# National Institute of Diabetes and Digestive and Kidney Diseases

# Triennial Report on the Inclusion of Women and Minorities in Clinical Research FY 2019 – FY 2021

## I. Overview and Background

### Mission

The mission of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) is to conduct and support medical research and research training and to disseminate science-based information on diabetes and other endocrine and metabolic diseases; digestive diseases, nutritional disorders, and obesity; and kidney, urologic, and hematologic diseases, to improve people's health and quality of life.

To guide his leadership of NIDDK's mission focused activities, Griffin P. Rodgers, M.D., M.A.C.P., Director, NIDDK, established several overarching principles, which have become known colloquially as "core values" (see https://www.niddk.nih.gov/about-niddk/meet-director/mission-vision). Among the five principles set out in the Director's vision statement is "*Support Pivotal Clinical Studies and Trials*." An indication that NIDDK has maintained focus on this principle is NIDDK's prioritization and continued high level of support of clinical research (see Figure 14 on NIDDK's "Funding Trends and Support of Core Values" webpage https://www.niddk.nih.gov/research-funding/funded-grants-grant-history/funding-trends-support-core-values).

While funding prioritization is one indication of "support" another indication is appropriate attention to the scientific requirements and the statutory and policy obligations to ensure the appropriate inclusion of women and minorities in NIH supported clinical research.

### History

In 1986 NIH established a policy for the inclusion of women in clinical research. This policy stemmed largely from a report of the Public Health Service Task Force on Women's Health in 1985. The policy was initially published in the NIH Guide to Grants and Contracts in 1987 and then later that year the policy was revised to include language encouraging the inclusion of minorities in clinical studies as well.

To ensure that NIH rigorously implement and enforce the inclusion policy, Congress included in The NIH Revitalization Act of 1993 (Public Law 103-43) a section entitled *Women and Minorities as Subjects in Clinical Research.* In 1994, NIH revised its policies to harmonize with the statutory language.

The revisions essentially reinforced NIH's existing policies, but included four additional requirements:

1. That NIH ensure that women and minorities and their subpopulations be included in all clinical research;
2. That women and minorities and their subpopulations be included in Phase III clinical trials in numbers adequate to follow for valid analyses of differences in intervention effect;
3. That cost is not allowed as an acceptable reason for excluding these groups and;
4. That NIH initiate programs and support for outreach efforts to recruit and retain women and minorities and their subpopulations as participants in clinical studies.

The 21st Century Cures Act of 2016 amended the NIH required reporting on the inclusion of women and minorities in clinical research from biennial reporting to triennial reporting. This report is the second such Triennial Inclusion Report.

# II. Strategies for Ensuring Compliance

## A. Peer Review

The implementation of inclusion guidelines involves the participation of review, program, policy, and grants management staff. Inclusion is first addressed by peer review. Reviewers on NIH peer review panels are given specific guidance on reviewing inclusion on the basis of sex/gender, race, ethnicity, and age when considering clinical research applications. Reviewers evaluate applications for the appropriateness of the proposed plan for inclusion by sex/gender, race and ethnicity. For Phase III studies, enrollment goals are further assessed for plans to conduct analyses of intervention effects among sex/gender, racial, and ethnic groups. Unacceptable inclusion plans must be reflected in the priority score of the application and documented in the minutes of the review session. Initial review groups make recommendations as to the acceptability of the proposed study population with respect to the inclusion policies. If issues are raised in review, program staff notify principal investigators, who are required to address these issues prior to funding. Applications with unacceptable inclusion plans receive a bar to funding; an award is not issued until an acceptable resolution is received.

### Extramural Research Awards: Bars-to-Funding and Resolutions

In cases where the study section 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 IMPAC II system that bars funding. For the application to be funded, the bar must be lifted and documentation of the grounds for lifting the bar must be included in the official grant file.

