Society for Women's Health Research

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Office of Clinical Research and Bioethics Policy
Office of Science Policy
National Institutes of Health
9000 Rockville Pike
Bethesda, MD 20892

To Whom It May Concern:

The Society for Women's Health Research (SWHR®) is pleased to submit comments on the NIH/FDA Draft Clinical Trial Protocol Template for Phase 2/3 trials. SWHR, a national non-profit organization based in Washington, D.C., is widely recognized as the thought leader in promoting research on sex differences and is dedicated to improving women's health through advocacy, education and research.

An updated template guidance is crucial to assist investigators in adequately considering the impact of research studies on participants. We believe this template significantly enhances trial design and protocol drafting over current submissions by the increased emphasis on recruiting and retaining, as well as ensuring the safety and protection of diverse participants (including women in general, pregnant women, and minority men).

SWHR finds this template to be very clear and easy to use. The sample text is clearly discernable from the instructional text (italics vs. non-italics) and specific for use in a variety of research trial designs. NIH and FDA have clearly identified sample text as modifiable throughout the entire instruction document. In addition, SWHR is incredibly supportive of Section 13: Ethics/Protection of Human Subjects and applauds NIH and FDA for their extensive work to ensure the protection of research participants.

SWHR finds the instructional text to be helpful in explaining the intended content for each section. In general, the instructional text for most sections is clear and easily understood. However, SWHR does recommend additional instructions that will assist in clarifying NIH/FDA priorities for the investigator.

1) *Section 2.3 Potential Risks and Benefits*: SWHR recommends NIH and FDA include an additional instruction that investigators address risks/benefits specific to individual populations that will be participating in the study. For example, if a research study includes women and men; risks and benefits of each population should be stated separately. If there are no risks or benefits, or they are unknown, investigators should be required to state so.

2) *Section 5.1 Participant Inclusion Criteria:* SWHR applauds NIH and FDA for recognizing that women and members of minority groups must be included in

Society for Women's Health Research

each research study, unless otherwise exempt, in accordance with NIH policies. However, enrolling women and minority populations to determine if a drug or device is safe will not be effective if they are not participating at levels adequate for analysis. As a result, SWHR recommends including a request that investigators enroll women and members of minority groups and their subpopulations at sufficient levels for separate analysis.

In addition, we recommend this section ensure that investigators recruit, to the extent possible, participants that reflect the real-world population that will be using this treatment. We recommend that the template be revised to require investigators to describe the potential population that will be using the treatment should it become available for widespread use, as well as their efforts to recruit and retain such individuals. If they do not intend to recruit such individuals, investigators should be required to justify their decisions.

3) *Section 5.3 Strategies for Recruitment and Retention:* In addition to the listed vulnerable participants, NIH and FDA should include a statement recognizing that this list is not exclusive. On occasion, other groups may be considered "vulnerable" as the definition of a vulnerable participant will vary depending on the type and scope of research. For example, a population may be considered vulnerable if the incentives are high enough to be considered coercion into the study (while not being a traditionally-designated vulnerable population).

SWHR applauds NIH and FDA for its instructional text listed under Section 8: Safety. Each subsection is clearly explained, research study related risks (i.e. adverse events) are clearly defined, and investigators are instructed to design a safety protocol that will take all measures into account to assure patient health and protection. We are especially pleased to see a separate section addressing pregnancy reporting, requiring investigators to develop a protocol that will ensure the safety of both mother and fetus. As stated, the instructional text does not stigmatize the inclusion of pregnant women in clinical trials research and follow-up; validating the importance of drug and device testing for safety and efficacy during pregnancy.

In Section 10.4.7.1: Safety Review, SWHR appreciates the emphasis on halting a study if specific study arms or participant subgroups may be experiencing adverse reactions to a drug or device. This reiterates the need to power studies to include diverse subpopulations at a level adequate for investigators to confidently conclude that a drug or device is safe for that specific population. SWHR applauds NIH and FDA for requesting investigators to complete Section 10.4.8: Additional Sub-Group Analyses which will assist with this issue; however, recognizes this should be reiterated throughout the document in the sections and manner as previously discussed to ensure compliance.

Finally, SWHR recommends NIH and FDA include hyperlinks to relevant NIH, FDA, or OHRP policies and regulations to facilitate investigator background research and knowledge on current policies.

Thank you for the opportunity to provide comment on this important tool for clinical research design.

Sincerely,

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