

National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)

Triennial Report

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

I. Background/Overview

The NIH and NIAMS are committed to the inclusion of women and minorities in all NIH-funded clinical research. As required by the NIH Revitalization Act of 1993 (Public Law 103-43), women and members of minority groups and their subpopulations as research participants must be included in all NIH-funded clinical research. Additionally, NIH-defined Phase III clinical trials must be carried out in a manner sufficient to analyze data by race, ethnicity, and sex/gender and report these results in accordance with policy. The overall goal of the NIH Inclusion Policy is to ensure that individuals are included in clinical research in a manner that is appropriate to the scientific question under study and the prevalence of the specific disease/condition in the population/subpopulation.

A. Mission of the NIAMS

The mission of the NIAMS is to support research into the causes, treatment, and prevention of arthritis and musculoskeletal and skin diseases; the training of basic and clinical scientists to carry out this research; and the dissemination of information on research progress in these diseases. The NIAMS supports a multidisciplinary program of basic, clinical, and translational investigations; epidemiologic research; research centers; and research training for scientists within its own facilities as well as grantees at universities and medical schools nationwide. It also supports the dissemination of research results and information through the NIAMS Information Clearinghouse and through the NIH Osteoporosis and Related Bone Diseases National Resource Center.

B. Description of the NIAMS Clinical Research Portfolio

The Institute's research portfolio includes five core mission areas: Systemic Rheumatic and Autoimmune Diseases, Bone Biology and Diseases, Muscle Biology and Diseases, Joint Biology and Diseases and Orthopaedics, and Skin Biology and Diseases.

Under Systemic Rheumatic and Autoimmune Diseases research area, the NIAMS supports:

- Arthritis Biology Program
- Rheumatic Diseases Integrative Biology Research Program
- Scleroderma, Fibrosis, and Autoinflammatory Disease Program
- Systemic Autoimmune Disease Biology Program

Under Bone Biology and Diseases research area, the NIAMS supports:

- Bone Biology, Metabolic Bone Disorders, and Osteoporosis Program
- Clinical, Integrative Physiology and Rare Diseases of Bone Program

Under Muscle Biology and Diseases research program, the NIAMS supports:

- Muscle Development and Physiology Program
- Muscle Disorders and Therapies Program

Under Joint Biology, Diseases, and Orthopaedics research program, the NIAMS supports:

- Cartilage and Connective Tissue Program
- Clinical Osteoarthritis and Diagnostic Imaging Program
- Musculoskeletal Tissue Engineering and Regenerative Medicine Program
- Orthopaedic Implant Science Program
- Orthopaedic Research Program

Under Skin Biology and Diseases research program, the NIAMS supports:

- Epidermis, Dermis, and Skin Senses Program
- Skin Immunology and Diseases, Skin Microbiome Program
- Skin Repair, Pigmentation and Appendages, Vasculature/Lymphatic Systems Program

In support of its research program goals and objectives, the NIAMS funds an extensive portfolio of clinical research, which includes interventional studies (i.e., clinical trials) and observational studies varying in size and complexity. While some of the diseases covered by the NIAMS mission are rare – affecting only a few thousand people worldwide, most are chronic and common, and many causes lifelong pain, disability, or disfigurement. They affect people of all ages, racial and ethnic populations, and economic groups. Many affect women and minorities disproportionately — both in increased numbers and increased disease severity. For example, women with systemic lupus erythematosus (SLE) outnumber men nine to one. African American women are three times as likely to have SLE as are white women, and the disease is also more

common in Hispanic, Asian, and American Indian women. SLE risk genes have been identified on the X chromosome, which provides potential evidence for this autoimmune disease's sex bias. Rheumatoid arthritis, osteoporosis, and osteoarthritis (in people over 45 years of age) are also more prevalent among women, whereas certain forms of ankylosing spondylitis (inflammation of the joints in the spine) occur more frequently in men. Given what is known about the populations affected by NIAMS diseases, it is important to ensure that the funded science is appropriately including individuals of diverse racial and ethnic groups.

II. Strategies for Ensuring Compliance in the Extramural Program

Strategies for ensuring compliance with the inclusion policy begins well before grant applications are received for peer review. In the funding opportunity announcement (FOA), specific language is included to support the inclusion of diverse populations in clinical studies. Any exclusion of a specific race/ethnicity, sex/gender or age group must be scientifically justified in the grant application. NIAMS scientific review, program, and grants management staff are aware of the NIH policies on inclusion on the basis of sex/gender, race/ethnicity, and age in clinical research. The NIAMS inclusion representative serves as a resource to answer questions about policy and compliance.

