# National Institutes of Health

# MONITORING ADHERENCE TO THE NIH POLICY ON THE INCLUSION OF WOMEN AND MINORITIES AS SUBJECTS IN CLINICAL RESEARCH

## Comprehensive Report
## (Fiscal Year 1998 & 1999 Tracking Data)

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# Monitoring Adherence to the NIH Policy on the Inclusion of Women and Minorities as Subjects in Clinical Research

**Background**

The establishment and implementation of policies for the inclusion of women and minorities in clinical research funded by the National Institutes of Health (NIH) has its origins in the women's health movement. Following the issuance of the report of the Public Health Service Task Force on Women's Health in 1985, the NIH established a policy in 1986 for the inclusion of women in clinical research. This policy, which ***urged*** the inclusion of women, was first published in the NIH Guide to Grants and Contracts in 1987. Later that year, minority and other scientists at the NIH recognized the need to address the inclusion of minority populations. Therefore, in a later 1987 version of the NIH guide, a policy ***encouraging*** the inclusion of minorities in clinical studies was first published.

In July 1989, an *NIH Memorandum on Inclusion* stated that research solicitations should encourage inclusion of women and minorities and require a rationale if excluded, and that executive secretaries of scientific review groups should ensure that responsiveness to policy would be addressed and indicated in summary statements. In 1990, the *Congressional Caucus for Women's Issues* requested the U.S. General Accounting Office (GAO) to conduct an investigation into the implementation of the guidelines for the inclusion of women by NIH. This report, in Congressional testimony, indicated that the implementation of the policy for the inclusion of women was slow, not well communicated, that gender analysis was not implemented, and that the impact of this policy could not be determined. The GAO testimony also indicated that there were differences in the implementation of the policy recommending the inclusion of minorities, and that not all Institutes and Centers (ICs) factored adherence to these policies into the scientific merit review.

In order to ensure the policies for inclusion were firmly implemented by NIH, the Congress made what had previously been policy into Public Law, through a section in the NIH Revitalization Act of 1993 (PL 103-43)[1], entitled *Women and Minorities as Subjects in Clinical Research*. In 1994, the NIH revised its inclusion policy to meet this mandate that women and minorities must be included in all of its clinical research studies. The Revitalization Act essentially reinforced the existing NIH policies, but with four major differences:

- that NIH ensure that women and minorities and their subpopulations be included in all clinical research;
- that women and minorities and their subpopulations be included in Phase III clinical trials in numbers adequate to allow for valid analyses of differences in intervention effect;
- that cost is not allowed as an acceptable reason for excluding these groups; and,
- that NIH initiate programs and support for outreach efforts to recruit and retain women and minorities and their subpopulations as participants in clinical studies.

Revised inclusion guidelines developed in response to this law were published in the *Federal Register*[2] in March 1994, and they became effective in September 1994. The result was that NIH could not and would not fund any grant, cooperative agreement or contract or support any intramural project to be conducted or funded in Fiscal Year 1995 and thereafter which did not comply with this policy. NIH's administrative procedures allow consideration of applications through a peer-review system. During initial peer review, the Scientific Review Group (SRG) evaluates the proposed enrollment of each project

involving human subjects and determines whether the plan to include women and minority subjects is scientifically acceptable. The implementation plan determines that an application may be unacceptable if it: 1) fails to provide sufficient information about target enrollment; 2) does not adequately justify limited or lack of inclusion of women or minorities; or 3) does not realistically address recruitment and retention. For NIH-defined Phase III clinical trials, the Scientific Review Group (SRG) also evaluates the description of plans to conduct analyses, as appropriate, to address differences in the intervention effect by sex/gender and/or racial/ethnic groups. Applications with unacceptable inclusion plans receive an unacceptable gender or minority code, resulting in a bar-to-funding. Such clinical research studies cannot be funded until NIH staff is assured of compliance from the investigators. This may involve requiring changes related to study design. Sometimes applicants are able to remedy the deficiencies found during initial review by providing additional information about the intended enrollment demographics. Research awards covered by this policy require the grantee to report annually on enrollment of women and men, and on the race and ethnicity of research participants so that accrual can be monitored. Annual progress reports submitted by the grantee contain information on research progress which includes research participant enrollment, retention, and when available, preliminary and/or final analyses including by sex/gender and race/ethnicity.

Strategies to ensure that the implementation of these revised guidelines was uniform across the NIH were developed through the establishment and deliberations of an NIH Tracking and Inclusion Committee made up of representatives of the directors of each of the ICs. This trans-NIH committee, convened by the Office of Research on Women's Health (ORWH) and co-chaired with a senior IC official, meets on a regular basis, focusing on consistent and widespread adherence to the NIH guidelines by all the ICs. Working in collaboration with the Office of Extramural Research (OER), the Office of Intramural Research (OIR), and other components of the NIH, the ORWH coordinates the activity of developing and establishing data collection and reporting methodologies to ensure uniform standards and definitions in the reporting of data on the participation of women and minority participants in NIH-funded clinical research.

To ensure universal adherence to the revised inclusion guidelines, in 1994 NIH conducted extensive training on the revised inclusion guidelines for more than 1,000 NIH staff members with review, program, grants management, and/or contract management responsibilities. Additionally, four publications were distributed to further reinforce adherence to the revised inclusion guidelines.[5-8] NIH staff, in turn, explained the requirements to applicants, reviewers, and other members of the research community. NIH staff members, reviewers, and applicants received written guidance about the requirements. This guidance outlined, in great detail, the circumstances under which it may be acceptable to use study populations deficient in women or minority participants, pointing out that the justification must be compelling and the scientific objectives of the research must be maintained. Training was especially important in response to 1990 GAO findings that an earlier policy was inconsistently applied and had not been well communicated or understood within the NIH or in the research community.

A variety of outreach activities were initiated to explain the revised policy to the scientific research community and to clear up common misunderstandings about the new requirements. Recognizing the importance of both recruitment and retention of human subject volunteers, NIH issued several articles[9-10] and an outreach notebook, entitled *Outreach Notebook for the NIH Guidelines on Inclusion of Women and Minorities as Subjects in Clinical Research*, that outlines elements of outreach processes, offers practical suggestions, and provides references to additional sources of information. The outreach notebook is available on the Office of Research on Women's Health Website http://www4.od.nih.gov/orwh/outreach.pdf. It also includes the full text of the 1994 implementation guidelines as well as a questions and answers document to provide more detailed policy guidance and

some of the more commonly asked questions. The ORWH also has available a full report of its workshop on "Recruitment and Retention of Women in Clinical Studies."

In June 1994, the ORWH convened a meeting of Institutional Review Board (IRB) chairs to discuss their role in implementing the revised policy. In 1996, ORWH reconvened these IRB chairs, along with representative members of the ORWH Recruitment and Retention Task Force, other experts, and representatives from NIH ICs, to discuss their experiences in implementing the 1994 guidelines. In these meetings, investigators expressed a number of lingering concerns, most notably whether it was realistic for the law to declare that cost is not a factor in designing clinical studies. Participants also raised questions about inclusion of women of childbearing potential, liability in clinical trials, and barriers to the recruitment of minority subjects. Other participants, however, noted that their worst fears about the 1994 guidelines did not materialize, in part because NIH focused on scientific considerations when developing its policy. They reported improved collaboration among institutions and emphasized the continued need for better outreach and for sharing information about effective recruitment strategies. Many noted the importance of considering community concerns, particularly those of minority populations who may feel that they are not included in enough research studies or who do not receive research results after participating in studies.

NIH has monitored aggregate demographic data for study populations through the existing NIH computerized tracking system since Fiscal Year 1994 and tracking the inclusion of women and minorities in clinical trials has been implemented in all ICs. The NIH Tracking and Inclusion Committee continues to work on ways to refine and improve data collection methods and the quality of the data entered by each IC into this system. Aggregate data is reported annually by Fiscal Year (FY). This report contains data for FY1998 and FY1999 and FY2000 data is currently being completed. Tables 1 to 10 provide aggregate enrollment data for extramural and intramural research protocols funded in FY1998 and FY1999. Aggregate enrollment figures FY1994 - 1997 for women and men and minority groups may be found on the ORWH website at http://www4.od.nih.gov/orwh/fy97-98trkg.pdf. Following the format of the aggregate extramural data tables, the aggregate intramural data for on-site and off-site research protocols are combined on a single table rather than separate data tables for on-site and off-site research protocols.

Analysis of the FY1999 inclusion data shows that substantial numbers of both women and minorities have been included as research subjects in Phase III clinical trials and other human subject research studies, in both intramural and extramural programs. During FY1999, more than 93% of applications involving human subjects met the inclusion requirements as submitted to the Initial Review Group [see Table A]. Of the remaining applications, approximately 7% were found to have unacceptable plans for inclusion at the time they were originally submitted. Of these, the applications that were otherwise considered acceptable for payment, were required to submit an acceptable plan for inclusion prior to funding [see Table B].

Aggregate enrollment data for extramural Phase III trials funded in FY1999 show that approximately 63.3% of the subjects were women. Among minority subjects,[1] representation in Phase III trials [Table 6] was highest for Black (not Hispanic) subjects (12.6%) and lowest for American Indians/Alaskan Natives subjects (0.8%). Asian/Pacific Islanders subjects were 4.8% of the extramural Phase III subjects; Hispanic subjects were 6.1%; and White (not Hispanic) subjects were 67.7%. Over six million subjects

[1]Racial and ethnic categories are in accord with the Office of Management and Budget (OMB) Directive No. 15.

were included in the research for which data were collected in the tracking system from among all extramural research active in FY 1999. This snapshot of aggregate enrollment data for FY 1999 extramural studies [Table 6] shows that approximately 61.6% of the subjects were women, approximately 37.7% were men, and approximately 0.6% were not identified by sex/gender.

Substantial numbers of women and minorities were also included in NIH intramural studies in FY 1999 [Table 10]. Approximately 47.3% of intramural subjects were women and approximately 51.8% were men. Among minority subjects, representation in intramural studies was highest for Asian/Pacific Islander subjects (20.5%) and lowest for American Indian/Alaskan native subjects (0.9%). Black - Not Hispanic subjects represented approximately 4.6% of the subjects; Hispanic subjects 1.7%; and White (not Hispanic) subjects represented 67.8% of the intramural research study population. Over two million subjects were included in the research for which data were collected in the tracking system from among intramural research active in FY 1999.

A review of intramural inclusion data indicates that the intramural research program is compliant with the reporting requirements adhered to by the extramural community and outlined in the NIH Implementation Guidelines on the Inclusion of Women and Minority Subjects in Research Studies. The Clinical Center Medical Executive Committee (MEC) has taken a proactive role in assuring that investigators conducting clinical research protocols in the Clinical Center are trained and competent in the conduct of clinical research. To this end, the MEC designed and endorsed the Standards for Clinical Research within the NIH Intramural Research Program. This set of standards, endorsed by the Clinical Center's Board of Governors and the NIH Institute Directors, sets forth guidelines for the infrastructure, training, education and monitoring required for the safe and effective conduct of clinical research and, the Clinical Center is actively engaged in outreach to minority groups to encourage participation in intramural clinical research.

**Current Activities**

Following a Congressional request for an assessment of NIH's progress in implementing the1994 guidelines on including women in clinical research, the GAO issued another report in May, 2000, entitled *Women's Health - NIH Has Increased Its Efforts to Include Women in Research*[3]. The conclusions of this report showed that in the past decade, NIH made significant progress in implementing a strengthened policy on including women in clinical research and highlighted several examples, including:

- NIH issued guidelines to implement the 1993 NIH Revitalization Act and conducted extensive training for scientists and reviewers;
- the review process for extramural research treats the inclusion of women and minorities as a matter of scientific merit, affecting a proposal's eligibility for funding;
- the intramural research program now implements the inclusion policy;
- NIH maintains a centralized inclusion tracking data system which serves as a tool for monitoring the implementation of the inclusion policy; and
- in fiscal year 1997, more that 62% of participants in NIH-funded clinical research studies were women; minority women were also well represented, however, the proportion of Hispanic women enrolled was below their proportion in the general population.

The GAO report also included two specific recommendations to the Director of NIH to ensure the following:

- that the requirement be implemented that Phase III clinical trials be designed and carried out to allow for the valid analysis of differences between women and men and communicate this requirement to applicants as well as requiring peer review groups to determine whether each proposed Phase III clinical trial is required to have such a study design, and that summary statements document the decision of the initial reviewers; and

- that the NIH staff who transmit data to the inclusion tracking data system receive ongoing training on the requirements and purpose of the system.

Immediately following the release of this report, an *NIH Subcommittee Reviewing Inclusion Issues* was formed, comprised of representatives from several ICs, ORWH, OER, and OIR, to reexamine NIH's system for tracking data on the inclusion of women and minorities in clinical research, recommend any necessary changes to improve the accuracy and performance of the system, and reiterate the NIH policy (See Appendix J). Four actions resulted to clarify the requirement for NIH-defined Phase III clinical trials to include women and minority groups, if scientifically appropriate, and for analysis of sex/gender and/or racial/ethnic differences to be planned and conducted by investigators engaged in NIH-funded research. These included:

- In October 2001, the NIH Policy and Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research and Amended Notice to the Guide for Grants and Contracts were updated and posted on the Internet with links to the ORWH home page and NIH web page, *Inclusion of Women and Minorities Policy Implementation* at: http://grants.nih.gov/grants/funding/women_min/women_min.htm. These documents supercede the 1994 Federal Register notice (http://grants.nih.gov/grants/guide/notice-files/not94-100.html) and the August 2000 notice in the NIH Guide to Grants and Contracts (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-048.html). These updated versions incorporate the definition of clinical research as reported in the 1997 Report of the NIH Director's Panel on Clinical research and the Office of Management and Budget (OMB) Directive 15 racial and ethnic categories to be used when reporting population data. They also provide additional guidance on reporting analyses of sex/gender and racial/ethnic differences in intervention effects for NIH-defined Phase III clinical trials (See Appendices E and F).

- In June 2001, clarified the definition for Clinical Research as reported in the 1997 Report of the NIH Director's Panel on Clinical research. NIH adopted the definition of clinical research as: (1) Patient-oriented research. Research conducted with human subjects (or on material of human origin such as tissues, specimens and cognitive phenomena) for which an investigator (or colleague) directly interacts with human subjects. Excluded from this definition are in vitro studies that utilize human tissues that cannot be linked to a living individual. Patient-oriented research includes: (a) mechanisms of human disease, (b) therapeutic interventions, (c) clinical trials, and (d) development of new technologies; (2) Epidemiologic and behavioral studies; and (3) Outcomes research and health services research http://www.nih.gov/news/crp/97report/execsum.htm

- The Office of Management and Budget (OMB) Directive 15 categories for reporting racial and ethnic population data were incorporated into the updated Guide Notice for Grants and Contracts. The primary difference from the previous categories were: (1) the Hispanic

population are considered an ethnicity and reported separately from other racial data; and (2) there is a separate racial category for Asian population data and Hawaiian and Pacific Islander population data (See Appendix G).

- On August 2, 2000, an NIH Guide Notice was posted on the Internet with a link to the web page, *Inclusion of Women and Minorities Policy Implementation* at: http://grants.nih.gov/grants/funding/women_min/women_min.htm. This restated that NIH-defined Phase III clinical trials must be designed and conducted in a manner sufficient to allow for a valid analysis of whether the variables being studied affected women or members of minority groups differently than other subjects.

- A new term and condition of award statement was developed and applied to awards made after October 1, 2000 that have NIH-defined Phase III clinical trials. This statement indicates that a description of plans to conduct analyses, as appropriate, by sex/gender and/or racial/ethnic groups must be included in clinical trial protocols and the results of subset analyses must be reported to NIH in Progress Reports, Competitive Renewal Applications (or Contract Renewals/Extensions) and in the required Final Progress Report.

- Effective October 1, 2000, language was incorporated in the NIH solicitations for grant applications and contract proposals [Program Announcements (PAs), Request for Applications (RFAs), and Request for Proposals (RFPs)] that stated the requirements for NIH-defined Phase III clinical trials clarifying the requirements that: a) all applications or proposals and/or protocols must provide a description of plans to conduct analyses, as appropriate, to address differences by sex/gender and/or racial/ethnic groups, including subgroups if applicable, and b) all investigators must report accrual, and conduct and report analyses, as appropriate, by sex/gender and/or racial/ethnic group differences.

- Guidelines and instructions for reviewers and Scientific Review Administrators (SRAs) were developed to emphasize and clarify the need to review research proposals that are classified as NIH-defined Phase III clinical trials for both inclusion requirements and issues related to analyses by sex/gender and/or race/ethnicity. Instructions were developed for the proper documentation to include in summary statements to address adherence to these policies (See Appendix I)

Following completion of the updated guidelines and instructions, training to ensure compliance with this policy was provided to NIH program and review officials, grants and contracts management staff and current and prospective research investigators. Since August 2000, several training initiatives have occurred:

- As part of an NIH Symposium: Human Subjects Update, the revised policy on inclusion of women and minorities and the revised *NIH Instructions to Reviewers Guidelines for Evaluating the Inclusion of Women and Minorities as Subjects in Clinical Research* were used as the basis for a required training session for NIH staff in October 2000. This symposium focused on the updated human subjects policy and the way in which it would be implemented. The training session included a question and answer session that provided an opportunity to emphasize the importance of the policy and the importance of reviewer evaluation of the changes related to valid analyses in Phase III clinical trials. About 450 were in attendance, 400 viewed the session at satellite centers and another 175 participated

through videocast. The training materials are permanently archived in the training materials for NIH staff at:
http://odoerdb2.od.nih.gov/oer/training/esa/human_subjects/esa_hs_symposium.htm

- An additional training session regarding a Grants Policy Update: Humans and Animals was held in December, 2000 where several hundred more extramural and intramural researchers were trained. It included a section regarding the inclusion of human subjects in clinical research studies. The training materials may be found at the following web address: http://odoerdb2.od.nih.gov/oer/training/esa/grants_policy_update/esa_grants_policy_update.htm

- In December 2000, the NIH Tracking and Inclusion Committee held a training session for all NIH program and grants management staff to discuss with members of the technical team, data entry and collection issues regarding the current population tracking system and IMPAC II as well as offer suggestions for the development of the new population tracking module.

- In July 2001, NIH issued the newly revised Applications for a DHHS Public Health Service Grant (PHS 398, rev. 5/01). The instructions in the PHS 398 (rev. 5/01) describe the requirements for designing Phase III clinical trails to provide valid analysis by sex/gender and race/ethnicity. These instructions continue to be the most frequently accessed NIH documents by the research, review, and NIH staff communities.

- In addition, the Questions and Answers section of the *Outreach Notebook for the NIH Guidelines on Inclusion of Women and Minorities as Subjects in Clinical Research* is currently being revised and will be published this fall as Frequently Asked Questions (FAQs) on the NIH website for the inclusion of women and minorities policy implementation at: http://grants.nih.gov/grants/funding/women_min/women_min.htm as well as on the ORWH website http://www4.od.nih.gov/orwh/fy97-98trkg.pdf. These FAQs are being developed and reviewed by members of the Tracking and Inclusion Committee to provide additional guidance to researchers and NIH staff on implementing the inclusion policy for women and minorities in clinical research, the new reporting requirements for inclusion data, and information for submitting an application, application submission, peer review and funding.

Throughout and following training, Program Officials continue to monitor, verify and document at the time of an award that policy requirements, including sex/gender analysis, are met and, when annual progress reports are submitted, they will continue to determine and document whether there is ongoing compliance with these policy requirements. In addition, Review Officials will introduce and discuss with reviewers the Guidelines/Instructions for reviewing Phase III clinical trials and the requirements for sufficient sample size to conduct valid analyses by sex/gender. When new and continuing applications are deficient in meeting the policy requirements, grants management and program officials will withhold funding until the Principal Investigator (PI) has satisfactorily addressed the policy requirements.

The *NIH Subcommittee Reviewing Inclusion Issues* also collected comments on the tracking system used prior to 2000 and identified issues relating to data entry, including quality control and the mechanisms of data entry. Improvements were recommended for the development of a new electronic database for grant administration and management which will include a user-friendly computerized information system for collecting and reporting inclusion data. In preparation for the launch of the new system, further training of

NIH staff responsible for monitoring and entering population data from NIH-funded investigators, will be undertaken.

## REFERENCES


1. Public Law 103-43. National Institutes of Health Revitalization Act of 1993. 42 USC 289 (a)(1).

2. NIH Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research, 59 Fed. Reg. 14508-14513 (1994).

3. *Women's Health: NIH Has Increased Its Efforts to Include Women in Research* (GAO/HEHS-00-96, May, 2000).

4. Updated: NIH Policy and Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research, NIH Guide for Grants and Contracts, (October, 2001).

5. Hayunga, E. G.,Costello, M. D. Pinn, V. W., "Demographics of Study Populations", *Applied Clinical Trials*, Vol. 6, No. 1, p. 41-45, 1997.

6. Hayunga, E. G. and Pinn V. W., "Implementing the 1994 NIH Guidelines", *Applied Clinical Trials*, Vol. 5, No. 10, p. 34-40, 1996.

7. Hayunga, E. G. and Pinn V. W., "NIH Response to Researchers' Concerns", *Applied Clinical Trials*, Vol. 5, No. 11, p. 59-64, 1996.

8. LaRosa, J. H., Seto, B., Caban, C. E., Hayunga, E. G., "Including Women and Minorities in Clinical Research", *Applied Clinical Trials*, Vol. 4, No. 5, p. 31-38, 1995.

9. McCarthy, C. R., "Historical Background of Clinical Trials Involving Women and Minorities", *Academic Medicine*, Vol. 69, No. 9, p. 695-698, 1994.

10. Pinn, V. W., "The Role of the NIH's Office of Research on Women's Health", *Academic Medicine,* Vol. 69, No. 9, p. 698-702, 1994.


