

NHLBI Report on Monitoring Adherence to the NIH Policy on the Inclusion of Women and Minorities in Clinical Research as Reported in FY2019 – FY2021

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.

Sex/Gender	Race	Ethnicity
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 21st 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 21st 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 triennial report provides information on

inclusion of participants in NIH clinical research from FY 2019 – 2021. One additional revision requires that NIH provide inclusion enrollment details by the Research, Condition, and Disease Categorization (RCDC) codes starting with the 2018 data. The most recent version of the RCDC data is available through this link: <https://report.nih.gov/RISR/>.

C. National Heart, Lung, and Blood Advisory Council Review

The first mandated inclusion monitoring report 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 2019, 2020, and 2021.

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.

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 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. The NHLBI Advisory Council performs the second level of review and makes

recommendations for funding to the NHLBI Director considering the overall impact score, percentile ranking, and summary statement in light of the research priorities for NHLBI. 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 requirements for plans and reporting of 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 examined 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 participants across the lifespan.
- 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 studies require investigators to provide plans for the appropriate inclusion of women and minorities and/or a justification whenever representation is limited or absent. These plans are considered during the scientific review process. With the annual scientific review and IRB review renewal, the investigator documents the number, sex/gender, race and ethnicity of those who were accrued during the past year; any issues with accrual are addressed and plan to increase recruitment reviewed by both the Institute and 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 (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. In April 2020, NIH Program Officials/Program Directors and Scientific Review Officers attended the 2020 Inclusion Training for Program Staff and the 2020 Inclusion Training for Review Staff. Staff may access the archived training on the NIH staff intranet. OER provides additional training materials through their website including archived training sessions available on video-cast or as slide shows. In addition, NHLBI Office of Clinical Research (OCR) conducts IC-level training sessions to address changes in policy and procedures, such as Division and Branch-level trainings on complying with Inclusion Across the Lifespan 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 2019-2021. 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 692,495 in 2019 to 973,955 in 2020, then a sharp drop to 476,746 in 2021. This fluctuation is attributed to two factors. The first factor is the reporting in 2020 from three hospital-based NHLBI studies utilizing large electronic health records systems to prospectively follow study participants. These three studies reported a total of over 400,000 participants. Two of these studies were completed in 2020, therefore not included in the 2021 totals, accounting for a drop of over 300,000 participants. The second factor is the impact of the COVID-19 pandemic on research activities. With institutions shifting efforts from research to clinical care, many of our awardees were forced to put recruitment and enrollment activities on hold and study participants were unable to attend visits. NHLBI worked closely with investigators to support their implementation of innovative solutions, such as electronic informed

consents or virtual visits. We expect that the COVID-19 pandemic will continue to impact the reported enrollment data into 2022.

- Percentage of Women Enrolled. Table 3-1-A also illustrates NHLBI's commitment to the inclusion of women, with enrollment greater than or equal to 50%. The decrease from 56.2% in 2019 to 50.1% in 2021 is largely driven by the completion of two large women-only studies. We also hypothesize that the COVID-19 pandemic and increased care-giving responsibilities may have played a role in fewer women enrolling in clinical research.
- Percentage of Minority Participants Enrolled. Table 5-1-1-C provides a breakdown of enrollment by sex/gender and minority status, showing in all three years across both females and males, racial and ethnic minority participation in NHLBI studies exceeded the 30% representation in the 2010 U.S census, the standard referenced in the [NHLBI Policy for the Inclusion of Women, Minorities, and Participants Across the Lifespan in Clinical Research](#). Total minority representation rose to 43.8% in 2021. This increase mirrors the new 2020 U.S. census, now reporting 40% minority population.

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 number of Phase III records reporting enrollment decreased slightly from 59 to 53 across the three years, with 94% requiring valid analyses by sex/gender and 93% requiring valid analyses by race and ethnicity (this requirement is not applicable for single-sex or minority-only trials). The drop in enrollment reported for Phase III Clinical Trials in 2020 is due to the completion of two large trials, comprising a total of over 80,000 participants. As mentioned above, we expect that the COVID-19 pandemic also impacted recruitment for Phase III trials.
- Percentage of Women Enrolled. From 2019 to 2020 the inclusion of women in Phase III trials decreased from 66.2% to 46.6% due to the completion of a women-only trial of approximately 50,000 participants, then increased in 2021 to 49.2%.

