

**DEPARTMENT OF HEALTH AND HUMAN SERVICES**

**National Institutes of Health**

**Office of the Director**

**2011 BIENNIAL ADVISORY COUNCIL REPORT  
CERTIFYING COMPLIANCE WITH THE  
NIH POLICY ON INCLUSION GUIDELINES**

A handwritten signature in black ink that reads "Eric Green". The signature is fluid and cursive, with the first name "Eric" and last name "Green" clearly distinguishable.

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National Human Genome Research Institute  
February, 2011**

**NATIONAL HUMAN GENOME RESEARCH INSTITUTE**  
**2011 BIENNIAL ADVISORY COUNCIL REPORT CERTIFYING**  
**COMPLIANCE WITH INCLUSION GUIDELINES**

**Background**

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:

- (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. Patient-oriented research includes: (a) mechanisms of human disease; (b) therapeutic interventions; (c) clinical trials; and (d) development of new technologies.
- (2) *Epidemiological and behavioral studies;* and
- (3) *Outcomes research and health services research.*

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 FY2010 for the NHGRI Extramural Research Program and the Office of Population Genomics in the NHGRI Director’s Office<sup>1</sup> and the FY2009 and FY2010 Intramural Research Program. It also includes the procedures followed by NHGRI staff to ensure gender and minority inclusion in all NHGRI research. The information contained in this report was discussed at the February 7-8, 2011 meeting of the National Advisory Council on Human Genome Research (NACHGR).

**Discussion of Data reported in FY 2009 and FY 2010**

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 specific populations, such as health or research

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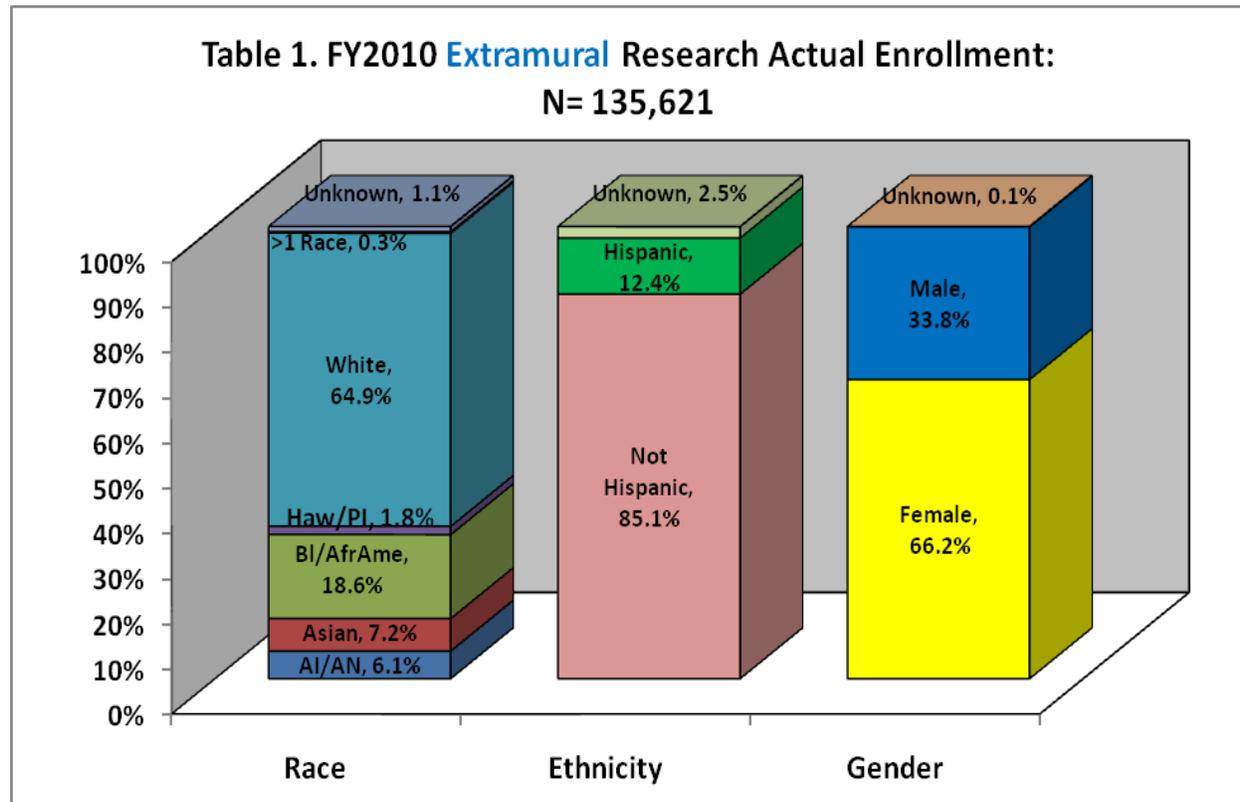
<sup>1</sup> For the remainder of this report, these two units will be described as extramural research.

