NIH Intramural 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

The mission of the NIH Intramural Research Program (IRP) is to conduct distinctive, high-impact laboratory, clinical, and population-based research; facilitate new approaches to improve the public health through prevention, diagnosis and treatment; respond to public health emergencies; and train the next generation of biomedical researchers. The mission of the NIH Clinical Center is to provide hope through pioneering clinical research to improve human health.

The Intramural Program is comprised of 24 Institutes and Centers conducting research, with approximately 2,000 active clinical protocols during a fiscal year. The majority of the intramural research, approximately 1,500 clinical protocols, are at the main NIH Clinical Center located at the Bethesda campus. The other 500 clinical protocols are at offsite locations such as Research Triangle Park, N.C. (NIEHS), Baltimore, MD (NIDA and NIA), Frederick, MD (NCI), Detroit, Michigan (NICHD) and Phoenix, AZ (NIDDK), as well as at other domestic and foreign locations.

The Intramural Program uses a centralized system, to capture data on active intramural clinical research protocols that fall under the auspices of the NIH Clinical Center. This system, Protrak, maintained by the Office of Protocol Services (OPS), includes protocol-related data for all protocols, and is the central system to capture planned and cumulative enrollment data. A second complementary system, the Clinical Research Information System (CRIS), the Electronic Health Record, captures accrual data relative to the ethnicity, sex/gender, race, and age as reported by each participant at the time of registration at the NIH Clinical Center. CRIS, along with the complementary Biomedical Translational Research Information System (BTRIS), a resource for investigators and clinicians to generate protocol-specific attribution for all clinical and research data. BTRIS provides an automated method of generating

cumulative enrollment data from demographic data received from the NIH Clinical Center CRIS system. The principal investigator or designee validate the data.

II. Strategies for Ensuring Compliance

A. Intramural Oversight

Since July of 2017, the Office of Clinical Research, under the leadership of the Chief Scientific Officer of the Clinical Center and NIH Associate Director for Clinical Research, oversees compliance with the Scientific Review Policy. The policy outlines the scientific compliance requirements that includes a plan for the appropriate inclusion of women and minorities and/or a justification whenever representation is limited or absent. Protocol review starts at the lab/branch level with concept review conducted by the lab/branch chief for feasibility, fit within the mission, and resources. Concept review considers the design, eligibility, statistical analysis and compliance with inclusion guidelines. Once concept review is approved, the Institutes' Scientific Review Committees conduct their review, with final submission of protocols to the Chief Scientific Officer to ensure compliance with all processes.

Quadrennial review is required for all protocols recruiting/following participants and considers the scientific justification for continuing the protocol. This parallels the process for a new protocol in which the first level is the concept review conducted by the Lab/Branch Chief, then review by the Institute Scientific Review Committee, and finally the Chief Scientific Officer of the Clinical Center. The investigator documents the aggregate number of participants accrued by sex/gender, race and ethnicity and identifies any issues related to recruitment with plan for resolution. In addition, annually, at the time of the protocols continuing review, the lab/branch chief review the protocol to evaluate the progress of the protocol, identify problems, and assure the protocol is progressing accordingly. A written report is prepared to summarize the review and submitted to the Institutional Review Board. A protocol must receive approval by the Institute Scientific Review Committee and the Chief Scientific Officer of the Clinical Center before it can receive IRB approval. Once approved by the IRB, the OPS receives the information for collation and reporting. The NIH Clinical Center's OPS collects the demographic data from

the investigators at the time of protocols' annual continuing review and coordinates the annual reporting to the Office of Extramural Research and the Office of Research on Women's Health.

B. Training

The Office of Human Subjects Research revised the training requirements in the NIH Human Research Protection Program Policy in 2019, creating SOP 103 Policy- Education Program. The policy outlines the training required for NIH Investigators conducting human subject's research and those non-NIH Investigators conducting human subject research on a protocol under the oversight of the NIH IRB. The degree of training required is commensurate with the roles and responsibilities of the research team participants. It is the responsibility of each investigator to complete the required initial human subjects training and refresher training as required. Upon review of the research, the IRB has the option to require additional training. The policy further outlines the required training for investigators conducting research exempt from IRB review as well as IRB Members.

