Reporting Screening and Enrollment Numbers to the IRB

General Considerations

Geisinger IRB (GIRB) reviews accrual into research studies as part of its oversight of human subjects research. The number of participants in a study relates to required IRB determinations of whether subject selection is equitable and whether the risks to participants are reasonable in relation to the anticipated benefits of the research. All participants in human subjects research are potentially exposed to some level of risk, even if that level is minimal, therefore the number of participants is monitored by the IRB. Investigators may not enroll more participants than the number specified in the application currently approved by the IRB unless a modification to increase enrollment is approved.

Definitions

Recognizing that enrollment of participants is a process, the GIRB has developed the following definitions to clarify how the GIRB considers enrollment numbers. Please note these definitions may differ from a study sponsor, clinical trial billing purposes, or other departments at Geisinger. Regardless of the other definitions, the IRB definitions should be used when corresponding with the IRB about a study. We realize with the many definitions used for these same terms that this can cause confusion. In addition, not every study is designed the same. Therefore, when opening a new study protocol it is important to layout these definitions for the study to be able to accurately report on them at continuing review. If you can't seem to fit your study to these definitions, please contact GIRB staff ahead of time.

In research studies without participant interaction and/or where consent is waived, the definitions are as follows (data- or biospecimen-only research):

- **Screened Participants** – individuals whose identifiable information (e.g., medical record) and/or biospecimens are used to determine who may potentially be eligible to be enrolled in a study.

- **Enrolled Participants** - individuals whose identifiable information (e.g., medical record) and/or biospecimens are eligible for inclusion (i.e., meet the inclusion criteria for the study) **and have been used in the study evaluation**.

- **Withdrawn Participants:** - individuals whose information have been withdrawn from use in study the evaluation for some reason (e.g., inclusion/ exclusion error)

In research studies with participant interaction, the definitions are as follows:

Pre-Screened Participants: describes the activities associated with selecting potentially eligible research participants prior to contacting them (e.g. data pull, chart review). Since there is no informed consent, research procedures or interventions may not take place during subject pre-screening unless a consent waiver has been approved. Please note the number planned to pre-screen does not need to be reported to the IRB. This is just for definition purposes.

Contacted Participants: individuals who have been contacted with information about the study to ascertain interest in learning more about or participating in the study (e.g. via phone, mail, email or in person).

Screened Participants: individuals who have given informed consent and participated in screening procedures to determine eligibility. Note that informed consent is required before any screening procedures are conducted.

Screen Failures: individuals who have given informed consent and participated only in screening procedures to determine eligibility, but who were determined to be ineligible to take part in the study. Screen failures **are not considered to have enrolled in a study.**

Enrolled Participants: individuals who are eligible for participation (i.e., meet the inclusion criteria for the study), have given informed consent (if applicable), completed the procedures that determine eligibility (if applicable) and participated in some or all study procedures.

Withdrawn Participants: individuals who have given informed consent and participated in some study procedures, but who withdrew or were withdrawn from the study. There are three main types of withdrawals that should be reported:

Active Withdraw with No Continued Follow-Up: participant or investigator initiates a formal complete withdraw from study (e.g., participant indicates they wish to withdraw themselves or investigator removes participant due to a reason)

Active Withdraw with Continued Follow-Up: participant or investigator initiates a formal withdraw from study, yet follow-up continues (e.g., participant indicates they wish to withdraw or investigator removes participant due to a reason, yet

participant agrees to ongoing follow-up to assess long-term survival, for example)

Passive Withdraw: informal withdrawal where an enrolled participant does not continue participating in study activities but does not communicate this to the study team (e.g. lost to follow-up)

Guidance/ Examples

As part of the annual continuing review process, investigators must provide information about accrual of participants during the study, including the total number enrolled to date, and, where the project involves a formal screening process to determine eligibility, the total number of screen failures. The total number of participants who withdrew or were withdrawn must also be reported. The reasons for all active withdrawals must be provided.

As noted above, investigators may not **enroll** more participants than the number specified on the approved IRB application until a modification to increase that number is approved. Participants who enroll but later withdraw, or are withdrawn, are counted in the total number enrolled. However, those who are only screened for eligibility (after consenting) are not counted in the total number enrolled.

1. For treatment studies:

    a) Study participants have completed the consent process, including signing an authorized consent form when appropriate, and have completed screening procedures* such that they meet inclusion and exclusion criteria and are considered eligible for the proposed study and;

    b) They have completed a baseline visit, such that their participation in the study will yield data for potential analysis.

Study participants who complete the procedures described in criterion #1a, but discontinue participation before a baseline visit, are not considered to have accrued. Similarly, study participants that sign a consent form but fail to meet inclusion/exclusion criteria are not considered to have accrued, because their participation (screening) does not yield data supporting the hypothesis.

*Note: If subjects undergo screening procedures that are not part of standard of care for their condition, these procedures are considered research activities. Consent must be obtained before a subject participates in such research activity.

2. For non-treatment studies where subjects have consented to participation:

Study participants are considered to have accrued if they participate in study procedures/activities that yield evaluable data.

The examples below clarify how enrollment is calculated based on different research scenarios.

Example A: An investigator plans to collect data using survey procedures and is granted approval to enroll 500 participants. A survey is sent to 500 persons, and 225 complete and return the survey.

Total enrollment at this point is 225. If the investigator wishes to collect additional data, he or she may contact more persons if the total number of those who complete the survey does not exceed 500.

NUMBERS

- Approved to enroll = 500
- Allowed to enroll an additional 275 participants
- Report at Continuing Review:
    - Contacted = 500
    - Screened = 22
    - Enrolled = 225
    - Completed = 225

Example B: An investigator is conducting a study involving intense exercise trials and has IRB approval to enroll 50 participants. Those with heart conditions or high blood pressure will be excluded to protect their safety. The investigator posts a flyer in several campus buildings and sends an email to 300 persons on campus. Fifty persons express interest in the study. They each give informed consent to participate in a medical history screening to determine whether they have heart conditions or high blood pressure. Of those, 30 are deemed eligible to take part in the study and complete the main study procedures.

Total enrollment in the study is 30 persons, and the total number of screen failures is 20. The investigator may continue recruitment and screening until a total of 50 participants give informed consent and participate in the study procedures.

NUMBERS

- Approved to enroll = 50
- Allowed to enroll an additional 20 participants
- Report at Continuing Review:
    - Contacted = 300
    - Screened = 50

- Screen failures = 20
- Enrolled = 30
- Completed = 30

Example C: As part of a long-term study on how economic conditions effect marital stress, couples are asked to complete surveys, interviews, and provide measures of blood pressure on an annual basis for five years. The investigator has approval to enroll a total of 700 participants. One thousand persons are contacted via telephone and asked if they would be willing to be in the study. Of those, 600 agree and give informed consent and complete all study procedures the first year. In the second year, the investigator is unable to collect data from 50 persons as their contact information is no longer valid and they cannot be located. Ten participants contact the investigator to say they no longer wish to be involved in the study because it is too time consuming. Data are collected in the second year from the remaining 540 participants.

At this point, total enrollment is still 600 even though 60 persons have withdrawn from the study (10 active withdrawals and 50 passive withdrawals). The investigator may enroll an additional 100 persons.

<u>NUMBERS</u>

- Approved to enroll = 700
- Allowed to enroll an additional 100 participants
- Report at Continuing Review (after year 2):
  - Contacted = 1000
  - Screened = 600
  - Enrolled = 600
  - Withdrawn (passive) = 50
  - Withdrawn (active) = 10
  - Completed = 0