professionals or individuals who have undergone genetic testing for specific diseases or conditions. These discrete target populations are not always racially or ethnically diverse. As a result, the demographic breakdown of NHGRI research enrollment can be slightly less representative than the US population, depending on the types of studies that are active in a given year. In addition, there are a handful of DIR studies with large enrollment numbers that report a high percentage of participants with “unknown” race, ethnicity and gender. These studies are using existing coded data to perform statistical analyses, which do not include demographic data. It should also be noted that NHGRI does not support any Phase III clinical trials.

**Extramural Research**

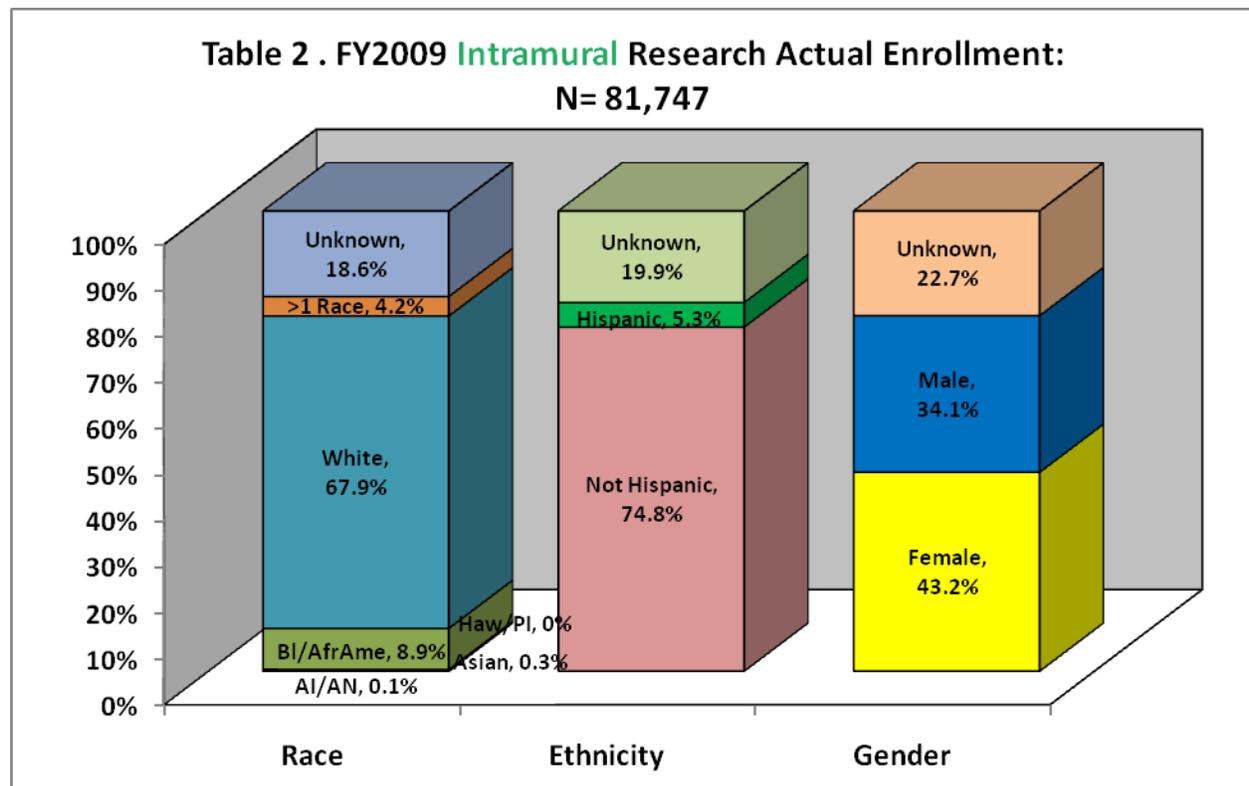
In FY 2010, 135,621 individuals were enrolled in 35 ongoing extramural research projects (Table 1). Approximately 65% of these individuals were White, 18.6% were Black/African American, 7.2% were Asian, 6.1% were American Indian/Alaskan Native, 1.8 % were Hawaiian/Pacific Islanders, and 0.3% reported identification of more than one race. Only 1.1% of the research participants had no racial identification, which is a drastic decrease from the previously reported figures of 17%. Also of note, figures significantly increased for Asians from 1.8% to 7.2% and for American Indian/Alaska Natives from 0.3% to 6.1%. The ethnic breakdown of the participants enrolled in studies reported in FY2010 was 12.4% Hispanic, 85.1% non-Hispanic, and 2.5% Unknown. The gender breakdown of these participants was 66.2% female, 33.8% male, and 0.1% Unknown.