For Additional Information on the implementation of the inclusion policy, please visit:

1. NIH Office of Extramural Research Inclusion of Women and Minorities Policy Implementation Website: http://grants.nih.gov/grants/funding/women_min/women_min.htm

2. Revitalization Act of 1993, 42 USC 289 (a)(1): http://grants.nih.gov/grants/guide/notice-files/not94-100.html

3. NIH Policy on Reporting Racial and Ethnicity Data: Subjects in Clinical Research, NIH Guide for Grants and Contracts Web page: http://grants.nih.gov/grants/guide/notice-files/NOT-OD-01-053.html

4. Office of Research on Women's Health Website: http://www4.od.nih.gov/orwh/fy97-98trkg.pdf

# Table A. Level of Compliance with Inclusion Policy in New Extramural Grant Applications as Assessed During Scientific Peer Review

| Council Dates | | Jan-95 | May-95 | Aug-95 | Oct-95 | Jan-96 | May-96 | Aug-96 | Oct-96 | Jan-97 | May-97 | Aug-97 | Oct-97 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Total Number of Applications Reviewed | (#) | 12,886 | 14,027 | 424 | 12,832 | 12,028 | 12,125 | 846 | 11,760 | 12,037 | 12,082 | 505 | 12,402 |
| | | | | | | | | | | | | | |
| Number of Applications with Human Subjects | (#) | 5,101 | 5,359 | 162 | 5,260 | 4,521 | 4,676 | 374 | 4,653 | 4,562 | 4,704 | 271 | 4,671 |
| | | | | | | | | | | | | | |
| Number (percent) of applications approved by IRG as submitted | (#) | 4,707 | 4,986 | 157 | 4,914 | 4,218 | 4,385 | 360 | 4,359 | 4,250 | 4,379 | 259 | 4,382 |
| | (%) | 92.28% | 93.04% | 96.91% | 93.42% | 93.30% | 93.78% | 96.26% | 93.68% | 93.16% | 93.09% | 95.57% | 93.81% |
| Number (percent) of applications with unacceptable minority inclusion | (#) | 175 | 131 | 1 | 126 | 146 | 115 | 4 | 129 | 134 | 115 | 2 | 104 |
| | (%) | 3.43% | 2.44% | 0.62% | 2.40% | 3.23% | 2.46% | 1.07% | 2.77% | 2.94% | 2.44% | 0.74% | 2.23% |
| Number (percent) of applications with unacceptable sex/gender inclusion | (#) | 33 | 29 | 2 | 22 | 21 | 23 | 1 | 14 | 17 | 20 | 6 | 20 |
| | (%) | 0.65% | 0.54% | 1.23% | 0.42% | 0.46% | 0.49% | 0.27% | 0.30% | 0.37% | 0.43% | 2.21% | 0.43% |
| Number (percent) of applications with both unacceptable minority AND sex/gender inclusion | (#) | 186 | 213 | 2 | 198 | 136 | 153 | 9 | 151 | 161 | 190 | 4 | 165 |
| | (%) | | | | | | | | | | | | |
| Total Number (percent) of applications with unacceptable minority inclusion | (#) | 361 | 344 | 3 | 324 | 282 | 268 | 13 | 280 | 295 | 305 | 6 | 269 |
| | (%) | 7.08% | 6.42% | 1.85% | 6.16% | 6.24% | 5.73% | 3.48% | 6.02% | 6.47% | 6.48% | 2.21% | 5.76% |
| Total Number (percent) of applications with unacceptable sex/gender inclusion | (#) | 219 | 242 | 4 | 220 | 157 | 176 | 10 | 165 | 178 | 210 | 10 | 185 |
| | (%) | 4.29% | 4.52% | 2.47% | 4.18% | 3.47% | 3.76% | 2.67% | 3.55% | 3.90% | 4.46% | 3.69% | 3.96% |
| Total number (percent) unacceptable applications as submitted | (#) | 394 | 373 | 5 | 346 | 303 | 291 | 14 | 294 | 312 | 325 | 12 | 289 |
| | (%) | 7.72% | 6.96% | 3.09% | 6.58% | 6.70% | 6.22% | 3.74% | 6.32% | 6.84% | 6.91% | 4.43% | 6.19% |

# Table A. Level of Compliance with Inclusion Policy in New Extramural Grant Applications as Assessed During Scientific Peer Review (continued)

| Council Dates | | Jan-98 | May-98 | Aug-98 | Oct-98 | Jan-99 | May-99 | Aug-99 | Oct-99 | Jan-00 | May-00 | Aug-00 | Oct-00 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | |
| Total Number of Applications Reviewed | (#) | 11,149 | 12,918 | 589 | 12,484 | 12,603 | 14,340 | 700 | 13,965 | 13,195 | 14,967 | 906 | 13,716 |
| | | | | | | | | | | | | | |
| Number of Applications with Human Subjects | (#) | 4,252 | 5,005 | 295 | 4,849 | 4,940 | 5,603 | 451 | 5,560 | 5,255 | 6,160 | 406 | 5,772 |
| | | | | | | | | | | | | | |
| Number (percent) of applications approved by IRG as submitted | (#) | 3,977 | 4,705 | 276 | 4,530 | 4,635 | 5,246 | 413 | 5,242 | 4,967 | 5,825 | 390 | 5,465 |
| | (%) | 93.53% | 94.01% | 93.56% | 93.42% | 93.83% | 93.63% | 91.57% | 94.28% | 94.51% | 94.56% | 96.05% | 94.68% |
| Number (percent) of applications with unacceptable minority inclusion | (#) | 114 | 118 | 7 | 120 | 133 | 115 | 20 | 133 | 115 | 119 | 8 | 112 |
| | (%) | 2.68% | 2.36% | 2.37% | 2.47% | 2.69% | 2.05% | 4.43% | 2.39% | 2.18% | 1.93% | 1.97% | 1.94% |
| Number (percent) of applications with unacceptable sex/gender inclusion | (#) | 27 | 24 | 3 | 26 | 20 | 28 | 5 | 23 | 30 | 25 | 0 | 28 |
| | (%) | 0.63% | 0.48% | 1.02% | 0.54% | 0.40% | 0.50% | 1.11% | 0.41% | 0.57% | 0.40% | 0.00% | 0.48% |
| Number (percent) of applications with both unacceptable minority AND sex/gender inclusion | (#) | 134 | 158 | 9 | 173 | 152 | 214 | 13 | 162 | 143 | 191 | 16 | 167 |
| | (%) | | | | | | | | | | | | |
| Total Number (percent) of applications with unacceptable minority inclusion | (#) | 248 | 276 | 16 | 293 | 285 | 329 | 33 | 295 | 258 | 310 | 16 | 279 |
| | (%) | 5.83% | 5.51% | 5.42% | 6.04% | 5.77% | 5.87% | 7.32% | 5.31% | 4.90% | 5.03% | 3.94% | 4.83% |

# Table B. Extramural Awards that Required the Lifting of a Bar-To-Funding

| Council Dates | | Jan-95 | May-95 | Aug-95 | Oct-95 | Jan-96 | May-96 | Aug-96 | Oct-96 | Jan-97 | May-97 | Aug-97 | Oct-97 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Total number of awards | (#) | 3,476 | 3,902 | 129 | 3,344 | 3,548 | 3,759 | 228 | 3,378 | 3,874 | 3,958 | 222 | 3,817 |
| | | | | | | | | | | | | | |
| Number of awards involving human subjects | (#) | 1,287 | 1,421 | 51 | 1,263 | 1,260 | 1,352 | 92 | 1,254 | 1,394 | 1,470 | 106 | 1,401 |
| | | | | | | | | | | | | | |
| Number (percent) of awards involving human subjects that met the inclusion | (#) | 1,224 | 1,330 | 50 | 1,189 | 1,178 | 1,277 | 89 | 1,198 | 1,305 | 1,374 | 101 | 1,324 |
| | (%) | 95.10% | 93.60% | 98.04% | 94.14% | 93.49% | 94.45% | 96.74% | 95.53% | 93.62% | 93.47% | 95.28% | 94.50% |
| Number (percent) of awards where *minority only* bar-to-funding was removed by program staff (M_U) | (#) | 29 | 26 | | 22 | 43 | 29 | 0 | 22 | 38 | 47 | 0 | 24 |
| | (%) | 2.25% | 1.83% | 0.00% | 1.74% | 3.41% | 2.14% | 0.00% | 1.75% | 2.73% | 3.20% | 0.00% | 1.71% |
| Number (percent) of awards where *sex/gender only* bar-to-funding was removed by program staff (G_U) | (#) | 3 | 6 | | 3 | 3 | 3 | 0 | 3 | 8 | 5 | 4 | 10 |
| | (%) | 0.23% | 0.42% | 0.00% | 0.24% | 0.24% | 0.22% | 0.00% | 0.24% | 0.57% | 0.34% | 3.77% | 0.71% |
| Number (percent) of awards where both minority AND sex/gender bar-to-funding was removed by program staff | (#) | 31 | 59 | 1 | 49 | 36 | 43 | 3 | 31 | 43 | 44 | 1 | 43 |
| | (%) | 2.41% | 4.15% | 1.96% | 3.88% | 2.86% | 3.18% | 3.26% | 2.47% | 3.08% | 2.99% | 0.94% | 3.07% |
| *Total number (percent) of awards where minority bar-to-funding was removed by program staff* | (#) | 60 | 85 | 1 | 71 | 79 | 72 | 3 | 53 | 81 | 91 | 1 | 67 |
| | (%) | 4.66% | 5.98% | 1.96% | 5.62% | 6.27% | 5.33% | 3.26% | 4.23% | 5.81% | 6.19% | 0.94% | 4.78% |
| *Total number (percent) of awards where sex/gender bar-to-funding was removed by program staff* | (#) | 34 | 65 | 1 | 52 | 39 | 46 | 3 | 34 | 51 | 49 | 5 | 53 |
| | (%) | 2.64% | 4.57% | 1.96% | 4.12% | 3.10% | 3.40% | 3.26% | 2.71% | 3.66% | 3.33% | 4.72% | 3.78% |
| Total number (percent) of awards where bar-to-funding was removed | (#) | 63 | 91 | 1 | 74 | 82 | 75 | 3 | 56 | 89 | 96 | 5 | 77 |
| | (%) | 4.90% | 6.40% | 1.96% | 5.86% | 6.51% | 5.55% | 3.26% | 4.47% | 6.38% | 6.53% | 4.72% | 5.50% |

# Table B. Extramural Awards that Required the Lifting of a Bar-To-Funding (continued)

| Council Dates | | Jan-98 | May-98 | Aug-98 | Oct-98 | Jan-99 | May-99 | Aug-99 | Oct-99 | Jan-00 | May-00 | Aug-00 | Oct-00 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Total number of awards | (#) | 3,863 | 4,363 | 209 | 4,019 | 4,247 | 4,824 | 298 | 4,278 | 4,415 | 4,960 | 307 | 4,389 |
| | | | | | | | | | | | | | |
| Number of awards involving human subjects | (#) | 1,431 | 1,594 | 104 | 1,442 | 1,625 | 1,832 | 156 | 1,616 | 1,633 | 1,964 | 129 | 1,683 |
| | | | | | | | | | | | | | |
| Number (percent) of awards involving human subjects that met the inclusion requirements as submitted | (#) | 1,368 | 1,524 | 98 | 1,370 | 1,556 | 1,753 | 143 | 1,552 | 1,582 | 1,893 | 124 | 1,632 |
| | (%) | 95.60% | 95.61% | 94.23% | 95.01% | 95.75% | 95.69% | 91.67% | 96.04% | 96.87% | 96.38% | 96.12% | 96.96% |
| Number (percent) of awards where *minority only* bar-to-funding was removed by program staff (M_U) | (#) | 30 | 17 | 3 | 30 | 21 | 31 | 5 | 25 | 18 | 27 | 1 | 23 |
| | (%) | 2.10% | 1.07% | 2.88% | 2.08% | 1.29% | 1.69% | 3.21% | 1.55% | 1.10% | 1.37% | 0.77% | 1.36% |
| Number (percent) of awards where *sex/gender only* bar-to-funding was removed by program staff (G_U) | (#) | 9 | 7 | 1 | 8 | 9 | 9 | 2 | 4 | 13 | 7 | 0 | 8 |
| | (%) | 0.63% | 0.44% | 0.96% | 0.55% | 0.55% | 0.49% | 1.28% | 0.25% | 0.79% | 0.35% | 0.00% | 0.47% |
| Number (percent) of awards where both minority AND sex/gender bar-to-funding was removed by program staff | (#) | 24 | 46 | 2 | 34 | 39 | 39 | 6 | 35 | 20 | 37 | 4 | 20 |
| | (%) | 1.68% | 2.89% | 1.92% | 2.36% | 2.40% | 2.13% | 3.85% | 2.17% | 1.22% | 1.88% | 3.10% | 1.18% |
| *Total number (percent) of awards where minority bar-to-funding was removed by program staff* | (#) | 54 | 63 | 5 | 64 | 60 | 70 | 11 | 60 | 38 | 64 | 5 | 43 |
| | (%) | 3.77% | 3.95% | 4.81% | 4.44% | 3.69% | 3.82% | 7.05% | 3.71% | 2.32% | 3.25% | 3.87% | 2.55% |
| *Total number (percent) of awards where sex/gender bar-to-funding was removed by program staff* | (#) | 33 | 53 | 3 | 42 | 48 | 48 | 8 | 39 | 33 | 44 | 4 | 28 |
| | (%) | 2.31% | 3.32% | 2.88% | 2.91% | 2.95% | 2.62% | 5.13% | 2.41% | 2.02% | 2.24% | 3.10% | 1.66% |
| Total number (percent) of awards where bar-to-funding was removed | (#) | 63 | 70 | 6 | 72 | 69 | 79 | 13 | 64 | 51 | 71 | 5 | 51 |
| | (%) | 4.40% | 4.39% | 5.77% | 4.99% | 4.25% | 4.31% | 8.33% | 3.96% | 3.12% | 3.61% | 3.87% | 3.03% |

# Table C. Inclusion by Sex in All Research Studies Receiving Funding in FY1998

| | Extramural Studies | | Intramural Studies | |
|---|---|---|---|---|
| | Phase III trials* | Other clinical research** | On-site | Off-site |
| Protocols reporting women only | 74 | 669 | 96 | 23 |
| Protocols reporting men only | 18 | 235 | 59 | 15 |
| Protocols reporting both women and men | 368 | 3,730 | 804 | 130 |
| Protocols involving men, women and Unknown*** | 38 | 221 | | 18 |
| Sex composition reported as Unknown | 2 | 45 | | 12 |
| Protocols reporting men and Unknown | 2 | 1 | | 1 |
| Protocols reporting women and Unknown | 1 | 6 | | |
| Early Stage studies where enrollment data has not yet been collected | 75 | 1,462 | 136 | 44 |
| **Totals** | **578** | **6,369** | **1,095** | **243** |

* According to the NIH Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research:, Phase III clinical investigations usually involve several hundred or more human subjects, for the purpose of evaluating an experimental intervention in comparison with standard or control intervention or comparing two or more existing treatments.

** Human subject studies that are not Phase III trials.

*** Many studies may be generic.

# Table C. Inclusion by Sex in All Research Studies Receiving Funding in FY1999

| | Extramural Studies | | Intramural Studies | |
|---|---|---|---|---|
| | Phase III trials* | Other clinical research** | On-site | Off-site |
| Protocols reporting women only | 114 | 774 | 90 | 36 |
| Protocols reporting men only | 34 | 294 | 64 | 14 |
| Protocols reporting both women and men | 369 | 4,329 | 848 | 155 |
| Protocols involving men, women and Unknown*** | 24 | 260 | | 26 |
| Sex composition reported as Unknown | 2 | 57 | | 10 |
| Protocols reporting men and Unknown | 2 | 6 | | 1 |
| Protocols reporting women and Unknown | 0 | 8 | | 1 |
| Early Stage studies where enrollment data has not yet been collected | 44 | 1,631 | 128 | 69 |
| **Totals** | **589** | **7,359** | **1,130** | **312** |

* According to the NIH Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research:, Phase III clinical investigations usually involve several hundred or more human subjects, for the purpose of evaluating an experimental intervention in comparison with standard or control intervention or comparing two or more existing treatments.

** Human subject studies that are not Phase III trials.

*** Many studies may be generic.

# Examples of Single Sex Extramural Research Studies

**Examples of Studies of Selected Protocols That Include Male-Only Human Subjects**

Managing Uncertainty in Advanced Prostate Cancer
Long Term Lithium for Aggressive Conduct Disorder
Dietary Fat Modulation of Androgen Metabolism in Men
Aging and Skeletal Muscle Fatty Acid Metabolism
Nutritional and Hormonal Biomarkers in Prostate Cancer
Head Injury & Alzheimer's Disease
Genetic Epidemiology of Alzheimer's Disease in Twins
Epidemiology of Male Infertility - Cryptorchidism
Medical Therapy for Benigh Prostatic Hyperplasia (BPH) - Data Coordinating Center
HIV Prevention Intervention for Young Men
Managing Uncertainty in Stage B Prostate Cancer
Comprehensive High Blood Pressure (HBP) Care for Young Urban Black Men
Serum Albumin, Orthostatic Hypotension in Frail
Psychophysiology of Visible and Invisible Trauma

**Examples of Studies of Selected Protocols That Include Female-Only Human Subjects**

Divalproex Sodium/Placebo in Bronchopulmonary Dysplasia (BPD)
Hormone Replacement and Metabolic Cardiovascular Risk
Detection of Presymptomatic Alzheimer Disease by functional Magnetic Resonance Imaging (fMRI)
Breastfeeding Services for Low Birth Weight (LBW) Infants-Outcomes and Cost
Epidemiology of Osteoporosis in Systemic Lupus Erythematosus (SLE)
Trials of Prevention of Cognitive Decline in Women
Breast Cancer Surveillance in a Defined Population
Diet, Activity and Adolescent Weight Changes
Women's Health Initiative
Cross Ethnic Nursing Study of Weight Management in Women
Women's Estrogen for Stroke Trial (WEST)
Persistence or Transience of HPV Infection in Women
Urine Screening Test to Detect Bacteriuria in Pregnancy
Infant Mortality in Rural Yunnan, China

# Table 1 (1998) Aggregate Enrollment Data for All Extramural Research Protocols

| | American Indians and Alaska Natives | | Asian and Pacific Islanders | | Black - Not Hispanic | | Hispanic | | White - Not Hispanic | | Other and Unknown | | Total | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | # | % | # | % | # | % | # | % | # | % | # | % | # | % |
| Female | 29,959 | 0.7% | 803,076 | 18.5% | 660,702 | 15.2% | 298,867 | 6.9% | 2,330,017 | 53.7% | 216,288 | 5.0% | 4,338,909 | 67.0% |
| | | | | | | | | | | | | | | |
| Male | 24,081 | 1.2% | 192,455 | 9.2% | 341,128 | 16.4% | 191,350 | 9.2% | 1,210,602 | 58.1% | 124,463 | 6.0% | 2,084,079 | 32.2% |
| | | | | | | | | | | | | | | |
| Unknown | 1,620 | 2.8% | 7,470 | 13.0% | 2,176 | 3.8% | 14,909 | 25.9% | 10,092 | 17.5% | 21,350 | 37.1% | 57,617 | 0.9% |
| | | | | | | | | | | | | | | |
| Total | 55,660 | 0.9% | 1,003,001 | 15.5% | 1,004,006 | 15.5% | 505,126 | 7.8% | 3,550,711 | 54.8% | 362,101 | 5.6% | 6,480,605 | 100.0% |

Number of Protocols: 6,947

# Table 2 (1999) Aggregate Enrollment Data for All Extramural Research Protocols

| | American Indians and Alaska Natives | | Asian and Pacific Islanders | | Black - Not Hispanic | | Hispanic | | White - Not Hispanic | | Other and Unknown | | Total | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | # | % | # | % | # | % | # | % | # | % | # | % | # | % |
| Female | 33,991 | 0.7% | 829,502 | 18.2% | 653,412 | 14.4% | 313,065 | 6.9% | 2,468,041 | 54.2% | 254,403 | 5.6% | 4,552,414 | 61.6% |
| | | | | | | | | | | | | | | |
| Male | 29,707 | 1.1% | 247,475 | 8.9% | 451,895 | 16.2% | 221,781 | 8.0% | 1,633,898 | 58.6% | 202,372 | 7.3% | 2,787,128 | 37.7% |
| | | | | | | | | | | | | | | |
| Unknown | 288 | 0.6% | 855 | 1.9% | 4,179 | 9.3% | 16,084 | 35.6% | 5,820 | 12.9% | 17,913 | 39.7% | 45,139 | 0.6% |
| | | | | | | | | | | | | | | |
| Total | 63,986 | 0.9% | 1,077,832 | 14.6% | 1,109,486 | 15.0% | 550,930 | 7.5% | 4,107,759 | 55.6% | 474,688 | 6.4% | 7,384,681 | 100.0% |

Number of Protocols: 7,948

# Aggregate Enrollment Data for All Extramural Research Protocols

FY98 Data Table Comments:

More females (4,338,909 or 67.0%) than males (2,084,079 or 32.2%) are enrolled in aggregate Extramural Research protocols.
Largest identified racial group is White, Not-Hispanic at 54.8%.
Largest identified racial minority groups are Black, Not-Hispanic at 15.5% and Asian/Pacific Islanders at 15.5%.
Smallest identified racial minority group is American Indian/Alaska Natives at 0.9%.