Responsibility for review and approval of finalized human subjects' research protocols resides with the Institutional Review Board (IRB) of record. NIH must receive certification of IRB approval before NIH funds can be used for human subject research. If certification of IRB approval cannot be provided prior to award, NIDDK may make restricted awards to allow the non-human subject research to go forward while human subjects concerns are addressed by the IRB. In general, once IRB approval is received, the

Grants Management Specialist will request review by the Program Officer before funding for human subjects research can be made.

**NIDDK Scientific Review Procedures for Inclusion**

Scientific Review Officers (SRO) read all applications and proposals and note if clinical research is being proposed and if the application complies with 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*" to scientists/clinicians that serve as peer reviewers on Scientific Review Panels to ensure they are up to date on all human subject policy issues when evaluating applications.

The study section evaluates each application during the initial review to determine if it is in compliance with the Inclusion Policy. The evaluation results are noted on the summary statement. In addition, reviewers are instructed to include compliance with the inclusion policy as a factor when assigning a priority score to an application.

Using specific codes, SROs document in the IMPAC II system any concerns regarding inclusion of women and minorities. Codes are also used to indicate and track studies that are Phase III clinical trials. If the study proposed is a clinical trial, then the type of trial (i.e., Phase I, Phase II or Phase III) is noted in the summary statement.

## B. Program Monitoring and Grants Management Oversight

Prior to award, program officials/directors are responsible for reviewing the inclusion information in the application and indicating whether the plans are scientifically appropriate. Program staff monitor actual enrollment progress in annual progress reports and provide consultation when necessary. For Phase III clinical trials, program officials monitor the requirement for sex/gender and race/ethnicity analyses in applications and annual progress reports. Grants management staff ensure appropriate terms and conditions of award are included in the Notice of Award, and that information is appropriately documented in the official grant file.

For multi-center clinical trials managed through a cooperative agreement or research contract there is typically a steering committee on which the responsible NIDDK program staff member serves. This committee monitors recruitment to make sure the ongoing study is on target with the initial study design approved through peer review. The committee will take corrective actions to ensure recruitment stays on target by employing appropriate enrollment strategies. These studies have, in addition, an outside advisory Data and Safety Monitoring Board (DSMB) that also monitors recruitment. The proceedings of the DSMB meetings are reported to the Institutional Review Boards (IRB) at all participating sites.

## C. Intramural

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, as part of their NIH protocol reviews. Intramural IRBs review intramural research protocols for compliance with inclusion guidelines and conduct annual monitoring. With each annual review and renewal, the

investigator documents the number, gender, and ethnicity of those who were accrued during the past year; any issues with accrual are addressed at the annual review by the investigator and reviewed by the pertinent IRB. The Clinical Center's Office of Protocol Services (OPS) coordinates annual reporting of demographic participant data to the Office of Extramural Research and the Office of Research on Women's Health.

## D. NIDDK Training Approaches

NIDDK Program Officials and Scientific Review Officers attended the 2020 Inclusion Training for Program Staff and the 2020 Inclusion Training for Review Staff in April 2020. Staff may access the archived training on the NIH staff intranet.

A section on inclusion guidelines is part of orientation training for all newly hired review and program staff members. In addition, the "NIDDK Extramural Program: Standard Operating Procedures (SOPs)," which are available on NIDDK's internal SharePoint site, include specific guidance to staff regarding inclusion. Some of the SOPs most focused on inclusion include:

- **SOP #8** - Preparing for Review Meetings At NIDDK: Administrative Review by the Scientific Review Officer
- **SOP #19** - Recording the Results of Review Meetings: Preparing and Releasing Summary Statements
- **SOP #27** - Staff Review of Applications Prior to Award: Resolving Concerns About the Inclusion of Women, Members of Minority Groups, and Children

NIDDK has a regularly updated section of its public website devoted to policies associated with conducting clinical trials that includes specific policies and implementation procedures for inclusion of women and minorities in clinical research (see https://www.niddk.nih.gov/research-funding/human-subjects-research/policies-clinical-researchers).

