSION OF POPULATIONS IN NHGRI-SUPPORTED RESEARCH GRANTS

The purpose of this document is to provide guidelines for NHGRI staff in tracking and reporting inclusion of human populations in NHGRI-funded studies.

Reporting of the Extramural Research Program (ERP) projects depends upon staff reviewing applications prior to funding to determine whether the grant is a candidate for population tracking and ensuring that the targeted/planned and inclusion enrollment data are accurate. The Type 5 applications are reviewed to ensure that inclusion efforts are consistent with the goals of the grant and that the data submitted by the PIs are accurate.

When projects that involve human participants are proposed or awarded, there are several points along the continuum from pre-application guidance to final progress report in which staff should be actively involved:

- Pre-Application Consultation.

When staff members are providing guidance to prospective applicants who plan to conduct studies on human participants, Principal Investigators should be apprised of the NHGRI requirement. In some proposed studies, it may not be appropriate to include certain populations or both genders; in such cases, there must be a strong justification for exclusion.

- Prior to Award.

There may be instances where an application has received a fundable score, but there is clear evidence that additional populations can be added to expand the diversity of the data set. In such cases, staff may discuss this with the Principal Investigator who may then request supplemental funding, if appropriate, to support the expansion,

If a study receives a fundable priority score and the study section has not flagged the application for study design concerns, but staff believes that the research can be improved or enhanced by adding additional populations, staff may take the application to Council with the recommendation that it be approved for high program priority (and funding) only on the condition that the additional populations be included.

- Award of Competing Applications.

Prior to making an award, staff must determine whether the recruitment/enrollment of human participants or the addition of new data on already-recruited participants will be tracked and indicate this decision on the grant checklist through the program module (PGM) of IMPAC II. Staff should use the guidelines provided by the Office of the Director, NIH, (see definition under "Background" of this document and list of exemption codes in http://impacii.nih.gov/popdoc/Tracking_Exception_codes_04-21-04.pdf). In addition, as noted above, studies that use already recruited populations but for which new data (such as genotyping data) are generated are also tracked.

- Changes in Human Subject Research Post Award.

Any change in research procedures in an active award that would result in an increased risk to human subjects will require prior NIH approval before implementation (<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-12-129.html>).

The institution must submit a separate request to the GMO of the funding IC no later than 30 days before the proposed change. The Program Director must review the request and it must be approved by the PD's supervisor before the change is implemented.

If program staff members are unsure of whether a project should be tracked, a small subcommittee of ERP staff will review the project with the Program Director and make a determination.

ROLES AND RESPONSIBILITIES:

- NHGRI staff will:

- (a) Apprise potential applicants proposing research involving human subjects (including the collection of new data from previously recruited subjects) of NHGRI's requirement. If the proposed project is a candidate for population tracking, then staff should discuss inclusion options;
- (b) Determine prior to Council whether additional populations would add value to the study and if so, discuss with the PI and propose a supplement to Council, if necessary;
- (c) If appropriate, propose to Council that an application be designated High Programmatic Priority only on the condition that the study population is enhanced to meet NHGRI's requirement for support;
- (d) Determine which grants need to be tracked in the population tracking database. If an exception code is warranted, indicate the code on the grant checklist so that it can be entered into IMPAC II (For more information see http://impacii.nih.gov/popdoc/Tracking_Exception_codes_04-21-04.pdf);
- (e) Determine the enrollment status of the grant: 1) pending enrollment (P) means that target data has been provided, but enrollment of participants has not started; 2) open enrollment (O) means that enrollment has started but is not complete; and 3) closed enrollment (C) means enrollment is completed and no more participants will be recruited. Enrollment forms submitted before enrollment begins should indicate the status as "P" or pending. After enrollment starts the form should indicate the status as "O" or open. When enrollment is completed, the enrollment status on the form would be "C" or closed.
- (f) If a project should be tracked but the protocol has not yet been developed and the target data is not available, indicate "ND" for protocol not developed on the target data form (this is sometimes the case with Center grants, or GWA studies that use existing samples);
- (g) Review targeted/planned and inclusion tables for accuracy (all the numbers add up) and completeness (all the appropriate cells filled);
- (h) Make sure that the "ethnic category: total of all subjects" equals the "racial category: total of all subjects";
- (i) If the targeted/planned inclusion for the grant is not representative of the US population, provide a brief explanation on the target/planned form (e.g. condition being studied is most prevalent in individuals of a particular gender, race or ethnic group; or research participants are

limited to members of a particular professional or community group which does not include representative gender or racial/ethnic diversity)