FY99 Data Table Comments:

More females (4,552,414 or 61.6%) than males (2,787,128 or 37.7) are enrolled in aggregate Extramural Research protocols.
Largest identified racial group is White, Not-Hispanic at 55.6%.
Largest identified racial minority groups is Black, Not-Hispanic at 15.0%.
Smallest identified racial minority group is American Indian/Alaska Natives at 0.9%.
The large Asian/Pacific Islander accrual reflects a number of NCI-supported epidemiology studies conducted in Asia, Hawaii and California

# Table 3 (1998) Aggregate Enrollment Data for All Extramural Research Protocols Excluding Male-Only & Female-Only Protocols Funded in FY1998

| | American Indians and Alaska Natives | | Asian and Pacific Islanders | | Black - Not Hispanic | | Hispanic | | White - Not Hispanic | | Other and Unknown | | Total | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | # | % | # | % | # | % | # | % | # | % | # | % | # | % |
| Female | 26,567 | 1.0% | 185,719 | 7.3% | 500,707 | 19.7% | 249,381 | 9.8% | 1,433,509 | 56.5% | 140,221 | 5.5% | 2,536,104 | 55.0% |
| | | | | | | | | | | | | | | |
| Male | 23,915 | 1.2% | 166,962 | 8.3% | 334,357 | 16.6% | 189,162 | 9.4% | 1,179,768 | 58.5% | 122,281 | 6.1% | 2,016,445 | 43.7% |
| | | | | | | | | | | | | | | |
| Unknown | 1,620 | 2.8% | 7,470 | 13.0% | 2,176 | 3.8% | 14,909 | 26.0% | 10,092 | 17.6% | 21,114 | 36.8% | 57,381 | 1.2% |
| | | | | | | | | | | | | | | |
| Total | 52,102 | 1.1% | 360,151 | 7.8% | 837,240 | 18.2% | 453,452 | 9.8% | 2,623,369 | 56.9% | 283,616 | 6.2% | 4,609,930 | 100.0% |

Number of Protocols: 4,413

# Table 4 (1999) Aggregate Enrollment Data for All Extramural Research Protocols Excluding Male-Only & Female-Only Protocols Funded in FY1999

| | American Indians and Alaska Natives | | Asian and Pacific Islanders | | Black - Not Hispanic | | Hispanic | | White - Not Hispanic | | Other and Unknown | | Total | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | # | % | # | % | # | % | # | % | # | % | # | % | # | % |
| Female | 29,853 | 1.2% | 167,725 | 6.8% | 504,250 | 20.4% | 258,584 | 10.4% | 1,318,085 | 53.2% | 197,183 | 8.0% | 2,475,680 | 50.1% |
| | | | | | | | | | | | | | | |
| Male | 29,459 | 1.2% | 159,956 | 6.6% | 420,593 | 17.3% | 216,121 | 8.9% | 1,402,815 | 57.8% | 197,582 | 8.1% | 2,426,526 | 49.1% |
| | | | | | | | | | | | | | | |
| Unknown | 288 | 0.7% | 855 | 1.9% | 4,179 | 9.5% | 16,084 | 36.5% | 5,820 | 13.2% | 16,840 | 38.2% | 44,066 | 0.9% |
| | | | | | | | | | | | | | | |
| Total | 59,600 | 1.2% | 328,536 | 6.6% | 929,022 | 18.8% | 490,789 | 9.9% | 2,726,720 | 55.1% | 411,605 | 8.3% | 4,946,272 | 100.0% |

Number of Protocols: 5,049

# Aggregate Enrollment Data for All Extramural Research Protocols Excluding Male-Only & Female-Only Protocols

FY98 Data Table Comments:

There were 6,947 protocols of which 743 were women-only protocols, 253 were men-only protocols and 1,538 were early stage studies where enrollment data have not yet been collected.
The remaining 4,413 protocols include both females (55%) and males (43%).
Largest identified racial group is White, Not-Hispanic at 2,623,369 or 56.9%.
Largest identified racial minority group is Black - Not Hispanic at 837,240 or 18.2%
Smallest identified racial minority group is American Indian/Alaska Native at 52,102 or 1.1%.

FY99 Data Table Comments:

There were 7,948 extramural protocols of which 888 were women-only protocols, 328 were men-only protocols and 1,683 were early stage studies where enrollment data have not yet been collected.
The remaining 5,049 protocols include both females (50%) and males (49%).
Largest identified racial group is White, Not-Hispanic at 2,726,720 or 55.1%.
Largest identified racial minority group is Black - Not Hispanic at 929,022 or 18.8%.
Smallest identified racial minority group is American Indian/Alaska Native at 59,600 or 1.2%.

# Table 5 (1998) Aggregate Enrollment Data for Extramural Phase III Protocols Funded in FY1998

| | American Indians and Alaska Natives | | Asian and Pacific Islanders | | Black - Not Hispanic | | Hispanic | | White - Not Hispanic | | Other and Unknown | | Total | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | # | % | # | % | # | % | # | % | # | % | # | % | # | % |
| Female | 2,195 | 0.6% | 11,796 | 3.5% | 50,052 | 14.7% | 24,008 | 7.1% | 235,271 | 69.3% | 16,211 | 4.8% | 339,533 | 67.2% |
| | | | | | | | | | | | | | | |
| Male | 1,480 | 0.9% | 8,477 | 5.2% | 26,456 | 16.1% | 16,291 | 9.9% | 100,802 | 61.5% | 10,444 | 6.4% | 163,950 | 32.5% |
| | | | | | | | | | | | | | | |
| Unknown | 10 | 0.7% | 3 | 0.2% | 413 | 28.6% | 268 | 18.5% | 630 | 43.6% | 122 | 8.4% | 1,446 | 0.3% |
| | | | | | | | | | | | | | | |
| Total | 3,685 | 0.7% | 20,276 | 4.0% | 76,921 | 15.2% | 40,567 | 8.0% | 336,703 | 66.7% | 26,777 | 5.3% | 504,929 | 100.0% |

Number of Protocols : 578

# Table 6 (1999) Aggregate Enrollment Data for Extramural Phase III Protocols Funded in FY1999

| | American Indians and Alaska Natives | | Asian and Pacific Islanders | | Black - Not Hispanic | | Hispanic | | White - Not Hispanic | | Other and Unknown | | Total | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | # | % | # | % | # | % | # | % | # | % | # | % | # | % |
| Female | 2,132 | 0.7% | 13,314 | 4.2% | 37,827 | 12.0% | 17,097 | 5.4% | 221,098 | 70.4% | 22,484 | 7.2% | 313,952 | 63.3% |
| | | | | | | | | | | | | | | |
| Male | 1,590 | 0.9% | 10,697 | 5.9% | 24,605 | 13.6% | 12,950 | 7.2% | 114,416 | 63.3% | 16,447 | 9.1% | 180,705 | 36.5% |
| | | | | | | | | | | | | | | |
| Unknown | 4 | 0.4% | 6 | 0.6% | 80 | 7.4% | 37 | 3.4% | 310 | 28.5% | 649 | 59.8% | 1,086 | 0.2% |
| | | | | | | | | | | | | | | |
| Total | 3,726 | 0.8% | 24,017 | 4.8% | 62,512 | 12.6% | 30,084 | 6.1% | 335,824 | 67.7% | 39,580 | 8.0% | 495,743 | 100.0% |

Number of Protocols : 589

# Aggregate Enrollment Data for Extramural Phase III Protocols

FY98 Data Comments:

Substantial numbers of women and minorities are enrolled in Phase III research protocols funded in 1998.
There were more females (339,533 or 67.2%) than males (163,950 or 32.5%) enrolled in Phase III research protocols.
Among minority subjects, the largest racial minority group is Black, Not-Hispanic at 76,921 or 15.2%.
Smallest identified racial group is American Indian/Alaska Natives at 3,685 or 0.7%.

FY99 Data Comments:

Substantial numbers of women and minorities are enrolled in Phase III research protocols funded in 1999.
There were more females (313,952 or 63.3%) than males (180,705 or 36.5%) enrolled in Phase III research protocols.
Among minority subjects, the largest racial minority group is Black, Not-Hispanic at 62,512 or 12.6%.
Smallest identified racial group is American Indian/Alaska Natives at 3,726 or 0.8%.

# Table 7 (1998) Aggregate Enrollment Data for Extramural Phase III Research Protocols Excluding Male-Only & Female-Only Protocols Funded in FY1998

| | American Indians and Alaska Natives | | Asian and Pacific Islanders | | Black - Not Hispanic | | Hispanic | | White - Not Hispanic | | Other and Unknown | | Total | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | # | % | # | % | # | % | # | % | # | % | # | % | # | % |
| Female | 1,408 | 1.0% | 7,856 | 5.3% | 26,145 | 17.8% | 16,419 | 11.2% | 81,669 | 55.5% | 13,528 | 9.2% | 147,025 | 47.7% |
| | | | | | | | | | | | | | | |
| Male | 1,468 | 0.9% | 8,441 | 5.3% | 25,587 | 16.0% | 16,148 | 10.1% | 97,724 | 61.2% | 10,393 | 6.5% | 159,761 | 51.8% |
| | | | | | | | | | | | | | | |
| Unknown | 10 | 0.7% | 3 | 0.2% | 413 | 28.6% | 268 | 18.5% | 630 | 43.6% | 122 | 8.4% | 1,446 | 0.5% |
| | | | | | | | | | | | | | | |
| Total | 2,886 | 0.9% | 16,300 | 5.3% | 52,145 | 16.9% | 32,835 | 10.7% | 180,023 | 58.4% | 24,043 | 7.8% | 308,232 | 100.0% |

Number of Protocols: 411

# Table 8 (1999) Aggregate Enrollment Data for Extramural Phase III Research Protocols Excluding Male-Only & Female-Only Protocols Funded in FY1999

| | American Indians and Alaska Natives | | Asian and Pacific Islanders | | Black - Not Hispanic | | Hispanic | | White - Not Hispanic | | Other and Unknown | | Total | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | # | % | # | % | # | % | # | % | # | % | # | % | # | % |
| Female | 1,422 | 1.1% | 9,070 | 6.9% | 22,144 | 16.9% | 10,939 | 8.3% | 68,168 | 51.9% | 19,571 | 14.9% | 131,314 | 45.9% |
| | | | | | | | | | | | | | | |
| Male | 1,557 | 1.0% | 10,109 | 6.6% | 21,097 | 13.7% | 11,589 | 7.5% | 94,761 | 61.4% | 15,099 | 9.8% | 154,212 | 53.8% |
| | | | | | | | | | | | | | | |
| Unknown | 4 | 0.5% | 6 | 0.7% | 80 | 9.3% | 37 | 4.3% | 310 | 36.0% | 423 | 49.2% | 860 | 0.3% |
| | | | | | | | | | | | | | | |
| Total | 2,983 | 1.0% | 19,185 | 6.7% | 43,321 | 15.1% | 22,565 | 7.9% | 163,239 | 57.0% | 35,093 | 12.3% | 286,386 | 100.0% |

Number of Protocols: 396

# Aggregate Enrollment Data for Extramural Phase III Research Protocols Excluding Male-Only & Female-Only Protocols

FY98 Data Table Comments

There were 578 protocols of which 74 were women-only protocols, 18 were men-only protocols and 75 protocols were early stage studies where enrollment data have not yet been collected.
The remaining 411 protocols include both females (47%) and males (51%).
Largest identified racial group is White, Not-Hispanic at 180,025 or 58.4%
Largest identified racial minority group is Black - Not Hispanic at 52,145 or 16.9%.
Smallest identified racial minority group is American Indian/Alaska Native at 2,886 or 0.9%.

FY99 Data Table Comments

There were 589 protocols of which 114 were women-only protocols, 34 were men-only protocols and 45 protocols were early stage studies where enrollment data have not yet been collected.
The remaining 396 protocols include both females (46%) and males (53%).
Largest identified racial group is White, Not-Hispanic at 163,239 or 57.0%.
Largest identified racial minority group is Black - Not Hispanic at 43,321 or 15.1%.
Smallest identified racial minority group is American Indian/Alaska Native at 2,983 or 1.0%.

## Table 9 (1998). Aggregate Enrollment Data for Intramural Research Protocols Funded in FY1998 (Includes On-site and Off-site)

| | American Indians and Alaska Natives | | Asian and Pacific Islanders | | Black - Not Hispanic | | Hispanic | | White - Not Hispanic | | Other and Unknown | | Total | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | # | % | # | % | # | % | # | % | # | % | # | % | # | % |
| Female | 8,304 | 1.1% | 232,972 | 30.5% | 42,459 | 5.6% | 10,205 | 1.3% | 446,675 | 58.5% | 22,782 | 3.0% | 763,397 | 50.8% |
| | | | | | | | | | | | | | | |
| Male | 7,460 | 1.2% | 192,976 | 30.7% | 34,406 | 5.5% | 11,145 | 1.8% | 368,736 | 58.7% | 13,266 | 2.1% | 627,989 | 41.8% |
| | | | | | | | | | | | | | | |
| Unknown | 12 | 0.0% | 73 | 0.1% | 339 | 0.3% | 84 | 0.1% | 104,844 | 93.4% | 6,894 | 6.1% | 112,246 | 7.5% |
| | | | | | | | | | | | | | | |
| Total | 15,776 | 1.0% | 426,021 | 28.3% | 77,204 | 5.1% | 21,434 | 1.4% | 920,255 | 61.2% | 42,942 | 2.9% | 1,503,632 | 100.0% |

Number of Protocols: 1,338

## Table 10 (1999). Aggregate Enrollment Data for Intramural Research Protocols Funded in FY1999 (Includes On-site and Off-site)

| | American Indians and Alaska Natives | | Asian and Pacific Islanders | | Black - Not Hispanic | | Hispanic | | White - Not Hispanic | | Other and Unknown | | Total | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | # | % | # | % | # | % | # | % | # | % | # | % | # | % |
| Female | 9,910 | 1.0% | 242,790 | 23.5% | 55,288 | 5.4% | 20,863 | 2.0% | 654,775 | 63.4% | 49,002 | 4.7% | 1,032,628 | 47.3% |
| | | | | | | | | | | | | | | |
| Male | 8,810 | 0.8% | 204,676 | 18.1% | 44,756 | 4.0% | 16,588 | 1.5% | 823,213 | 72.7% | 33,894 | 3.0% | 1,131,937 | 51.8% |
| | | | | | | | | | | | | | | |
| Unknown | 22 | 0.1% | 94 | 0.5% | 239 | 1.2% | 27 | 0.1% | 3,195 | 16.1% | 16,274 | 82.0% | 19,851 | 0.9% |
| | | | | | | | | | | | | | | |
| Total | 18,742 | 0.9% | 447,560 | 20.5% | 100,283 | 4.6% | 37,478 | 1.7% | 1,481,183 | 67.8% | 99,170 | 4.5% | 2,184,416 | 100.0% |

Number of Protocols: 1,442

# Aggregate Enrollment Data for Intramural Research Protocols

FY98 Data Comments:

There were more females (763,397 or 50.8%) than males (627,989 or 41.8%) enrolled in aggregate Intramural research protocols.
Largest identified racial minority group is Asian/Pacific Islanders at 426,021 or 28.3%.
Smallest identified racial minority group is American Indian/Alaska Native at 15,731 or 1.1%.

FY99 Data Comments

There were more males (1,131,937 or 51.8%) than females (1,032,628 or 47.3%) enrolled in aggregate Intramural research protocols.
Differences in the enrollment of males and females is attributed primarily to improvements in reporting procedures. (ie, ensuring gender declaration and recording at enrollment).
The racial minority group with the largest increase in enrollment is Hispanic - an increase of 75% from FY98 to FY99.
The number of Black - Not Hispanic enrollees increased by 30% from FY98 to FY99.
Largest identified racial minority group is Asian/Pacific Islanders at 446,918 or 20.6%.
The large Asian/Pacific Islander population is due in part to a large clinical study being conducted in Vietnam.
Smallest identified racial minority group is American Indian/Alaska Native at 18,692 or 0.9%.
Patient enrollment in the intramural research program at the Warren Grant Magnuson Clinical Cener increased by 45% in FY99 compared to FY98.

## Appendix A

### Explanation of Sex and Minority Codes

| | |
|---|---|
| G1A | Includes both genders, scientifically acceptable. |
| G2A | Includes only women, scientifically acceptable. |
| G3A | Includes only men, scientifically acceptable. |
| G4A | Gender representation unknown, scientifically acceptable. |
| G1U | Includes both genders, but scientifically unacceptable. |
| G2U | Includes only women, scientifically unacceptable. |
| G3U | Includes only men, scientifically unacceptable. |
| G4U | Gender representation unknown, scientifically unacceptable. |

| | |
|---|---|
| M1A | Includes minorities and non-minorities, scientifically acceptable. |
| M2A | Includes only minorities, scientifically acceptable. |
| M3A | Includes only non-minorities, scientifically acceptable. |
| M4A | Minority representation unknown, scientifically acceptable. |
| M1U | Includes minorities and non-minorities, but scientifically unacceptable. |
| M2U | Includes only minorities, scientifically unacceptable. |
| M3U | Includes only non-minorities, scientifically unacceptable. |
| M4U | Minority representation unknown, scientifically unacceptable. |

When an application receives a "U" (unacceptable) code it automatically receives a bar-to-funding as well. If the bar is removed, the "U" is converted to "R" to designate that change in status.

# Appendix B

NIH Tracking and Inclusion Committee Members
- Full Committee
- Subcommittee Reviewing Inclusion Issues

# NIH Tracking and Inclusion Committee
# List of Members
# Year 2000-2001

**Office of the Director**

Yvonne Maddox

**Office of Research on Women's Health**

Vivian Pinn (Co-Chair), Angela Bates, Lisa Begg, Joyce Rudick, Virginia Hartmuller, Kay Anderson, Marietta Anthony

**Office of Extramural Research**

Della Hann*, Larry Fanning, Carlos Caban, Carla Flora, Vicki Fadeley, Donna Frahm, Sherry Zucker, Jan Heffernan, Chuck Selden, Belinda Seto, Jim Tucker, Rene Edwards, Aileen Kelly

**National Cancer Institute**

Marvin Kalt*, Diane Bronzert, Marilyn Gaston, Joe Harford, Michaele Christian, Paulette Gray, Karen Bashir, George Alexander, Ann Carpenter, Otis Brawley

**National Eye Institute**

Lore Anne McNicol*, Jack McLaughlin, William Darby

**National Heart, Lung, and Blood Institute**

Carl Roth (Co-Chair), Barbara Liu, Nancy Morris, Sharry Palagi, Ralph Van Wey, Juanita Coen

**National Human Genome Research Institute**

Monique Mansoura *, Joy Boyer, Emily Linde, Peggy McKoy

**National Institute on Aging**

Miriam Kelty *, Karen Bashir, Taylor Harden, David Reiter

**National Institute on Alcohol Abuse and Alcoholism**

Lorraine Gunzerath *; Mary Westcott, Carmen Richardson, Deborah Hendry

**National Institute of Allergy and Infectious Diseases**

Lai Tan *, Diane Adger-Johnson, Susan Schafer, Waquita Smith, Joyce Woodford, Diane Yerg, Milton Hernandez, Joan Kondratick

**National Institute of Arthritis and Musculoskeletal and Skin Diseases**

Christine Densmore *, Julia Freeman, Marcia Hahn, Kristen Ehrenspeck, Joanne Odenkirchen

* Indicates the IC Lead Representative to the Tracking and Inclusion Committee

## List of Members, continued...

**National Institute of Child Health and Human Development**
Darlene Levenson *, Douglas Shawver, Yvonne Maddox, Sandra Occipinti

**National Institute on Deafness and Other Communication Disorders**
Julie Gulya*, Sue Hamilton, Lynnette Hemsley, Jackie Jones

**National Institute of Dental and Craniofacial Research**
Norman Braveman *, Maryann Redford, Susan Hamilton, Trenita Davis

**National Institute of Diabetes, Digestive and Kidney Disorders**
Beth Paterson *, Patricia Robuck, Walter Stolz

**National Institute on Drug Addiction**
Jack Manischewitz *, Mark Swieter

**National Institute of Environmental Health Sciences**
Martha Barnes *

**National Institute of General Medical Sciences**
John Matala *, Alison Cole, Judit Camacho, Marcia Hahn

**National Institute of Mental Health**
Mary Lou Prince *, Mary Blehar, William Radcliffe, Pamela Wexler, Tracy Soto

**National Institute of Neurological Disorders and Stroke**
Meredith Temple *, Connie Atwell, Gladys Melendez-Bohler, Mary Beth Cheung, James Washington, Mary Graham

**National Institute of Nursing Research**
Carole Hudgings *, Robin Gruber

**National Library of Medicine**
Rita Richey *, Dwight Mowery

**Warren G. Magnuson Clinical Center**
Kim Jarema *, Dee Koziol, Kai Lakeman, Kim Hunt, Jerry King

**National Center for Complementary and Alternative Medicine**
Carol Fitzpatrick*, Eugene Hayunga, Dean Batten, Victoria Putprush, Joan Talley, Maliaka Pinkney

* Indicates the IC Lead Representative to the Tracking and Inclusion Committee

## List of Members, continued...

**National Center for Research Resources**
Louise Ramm *, Delores Lee, Patricia Newman, Stephen Seidel, Geoffrey Cheung

**Fogarty International Center**
Kathleen Michels *, Janice Solomon

**Center for Scientific Review**
Elliot Postow *

**Office of Intramural Research**
Alan Sandler

**National Center for Minority Health and Health Disparaties**
Eric Bailey*, John Ruffin

**National Institute of Biomedical Imaging and Bioengineering**
Joan Harmon *

* Indicates the IC Lead Representative to the Tracking and Inclusion Committee

# Subcommittee Reviewing Inclusion Issues
# List of Members
# Year 2000-2001

**Miriam Kelty**, **Chair**, National Institute of Aging
**Virginia Hartmuller**, Office of Research on Women's Health
**Angela Bates**, Office of Research on Women's Health

**Vickie Fadeley**, Office of Extramural Research
**Larry Fanning**, Office of Extramural Research
**Carla Flora**, Office of Extramural Research
**Donna Frahm**, Office of Extramural Research
**Carlos Caban**, Office of Extramural Research
**Renee Edwards**, Center for Information Technology
**Aileen Kelly**, Center for Information Technology
**Zaiga Tums**, Office of Acquisition Management and Policy
**Barbara Levy**, Office of Acquisition Management and Policy
**Mary Ellen Cheung**, National Institute on Neurological Disorders
**Meredith Temple**, National Institute on Neurological Disorders
**Darlene Levenson**, National Institute on Child Health and Human Development
**Jack Manischewitz**, National Institute on Drug Addiction
**Sharry Palagi**, National Heart, Lung, and Blood Institute
**Lai Tan**, National Institute of Allergy and Infectious Diseases
**Beth Paterson**, National Institute of Diabetes, Digestive and Kidney Disorders
**Kim Jarema,** Warren G. Magnuson Clinical Center
**Dee Koziol,** Warren G. Magnuson Clinical Center
**Margaret Holmes**, National Cancer Insitute
**Kim Witherspoon**, National CancerInstitute
**Martha Barnes,** National Institute of Environmental Health Sciences

# Appendix C

## Responses to the General Accounting Office (GAO) Report: "Women's Health: NIH Has Increased Its Efforts to Include Women in Research" GAO/HEHS-00-96, August 2001

**Status Report on Actions Taken on General Accounting Office (GAO) Report, "Women's Health: NIH Has Increased Its Efforts to Include Women in Research", GAO/HEHS-00-96, August 2001**

This document represents a status report of actions taken by the National Institutes of Health in response to recommendations of the May 2000 General Accounting Office Report, "Women's Health: NIH Has Increased Its Efforts to Include Women in Research."

