

**2016-2018 Triennial Advisory Council Report Certifying
Compliance with Inclusion Guidelines
National Institute of Environmental Health Sciences**

I. Background/Overview

Among the 27 research institutes and centers that comprise the National Institutes of Health (NIH), the National Institute of Environmental Health Sciences (NIEHS) is the institute most focused on prevention rather than diagnosis or treatment of health issues. The mission of the National Institute of Environmental Health Sciences is to discover how the environment affects people in order to promote healthier lives. Our vision is to provide global leadership for innovative research that improves public health by preventing disease and disability.

The NIEHS research agenda is based on the concept that all complex diseases have both an environmental and a genetic component, and the Institute focuses on understanding the environmental component and the interaction of environment with genetics. Research programs cover the effects of environmental exposures throughout the lifespan, from preconception to old age. Funded studies range from computational and cell-based models to epidemiological studies with human subjects. The more we know about environmental exposures and how they affect health outcomes, the greater our ability to create healthy environments by reducing or preventing hazardous exposures. To this end, NIEHS investments are significant and measurable.

The Extramural Division includes review, grants management, program analysis and five program branches that focus on different aspects of the grant portfolio. DERT staff plans, reviews, approves, directs, fiscally administers, and evaluates performance of the Institute's grant and cooperative agreement that support research and training in environmental health science. All five branches support human subjects research to a greater or lesser extent, with the Population and Health Branch managing approximately 60% of human research studies. In addition, the extramural review staff review the research contracts that support the intramural human studies.

The Intramural Division conducts a broad range of clinical, translation and basic investigations at both the NIEHS and NIH Clinical Centers as well as at sites around the country. In addition, the human studies performed within the National Toxicology Program fall within the Intramural umbrella.

II. Strategies for Ensuring Compliance (Required)

Peer Review

The implementation of inclusion guidelines involves the participation of review, program, and grants management staff. Inclusion is first addressed by peer review. Reviewers on NIH and NIEHS 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 or discovered by staff, program staff notify principal investigators, who are required to address these issues prior to funding. For applications with unacceptable inclusion plans an award is not issued until an acceptable resolution is received.

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 officials 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.

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 race 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 (OER) and the Office of Research on Women's Health. At NIEHS, Intramural

data includes data from the human studies performed as part of the National Toxicology Program.

NIEHS training approaches

All Program Officials, Grants Management Specialists, and Scientific Review Officers attended the May 11, 2018 training, *Ensuring Inclusion in NIH Clinical Research: Policies and Procedures for Grants and Contracts*. Training was tracked internally to ensure 100% compliance.

Program Officers and Grants Management Specialists also attended the NIH training on the use of the new Human Subjects System session designed for their respective position.

All scientific staff including Grants Management, Scientific Review, and Program staff completed the required Good Clinical Practices Training in 2016 and will take the refresher training in 2019. Other trainings taken by staff include the Revised Common Rule Webinar with OHRP held on September 20, 2019; the Webinar on Implementing the NIH Single IRB Policy for NIH Extramural Staff on March 30, 2017; and the Single IRB and the Exceptions Process Webinar on October 11, 2017. If not able to attend at the time of the original presentation, all webinars are archived and available online. In addition, the NIEHS representative to the Inclusion Operating Workgroup is available to provide guidance to staff.

III. Analysis and Interpretation of Data

Tables of NIEHS inclusion data covering the three-year period of this report are provided in the appendix. All data tables include combined extramural and intramural data for fiscal years (FY) 2016-2018.

As shown in Table 2-1, the number of Inclusion Enrollment Records (IERs) increased approximately 35% from 304 in FY2016 to 414 in FY2018. The majority of the IERs (75-80%) are enrolling from US sites. It is important to note that as many of our studies include mother or caregiver (which is usually the mother) /child pairs, NIEHS Extramural Division reports adults separately from children. Reporting adults separately from children ensures staff knows the number of females who have been recruited are adult women/men or girls/boys. For this reason, a significant percentage of the IERs are female only. The male only studies include studies of toxicants on male development, fertility or prostate cancer.

The NIEHS inclusion enrollment records show in Table 5-1-1-C that enrollment has fluctuated between the years. Overall, however, the number of females has

increased between 2016 and 2018 while the numbers of male participants has remained about the same. At the same time, while the percentage of non-Hispanic females has remained the same, the percentage of non-Hispanic males has dropped. These changes are not attributable to a single study but are the result of natural fluctuation in funded studies.