The NIDDK Division of Extramural Activities (DEA) currently schedules inclusion refresher training at the NIDDK Extramural Program (EP) Staff meeting (includes review, program, and grants management staff) to ensure that staff members are familiar with the materials and to address any questions that may arise. This refresher training was last presented at the November 13, 2019 EP Staff Meeting by the NIH Inclusion Policy Officer, Ms. Dawn Corbett MPH. Regular updates on inclusion policy are presented at the monthly EP Staff Meeting throughout the year.

## E. Additional NIDDK Actions to Ensure Compliance with the Inclusion Policy

The NIDDK DEA conducts an annual review of ongoing efforts associated with inclusion policy compliance and provides data to the NIH Office of Research on Women's Health. The DEA Director oversees the process and provides policy leadership to all NIDDK Extramural Divisions. Within DEA, the Office of Research Evaluation and Operations (OREO) manages most inclusion monitoring and reporting activities, including the coordination of the triennial inclusion report. Each NIDDK Extramural Division has a designated inclusion program analyst or clinical trial specialist for data quality assurance and tracking

at the division level. All NIDDK Program Officers are responsible for monitoring the clinical studies within their respective programs. The NIDDK Inclusion Policy Officer within OREO works closely with the division inclusion analysts to monitor reporting progress and reports any problems to the OREO director.

## III. Analysis and Interpretation of Data

In June 2018, NIH transitioned from the previous Inclusion Management System (IMS) to the Human Subject System (HSS). In HSS, the Principal Investigator (PI) directly uploads their inclusion data, which is then reviewed and approved by the program official.

Starting with fiscal year 2019 (FY19) inclusion data, the NIH Office of Extramural Research in the Office of the Director requires that Institute/Center (IC) Directors review and approve the previous year's inclusion data after the IC's Advisory Council has the opportunity to review and concur. This analysis and interpretation provide a summarized overview of the FY19 to FY21 inclusion data for the NIDDK Director's review and approval.

Annual data checks and certifications are part of new NIH standard operating procedures to ensure the inclusion data are as accurate as possible. Note that in cases where the total percentages are not 100%, this can occur as multiple selections are allowed in some categories.

NIDDK staff members have continued their efforts to ensure that persons of both genders and all ethnic and racial backgrounds are included in studies involving human subjects (see data in Appendix, Tables 1-4).

**All NIDDK Clinical Research (Intramural and Extramural)**

The total number of Inclusion Enrollment Records (IERs) with enrollment (some IERs are registered by studies but have not yet started recruiting) was 970 in FY21 compared to 1,006 in FY20 and 1,010 in FY19 (Appendix Table 1).

The total number of Black/African-American females enrolled in NIDDK clinical research in FY20 was 33,802 and in FY21 was 23,407; a decrease in FY21 of 10,395 (31% decrease; Appendix Table 2). The total number of White females enrolled in NIDDK clinical research in FY20 was 115,869 and in FY21 was 97,728; a decrease in FY21 of 18,141 (16% decrease; Appendix Table 2). The total number of Black/African-American males enrolled in NIDDK clinical research in FY20 was 24,942 and in FY21 was 20,970; a decrease in FY21 of 3,972 (16% decrease; Appendix Table 2). The total number of White males enrolled in NIDDK clinical research in FY20 was 92,780 and in FY21 was 86,819; a decrease in FY21 of 5,961 (6% decrease; Appendix Table 2). This general decrease in enrollment in FY21 could be the result of various factors, including but not limited to COVID-19-related delays or terminations of projects and the sunsetting of some studies. Other trends may emerge as some studies end and others are established.