The Office of Clinical Research was established in 2016, with a vision to facilitate clinical research and research training applicable to the NIH Intramural Program, the rest of the United States, and international investigators. Several comprehensive training programs are offered and ensure investigators conducting research are educated about the conduct of clinical research. Over the years enrollment has expanded and uses videotaped lectures. The educational opportunities include:

Introduction to the Principles and Practice of Clinical Research

This course, which is part of the Clinical Center's core curriculum in clinical research, is designed to train participants on how to effectively conduct clinical research. The course focuses on the spectrum of clinical research and clinical research processes by highlighting statistical methods, study design, protocol preparation, patient monitoring, quality assurance, and Food and Drug Administration (FDA) issues. Other areas covered include data management, building a research budget and bioethical

issues, including protection of human subjects, plus many special topics. For the 2020-2021 course, 11,628 participated via long distance learning from 156 different countries. Since initiation of the course in 1995, there have been over 76,000 registrants.

Principles of Clinical Pharmacology

This course is designed to meet the needs of researchers, fellows in training, and others who have an interest in the clinical pharmacologic aspects of contemporary drug development and utilization. This course consists of videotaped lectures covering the fundamentals of pharmacokinetics, pharmacodynamics, drug metabolism, pharmacogenomics, adverse drug reactions, drug discovery and development, FDA regulations, and optimization of therapy in special populations (pediatrics, geriatrics, in pregnancy and lactation), viewing clinical pharmacology as a translational scientific discipline focused on rational drug development and utilization. For the 2020-2021 course, 6,647 participated via long distance learning from 132 different countries. Since initiation of the course in 1998, there have been 22,534 participants.

Ethical and Regulatory Aspects of Human Subjects Research

Implemented in 1999, the course offers formal education and training in research ethics. Participants are exposed to a broad range of issues important to the ethical conduct of clinical research. Individual lectures and group institutional review board (IRB) reviews are presented by leading experts in various areas of clinical research ethics. There have been 10,348 students enrolled in the course since its inception and around 4,000 students have earned the certificate as of March 2021.

III. Analysis and Interpretation of Data

The Office of Protocol Services submits data to the NIH Office of Extramural Research (OER) annually, who generates the intramural data provided in the appended tables. These data represent the aggregate number of participants enrolled over the life of the protocol through the fiscal years reported, at the NIH Clinical Center, other intramural locations

including collaborative sites, as well as foreign locations. Subjects participating in multiple protocols are counted in each protocol. With the implementation of the revised Common Rule, the NIH IRB identified 21 protocols that did not meet the definition of human subject's research and re-classified as non-human subjects research.

A. Enrollment for Intramural NIH-Defined Clinical Research

Of the total number of participants enrolled in FY19 (2,415,354), 13% (304,540) are attributed to protocols conducted at the NIH Clinical Center while the remaining 87% (2,110,814) are from protocols conducted at other intramural locations, collaborative sites. In FY21 (2,122,798) participants were enrolled with 14% (303,838) at the NIHCC.

Table 1 summarizes the aggregate number of participants reported in FY2019, FY2020 and FY2021. The data show in FY 2019, of the 2,415,354 enrolled, 54.4% were females. This trend continues in FY2020 with 2,400,636 participants enrolled 54.9% females and in FY2021, 2,122,798 participants enrolled with 54.8% females. In each fiscal year, females represent approximately 12% more of the population enrolled over males. The data show a decrease in total enrollment from FY2019 to FY2021. In FY2020, in association with COVID, the number of protocols that closed increased by 40% from previous years.

The trend of enrolling more females than males continued with total enrollment in the U.S., summarized in table 2, with approximately 51% of participants enrolled being females and 46% males, for FY2019, FY2020, and FY2021.

