

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**

A handwritten signature in blue ink, appearing to read "George Koob", is written over a horizontal line.

George Koob, Ph.D.

Director

National Institute on Alcohol Abuse and Alcoholism

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Note to NIAAA Advisory Council Members:

The NIH is mandated by law (Public Health Service Act sec. 492B, 42 U.S.C. sec. 289a-2) to ensure the inclusion of women and minority groups as participants in clinical research. The goal is to ensure that individuals are included in clinical research in a manner that is appropriate to the scientific question under study. As a result, NIH instituted the NIH Policy on the Inclusion of Women and Minorities as Subjects in Clinical Research.

Federal law also requires that the Advisory Council of each NIH Institute/Center prepares a triennial report describing how the Institute has complied with the inclusion policy. The attached draft triennial report, prepared on behalf of the National Advisory Council on Alcohol Abuse and Alcoholism, responds to this requirement. The current triennial report covers fiscal years 2016, 2017, and 2018 and includes aggregate enrollment data by sex/gender and race/ethnicity for NIAAA clinical research studies, including NIH-defined Phase III clinical trials. The format of the report is per NIH guidance.

During its February 2019 meeting, the National Advisory Council on Alcohol Abuse and Alcoholism will formally review NIAAA's performance regarding this requirement and certify the Institute's compliance with the NIH inclusion policy.

Compliance with the NIH Policy on Inclusion Guidelines

National Institute on Alcohol Abuse and Alcoholism

Overview

The mission of the National Institute on Alcohol Abuse and Alcoholism (NIAAA) is to generate and disseminate fundamental knowledge about the effects of alcohol on health and well-being, and apply that knowledge to improve diagnosis, prevention, and treatment of alcohol-related problems, including alcohol use disorder (AUD), across the lifespan.

NIAAA supports and conducts research on the impact of alcohol use on human health and well-being through its extramural and intramural research programs. It is the largest funder of alcohol research in the world.

NIAAA leads the national effort to reduce alcohol-related problems by:

- Conducting and supporting a portfolio of alcohol-related research in a wide range of scientific areas including neuroscience and behavior, epidemiology and prevention, treatment and recovery, and metabolism and health effects.
- Coordinating and collaborating with other research institutes and federal programs on alcohol-related issues.
- Collaborating with international, national, state, and local institutions, organizations, agencies, and programs engaged in alcohol-related work.
- Translating and disseminating research findings to health care providers, researchers, policymakers, and the public.

By supporting a broad range of basic, translational, and clinical research, NIAAA aims to:

- Better understand the health effects of alcohol consumption, including why it can cause addiction.
- Reveal the biological and socio-cultural origins of alcohol misuse.
- Remove the stigma associated with alcohol problems.
- Develop effective prevention and treatment strategies that address the physical, behavioral, and social risks that result from underage drinking and alcohol misuse among adults.

NIAAA-funded discoveries have important implications for improving the health and well-being of all people. For more information about NIAAA's research priorities, visit <https://www.niaaa.nih.gov/strategic-plan>

Recent Changes to the NIH Policy on Inclusion Guidelines

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.

NIAAA Strategies for Ensuring Compliance with NIH Inclusion Guidelines

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 valid analyses of intervention effects by sex/gender, race, and ethnicity. 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. Applications with unacceptable inclusion plans receive a bar to funding; an award is not issued until an acceptable resolution is received.

Program Monitoring and Grants Management Oversight

Prior to an award, program officials 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.

Phase III Clinical Trials

NIAAA works to ensure that each NIH-defined Phase III clinical trial meets NIH requirements for inclusion of minorities and women. Phase III clinical trial investigators are required to design and conduct their studies such that valid analyses, i.e. unbiased assessments of the differences in intervention effects among sex/gender, racial, and ethnic groups, can be accomplished.

