# DEPARTMENT OF HEALTH AND HUMAN SERVICES

**National Institutes of Health**

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# 2019 TRIENNIAL ADVISORY COUNCIL REPORTS CERTIFYING COMPLIANCE WITH THE NIH POLICY ON INCLUSION GUIDELINES

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# NIH Intramural Report on Monitoring Adherence to the NIH Policy on the Inclusion of Women and Minorities in Clinical Research as Reported in FY2016 – FY2018

## I. Background/Overview

A. The mission of the NIH Intramural Research Program (IRP) is to conduct distinctive, high-impact laboratory, clinical, and population-based research; facilitate new approaches to improve the public health through prevention, diagnosis and treatment; respond to public health emergencies; train the next generation of biomedical researchers; and maximize the impact of IRP discoveries through information sharing and partnerships with academia, industry, and other government agencies. It's the mission of the NIH Clinical Center to provide a model environment for: clinical research, patient care and safety, and training.

B. The Intramural Program is comprised of 21 Institutes conducting research with approximately 2,150 active protocols during a fiscal year. The majority of the intramural research, approximately 1,600 protocols, are conducted at the main NIH Clinical Center located at the Bethesda campus. The other 520 protocols are conducted at offsite locations such as Research Triangle Park, N.C. (NIEHS), Baltimore, MD (NIDA and NIA), Frederick, MD (NCI), Detroit, Michigan (NICHD) and Phoenix, AZ (NIDDK), as well as at foreign locations.

C. The Intramural Program uses a centralized system, to capture data on all active intramural clinical research protocols and falls under the auspices of the NIH Clinical Center. This system, Protrak, maintained by the Office of Protocol services, includes protocol-related data for all protocols, and is the central system to capture planned and cumulative enrollment data. A second complementary system, the Clinical Research Information System (CRIS), captures actual accrual data relative to the ethnicity, sex/gender, and race as reported by each participant at the time of registration at the NIHCC. CRIS, along with the Biomedical Translational Research Information System (BTRIS), make up the Electronic Health Record and provides a resource for investigators and clinicians to generate protocol-specific attribution. BTRIS provides an automated method of generating cumulative enrollment data from demographic data received from the NIH Clinical Center CRIS system. The principal investigator or designee can validate the data. If users note discrepancies in the data, they submit a correction request which is sent to the Health Information Management Department, where the required follow-up is conducted.

## II. Strategies for Ensuring Compliance

A. Intramural Oversight
All intramural clinical research studies require investigators to provide plans for the appropriate inclusion of women and minorities and/or a justification whenever representation is limited or absent. In July of 2017, the Office of Clinical Research, under the leadership of the Chief Scientific Officer, implemented a new Scientific Review Policy that outlined the scientific compliance requirements. Protocols are initially reviewed by the lab/branch chief for feasibility, fit within the mission, and resources.

Concept review considers the design, eligibility, statistical analysis and compliance with inclusion guidelines. Once approved, it is then reviewed by the Institute's Scientific Review Committee, with final submission to the Chief Scientific Officer to ensure compliance has been adhered to. New to the process, and a part of the policy, is the quadrennial review that considers the scientific justification for continuing the protocol. This parallels the process of a new protocol in which the first level is the concept review conducted the Lab/Branch Chief, then the Institute Scientific Review Committee, and finally the Chief Scientific Officer. Here again, the investigator documents the number, sex/gender, race and ethnicity of those who were accrued during the past year; identifies any issues related to recruitment with plan for resolution. Annually, at the time of protocol's continuing review, the protocol is reviewed by the lab/branch chief to evaluate the progress of the protocol, identify problems assure protocol is progressing accordingly. As part of this review, the investigator provides summary documents reporting the number, sex/gender, race and ethnicity of those who were accrued during the past year; identifies any issues with accrual and how they will be addressed. A written report is prepared to summarize the review and becomes a part of the protocol documentation submitted to the Institutional Review Board. Once the protocol receives approval of the Institute Scientific Review Committee and the NIH CC Chief Scientific Officer, it is submitted to the IRB for approval and then on to OPS for collation and reporting The NIH Clinical Center's OPS collects the demographic data from the investigators at the time of protocols' annual continuing review, and coordinates the annual reporting to the Office of Extramural Research and the Office of Research on Women's Health.

B. Training

In 2016 the Office of Human Subjects Research revised the existing Standard Operating Procedure, "Training Requirements for the NIH Human Research Protection Program (HRPP)", that outlines the training for each type of research (clinical trial vs. natural history). In addition, all intramural research scientists are required to complete the training and demonstrate understanding when involved in human subjects research. The degree of training required is commensurate with their roles, responsibilities, and type of research. It's the responsibility of the Principal Investigator to verify training and certify to the IRB the completion of training. Upon review of the research, the IRB has the option to require additional training. Every three years, investigators are required to complete a refresher course that is consistent with the type of research conducted. The policy further outlines the required training for IRB Members.