**RECOMMENDATION #1**

**To strengthen the capacity of biomedical research to produce health information applicable to all segments of the population, we recommend that the director of NIH ensure that the agency implements the requirement that Phase III clinical trials be designed and carried out to allow for valid analysis of differences by sex as fully as it implements other elements of the inclusion policy. Specifically, we recommend that NIH appropriately communicate this requirement to applicants, that peer review groups explicitly determine whether each Proposed Phase III clinical study is required to have such a study design, and that Summary Statements document the initial reviewer's decision.**

- **NIH STATEMENT: Language in the NIH Guide Notice of August 1, 2000 would be incorporated in the IC guidelines and instructions for the submission and review of applications and proposals, to be effective October 1, 2000.**

  **CURRENT STATUS:**
  The NIH policy on the inclusion of women and minorities as subjects in clinical research was updated in August, 2000 for active grants, cooperative agreements, and contracts and applied to all new grant, cooperative agreement, and contract submissions beginning in October, 2000. The updated policy can be accessed at the following NIH Grants Policy website address: http://grants.nih.gov/grants/funding/women_min/women_min.htm. The *NIH Guide for Grants and Contracts* serves, in lieu of the Federal Register's compliance with the Administrative Procedures Act, as the official publication of NIH policies, procedures, and availability of funds. Researchers can access this information from the NIH Grants website through the URL: http://grants.nih.gov/grants/policy/policy.htm. The NIH website is one of the most frequently accessed sites by researchers and by the public and is used for both administrative announcements and reporting of more general scientific issues.

  Beginning with the October, 2000 receipt date, grant, cooperative agreement, and contract submissions requesting support for an NIH-defined Phase III clinical trial must adhere to this updated policy which specifies when a valid analysis by sex/gender and race/ethnicity of the intervention effect is required. All applications or proposals and/or protocols for a Phase III clinical trial require the research design and inclusion plan not only to describe the composition of the proposed study population but also to address differences by sex/gender and race/ethnicity describe plans to conduct valid analyses to address these differences. The

final protocol approved by the Institutional Review Board must include these plans for analysis.

In addition to the general announcements for all applicants, special steps have been taken to reinforce the NIH policy. As of October, 2000, investigators who respond to a Request for Applications (RFA), a Program Announcement (PA), or a Request for Proposals (RFP) are required to adhere to the specific requirements for NIH-defined Phase III clinical trials. The revision requires the inclusion of a description of plans to conduct analyses to address sex/gender and racial/ethnic differences and instructions that all investigators must report accrual of subjects and conduct as well as report analyses by sex/gender and~~/or~~ racial/ethnic group differences. Once the research study has been completed, analyses by sex/gender and~~/or~~ racial/ethnic differences are to be submitted to the NIH as part of the final progress report.

Relevant information for inclusion of women and minorities in clinical research studies may also be accessed through the *Inclusion of Women and Minorities Policy Implementation* web page at the following URL:
http://grants.nih.gov/grants/funding/women_min/women_min.htm.

- **NIH STATEMENT: Guidelines/Instructions for reviewers and SRAs would be developed that would emphasize and clarify the need to review research proposals containing NIH-defined Phase III clinical trials for both inclusion requirements and those related to sex/gender. Instructions were to be provided on the proper documentation to be included in summary statements to address adherence to these policies.**

  **CURRENT STATUS:**
  In February 2001, NIH issued new "NIH Instructions to Reviewers for Evaluating Research Involving Human Subjects in Grant and Cooperative Agreement Applications" as part of its commitment to the protection of human subjects from research risks and to the inclusion of women, minorities, and children in clinical research. These instructions consolidate information and instructions for reviewers concerning new, revised, or existing NIH policies for human subject protection, data and safety monitoring plans, and inclusion of women, minorities and children in clinical research. These instructions are available on the NIH website: http://grants.nih.gov/grants/peer/hs_review_inst.pdf . In the instruction document, the Scientific Review Groups are instructed that they must evaluate applications on these factors independently of any other review by Institutional Review Boards, NIH staff, or others.

  The instructions emphasize the importance of a thorough evaluation of the requirements for inclusion of women and minorities in clinical research applications submitted to the NIH. They specifically describe the requirements that clinical trials be designed to provide for valid analysis by sex/gender and race/ethnicity. The instructions remind reviewers that failure to address the issues related to inclusion of women and minorities adequately, must have a negative impact on the priority scores assigned for scientific and technical merit. Moreover,

the designation of an unacceptable plan for the inclusion of women and minorities results in a bar-to-funding by the NIH until the deficiencies are resolved.

- **NIH STATEMENT: Following completion of these actions, training would be provided to program and review official and grants and contracts management staff.**

  **CURRENT STATUS:**
  Since August 2000, several training initiatives have occurred and are ongoing. As part of an NIH Symposium: Human Subjects Update, the revised policy on inclusion of women and minorities and the revised *NIH Instructions to Reviewers for Evaluating the Inclusion of Women and Minorities as Subjects in Clinical Research* were used as the basis for a required training session for NIH staff in October 2000. This symposium focused on the updated human subjects policy and the way in which it would be implemented. The training session included a question and answer session that provided an opportunity to emphasize the importance of the policy and the importance of reviewer evaluation of the changes related to valid analyses in Phase III clinical trials. Some 450 NIH staff were in attendance, 400 viewed the remote session at satellite centers and another 175 participated through videocast. The training materials are permanently archived in the training materials for NIH staff at: http://odoerdb2.od.nih.gov/oer/training/esa/human_subjects/esa_hs_symposium.htm

  An additional training session regarding a Grants Policy Update: Humans and Animals was held in December, 2000 where several hundred more extramural and intramural researchers were provided updated instructions about inclusion of human subjects in clinical research studies. The training materials may be found at the following web address: http://odoerdb2.od.nih.gov/oer/training/esa/grants_policy_update/esa_grants_policy_update.htm

  In July 2001, NIH issued the newly revised Applications for a DHHS Public Health Service Grant (PHS 398, rev. 5/01). The instructions in the PHS 398 (rev. 5/01) describe the requirements for designing Phase III clinical trails to provide valid analysis by sex/gender and race/ethnicity. These instructions are the most frequently accessed NIH documents by the research, review, and NIH staff communities.

  In addition, the Questions and Answers section of the *Outreach Notebook for the NIH Guidelines on Inclusion of Women and Minorities as Subjects in Clinical Research* is currently being revised and will be published this fall as Frequently Asked Questions (FAQs) on the NIH website for the inclusion of women and minorities policy implementation at: http://grants.nih.gov/grants/funding/women_min/women_min.htm. These FAQs are being developed and reviewed by members of the NIH-wide Tracking and Inclusion Committee. They provide additional guidance to researchers and NIH staff on implementing the inclusion policy for women and minorities in clinical research, the new reporting requirements for inclusion data, and information for submitting an application, peer review and funding.

- **NIH STATEMENT: Program Officials would monitor, verify, and document, at time of award, whether policy requirements are met and, when annual progress reports are submitted, will determine and document whether compliance has continued.**

  **CURRENT STATUS:**
  Throughout and following training on these actions, Program Officials continue to monitor, verify and document, at time of award, whether policy requirements are met. At the time annual progress reports are submitted, they continue to determine and document whether there is ongoing compliance. When applications or proposals are deficient in meeting the policy requirements, grants and contracts management staff along with program officials will withhold funding until the Principal Investigator has satisfactorily addressed the policy requirements.

  Advisory Councils of each Institute and Center (IC) prepare biennial reports describing the manner in which they have complied with the inclusion guidelines mandated by law in the NIH Revitalization Act of 1993, Public Law 103-43, Section 485B (2)(f). In December, 2000, the Office of Research on Women's Health (ORWH) requested each IC Director to address compliance with the inclusion guidelines in their report submitted to members at their January or February, 2001 Advisory Council meetings. As of August 2001, ORWH has received reports from the ICs to be included in the *2000 Biennial Report Certifying Compliance with the NIH Policy on the Inclusion of Women and Minorities as Subjects in Clinical Research*. In their reports, ICs were asked to address procedures used to ensure compliance with the May 2000 GAO recommendations, including the requirements that clinical trials be designed to provide for a valid analysis of sex/gender and racial/ethnic differences.

**RECOMMENDATION #2**

**To improve the accuracy of NIH's tracking data on the inclusion of women and minorities, we recommend that the Director of the NIH ensure that the NIH staff who transmit data to the tracking system receive ongoing training on the requirements and purpose of the system.**

**5. NIH STATEMENT: The launch of a new electronic database for grant review, management and administration, which would include a computerized system for standardizing and collecting inclusion data, would occur before the end of the calendar year 2000.**

**CURRENT STATUS:**
The data tracking system for monitoring inclusion of women and minorities in clinical research is going through significant re-engineering. This re-engineering is driven by three main issues: (1) the need to develop a system that provides easy-to-use data entry and project monitoring by staff; (2) the ability to create clear, accurate, and timely NIH reports on inclusion data; and (3) the need to incorporate the 1997 OMB Directive 15 - standards for the classification of federal data on race and ethnicity.

The re-engineering of the NIH electronic tracking system was begun by OER in 2000. This system now includes a web-based set of tools that provides user-friendly access and data entry by NIH staff. In addition, the new system is part of the NIH enterprise data system, IMPAC II, and as such will be integral to extramural research grant administration that includes grant review, grants management and program operations. The new system will incorporate data reported using the new classifications in OMB Directive 15 and is consistent with the instructions and forms provided in the newly revised PHS 398 and 2590 (rev. 5/01). The design of the new system is currently being reviewed and accepted by NIH committees representing tracking and inclusion, grants management, health services administration, electronic research administration, and extramural policy and management. Development and testing of the new system is expected to continue through April 2002, with full deployment in May 2002. Analyses of inclusion data reported in FY2002 will be conducted with the new system. After completion of the re-engineered electronic database by OER, the ORWH will collaborate with OER and the Division of Workforce Development to develop training on the new system prior to its full implementation.

| Status of Activities on GAO Report on Women's Health (GAO/HEHS-00-96, May 2000) | | | |
|---|---|---|---|
| **Activity** | **Due Date** | **Status** | **Date Completed** |
| Notice in NIH Guide to Grants & Contracts - clarifies policy for gender analyses for Phase III clinical trials | *8/1/2000* | Completed - link from Women and Minorities Web Page at: http://grants.nih.gov/grants/funding/women_min/women_min.htm | *8/2/2000* |
| Language incorporated in NIH solicitations for grant applications and contract proposals (PA/RFA/RFP) indicating requirements for applications and reporting for Phase III clinical trials | *Effective 10/1/2000* | Completed document | *8/2/2000* |
| A new Terms and Conditions for Awards will be included in all grant, cooperative agreement, & contract awards containing Phase III clinical trials | *Effective 10/1/2000* | Completed document | *8/2/2000* |
| Guidelines/instructions for reviewers & SRAs developed clarifying the need to review research proposals containing Phase III clinical trials. Documentation required in summary statements addressing adherence to these policies | *10/26/2000* | Completed document http://grants.nih.gov/grants/peer/hs_review_inst.pdf | *02/2001* |

| Status of Activities on GAO Report on Women's Health (GAO/HEHS-00-96, May 2000) | | | |
|---|---|---|---|
| **Activity** | **Due Date** | **Status** | **Date Completed** |
| Train NIH program & review officials and grants & contracts management staff on updated policy for Phase III clinical trials (workshops, presentations at professional meetings & advisory committees; web-site didactic instructions; & on-line Q&A and fact sheets) | *Fall 2000* | Symposium training session for extramural staff (450) occurred on10/16 on new policies and procedures regarding human subjects. An additional 400 individuals viewed the symposium in satellite centers and 175 additional NIH staff utilized a VideoCast system.<br><br>An additional training session regarding a Grants Policy Update: Humans and Animals targeting extramural and intramural research, program and grants management, and review staff.<br><br>Video tapes and web-video access from the 10/16 and 12/11 training are available to NIH staff as needed.<br><br>Frequently Asked Questions document drafted<br><br>Training of Extramural and Intramural staff at December 2000 Full Tracking and Inclusion Committee Meeting. | *10/16/00*<br><br>*12/11/00*<br><br>*12/11/00* |
| ORWH & OER work together to ensure NIH staff are well-informed about data collection requirements of current tracking system | No end date | Continuing | |

| Status of Activities on GAO Report on Women's Health (GAO/HEHS-00-96, May 2000) | | | |
|---|---|---|---|
| **Activity** | **Due Date** | **Status** | **Date Completed** |
| NIH develop specific tracking/inclusion module to interface w/ IMPAC2 system. | 12/31/2000 | CIT/OER proposal for Sex/Gender and Minority Population Tracking System Development submitted on 10/27. Requirements analysis started 10/31 - to be completed by 12/15. | |
| NIH staff training on tracking system module to interface w/ IMPAC2 system. | Begin training when system developed | | |
| Training on current *NIH Tracking System* to members of *Full Tracking & Inclusion Committee*. | 12/11/2000 | OER conducted training on the current tracking system at the 12/11 *Full Tracking & Inclusion Committee* meeting. | 12/11/2000 |

## Appendix D

## Internet Homepage:
## Inclusion of Women and Minorities Policy Implementation

**http://grants.nih.gov/grants/funding/women_min/women_min.htm**

NATIONAL INSTITUTES OF HEALTH
Office of Extramural Research

# Inclusion of Women and Minorities Policy Implementation

**Current Policy Documents and References:**

**10/09/2001 NIH Guide Notice** - The NIH Policy on the Inclusion of Women and

Minorities as Subjects in Clinical Research was amended October 2001. Click here for a complete copy of the Amended Policy that provides full explanation of the October 2001 policy notice.

**08/08/2001 NIH Guide Notice** - NIH Policy on Reporting Race and Ethnicity Data:

Subjects in Clinical Research. This notice provides additional guidance and instruction for using the revised minimum standards for maintaining, collecting, and presenting data on race and ethnicity found in the PHS 398 (rev. 5/01) and PHS 2590 (rev. 5/01) instructions and forms.

**Inclusion Table (07/25/2001)** - Prior format for reporting sex/gender and race/ethnicity data using the 1977 OMB standards for the classification of federal data on race and ethnicity. This format is superceded by the Target/Planned Enrollment Table and Inclusion Enrollment Reports that use the 1997 OBM standards for the classification of federal data on race and ethnicity.

**Women's Inclusion as Participants in Research** - Page from the Office of Research on Women's Health (ORWH) Web site.

**Outreach Notebook for the NIH Guidelines on Inclusion of Women and Minorities as Subjects in Clinical Research** - To help investigators to understand and comply with the NIH's inclusion policies, the ORWH collaborated in the preparation and publication of this Notebook, available here in Adobe Acrobat (PDF) format. This publication contains two appendices. Appendix A summarizes the inclusion guidelines; Appendix B contains sample questions and answers to assist investigators in preparing their applications in accordance with the inclusion guidelines.

OUTREACH NOTEBOOK (Pages 1-39 of PDF file)
INCLUSION GUIDELINES (Pages 40-51 of PDF file)
QUESTIONS AND ANSWERS (Pages 52-87 of PDF file)

**Historical Documents and References:**

**08/02/2000 NIH Guide Notice** - NIH Guidelines on The Inclusion of Women and

Minorities as Subjects in Clinical Research - Updated August 2, 2000. Changes to the Guidelines, Sections 'III.B. NIH Phase III Clinical Trials' and 'V. Definitions' are highlighted in **bold** type.

**NIH Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research - Updated August 2, 2000** - A complete text of the Updated Guidelines, with changes to the Guidelines, Sections 'III.B. NIH Phase III Clinical Trials' and 'V. Definitions' highlighted in **bold** type. The list of NIH Contacts has also been updated.

**03/18/1994 NIH Guide Notice** - NIH Guidelines on The Inclusion of Women and Minorities as Subjects in Clinical Research.

Weblink: http://grants.nih.gov/grants/funding/women_min/women_min.htm

# Appendix E

## Amendment
## NIH Policy and Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research - October, 2001

**AMENDMENT: NIH POLICY AND GUIDELINES ON THE INCLUSION OF WOMEN AND MINORITIES AS SUBJECTS IN CLINICAL RESEARCH - OCTOBER, 2001**

Release Date: October 9, 2001

NOTICE: NOT-OD-02-001

National Institutes of Health

The National Institutes of Health policy on the Inclusion of Women and Minorities as Subjects in Clinical Research has been amended. A complete copy of the amended policy may be found on the "Inclusion of Women and Minorities Policy Implementation" web site: http://grants.nih.gov/grants/funding/women_min/women_min.htm. The October 2001 policy provides a consolidated, concise, and clear document of the updates and changes to the NIH policies to implement the original legislation (PL 103-43), the 1994 Federal Register notice (http://grants.nih.gov/grants/guide/notice-files/not94-100.html) and the August 2000 notice in the NIH Guide to Grants and Contracts (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-048.html).

EFFECTIVE DATE: This amended policy is effective immediately and applies to all grants and cooperative agreements currently active and to be awarded. Contract solicitations issued as of October 2001 must adhere to the amended policy.

The amended policy incorporates the following four points:

1. The definition of clinical research as reported in the "1997 Report of the NIH Director''s Panel on Clinical Research" is used to implement the NIH policy on the inclusion of women and minorities as subjects in clinical research. In June 2001, NIH adopted the definition of clinical research as: (1) Patient-oriented research. Research conducted with human subjects (or on material of human origin such as tissues, specimens and cognitive phenomena) for which an investigator (or colleague) directly interacts with human subjects. Excluded from this definition are in vitro studies that utilize human tissues that cannot be linked to a living individual. Patient-oriented research includes: (a) mechanisms of human disease, (b) therapeutic interventions, (c) clinical trials, and (d) development of new technologies; (2) Epidemiologic and behavioral studies; and (3) Outcomes research and health services research http://www.nih.gov/news/crp/97report/execsum.htm

2. Racial and ethnic categories have been updated in order to comply with the new standards issued by the Office of Management and Budget (OMB) in Directive No. 15 http://www.whitehouse.gov/omb/fedreg/ombdir15.html. This directive defines the minimum standards for maintaining, collecting, and presenting data on race and ethnicity for all Federal reporting. NIH is required to use these definitions to allow comparisons to other federal databases, especially the census and national health databases. The categories in this classification are social-political constructs and should not be interpreted as anthropological in nature.

3. Language governing NIH-defined Phase III clinical trials has been clarified in order to be consistent with the mandate for the inclusion of women and minorities as subjects in clinical research (PL103-43), the new PHS 398 form and OMB Directive 15. The amended policy provides additional guidance on the analyses and reporting of analyses of sex/gender, racial/ethnic and relevant subpopulation differences in intervention effects for NIH-defined Phase III clinical trials.

4. Roles and responsibilities of NIH staff and the extramural community have been updated with regard to the implementation of the NIH policy on the inclusion of women and minorities as subjects in clinical research. While this policy applies to all applicants/offerors for NIH-fundeded clinical research, certain individuals and groups have special roles and responsibilities with regard to its implementation.

# Appendix F

## NIH Policy and Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research Amended, October, 2001

# NIH POLICY AND GUIDELINES ON THE INCLUSION OF WOMEN AND MINORITIES AS SUBJECTS IN CLINICAL RESEARCH — Amended, October, 2001.

**NOTE:** Additional information concerning the NIH Policy on Inclusion of Women and Minorities as Subjects in Clinical Research is available at http://grants.nih.gov/grants/funding/women_min/women_min.htm.

**SUMMARY:** This notice updates the NIH policy on the inclusion of women and minorities as subjects in clinical research. It supercedes the 1994 Federal Register notice (http://grants.nih.gov/grants/guide/notice-files/not94-100.html) and the August 2000 notice in the NIH Guide to Grants and Contracts (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-048.html). It incorporates the definition of clinical research as reported in the 1997 Report of the NIH Director''s Panel on Clinical research. Also, this notice provides additional guidance on reporting analyses of sex/gender and racial/ethnic differences in intervention effects for NIH-defined Phase III clinical trials. The guidelines ensure that all NIH-funded clinical research will be carried out in a manner sufficient to elicit information about individuals of both sexes/genders and diverse racial and ethnic groups and, particularly in NIH-defined Phase III clinical trials, to examine differential effects on such groups. Since a primary aim of research is to provide scientific evidence leading to a change in health policy or standard of care, it is imperative to determine whether the intervention or therapy being studied affects women or men or members of minority groups and their subpopulations differently.

In June 2001, NIH adopted the definition of clinical research as: (1) Patient-oriented research. Research conducted with human subjects (or on material of human origin such as tissues, specimens and cognitive phenomena) for which an investigator (or colleague) directly interacts with human subjects. Excluded from this definition are in vitro studies that utilize human tissues that cannot be linked to a living individual. Patient-oriented research includes: (a) mechanisms of human disease, (b) therapeutic interventions, (c) clinical trials, and (d) development of new technologies; (2) Epidemiologic and behavioral studies; and (3) Outcomes research and health services research http://www.nih.gov/news/crp/97report/execsum.htm.

**EFFECTIVE DATE:** This amended policy is effective immediately and applies to all grants and cooperative agreements currently active and to be awarded. Contract solicitations issued as of October 2001 must adhere to the amended policy.

## I. LEGISLATIVE BACKGROUND

The NIH Revitalization Act of 1993, PL 103-43, signed into law on June 10, 1993, directed the NIH to establish guidelines for inclusion of women and minorities in clinical research.