An applicant institution is responsible for designating studies as Phase III clinical trials, and NIAAA grants management officers, scientific review officers, and program officials also work together to ensure that Phase III clinical trials are identified. A clinical trial grant application is subjected to peer review using the recently updated clinical trial review criteria as described in Funding Opportunity Announcements (FOA). If an application is funded, NIAAA staff ensure that all requirements are followed by the grantee institution before recruitment of patients. For example, NIAAA staff must confirm that the data and safety monitoring plans and Internal Review Boards are in place. NIAAA staff are also responsible for programmatic oversight of a given Phase III clinical trial with special attention to the study and distinctive coding in the NIH IMPAC II system. Designated NIAAA staff work with NIAAA program officials as needed to assist in proper monitoring of planned and actual enrollment data.

Intramural Research

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 institutional review boards (IRB) 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 coordinates annual reporting of demographic participant data to the NIH Office of Extramural Research (OER) and the NIH Office of Research on Women's Health.

NIAAA Staff Training on the NIH Inclusion Policy and the NIH Human Subjects System

NIAAA program officials and scientific review officers (SRO) attended the May 11, 2018 NIH training, "Ensuring Inclusion in NIH Clinical Research: Policies and Procedures for Grants and Contracts." Staff may access the archived training on the OER intranet.

NIAAA also invited the NIH Inclusion Policy Officer, OER, who provided training on use of the new NIH Human Subjects System which replaced the previous NIH system for inclusion monitoring. The HSS is a shared system that enables grant recipients to electronically report and

update data on human subjects and clinical trials in a single place, allows NIH staff to monitor and manage the data, and promotes increased transparency by displaying the same information to grant recipients and NIH staff in the same system.

NIAAA Aggregate Inclusion Data for Reporting Period FY 2016-2018: Summary

Tables 1-10 (see Appendix) include aggregate inclusion data for NIAAA-supported clinical research during fiscal years (FY) 2016, 2017 and 2018. NIAAA inclusion data for FY 2018 can be viewed for NIH's research, condition, and disease funding categories at <https://report.nih.gov/RISR/>

Table 1 shows the number of NIAAA-supported intramural and extramural protocols involving human research participants that required inclusion monitoring (also known as an Inclusion Data Record (IDR)) during FYs 2016, 2017 and 2018. The protocols included research conducted at foreign sites.

Tables 2-4 present enrollment data by sex/gender, race, and ethnicity for NIAAA-supported clinical research, including Phase III clinical trials. These tables also present enrollment percentages that exclude large studies with enrollment of more than 50,000 participants. Tables 5-7 present disaggregated enrollment data by sex/gender, race and ethnicity and include the large studies described above. Tables 8-10 present disaggregated data for Phase III clinical trials.

NIAAA supported 279, 320 and 310 extramural and intramural research protocols in FY 2016, FY 2017, and FY 2018, respectively (Table 1). There was about a 13% increase in the number of protocols from FY 2016 to FY 2017 and about a 3% decrease in the number of protocols from FY 2017 to FY 2018.

The Total Enrollment was 383,605 participants in FY 2016, 218,160 participants in FY 2017, and 218,213 participants in FY 2018 (Table 2). NIAAA-supported clinical research comprises primarily protocols that involved less than 1,000 participants with various sex/gender, race, and ethnicity distributions. In each fiscal year, however, one study with a large sample size, i.e. greater than 50,000 participants, reported data that significantly increased enrollment for specific categories and affected the distributions of the aggregate data for the fiscal year. For example, in FY 2016, a large social media study (228,504 participants) reported enrollment only in the Unknown categories for sex/gender, race, and ethnicity. This caused a dramatic reduction in the female and male percentages (Table 2) and significant fluctuations in race and ethnicity categories (Tables 3, 4). A similar but much less dramatic effect was also observed in FY 2017 when another large study (56,640 participants) reported enrollment only in those same Unknown categories. Some studies, such as those that involve internet surveys, do not collect sex/gender, race or ethnicity information, contributing to higher unknown sex/gender and race/ethnicity enrollment percentages and lower percentages for "known" categories. Also, in FY 2018, a very large observational study of veterans with a high proportion of males relative to females (160,415 males: 4,241 females) reported enrollment primarily in the African-American and White race categories. This resulted in large shifts in enrollment numbers and percentages for sex/gender as well as certain race and ethnicity categories compared to FY 2017 (Tables 2, 3,

and 4). When these large studies were excluded (see percentages in parentheses), the percentages were mostly consistent across the reporting period for sex/gender, race, and ethnicity. Sex/gender enrollment data by race and ethnicity for fiscal years 2016-2018 are also presented in Tables 5-7 and include the large studies with a sample size greater than 50,000 participants.