The biggest change in demographics is the significant drop in Asians between 2016 and 2017, due to the completion of enrollment of a study of more than 30,000 participants in Bangladesh. In all other underrepresented minority categories between 2016 and 2018 the percentages increased. However, it is concerning to note that, after years of dropping, reports of the number of participants of unknown gender/race/ethnicity has grown between 2016 and 2018. This also is not attributable to a single study. Gender/Race/Ethnicity are self-reported. While participants from the Latino population often choose not to provide demographic information, it is not discernable from the data why the numbers are again increasing. Staff will be reminded to work with their grantees to reduce the number of unknowns.

NIEHS recognizes the importance of diversity in human subjects' research. As part of the strategy to increase diversity, staff have created programs in community-based research, research to action, and have added community outreach and education to multi-project grants. To help increase the participation of Native Americans/Alaska Natives and Native Hawaiian/Pacific Islanders in research, an NIEHS program officer participates in national and local meetings of tribal organizations, participates in trans-federal tribal focused working groups, has organized an NIH workshop about traditional ecological knowledge, and has co-authored publications with tribal affiliated investigators. In addition, the institute director and program staff have made several site visits to Indian Country and participated in listening sessions and community events in tribal communities. While the numbers for these groups are still small, there has been an almost three-fold increase in the raw numbers of Native Americans/Alaska Natives and a doubling of Native Hawaiian/Pacific Islanders participating in NIEHS funded research.

Table 5-2-2-C shows the number of NIEHS Phase III clinical trials. In FY2016 there were three IERs associated with two Phase III Clinical Trials, one each from Extramural and Intramural. From FY2016-2018, the two extramural IERs were associated with a study to reduce indoor nitrogen dioxide and/or particle exposure in children with asthma. Caregivers, usually mothers, were enrolled as they were consented to provide health and other survey information on themselves and family members. This study has been slow to enroll subjects. A corrective plan was put in place and the PI is expected to be able to fully enroll subjects into the trial before the grant ends. While the study is not

expected to yield differences for sex/gender or race/ethnicity, the PI plans to do the analyses.

The Intramural IER shows the final enrollment of the Treatment of Lead-Exposed Children Study, which looked at succimer chelation of lead versus placebo on child development. Enrollment is closed but the study was kept open by the IRB while the secondary analyses were being completed. An analysis for sex/gender was done, and the result was essentially the same in boys and girls. As the study participants were 75% African American, analysis by race/ethnicity was not considered appropriate.

Recognizing the importance of keeping the American people informed about how their tax dollars are spent to support medical research, in January 2009, the NIH added the Research, Condition, and Disease Categorization (RCDC) reports to the RePORT site. RCDC is a computerized process the NIH uses to categorize and report the amount it funded in each of the more than 280 reported categories of disease, condition, or research area. As of January 2019, as part of the RCDC reporting, the data now also can be viewed by the NIH Inclusion of Women and Minorities categories of Gender/Race/Ethnicity (<https://report.nih.gov/RISR/>). Using the dropdown boxes at the top, the data can be viewed for all of NIH or broken out by the individual Institutes.

Please note that the inclusion categories are not mutually exclusive, so the same projects may appear in more than one category. All participants enrolled in a project's studies are included in all categories associated with that project. Individual research projects can be included in multiple categories so amounts depicted within each column of this table do not add up to the total participants enrolled in NIH-funded research.

IV. Additional information

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 first triennial report provides information on inclusion of participants in NIH clinical research from FY 2016 – 2018. Section IV of the [Report of the Advisory Committee on Research on Women's Health](#) includes IC reports on monitoring adherence to the NIH Policy on the Inclusion of Women and Minorities as Subjects in Clinical Research for FY 2015 and 2016.

Appendix: NIEHS Tables

Section 2: Metrics Based on Inclusion Data Records (IERs)

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

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*
2016	304	59	245	186	59	61	4	180
2017	338	48	290	232	58	78	6	206
2018	414	74	340	272	68	92	10	238

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

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

Total Enrollment: All NIH-Defined Clinical Research

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

Year	Year	Sex Gender	Minority *	% Minority	Total Enrollment	% Total	Not Hispanic	% Not Hispanic	Hispanic Latino	% Hispanic Latino	Unknown Not Reported	% Unknown Not Reported
2016	2016	Female	78,382	32.1	244,274	71.7	219,972	90.1	20,743	8.5	3,559	1.5
2016	2016	Male	48,777	51.8	94,085	27.6	80,817	85.9	11,288	12.0	1,980	2.1
2016	2016	Unknown	1,882	76.4	2,464	0.7	2,145	87.1	224	9.1	95	3.9
2017	2017	Female	63,245	26.8	236,170	70.5	207,700	87.9	23,762	10.1	4,708	2.0
2017	2017	Male	42,051	44.0	95,552	28.5	74,172	77.6	17,955	18.8	3,425	3.6
2017	2017	Unknown	1,697	53.7	3,160	0.9	2,036	64.4	132	4.2	992	31.4
2018	2018	Female	71,323	23.5	303,387	75.9	273,162	90.0	23,613	7.8	6,612	2.2
2018	2018	Male	38,389	40.7	94,423	23.6	75,401	79.9	13,836	14.7	5,186	5.5
2018	2018	Unknown	266	12.9	2,059	0.5	631	30.6	147	7.1	1,281	62.2