The Office of Clinical Research (OCR) was established in 2016 with a vision to facilitate clinical research and research training applicable to the NIH Intramural Program, the rest of the United States, and international investigators. A number of comprehensive training programs are provided to ensure investigators conducting research are educated about the aspects to conduct clinical research. Over the years enrollment has expanded and includes teleconferencing to external sites. The educational opportunities include:

<u>Introduction to the Principles and Practice of Clinical Research</u>
This program, which is part of the Clinical Center's core curriculum in clinical research, is designed to train participants on how to effectively conduct clinical research. The course focuses on the spectrum of clinical research and clinical

research processes by highlighting epidemiologic methods, study design, protocol preparation, patient monitoring, quality assurance, and Food and Drug Administration (FDA) issues. Other areas covered include data management, building a research budget and bioethical issues, including protection of human subjects, plus many special topics. For the 2016-2018 course, 419 remote sites (183 nationally and 236 internationally) participated via long distance learning reaching 50 different countries. Since the course was initiated in 1995, there have been 50,056 registrants.

Principles of Clinical Pharmacology
This course is designed to meet the needs of researchers, fellows in training, and others who have an interest in the clinical pharmacologic aspects of contemporary drug development and utilization. This course consists of weekly lectures covering the fundamentals of pharmacokinetics, pharmacodynamics, drug metabolism, pharmacogenomics, adverse drug reactions, drug discovery and development, FDA regulations, and optimization of therapy in special populations (pediatrics, geriatrics, pregnancy and lactation), viewing clinical pharmacology as a translational scientific discipline focused on rational drug development and utilization. For the 2016-2018 course, in addition to the NIH Clinical Center, 29 sites (17 nationally, 12 internationally) participated via long distance learning. There have been 9,633 registrants since the course was initiated in 1998.

Ethical and Regulatory Aspects of Human Subjects Research
Implemented in 1999, the course offers formal education and training in research ethics. Participants are exposed to a broad range of issues important to the ethical conduct of clinical research. Individual sessions and group institutional review board (IRB) reviews are presented by leading experts in various areas of clinical research ethics. The average number of students enrolled for Fiscal Years 2016, 2017 and 2018, is 687. This is a 50% increase from prior years which had an average enrolled 300 students. The course is also broadcast by satellite and the internet to participants at remote sites which accounts for 68.4% of the students enrolled.

## III. Analysis and Interpretation of Data

A. Enrollment Data for the Intramural Research Program
The Office of Protocol Services submits data to the NIH Office of Extramural Research (OER) annually, who generate the intramural data provided in the appended tables. This data represents the aggregate number of participants enrolled over the life of the protocol through the fiscal year reported, at the NIH Clinical Center, other intramural locations including collaborative sites, as well as foreign locations. Prior to submitting the FY2018 data, a review of protocols reporting more than 100,000 participants was conducted. Six protocols were identified as secondary analysis protocols and removed from the FY2018 reporting data, accounting for 1,056,181 participants.

Total Number of Participants Enrolled: The total number of participants enrolled in table 3-1-C shows a decrease from FY2016 to FY2017 to FY2018. After removing the secondary analysis protocols with the submission of FY2018 data, there is a 38% decrease from FY2016 to FY2018. Of the total number of participants enrolled in FY18 (2,383,823), 12% (302,851) are attributed to protocols conducted at the NIH

Clinical Center. The remaining 88% (2,080,972) are from protocols conducted at other intramural locations, collaborative sites, in addition to foreign locations. Of the 2,080,972 participants enrolled, 10 protocols accounting for 1,182,378 participants enrolled is directly attributed to epidemiology studies.

Percentage of Participants by Gender/Sex: Table 3-1-C shows a decrease in the number of females and an increase in the number of males when comparing FY2016 to FY2018. The difference is again attributed to the removal of the secondary analysis protocol. The FY2018 data shows a12.1% increase over males enrolled, with the number of unknowns reported dropping to 2.9%.

Percentage of Enrollment by Race/Ethnicity: The percentage of minority enrollment remains almost consistent from FY2017 to FY2018 with a 1% increase as seen in table 4-1-1-E. Enrollment by Ethnicity, Table 4-1-F, shows an increase in Not Hispanic population by 34% and a decrease of 35.8% in Unknown. The changes are attributed to the removal of the secondary analysis protocols.

B. Enrollment Data for the Intramural Research Program Phase III Clinical Trials
From the total number of protocols conducted by the intramural program, only 4% (47 protocols) are Phase III clinical trials and of these, the majority are conducted at the NIH Clinical Center. Tables 3-3, 4-2-1-C and 4-2-1-D summarize the data.