- Percentage of Minority Participants Enrolled. The 2020 and 2021 enrollment data show a spike in minority enrollment in Phase III trials with both female and male minority participants above 60%. This spike, comprised of increases in Asian, African American, and Hispanic/Latino participants, is attributed to foreign and minority-focused trials, including a household air pollution trial among pregnant women in developing countries, a statin trial among people living with HIV, and an implementation trial among underserved populations.

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.

C. New Data for Age at Enrollment

After the implementation of the new NIH Inclusion Across the Lifespan Policy, the 2021 data are the first to include details about study participants' age at enrollment. The requirement applies to new projects from applications or proposals submitted for 2019 due dates, and this first batch of data includes 38,992 individuals from 285 new studies. This is approximately 26% of the studies reporting enrollment data in 2021. As shown in Tables 6 and 7, 49.5% of NHLBI participants from these applicable studies fell into the older adult age category defined as individuals 65 years or older. This older study population reflects the chronic nature of many NHLBI research portfolios. As additional data are compiled, we look forward to the ability to make more inferences and support investigators to ensure full inclusion of participants of all ages.

Conclusion

The mandate of the NIH Revitalization Act of 1993 was to ensure inclusion of women and minorities in all NIH-supported clinical studies. The data demonstrate that the Institute has done far more than that minimal standard. Women and minority participants 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 as well as the new 2020 census.

APPENDIX 1. DATA TABLES

Table 2-1. Total Inclusion Data 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	2,100	638	1,462	1,400	62	82	38	1,342
2020	2,303	843	1,460	1,398	62	86	46	1,328
2021	2,480	996	1,484	1,411	73	105	45	1,334

*Inclusion Data Records (IERS) 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 Fiscal Years 2019 and 2021

Fiscal Year	Total Enrollment	Total Females	% Females	Total Males	% Males	Total Unknown	% Unknown
2019	692,495	389,453	56.2	277,941	40.1	25,101	3.6
2020	973,955	523,236	53.7	418,272	42.9	32,447	3.3
2021	476,746	238,678	50.1	223,543	46.9	14,525	3.0

Fiscal Year	Total Enrollment	Enrollment in Female only	% Female only	Enrollment in Male only	% Male only	Females, Excluding Female only	% Females, Excluding Female only	Males, Excluding Male only	% Males, Excluding Male only
2019	692,495	113,108	16.3	3,235	0.5	276,345	39.9	274,706	39.7
2020	973,955	64,716	6.6	2,797	0.3	458,520	47.1	415,475	42.7
2021	476,746	5,864	1.2	426	0.1	232,814	48.8	223,117	46.8

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

Fiscal Year	Sex Gender	Minority	% Minority	Total Enrollment	% Total	Not Hispanic	% Not Hispanic	Hispanic Latino	% Hispanic Latino	Unknown Not Reported	% Unknown Not Reported
2019	Female	127,436	32.7	389,453	56.2	332,934	85.5	31,072	8.0	25,447	6.5
2019	Male	95,069	34.2	277,941	40.1	228,050	82.0	22,815	8.2	27,076	9.7
2019	Unknown	435	1.7	25,101	3.6	1,431	5.7	204	0.8	23,466	93.5
2020	Female	239,841	45.8	523,236	53.7	430,455	82.3	74,411	14.2	18,370	3.5
2020	Male	178,814	42.8	418,272	42.9	357,547	85.5	42,146	10.1	18,579	4.4
2020	Unknown	872	2.7	32,447	3.3	2,032	6.3	591	1.8	29,824	91.9
2021	Female	112,659	47.2	238,678	50.1	189,940	79.6	28,066	11.8	20,672	8.7
2021	Male	95,190	42.6	223,543	46.9	180,258	80.6	22,736	10.2	20,549	9.2
2021	Unknown	800	5.5	14,525	3.0	1,006	6.9	352	2.4	13,167	90.7

Fiscal 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
2019	Female	3,066	0.8	11,898	3.1	79,767	20.5	1,576	0.4	266,609	68.5	6,418	1.6	20,119	5.2
2019	Male	2,055	0.7	12,851	4.6	55,832	20.1	1,224	0.4	184,235	66.3	4,448	1.6	17,296	6.2
2019	Unknown	79	0.3	8	0.0	148	0.6	3	0.0	304	1.2	28	0.1	24,531	97.7
2020	Female	2,546	0.5	19,554	3.7	134,556	25.7	1,417	0.3	324,366	62.0	19,630	3.8	21,167	4.0
2020	Male	2,254	0.5	17,874	4.3	107,820	25.8	1,384	0.3	254,175	60.8	15,286	3.7	19,479	4.7
2020	Unknown	11	0.0	30	0.1	243	0.7	5	0.0	1,817	5.6	36	0.1	30,305	93.4
2021	Female	1,395	0.6	10,855	4.5	71,553	30.0	971	0.4	133,918	56.1	4,455	1.9	15,531	6.5
2021	Male	1,364	0.6	10,055	4.5	60,295	27.0	984	0.4	133,298	59.6	3,429	1.5	14,118	6.3
2021	Unknown	8	0.1	23	0.2	398	2.7	5	0.0	525	3.6	34	0.2	13,532	93.2