The FY 2009 Enrollment Data was not accepted into the database due to a technical problem. However, as the data is largely cumulative, the enrollment data from FY 2009 is mostly reflected in the FY 2010 figures. In addition, unfortunately, after the system had been shut down at the end of this fiscal year for reporting purposes, we discovered an error in the entry of Hispanics and Asians in our total data reported in the database. We have since made the corrections, which are reflected in the figures in this report, and have presented the appropriate figures in our presentation to the NACHGR.



**Intramural Research**

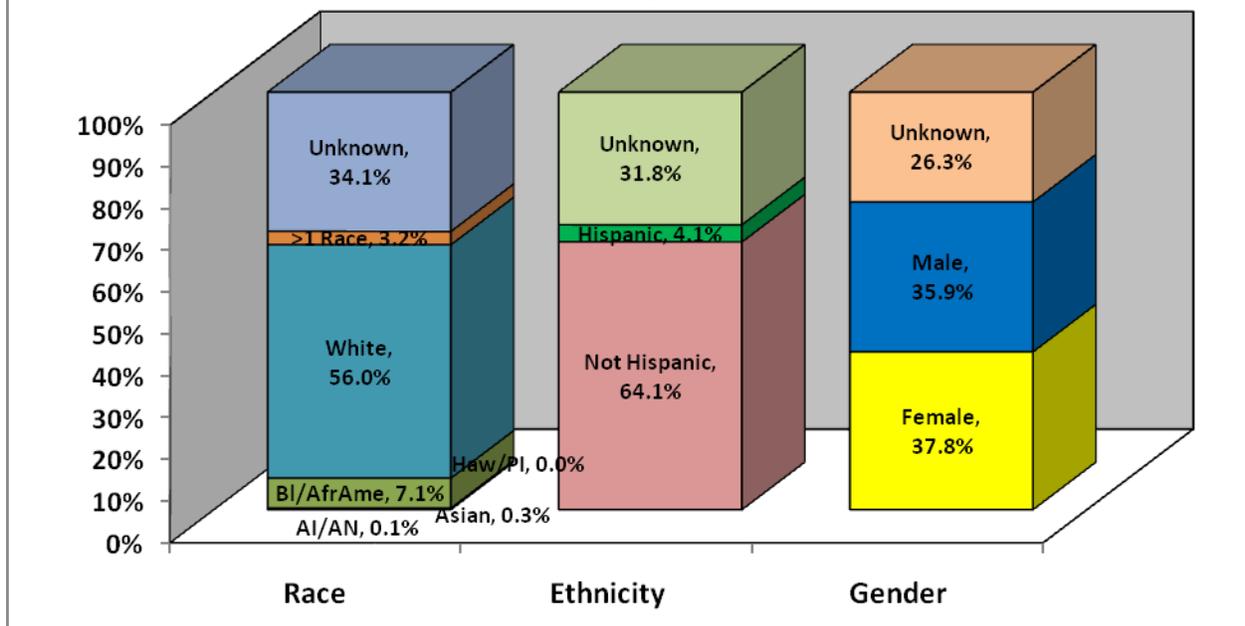
In FY 2009, NHGRI intramural research grants reported 81,747 research participants enrolled in 69 ongoing research studies (Table 2). Approximately 67.9% of these individuals were White, 9% were Black/African American, 0.3% were Asian, 0.1% were American Indian/Alaskan Native, 4.2% identified themselves as more than one race, and there were no Hawaiian/Pacific Islanders. Approximately 18.6% of the research participants reported no racial identification. The ethnic breakdown of these participants was 5.3% Hispanic, 74.8% Non-Hispanic and 19.9% Unknown. The gender breakdown was 43.2% female, 34.1% male and 22.7% unknown. The relatively high percentage of participants with “unknown” race, ethnicity and gender is due to a small number of studies (with relatively large enrollment totals) in which DIR investigators receive coded data for statistical analyses, for which demographic data are not relevant and not provided. These studies are now usually considered "not human subjects research" and exempt from IRB review and tracking, but in FY 2009 and FY 2010, DIR investigators kept open several protocols that were already in the system.