Total Enrollment for NIH-Defined Phase III Trials: The number of participants enrolled in Phase III clinical trials remained consistent from fiscal year to fiscal year, ending in FY2018 with a slightly larger number of participants enrolled.

Percentage of Participants by Gender/Sex: On average for the fiscal years, females accounted for 78% of the participants enrolled while males accounted for 22% of the participants enrolled. The percentage of females increased from FY2016 to FY2017 and decreased from FY2017 to FY2018. This is attributed to the closure of protocols in FY2016 and FY2017 and the addition of new protocols in FY2018.

Percentage of Enrollment by Race/Ethnicity: The percentage of minority enrollment decreased by 3% from FY2016 to FY2018, even though the total number of participants increased. This is attributed to one protocol reporting the majority of its population as white. This protocol also accounts for the percentage increase/decrease for other race categories. Enrollment by Ethnicity on average reflects 63% of enrollees are Not Hispanic and 37% are Hispanic Latino. These percentages reflect little change within the fiscal years.

## IV. Additional information

A. With the implementation of the 21st Century Cures Act, the intramural adapted policies and procedures to comply.
   - The Office of Human Subjects Research Protection has worked with the Office of General Council to incorporate required language into the existing informed consent template. Some institutes took the initiative to incorporate this language into the body of the informed consent prior to the initiation of the template across the program. Simultaneously, the Policy for “Informed Consent” was modified to include the protections of Certificate of

Confidentiality. Previously both the informed consent template and policy only addressed the Privacy Act of 1974.

- The Policy for Privacy and Confidentiality was also amended to comply with the 21st Century Cures Act. As a result, the Certificate of Confidentiality has been issued automatically to the Intramural Research Program for research covered by the policy vs. individual certificates.

- On October 13, 2017, The Deputy Director of Intramural Research issued a desk-to-desk memo informing investigators and researchers of this change.

- When the NIH Intramural Institutional Review Board (IRB) is not the IRB of record, and when the NIH relies on a non-NIH Institutional Review Board, NIH provides the privacy and confidentiality local context information in order to convey the requirements of the Privacy Act of 1974 and the protections of the Certificate of Confidentiality under the 21st Century Cures Act.

- Lastly, the Material Transfer agreements and CRADA agreements were updated to include the obligations under the Certificates of Confidentiality and the 21st Century Cures Act for recipients of data from the NIH. The Tech Transfer Community was educated regarding the changes February of 2018.

B. The intramural research program has recently created a Central Institutional Review Board Office (IRBO), and is working to consolidate the Institute Institutional Review Boards into Panels under the auspices of the Director of the Human Subjects Research Program. With this change comes the adoption of one computerized system, the NIH iRIS. This provides investigators a single source to collect information and report out to the Office of Protocol Services. As regulations/policies change, the central NIH iRIS, allows for ease in implementing the requirements and ensure compliance.

Appendix 1. Data Tables

**Table 3-1-C. Total Enrollment for All NIH-Defined Intramural Clinical Research Between FY2016 and FY2018**

| Fiscal Year | Total Enrollment | Total Females | % Females | Total Males | % Males | Total Unknown | % Unknown |
|---|---|---|---|---|---|---|---|
| 2016 | 3,854,483 | 2,596,487 | 67.4 | 1,107,746 | 28.7 | 150,250 | 3.9 |
| 2017 | 3,161,520 | 1,649,851 | 52.2 | 1,381,695 | 43.7 | 129,974 | 4.1 |
| 2018 | 2,383,823 | 1,301,006 | 54.6 | 1,013,229 | 42.5 | 69,588 | 2.9 |

**Table 3-2-C. US Site Enrollment for All NIH-Defined Intramural Clinical Research**

| Fiscal Year | Total Enrollment | Total Females | % Females | Total Males | % Males | Total Unknown | % Unknown |
|---|---|---|---|---|---|---|---|
| 2016 | 3,200,719 | 2,176,309 | 68.0 | 896,680 | 28.0 | 127,730 | 4.0 |
| 2017 | 2,500,323 | 1,227,511 | 49.1 | 1,165,510 | 46.6 | 107,302 | 4.3 |
| 2018 | 1,722,757 | 887,786 | 51.5 | 787,488 | 45.7 | 47,483 | 2.8 |