A. Peer Review

The implementation of inclusion guidelines involves the participation of NIAMS review, program, clinical management, and grants management staff. Inclusion is first addressed during the peer review process. 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/ethnicity, and age. 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. Initial review groups make recommendations as to the acceptability of the proposed study population with respect to the inclusion policies. Unacceptable inclusion plans must be reflected in the priority score of the application and documented in the minutes of the review session. 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 officials/program directors are responsible for reviewing the inclusion information in the application and indicating whether the plans are scientifically appropriate. NIAMS program officials discuss issues of non-compliance with applicants and advise them on how to resolve problems. The applicant then modifies the project or provides additional information to address reviewer concerns. These procedures ensure that NIAMS funds no application with unacceptable inclusion of women, minorities, and age groups. Program staff monitor enrollment in annual progress reports and provide consultation to investigators for enhancing outreach to particular populations as needed. 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. For NIH-defined Phase III clinical trials, program staff monitor the requirement for sex/gender and race/ethnicity analyses in annual progress reports. The Clinical Management Team is involved with monitoring inclusion data within the Human Subjects System (HSS) and addressing any technical issues that arise. They also provide expertise in devising strategies to help studies that are not meeting their inclusion goals and keep up-to-date on all inclusion policies.

C. NIAMS Training Approaches

NIAMS Program Officials/Program Directors and Scientific Review Officers attended the 2020 Inclusion Training for Program Staff and the 2020 Inclusion Training for Review Staff in April 2020 conducted by the NIH Office of Extramural Research (OER). The purpose of this training was to train NIH program and review staff on the NIH inclusion policies and procedures for the inclusion of women, minorities, and individuals across the lifespan. Staff may access the archived trainings on the NIH staff intranet. New NIAMS staff may also attend the NIH Integrated Core Curriculum training, which provides an intensive overview of the grants process and covers topics including initiative development, application submission, scientific peer review, resources and tools, council and pre-award, and post-award.

NIAMS Clinical Management staff host a monthly Clinical Trial Crosscutting Group meeting, attended by NIAMS program, review, and grants management staff. During this meeting, the Clinical Management staff discuss any updates on inclusion processes and address frequently asked inclusion and HSS questions.

D. NIAMS Specific Procedures

Additionally, some NIAMS clinical research studies, specifically clinical trials have an additional level of oversight implemented through a NIAMS-appointed Data and Safety Monitoring Board (DSMB) or a NIAMS-appointed Safety Officer (SO) who pays special attention to enrollment of participants and whether the researchers are meeting specified sex/gender and race/ethnicity targets. If a study is falling behind on reaching its minority goals, the monitoring body will request a plan from the principal investigator (PI) to improve the study's outreach to a particular population. The NIAMS and the monitoring body also pay careful attention to PI requests to add or replace clinical study sites to ensure that a new recruitment site will contribute the appropriate patient population in order to reach the study's inclusion targets. PIs must provide the following information before additional sites will be approved:

- Description of the patient population pool/catchment area of the new site (3-4 sentences)
- Overall study target enrollment
- Target enrollment for new site
- Description of the expected minority population pool of the new site
- Target minority enrollment for new site

III. Strategies for Ensuring Compliance for Intramural Research

NIAMS requires all intramural investigators conducting clinical research to provide plans for the appropriate inclusion of women and minorities, or a justification whenever representation is limited or absent, as part of their NIH protocol reviews. Intramural Institutional Review Boards (IRB) review the research protocols for compliance with inclusion guidelines and conduct annual Continuing Reviews. With each annual review and renewal, the investigator documents the number, sex, and race and ethnicity of participants 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 coordinates annual reporting of participant demographic data to the Office of Extramural Research (OER) and the Office of Research on Women's Health. As part of a quadrennial review policy, any clinical protocols that are open for four years or more involve discussion among the Institute Clinical Director and the PIs to discuss the adequacy of enrollment goals and any issues related to meeting them. Additionally, the NIAMS Clinical Director and Clinical Operations Manager meet yearly with individual PIs to carefully review study progress regarding target enrollment.

IV. Analysis and Interpretation of Data

The appended tables show the NIAMS inclusion enrollment data for extramural and intramural clinical research studies in fiscal years (FY) 2019 through 2021. Please note that data reflected for FY20 incorrectly included two Inclusion Enrollment Records (IERs) in the reporting that contained existing datasets with enrollment data of 140,212 participants. For the purposes of reporting inclusion data, existing datasets are not counted. This error incorrectly inflated our FY20 enrollment numbers; however, this was corrected, and data are reflected correctly for FY21.