**NIDDK Phase III Clinical Trials (Intramural and Extramural)**

The total number of minorities enrolled in NIDDK Phase III trials in FY20 was 2,270 and in FY21 was 3,801; an increase in FY21 of 1,531 (67% increase; Appendix Table 3). The total number of Black/African-American females enrolled in NIDDK clinical research in FY20 was 493 and in FY21 was 773; an increase in FY21 of 280 (57% increase; Appendix Table 3). The total number of White females enrolled in NIDDK clinical research in FY20 was 4,303 and in FY21 was 1,532; a decrease in FY21 of 2,771 (64% decrease; Appendix Table 3). The total number of Black/African-American males enrolled in NIDDK clinical research in FY20 was 425 and in FY21 was 777; an increase in FY21 of 352 (83% increase; Appendix Table 3). The total number of White males enrolled in NIDDK clinical research in FY20 was 3,130 and in FY21 was 2,709; a decrease in FY21 of 421 (13% decrease; Appendix Table 3).

In accordance with the NOT-OD-18-014 amendment to the "*NIH Policy and Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research*," all grant recipients conducting applicable NIH-defined Phase III clinical trials must ensure results of valid analyses by sex/gender, race, and/or ethnicity are submitted to Clinicaltrials.gov. The total number of NIDDK Phase III trials requiring valid analyses by sex and gender was 31 (97%) in FY19; 37 (97%) in FY20; and 36 (84%) in FY21. The total number of NIDDK Phase Trials III requiring valid analyses by race and ethnicity was 32 in F19 and 36 in FY20 and FY21 (Appendix Table 4).

Inclusion enrollment data summarized by this report can be further explored using the Research Condition and Disease Categorization (RCDC) module through this link: https://report.nih.gov/RISR/.

NIDDK staff will continue to encourage participation of all minority groups in clinical research, to maintain diversity and scientific integrity of the Institute's funded clinical research. In addition, the NIDDK will continue to seek out and fund clinical research in areas of high relevance to either a specific gender or racial group.

# IV. APPENDIX

## Table 1: Metrics Based on Inclusion Enrollment Records (IERs) - NIDDK

**Total Inclusion Enrollment Records (IERs) for NIH-Defined Extramural and Intramural Clinical Research Reported Between Fiscal Years 2019 and 2021**

| Fiscal Year | Total IERs | IERs Without Enrollment | IERs With Enrollment | US Site IERs | Non-US Site IERs | Female Only IERs | Male Only IERs | IERs Excluding Male only and Female only* |
|---|---|---|---|---|---|---|---|---|
| 2019 | 1,395 | 385 | 1,010 | 957 | 53 | 58 | 29 | 923 |
| 2020 | 1,607 | 601 | 1,006 | 969 | 37 | 83 | 32 | 891 |
| 2021 | 1,576 | 606 | 970 | 943 | 27 | 81 | 34 | 855 |

*Inclusion Enrollment Records (IERs) excluding male only and female only include unknown sex/gender, and combination of unknown and any sex/gender(s).

## Table 2: Total Enrollment: All NIH-Defined Clinical Research – NIDDK

### NIDDK Total Enrollment for All NIH-Defined Clinical Research, Sex/Gender by Race and Ethnicity

| Fiscal Year | Sex Gender | Minority | % Minority | Total Enrollment | % Total | American Indian Alaska Native | % American Indian Alaska Native | Asian | % Asian | Black African American | % Black African American | Native Hawaiian Pacific Islander | % Native Hawaiian Pacific Islander | White | % White |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 2019 | Female | 106,702 | 47.7 | 223,842 | 52.4 | 14,136 | 6.3 | 10,991 | 4.9 | 53,107 | 23.7 | 1,806 | 0.8 | 119,667 | 53.5 |
| 2019 | Male | 84,070 | 42.7 | 196,720 | 46.1 | 12,257 | 6.2 | 10,455 | 5.3 | 41,095 | 20.9 | 1,434 | 0.7 | 111,459 | 56.7 |
| 2019 | Unknown | 355 | 5.4 | 6,562 | 1.5 | 129 | 2.0 | 49 | 0.7 | 81 | 1.2 | 1 | 0.0 | 196 | 3.0 |
| 2020 | Female | 98,569 | 49.3 | 199,872 | 53.8 | 14,129 | 7.1 | 14,519 | 7.3 | 33,802 | 16.9 | 1,784 | 0.9 | 115,869 | 58.0 |
| 2020 | Male | 72,213 | 45.5 | 158,846 | 42.8 | 12,062 | 7.6 | 10,700 | 6.7 | 24,942 | 15.7 | 1,534 | 1.0 | 92,780 | 58.4 |
| 2020 | Unknown | 2,495 | 19.4 | 12,846 | 3.5 | 152 | 1.2 | 439 | 3.4 | 1,084 | 8.4 | 1 | 0.0 | 4,744 | 36.9 |
| 2021 | Female | 78,014 | 47.3 | 164,906 | 51.4 | 12,682 | 7.7 | 13,736 | 8.3 | 23,407 | 14.2 | 1,532 | 0.9 | 97,728 | 59.3 |
| 2021 | Male | 60,765 | 42.2 | 143,957 | 44.9 | 11,120 | 7.7 | 10,136 | 7.0 | 20,970 | 14.6 | 1,474 | 1.0 | 86,819 | 60.3 |
| 2021 | Unknown | 2,273 | 19.2 | 11,859 | 3.7 | 4 | 0.0 | 433 | 3.7 | 1,036 | 8.7 | 4 | 0.0 | 5,270 | 44.4 |

