

2015 NIMH BIENNIAL REPORT CERTIFYING COMPLIANCE WITH INCLUSION GUIDELINES

Overview

The National Institutes of Health (NIH) Revitalization Act of 1993 (PL 103-43) mandates the advisory council of each Institute prepare a biennial report describing the manner in which the Institute has complied with requirements regarding the inclusion of women and minorities in clinical research. NIH guidelines ensure that women and minorities are included in NIH-funded clinical research, and that NIH-defined Phase III clinical trials are designed in a manner sufficient to examine differential effects of interventions on both women and men, as well as individuals of diverse racial and ethnic groups.¹

This report details NIMH strategies for maintaining compliance with the inclusion guidelines and includes data on extramural clinical research, extramural Phase III clinical trials, and intramural clinical research. As the NIH inclusion guidelines apply to studies both within and outside the U.S., data are presented for all NIMH studies (both domestic and foreign), as well as participants recruited in the U.S. only. The data reflect the breadth of the clinical research supported by NIMH to fulfill its mission to transform the understanding and treatment of mental illnesses through basic and clinical research, paving the way for prevention, recovery, and cure. The NIMH clinical research portfolio includes large-scale clinical trials and observational studies, as well as smaller studies in basic, translational and services research.

Strategies for Ensuring Compliance

NIMH follows several steps to ensure compliance with the inclusion guidelines. The Institute relies on review, program, policy, and grants management staff to implement these guidelines. Inclusion is addressed first by NIMH review administrators. Review administrators evaluate applications for the appropriateness of sex/gender, racial and ethnic minority enrollment goals; recruitment plans that demonstrate how the investigator will meet these goals; and, for Phase III studies, plans to conduct analyses to detect significant differences in 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 policy. If issues are raised in review, then program staff will notify principal investigators, who are required to address these issues prior to funding. Applications with unacceptable inclusion plans receive a bar to funding, which must be resolved prior to award of the grant or cooperative agreement. In the case of a bar to funding, the program official forwards the revised enrollment plan to the Office of Clinical Research (OCR), for review. If satisfactory, the enrollment plan is returned to the program official and the grants management branch and the bar to funding is then lifted. This response is kept in the official grant file along with a record of administrative actions taken.

¹ For further information about the guidelines, please see http://grants.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm.

Prior to award NIMH program officials are responsible for approving the inclusion information submitted by the Principal Investigator. For Phase III clinical trials, program officials monitor the requirement for valid analysis of significant differences in applications and annual progress reports.

OCR monitors the entry of inclusion data, performs quality assurance tasks, prepares aggregate reports for the NAMHC and the NIH Office of Research on Women's Health (ORWH), and provides up-to-date training on procedures for ensuring the accuracy of inclusion data, as well as on the use of the electronic inclusion monitoring system. OCR provides this training through individual assistance, workshops for staff, and the provision of training materials to employees.

Monitoring of intramural research is coordinated by the Clinical Center's Office of Protocol Services (OPS). Intramural IRBs review intramural research protocols for compliance with inclusion guidelines and conduct annual monitoring. The NIH Clinical Center maintains centralized systems for capturing accrual data including sex/gender, ethnic, and racial status, and individual investigators conduct validation of these data in collaboration with the Clinical Center's Medical Record Department. OPS, in collaboration with the Department of Clinical Research Informatics, prepares and submits inclusion data to the Office of Research on Women's Health for review and analysis.

Analysis and Interpretation of Data

The appended tables show enrollment data for the fiscal years (FY) 2013 and 2014. Included in the tables are enrollment data for all extramural clinical research, for extramural Phase III clinical trials only, and for intramural research. Inclusion data are reported using the Office of Management and Budget's (OMB) revised 1997 racial and ethnic categories, which are required for the collection, tabulation, and presentation of race and ethnicity data within the Federal statistical system.² When assessing inclusion data, it is important to keep in mind that the number of individuals in sex/gender, racial, and ethnic subgroups included in a particular study depends upon the scientific questions addressed in the study and the prevalence or incidence among these subgroups of the disease, disorder, or condition under investigation.

Tables 1 and 2: Aggregate Data for all Extramural Research

Tables 1 and 2 display the sex/gender, racial, and ethnic distribution of participants in NIMH extramural clinical research in FY 2013 and FY 2014, respectively.

In FY 2013, NIMH extramural studies enrolled 465,988 participants; 42% of participants identified as female, and 57% identified as male, while less than 2% did not identify a sex or gender. In FY 2014, NIMH extramural studies enrolled 315,492 participants; 49% of participants identified as female and 50% identified as male, and 1% did not identify a sex or gender. From FY 2013 to FY 2014, decreases in both overall participants and the percentage of male participants are due in part to the inclusion of

² For more information about racial and ethnic categories required by OMB revisions to Statistical Policy Directive 15, see http://www.whitehouse.gov/omb/fedreg_1997standards/.

enrollment data for Army Study to Assess Risk and Resilience in Servicemembers (ARMY STARRS), which was last awarded in FY 2013 and is not included in the FY 2014 data. Army STARRS is the largest study of mental health risk and resilience ever conducted among military personnel. As of FY 2013, Army STARRS had enrolled over 100,000 participants, and 83% of those participants are male.

