Sheet 11 INCLUSION OF WOMEN AND MINORITIES IN STUDY POPULATIONS: GUIDANCE FOR IRBs AND PRINCIPAL INVESTIGATORS

The principle of Justice as outlined in the Belmont Report requires that research subjects be treated fairly. For example, subjects should be carefully and equitably chosen to insure that certain individuals, or classes of individuals are not systematically selected or excluded, unless there are scientifically or ethically valid reasons for doing so.

Consistent with this principle, the NIH Revitalization Act of 1993 legislated that special attention be given to the inclusion of women and minority groups in all clinical research conducted or supported by the NIH.

On March 9, 1994, the NIH issued Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research (copy available from OHSR). These Guidelines focus on the requirement for appropriate representation of women and minority groups in all NIH-supported or -conducted clinical research, particularly in Phase III clinical trials. On August 2, 2000, the NIH updated the Guidelines to reflect the requirement to include in the research plan of Phase III trials a description of how valid analyses will be conducted to detect significant differences in intervention effect among different populations. To review the update, see http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-048.html. Even though most Intramural Research Program (IRP) clinical research does not consist of Phase III clinical trials, the Guidelines nevertheless direct that all IRP clinical research projects should strive to recruit and enroll the most diverse study population consistent with the purpose of the project.

The Guidelines contain the following policy statements:

> **"It is the policy of the NIH that women and members of minority groups and their subpopulations must be included in all NIH-supported biomedical and behavioral research projects involving human subjects, unless a clear and compelling rationale and justification establishes to the satisfaction of the relevant Institute or 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. All NIH-supported biomedical and behavioral research involving human subjects is defined as clinical research. This policy applies to research subjects of all ages."**
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> **"The inclusion of women and members of minority groups and their subpopulations must be addressed in developing a research design appropriate to the scientific objectives of the study. The research plan should describe the composition of the proposed study population in terms of gender and racial/ethnic group, and provide a rationale for selection for such subjects. Such a plan should contain a description of the proposed outreach programs for recruiting women and minorities as participants."**

NIH Intramural Research Program Principal Investigators (PIs) and Institutional Review Boards (IRBs) implement these Guidelines as follows:

1. Design of protocols: In their clinical research protocols, PIs must include in the protocol's headed section entitled Human Subject Protections:

   a. the rationale for the research subject selection based on a review of the gender and population category(ies) at risk for the disease or condition being studied;

b. strategies and procedures for recruiting the subject population selected in (a) above, and

c. justification for exclusions, if any, of women and/or individuals from particular population categories.

A Targeted/Planned Enrollment Table should be included in the protocol for Phase III and IV trials. The format for this table can be found in the NIH Standard Operating Procedures for IRBs, 6-6a. See OHSR website at http://ohsr.od.nih.gov/irb/procedures.html

2. Initial IRB review of protocols: The IRB is required to review and approve the rationale for research subject selection; the strategies and procedures for recruiting subjects, and the justification for exclusion of women and/or individuals from particular population categories. Exclusions may be warranted because of the nature of the disease or condition being studied, or there may be other justifiable reasons.

3. Continuing IRB review of protocols: Continuing review and approval of clinical research protocols by IRBs must include a review of the cumulative number of subjects accrued by gender and ethnic/racial category(ies), provided by the PI on the Inclusion Enrollment Report form, found in the NIH Standard Operating Procedures for IRBs, 6-6b. See OHSR website at http://ohsr.od.nih.gov/irb/procedures.html

In the course of its continuing reviews of a particular protocol, the IRB may find that the cumulative data on subject enrollment are inconsistent with its previously approved subject selection (see 1. and 2., above). In these cases, the IRB has broad discretion in exercising its judgment on how to proceed. Actions from which it may choose include: (a) continuation of subject accrual with referral of the matter to the IC Clinical Director for evaluation of recruitment strategies and additional resources, or (b) termination of the protocol for failure to meet the terms and conditions of IRB approval.

4. As with any other protocol submission determined by the IRB to be incomplete, IRBs are expected to defer initial or continuing review of any protocol that does not include items (1), or (3) above, respectively.

A primary aim of clinical research is to provide scientific evidence leading to a change in health policy or a standard of care, and therefore it is imperative to determine whether the experimental intervention or therapy affects women, men or individuals from various racial and ethnic groups differently. The objective is to recruit actively the most diverse study population consistent with the purpose of a research project. At the NIH, this objective is met by the conscientious implementation of the Guidelines by PIs and IRBs.