The statute states that:

> In conducting or supporting clinical research for the purposes of this title, the Director of NIH shall ... ensure that (a) women are included as subjects in each project of such research; and (b) members of minority groups are included in such research. 492B(a)(1)

The statute further directed the NIH to establish guidelines to specify:

(a) the circumstances under which the inclusion of women and minorities as subjects in projects of clinical research is inappropriate ……;
(b) the manner in which clinical trials are required to be designed and carried out ……; and
(c) the operation of outreach programs …… 492B(d)(1)

The statute defines "clinical research" to include "clinical trials" and states that:

In the case of any clinical trial in which women or members of minority groups will be included as subjects, the Director of NIH shall ensure that the trial is designed and carried out in a manner sufficient to provide for valid analysis of whether the variables being studied in the trial affect women or members of minority groups, as the case may be, differently than other subjects in the trial. 492B(c)

Specifically addressing the issue of minority groups, the statute states that:

The term "minority group" includes subpopulations of minority groups. The Director of NIH shall, through the guidelines established...define the terms "minority group" and "subpopulation" for the purposes of the preceding sentence. 492B(g)(2)

The statute speaks specifically to outreach and states that:

The Director of NIH, in consultation with the Director of the Office of Research on Women's Health and the Director of the Office of Research on Minority Health, shall conduct or support outreach programs for the recruitment of women and members of minority groups as subjects in the projects of clinical research. 492B(a)(2)

The statute includes a specific provision pertaining to the cost of clinical research and, in particular clinical trials.

(A)(i) In the case of a clinical trial, the guidelines shall provide that the costs of such inclusion in the trial is (sic) not a permissible consideration in determining whether such inclusion is inappropriate. 492B(d)(2)

(ii) In the case of other projects of clinical research, the guidelines shall provide that the costs of such inclusion in the project is (sic) not a permissible consideration in determining whether such inclusion is inappropriate unless the data regarding women or members of minority groups, respectively, that would be obtained in such project (in the event that such inclusion were required) have been or are being obtained through other means that provide data of comparable quality. 492B(d)(2)

Exceptions to the requirement for inclusion of women and minorities are stated in the statute, as follows:

The requirements established regarding women and members of minority groups shall not apply to the project of clinical research if the inclusion, as subjects in the project, of women and members of minority groups, respectively-

(1) is inappropriate with respect to the health of the subjects;
(2) is inappropriate with respect to the purpose of the research; or
(3) is inappropriate under such other circumstances as the Director of NIH may designate. 492B(b)

(B) In the case of a clinical trial, the guidelines may provide that such inclusion in the trial is not required if there is substantial scientific data demonstrating that there is no significant difference between-

(i) the effects that the variables to be studied in the trial have on women or members of minority groups, respectively; and

(ii) the effects that the variables have on the individuals who would serve as subjects in the trial in the event that such inclusion were not required. 492B(d)(2)

**II. POLICY**

A. Inclusion of Women and Minorities as Subjects in Clinical Research

It is the policy of NIH that women and members of minority groups and their subpopulations must be included in all NIH-funded clinical research, unless a clear and compelling rationale and justification establishes to the satisfaction of the relevant Institute/Center Director that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. Exclusion under other circumstances may be made by the Director, NIH, upon the recommendation of an Institute/Center Director based on a compelling rationale and justification. Cost is not an acceptable reason for exclusion except when the study would duplicate data from other sources. Women of childbearing potential should not be routinely excluded from participation in clinical research. This policy applies to research subjects of all ages in all NIH-supported clinical research studies.

The inclusion of women and members of minority groups and their subpopulations must be addressed in developing a research design or contract proposal appropriate to the scientific objectives of the study/contract. The research plan/proposal should describe the composition of the proposed study population in terms of sex/gender and racial/ethnic group, and provide a rationale for selection of such subjects. Such a plan/proposal should contain a description of the proposed outreach programs for recruiting women and minorities as participants.

B. NIH-defined Phase III Clinical Trials: Planning, Conducting, and Reporting of Analyses for Sex/Gender and Race/Ethnicity Differences.

When an NIH-defined Phase III clinical trial is proposed, evidence must be reviewed to show whether or not clinically important sex/gender and race/ethnicity differences in the intervention effect are to be expected. This evidence may include, but is not limited to, data derived from prior animal studies, clinical observations, metabolic studies, genetic studies, pharmacology studies, and observational, natural history, epidemiology and other relevant studies.

Investigators must consider the following when planning, conducting, analyzing, and reporting an NIH-Defined Phase III clinical trial. Based on prior studies, one of the three situations below will apply:

1. Prior Studies Support the Existence of Significant Differences

If the data from prior studies strongly support the existence of significant differences of clinical or public health importance in intervention effect based on sex/gender, racial/ethnic, and relevant subpopulation comparisons, the primary question(s) to be addressed by the proposed NIH-defined Phase III clinical trial and the design of that trial must specifically accommodate this. For example, if men and women are thought to respond differently to an intervention,

then the Phase III clinical trial must be designed to answer two separate primary questions, one for men and the other for women, with adequate sample size for each.

The Research Plan (for grant applications) or Proposal (for contract solicitations) must include a description of plans to conduct analyses to detect significant differences in intervention effect (see DEFINITIONS - Significant Difference) by sex/gender, racial/ethnic groups, and relevant subpopulations, if applicable. The final protocol(s) approved by the Institutional Review Board (IRB) must include these plans for analysis. The award will require that for each funded protocol, investigators must report in their annual Progress Report cumulative subject accrual and progress in conducting analyses for sex/gender and race/ethnicity differences. If final analyses of sex/gender and race/ethnicity are not available at the time of the Final Progress Report or Competing Continuation for the grant, a justification and plan ensuring completion and reporting of the analyses are required. If final analyses are required as part of the contract, these analyses must be included as part of the deliverables. These requirements will be cited in the terms and conditions of all awards for grants, cooperative agreements and contracts supporting NIH-defined Phase III clinical trials.

Inclusion of the results of sex/gender, race/ethnicity and relevant subpopulations analyses is strongly encouraged in all publication submissions. If these analyses reveal no differences, a brief statement to that effect, indicating the groups and/or subgroups analyzed, will suffice.

2. Prior Studies Support No Significant Differences

If the data from prior studies strongly support no significant differences of clinical or public health importance in intervention effect based on sex/gender, racial/ethnic and/or relevant subpopulation comparisons, then sex/gender and race/ethnicity will not be required as subject selection criteria. However, the inclusion and analysis of sex/gender and/or racial/ethnic subgroups is still strongly encouraged.

3. Prior Studies Neither Support nor Negate Significant Differences

If the data from prior studies neither strongly support nor strongly negate the existence of significant differences of clinical or public health importance in intervention effect based on sex/gender, racial/ethnic, and relevant subpopulation comparisons, then the NIH-defined Phase III clinical trial will be required to include sufficient and appropriate entry of sex/gender and racial/ethnic participants, so that valid analysis of the intervention effects can be performed. However, the trial will not be required to provide high statistical power for these comparisons.

The Research Plan (for grant applications) or Proposal (for contract solicitations) must include a description of plans to conduct valid analysis (see DEFINITIONS - Valid Analysis) by sex/gender, racial/ethnic groups, and relevant subpopulations, if applicable. The final protocol(s) approved by the Institutional Review Board (IRB) must include these plans for analysis. The award will require that for each funded protocol, investigators must report in their annual Progress Report cumulative subject accrual and progress in conducting analyses for sex/gender and race/ethnicity differences. If final analyses of sex/gender and race/ethnicity are not available at the time of the Final Progress Report or Competing Continuation for the grant, a justification and plan ensuring completion and reporting of the analyses are required. If final analyses are required as part of the contract, these analyses must be included as part of the deliverables. These requirements will be cited in the terms and

conditions of all awards for grants, cooperative agreements and contracts supporting NIH-defined Phase III clinical trials.

Inclusion of the results of sex/gender, race/ethnicity and relevant subpopulations analyses is strongly encouraged in all publication submissions. If these analyses reveal no differences, a brief statement to that effect, indicating the groups and/or subgroups analyzed, will suffice.

For all three situations, cost is not an acceptable reason for exclusion of women and minorities from clinical trials.

**III. ROLES AND RESPONSIBILITIES**

While this policy applies to all applicants/offerors for NIH-supported clinical research, certain individuals and groups have special roles and responsibilities with regard to its implementation.

1. NIH Staff

The NIH staff provide educational opportunities for the extramural and intramural communities concerning this policy; monitor its implementation during the development, review, award and conduct of research; and manage the NIH research portfolio to comply with the policy.

2. Principal Investigators

Principal investigators should assess the theoretical and/or scientific linkages between sex/gender, race/ethnicity, and their topic of study. Following this assessment, the principal investigator and the applicant/offeror institution will address the policy in each application and proposal, providing the required information on inclusion of women and minorities and their subpopulations in clinical research projects, and any required justifications for exceptions to the policy.

For foreign awards and domestic awards with a foreign component, the NIH policy on inclusion of women and minority groups in research is the same as that for research conducted in the U.S. If there is scientific rationale for examining subpopulation group differences within the foreign population, investigators should consider designing their studies to accommodate these differences.

Investigators and their staff(s) are urged to develop appropriate and culturally sensitive outreach programs and activities commensurate with the goals of the study or objectives of the contract. The objective should be to actively recruit and retain the most diverse study population consistent with the purposes of the research project. Indeed, the purpose should be to establish a relationship between the investigator(s) and staff(s) and populations and community(ies) of interest such that mutual benefit is derived for participants in the study. Investigator(s) should take precautionary measures to ensure that ethical issues are considered, such that there is minimal possibility of coercion or undue influence in the incentives or rewards offered in recruiting into or retaining participants in studies.

To assist investigators and potential study participants, NIH staff have prepared educational materials, including a notebook titled the, "NIH Outreach Notebook On the Inclusion of Women and Minorities in Biomedical and Behavioral Research." The notebook as well as the Frequently Asked Questions document, are located at the following URL: http://grants.nih.gov/grants/funding/women_min/women_min.htm

3. Institutional Review Boards (IRBs)

It is the responsibility of the IRBs to address the ethical issues as outlined in Section IV(2) for Principal Investigators. As the IRBs implement the regulation for the protection of human subjects as described in Title 45 CFR Part 46, "Protection of Human Subjects", http://ohrp.osophs.dhhs.gov/humansubjects/guidance/45cfr46.htm they must also attend to the guidelines for the inclusion of women and minorities and their subpopulations in clinical research. They should take into account the Food and Drug Administration's "Guidelines for the Study and Evaluation of Gender Differences in the Clinical Evaluation of Drugs," Vol. 58 Federal Register 39406 http://www.fda.gov/cder/guidance/old036fn.pdf.

4. Peer Review Groups

In conducting peer review for scientific and technical merit, appropriately constituted initial review groups (including study sections), technical evaluation groups, and intramural review panels are instructed, as follows:

evaluate the proposed plan for the inclusion of minorities and both genders for appropriate representation or to evaluate the proposed justification when representation is limited or absent,

to evaluate the proposed exclusion of minorities and women on the basis that a requirement for inclusion is inappropriate with respect to the health of the subjects,

to evaluate the proposed exclusion of minorities and women on the basis that a requirement for inclusion is inappropriate with respect to the purpose of the research,

to determine whether the design of clinical trials is adequate to measure differences when warranted,

to evaluate the plans for valid analysis for NIH-defined Phase III clinical trials,

to evaluate the plans for recruitment/outreach for study participants, and

to include these criteria as part of the scientific assessment and evaluation.

The review instructions for grants are available on line at the following URL: http://grants.nih.gov/grants/peer/hs_review_inst.pdf

For contracts, the contracting officer will provide instructions for contract reviewers. Further information on instructions for contracts may be obtained at the following URL: http://oa.od.nih.gov/oamp/index.html.

Or contact:

National Institutes of Health
Division of Acquisition Policy and Evaluation
Office of Acquisition Management and Policy
6100 Executive Boulevard, Room 6C01
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Fax: 301- 402-1199

5. NIH Advisory Councils

In addition to other responsibilities for review of projects where the peer review groups have raised questions about the appropriate inclusion of women and minorities, the Advisory Council/Board of each Institute/Center shall prepare biennial reports, for inclusion in the overall NIH Director's biennial report, describing the manner in which the Institute/Center has complied with the provisions of the statute.

6. Institute/Center Directors

Institute/Center Directors and their staff shall ensure compliance with the policy.

7. NIH Director

The NIH Director may approve, on a case-by-case basis, the exclusion of projects, as recommended by the Institute/Center Director, that may be inappropriate to include within the requirements of these guidelines on the basis of circumstances other than the health of the subjects, the purpose of the research, or costs.

## IV. DEFINITIONS

Throughout the section of the statute pertaining to the inclusion of women and minorities, terms are used which require definition for the purpose of implementing these guidelines. These terms, drawn directly from the statute, are defined below.

A. Clinical Research

Clinical research is defined as:

(1) Patient-oriented research. Research conducted with human subjects (or on material of human origin such as tissues, specimens and cognitive phenomena) for which an investigator (or colleague) directly interacts with human subjects. Excluded from this definition are in vitro studies that utilize human tissues that cannot be linked to a living individual. Patient-oriented research includes: (a) mechanisms of human disease, (b) therapeutic interventions, (c) clinical trials, and (d) development of new technologies, (2) Epidemiologic and behavioral studies, (3) Outcomes research and health services research. http://www.nih.gov/news/crp/97report/execsum.htm

B. NIH-defined Clinical Trial

For the purpose of these guidelines, an NIH-defined "clinical trial" is a broadly based prospective Phase III clinical investigation, usually involving several hundred or more human subjects, for the purpose of evaluating an experimental intervention in comparison with a standard or control intervention or comparing two or more existing treatments. Often the aim of such investigation is to provide evidence leading to a scientific basis for consideration of a change in health policy or standard of care. The definition includes pharmacologic, non-pharmacologic, and behavioral interventions given for disease prevention, prophylaxis, diagnosis, or therapy. Community trials and other population-based intervention trials are also included.

C. Valid Analysis

The term "valid analysis" means an unbiased assessment. Such an assessment will, on average, yield the correct estimate of the difference in outcomes between two groups of subjects. Valid analysis can and should be conducted for both small and large studies. A valid analysis does not need to have a high statistical power for detecting a stated effect. The principal requirements for ensuring a valid analysis of the question of interest are:

allocation of study participants of both sexes/genders (males and females) and different

racial/ethnic groups to the intervention and control groups by an unbiased process such as randomization,

unbiased evaluation of the outcome(s) of study participants, and

use of unbiased statistical analyses and proper methods of inference to estimate and compare the intervention effects among the sex/gender and racial/ethnic groups.

D. Significant Difference

For purposes of this policy, a "significant difference" is a difference that is of clinical or public health importance, based on substantial scientific data. This definition differs from the commonly used "statistically significant difference," which refers to the event that, for a given set of data, the statistical test for a difference between the effects in two groups achieves statistical significance. Statistical significance depends upon the amount of information in the data set. With a very large amount of information, one could find a statistically significant, but clinically small difference that is of very little clinical importance. Conversely, with less information one could find a large difference of potential importance that is not statistically significant.

E. Racial and Ethnic Categories

1. Minority Groups

A minority group is a readily identifiable subset of the U.S. population that is distinguished by racial, ethnic, and/or cultural heritage.

The Office of Management and Budget (OMB) Directive No. 15 http://www.whitehouse.gov/omb/fedreg/ombdir15.html defines minimum standards for maintaining, collecting and presenting data on race and ethnicity for all Federal reporting. NIH is required to use these definitions to allow comparisons to other federal databases, especially the census and national health databases. The categories in this classification are social-political constructs and should not be interpreted as anthropological in nature.

When an investigator is planning data collection on race and ethnicity, these categories shall be used. The collection of greater detail is encouraged. However, more detailed items should be designed in a way that they can be aggregated into these required categories. Using respondent self-report or self-identification to collect an individual''s data on ethnicity and race, investigators should use two separate questions with ethnicity information collected first

followed by the option to select more than one racial designation. Respondents shall be offered the opportunity to select more than one racial designation. When data are collected separately, provision shall be made to report the number of respondents in each racial category who are Hispanic or Latino.

The following definitions apply for ethnic categories.

**Hispanic or Latino** - a person of Cuban, Mexican, Puerto Rican, South or Central American, or other Spanish culture or origin, regardless of race. The term "Spanish origin" can also be used in addition to "Hispanic or Latino."

**Not Hispanic or Latino**

The following definitions apply for racial categories.

**American Indian or Alaska Native** - a person having origins in any of the original peoples of North, Central, or South America, and who maintains tribal affiliations or community attachment.

**Asian** - a person having origins in any of the original peoples of the Far East, Southeast Asia, or the Indian subcontinent including, for example, Cambodia, China, India, Japan, Korea, Malaysia, Pakistan, the Philippine Islands, Thailand, and Vietnam. (Note: Individuals from the Philippine Islands have been recorded as Pacific Islanders in previous data collection strategies.)

**Black or African American** - a person having origins in any of the black racial groups of Africa. Terms such as "Haitian" or "Negro" can be used in addition to "Black or African American."

**Native Hawaiian or Other Pacific Islander** - a person having origins in any of the original peoples of Hawaii, Guam, Samoa, or other Pacific Islands.

2. Majority Group

**White** - a person having origins in any of the original peoples of Europe, the Middle East, or North Africa.

NIH recognizes the diversity of the U.S. population and that changing demographics are reflected in the changing racial and ethnic composition of the population. The terms "minority groups" and "minority subpopulations" are meant to be inclusive, rather than exclusive, of differing racial and ethnic categories.

3. Subpopulations

Each racial and ethnic group contains subpopulations that are delimited by geographic origins, national origins and/or cultural differences. It is recognized that there are different ways of defining and reporting racial and ethnic subpopulation data. The subpopulation to which an individual is assigned depends on self-reporting of specific origins and/or cultural heritage. Attention to subpopulations also applies to individuals who self identify with more than one race or ethnicity. Researchers should be cognizant of the possibility that these racial/ethnic combinations may have biomedical, behavioral, and/or social-cultural implications related to the scientific question under study.

F. Outreach Strategies

These are outreach efforts by investigators and their staff(s) to appropriately recruit and retain populations of interest into research studies. Such efforts should represent a thoughtful and culturally sensitive plan of outreach and generally include involvement of other individuals and organizations relevant to the populations and communities of interest, e.g., family, religious organizations, community leaders and informal gatekeepers, and public and private institutions and organizations. The objective is to establish appropriate lines of communication and cooperation to build mutual trust and cooperation such that both the study and the participants benefit from such collaboration.

## V. NIH CONTACTS FOR MORE INFORMATION

The following senior extramural staff from the NIH Institutes and Centers may be contacted for further information about the policy and relevant Institute/Center programs:

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# Appendix G

# NIH Policy on
# Reporting Race and Ethnicity Data:
# Subjects in Clinical Research

**NIH POLICY ON REPORTING RACE AND ETHNICITY DATA: SUBJECTS IN CLINICAL RESEARCH**

Release Date: August 8, 2001

NOTICE: NOT-OD-01-053

National Institutes of Health

POLICY: The NIH has adopted the 1997 Office of Management and Budget (OMB) revised minimum standards for maintaining, collecting, and presenting data on race and ethnicity for all grant applications, contract and intramural proposals and for all active research grants, cooperative agreements, contract and intramural projects. The minimum standards are described in the 1997 OMB Directive 15, http://www.whitehouse.gov/OMB/fedreg/ombdir15.html.

SUMMARY: This document provides additional guidance and instruction for using the revised minimum standards for maintaining, collecting, and presenting data on race and ethnicity found in the PHS 398 (rev. 5/01) and PHS 2590 (rev.5/01) instructions and forms http://grants.nih.gov/grants/forms.htm. Comparable information will be provided in research and development contract solicitations and awards for intramural projects. This document should be used in conjunction with the instructions in the PHS 398 and PHS 2590 instructions and forms.

The 1997 OMB revised minimum standards include two ethnic categories (Hispanic or Latino, and Not Hispanic or Latino) and five racial categories (American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or Other Pacific Islander, and White). The categories in this classification are social-political constructs and should not be interpreted as being anthropological in nature. Using self-reporting or self-identification to collect an individual''s data on ethnicity and race, investigators should use two separate questions with ethnicity information collected first followed by the option to select more than one racial designation.

Collection of this information and use of these categories is required for research that meets the NIH definition of clinical research.

EFFECTIVE DATE: This policy applies to all new applications and proposals, annual progress reports, competing continuation applications, competing supplement applications for research grants, contracts, and intramural projects as of January 10, 2002.

I. Revised Minimum Standards for Maintaining, Collecting, and Presenting Federal Data on Race and Ethnicity

The following are the ethnic and racial definitions for the minimum standard categories (1997 OMB Directive 15).

Ethnic Categories:

Hispanic or Latino: A person of Cuban, Mexican, Puerto Rican, South or Central American, or other Spanish culture or origin, regardless of race. The term "Spanish origin" can also be used in addition to "Hispanic or Latino."

Not Hispanic or Latino

Racial Categories:

American Indian or Alaska Native: A person having origins in any of the original peoples of North, Central, or South America, and who maintains tribal affiliations or community attachment.

Asian: A person having origins in any of the original peoples of the Far East, Southeast Asia, or the Indian subcontinent including, for example, Cambodia, China, India, Japan, Korea, Malaysia, Pakistan, the Philippine Islands, Thailand, and Vietnam. (Note: Individuals from the Philippine Islands have been recorded as Pacific Islanders in previous data collection strategies.)

Black or African American: A person having origins in any of the black racial groups of Africa. Terms such as "Haitian" or "Negro" can be used in addition to "Black or African American."

Native Hawaiian or Other Pacific Islander: A person having origins in any of the original peoples of Hawaii, Guam, Samoa, or other Pacific Islands.

White: A person having origins in any of the original peoples of Europe, the Middle East, or North Africa.

Using respondent self-report or self-identification to collect an individual's data on ethnicity and race, investigators should use two separate questions with ethnicity information collected first followed by the option to select more than one racial designation.

When reporting these data in the aggregate, investigators should report: (a) the number of respondents in each ethnic category; (b) the number of respondents who selected only one category for each of the five racial categories; (c) the total number of respondents who selected multiple racial categories reported as the "number selecting more than one race"; and, (d) the number of respondents in each racial category who are Hispanic or Latino. Investigators may provide the detailed distributions, including all possible combinations, of multiple responses to the racial designations as additional information. However, more detailed items should be designed in a way that they can be aggregated into the required categories for reporting purposes. NIH is required to use these definitions to allow comparisons to other federal databases, especially the census and national health databases. Federal agencies will not present data on detailed categories if doing so would compromise data quality or confidentiality standards.