The trends in the racial and ethnic distribution of participants in NIMH extramural clinical research are similar in FY 2013 and FY 2014. The majority of participants identified as White (56% in FY 2013 and 53% in FY 2014), and the largest racial minority groups were Black or African American (23% in FY 2013 and 25% in FY 2014) and Asian (9% in FY 2013 and 10% in FY 2014). The percentage of American Indian/Alaska Native participants decreased from 1% in FY 2013 to 0.7% in FY 2014, and the percentage of Hawaiian/Pacific Islanders decreased from 0.4% to 0.3%. The percentage of participants identifying as More Than One Race was 3% in both years. Participants of Hispanic ethnicity, who may identify as any race, constituted 11% of participants enrolled in FY 2013 and 9% in FY 2014.

Tables 3 and 4: Aggregate Data for Extramural Phase III Research

Tables 3 and 4, respectively, display the distribution of participants in NIMH extramural Phase III clinical trials for FY 2013 and FY 2014. In FY 2013, 22,919 participants were enrolled in NIMH extramural Phase III clinical trials, whereas 23,093 participants were enrolled in FY 2014. Most participants reported in NIMH Phase III clinical research in both FY 2013 and FY 2014 were enrolled in an ancillary study of the National Cancer Institute-supported *VITamin D and OmegA-3 Trial*, which investigates whether taking daily dietary supplements of vitamin D3 or omega-3 fatty acids reduces the risk of developing cancer, heart disease, and stroke in people who do not have prior history of these illnesses. The NIMH-supported study, *VITAL-DEP: Depression Endpoint Prevention in the VITamin D and OmegA-3 Trial*, examines the effects of these supplements on depression and mood over time compared to placebo.

In both FY 2013 and FY 2014, 53% of participants in NIMH Phase III extramural research were female and 47% were male. In both years, the largest racial minority group was Black or African American (22%), followed by More Than One Race and Asian (both 1%). In FY 2013, 0.5% of participants identified as American Indian/Alaska Native, and 0.4% identified as American Indian/Alaska Native in FY 2014. In both years, 0.2% were Native Hawaiian/Pacific Islander. In FY 2013 and FY 2014, 6% of participants identified their ethnicity as Hispanic.

Tables 5 and 6: Aggregate Data for Intramural Research

Tables 5 and 6 display data for NIMH intramural clinical protocols for FY 2013 and FY 2014, respectively.

NIMH intramural studies enrolled 48,138 participants in FY 2013 and 50,253 in FY 2014. Tables 5 and 6 show the trends in the distribution of sex, race, and ethnicity were relatively stable from FY 2013 to FY 2014. In both years, 53% of participants were female and 47% were male. The majority of participants identified as

White (69% in FY 2013 and 68% in FY 2014). The largest racial minority group was Black or African American (18%), followed by Asian (5%), American Indian/Alaska Native (0.2%), and Hawaiian/Pacific Islander (0.1%), and 2% of participants identified as More Than One Race. Enrollment for participants of Hispanic ethnicity was 5% in both years.

Additional Information

As mentioned above, the NIH inclusion guidelines require Phase III clinical trials to be designed in a way that allows for a valid analysis of significant differences by sex, race, and ethnicity. Although subgroup analyses are still in progress for most trials, published results on subgroup analyses by sex are available for the NIMH-supported trial, *Sustaining Remission of Psychotic Depression*.³

Separate from the inclusion policy, but critical to monitoring ongoing recruitment in research studies, NIMH adopted the Policy for the Recruitment of Participants in Clinical Research on June 1, 2005. This policy allows for benchmarking and regular monitoring of recruitment for studies involving 150 or more human subjects.⁴ NIMH is one of the few NIH Institutes to have such a policy.

On February 6, 2015, the National Advisory Mental Health Council concurred that NIMH is in compliance with the requirement to include women and minorities in clinical research as directed by the 1993 Revitalization Act.

³ Deligiannidis, K. M., Rothschild, A. J., Barton, B. A., Kroll-Desrosiers, A. R., Meyers, B. S., Flint, A. J., Whyte, E. M., Mulsant, B. H., & , STOP PD Study Group. (2013). A gender analysis of the study of pharmacotherapy of psychotic depression (STOP-PD): gender and age as predictors of response and treatment-associated changes in body mass index and metabolic measures. *The Journal of clinical psychiatry*, 10, 1003–1009; Davies, S. J., Mulsant, B. H., Flint, A. J., Rothschild, A. J., Whyte, E. M., Meyers, B. S., & , STOP PD Study Group. (2014). Differential impact of anxiety symptoms and anxiety disorders on treatment outcome for psychotic depression in the STOP-PD study. *Comprehensive psychiatry*, 5, 1069–1076.