A. NIAMS Aggregate Inclusion Enrollment Data

Inclusion enrollment data are reported by clinical research study and contained within IERs in the HSS. A study may have one or more IERs representing different study populations, depending upon how the record for a project is setup for reporting inclusion.

Table 2-1 (see Appendix 1) shows the number of IERs for NIAMS Extramural and Intramural clinical research projects that reported inclusion data between FY19 and FY21. The majority of records were from grants conducting research at U.S. (domestic) sites. IERs without enrollment indicate studies that have not recruited any participants. Female only or male only IERs indicate studies that were scientifically justified to recruit only single sex. The total number of records reporting inclusion data increased from 2019 to 2020 and slightly decreased from 2020 to 2021, with an overall 6.6% increase in records reporting data between 2019 (273 IERs) and 2021 (291 IERs).

The total enrollment for all NIAMS intramural and extramural Clinical Research by sex/gender, race, and ethnicity is displayed in Table 5-1-1-C (see Appendix 2). The NIAMS total enrollment counts for females and males in 2019 (180,434) and 2021 (194,983) show an increase in the number of participants enrolled. The increase in the number of participants may be attributed to more inclusion records, larger cohorts enrolled, and more accurate reporting of sex/gender based on the decreased number of participants with *unknown* information. The percentage of females (63.3%) enrolled in clinical research in 2019 has remained the same in 2021 and was almost twice that of males (32.4% in 2019; 33.0% in 2021). This ratio has been consistent and is not surprising given the prevalence of many NIAMS diseases affecting women disproportionately.

The percentage of minority enrollment for NIAMS clinical research studies has slightly increased from 24.8% in 2019 to 25.0% in 2021. The percentages of American Indian/Alaska Native

(0.2%) and Native Hawaiian/Pacific Islander (0.0%) enrolled in 2019 have remained the same in 2021. The percentage of Asian participants has increased from 3.3% in 2019 to 4.7% in 2021 while Black/African American have slightly decreased from 13.1% in 2019 to 12.2% in 2021. The percentage of ethnic minority (Hispanic/Latin) enrollment has slightly decreased from 7.9% in 2019 to 7.5% in 2021.

The total enrollment for NIH-wide intramural and extramural Clinical Research by sex/gender, race, and ethnicity is displayed in Table 5-1-1-C (see Appendix 4). When NIAMS sex/gender and race/ethnicity data are compared to the NIH-wide data, NIAMS has more female participants (66.3% in 2021 for NIAMS; 58.5% in 2021 for NIH-wide) and less Hispanic participants (7.5% in 2021 for NIAMS; 10.2% in 2021 for NIH-wide). Also, compared to the NIH data, NIAMS has enrolled a greater number of White participants (74.4% in 2021 for NIAMS; 53.4% in 2021 for NIH-wide). For minority enrollment, NIAMS has lower enrollment percentages across all racial minority categories. Overall, NIAMS is below (25.0% in 2021) NIH in minority enrollment (41.8% in 2021). The NIH total in minority enrollment has shown an increase from 2019 (40.1%) to 2021 (41.8%).

B. NIAMS supported NIH-Defined Phase III Trials

NIAMS supports NIH-defined Phase III clinical trials. NIAMS extramural currently supports two NIH-defined phase III clinical trials that require valid analyses by sex/gender and race/ethnicity, which includes four IERs.

The total enrollment for all NIAMS supported NIH-Defined Phase III Clinical Trials by sex/gender, race, and ethnicity is displayed in Table 5-2-2-C (see Appendix 3). The total enrollment number for NIH-defined phase III clinical trials has increased from 88 in 2019 to 248 in 2021. The percentage of females enrolled has decreased from 90.9% in 2019 to 85.5% in 2021. The overall percentage of minority enrollment has increased from 12.5% in 2019 to 18.1% in 2021. The percentage of Hispanic/Latino enrolled also has increased from 4.5% in 2019 to 5.2% in 2021.

C. Research, Condition, and Disease Categorization (RCDC) Report

As of March 1, 2022, NIAMS clinical research inclusion enrollment data by RCDC category are available on the NIH RePORT website through this link: <https://report.nih.gov/RISR/>

V. Additional information

A. NIAMS efforts to monitor inclusion of women and racial/ethnic minority enrollment in clinical research during the COVID-19 pandemic

The COVID-19 pandemic has resulted in many unique challenges for clinical research studies, especially with regard to recruitment and retention of minority and other hard to reach populations. To this end, NIAMS introduced a new process to closely monitor the impact of COVID-19 on recruitment and inclusion of women and racial/ethnic minorities in clinical research studies it supports. For studies that NIAMS monitors using an independent Safety Officer, studies are required to report the impact of COVID-19 on the study and submit data tables that show recruitment progress by sex/gender, race, and ethnicity as part of their safety report. The Safety Officers review these data and provide comment and feedback to help overcome challenges the study may be facing. For studies that are monitored by an independent Data and Safety Monitoring Board (DSMB), a similar process is followed, and the meeting agenda includes a targeted discussion about how the study is meeting its minority enrollment targets and what additional support it may need to reach certain populations. Frequent and open communication and consultation/support to the research teams is one strategy NIAMS hopes can help ease the challenges brought on by the ongoing COVID-19 pandemic.