In Table 3, underrepresented minority patients comprised 28.7% in FY2019, 28.7% in FY2020, and a slight increase in FY2021 with 30.0%. Of the underrepresented minority patient population, Asian participants were consistent with approximately 11.3% across all three years and Black African American participants increased by 0.7% from FY2019 to FY2021. Table 4 reflects the US Site enrollment reporting 18.2% minorities in FY2019, 17.7% in FY2020 and 19.1% in FY2021. White participants are the largest percentage across the fiscal years averaging 68%, followed by Black African American averaging 9.4% across the fiscal years.

B. Enrollment Data for the Intramural Research Program Phase III Clinical Trials

Phase III Clinical trials represent approximately 4% (41) of the protocols within the intramural program. Of the 41 Phase III protocols, the majority see patients at the NIHCC. Of the total number of participants on Phase III protocols, approximately 50% are from within the US and the other 50% from foreign locations. Table 5 shows the number of females is greater for all three years with 72.7% in FY2019, 73.6% in FY2020 and 77.4% in FY2021. The Black African American patient population consistently represented a larger percent of female patients with an average of 10.5% compared to other races. For Phase III clinical trials, minorities represented 65% of the population in FY2019, 67% in FY2020 and 61% in FY2021. The decrease in the Asian patients in FY2021 is attributed to a protocol conducted in China that closed in FY2020.

IV. Additional information

As a result of the COVID-19 virus pandemic, the NIH Clinical Center deferred all elective admissions and elective out-patient visits during FY2020-FY 2021. This included all participants to natural history studies. Exceptions were handled on a case-by-case basis. As COVID-19 positivity rates decreased, the NIH Clinical Center returned operations back towards normal allowing admissions to protocols. Because of the admissions deferred and restrictions on participants traveling to the NIH Clinical Center, the number of new participants declined. In response COVID pandemic, the intramural program initiated 33 new protocols in FY2020 and 20 new protocols in FY2021 addressing COVID 19. In addition, investigators modified protocols already in existence to include research related to the virus.

In 2019 the NIH completed the consolidation of the NIH Institutional Review Boards into a single panel, operating out of the Institutional Review Board Office (IRBO), Office of Human Research Protection. As a result, the intramural program uses a single centralized electronic system for the submission of protocols. The Institutional Review Board Office has focused on revising Standard Operating Procedures and Policies as regulations and policies have changed, to ensure compliance.

Appendix 1. Data Tables

Table 1

Table 3-1-C. Total Enrollment for All NIH-Defined Intramural Clinical Research Between FY2019 and 2021

Fiscal Year	Total Enrollment	Total Females	% Females	Total Males	% Males	Total Unknown	% Unknown
2019	2,415,354	1,313,080	54.4	1,023,233	42.4	79,041	3.3
2020	2,400,636	1,317,850	54.9	1,004,923	41.9	77,863	3.2
2021	2,122,798	1,162,926	54.8	902,474	42.5	57,398	2.7

Table 2

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

Fiscal Year	Total Enrollment	Total Females	% Females	Total Males	% Males	Total Unknown	% Unknown
2019	1,738,647	89,400	51.2	793,508	45.6	54,739	3.1
2020	1,715,049	877,577	51.2	783,153	45.7	54,319	3.2
2021	1,490,499	746,559	50.1	707,490	47.5	36,450	2.4

Table 3

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

Fiscal Year	Total Enrollment	No. Inclusion Data Records	Minority Enrollment	% Minority Enrollment	American Indian Alaska Native	% American Indian Alaska Native	Asian	% Asian
2019	2,415,354	1,855	693,285	28.7	29,910	1.2	272,479	11.3
2020	2,400,636	1,778	689,575	28.7	29,510	1.2	274,184	11.4
2021	2,122,798	1,694	637,214	30.0	28,863	1.4	239,765	11.3

Fiscal Year	Black African American	% Black African American	Native Hawaiian Pacific Islander	% Native Hawaiian Pacific Islander	White	% White	More Than One Race	% More Than One Race	Unknown Not Reported	% Unknown Not Reported
2019	220,922	9.1	4,606	0.2	1,642,939	68.0	14,334	0.6	230,164	9.5
2020	219,809	9.2	4,152	0.2	1,626,300	67.7	14,243	0.6	232,438	9.7
2021	207,309	9.8	4,095	0.2	1,448,121	68.2	13,593	0.6	181,052	8.5