⁴ The full policy statement is available at <http://www.nimh.nih.gov/research-funding/grants/nimh-policy-for-the-recruitment-of-participants-in-clinical-research.shtml>.

Table 1 - FY 2013 Aggregate Enrollment Data for All Extramural Research Protocols

	U.S. ONLY	ALL NIMH STUDIES
Female	40.54%	41.55%
Male	57.93%	56.94%
American Indian/Alaska Native	0.94%	1.05%
Asian	5.49%	9.37%
Hawaiian/Pacific Islander	0.52%	0.43%
Black or African American	19.23%	23.23%
Hispanic	12.55%	10.88%
White	62.50%	55.95%
More Than One Race	3.82%	3.25%
Unknown/Not Reported (Race)	7.50%	6.71%
Unknown/Not Reported (Ethnicity)	5.45%	5.68%
Total Participants	383,286	465,988
Total Protocol Records*	873	934

*A protocol record is an enrollment data record for a research protocol. A research protocol may have one or more assigned protocol records.
Data Source: NIH Population Tracking Module, Retrieved 12/16/14

Table 2 - FY 2014 Aggregate Enrollment Data for All Extramural Research Protocols

	U.S. ONLY	ALL NIMH STUDIES
Female	51.28%	49.06%
Male	47.45%	49.91%
American Indian/Alaska Native	0.89%	0.73%
Asian	6.05%	10.18%
Hawaiian/Pacific Islander	0.31%	0.25%
Black or African American	21.27%	24.57%
Hispanic	10.80%	9.16%
White	58.98%	53.48%
More Than One Race	3.42%	2.94%
Unknown/Not Reported (Race)	9.07%	7.86%
Unknown/Not Reported (Ethnicity)	8.61%	7.82%
Total Participants	253,454	315,492
Total Protocol Records	768	821

Data Source: NIH Population Tracking Module, Retrieved 12/16/14

Table 3 - FY 2013 Aggregate Enrollment Data for Extramural Phase III Research Protocols

	U.S. ONLY	ALL NIMH STUDIES
Female	52.81%	52.84%
Male	46.72%	46.69%
American Indian/Alaska Native	0.45%	0.45%
Asian	1.21%	1.26%
Hawaiian/Pacific Islander	0.15%	0.15%
Black or African American	22.03%	21.96%
Hispanic	6.27%	6.32%
White	73.66%	73.69%
More Than One Race	1.36%	1.36%
Unknown/Not Reported (Race)	1.13%	1.13%
Unknown/Not Reported (Ethnicity)	9.82%	9.77%
Total Participants	22,816	22,919
Total Protocol Records	11	13

Data Source: NIH Population Tracking Module, Retrieved 12/16/14

Table 4 - FY 2014 Aggregate Enrollment Data for Extramural Phase III Research Protocols

	U.S. ONLY	ALL NIMH STUDIES
Female	52.70%	52.73%
Male	46.83%	46.81%
American Indian/Alaska Native	0.44%	0.44%
Asian	1.20%	1.25%
Hawaiian/Pacific Islander	0.16%	0.16%
Black or African American	22.11%	22.04%
Hispanic	6.33%	6.38%
White	73.46%	73.50%
More Than One Race	1.41%	1.40%
Unknown/Not Reported (Race)	1.22%	1.21%
Unknown/Not Reported (Ethnicity)	9.74%	9.70%
Total Participants	22,990	23,093
Total Protocol Records	11	13

Data Source: NIH Population Tracking Module, Retrieved 12/16/14

Table 5 - FY 2013 Aggregate Enrollment Data for Intramural Research Protocols

	U.S. ONLY	ALL NIMH STUDIES
Female	52.95%	52.85%
Male	46.97%	47.08%
American Indian/Alaska Native	0.21%	0.20%
Asian	5.15%	5.04%
Hawaiian/Pacific Islander	0.12%	0.12%
Black or African American	16.51%	18.25%
Hispanic	4.96%	4.85%
White	70.18%	68.72%
More Than One Race	1.70%	1.67%
Unknown/Not Reported (Race)	6.12%	6.00%
Unknown/Not Reported (Ethnicity)	2.82%	2.76%
Total Participants	47,136	48,138
Total Protocol Records	117	118

Data Source: NIH Population Tracking Module, Retrieved 12/16/14

Table 6 - FY 2014 Aggregate Enrollment Data for Intramural Research Protocols

	U.S. ONLY	ALL NIMH STUDIES
Female	52.87%	52.78%
Male	47.05%	47.15%
American Indian/Alaska Native	0.22%	0.21%
Asian	5.29%	5.18%
Hawaiian/Pacific Islander	0.11%	0.11%
Black or African American	16.68%	18.34%
Hispanic	5.05%	4.95%
White	69.54%	68.16%
More Than One Race	1.86%	1.82%
Unknown/Not Reported (Race)	6.30%	6.18%
Unknown/Not Reported (Ethnicity)	3.04%	2.98%
Total Participants	49,251	50,253
Total Protocol Records	115	116

Data Source: NIH Population Tracking Module, Retrieved 12/16/14