NIAAA supports very few Phase III clinical trials; therefore, enrollment in these studies represents a very small proportion of the total NIAAA enrollment (Tables 8-10). The enrollment categories remained stable with slight fluctuations during the reporting period. One exception was the Asian enrollment categories which increased from FY 2016 to FY 2017 for females and decreased for males.

In summary, noticeable shifts in enrollment for sex/gender and certain race categories occurred during the reporting period. While it is not uncommon for fluctuations to occur with turnover of grant awards, several large changes were observed that were attributed to studies that reported large sample sizes, resulting in skewing of the enrollment distributions. In addition, there were major changes in the system used to monitor inclusion data as well as several policy changes that could have impacted the enrollment data during the reporting period, e.g. launch of new systems for reporting and monitoring of inclusion data and changes regarding the reporting of existing data sets. It is also important to note that NIAAA had 62 protocols without enrollment data in the new Human Subjects System in FY 2018 (compared to 25 protocols in FY 2016 and 39 protocols in FY 2017). This large number of protocols without enrollment data could have affected the total enrollment for FY 2018. NIAAA will continue to closely monitor its enrollment numbers and work with grantees to ensure accurate reporting and compliance with the NIH inclusion guidelines.

Appendix: NIAAA Aggregate Inclusion Data Tables for Reporting Period FY 2016-2018

Table 1. Inclusion Data Records for NIH-Defined Extramural and Intramural Clinical Research Reported Between 2016 & 2018

Fiscal Year	2016	2017	2018
US Site	241	268	233
Non-US Site	13	13	15
Female Only	14	10	15
Male Only	6	16	18
Excluding Male-only & Female-only*	234	255	215
Without Enrollment	25	39	62
With Enrollment	254	281	248
Total	279	320	310

The data presented in this report show only inclusion data records labeled as prospective data. Inclusion data records labeled as existing data are excluded. *Inclusion Data Records excluding male-only and female-only include unknown sex/gender, and combination of unknown and any sex/gender(s).

Table 2. Enrollment for All NIH-Defined Clinical Research by Sex/Gender

Sex/Gender	FY 2016	FY 2017	FY 2018
Female	83,496	82,928	29,795
	21.8% (53.8%)	38.0% (51.3%)	13.7% (47.7%)
Male	69,218	77,756	188,046
	18.0% (44.6%)	35.6% (48.1%)	86.2% (51.6%)
Unknown	230,891	57,476	372
	60.2% (1.6%)	26.3% (0.5%)	0.2% (0.7%)
Total Enrollment	383,605	218,160	218,213

*Percentages in parentheses exclude studies with enrollment of greater than 50,000 participants.

Table 3. Enrollment for All NIH-Defined Clinical Research by Race

Race	FY 2016	FY 2017	FY 2018
American Indian/Alaska Native	3,803 1.0% (2.5%)	4,762 2.2% (2.9%)	1,439 0.7% (1.6%)
Asian	6,453 1.7% (4.2%)	10,665 4.9% (6.6%)	8,586 3.9% (14.9%)
Black/African American	23,806 6.2% (15.3%)	26,706 12.2% (16.5%)	90,216 41.3% (18.3%)
Native Hawaiian/Pacific Islander	652 0.2% (0.4%)	623 0.3% (0.4%)	731 0.3% (0.4%)
White	102,281 26.7% (65.9%)	106,849 49.0% (66.2%)	101,599 46.6% (51.1%)
More Than One Race	5,981 1.6% (3.9%)	5,590 2.6% (3.5%)	10,737 4.9% (4.5%)
Unknown/Not Reported	240,629 62.7% (7.9%)	62,965 28.9% (3.9%)	4,905 2.2% (9.2%)
Total Enrollment	383,605	218,160	218,213

*Percentages in parentheses exclude studies with enrollment of greater than 50,000 participants.