- (j) If the target/planned gender and minority status of grant participants is unknown, provide a brief justification for this (e.g. study design limits ability to collect demographic data.)
- (k) Contact the Principal Investigator if there are questions about the form(s) BEFORE giving it (them) to the extramural assistant;
- (l) Ensure that each table is labeled properly and consistently (it is particularly important that the protocol titles on inclusion enrollment forms are consistent from year to year to ensure that duplicate protocols are not inadvertently created in the database.)
- (m) Provide separate tables for foreign and domestic participants, defined by their place of residence. All foreign subjects in a given protocol can be lumped together and provided on a single tracking sheet, with the areas of residence that are included listed at the top of the sheet (an individual breakdown of participants by country of residence is not necessary).
- (n) Determine how many different protocols are eligible for tracking, and give only the tables for these protocols to the extramural assistant;
- (o) Ensure that the grant number, year, and PI name are on each protocol that is given to the extramural assistant; and
- (p) Initial and date the form certifying that all of the above steps have been completed.

Summary of Program Staff duties:

1. Ensure that the proposed gender and minority inclusion plan is appropriate prior to funding.
 2. Enter the correct tracking code and answer all appropriate questions on the grant checklist.
 3. Ensure that the appropriate tracking form has been accurately completed by the PI (*Target forms are shorter and are provided at the beginning of the protocol, usually before enrollment has started. Inclusion forms are longer and are provided with each progress report after enrollment has started*).
 4. Note the enrollment status of the protocol (P, O, C, or ND) on the tracking form and provide a justification if the inclusion data is not representative of the US population or if a significant number of research participants' gender/race/ethnicity is reported as unknown.
 5. Ensure that the enrollment form includes the correct grant number, PI name and protocol title (*For grants with multiple protocols, it is critical that protocol titles are consistent between the target data form and all the subsequent enrollment forms!*)
 6. Submit completed forms to the extramural assistant staff.
- Extramural Assistants will:
 - (a) Make a printed copy of the target/planning and inclusion forms by budget period.
 - (b) Discuss with NHGRI staff the list of protocols for inclusion/enrollment data to be sure that the protocols for targeted/planned enrollment match the protocols for inclusion enrollment; this must be done BEFORE the extramural assistant enters the data.
 - (c) Ensure that each protocol has been initialed BEFORE entering the data.
 - (d) Ask the NHGRI staff to resolve any discrepancies in target or planned/enrollment numbers, protocol labeling, number of protocols, etc.

(e) Provide the NHGRI approval officer (Carolyn Taylor and Ian Marpuri) with a copy of the forms for her approval in the population tracking database.

- NHGRI Approval Officer

Approval Officers must review and approve the data entered. If there are discrepancies, the extramural assistant must be contacted to resolve the discrepancies.

All Principal Investigators whose projects require population tracking will be sent a letter at the time of award to encourage them to submit data that are accurate and correct and to ensure that the protocol titles are consistent throughout the study.

TRAINING:

The number of protocols handled by NHGRI staff is small. Therefore, there is a need to have refresher sessions periodically as described below:

- An orientation will be provided for NHGRI staff about what types of projects should/should not be included in the population tracking database.
- As new ERP staff are hired, the population tracking contact should set up a training session to orient new staff to the requirements for population tracking.
- In December 2013, Inclusion Policy Officer Don Everett of NEI provided a training session for NHGRI staff to update them on the latest policies.