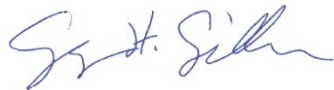


**DEPARTMENT OF HEALTH AND HUMAN SERVICES**

**National Institutes of Health**

**Office of the Director**

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



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**NHLBI 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. NHLBI Mission Statement**

The National Heart, Lung, and Blood Institute (NHLBI) provides global leadership for a research, training, and education program to promote the prevention and treatment of heart, lung, and blood diseases and enhance the health of all individuals so that they can live longer and more fulfilling lives.

The NHLBI stimulates basic discoveries about the causes of disease, enables the translation of basic discoveries into clinical practice, fosters training and mentoring of emerging scientists and physicians, and communicates research advances to the public. It creates and supports a robust, collaborative research infrastructure in partnership with private and public organizations, including academic institutions, industry, and other government agencies. The Institute collaborates with patients, families, health care professionals, scientists, professional societies, patient advocacy groups, community organizations, and the media to promote the application of research results and leverage resources to address public health needs. The NHLBI also collaborates with international organizations to help reduce the burden of heart, lung, and blood diseases worldwide.

**B. History of Inclusion Policy**

The NIH Revitalization Act of 1993 (PL 103-43) directed the NIH to ensure that women and minorities are included as subjects in the clinical research it supports. The NIH policy on the inclusion of women and minorities as participants in clinical research was published as a notice in the *Federal Register* on March 28, 1994, (Vol. 59, No. 59) and became effective in September 1994 for all grant applications and contract proposals submitted after June 1, 1994. As stated in the notice,

“It is the policy of the NIH that women and members of minority groups and their subpopulations must be included in all NIH-supported biomedical and behavioral research projects involving human subjects, 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.”

The law also included the following provision:

“The advisory council of each national institute shall prepare biennial reports describing the manner in which the institute has complied with this section.”

Most recently revised in January 2002, the sex/gender, race, and ethnicity categories required by the Office of Management and Budget (OMB), are shown below. Investigators are instructed to collect these data through participant self-report and are permitted to collect more detailed information as applicable to their research topics, but are required to collapse their data into the OMB-specified categories. Also dependent upon the research topic is whether investigators choose to collect sex or gender data from participants.

<b>Sex/Gender</b>	<b>Race</b>	<b>Ethnicity</b>
Female	American Indian, Alaska Native	Hispanic, Latino
Male	Asian	Not Hispanic or Latino
Unknown or Not Reported	Black, African American	Unknown or Not Reported
	Native Hawaiian, Pacific Islander	
	White	
	More than One Race	
	Unknown or Not Reported	

### *Recent Revisions*

The 21<sup>st</sup> Century Cures Act, enacted December 13, 2016, included several new requirements related to inclusion of participants in clinical research. As a result, NIH updated its policy on the Inclusion of Women and Minorities as Subjects in Clinical Research on November 28, 2017, to require studies that are both NIH-defined Phase III clinical trials and applicable clinical trials to report the results of analyses by sex/gender and/or race/ethnicity to ClinicalTrials.gov. This requirement is effective for competing grant awards on or after December 13, 2017, as well as contract solicitations and intramural studies initiated after this date. Additionally, NIH revised its Inclusion of Children Policy on December 19, 2017. The revised policy, now called the NIH Policy and Guidelines on the Inclusion of Individuals Across the Lifespan as Participants in Research Involving Human Subjects, applies to individuals of all ages and requires reporting of participant age at enrollment in annual progress reports. The policy is effective for applications submitted on or after January 25, 2019, and contract solicitations and intramural studies initiated after this date. The 21<sup>st</sup> Century Cures Act amended the frequency of the Report of the NIH Director on the inclusion of women and minorities from biennial to triennial. Thus, this first triennial report provides information on inclusion of participants in NIH clinical research from FY 2016 – 2018. One additional revision requires that NIH provide inclusion enrollment details by the Research, Condition, and Disease Categorization (RCDC) codes starting with the 2018 data. These data can be found on the new website <https://report.nih.gov/RISR/>.

### ***National Heart, Lung, and Blood Advisory Council Review***

The first of such reports was prepared for the NIH and its constituent Institutes and Centers (ICs) in 1997. As it did in each of the previous report years, the NIH has elected to prepare centrally a summary report. The report, which is to be developed by the NIH Office of Extramural Research, will include statements related to each of the national advisory councils. Because recruitment data are only required to be provided to the NIH as part of noncompeting renewal applications, there is always a lag in the data presented. The data provided as part of this report reflect enrollment of participants in NHLBI clinical research studies in fiscal years 2016, 2017, and 2018.

