

**PREMIER Clinical Manual of Procedures**

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## **Summary of Edits**

### **Summary of changes between version 1.0 and version 1.1**

- Baton Rouge consent description updated to reflect that the second consent, covering part of screening and all activities following randomization, is obtained at SV2.

## **4. Human Subjects**

To participate in PREMIER, participants must provide written informed consent using procedures reviewed and approved by each clinical center's local IRB. This consent should cover screening visits, interim measures, and intervention. The number and timing of these consents are determined by the local IRBs and may vary across the clinical centers. At a minimum, an initial consent is obtained prior to commencing the SV1 visit to cover screening activities and baseline measurements, and a separate consent is obtained after SV3 and prior to randomization to cover intervention measurements and activities.

Information leading to informed consent must be provided in a language that is understandable to the participant. Even when extensive printed information is provided, the investigator or interviewer must verify that the participant understands what he/she has read and heard. The participant must be given the opportunity to ask questions, and the interviewer should ask questions to determine the participant's level of understanding.

Summary descriptions of each clinical center's consent procedures are included as part of this chapter.

### ***Principles of Informed Consent***

In seeking informed consent, the following information should be provided to each participant:

1. A statement that the study involves research, an explanation of the purpose of the research, the expected duration of the individual's participation, a description of the procedures, and identification of any experimental procedures.
2. A description of any reasonably foreseeable risks or discomforts to the participants.
3. A description of any benefits to the participants (or to others) that may reasonably be expected from the research.
4. A statement describing the extent to which confidentiality of records identifying the participant is maintained.
5. An explanation as to whether any compensation or medical intervention is available if injury occurs and, if so, what it consists of, or where further information may be obtained.
6. An explanation of whom to contact for answers to pertinent questions about the research and the participant's rights, and whom to contact in the event of a research-related injury to the participant.
7. A statement that participation is voluntary, that refusal to participate will involve no penalty or loss of benefits to which the participant may otherwise be entitled, and that the participant may discontinue participation at any time without penalty or loss of benefits to which the participant may otherwise be entitled.

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8. Anticipated circumstances under which the individual's participation may be terminated by the investigator without regard to the individual's consent.

### ***Process of Obtaining Informed Consent***

Various studies indicate that the circumstances under which consent is obtained in clinical trials can have a profound influence on the participant's interpretation of information communicated during the consent discussion and on the freedom of participants to make their own decision. All clinical centers will therefore follow the guidelines listed below when obtaining informed consent.

1. Participants should have adequate time to evaluate the pros and cons of participation. Allow the participant to take the consent form home to review if necessary.
2. Participants should be encouraged to discuss the study with anyone they wish, particularly family and friends who might be affected (e.g., persons who might be needed to provide transportation).
3. To be eligible for participation in the study, participants must have the capacity to give their own consent. If a participant is incapable of understanding what is expected of him or her as a participant in the study, it is not permissible to obtain informed consent from a guardian. The study requires daily responsibilities that cannot be easily assumed by other persons.
4. The setting in which the consent is obtained should be as private as possible so participants can freely ask questions without embarrassment.
5. To avoid pressuring the participant only one person associated with the study should be present when the participant reviews the consent form. Additional staff may be present for other purposes, such as training, if participant permission is obtained.
6. The participant should be given a copy of the consent form after it is signed and witnessed.
7. Participants should be encouraged to keep the consent form because it contains useful information about the study that they can review from time to time.
8. In situations where the person or organization responsible for obtaining the participant's consent is also involved in that participant's regular medical care, the participant must be told in no uncertain terms that they will be treated with the same degree of interest and concern regardless of whether or not they participate in the study. It is desirable, therefore, that someone other than the participant's health care provider be the person responsible for obtaining the informed consent.

### ***Summary of Site-Specific Consent Procedures***

This section contains a brief summary of the process for obtaining informed consent at each site.

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### *Baltimore*

Consent for PREMIER volunteers at Johns Hopkins ProHealth occurs in two stages. Screening consent is obtained at SV1 and covers all aspects of screening, including data collection conducted at the R/I visit prior to the randomization event. Randomization consent occurs no sooner than the end of SV3 and covers all participant activities that occur following randomization.

### *Baton Rouge*

Consent for PREMIER participants at the Pennington Biomedical Research Center occurs in two stages. At SV1, all participants sign an informed consent that covers all aspects of PREMIER screening. This consent also includes consent for a battery of phlebotomy, body composition, and other evaluations that are performed on all participants receiving evaluations for any study at the Pennington Center. A second consent is obtained at SV2, and covers all participant activities that occur for the rest of screening and all activities that occur following randomization.

### *Portland*

Consent for PREMIER volunteers at the Portland clinical site will be obtained four times; at each of the three screening visits, and at the R/I visit. Each of the three screening visit consents will cover all aspects of that individual visit. In addition, the SV3 consent will include the activities at the interim visit. The randomization consent will be obtained at the beginning of the R/I visit, and covers all participant activities that occur during the R/I visit and following randomization.