| Fiscal Year | Sex Gender | More Than One Race | % More Than One Race | Unknown Not Reported | % Unknown Not Reported | Not Hispanic | % Not Hispanic | Hispanic Latino | % Hispanic Latino | Unknown Not Reported | % Unknown Not Reported |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 2019 | Female | 5,549 | 2.5 | 18,586 | 8.3 | 144,071 | 64.4 | 25,778 | 11.5 | 53,993 | 24.1 |
| 2019 | Male | 4,509 | 2.3 | 15,511 | 7.9 | 119,361 | 60.7 | 17,747 | 9.0 | 59,612 | 30.3 |
| 2019 | Unknown | 60 | 0.9 | 6,046 | 92.1 | 1,229 | 18.7 | 42 | 0.6 | 5,291 | 80.6 |
| 2020 | Female | 5,337 | 2.7 | 14,432 | 7.2 | 160,431 | 80.3 | 33,154 | 16.6 | 6,287 | 3.1 |
| 2020 | Male | 3,617 | 2.3 | 13,211 | 8.3 | 130,649 | 82.2 | 22,616 | 14.2 | 5,581 | 3.5 |
| 2020 | Unknown | 670 | 5.2 | 5,756 | 44.8 | 1,396 | 10.9 | 751 | 5.8 | 10,699 | 83.3 |
| 2021 | Female | 4,891 | 3.0 | 10,930 | 6.6 | 135,675 | 82.3 | 25,578 | 15.5 | 3,653 | 2.2 |
| 2021 | Male | 3,440 | 2.4 | 9,998 | 6.9 | 123,484 | 85.8 | 16,774 | 11.7 | 3,699 | 2.6 |
| 2021 | Unknown | 648 | 5.5 | 4,464 | 37.6 | 1,728 | 14.6 | 762 | 6.4 | 9,369 | 79.0 |

The data presented in this report show only inclusion data records labeled as prospective data. Inclusion data records labeled as existing data are excluded.

## Table 3: Total Enrollment: All NIH-Defined Phase III Trials - NIDDK

### NIDDK Total Enrollment for NIH-Defined Extramural and Intramural Phase III Clinical Research, Sex/Gender by Race and Ethnicity