In FY 2010, NHGRI intramural research grants reported 109,942 research participants enrolled in 79 ongoing research studies (Table 3). Approximately 56% of these individuals were White, 7.1% were Black/African American, 0.3% were Asian, 0.1% were American Indian/Alaskan Native, 0% were Hawaiian/Pacific Islanders, and 3.2% identified themselves as more than one race. Approximately 34.1% of the research participants had no racial identification. The ethnic breakdown of these participants was 4.1% Hispanic, 64.1% Non-Hispanic and 31.8% Unknown. The gender breakdown was 37.8% female, 35.9% male and 26.3% unknown. Again, the number of participants with “unknown” race, ethnicity and gender is due to the inclusion of data from studies performing statistical analyses of coded data that do not include gender, race or ethnicity information.

Several recently initiated DIR protocols will target African Americans and individuals of West African origin to study common, complex genetic disorders; it is expected that these will lead to increased representation of African Americans in NHGRI DIR studies in future years.

**Table 3. FY2010 Intramural Research Actual Enrollment:  
N= 109,942**



**NHGRI Data Compared to 2010 NIH Aggregate Data and 2005 – 2009 Estimated Census Data**

The following table (Table 4) provides a comparison between the NHGRI extramural and intramural actual enrollment, the aggregate actual enrollment data reported in FY 2010 for all of NIH, and the demographic breakdown from the Estimated 2005-2009 Census.

**Table 4. Comparison with NIH Aggregate Data and 2005-2009 Census Data**

Category	2009	2010		2010	2005-2009 estimates
	Intramural	Extramural	Intramural	*NIH ALL	Census
Hispanic	5.3%	12.4%	4.1%	8.4%	15.1%
Not Hispanic	74.8%	85.1%	64.1%	82.2%	84.9%
Unknown	19.9%	2.5%	31.8%	9.3%	
Am Ind/AL	0.1%	6.1%	0.1%	1.5%	0.8%
Asian	0.3%	7.2%	0.3%	9.2%	4.4%
Haw/Pacif	0.0%	1.8%	0.0%	0.6%	0.1%
Black/AfrAmer	8.9%	18.6%	7.1%	12.8%	12.4%
White	67.9%	64.9%	55.9%	66.3%	74.5%
>1 Race	4.2%	0.3%	3.2%	1.5%	2.2%
Unknown	18.6%	1.1%	34.1%	8.1%	5.6%
Female	43.2%	66.2%	37.8%	56.1%	50.7%
Male	34.1%	33.8%	35.9%	43.0%	49.3%
Unknown	22.7%	0.1%	26.5%	0.9%	
<b>Total #</b>	<b>81,747</b>	<b>135,621</b>	<b>109,942</b>	<b>23,363,635</b>	<b>301,461,533</b>

\*The NIH Aggregate totals are figures based on FY2010 reported totals combining the data from the Old Form and New Form (Part A)

In FY 2010, the NHGRI extramural figures were significantly higher than the NIH in the inclusion of Hispanics at 12.4% vs. NIH at 8.4%. Although, these figures were still slightly lower than the Census at 15.1%. Also, in FY 2010, the NHGRI extramural actual enrollment figures for American Indian/Alaska Natives, Asians, and Hawaiian/Pacific Islanders were much higher than the 2005-2009 estimated Census, and mostly higher than the NIH figures, except the enrollment for Asians was slightly lower. Of important note, African American inclusion figures were significantly higher than both NIH and Census figures. Lastly, there were considerably fewer Unknown individuals reported for race, ethnicity and gender than both NIH and the Census.