Year	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	More Than One Race	% More Than One Race	Unknown Not Reported	% Unknown Not Reported
2016	2016	Female	78,382	32.1	244,274	71.7	1,055	0.4	29,179	11.9	26,058	10.7	164	0.1	174,691	71.5	3,719	1.5	9,408	3.9
2016	2016	Male	48,777	51.8	94,085	27.6	798	0.8	19,772	21.0	15,571	16.5	113	0.1	47,550	50.5	2,520	2.7	7,761	8.2
2016	2016	Unknown	1,882	76.4	2,464	0.7	0	0.0	147	6.0	1,504	61.0	1	0.0	587	23.8	89	3.6	136	5.5
2017	2017	Female	63,245	26.8	236,170	70.5	1,802	0.8	9,163	3.9	27,976	11.8	204	0.1	180,906	76.6	4,050	1.7	12,069	5.1
2017	2017	Male	42,051	44.0	95,552	28.5	1,812	1.9	6,950	7.3	14,877	15.6	140	0.1	59,401	62.2	2,772	2.9	9,600	10.0
2017	2017	Unknown	1,697	53.7	3,160	0.9	10	0.3	43	1.4	1,503	47.6	0	0.0	491	15.5	39	1.2	1,074	34.0
2018	2018	Female	71,323	23.5	303,387	75.9	3,206	1.1	11,353	3.7	31,232	10.3	480	0.2	237,440	78.3	6,884	2.3	12,792	4.2
2018	2018	Male	38,389	40.7	94,423	23.6	2,306	2.4	6,057	6.4	15,829	16.8	112	0.1	59,130	62.6	3,419	3.6	7,570	8.0
2018	2018	Unknown	266	12.9	2,059	0.5	9	0.4	9	0.4	94	4.6	2	0.1	560	27.2	67	3.3	1,318	64.0

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

*includes NA/AN, Asian, AA/Black, NH/PI, More Than One Race, and Hispanic participants. Total adjusted for participants that are both Hispanic and of another racial minority category.

Total Enrollment: All NIH-Defined Phase III Trials

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	262	74.9	350	44.4	283	80.9	24	6.9	43	12.3
2016	Male	342	78.1	438	55.6	361	82.4	25	5.7	52	11.9
2016	Unknown	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
2017	Female	20	90.9	22	78.6	10	45.5	12	54.5	0	0.0
2017	Male	6	100.0	6	21.4	2	33.3	4	66.7	0	0.0
2017	Unknown	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
2018	Female	81	82.7	98	66.7	52	53.1	45	45.9	1	1.0
2018	Male	44	89.8	49	33.3	23	46.9	26	53.1	0	0.0
2018	Unknown	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

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	More Than One Race	% More Than One Race	Unknown Not Reported	% Unknown Not Reported
2016	Female	262	74.9	350	44.4	2	0.6	1	0.3	235	67.1	0	0.0	46	13.1	1	0.3	65	18.6
2016	Male	342	78.1	438	55.6	0	0.0	1	0.2	316	72.1	0	0.0	45	10.3	0	0.0	76	17.4
2016	Unknown	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
2017	Female	20	90.9	22	78.6	0	0.0	0	0.0	8	36.4	0	0.0	3	13.6	1	4.5	10	45.5
2017	Male	6	100.0	6	21.4	1	16.7	0	0.0	0	0.0	0	0.0	1	16.7	3	50.0	1	16.7
2017	Unknown	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
2018	Female	81	82.7	98	66.7	0	0.0	1	1.0	34	34.7	1	1.0	21	21.4	14	14.3	27	27.6
2018	Male	44	89.8	49	33.3	1	2.0	1	2.0	13	26.5	0	0.0	11	22.4	10	20.4	13	26.5
2018	Unknown	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

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

*includes NA/AN, Asian, AA/Black, NH/PI, More Than One Race, and Hispanic participants. Total adjusted for participants that are both Hispanic and of another racial minority category.