On February 5, 2019, the National Heart, Lung, and Blood Advisory Council (NHLBAC) reviewed:

- NHLBI's procedures for implementation of the NIH policy for inclusion of women and minorities in clinical studies and
- The results of that implementation.

They determined that NHLBI is in compliance.

In 1997 and in each of the report years since then, the NHLBAC found that the NHLBI had complied with the policy mandate. Information and data are provided herein to support a similar conclusion in 2019.

## **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 NIH-defined Phase III clinical trials, 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 Summary Statement. 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.

## **B. Program Monitoring and Grants Management Oversight**

Prior to an award, program staff 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 NIH-defined Phase III clinical trials, program staff monitor the requirement for sex/gender and race/ethnicity analyses in applications and annual progress reports. Grants management staff ensure that appropriate terms and conditions of award are included in the Notice of Award, and that this information is appropriately documented in the official grant file.

The NHLBI relies upon a four-step process involving its program officials (POs) for ensuring compliance with the NIH policy. Since the inception of the NIH policy, the NHLBI has scrutinized each project—even those that were rated acceptable for inclusion of women and minorities during peer review. The NHLBI procedure is to have:

- The POs evaluate all clinical research applications for appropriate representation of women, minorities, and children.
- The POs discuss any concerns regarding the extent to which an application is in compliance with the policy with senior Institute staff.
- The POs discuss those issues needing further attention and their possible solution with the applicants.
- The POs evaluate cumulative enrollment data from annual progress reports and work with investigators to develop plans for enhancing enrollment of under-represented groups.

## **C. Intramural Oversight**

All intramural clinical research trials stipulate in their consent forms that *“subjects will not be excluded from participation based on gender, race or ethnicity”*. Intramural IRBs monitor annual intramural research protocol enrollment for compliance with inclusion guidelines. During annual IRB continuing review of protocols, investigators must provide to the IRB an explanation and/or justification for enrollment patterns inconsistent with this stipulation. With each continuing review, the investigator documents the number, gender, race, and ethnicity of participants accrued during the past year. The Clinical Center’s Office of Protocol Services (OPS) coordinates annual reporting of participant demographic data to the Office of Extramural Research (OER) and the Office of Research on Women’s Health.

## **D. Training Approaches**

The NIH has developed numerous training documents, FAQs, and tools related to tracking study populations and addressing compliance with the Inclusion Policy. NHLBI program staff have access to these resources. Most recently, the NIH Office of Extramural Research (OER) provided the May 11, 2018 training, Ensuring Inclusion in NIH Clinical Research: Policies and Procedures for Grants and Contracts. A member of the NHLBI Office of Clinical Research (OCR) participated in this training as a presenter. OER also provides training materials through their website including archived training sessions available on video-cast or as slide shows. In addition, NHLBI OCR conducts IC-level training sessions to address changes in policy and procedures, such as Division and Branch-level trainings on the new 21<sup>st</sup> Centuries Cures policies and Human Subjects System (HSS). One-on-one training is always available.

### III. Analysis and Interpretation of Data

#### A. Enrollment Data for NHLBI Clinical Research

As mentioned above, the NIH Office of Extramural Research (OER) generates both NIH and IC-level data tables describing the enrollment into human subjects research studies reported during the fiscal years 2016-2018. These NHLBI tables are presented in the Appendix. These data represent only prospective enrollment and do not include secondary analyses of existing datasets. Further details describing enrollment of participants in Phase III Clinical Trials is provided below in Section B. The trends and key points illustrated in the data tables are summarized below:

- Total Number of Participants Enrolled. The total enrollment figures in Table 3-1-A show an increase in participants reported from 487,191 in 2016, 846,020 in 2017, and 988,868 in 2018. This consistent increase is attributed to two factors. The first factor is an NIH-wide change in electronic tracking systems and enforcement procedures, leading to a more comprehensive data capturing process. The second factor is an increase in NHLBI studies utilizing large electronic health records systems to prospectively follow study participants.
- Percentage of Women Enrolled. Table 3-1-A also illustrates the increase in the enrollment of women, with 56.5% female participants in 2018. This trend was also seen when single-sex studies were removed, with 45.3% female enrollment in 2018 versus 41.6% in 2016 in studies that enrolled both males and females.
- Percentage of Minority Participants Enrolled. Table 5-1-1-C provides a breakdown of enrollment by sex/gender and minority status, showing that minority participation in NHLBI studies exceeded the 30% representation in the 2010 U.S. census in all three years across both females and males, with minority representation rising above 40% in 2018.