Appendix 1

Table 2-1. Total Inclusion Data Records (IERs) for NIAMS Extramural and Intramural Clinical Research Reported Between FY2019 and FY2021

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	427	154	273	266	7	25	12	236
2020	478	159	319	312	7	30	11	278
2021	473	182	291	287	4	18	7	266

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

Appendix 2

Table 5-1-1-C. Enrollment for All NIAMS Extramural and Intramural 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	32,759	27.0	121,218	66.3	108,450	89.5	10,393	8.6	2,375	2.0
2019 Male	12,116	20.5	59,216	32.4	53,790	90.8	3,505	5.9	1,921	3.2
2019 Unknown	507	22.1	2,297	1.3	111	4.8	504	21.9	1,682	73.2
2020 Female	113,534	43.8	259,493	76.7	224,160	86.4	31,987	12.3	3,346	1.3
2020 Male	19,716	25.9	76,150	22.5	68,424	89.9	5,664	7.4	2,062	2.7
2020 Unknown	611	23.0	2,652	0.8	230	8.7	503	19.0	1,919	72.4
2021 Female	34,789	26.7	130,201	66.3	117,428	90.2	10,432	8.0	2,341	1.8
2021 Male	13,897	21.5	64,782	33.0	59,495	91.8	3,824	5.9	1,463	2.3
2021 Unknown	517	34.8	1,487	0.8	91	6.1	515	34.6	881	59.2

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	213	0.2	3,897	3.2	17,863	14.7	28	0.0	87,834	72.5	1,841	1.5	9,542	7.9
2019 Male	109	0.2	2,132	3.6	6,063	10.2	33	0.1	46,858	79.1	492	0.8	3,529	6.0
2019 Unknown	1	0.0	1	0.0	1	0.0	1	0.0	53	2.3	0	0.0	2,240	97.5
2020 Female	1,715	0.7	7,522	2.9	68,524	26.4	924	0.4	145,471	56.1	24,559	9.5	10,778	4.2
2020 Male	238	0.3	2,926	3.8	10,144	13.3	141	0.2	56,335	74.0	2,614	3.4	3,752	4.9
2020 Unknown	1	0.0	5	0.2	12	0.5	0	0.0	47	1.8	91	3.4	2,496	94.1
2021 Female	250	0.2	5,638	4.3	17,915	13.8	49	0.0	95,070	73.0	1,676	1.3	9,603	7.4
2021 Male	92	0.1	3,552	5.5	6,025	9.3	33	0.1	51,165	79.0	655	1.0	3,260	5.0
2021 Unknown	1	0.1	0	0.0	0	0.0	0	0.0	33	2.2	14	0.9	1,439	96.8

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

Appendix 3

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

Fiscal Year / Sex Gender	Minority		Total Enrollment		Not Hispanic	% Not Hispanic	Hispanic Latino	% Hispanic Latino	Unknown Not Reported	% Unknown Not Reported
	Minority	% Minority	Enrollment	% Total						
2019 Female	10	12.5	80	90.9	76	95.0	3	3.8	1	1.3
2019 Male	0	0.0	5	5.7	5	100.0	0	0.0	0	0.0
2019 Unknown	1	33.3	3	3.4	2	66.7	1	33.3	0	0.0
2020 Female	27	18.4	147	86.5	138	93.9	9	6.1	0	0.0
2020 Male	1	6.7	15	8.8	14	93.3	0	0.0	1	6.7
2020 Unknown	2	25.0	8	4.7	7	87.5	1	12.5	0	0.0
2021 Female	38	17.9	212	85.5	200	94.3	12	5.7	0	0.0
2021 Male	5	18.5	27	10.9	26	96.3	0	0.0	1	3.7
2021 Unknown	2	22.2	9	3.6	8	88.9	1	11.1	0	0.0