Table 4. Enrollment for All NIH-Defined Clinical Research by Ethnicity

Ethnicity	FY 2016	FY 2017	FY 2018
Not Hispanic	123,245 32.1% (79.4%)	191,390 87.7% (83.4%)	196,129 89.9% (81.6%)
Hispanic/Latino	27,089 7.1% (17.5%)	23,303 10.7% (14.4%)	20,967 9.6% (16.3%)
Unknown/Not Reported	233,271 60.8% (3.1%)	3,467 1.6% (2.1%)	1,117 0.5% (2.1%)
Total Enrollment	383,605	218,160	218,213

*Percentages in parentheses exclude studies with enrollment of greater than 50,000 participants.

Table 5. Enrollment for All NIH-Defined Clinical Research, Sex/Gender by Race and Ethnicity, FY 2016

	Sex/Gender	Female	Male	Unknown
	Total Enrollment	83,496	69,218	230,891
	%	21.8	18.0	60.2
	Minority	35,723	27,620	103
	%	42.8	39.9	0.0
Race	American Indian/Alaska Native	2,230	1,567	6
	%	2.7	2.3	0.0
	Asian	3,369	3,073	11
	%	4.0	4.4	0.0
	Black/African American	13,389	10,398	19
	%	16.0	15.0	0.0
	Native Hawaiian/Pacific Islander	333	319	0
	%	0.4	0.5	0.0
	White	55,419	46,362	500
	%	66.4	67.0	0.2
	More Than One Race	3,288	2,666	27
	%	3.9	3.9	0.0
	Unknown/Not Reported	5,468	4,833	230,328
	%	6.5	7.0	99.8
Ethnicity	Not Hispanic	66,409	56,106	730
	%	79.5	81.1	0.3
	Hispanic/Latino	15,457	11,578	54
	%	18.5	16.7	0.0
	Unknown/Not Reported	1,630	1,534	230,107
	%	2.0	2.2	99.7

Table 6. Enrollment for All NIH-Defined Clinical Research, Sex/Gender by Race and Ethnicity, FY 2017

	Sex/Gender	Female	Male	Unknown
	Total Enrollment	82,928	77,756	57,476
	%	38.0	35.6	26.3
	Minority	33,830	32,828	130
	%	40.8	42.2	0.2
Race	American Indian/Alaska Native	2,854	1,900	8
	%	3.4	2.4	0.0
	Asian	4,419	6,240	6
	%	5.3	8.0	0.0
	Black/African American	13,543	13,155	8
	%	16.3	16.9	0.0
	Native Hawaiian/Pacific Islander	319	303	1
	%	0.4	0.4	0.0
	White	55,549	50,866	434
	%	67.0	65.4	0.8
	More Than One Race	2,887	2,648	55
	%	3.5	3.4	0.1
	Unknown/Not Reported	3,357	2,644	56,964
	%	4.0	3.4	99.1
Ethnicity	Not Hispanic	68,706	65,770	56,914
	%	82.9	84.6	99.0
	Hispanic/Latino	12,330	10,914	59
	%	14.9	14.0	0.1
	Unknown/Not Reported	1,892	1,072	503
	%	2.3	1.4	0.9

Table 7. Enrollment for All NIH-Defined Clinical Research, Sex/Gender by Race and Ethnicity, FY 2018