**Table 3-3. Total Enrollment for All NIH-Defined Phase III Trials Reporting Between FY2016 and FY2018**

| Fiscal Year | Total Enrollment | Total Females | % Females | Total Males | % Males | Total Unknown | % Unknown |
|---|---|---|---|---|---|---|---|
| 2016 | 22,351 | 17,755 | 79.4 | 4,592 | 20.5 | 4 | 0.0 |
| 2017 | 21,341 | 17,317 | 81.1 | 4,022 | 18.8 | 2 | 0.0 |
| 2018 | 22,421 | 16,425 | 73.3 | 5,976 | 26.7 | 20 | 0.1 |

**Table 4-1-1-E. Total Enrollment of NIH-Defined Intramural Clinical Research**

| Fiscal Year | Total Enrollment | No. Inclusion Data Records | Minority Enrollment | % Minority Enrollment | American Indian Alaska Native | % American Indian Alaska Native | Asian | % Asian |
|---|---|---|---|---|---|---|---|---|
| 2016 | 3,854,483 | 1,895 | 761,594 | 19.8 | 28,630 | 0.7 | 272,218 | 7.1 |
| 2017 | 3,161,520 | 1,909 | 860,770 | 27.2 | 31,166 | 1.0 | 293,316 | 9.3 |
| 2018 | 2,383,823 | 1,864 | 673,286 | 28.2 | 29,475 | 1.2 | 267,186 | 11.2 |

| Fiscal Year | Black African American | % Black African American | Native Hawaiian Pacific Islander | % Native Hawaiian Pacific Islander | White | % White | More Than One Race | % More Than One Race | Unknown Not Reported | % Unknown Not Reported |
|---|---|---|---|---|---|---|---|---|---|---|
| 2016 | 266,909 | 6.9 | 5,379 | 0.1 | 1,724,887 | 44.8 | 13,235 | 0.3 | 1,543,225 | 40.0 |
| 2017 | 319,709 | 10.1 | 5,490 | 0.2 | 2,184,977 | 69.1 | 15,120 | 0.5 | 311,742 | 9.9 |
| 2018 | 212,100 | 8.9 | 4,457 | 0.2 | 1,634,659 | 68.6 | 13,676 | 0.6 | 222,270 | 9.3 |

**Table 4-1-1-F. Total Enrollment of All NIH-Defined Intramural Clinical Research**

| Fiscal Year | Not Hispanic | % Not Hispanic | Hispanic Latino | % Hispanic Latino | Unknown Not Reported | % Unknown Not Reported |
|---|---|---|---|---|---|---|
| 2016 | 1,904,670 | 49.4 | 184,047 | 4.8 | 1,765,766 | 45.8 |
| 2017 | 2,388,515 | 75.5 | 204,984 | 6.5 | 568,021 | 18.0 |
| 2018 | 1,988,228 | 83.4 | 155,344 | 6.5 | 240,251 | 10.1 |

**Table 4-2-1-C. Total Enrollment of All NIH-Defined Phase III Trials**

| Fiscal Year | Total Enrollment | No. Inclusion Data Records | Minority Enrollment | % Minority Enrollment | American Indian Alaska Native | % American Indian Alaska Native | Asian | % Asian |
|---|---|---|---|---|---|---|---|---|
| 2016 | 22,351 | 50 | 15,177 | 67.9 | 400 | 1.8 | 3,714 | 16.6 |
| 2017 | 21,341 | 48 | 14,510 | 68.0 | 463 | 2.2 | 3,732 | 17.5 |
| 2018 | 22,421 | 46 | 14,553 | 64.9 | 519 | 2.3 | 3,780 | 16.9 |

| Fiscal Year | Black African American | % Black African American | Native Hawaiian Pacific Islander | % Native Hawaiian Pacific Islander | White | % White | More Than One Race | % More Than One Race | Unknown Not Reported | % Unknown Not Reported |
|---|---|---|---|---|---|---|---|---|---|---|
| 2016 | 2,935 | 13.1 | 5 | 0.0 | 7,369 | 33.0 | 50 | 0.2 | 7,878 | 35.2 |
| 2017 | 2,229 | 10.4 | 6 | 0.0 | 7,138 | 33.4 | 50 | 0.2 | 7,723 | 36.2 |
| 2018 | 2,326 | 10.4 | 5 | 0.0 | 8,043 | 35.9 | 58 | 0.3 | 7,690 | 34.3 |

**Table 4-2-1-D. Total Enrollment of All NIH-Defined Phase III Trials**

| Fiscal Year | Not Hispanic | % Not Hispanic | Hispanic Latino | % Hispanic Latino | Unknown Not Reported | % Unknown Not Reported |
|---|---|---|---|---|---|---|
| 2016 | 13,972 | 62.5 | 8,177 | 36.6 | 202 | 0.9 |
| 2017 | 13,093 | 61.4 | 8,146 | 38.2 | 102 | 0.5 |
| 2018 | 14,373 | 64.1 | 7,985 | 35.6 | 63 | 0.3 |