II. Guidance on Reporting Ethnicity/Race and Sex/Gender in Clinical Research

NIH requires all grants, contracts, and intramural projects conducting clinical research to address the Inclusion of Women and Minorities (see http://grants.nih.gov/grants/funding/women_min/women_min.htm). NIH defines clinical

research as: (1) Patient-oriented research. Research conducted with human subjects (or on material of human origin such as tissues, specimens and cognitive phenomena) for which an investigator (or colleague) directly interacts with human subjects. Excluded from this definition are in vitro studies that utilize human tissues that cannot be linked to a living individual. Patient-oriented research includes: (a) mechanisms of human disease, (b) therapeutic interventions, (c) clinical trials, or (d) development of new technologies. (2) Epidemiologic and behavioral studies. (3) Outcomes research and health services research.

New Applications (type 1), Competing Continuations (type 2), Requests for Proposals, and Intramural Projects

Submitting Applications or Proposals Involving the Collection of New/Additional Data in Clinical Research:

Investigators are instructed to provide plans for the total number of subjects proposed for the study and to provide the distribution by ethnic/racial categories and sex/gender. This information must be reported using the newly revised categories and according to the new format provided in the Targeted/Planned Enrollment table
http://grants.nih.gov/grants/funding/phs398/enrollment.pdf

Submitting Applications or Proposals Using Existing Data in Clinical Research with No Plans for Collecting New/Additional Data:

Investigators are instructed to provide plans for the total number of subjects proposed for the study and to provide the distribution by ethnic/racial categories and sex/gender. Under these circumstances, investigators are not required to re-contact subjects solely to comply with the newly revised categories. If the existing data on ethnicity and race allows accurate correspondence with the new categories, the investigator can use the format in the Targeted/Planned Enrollment table. However, if the existing data do not allow accurate correspondence with the new categories, information may be reported using the former categories and according to the format in the 4/98 Version of the Inclusion Table
http://grants.nih.gov/grants/funding/women_min/InclusionOld_Form.pdf

Annual Progress Reports (type 5) and Competing Supplement Applications

In Annual Progress Reports and Competing Supplement Applications, investigators conducting clinical research are required to provide the cumulative total enrollment of subjects to-date (as well as any proposed additions to the Targeted/Planned enrollment in the case of Competing Supplement Applications) and to present the distribution by ethnic/racial categories and sex/gender.

If Data Collection is Ongoing, Such that New Subjects Will be Enrolled and/or Additional Data Will be Collected from Human Subjects:

Investigators may choose to report ethnicity/race and sex/gender sample composition using EITHER the format in the former 4/98 Version of the Inclusion Table OR the new Inclusion Enrollment Report http://grants.nih.gov/grants/funding/phs398/enrollmentreport.pdf [Note: If

investigators with on-going data collection choose to report information using the new Inclusion Enrollment Report, they must continue to use this format for the remaining years of the project.]

If Data Collection is Complete, Such that No New/Additional Subject Contact is Planned:

Investigators may EITHER continue to report using the former categories and according to the 4/98 Version of the Inclusion Table, OR, if data allow accurate correspondence with the new categories, use the format in the new Inclusion Enrollment Report.

III. Frequently Asked Questions

1. What categories should I use in my application to estimate race and ethnicity, given the new OMB standards?

Investigators should use the categories described in the PHS 398 instructions and listed in the table "Targeted/Planned Enrollment Table" for New Applications. First, the investigator should report the anticipated total number of males and females to be enrolled by Ethnicity (Hispanic or Latino, Not Hispanic or Latino). Then, the investigator should report the anticipated total number of males and females by Racial Categories (American Indian or Alaska Native, Asian, Native Hawaiian or Other Pacific Islander, Black or African American, White). The total number of subjects in the Ethnic Category section of the table should equal the total number of subjects in the Racial Categories section. Investigators do not need to estimate the anticipated number of individuals reporting multiple racial categories (either total number reporting multiple categories or number reporting specific combinations) for New Applications. However, the investigator must follow the OMB guidelines, which include allowing respondents to select multiple race categories, once data collection commences.

2. What if my new application involves analyzing secondary data in which the race and ethnicity categories do not comply with the new OMB guidelines?

If an investigator is using secondary data sets that do not conform to the new OMB guidelines and does not plan to collect any new/additional data from the subjects, this should be noted in the New Application. In this circumstance, the investigator should complete the "Targeted/Planned Enrollment Table" for a New Application and the "Inclusion Enrollment Report" for Continuation Applications, Competing Supplement Applications, and Annual Grant Progress Reports if the data allow. However, if the existing data do not allow accurate correspondence with the new categories, the investigator should report the information using the prior categories and use the 4/98 Version of the Inclusion Table.

3. There are many ways of tabulating the multiple race and ethnicity responses, particularly since the race and ethnicity categories are not mutually exclusive. Do the numbers I report have to "add up"?

The numbers in several parts of the two tables must be the same. In both the "Targeted/Planned Enrollment Table" for a New Application and the "Inclusion Enrollment Report " for Continuation Applications, Competing Supplement Applications, and Annual Progress Reports, the sum in "Ethnic Category: Total of All Subjects" must equal the sum in "Racial Categories:

Total of All Subjects." In addition, the "Racial Categories: Total Hispanics or Latinos" in Part B of the "Inclusion Enrollment Report Table" must equal the Total Hispanic or Latino number reported in Part A of the "Inclusion Enrollment Report." Footnotes in the tables clearly identify which numbers must be the same.

4. Can I use the Targeted/Planned Enrollment Table or the Enrollment Inclusion Report to collect data from individuals?

Neither the Targeted/Planned Enrollment Tablet nor the Enrollment Inclusion Report should be used for collecting data from individuals. These tables are only to be used for reporting aggregate data.

To collect data from an individual respondent, investigators should use respondent self-report or self-identification and use two separate questions. The first question should be about ethnicity, followed by a question that provides the option of selecting one or more racial designations. An example of a format for collecting information from an individual can be found in the ""Ethnic Origin and Race"" section of the Personal Data Form Page in the PHS 398 (rev. 5/01) http://grants.nih.gov/grants/funding/phs398/personal.pdf

5. Can I ask more detailed questions about ethnicity and race than these guidelines indicate?

The revised OMB guidelines provide minimal standards for data collection. Indeed, researchers are encouraged to explore collecting additional types of information on race and ethnicity that will provide additional insights into the relationships between race and ethnicity and health. For example, after asking the ethnicity and then the race questions, researchers may opt to ask study participants who choose multiple categories to identify the group that they identify with primarily. Further questions identifying membership in subpopulations within the ethnic and racial categories provided by OMB may also be considered. The scientific question being addressed in the study should guide investigators' decisions regarding collection of any additional information on ethnicity or race. Information on subpopulations may be reported by listing the information in an attachment to the required table.

6. I have already begun data collection and my categories do not comply with the new OMB standards. Do I need to change my questions on race and ethnicity in the middle of the study?

If data collection has already begun, we do not expect investigators to change their questions on race and ethnicity prior to the completion of the study. For Annual Progress Reports, in this circumstance, investigators should note that the research project was initiated prior to the implementation of the new reporting guidelines. If the data do not accurately correspond with the new categories, the investigator may continue to use the format in the 4/98 Version of the Inclusion Table.

7. I began data collection prior to the new standards, but my race and ethnicity questions comply with the new standards. I submitted my original estimates of the study composition using the old standards. How should I present the data in the progress report?

If you began your data collection prior to the implementation of the new standards but your questions on race and ethnicity comply with the new standards, the choice is left up to the investigator as to how to present the data for Annual Progress Reports. We suggest completion of the new Inclusion Enrollment Report.

8. How should I report race and ethnicity data when my research involves a foreign population?

Investigators are encouraged to design their data collection instruments in ways that allow respondent self-identification of their racial and ethnic affiliation. However, these items should be designed in a way that they can be aggregated into the required categories. Also, the investigator can report on any racial/ethnic subpopulations by listing this information in an attachment to the required table. This may be particularly useful when distinctive subpopulations are relevant to the scientific hypotheses being studied.

When completing the tables, investigators should asterisk and footnote the table indicating that data includes foreign participants. If the aggregated data only includes foreign participants, the investigator should provide information in one table with an asterisk and footnote. However, if the study includes both domestic and foreign participants, we suggest the investigator complete two separate tables — one for domestic data and one for foreign data, with an asterisk and footnote accompanying the table with foreign data.

9. How do the 1997 OMB revised standards differ from the previous standards?

OMB issued the previous standards for maintaining, collecting, and presenting data on race and ethnicity in 1977. The minimum acceptable categories were: American Indian or Alaska Native; Asian or Pacific Islander; Black, not of Hispanic origin; Hispanic; White, not of Hispanic origin.

The 1997 OMB revised standards now include two ethnic categories (Hispanic or Latino or Not Hispanic or Latino) and five racial categories (American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or Other Pacific Islander, and White). When using self-reporting or self-identification to collect data on ethnicity and race, investigators should use two separate questions with ethnicity information collected first followed by the option to select more than one racial designation.

Additional Information and NIH Contacts Additional information on NIH policy regarding the Inclusion of Women and Minorities in Clinical Research can be found at the website http://grants.nih.gov/grants/funding/women_min/women_min.htm.

The following senior extramural staff from the NIH Institutes and Centers may be contacted for further information about the policy and relevant Institute/Center programs:

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# APPENDIX H

## NIH Inclusion Tables for Target and Enrollment Data

- **Old Table for Target & Enrollment Data Collection**
- **New Table for Target Data Collection**
- **New Table for Enrollment Data Collection**

OLD TABLE - TARGET/ENROLLMENT DATA

**INCLUSION TABLE**

**This report format should NOT be used for data collection from study participants.**

**Principal Investigator/Project Director** _____
**(Last, First, Middle)**

**Grant Number (if known):** _____

**STUDY TITLE:** _____

**Total Enrollment:** _____ **Protocol Number:** _____

| | American Indian or Alaskan Native | Asian or Pacific Islander | Black, not of Hispanic Origin | Hispanic | White, not of Hispanic Origin | Other or Unknown | Total |
|---|---|---|---|---|---|---|---|
| Female | | | | | | | |
| Male | | | | | | | |
| Unknown | | | | | | | |
| Total | | | | | | | |

NEW TABLE - TARGET DATA

Principal Investigator/Program Director *(Last, first, middle):* _____

**Targeted/Planned Enrollment Table**

**This report format should NOT be used for data collection from study participants.**

**Study Title:**

**Total Planned Enrollment:**

| **TARGETED/PLANNED ENROLLMENT: Number of Subjects** | | | |
|---|---|---|---|
| **Ethnic Category** | **Sex/Gender** | | |
| | **Females** | **Males** | **Total** |
| Hispanic or Latino | | | |
| Not Hispanic or Latino | | | |
| Ethnic Category Total of All Subjects* | | | |
| **Racial Categories** | | | |
| American Indian/Alaska Native | | | |
| Asian | | | |
| Native Hawaiian or Other Pacific Islander | | | |
| Black or African American | | | |
| White | | | |
| Racial Categories: Total of All Subjects * | | | |

*The "Ethnic Category Total of All Subjects" must be equal to the "Racial Categories Total of All Subjects."

NEW TABLE - ENROLLMENT DATA

●

Principal Investigator/Program Director *(Last, first, middle):* _____

**Inclusion Enrollment Report**

**This report format should NOT be used for data collection from study participants.**

**Study Title:**

**Total Enrollment:** _____ **Protocol Number:** _____

**Grant Number:** _____

| **PART A. TOTAL ENROLLMENT REPORT: Number of Subjects Enrolled to Date (Cumulative) by Ethnicity and Race** | | | | |
|---|---|---|---|---|
| **Ethnic Category** | **Sex/Gender** | | | |
| | **Females** | **Males** | **Unknown or Not Reported** | **Total** |
| Hispanic or Latino | | | | ** |
| Not Hispanic or Latino | | | | |
| Unknown (Individuals not reporting ethnicity) | | | | |
| Ethnic Category: Total of All Subjects* | | | | * |
| **Racial Categories** | | | | |
| American Indian/Alaska Native | | | | |
| Asian | | | | |
| Native Hawaiian or Other Pacific Islander | | | | |
| Black or African American | | | | |
| White | | | | |
| More than one race | | | | |
| Unknown or not reported | | | | |
| **Racial Categories: Total of All Subjects*** | | | | * |

| **PART B. HISPANIC ENROLLMENT REPORT: Number of Hispanics or Latinos Enrolled to Date (Cumulative)** | | | | |
|---|---|---|---|---|
| **Racial Categories** | **Females** | **Males** | **Unknown or Not Reported** | **Total** |
| American Indian or Alaska Native | | | | |
| Asian | | | | |
| Native Hawaiian or Other Pacific Islander | | | | |
| Black or African American | | | | |
| White | | | | |
| More Than One Race | | | | |
| Unknown or not reported | | | | |
| **Racial Categories: Total of Hispanics or Latinos**** | | | | ** |

* These totals must agree.
** These totals must agree.

# Appendix I

# NIH Instructions to Reviewers for Evaluating Research Involving Human Subjects in Grant and Cooperative Agreement Applications

## NIH INSTRUCTIONS TO REVIEWERS FOR EVALUATING RESEARCH INVOLVING HUMAN SUBJECTS IN GRANT AND COOPERATIVE AGREEMENT APPLICATIONS
**April 25, 2001**

Please read the instructions contained in this document, whether this is your first time as a reviewer or you have reviewed previously. **NIH has revised the reviewer responsibilities and applicant requirements with respect to the human subjects elements identified below.** Each assigned application and project within an application involving human subjects must be evaluated with respect to elements listed below.

**Note:** The first two pages of this document summarize the reviewer responsibilities, and the subsequent pages of the document provide additional details, explanations and guidance.

### REVIEWER CRITIQUE HEADINGS AND EVALUATION CODING OPTIONS

**1. PROTECTION OF HUMAN SUBJECTS FROM RESEARCH RISK: (page 3)**

**Absent** (no information provided in the application – Call the Scientific Review Administrator.) or
**No Concern** (acceptable risks and/or adequate protections) or
**Concerns** (unacceptable risks and/or inadequate protections) or
**Exempt** (See Glossary for Exemption Categories)

**2. DATA AND SAFETY MONITORING PLAN: (required only for clinical trials - page 4)**

**Absent** (no information provided in the application – Call the Scientific Review Administrator.) or
**Acceptable** or
**Unacceptable**

**3. INCLUSION OF WOMEN PLAN: (required for clinical research - page 5)**

**Not an NIH-defined Phase III Clinical Trial:**
**Absent** (no information provided in the application – Call the Scientific Review Administrator.) or
**Acceptable** (representation coded 1-4, see instructions) or
**Unacceptable** (representation coded 1-4 see instructions) or

NIH-defined Phase III Clinical Trial: (see special analyses requirements)
**Absent** (no information provided in the application – Call the Scientific Review Administrator.) or
**Acceptable** (representation coded 1-4, see instructions) or
**Unacceptable** (representation coded 1-4)

**4. INCLUSION OF MINORITIES PLAN: (page 6)**
**Not an NIH-defined Phase III Clinical Trial:**
**Absent** (no information provided in the application – Call the Scientific Review Administrator.) or
**Acceptable** (representation coded 1-5, see instructions) or
**Unacceptable** (representation coded 1-5) or

NIH-defined Phase III Clinical Trial: (see special analyses requirements):
**Absent** (no information provided in the application – Call the Scientific Review Administrator.) or
**Acceptable** (representation coded 1-5, see instructions) or
**Unacceptable** (representation coded 1-5)

**5. INCLUSION OF CHILDREN PLAN: (page 9)**

**Absent** (no information provided in the application – Call the Scientific Review Administrator.) or
**Acceptable** or
**Unacceptable**

APPLICANT REQUIREMENTS (Page 2)

GLOSSARY OF TERMS (page 10)

### ADDITIONAL GUIDANCE

**Please refer to the Decision Trees on the NIH Peer Review Policy web page:**

(http://grants.nih.gov/grants/peer/peer.htm)

Protection of Humans

Women in Clinical Research

Women in NIH-Defined Phase III Clinical Trials

Minorities in Clinical Research

Minorities in NIH-Defined Phase III Clinical Trials

Children in Human Subjects Research

Data and Safety Monitoring Plans in Clinical Trials

**APPLICANT REQUIREMENTS:**

**1. PROTECTION OF HUMAN SUBJECTS FROM RESEARCH RISK (page 3)**

In the Human Subjects Research section, applicants must (1) address the involvement of human subjects and protections from research risk relating to their participation in the proposed research plan, or (2) provide sufficient information on the research subjects to allow a determination by peer reviewers and NIH staff that a designated exemption is appropriate.

Note: NIH policy no longer requires documentation of Institutional Review Board (IRB) approval at the time of the initial peer review. http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-031.html.

**2. DATA AND SAFETY MONITORING PLAN (page 5)**

As of the October 2000 receipt date (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-038.html) applicants must supply a general description of the Data and Safety Monitoring Plan for all clinical trials (see glossary definition) as part of the research application. The principles of data and safety monitoring require that all biomedical and behavioral clinical trials be monitored to ensure the safe and effective conduct of human subjects research, and to recommend conclusion of the trial when significant benefits or risks are identified or if it is unlikely that the trial can be concluded successfully. Risks associated with participation in research must be minimized to the extent practical and the method and degree of monitoring should be commensurate with risk.

**3. WOMEN AND MINORITY INCLUSION (page 5)**

The NIH Revitalization Act of 1993 (Public Law 103-43) requires that women and minorities must be included in all NIH-supported biomedical and behavioral clinical research projects involving human subjects, unless a clear and compelling rationale and justification establishes that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research.

The most recent "NIH Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research" (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-048.html) were published in the NIH Guide on August 2, 2000. All human clinical research (see glossary definition) is covered by this NIH policy. Each project of a multi-project application must be individually evaluated for compliance with the policy.

Since a primary aim of clinical research is to provide scientific evidence leading to a change in health policy or a standard of care, it is imperative to determine whether the intervention or therapy being studied affects women or men or members of minority groups and their subpopulations differently.

Applicants must include a description of plans to conduct valid analyses (see glossary definition) to detect significant differences (see glossary definition) in intervention effect for an NIH-defined Phase III Clinical Trial (see glossary definition).

**4. INCLUSION OF CHILDREN (page 9)**

NIH requires that children (i.e., individuals under the age of 21) must be included in all human subjects research, conducted or supported by the NIH, unless there are scientific and ethical reasons not to include them.

This policy (http://grants.nih.gov/grants/guide/notice-files/not98-024.html ) applies to all NIH conducted or supported research involving human subjects, including research that is otherwise "exempt" in accord with Sections 101(b) and 401(b) of 45 CFR 46 - Federal Policy for the Protection of Human Subjects. The inclusion of children as subjects in research must be in compliance with all applicable subparts of 45 CFR 46 as well as with other pertinent federal laws and regulations. Therefore, applications for research involving human subjects must include a description of plan for including children. If children will be excluded from the research, the application must present an acceptable justification for the exclusion. This policy applies to all initial applications (Type 1) proposals and intramural projects submitted for receipt dates after October 1, 1998.

**PROTECTION OF HUMAN SUBJECTS FROM RESEARCH RISK**

**REVIEWER RESPONSIBILITIES:** Create a "**Protection Of Human Subjects From Research Risk**" heading in your written critique (using upper and lower case letters as shown).

Federal regulations (45 CFR 46.120) require that the information provided in the application (Human Subjects section e or other sections of the application) must be evaluated with reference to the following criteria:

Risk To Subjects; Adequacy Of Protection Against Risks; Potential Benefits Of The Proposed Research To The Subjects And Others; Importance Of The Knowledge To Be Gained.

Evaluate the information provided in the application, and indicate that the information is **"Absent" or** there are **"No Concerns"** or that there are **"Concerns"** or that the proposed research is **"Exempt".**

**Scoring Considerations:**

If concerns are identified, they should be reflected in the priority score for scientific and technical merit assigned to the application. The negative impact on the score should reflect the seriousness of the human subjects concerns. Reviewers may also recommend limitations on the scope of the work proposed, imposition of restrictions, or elimination of objectionable (risky) procedures involving human subjects.

If the research risks are sufficiently serious and protections against the risks are so inadequate as to consider the proposed research unacceptable on ethical grounds, reviewers may recommend that no further consideration be given to the application and score the application as **NRFC** (Not Recommended for Further Consideration - An NRFC).

Your evaluation is independent of any other group who will review the research. (NIH policy no longer requires documentation of Institutional Review Board (IRB) approval at the time of the initial peer review http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-031.html ).

**Absent** If the applicant does not address any of the Human Subjects elements that are specifically required in the PHS 398 instructions, begin your comments in the Human Subjects section with the words **"Human Subjects Information Absent" and** call the Scientific Review Administrator.

**No Concerns (acceptable risks and/or adequate protections):** If the applicant has adequately and appropriately addressed the Human subjects criteria and there are no concerns as defined in the glossary of terms, then, enter the words "No Concerns (acceptable risks and/or adequate protections)".

Other issues related to the inclusion of human subjects, which are not concerns, may be communicated to the applicant or NIH staff in this section of your critique.

**Concerns (actual or potentially unacceptable risk, or inadequate protection against risk, to human subjects):** If the applicant has not adequately and appropriately addressed the four criteria in the application and/or you identify human subjects concerns, (defined below), then, begin your comments with the words "**Concerns (unacceptable risks and/or inadequate protections).**" Document and specify the actual or potential issues that constitute the unacceptable risks or inadequate protections against risks.

Concerns should be described in your reviews, whether or not you recommend that the application be scored.

**Exempt:** If the application indicates that the Human Subjects research is exempt from coverage by the regulations, then determine whether the information provided conforms to one of the categories of exempt research and whether the information justifies the exemption claimed. If it is exempt, state "**Exempt**" and specify which exemption or exemptions apply (see Glossary for list of Exemption categories).