| Fiscal Year | Sex Gender | Minority | % Minority | Total Enrollment | % Total | American Indian Alaska Native | % American Indian Alaska Native | Asian | % Asian | Black African American | % Black African American | Native Hawaiian Pacific Islander | % Native Hawaiian Pacific Islander | White | % White |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 2019 | Female | 1,905 | 56.8 | 3,354 | 44.5 | 356 | 10.6 | 95 | 2.8 | 641 | 19.1 | 16 | 0.5 | 1,836 | 54.7 |
| 2019 | Male | 1,786 | 42.8 | 4,176 | 55.5 | 184 | 4.4 | 195 | 4.7 | 599 | 14.3 | 28 | 0.7 | 2,812 | 67.3 |
| 2019 | Unknown | 0 | 0.0 | 1 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 1 | 100.0 |
| 2020 | Female | 1,327 | 23.1 | 5,747 | 58.3 | 415 | 7.2 | 200 | 3.5 | 493 | 8.6 | 7 | 0.1 | 4,303 | 74.9 |
| 2020 | Male | 943 | 23.0 | 4,095 | 41.6 | 147 | 3.6 | 202 | 4.9 | 425 | 10.4 | 7 | 0.2 | 3,130 | 76.4 |
| 2020 | Unknown | 0 | 0.0 | 10 | 0.1 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| 2021 | Female | 1,950 | 61.4 | 3,176 | 43.1 | 500 | 15.7 | 75 | 2.4 | 773 | 24.3 | 9 | 0.3 | 1,532 | 48.2 |
| 2021 | Male | 1,851 | 44.2 | 4,185 | 56.8 | 211 | 5.0 | 185 | 4.4 | 777 | 18.6 | 22 | 0.5 | 2,709 | 64.7 |
| 2021 | Unknown | 0 | 0.0 | 3 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 2 | 66.7 |

| Fiscal Year | Sex Gender | More Than One Race | % More Than One Race | Unknown Not Reported | % Unknown Not Reported | Not Hispanic | % Not Hispanic | Hispanic Latino | % Hispanic Latino | Unknown Not Reported | % Unknown Not Reported |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 2019 | Female | 197 | 5.9 | 213 | 6.4 | 2,164 | 64.5 | 777 | 23.2 | 413 | 12.3 |
| 2019 | Male | 201 | 4.8 | 157 | 3.8 | 3,146 | 75.3 | 734 | 17.6 | 296 | 7.1 |
| 2019 | Unknown | 0 | 0.0 | 0 | 0.0 | 1 | 100.0 | 0 | 0.0 | 0 | 0.0 |
| 2020 | Female | 39 | 0.7 | 290 | 5.0 | 5,149 | 89.6 | 224 | 3.9 | 374 | 6.5 |
| 2020 | Male | 16 | 0.4 | 168 | 4.1 | 3,773 | 92.1 | 168 | 4.1 | 154 | 3.8 |
| 2020 | Unknown | 0 | 0.0 | 10 | 100.0 | 0 | 0.0 | 0 | 0.0 | 10 | 100.0 |
| 2021 | Female | 180 | 5.7 | 107 | 3.4 | 2,347 | 73.9 | 593 | 18.7 | 236 | 7.4 |
| 2021 | Male | 193 | 4.6 | 88 | 2.1 | 3,289 | 78.6 | 623 | 14.9 | 273 | 6.5 |
| 2021 | Unknown | 0 | 0.0 | 1 | 33.3 | 2 | 66.7 | 0 | 0.0 | 1 | 33.3 |

The data presented in this report show only inclusion data records labeled as prospective data. Inclusion data records labeled as existing data are excluded.

## Table 4: Valid Analysis by Sex/Gender and Race/Ethnicity

**Valid Analysis Requirements for NIH-Defined Phase III Extramural Grants Reported Between Fiscal Years 2019 and 2021**

| Fiscal Year | Total IERs | IERs Requiring Race Ethnicity Valid Analysis | % IERs Requiring Race Ethnicity Valid Analysis | IERs Requiring Sex Gender Valid Analysis | % IERs Requiring Sex Gender Valid Analysis |
|---|---|---|---|---|---|
| 2019 | 32 | 31 | 96.9 | 31 | 96.9 |
| 2020 | 38 | 36 | 94.7 | 37 | 97.4 |
| 2021 | 43 | 36 | 83.7 | 36 | 83.7 |

Current methodology to monitor valid analysis began in 2019 and differs from what was used in 2018 (N/A in 2018). Plans for valid analysis methodologies specified in the project application are reported for all IERs, including IERs that have no reported actual enrollment at the time of reporting.