

2015 Biennial National Advisory Eye Council Report Certifying Compliance with Inclusion Guidelines

Background/Overview: As part of the Federal government's National Institutes of Health (NIH), the National Eye Institute (NEI) was established to protect and prolong the vision of the American people. The National Eye Institute's mission is to "conduct and support research, training, health information dissemination, and other programs with respect to blinding eye diseases, visual disorders, and mechanisms of visual function. NEI research leads to sight-saving treatments, reduces visual impairment and blindness, and improves the quality of life for people of all ages. NEI-supported research has advanced our knowledge of how the visual system functions in health and disease.

The NEI supports a significant numbers of clinical research projects on potentially blinding eye diseases and other visual disorders. Examples include diabetic retinopathy, amblyopia, age-related macular degeneration, glaucoma, retinopathy of prematurity, corneal stromal keratitis, cytomegalovirus retinitis, uveitis, retinitis pigmentosa, Leber's congenital amaurosis and myopia (nearsightedness).

The National Eye Institute has developed procedures to implement the inclusion policies mandated by the NIH Revitalization Act of 1993, Part I--Women and Minorities as Subjects in Clinical Research. This Act enjoins the NIH to ensure that women and minorities and their subpopulations are included in all human subject research. In addition, for Phase III clinical trials, the Act requires that women and minorities and their subpopulations be included such that valid analyses of differences in intervention effect can be accomplished. In 1994, the NIH revised its inclusion policy to meet this mandate.

NEI Strategies for Ensuring Compliance: The Director, Division of Extramural Research (DER), NEI, is the official with responsibility for ensuring compliance. In order to educate the vision research community, inclusion policies are highlighted on the NEI

extramural research website. The policy is also explicitly detailed in all NEI Funding Opportunity Announcements, Requests for Applications, and Requests for Proposals. The scientific and clinical bases underlying gender and minority differences in ocular diseases and conditions such as dry eye, glaucoma, diabetic retinopathy, macular degeneration, and myopia are discussed in the NEI strategic planning document, "Vision Research: Needs, Gaps and Opportunities", (August 2012). This document was developed in conjunction with experts from all fields of vision research, who were assembled to make recommendations on research priorities. Several of the priority recommendations made by these groups were related to health disparities. They included research on glaucoma, diabetic retinopathy, myopia, health services research, and eye health education. Over 60 professional, scientific, or advocacy organizations that support vision research were asked to review the draft plan to ensure that important areas of research or specific issues of importance to vision research had not been overlooked. The final plan reflects the comments and input received during that process.

NEI Scientific Review Officers ensure that applications are reviewed for appropriate inclusion criteria. All peer-reviewers are educated about the inclusion requirements and are instructed to evaluate the appropriateness of study participant inclusion in NEI-supported projects. NEI program staff and grants management staff review inclusion issues on each application prior to award. Any concerns are resolved before funding actions are finalized, and the individual grant files include documentation of the compliance review. NEI staff maintains a computerized tracking system to follow inclusion, and data in the system are analyzed annually by the Director, DER. Results are discussed at general staff meetings.

NEI DER staff are required to participate in the NIH Training on Gender, Race and Ethnicity. The Director, DER, routinely distributes policy updates to all staff and holds at least quarterly staff meetings to discuss and review tracking issues. DER staff members participate in several trans-NIH committees regularly involved with compliance and policy issues.

All NEI-funded Phase III clinical trials are supported through the cooperative agreement mechanism. NEI Clinical Program Directors collaborate with the study team to ensure that all protocols are designed with appropriate inclusion goals before funding. Most Phase III trials are multicenter, which permits broader sampling of minority subpopulations. NEI staff monitor enrollment in all Phase III trials routinely and document inclusion in the grant file. NEI staff work collaboratively with study biostatisticians to ensure that appropriate valid analyses of differences in intervention effect are performed.

The NEI collaborates with the National Institutes of Health, Office of Research on Women's Health and the National Institute on Minority Health and Health Disparities to obtain funding to add special populations to selected clinical trials. This collaboration has provided opportunities such as the addition of urban Latino and African-American participants to epidemiologic studies of eye diseases, the addition of a larger group of Asian-Americans, African-Americans and Native Americans to a study of myopia development in children, and the addition of Native Americans to projects studying the development and treatment of astigmatism and amblyopia.

Members of the NEI program staff have reviewed the May 2000 Government Accounting Office report regarding compliance, and actively implement the recommendations for valid analysis of sex differences in Phase III clinical trials and for improved accuracy of inclusion tracking data.

Analysis and Interpretation of Data: The National Advisory Eye Council (NAEC) reviewed NIH policy documents and NEI-specific inclusion data for FY2013 and FY2014 at their January 22, 2015, meeting. Data for all domestic clinical research, NIH-defined Phase III clinical trials, extramural and intramural research was reviewed. For aggregate studies, the NEI portfolio showed a preponderance of women subjects. This is an expected observation given that many of the eye diseases under study impact older populations and women make up a higher percentage of this age group.

There was good representation of minority groups in research protocols overall. There was a slight over-representation of Asian-American subjects. This is an expected observation given the NEI is currently supporting a large epidemiologic study of eye diseases in Chinese-Americans. There was a slight under-representation of African-American subjects. This is an expected observation given that a large study of glaucoma was completed and no longer appears in the recent inclusion results. Glaucoma disproportionately impacts African-Americans. For all clinical research projects, the NEI had high representation of Hispanic participants. NAEC members discussed the tracking data and concluded that it was acceptable.

In NEI-sponsored Phase III clinical trials, women and men study participants were equally represented. Inclusion of minority groups in Phase III clinical trials was commensurate with United States population averages. Inclusion of Hispanic participants in Phase III clinical trials was commensurate with United States population averages as well. All NEI-funded Phase III clinical trials are designed with enrollment targets for gender, race, and ethnicity which result in sufficient power for valid subgroup analyses as required by policy. Members of the Council discussed the target data and the corresponding tracking and inclusion data and concluded that it was acceptable.

Additional Information: The NEI supports a large portfolio of clinical research. The NAEC reviewed the inclusion data and concluded that the NEI has complied with the NIH Policy on Inclusion of Women & Minorities in Clinical Research. Overall, inclusion of minority groups in NEI clinical research was commensurate with United States population averages. Recently, the NEI funded a clinical trial of dry eye disease which is expected to enroll substantial number of female patients and two large glaucoma projects which are expected to enroll significant numbers of African-American subjects. NEI Program staff actively monitor scientific portfolios and individual clinical research projects for the appropriate inclusion of women and minority populations.