In FY 2010, the NHGRI intramural figures lagged behind the NIH at 4.1% inclusion of Hispanics and the Census at 15.1%, a slight decrease from FY 2009. In addition, the intramural actual enrollment figures fell below both the NIH and Census figures for African Americans, American Indian/Alaska Natives, Asians, and Hawaiian/Pacific Islanders. Overall, there were no significant differences in race, ethnicity and gender between FY 2009 and FY 2010 for intramural. The largest difference is an increase in the number of Unknown individuals reported, from 19.9% in FY 2009 to 31.8% in FY 2010, and this is mostly attributed to intramural studies with large enrollment numbers that report a high percentage of participants with “unknown” race, ethnicity and gender. These studies use existing coded data to perform statistical analyses, which do not include demographic data.

## **Staff Responsibilities and Procedures to Ensure Compliance with Inclusion Guidelines**

### **Extramural Research**

- Extramural conducts an annual review of NHGRI's inclusion efforts and provides data to the NIH Office of Research on Women's Health. As Director of the Division of Extramural Research, Dr. Mark Guyer oversees the process and provides leadership. He is assisted in this task by Ms. Joy Boyer and Dr. Bettie Graham. The NHGRI staff is assisted by Division of Extramural Activities Support (DEAS) administrative staff members who are responsible for inputting the data into the Population Tracking Database. The NHGRI and DEAS staff works cooperatively to ensure that the data are submitted correctly and in a timely manner.
- The Extramural 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 DEAS staff members that input the information into the Population Tracking Database. Ms. Anna Rossoshek and Ms. Lin Gyi review, approve, and sign-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 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://grants2.nih.gov/grants/peer/hs\\_review\\_instruct.pdf](http://grants2.nih.gov/grants/peer/hs_review_instruct.pdf)) to scientist/clinicians 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 a priority score.
- SROs document the gender and minority codes for 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 for program directors and DEAS staff 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. DEAS staff members who are responsible for inputting the data are trained by OD to perform this function.

### **Intramural Research**

- 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.shtml> 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. In addition to PIs, nearly a 1000 students a year register for the course, about half come in via long distance learning. A companion text, the second edition, is also available. The Master's degree in partnership with Duke is made available but is not required; about 50 NIH people have received their Masters Degree in Clinical Research in recent years. 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 stated on the Office of Human Subjects Research web site, "All researchers newly employed at the NIH and all persons who conduct or support the conduct of research involving human subjects are required to register completion of the computer based training (CBT) program entitled "Protecting Human Subjects" found at <http://ohsr.od.nih.gov/cbt/cbt.html>. The human research training requirements are in the process of being revised and updated by the NIH Office of Human Subjects Research Protections (OHSRP); however, all principal investigators were required to complete the training described above for the conduct of the FY 2009-2010 protocols covered in this report.
- The intramural scientists who are conducting clinical studies submit their clinical research protocols to the Intramural Institutional Review Board (IRB) for evaluation. 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 compliance. Enrollment data are submitted annually to the Clinical Center for inclusion in their central database. NHGRI receives this data on an annual basis for reporting purposes.

## 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 Division of Extramural Research (DER) and Office of Population Genomics (OPG) 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](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.

If program staff members are unsure of whether a project should be tracked, a small subcommittee, consisting of a representative from the ELSI Program and the Office of Population Genomics will review the project with the Program Director and make a determination. The current representatives are: Lin Gyi for OPG and Anna Rossoshek for DER.

## 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](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 DEAS staff;
  - (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 DEAS staff;

- (o) Ensure that the grant number, year, and PI name are on each protocol that is given to the DEAS staff; 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 DEAS staff.**
- DEAS staff will:
    - (a) Make a hard copy folder for each grant and within each folder, a 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 DEAS staff member enter 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 (Anna Rossoshek or Lin Gyi) with a copy of the forms for her approval in the population tracking database.
  - NHGRI Approval Officer must review and approve the data ENTERED by the DEAS staff. If there are discrepancies, the DEAS staff 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 DER and OPG staff are hired, the DER and OPG contacts should set up a training session to orient new staff to the requirements for population tracking.