If an exemption is claimed and you determine that the information provided does not justify the exemption, then, indicate that there is a "**Concern**" and indicate why you have determined that the information provided does not justify the exemption.

Where is the human subjects information located in an application?

The PHS form 398 grant application requires that applicants provide information about human subjects involvement and protections from research risk in the RESEARCH PLAN and the Appendices (if applicable).

See decision tree for **Protection of Humans**

http://grants.nih.gov/grants/peer/tree_protection_hs.pdf

## DATA AND SAFETY MONITORING PLAN

**REVIEWER RESPONSIBILITIES:** If the application contains clinical trials research, create a "**Data and Safety Monitoring Plan**" heading in your written critique (using upper and lower case letters as shown). **Required only if the application is clinical trials (see Glossary).**

Evaluate the acceptability of the proposed Data and Safety Monitoring Plan provided in the application's research plan. Data and Safety Monitoring Plan are required (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-038.html) of all applications that involve a clinical trial.

On the basis of the information provided in the application, document the extent to which you judge the plan is "**Absent",** "**Acceptable**," or "**Unacceptable.**"

**Scoring Considerations:** If the Data And Safety Monitoring Plan is unacceptable, then, the unacceptability must be reflected in the priority score that you assign to the application.

The Data and Safety Monitoring Plan must be appropriate with respect to the potential risks to human participants, and complexity of study design.

**Absent**: If the applicant does not provide information about a Data and Safety Monitoring Plan, indicate "**Absent**" in the Data and Safety Monitoring section of the critique and call the Scientific Review Administrator.

**Acceptable:** If the general description of the Data and Safety Monitoring Plan is adequate, (e.g. defines the general structure of the monitoring entity and mechanisms for reporting Adverse Events to the NIH, the IRB, etc.), begin your comments with the word, "**Acceptable**" in the Data and Safety Monitoring section.

**Unacceptable:** If the information provided about Data and Safety Monitoring is inadequate, begin your comments with the word, "**Unacceptable**" and subsequently specify what is unacceptable about the plan and/or what information is missing.

### Components of a Monitoring Plan

NIH requires the establishment of Data and Safety Monitoring Boards (DSMBs) for multi-site clinical trials involving interventions that entail potential risk to the participants.

(http://grants.nih.gov/grants/guide/notice-files/not98-084.html ).

Generally, NIH-defined Phase III Clinical Trials require DSMBs. Smaller and earlier phase clinical trials may not require this level of oversight, and alternate monitoring plans may be more appropriate.

Applicants must submit a general description of the Data and Safety Monitoring Plan for all clinical trials. Monitoring plans are also required as part of the PHS 398 section "e. Human Subjects".

The general description of the Data and Safety Monitoring Plan should describe the entity that will be responsible for monitoring, and the policies and procedures for adverse event reporting. All monitoring plans must include a description of how Adverse Events (AEs) will be reported to the Institutional Review Board (IRB), the NIH, the Office of Biotechnology Activities (OBA) (if required), and the Food and Drug Administration (FDA) in accordance with IND or IDE regulations.

Monitoring entities may include, but are not limited to:

Principal Investigator
Independent individual/Safety Officer
Designated medical monitor
Internal Committee or Board with explicit guidelines
DSMB (required for multi-site NIH-defined Phase III Clinical Trials)
IRB (required)

A detailed Data and Safety Monitoring plan will be submitted to the applicant's IRB and subsequently to the funding IC for approval prior to award. The detailed monitoring plan must be approved by the funding IC prior to the accrual of human participants.

(http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-038.html )

In addition applications involving human gene transfer research must comply with NIH Guidelines for Research Involving Recombinant DNA Molecules be and must submit protocols to the NIH Office of Biotechnology Activities (OBA), for review by the Recombinant DNA Advisory Committee(RAC) prior to final approval by the Institutional Biosafety Committee. OBA recommends that RAC review also occur prior to IRB review and submission to FDA for regulatory permission to proceed with the study.

See decision tree for **Data and Safety Monitoring Plans in Clinical Trials**

http://grants.nih.gov/grants/peer/tree_dsm_plans.pdf

## WOMEN AND MINORITY INCLUSION

**Reviewer Responsibilities:**

Create two headings: **"Inclusion of Women" and "Inclusion of Minorities"** in your written critique (using upper and lower case letters as shown). Evaluate the assigned applications and each individual project within multicomponent applications to assess the plan for the inclusion of Women and Minorities or the acceptability of the justifications for exclusion provided in the application's research plan.

On the basis of the information provided in the application, designate that the information is **"Absent," "Acceptable"** or **"Unacceptable."**

**Scoring Considerations:** If the Inclusion Plan is unacceptable, then, the unacceptability must be reflected in the priority score that you assign to the application.

Provide a brief narrative text to answer each of the following questions separately for women and for minorities:

**Inclusion Plan -** Does the applicant propose a plan for the inclusion of minorities and both genders for appropriate representation? How does the applicant address the inclusion of women and members of minority groups and their subpopulations in the development of a research design that is appropriate to the scientific objectives of the study? Does the research plan describe the composition of the proposed study population in terms of sex/gender and racial/ethnic group, and does it provide a rationale for selection of such subjects.

**Exclusion -** Does the applicant propose justification when representation is limited or absent? Does the applicant propose exclusion of minorities and women on the basis that a requirement for inclusion is inappropriate with respect to the health of the subjects and/or with respect to the purpose of the research? Reviewers shall evaluate the justifications and assess whether they are acceptable.

**Analysis Plans -** Does the applicant propose an NIH-defined Phase III Clinical Trial (see Glossary for definition)? If yes, does the research plan include either (a) an adequate description of plans to conduct analyses to detect significant differences of clinical or public health importance in intervention effect by sex/gender and/or racial/ethnic subgroups when the intervention effect(s) is expected in the primary analyses, or (b) an adequate description of plans to conduct valid analyses (see Glossary) of the intervention effect in subgroups when the intervention effect(s) is not expected in the primary analyses.

**Evaluation And Coding:** For single project applications, assign an overall code as described below. For multi-project applications, a code should be assigned to each individual project or subproject in an application containing multiple projects or involving distinct populations or specimen collections. If only one project in a multiproject application involves clinical research, the codes assigned to that project will apply to the overall document; if there is more than one project covered by the policy, ALSO assign an overall code to the entire application as follows:

**Absent**: If no information is provided about the Inclusion of Women, indicate "**Absent**" in the appropriate heading section. In the absence of information or proposed plans for inclusion, reviewers should call the Scientific Review Administrator.

**Representation Proposed in Project.** Coding should reflect the total representation proposed for all projects or subprojects, even if some are single-gender.

**Gender Codes**

**Format.** Each code is a three digit alphanumeric string:

1st character **G** (indicates gender code)
2nd character **1, 2, 3, or 4** (representation proposed in project – see below)
3rd character **A or U** (acceptable or unacceptable – see guidance below)

**Representation Proposed in Project**

(2nd character)

**1** = both genders
**2** = only women
**3** = only men
**4** = gender unknown

| GENDER CODES | | |
|---|---|---|
| **Gender Representation** | **Scientifically… Acceptable** | **Unacceptable** |
| both included | G1A | G1U |
| women only | G2A | G2U |
| men only | G3A | G3U |
| unknown | G4A | G4U |

**Gender Inclusion In Clinical Research (Not A NIH-Defined Phase III Clinical Trial)**

**Acceptable:** One or more of the following may apply:

Both genders are included in the study in scientifically appropriate numbers.

One gender is excluded from the study because: inclusion of these individuals would be inappropriate with respect to their health; or the research question addressed is relevant to only one gender; or evidence from prior research strongly demonstrates no difference between genders; or sufficient data already exist with regard to the outcome of comparable studies in the excluded gender, and duplication is not needed in this study.

One gender is excluded or severely limited because the purpose of the research constrains the applicant's selection of study subjects by gender (e.g., uniquely valuable stored specimens or existing datasets are single gender; very small numbers of subjects are involved; or overriding factors dictate selection of subjects, such as matching of transplant recipients, or availability of rare surgical specimens).

Gender representation of specimens or existing datasets cannot be accurately determined (e.g., pooled blood samples, stored specimens, or data-sets with incomplete gender documentation are used), and this does not compromise the scientific objectives of the research.

**Unacceptable:** Representation fails to conform to NIH policy guidelines summarized in this document and the NIH Guidelines pertinent to the scientific purpose and type of study; or the application provides insufficient information, or does not adequately justify limited representation of one gender.

**Gender Requirements for NIH-defined Phase III Clinical Trials:**

**Acceptable:** One or more of the following may apply based on review of prior evidence:

Available evidence strongly indicates significant gender differences of clinical or public health importance in intervention effect, and the study design is appropriate to answer two separate primary questions -- one for males and one for females -- with adequate sample size for each gender. **The research plan must include a description of plans to conduct analyses to detect** significant differences **in intervention effect.**

Available evidence strongly indicates there is no significant difference of clinical or public health importance between males and females in relation to the study variables. (Representation of both genders is not required; however, inclusion of both genders is encouraged.)

There is no clear-cut scientific evidence to rule out significant differences of clinical or public health importance between males and females in relation to study variables, and study design includes sufficient and appropriate representation of both genders to permit valid analyses of a differential intervention effect. **The research plan must include a description of plans to conduct the** valid analyses **(see glossary definition) of the intervention effect.**

One gender is excluded from the study because:

inclusion of these individuals would be inappropriate with respect to their health; or

Inclusion of these individuals would be inappropriate with respect to the purposes of the research (e.g., the research question addressed is only relevant to one gender).

**Unacceptable:** Representation fails to conform to NIH policy guidelines summarized in this document and the NIH Guidelines pertinent to the scientific purpose and type of study; or the application fails to provide an appropriate analysis plan.

**MINORITY CODING**

A minority group is defined as "...a readily identifiable subset of the US population which is distinguished by either racial, ethnic and/or cultural heritage." In accordance with OMB Directive No.15, the basic racial and ethnic categories are: American Indian or Alaska Native; Asian; Black or African American, Hispanic or Latino; Native Hawaiian or Other Pacific Islander and White. It is not anticipated that every study will include all minority groups and subgroups. The inclusion of minority groups should be determined by the scientific questions under examination and their relevance to racial or ethnic groups. Applications should describe the subgroups that will be included in the research.

In foreign research projects involving human subjects, the definition of minority groups may be different than in the US; if there are scientific reasons for examining minority group or subgroup differences in such settings, studies should be designed to accommodate such differences.

**Minority Codes**

**Format**. Each code is a three digit alphanumeric string:

1st character **M** ( indicated minority code)
2nd character **1, 2, 3, 4, or 5** (representation proposed in project – see below)
3rd character **A or U** (scientifically acceptable or unacceptable – see below)

**Representation Proposed in Project** (2nd character)

**1** = minority and nonminority
**2** = only minority
**3** = only nonminority
**4** = minority representation unknown
**5** = only foreign subjects in study population (no U.S. subjects). If the study population includes both foreign and U.S. study subjects then use codes 1 thru 4 to describe the U.S. component (do not use code 5).

**Acceptability/Unacceptability of Representation of Minorities** (3rd character)

**A** = Representation is scientifically acceptable and recruitment/retention has been realistically addressed, or an acceptable justification for exclusion has been provided.

**U** = Representation is unacceptable. Application fails to conform to NIH policy guidelines in relation to the scientific purpose of the study; or fails to provide sufficient information; or does not adequately justify exclusion of minority consideration in subjects; or does not realistically address recruitment/retention.

**MINORITY CODES**

| Minority Representation | Scientifically… Acceptable | Unacceptable |
|---|---|---|
| minorities and non-minorities included | M1A | M1U |
| minorities only | M2A | M2U |
| non-minorities only | M3A | M3U |
| Unknown | M4A | M4U |
| Foreign | M5A | M5U |

Minority Inclusion in Clinical Research; Not a NIH defined NIH-defined Phase III Clinical Trial.

**Acceptable:** One or more of the following may apply:

Minority individuals are included in scientifically appropriate numbers.

Some or all minority groups or subgroups are excluded from the study because:

Inclusion of these individuals would be inappropriate with respect to their health; or

The research question addressed is relevant to only one racial or ethnic group; or

Evidence from prior research strongly demonstrates no differences between racial or ethnic groups on the outcome variables; or a single minority group study is proposed to fill a research gap; or

Sufficient data already exists with regard to the outcome of comparable studies in the excluded racial or ethnic groups and duplication is not needed in this study; or

3. Some minority groups or subgroups are excluded or poorly represented because the geographical location of the study has only limited numbers of these minority groups who would be eligible for the study, and the investigator has satisfactorily addressed this issue in terms of the size of the study, the relevant characteristics of the disease, disorder or condition, or the feasibility of making a collaboration or consortium or other arrangements to include representation.

4. Some minority groups or subgroups are excluded or poorly represented because the purpose of the research constrains the applicant's selection of study subjects by race or ethnicity (e.g., uniquely valuable cohorts, stored specimens or existing datasets are of limited minority representation, very small numbers of subjects are involved, or overriding factors dictate selection of subjects, such as matching of transplant recipients or availability of rare surgical specimens).

5. Racial or ethnic origin of specimens or existing datasets cannot be accurately determined (e.g., pooled blood samples, stored specimens or data sets with incomplete racial or ethnic documentation are used) and this does not compromise the scientific objectives of the research.

**Unacceptable:** Minority representation fails to conform to NIH policy guidelines summarized in this document and in the NIH Guidelines pertinent to the scientific purpose and type of study, insufficient information is provided; or the application does not adequately justify limited representation of minority groups or subgroups.

**Minority Requirements for NIH-defined Phase III Clinical Trials**

**Acceptable:** One or more may apply:

Available evidence strongly indicates significant racial or ethnic differences in intervention effects, and the study design is appropriate to answer separate primary questions for each of the relevant racial or ethnic subgroups, with adequate sample size for each. **The research plan must include a description of plans to conduct analyses to detect significant differences in intervention effect.**

Available evidence strongly indicates that there are no significant differences of clinical or public health importance among racial or ethnic groups or subgroups in relation to the effects of study variables. (Minority representation is not required as a subject selection criterion; however, inclusion of minority group or subgroup members is encouraged.)

There is no clear-cut scientific evidence to rule out significant differences of clinical or public health importance among racial or ethnic groups or subgroups in relation to the effects of study variables, and the study design includes sufficient and appropriate representation of minority groups to permit valid analyses (see note below) of a differential intervention effect. **The Research Plan in the application or proposal must include a description of plans to conduct the valid analyses (see Glossary definition) of the intervention effect in subgroups.**

Some minority groups or subgroups are excluded from the study because:

Inclusion of these individuals would be inappropriate with respect to their health; or

Inclusion of these individuals would be inappropriate with respect to the purposes of the research (e.g., the research question addressed is not relevant to all subgroups).

**Unacceptable:** Minority representation fails to conform to NIH policy guidelines summarized in this document and in the NIH Guidelines pertinent to the scientific purpose and type of study, insufficient information is provided; or the application does not adequately justify limited representation of minority groups or subgroups, or the application fails to provide an appropriate analysis plan.

See decision trees for:

Women in Clinical Research

http://grants.nih.gov/grants/peer/tree_women_clinical_research.pdf

Women in NIH-Defined Phase III Clinical Trials

http://grants.nih.gov/grants/peer/tree_women_clinical_trials.pdf

Minorities in Clinical Research

http://grants.nih.gov/grants/peer/tree_minorities_clinical_research.pdf

Minorities in NIH-Defined Phase III Clinical Trials

http://grants.nih.gov/grants/peer/tree_minorities_clinical_trials.pdf

**INCLUSION OF CHILDREN IN HUMAN SUBJECTS RESEARCH**

**REVIEWER RESPONSIBILITIES:** Create an "**Inclusion of Children Plan**" heading in your written critique (using upper and lower case letters as shown)

Evaluate the acceptability of the proposed plan for the inclusion of children or the acceptability of the justifications for exclusion provided in the application's research plan.

On the basis of the information provided in the application document the extent to which you judge the plan is "**Absent",** "**Acceptable**," or "**Unacceptable.**"

**Scoring Considerations:** If the Inclusion Plan is unacceptable, then, the unacceptability must be reflected in the priority score that you assign to the application.

Reviewers are asked to evaluate the appropriateness of the population studied in terms of the aims of the research and ethical standards, the expertise of the investigative team in dealing with children at the ages included, and the appropriateness of the facilities. Evaluate and code (see instructions below) each project and subproject separately for inclusion of children.

The PI must describe in the application, under a section "Participation of Children," the plans to include children and a rationale for selecting or excluding a specific age range of child, or an explanation of the reason(s) for excluding children. Additional information is provided in the Human Subjects section.

**Absent**: If no information is provided about the Inclusion of Children, indicate "**Absent**" in the heading section.

In the absence of information on the proposed plans for inclusion, reviewers should call the Scientific Review Administrator.

An **Acceptable** plan is one in which the representation of children is scientifically appropriate and recruitment/retention has been realistically addressed, or an appropriate justification for exclusion has been provided.

For those plans, which are "**Acceptable**" provide one of the following codes:

**C1A** Both children and adults are included (e.g. inclusion is scientifically acceptable).

**C2A** Only children are represented in the study (e.g. inclusion is scientifically acceptable).

**C3A** No children included (e.g. acceptable justification for exclusion is provided).

**C4A** Representation of children is not known (e.g. The information on age of individuals providing specimens or in existing datasets cannot be accurately determined (e.g., pooled blood samples, stored specimens), and this does not compromise the scientific objectives of the research).

An **Unacceptable** plan is one, which fails to conform to NIH policy guidelines in relation to the scientific purpose of the study; or fails to provide sufficient information; or does not adequately justify that children are not included; or does not realistically address recruitment/retention

For those plans that are **Unacceptable** provide one of the following codes**:**

**C1U** Both children and adults are included; (e.g. no rationale is provided for selecting or excluding a specific age range of children).

**C2U** Only children are represented in the study (e.g. but age range is too restricted to be scientifically acceptable, such as including only children of ages 18-21).

**C3U** No children included (e.g. acceptable justification for exclusion is not provided).

**C4U** Representation of children is not known (e.g. the application does not provide sufficient information about the age distribution of the study population. the application does not comply with requirements and is unacceptable).

In all cases explain the basis for your judgment.

## GLOSSARY OF TERMS

### AMERICAN INDIAN OR ALASKA NATIVE:

A person having origins in any of the original peoples of North, Central, or South America and maintains tribal affiliation or community

### ASIAN:

A person having origins in any of the original peoples of the Far East, Southeast Asia, or the Indian subcontinent including, for example, Cambodia, China, India, Japan, Korea, Malaysia, Pakistan, the Philippine Islands, Thailand, and Vietnam

### BLACK OR AFRICAN AMERICAN:

A person having origins in any of the black racial groups of Africa. Terms such as "Haitian" or "Negro" can be used in addition to "Black or African American."

### CHILD:

For purposes of this policy, a child is an individual under the age of 21 years. This policy and definition do not affect the human subject protection regulations for research on children 45 CFR 46) and their provisions for assent which remain unchanged.

It should be noted that the definition of child described above will pertain notwithstanding the FDA definition of a child as an individual from infancy to 16 years of age, and varying definitions employed by some states. Generally, state laws define what constitutes a "child," and such definitions dictate whether or not a person can legally consent to participate in a research study. However, state laws vary, and many do not address when a child can consent to participate in research. Federal Regulations (45 CFR 46, subpart D, Sec.401-409) address DHHS protections for children who participate in research, and rely on state definitions of "child" for consent purposes. Consequently, the children included in this policy (persons under the age of 21) may differ in the age at which their own consent is required and sufficient to participate in research under state law. For example, some states consider a person age 18 to be an adult and, therefore, one who can provide consent without parental permission (see also http://grants.nih.gov/grants/guide/notice-files/not98-024.html).

### CLINICAL RESEARCH:

The NIH definition of clinical research is based on the 1997 Report of the NIH Director's Panel on Clinical Research that defines clinical research in the following three parts:

(1) Patient-oriented research. Research conducted with human subjects (or on material of human origin such as tissues, specimens and cognitive phenomena) for which an investigator (or colleague) directly interacts with human subjects. Excluded from this definition are in vitro studies that utilize human tissues that cannot be linked to a living individual. Patient-oriented research includes: (a) mechanisms of human disease, (b) therapeutic interventions, (c) clinical trials, or (d) development of new technologies.

(2) Epidemiologic and behavioral studies,

(3) Outcomes research and health services research.

Note: Autopsy material is not covered by the policy. When the research under review is essentially a service (e.g., statistical center or analysis laboratory) in support of another activity already found to be in compliance with this policy, a second review is not necessary.

Training grants (T32, T34, T35) are exempt from coding requirements but a term or condition of award will specify that all projects to which trainees are assigned must already be in compliance with the NIH policy on inclusion of women and minorities in clinical research.

### CLINICAL TRIAL:

For purposes of reviewing applications submitted to the NIH, a clinical trial is operationally defined as a prospective biomedical or behavioral research study of human subjects that is designed to answer specific questions about biomedical or behavioral interventions (drugs, treatments, devices, or new ways of using known drugs, treatments, or devices).

Clinical trials are used to determine whether new biomedical or behavioral interventions are safe, efficacious and effective. Clinical trials of experimental drug, treatment, device or behavioral intervention may proceed through four phases:

Phase I clinical trials are done to test a new biomedical or behavioral intervention in a small group of people (e.g. 20-80) for the first time to evaluate safety (e.g. determine a safe dosage range, and identify side effects).

Phase II clinical trials are done to study the biomedical or behavioral intervention in a larger

group of people (several hundred) to determine efficacy and to further evaluate its safety.

Phase III studies are done to study the efficacy of the biomedical or behavioral intervention in large groups of human subjects (from several hundred to several thousand) by comparing the intervention to other standard or experimental interventions as well as to monitor adverse effects, and to collect information that will allow the intervention to be used safely.

Phase IV studies are done after the intervention has been marketed. These studies are designed to monitor effectiveness of the approved intervention in the general population and to collect information about any adverse effects associated with widespread use.