#### B. Enrollment Data for NHLBI-funded Phase III Clinical Trials

As mentioned above, there are additional policy requirements for Phase III Clinical Trials, requiring attention to be focused on the inclusion of women and minorities. One key provision is to ensure that each Phase III trial provides a plan to conduct valid analyses by sex/gender, race, and ethnicity. All of the NHLBI-funded Phase III trials met this requirement. The enrollment trends and key points illustrated in Table 5-2-2-C are summarized below:

- Total Enrollment. The spike in enrollment reported for Phase III Clinical Trials in 2017 is the result of a large pragmatic trial which studied over 200,000 participants that year. After the completion of this large trial, the Phase III enrollment dropped in 2018 but still remained considerably higher than 2016 levels due to the initiation of two large trials.
- Percentage of Women Enrolled. From 2016 to 2018 the inclusion of women in Phase III trials improved from 35.0% to 65.0%. The low inclusion in 2016 is attributed to a large VA-based trial that enrolled a high percentage of men. The increase in 2018 is attributed to the two large trials mentioned above that enroll only women.
- Percentage of Minority Participants Enrolled. The 2016 enrollment data show a spike in minority enrollment in Phase III trials with both female and male minority participants above 60%. This spike is attributed to a large trial among Asian participants that ended in 2016. A drop in minority enrollment in 2017 is due to an increase in “unknown” race and ethnicity reporting attributed to a single trial. Minority participation in Phase III trials improved in 2018, but female minority participation still falls below the 30% reported in the 2010 census.

To facilitate further improvements, the Institute will continue to share lessons learned across portfolios and encourage investigators to develop novel strategies for the recruitment of women and minorities in Phase III clinical trials.

### **Conclusion**

The mandate of the NIH Revitalization Act of 1993 was to ensure inclusion of women and minorities in all NHLBI-supported clinical studies. The data demonstrate that the Institute has done far more than that minimal standard. Women, African Americans, American Indian/Alaskan Natives, Asians, Native Hawaiians/Pacific Islanders, and Hispanics/Latinos are all represented in NHLBI-supported clinical studies at rates that are near or exceed their corresponding representation in the U.S. population according to the 2010 census.

## APPENDIX 1. DATA TABLES

**Table 2-1. Total Inclusion Data Records for NIH-Defined Extramural and Intramural Clinical Research Reported Between FY2016 and FY2018**

<b>Fiscal Year</b>	<b>Total Records</b>	<b>Records Without Enrollment</b>	<b>Records With Enrollment</b>	<b>US Site Records</b>	<b>Non-US Site Records</b>	<b>Female Only Records</b>	<b>Male Only Records</b>	<b>Records Excluding Male-only and Female-only*</b>
2016	1,182	110	1,072	1,041	31	43	29	1,000
2017	1,427	182	1,245	1,208	37	58	33	1,154
2018	1,617	252	1,365	1,320	45	67	33	1,265

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

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

<b>Fiscal Year</b>	<b>Total Enrollment</b>	<b>Total Females</b>	<b>% Females</b>	<b>Total Males</b>	<b>% Males</b>	<b>Total Unknown</b>	<b>% Unknown</b>
2016	487,191	260,812	53.5	219,627	45.1	6,752	1.4
2017	846,020	460,155	54.4	368,119	43.5	17,746	2.1
2018	988,868	558,580	56.5	413,769	41.8	16,519	1.7

<b>Fiscal Year</b>	<b>Total Enrollment</b>	<b>Enrollment in Female-only</b>	<b>% Female-only</b>	<b>Enrollment in Male-only</b>	<b>% Male-only</b>	<b>Females, Excluding Female-only</b>	<b>% Females, Excluding Female-only</b>	<b>Males, Excluding Male-only</b>	<b>% Males, Excluding Male-only</b>
2016	487,191	58,170	11.9	875	0.2	202,642	41.6	218,752	44.9
2017	846,020	106,665	12.6	1,020	0.1	353,490	41.8	367,099	43.4
2018	988,868	110,150	11.1	977	0.1	448,430	45.3	412,792	41.7



**Table 5-1-1-C Enrollment for All NIH-Defined Clinical Research, Sex/Gender by Race and Ethnicity**

Year	Sex Gender	Minority	% Minority	Total		Not Hispanic	% Not Hispanic	Hispanic Latino	% Hispanic Latino	Unknown Not Reported	% Unknown Not Reported
				Enrollment	% Total						
2016	Female	116,878	44.8	260,812	53.5	212,206	81.4	41,131	15.8	7,475	2.9
2016	Male	102,859	46.8	219,627	45.1	179,584	81.8	33,158	15.1	6,885	3.1
2016	Unknown	345	5.1	6,752	1.4	467	6.9	127	1.9	6,158	91.2
2017	Female	145,641	31.7	460,155	54.4	369,381	80.3	50,718	11.0	40,056	8.7
2017	Male	113,910	30.9	368,119	43.5	287,046	78.0	39,412	10.7	41,661	11.3
2017	Unknown	666	3.8	17,746	2.1	475	2.7	425	2.4	16,846	94.9
2018	Female	245,261	43.9	558,580	56.5	426,328	76.3	111,202	19.9	21,050	3.8
2018	Male	176,367	42.6	413,769	41.8	310,390	75.0	79,406	19.2	23,973	5.8
2018	Unknown	379	2.3	16,519	1.7	1,043	6.3	169	1.0	15,307	92.7