Fiscal Year / Sex Gender	American Indian		Asian		Black African American		Native Hawaiian Pacific Islander		White		More Than One Race		Unknown Not Reported	% Unknown Not Reported
	Alaska Native	% American Indian Alaska Native	Asian	% Asian	African American	% Black African American	Pacific Islander	% Native Hawaiian Pacific Islander	White	% White	More Than One Race	% More Than One Race		
2019 Female	0	0.0	0	0.0	4	5.0	1	1.3	72	90.0	2	2.5	1	1.3
2019 Male	0	0.0	0	0.0	0	0.0	0	0.0	5	100.0	0	0.0	0	0.0
2019 Unknown	1	33.3	0	0.0	0	0.0	0	0.0	2	66.7	0	0.0	0	0.0
2020 Female	1	0.7	4	2.7	7	4.8	1	0.7	127	86.4	7	4.8	0	0.0
2020 Male	0	0.0	0	0.0	0	0.0	0	0.0	13	86.7	1	6.7	1	6.7
2020 Unknown	1	12.5	0	0.0	0	0.0	0	0.0	6	75.0	1	12.5	0	0.0
2021 Female	1	0.5	6	2.8	12	5.7	1	0.5	182	85.8	9	4.2	1	0.5
2021 Male	0	0.0	0	0.0	4	14.8	0	0.0	21	77.8	1	3.7	1	3.7
2021 Unknown	1	11.1	0	0.0	0	0.0	0	0.0	7	77.8	1	11.1	0	0.0

Appendix 4

Table 5-1-1-C. Enrollment for All NIH-Wide Extramural and Intramural Clinical Research, Sex/Gender by Race and Ethnicity

Fiscal Year / Sex Gender	Minority		Total Enrollment		Not Hispanic	% Not Hispanic	Hispanic Latino	% Hispanic Latino	Unknown Not Reported	% Unknown Not Reported
	Minority	% Minority	Total Enrollment	% Total						
2019 Female	3,027,503	43.9	6,894,390	52.1	5,470,825	79.4	844,013	12.2	579,552	8.4
2019 Male	2,219,465	37.4	5,930,000	44.8	4,851,599	81.8	565,538	9.5	512,863	8.6
2019 Unknown	59,734	14.3	417,023	3.1	85,697	20.5	29,156	7.0	302,170	72.5
2020 Female	3,133,281	41.5	7,552,684	55.1	5,933,042	78.6	879,883	11.6	739,759	9.8
2020 Male	2,202,943	39.8	5,532,650	40.4	4,532,188	81.9	574,608	10.4	425,854	7.7
2020 Unknown	86,053	13.9	620,325	4.5	96,918	15.6	52,354	8.4	471,053	75.9
2021 Female	3,295,858	43.5	7,572,143	58.5	6,064,750	80.1	797,932	10.5	709,461	9.4
2021 Male	2,016,535	40.0	5,047,190	39.0	4,144,316	82.1	475,840	9.4	427,034	8.5
2021 Unknown	92,191	29.0	317,823	2.5	95,320	30.0	52,274	16.4	170,229	53.6

Fiscal Year / Sex Gender	American Indian		Asian		Black African American		Native Hawaiian Pacific Islander		White		More Than One Race	% More Than One Race	Unknown Not Reported	% Unknown Not Reported
	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	221,459	3.2	791,042	11.5	1,269,976	18.4	13,338	0.2	3,895,837	56.5	151,836	2.2	550,902	8.0
2019 Male	109,470	1.8	456,922	7.7	1,101,038	18.6	11,681	0.2	3,641,423	61.4	121,853	2.1	487,613	8.2
2019 Unknown	1,910	0.5	17,042	4.1	11,706	2.8	90	0.0	20,389	4.9	1,753	0.4	364,133	87.3
2020 Female	69,957	0.9	569,335	7.5	1,535,430	20.3	17,532	0.2	4,273,974	56.6	210,974	2.8	875,482	11.6
2020 Male	54,337	1.0	385,652	7.0	1,134,775	20.5	14,818	0.3	3,281,452	59.3	144,076	2.6	517,540	9.4
2020 Unknown	813	0.1	15,393	2.5	15,858	2.6	120	0.0	27,678	4.5	3,042	0.5	557,421	89.9
2021 Female	55,984	0.7	963,278	12.7	1,392,649	18.4	44,193	0.6	4,037,094	53.3	145,474	1.9	933,471	12.3
2021 Male	40,262	0.8	565,616	11.2	880,182	17.4	39,492	0.8	2,842,637	56.3	102,412	2.0	576,589	11.4
2021 Unknown	541	0.2	22,027	6.9	16,358	5.1	194	0.1	22,567	7.1	6,928	2.2	249,208	78.4