	Sex/Gender	Female	Male	Unknown
	Total Enrollment	29,795	188,046	372
	%	13.7	86.2	0.2
	Minority	15,604	113,219	69
	%	52.4	60.2	18.5
Race	American Indian/Alaska Native	464	971	4
	%	1.6	0.5	1.1
	Asian	1,693	6,885	8
	%	5.7	3.7	2.2
	Black/African American	7,489	82,717	10
	%	25.1	44.0	2.7
	Native Hawaiian/Pacific Islander	132	598	1
	%	0.4	0.3	0.3
	White	15,784	85,758	57
	%	53.0	45.6	15.3
	More Than One Race	1,679	9,051	7
	%	5.6	4.8	1.9
	Unknown/Not Reported	2,554	2,066	285
	%	8.6	1.1	76.6
Ethnicity	Not Hispanic	24,199	171,872	58
	%	81.2	91.4	15.6
	Hispanic/Latino	5,193	15,728	46
	%	17.4	8.4	12.4
	Unknown/Not Reported	403	446	268
	%	1.4	0.2	72.0

Table 8. Enrollment for NIH-Defined Extramural and Intramural Phase III Clinical Research, Sex/Gender by Race and Ethnicity, FY 2016

	Sex/Gender	Female	Male	Unknown
	Total Enrollment	1376	613	20
	%	68.5	30.5	1.0
	Minority	385	303	0
	%	28.0	49.4	0.0
Race	American Indian/Alaska Native	5	3	0
	%	0.4	0.5	0.0
	Asian	53	131	0
	%	3.9	21.4	0.0
	Black/African American	135	97	0
	%	9.8	15.8	0.0
	Native Hawaiian/Pacific Islander	1	0	0
	%	0.1	0.0	0.0
	White	1098	359	0
	%	79.8	58.6	0.0
	More Than One Race	62	16	0
	%	4.5	2.6	0.0
	Unknown/Not Reported	22	7	20
%	1.6	1.1	100.0	
Ethnicity	Not Hispanic	1203	526	0
	%	87.4	85.8	0.0
	Hispanic/Latino	169	86	0
	%	12.3	14.0	0.0
	Unknown/Not Reported	4	1	20
	%	0.3	0.2	100.0

Table 9. Enrollment for NIH-Defined Extramural and Intramural Phase III Clinical Research, Sex/Gender by Race and Ethnicity, FY 2017

	Sex/Gender	Female	Male	Unknown
	Total Enrollment	1672	602	21
	%	72.9	26.2	0.9
	Minority	489	230	1
	%	29.2	38.2	4.8
Race	American Indian/Alaska Native	5	3	0
	%	0.3	0.5	0.0
	Asian	94	39	0
	%	5.6	6.5	0.0
	Black/African American	156	99	0
	%	9.3	16.4	0.0
	Native Hawaiian/Pacific Islander	2	0	0
	%	0.1	0.0	0.0
	White	1313	427	0
	%	78.5	70.9	0.0
	More Than One Race	74	21	0
	%	4.4	3.5	0.0
	Unknown/Not Reported	28	13	21
	%	1.7	2.2	100.0
Ethnicity	Not Hispanic	1459	499	0
	%	87.3	82.9	0.0
	Hispanic/Latino	209	102	1
	%	12.5	16.9	4.8
	Unknown/Not Reported	4	1	20
	%	0.2	0.2	95.2

Table 10. ALL Enrollment for NIH-Defined Extramural and Intramural Phase III Clinical Research, Sex/Gender by Race and Ethnicity, FY 2018

Sex/Gender		Female	Male	Unknown
Total Enrollment		1722	602	21
%		73.4	25.7	0.9
Minority		520	230	1
%		30.2	38.2	4.8
Race	American Indian/Alaska Native	5	3	0
	%	0.3	0.5	0.0
	Asian	113	39	0
	%	6.6	6.5	0.0
	Black/African American	163	99	0
	%	9.5	16.4	0.0
	Native Hawaiian/Pacific Islander	3	0	0
	%	0.2	0.0	0.0
	White	1336	427	0
	%	77.6	70.9	0.0
	More Than One Race	74	21	0
	%	4.3	3.5	0.0
	Unknown/Not Reported	28	13	21
%	1.6	2.2	100.0	
Ethnicity	Not Hispanic	1505	499	0
	%	87.4	82.9	0.0
	Hispanic/Latino	213	102	1
	%	12.4	16.9	4.8
	Unknown/Not Reported	4	1	20
%	0.2	0.2	95.2	