Year	Sex Gender	% American Indian Alaska Native		Asian	% Asian	% Black African American		% Native Hawaiian Islander		White	% White	% More Than One Race	% More Than One Race	Unknown Not Reported	% Unknown Not Reported
		Indian Alaska Native	% Indian Alaska Native			Black African American	% Black African American	Native Hawaiian Islander	% Native Hawaiian Islander						
2016	Female	4,605	1.8	19,119	7.3	49,630	19.0	3,716	1.4	157,819	60.5	7,170	2.7	18,753	7.2
2016	Male	2,828	1.3	27,351	12.5	36,926	16.8	2,891	1.3	126,167	57.4	6,207	2.8	17,257	7.9
2016	Unknown	4	0.1	16	0.2	207	3.1	4	0.1	164	2.4	16	0.2	6,341	93.9
2017	Female	5,982	1.3	19,238	4.2	70,608	15.3	723	0.2	326,048	70.9	8,850	1.9	28,706	6.2
2017	Male	3,760	1.0	20,151	5.5	50,664	13.8	471	0.1	260,048	70.6	5,655	1.5	27,370	7.4
2017	Unknown	16	0.1	40	0.2	171	1.0	4	0.0	208	1.2	41	0.2	17,266	97.3
2018	Female	2,837	0.5	35,590	6.4	97,603	17.5	889	0.2	349,675	62.6	40,280	7.2	31,706	5.7
2018	Male	1,887	0.5	33,209	8.0	61,466	14.9	787	0.2	253,056	61.2	35,049	8.5	28,315	6.8
2018	Unknown	97	0.6	16	0.1	113	0.7	3	0.0	208	1.3	23	0.1	16,059	97.2

**Table 5-2-2-C. All Enrollment for NIH-Defined Extramural and Intramural Phase III Clinical Research, Sex/Gender by Race and Ethnicity**

Year	Sex Gender	Minority	% Minority	Total Enrollment	% Total	Not Hispanic	% Not Hispanic	Hispanic Latino	% Hispanic Latino	Unknown Not Reported	% Unknown Not Reported
2016	Female	11,301	65.2	17,334	35.0	13,210	76.2	3,936	22.7	188	1.1
2016	Male	19,708	61.4	32,090	64.9	27,984	87.2	3,797	11.8	309	1.0
2016	Unknown	5	10.0	50	0.1	0	0.0	5	10.0	45	90.0
2017	Female	38,898	16.5	235,606	60.3	198,666	84.3	8,763	3.7	28,177	12.0
2017	Male	24,900	16.0	155,332	39.7	118,528	76.3	5,865	3.8	30,939	19.9
2017	Unknown	14	13.3	105	0.0	12	11.4	5	4.8	88	83.8
2018	Female	19,930	23.6	84,293	65.0	78,176	92.7	5,692	6.8	425	0.5
2018	Male	13,548	30.1	45,020	34.7	40,238	89.4	3,776	8.4	1,006	2.2
2018	Unknown	44	15.8	278	0.2	54	19.4	1	0.4	223	80.2

Year	Sex Gender	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	More Than One Race	% More Than One Race	Unknown Not Reported	% Unknown Not Reported
2016	Female	42	0.2	3,782	21.8	3,509	20.2	17	0.1	9,390	54.2	185	1.1	409	2.4
2016	Male	69	0.2	11,670	36.4	4,061	12.7	39	0.1	15,441	48.1	224	0.7	586	1.8
2016	Unknown	0	0.0	0	0.0	1	2.0	0	0.0	0	0.0	0	0.0	49	98.0
2017	Female	533	0.2	4,947	2.1	24,701	10.5	56	0.0	193,110	82.0	1,971	0.8	10,288	4.4
2017	Male	308	0.2	4,676	3.0	14,048	9.0	55	0.0	125,224	80.6	382	0.2	10,639	6.8
2017	Unknown	1	1.0	0	0.0	2	1.9	0	0.0	5	4.8	6	5.7	91	86.7
2018	Female	518	0.6	3,254	3.9	10,568	12.5	86	0.1	66,564	79.0	141	0.2	3,162	3.8
2018	Male	333	0.7	3,933	8.7	5,629	12.5	117	0.3	33,139	73.6	280	0.6	1,589	3.5
2018	Unknown	0	0.0	0	0.0	43	15.5	0	0.0	16	5.8	0	0.0	219	78.8