**NIH-Defined Phase III Clinical Trial:**

For the purpose of the Guidelines on the Inclusion of Women and Minorities, an NIH-defined Phase III clinical trial is a broadly based prospective NIH-defined Phase III clinical investigation, usually involving several hundred or more human subjects, for the purpose of evaluating an experimental intervention in comparison with a standard or control intervention or comparing two or more existing treatments. Often the aim of such investigation is to provide evidence leading to a scientific basis for consideration of a change in health policy or standard of care. The definition includes pharmacologic, non-pharmacologic, and behavioral interventions given for disease prevention, prophylaxis, diagnosis, or therapy. Community trials and other population-based intervention trials are also included.

**EXEMPTION CATEGORIES:**

The six categories of research that qualify for exemption from coverage by the regulations include activities in which the only involvement of human subjects will be in one or more of the following six categories:

The six categories of research that qualify for exemption from coverage by the regulations include one or more of the following six categories:

Exemption 1: Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as (a) research on regular and special education instructional strategies, or (b) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

Exemption 2: Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior, unless: (a) information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and (b) any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.

Exemption 3: Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under paragraph (2)(b) of this section, if: (a) the human subjects are elected or appointed public officials or candidates for public office; or (b) Federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.

Exemption 4: Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

Exemption 5: Research and demonstration projects which are conducted by or subject to the approval of department or agency heads, and which are designed to study, evaluate, or otherwise examine: (a) public benefit or service programs; (b) procedures for obtaining benefits or services under those programs; (c) possible changes in or alternatives to those programs or procedures; or (d) possible changes in methods or levels of payment for benefits or services under those programs.

Exemption 6: Taste and food quality evaluation and consumer acceptance studies, (a) if wholesome foods without additives are consumed or (b) if a food is consumed that contains a food ingredient at or below the level and use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

**GENDER:**

Refers to the classification of research subjects into either or both of two categories: women and men. In some cases, representation is unknown, because gender composition cannot be accurately determined (e.g., pooled blood samples or stored specimens without gender designation).

**HISPANIC OR LATINO:**

A person of Cuban, Mexican, Puerto Rican, South or Central American, or other Spanish culture or origin, regardless of race. The term, "Spanish origin," can be used in addition to "Hispanic or Latino".

**HUMAN SUBJECTS:**

The CODE OF FEDERAL REGULATIONS, TITLE 45, PART 46, PROTECTION OF HUMAN SUBJECTS (45-CFR-46) defines human subjects as follows:

Human subject means a living individual about whom an investigator (whether professional or student) conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information. Intervention includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes. Interaction includes communication or interpersonal contact between investigator and subject. Private information includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects (see also the decision charts provided by the Office of Human Research Protection)

Legal requirements to protect human subjects apply to a much broader range of research than many investigators realize, and researchers using human tissue specimens are often unsure about how regulations apply to their research. Legal obligations to protect human subjects apply, for example, to research that uses–

Bodily materials, such as cells, blood or urine, tissues, organs, hair or nail clippings, even if you did not collect these materials

Residual diagnostic specimens, including specimens obtained for routine patient care that would have been discarded if not used for research

Private information, such as medical information, that can be readily identified with individuals, even if the information was not specifically collected for the study in question.

Research on cell lines or DNA samples that can be associated with individuals falls into this category.

**HUMAN SUBJECTS CONCERN:**

A human subject concern is defined as any actual or potential unacceptable risk, or inadequate protection against risk, to human subjects as described in any portion of the application.

**HUMAN SUBJECTS RISK AND PROTECTION ISSUES:**

The PHS 398 application instructions require that applicants address the following items in the Research Plan – Section e of their applications:

**1. Subjects Involvement and Characteristics.** Provide a detailed description of the proposed involvement of human subjects in the work previously outlined in the Research Design and Methods section. Describe the characteristics of the subject population, including their anticipated number, age range, and health status. Identify the criteria for inclusion or exclusion of any subpopulation. Explain the rationale for the involvement of special classes of subjects, such as fetuses, pregnant women, children, prisoners, institutionalized individuals, or others who are likely to be vulnerable populations.

**2. Sources of Materials.** Identify the sources of research material obtained from individually identifiable living human subjects in the form of specimens, records, or data. Indicate whether the material or data will be obtained specifically for research purposes or whether use will be made of existing specimens, records, or data.

**3. Recruitment and Informed Consent.** Describe plans for the recruitment of subjects and the consent procedures to be followed. Include the circumstances under which consent will be sought and obtained, who will seek it, the nature of the information to be provided to prospective subjects, and the method of documenting consent. The

informed consent document should be submitted to the PHS only if requested.

**4. Potential Risks.** Describe the potential risks to subjects (physical, psychological, social, legal, or other) and assess their likelihood and seriousness to the subjects. Describe the procedures for protecting against or minimizing potential risks, including risks to confidentiality, and assess their likely effectiveness. Where appropriate, discuss provisions for ensuring necessary medical or professional intervention in the event of adverse effects to the subjects. Also, where appropriate, describe the provisions for monitoring the data collection to ensure the safety of subjects.

**5. Protection Against Risk.** Describe the procedures for protecting against or minimizing potential risks, including risks to confidentiality, and assess their likely effectiveness. Where appropriate, discuss provisions for ensuring necessary medical or professional intervention in the event of adverse effects to the subjects. Also, where appropriate, describe the provisions for monitoring the data collected to ensure the safety of subjects.

**6. Benefits.** Discuss the potential benefits of the research to the subjects and others, and the importance of the knowledge gained or to be gained. Discuss why the risks to subjects are reasonable in relation to the anticipated benefits to subjects and in relation to the importance of the knowledge that may reasonably be expected to result. Where appropriate, describe alternative treatments and procedures that might be advantageous to the subjects.

**MAJORITY GROUP:**

White, not of Hispanic Origin: A person having origins in any of the original peoples of Europe, North Africa, or the Middle East.

NIH recognizes the diversity of the U.S. population and that changing demographics are reflected in the changing racial and ethnic composition of the population. The terms "minority groups" and "minority subpopulations" are meant to be inclusive, rather than exclusive, of differing racial and ethnic categories.

**MINORITY GROUPS:**

A minority group is a readily identifiable subset of the U.S. population, which is distinguished by racial, ethnic, and/or cultural heritage.

It is not anticipated that every study will include all minority groups and subgroups. The inclusion of minority groups should be determined by the scientific questions under examination and their relevance to racial or ethnic groups.

Applicants should describe the subgroups to be included in the research. In foreign research projects involving human subjects, the definition of minority groups may be different than in the US.

**NATIVE HAWAIIAN OR OTHER PACIFIC ISLANDER:**

A person having origins in any of the original peoples of Hawaii, Guam, Samoa, or other Pacific Islands.

**NIH-DEFINED PHASE III CLINICAL TRIAL:**

For the purpose of the Guidelines on the Inclusion of Women and Minorities, an NIH-defined Phase III Clinical Trial is a broadly based prospective NIH-defined Phase III clinical investigation, usually involving several hundred or more human subjects, for the purpose of evaluating an experimental intervention in comparison with a standard or control intervention or comparing two or more existing treatments. Often the aim of such investigation is to provide evidence leading to a scientific basis for consideration of a change in health policy or standard of care. The definition includes pharmacologic, non-pharmacologic, and behavioral interventions given for disease prevention, prophylaxis, diagnosis, or therapy. Community trials and other population-based intervention trials are also included.

**OUTREACH STRATEGIES:**

These are outreach efforts by investigators and their staff(s) to appropriately recruit and retain populations of interest into research studies. Such efforts should represent a thoughtful and culturally sensitive plan of outreach and generally include involvement of other individuals and organizations relevant to the populations and communities of interest, e.g., family, religious organizations, community leaders and informal gatekeepers, and public and private institutions and organizations. The objective is to establish appropriate lines of communication and cooperation to build mutual trust and cooperation such that both the study and the participants benefit from such collaboration.

**RACIAL AND ETHNIC CATEGORIES:**

The Office of Management and Budget (OMB) Directive No. 15 defines the minimum standard of basic racial and ethnic categories, which are used by NIH. These definitions are used because they allow comparisons to many national databases, especially national health databases. Therefore, the racial and

ethnic categories described in this document should be used as basic guidance, cognizant of the distinction based on cultural heritage.

**RESEARCH PORTFOLIO:**

Each Institute and Center at the NIH has its own research portfolio, i.e., its "holdings" in research grants, cooperative agreements, contracts and intramural studies. The Institute or Center evaluates the research awards in its portfolio to identify those areas where there are knowledge gaps or which need special attention to advance the science involved. NIH may consider funding projects to achieve a research portfolio reflecting diverse study populations. With the implementation of this new policy, there will be a need to ensure that sufficient resources are provided within a program to allow for data to be developed for a smooth transition from basic research to NIH-defined Phase III clinical trials that meet the policy requirements

**SCIENTIFICALLY ACCEPTABLE OR UNACCEPTABLE:**

A determination, based on whether or not the gender or minority representation proposed in the research protocol conforms with NIH policy guidelines pertinent to the scientific purpose and type of study. A determination of unacceptable is reflected in the priority score assigned to the application. In addition, the definition of what constitutes SCIENTIFICALLY ACCEPTABLE OR UNACCEPTABLE changes if the research being conducted is a clinical trial, as opposed to merely being clinical research.

**SIGNIFICANT DIFFERENCE:**

For purposes of the NIH policies, a "significant difference" is a difference that is of clinical or public health importance, based on substantial scientific data. This definition differs from the commonly used "statistically significant difference," which refers to the event that, for a given set of data, the statistical test for a difference between the effects in two groups achieves statistical significance. Statistical significance depends upon the amount of information in the data set. With a very large amount of information, one could find a statistically significant, but clinically small difference that is of very little clinical importance. Conversely, with less information one could find a large difference of potential importance that is not statistically significant.

**SUBPOPULATIONS:**

Each minority group contains subpopulations, which are delimited by geographic origins, national origins and/or cultural differences. It is recognized that there are different ways of defining and reporting racial and ethnic subpopulation data. The subpopulation to which an individual is assigned depends on self-reporting of specific racial and ethnic origin. Attention to subpopulations also applies to individuals of mixed racial and/or ethnic parentage. Researchers should be cognizant of the possibility that these racial/ethnic combinations may have biomedical and/or cultural implications related to the scientific question under study.

**VALID ANALYSIS:**

The term "valid analysis" means an unbiased assessment. Such an assessment will, on average, yield the correct estimate of the difference in outcomes between two groups of subjects. Valid analysis can and should be conducted for both small and large studies. A valid analysis does not need to have a high statistical power for detecting a stated effect. The principal requirements for ensuring a valid analysis of the question of interest are:

Allocation of study participants of both sexes/genders (males and females) and from different racial/ethnic groups to the intervention and control groups by an unbiased process such as randomization,

Unbiased evaluation of the outcome(s) of study participants, and

Use of unbiased statistical analyses and proper methods of inference to estimate and compare the intervention effects among the gender and racial/ethnic groups.

**WHITE:**

A person having origins in any of the original peoples of Europe, the Middle East, or North Africa.

# Appendix J

## Subcommittee Reviewing Inclusion Issues: Summary Report on Actions to the NIH Tracking and Inclusion Committee

# Summary Report to the NIH Tracking and Inclusion Committee on the Actions of the Subcommittee Review Inclusion Issues

Between 1994 and 2000, a number of changes occurred at the NIH that affected extramural policies and the subsequent implementation of a tracking system for the inclusion of women and minorities in clinical research. As a result of these changes and the May 2000 GAO report, the Chair of the NIH Tracking and Inclusion Committee created an ad hoc Subcommittee composed of representatives of Institutes and Centers (ICs), the Office on Women's Health Research (ORWH), the Office of Extramural Research (OER), and the Office of Intramural Research (OIR). A list of the subcommittee members follows this report.

The purpose of the subcommittee was to examine NIH's policy and information system for tracking data on the inclusion of women and minorities in clinical research, recommend changes to improve the accuracy and performance of the system, and recommend improvements needed in the NIH policy.

The *NIH Subcommittee Reviewing Inclusion Issues* surveyed and collected comments from ICs on their interpretation and implementation of the inclusion policy and the tracking of inclusion data. A random sampling of files confirmed that there were inconsistencies in the interpretation and implementation of the requirements as well as in the collection and reporting of data. Based on these comments, the Subcommittee identified as immediate issues to be addressed: (1) updates, clarifications, and implementation of the policies regarding inclusion of women and minorities as subjects in clinical research including the definition of clinical research and the clarification of the gender analysis requirements; (2) quality and consistency of data entered and mechanisms of data entry; and (3) improvements necessary for the computerized information system.

The Subcommittee (1) updated the NIH policy on the inclusion of women and minorities as subjects in clinical research, (2) clarified the NIH definition of clinical research as it pertains to inclusion issues, (3) clarified the requirements for analysis for sex differences in NIH defined Phase III clinical trials, and (4) proposed and made substantive recommendations for the design of a new tracking system that will be fully compatible with the IMPAC II database. In addition, the subcommittee (5) recommended additional training on the inclusion policy and the proposed system for NIH staff, (6) incorporated and communicated the Office of Management and Budget (OMB) Directive 15 racial and ethnic categories into the NIH inclusion policies and guidelines, (7) prepared and reviewed relevant sections of the new 398/2590 Grant Application Instructions and Forms, (8) and revised the Frequently Asked Questions section of the Outreach Notebook used by the extramural community to ensure that the inclusion policy is understood and fully implemented.

A number of operational details required attention. Our initial activities involved the clarification of the requirement for NIH-defined Phase III clinical trials to provide analysis of sex differences. The NIH Policy and Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research updated August 1, 2000 reflected this clarification of requirements specific to NIH defined Phase III clinical trials. Language was incorporated into the announcements of research initiatives to the extramural research community (PA/RFA/RFP), and the Terms and Conditions of Awards to clarify the requirement for Phase III clinical trials to provide analysis for sex differences. Moreover, the instructions for reviewers and for the Scientific Review Administrators were updated to emphasize and clarify the need to review research proposals for inclusion requirements, analyses by sex/gender, the new OMB Directive 15 standards for reporting racial and ethnic data, as well as the proper documentation to be included in summary statements to address adherence to these policies.

Once these policy changes were approved by the full tracking and inclusion committee and governing committees of NIH (Review Policy Committee (RPC); Grants Management Advisory Committee (GMAC); Acquisition Management Committee (AMC); and Extramural Program Management Committee (EPMC)), the subcommittee began to outline design requirements for a new computerized tracking system for the inclusion of women and minorities as subjects in clinical research. The subcommittee worked closed with the technology team and members from the Office of Extramural Research (OER) and the Center for Information Technology (CIT). As well, many of the subcommittee members participated on the Joint Application Development/Design (JAD) team to design the new tracking system and assisted in the development of the Initial Critical Design Review (ICDR) document.

The subcommittee also was instrumental in the organization and design of training sessions and documents for NIH staff and the extramural community. Members worked closely with Dr. Chuck Selden, the OER Extramural Staff Training Officer, to design and conduct training sessions on the new/updated inclusion policies and assisted in the training sessions as faculty. As well, subcommittee members made periodic presentations to the GMAC, POPOF, and EPMC to keep them abreast of changes and receive input on updates to the inclusion policy.

In spring 2001, after final approval was given to update the definition of clinical research, additional updates and clarifications were needed in the inclusion policy. These included the incorporation of the new OMB Directive 15 standards on reporting race and ethnicity data, and further specification of the sex/gender analysis required for NIH-defined phase III clinical trials. The Subcommittee developed the October 2001 Amended Guidelines that provide a consolidation of the original legislation (PL 103-43) and the Federal Register notice and provide a clear and concise reference document for NIH staff and the extramural community. An abbreviated guide notice, dated October 2001, will be posted in the NIH Guide for Grants and Contracts with the fully amended policy posted on the OER Inclusion of Women and Minorities Policy Implementation web site http://grants.nih.gov/grants/funding/women_min/women_min.htm. Also, the Subcommittee provided substantive recommendations in the development of the NIH Policy on Reporting Race and Ethnicity Data: Subjects in Clinical Research (also available through the OER Inclusion of

Women and Minorities Policy Implementation web site ) which provides NIH staff and the extramural community guidance on collecting and reporting data consistent with the new OMB standards regarding race and ethnicity data.

In concert with the October 2001 Amended Guidelines, the Frequently Asked Question (FAQ's) section of the Outreach Notebook is being updated. These updated FAQ's will reflect the Amended Policy, the newly revised 398/2590 application instructions (rev. 5/01), and the new data tables for collecting target and enrollment data. The FAQ's will be posted on the ORWH website and the OER Inclusion of Women and Minorities Policy Implementation website.

The *Subcommittee Reviewing Inclusion Issues* has accomplished the three objectives that constituted it's charge. A detailed listing of actions completed by the *Subcommittee Reviewing Inclusion Issues*, work in progress, and new issues is attached. A final recommendation from the Subcommittee is that the ongoing activities be monitored by a new subcommittee of the NIH Tracking and Inclusion Committee.

# Actions Taken by Subcommittee Reviewing Inclusion Issues

October 2001

**Actions Completed**

1. **Updates to NIH Policy and Guidelines on Inclusion**
   a. A **Notice** was announced on August 2, 2000 in the *NIH Guide to Grants and Contracts*, which reiterated and clarified the policy for inclusion and restated that Phase III clinical trials must be designed and conducted in a manner sufficient to allow for a valid analysis to determine whether differences exist in intervention effect for women or members of minority groups. This notice would apply to all intramural and extramural research.
   b. A new **Terms and Conditions of Award** was applied to awards made after October 1, 2000 that have Phase III clinical trials.
   c. An **Amended Notice** was prepared for release in October 2001. This document will essentially replace the Federal Register Notice as a reference and the update from August 2, 2000; it is significantly shortened however it incorporates statute language; change in language to reflect new OMB standards, insertion of new definition for clinical research ( replace "human subject" references with "clinical research") and provides further clarification on sex/gender analysis in NIH-defined phase III clinical trials.
   d. Approved by full committee in September 2001 and posted October 2001.
   e. Separate 1-page notice of the new guidelines will be placed in electronic version for NIH Guide for Grants and Contracts. Posted in October 2001.

2. **New Policy and Guidelines on Reporting Data Sex/Gender and Race/Ethnicity**
   a. Policy developed by OER; distributed to full tracking committee for comment.
   b. Outlines OMB Directive 15 requirements for reporting race and ethnicity data.
   c. Includes FAQ questions - new concept to include in policy.

3. **Tracking System Module for IMPAC 2 - Initial Design**
   a. November 2000, proposal developed by CIT and OER
   b. December 2000, Joint Application Design (JAD) team formed to discuss recommendations and design implications.
   c. Spring/Summer 2001, Initial design for tracking system module discussed and presented to the full tracking committee and NIH functional committees.

4. **Training for NIH staff**
   a. October 16, 2000, a one-day training session was held on new policies and procedures regarding human subjects and the inclusion of women and minorities in clinical trials was addressed.
   b. December 11, 2000, a half-day training session was held on additional policy issues related to the inclusion of women and minorities, including the new OMB reporting requirements for data on race and ethnicity.
   c. December 11, 2000, L. Fanning conducted a training session on the existing population tracking system for the full committee.

5. **Activity Codes that must be tracked**

a. Document approved in March 2001.
b. All F's and T's and K's are not to be tracked.
c. Activity Codes will be used for development of exception codes and business rules for new tracking system.

**6. Creation of NIH Website for the Implementation of Policy for Inclusion of Women and Minorities as Subjects in Clinical Research**

**7. Preparation of GAO Status Reports**

**8. SRA Reviewer Instructions**
(website-- http://grants.nih.gov/grants/peer/hs_review_inst.pdf)
a. Document approved and published on Website in April 2001(website)
b. New definition for Clinical research and Phase III clinical trials included

**9. _Definitions and Communication**
a. NIH definition for Phase III Clinical Trials
b. NIH definition for Clinical Research
c. Racial/Ethnic Categories and Data Tables

**10. Policy**: Applications for Phase I toxicity studies will not require the inclusion of target data tables. (see attachment I) - **Recommendation Approved by Full Committee**
a. Motion approved by committee in May 2001.
b. NCI requested exception for Phase II clinical studies.

**11. New 398/2590 Application Instructions and Forms**
a. Issue: The form does not include a field to identify whether a study is "clinical research". Of great concern to NIH staff. Comments given to OER. Context changes to reflect clinical research instead of the words "human subjects".

**Work in Progress**

**1. Update to the Frequently Asked Questions (FAQ) Document**
a. Needs to be posted on Women and Minorities Home Page
b. Questions to reflect new 398 and Amendment to the Inclusion Policy
c. Reflects additions and changes since the release of the May 2000 GAO report
d. Document has been approved in concept by full committee; will pass by committee for final approval.
e. Anticipated posting October 2001.

**2. Update to the Outreach Notebook**
a. Needs to be finalized and posted on Women and Minorities Home Page
b. Separate committee chaired by Taylor Harden

**3. Exception Categories**

a. Exception codes reduced from 11 to 6 or 7.
b. Explanations provided for each code.
c. New codes provide a separate acronym to be used and correlate with old code, if appropriate.
d. Recommend addition of a code to cover "parent projects" where the data is stored in sub-projects or protocols. This code will need to be re-assessed when JAD conducts beta testing.
e. Question regarding interpretation and implementation of exception categories remains.

**4. Tracking System**

a. Interim MS Excel spreadsheets to be developed for IC's to use when entering data reported in FY 02.
b. No FY 02 data should be entered into the old system.
c. JAD to be re-convened Fall 01 to refine, design and assist in beta testing.
d. New system to be deployed April/May 02.

**New Issues**

**1. Transition of Subcommittee to Steering Committee - Recommendation**

a. Committee has addressed the recommendation of the GAO
b. Steering to assume Subcommittee committee functions to monitor and make recommendations regarding the inclusion policy and new population tracking system.

**2. Training NIH staff and extramural community**

a. In the Fall 2001, need to develop training materials and organize training sessions regarding the revised inclusion policy, new forms and tables for reporting data on women and minorities, the new data tracking codes, and the new IMPAC II tracking module. Should include written information, verbal presentations, and web-based tutorials for NIH staff and extramural community.
b. Develop a list of important meetings and associated NIH staff to provide training to extramural community.
c. Develop training