Table 4

Table 4-1-4-B. US Site Enrollment of NIH-Defined Intramural Clinical Research

Fiscal Year	Total Enrollment	No. Inclusion Data Records	Minority Enrollment	% Minority Enrollment	American Indian Alaska Native	% American Indian Alaska Native	Asian	% Asian
2019	1,738,647	1,698	316,184	18.2	29,017	1.7	33,452	1.9
2020	1,715,049	1,626	303,923	17.7	28,616	1.7	34,282	2.0
2021	1,490,499	1,565	284,585	19.1	28,067	1.9	29,832	2.0

Fiscal Year	Black African American	% Black African American	Native Hawaiian Pacific Islander	% Native Hawaiian Pacific Islander	White	% White	More Than One Race	% More Than One Race	Unknown Not Reported	% Unknown Not Reported
2019	159,191	9.2	4,602	0.3	1,314,994	75.6	12,871	0.7	184,520	10.6
2020	151,941	8.9	4,148	0.2	1,296,815	75.6	12,811	0.7	186,436	10.9
2021	143,567	9.6	4,092	0.3	1,139,009	76.4	12,157	0.8	133,775	9.0

Table 5

Table 5-2-4-C. Total Enrollment of All NIH-Defined Phase III Trials

Fiscal Year	Sex Gender	Minority	% Minority	Total Enrollment	% Total	American Indian Alaska Native	% American Indian Alaska Native	Asian	% Asian
2019	Female	11,747	71.8	16,358	72.7	371	2.3	1,869	11.4
2019	Male	2,771	45.4	6,108	27.2	132	2.2	1,902	31.1
2019	Unknown	19	95.0	20	0.1	0	0.0	0	0.0
2020	Female	13,101	74.6	17,561	73.6	498	2.8	1,867	10.6
2020	Male	2,825	44.9	6,286	26.3	148	2.4	1,913	30.4
2020	Unknown	19	95.0	20	0.1	0	0.0	0	0.0
2021	Female	11,426	72.3	15,809	77.4	518	3.3	207	1.3
2021	Male	1,086	23.7	4,582	22.4	153	3.3	167	3.6
2021	Unknown	31	100.0	31	0.2	0	0.0	0	0.0

Fiscal Year	Black African American	% Black African American	Native Hawaiian Pacific Islander	% Native Hawaiian Pacific Islander	White	% White	More Than One Race	% More Than One Race	Unknown Not Reported	% Unknown Not Reported
2019	1,743	10.7	1	0.0	4,753	29.1	32	0.2	7,589	46.4
2019	577	9.4	1	0.0	3,370	55.2	35	0.6	91	1.5
2019	0	0.0	0	0.0	1	5.0	1	5.0	18	90.0
2020	1,749	9.9	0	0.0	4,605	26.2	33	0.2	8,824	50.2
2020	600	9.5	1	0.0	3,487	55.5	32	0.5	105	1.7
2020	0	0.0	0	0.0	1	5.0	1	5.0	18	90.0
2021	1,712	10.8	0	0.0	4,515	28.6	31	0.2	8,826	55.8
2021	610	13.3	1	0.0	3,524	76.9	32	0.7	95	2.1
2021	0	0	0	0.0	0	0.0	1	3.2	30	96.8

Table 5

Table 5-2-4-C. Total Enrollment of All NIH-Defined Phase III Trials – Con't

Fiscal Year	Not Hispanic	% Not Hispanic	Hispanic Latino	% Hispanic Latino	Unknown Not Reported	% Unknown Not Reported
2019	8,491	51.9	7,819	47.8	48	0.3
2019	5,946	97.3	148	2.4	14	0.2
2019	0	0.0	19	95.0	1	5.0
2020	8,453	48.1	9,058	51.6	50	0.3
2020	6,116	97.3	153	2.4	17	0.3
2020	0	0.0	19	95.0	1	5.0
2021	6,703	42.4	9,053	57.3	53	0.3
2021	4,415	96.4	147	3.2	20	0.4
2021	0	0.0	31	100.0	0	0.0