Table 5-2-2-C. All 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	Not Hispanic	% Not Hispanic	Hispanic Latino	% Hispanic Latino	Unknown Not Reported	% Unknown Not Reported
2019	Female	20,386	22.7	89,809	66.2	83,989	93.5	5,114	5.7	706	0.8
2019	Male	13,617	30.0	45,417	33.5	40,601	89.4	3,654	8.0	1,162	2.6
2019	Unknown	94	26.8	351	0.3	77	21.9	34	9.7	240	68.4
2020	Female	16,832	68.9	24,437	46.6	16,048	65.7	7,722	31.6	667	2.7
2020	Male	14,907	54.5	27,339	52.1	19,405	71.0	6,974	25.5	960	3.5
2020	Unknown	338	51.4	658	1.3	132	20.1	309	47.0	217	33.0
2021	Female	15,214	68.7	22,152	49.2	14,989	67.7	6,609	29.8	554	2.5
2021	Male	12,350	54.2	22,792	50.6	16,781	73.6	5,194	22.8	817	3.6
2021	Unknown	17	23.9	71	0.2	39	54.9	4	5.6	28	39.4

Fiscal 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
2019	Female	664	0.7	3,170	3.5	11,508	12.8	55	0.1	72,821	81.1	202	0.2	1,389	1.5
2019	Male	421	0.9	3,714	8.2	5,647	12.4	67	0.1	33,515	73.8	712	1.6	1,341	3.0
2019	Unknown	0	0.0	1	0.3	57	16.2	0	0.0	52	14.8	3	0.9	238	67.8
2020	Female	313	1.3	2,161	8.8	6,774	27.7	55	0.2	13,343	54.6	271	1.1	1,520	6.2
2020	Male	396	1.4	1,626	5.9	6,130	22.4	65	0.2	16,762	61.3	417	1.5	1,943	7.1
2020	Unknown	6	0.9	3	0.5	18	2.7	0	0.0	110	16.7	6	0.9	515	78.3
2021	Female	132	0.6	2,395	10.8	6,152	27.8	26	0.1	11,880	53.6	184	0.8	1,383	6.2
2021	Male	169	0.7	1,743	7.6	5,449	23.9	40	0.2	13,389	58.7	257	1.1	1,745	7.7
2021	Unknown	1	1.4	0	0.0	8	11.3	1	1.4	30	42.3	4	5.6	27	38.0

Table 6. Age Distribution Using Broad Age Groups for NIH-Defined Extramural and Intramural Clinical Research Reported for Fiscal Year 2021

Children (<18 years)	Adults (18-64 years)	Older Adults (65+ years)	Unknown or Not Reported	Total
4,296 11.0%	14,426 37.0%	19,286 49.5%	984 2.5%	38,992 100%

Table 7. Age Distribution Using Detailed Age Groups for NIH-Defined Extramural and Intramural Clinical Research Reported for Fiscal Year 2021

0 - 28 Days	29-364 Days	<1 year, values other than 0-28 or 29-364 days *	<1 year, Total **	1-5 Years	6-12 Years	13-15 Years	16-17 Years	18-21 Years	22-25 Years	26-34 Years	35-44 Years	45-54 Years	55-64 Years	65-69 Years	70-74 Years	75-79 Years	80-84 Years	85-89 Years	90+ Years	Unknown or Not Reported	Total
25 0.1%	83 0.2%	487 1.2%	595 1.5%	909 2.3%	1,987 5.1%	435 1.1%	370 0.9%	867 2.2%	779 2.0%	2,152 5.5%	2,313 5.9%	2,804 7.2%	5,511 14.1%	2,162 5.5%	1,838 4.7%	5,567 14.3%	5,040 12.9%	3,142 8.1%	1,537 3.9%	984 2.5%	38,992 100%

* Includes ages reported in weeks, months, or years that are equivalent to less than 1 year.

**Includes all ages equivalent to less than one year, including all those reported in days, weeks, months and years.