### *Durham*

Consent for PREMIER volunteers at the Duke clinical site is obtained twice. The first consent covers all screening activities and is obtained at the SV1 visit. The second consent is obtained at the randomization visit and covers all participant activities that occur following randomization.

### ***Assurance of Informed Consent***

The CC receives a blank copy of all consent documents used at each site as well as copies of each site's IRB assurances forms. In addition, during site visits the CC verifies properly signed consent documents on a random subset of participants.

### ***Confidentiality***

All participant information, including the fact that an individual is participating in the study, is considered confidential. This confidentiality is assured in PREMIER through several

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mechanisms. First, each participant is assigned an anonymous study ID, which is then used on all study forms. Only where absolutely necessary to assure data integrity is a participant's name also included on study forms.

Second, all study forms, biological specimens, and paper records that contain participant information (e.g., address lists, phone lists) are kept in secured, locked areas when not in use. In addition, such materials, when in use, are kept away from public scrutiny. Materials and specimens that need to be discarded are destroyed.

Third, access to all participant data and information, including laboratory specimens, is restricted to authorized personnel. In the case of computerized data, this restricted access is assured in several ways. At the clinical centers, the data are maintained on stand-alone personal computers (PCs) that are not networked to any other PC. Further, access to the study data on these machines is password protected. Staff members receive individualized account numbers and passwords that allow them access only to those elements of the data management system to which they are authorized. At the Coordinating Center, access to computerized data is restricted in two ways. First, only authorized personnel are granted access to the data, and, second, this access is further restricted by password protection. In addition, Coordinating Center personnel are annually required to sign a confidentiality statement affirming that they agree to abide by the Center for Health Research's policies on research confidentiality and ethics.

When the study database is made available to clinical centers, to the Project Office, and, ultimately, to the public, it will not include actual identities and contact information for participants. Such information is retained under lock and key at the individual clinical centers and at the Coordinating Center for use in the event that future follow-up of the study participants is necessary.

Finally, participants are not identified by name in any reports or publications, nor are data presented in such a way that the identity of individual participants can be inferred.

### ***Data Integrity***

Data maintained at the clinical centers are internally backed up each day onto a second hard drive located in the PC. Copies of the master database maintained at the Coordinating Center are backed up daily and archived off-line on a daily, weekly, monthly, and yearly basis.

### ***Risks***

The PREMIER eligibility criteria are designed to exclude those individuals at undue risk for cardiac events or for whom the PREMIER interventions would be inappropriate. Wherever feasible, we have followed national guidelines in determining these criteria. We have also followed national guidelines in setting our blood pressure escape monitoring criteria, and all

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participants meeting escape thresholds are referred to a physician for further evaluation. If these escape thresholds are met prior to randomization, the participant is also excluded from participating in PREMIER.

As a result of these safeguards, the PREMIER study should not pose any major health risk to participants. The most likely physical health risks associated with participation are gastrointestinal upset (e.g., bloating), increased frequency and bulk of stools (resulting from the high fiber content associated with adherence to some of the study dietary recommendations), minor discomfort from the venipunctures, and possible increase in minor injuries (muscle strains, sprains, etc) associated with the adoption of a physical activity regimen. These effects are either transient or readily reversible when intervention procedures are stopped. Participants are monitored for reactions to study procedures and these procedures can be terminated if necessary.

Additional risks and inconveniences to study participants include: accidental breach of confidentiality; the inconvenience of having to come to clinic or counseling sessions on a frequent basis; the inconvenience of collecting 24-hour urine specimens; and the inconvenience of receiving data collection interviews via the telephone within specified time windows.

The PREMIER protocol also provides for regular monitoring of participants for other adverse health outcomes, and all adverse outcomes are routinely reported to the trial's Data and Safety Monitoring Board, which may propose termination or modification of the study if it determines that participants in any of the intervention groups are being placed at undue risk through their participation in PREMIER.

### ***Benefits***

The benefits associated with participation in the study include: counseling for positive health related behavior change, regular blood pressure monitoring, cash reimbursement (amounts vary by center and may not be provided at all centers), and free laboratory tests that have a small possibility for early diagnosis of an illness. Participants also have the satisfaction of participating in a clinical trial with potentially major public health implications.

Based on the results of earlier behavioral research, we anticipate that a majority of participants randomized to the active interventions will experience a reduction in blood pressure while participating in PREMIER. Moreover, we anticipate that those participants in the weight loss component of the active interventions will lose a significant amount of weight. We also anticipate an increase in regular physical activity and a resulting improvement in fitness measures among those in the active interventions. Even participants randomized to the advice group will receive, over the course of the 18-month follow-up period, three one-hour individual counseling sessions to discuss lifestyle change strategies and options.

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### ***Gender and Minorities***

The PREMIER study will recruit a population that is 40% African American and 50% female. Recruitment of minorities and women is formally monitored quarterly and reports forwarded to NHLBI. Minorities other than Blacks are also eligible to participate, although no targets are set for these categories. Further, we have specifically designed the study to have good power to detect effects on the primary study endpoints for race and gender subgroups.