

Enrollment and Accrual of Study Participants

Background

The number of participants in a study relates to required determinations of whether or not subject selection is equitable and whether the risks to participants are reasonable in relation to the anticipated benefits of the study. It may also affect the extent to which confidentiality can be protected when study results are shared. As such, investigators must provide an estimate of the number of participants to be *enrolled* in the study when seeking IRB approval.¹ Investigators conducting non-exempt research 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 ISU IRB has developed the following definitions to clarify the point at which a participant is considered to be enrolled in research.

Enrolled participants: individuals who are eligible for participation (i.e., meet the inclusion criteria for the study), have given informed consent and participated in some or all of the study procedures (excluding screen failures who only took part in screening procedures).

Screened participants: individuals who have given informed consent and participated in screening procedures to determine eligibility. Note that informed consent is required before any data can be collected for screening purposes. A screening process where persons are simply informed of inclusion/exclusion criteria and allowed to self-identify as eligible for enrollment does not require informed consent because no data about the individuals are collected.

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.

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individuals who have given informed consent and participated in some study procedures, but who withdrew or were withdrawn from the study.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

Active withdrawal: formal withdrawal initiated either by the participant or investigator where communication about the reason for withdrawal is initiated/provided (e.g., a participant indicates he/she no longer wishes to participate because of time constraints, discomfort with the procedures, etc.; an investigator removes a participant from the study due to noncompliance with study procedures or because it is in the participant's best interests to discontinue).

Passive withdrawal: informal withdrawal where an enrolled participant does not take part in some study procedures but does not communicate any reasons or intention to withdraw (e.g., the enrolled participant does not show up for study sessions or completes initial components and then "disappears," etc.).

¹ For special circumstances where total enrollment cannot be estimated, please contact the Office of Research Ethics for guidance.

Guidance

As part of the continuing review process, investigators must provide information about accrual of participants during the course of 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 conducting non-exempt research 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 are not counted in the total number enrolled. The examples below clarify how enrollment is calculated based on different research scenarios.

Examples

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 as long as the total number of those who complete the survey does not exceed 500.

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.

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 only enroll an additional 100 persons. If replacement of the 60 individuals who withdrew is desired, the investigator may do so, provided that total enrollment does not exceed 700.

References

HHS Protection of Human Subjects, 45 CFR 46

<https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/index.html>

FDA Protection of Human Subjects, 21 CFR 50

<https://www.ecfr.gov/cgi-bin/text-idx?SID=31424e80d54698429ea54ae56d6f3727&mc=true&node=pt21.1.50&rgn=div5>

FDA Institutional Review Boards, 21 CFR 56

<https://www.ecfr.gov/cgi-bin/text-idx?SID=4059d602ddef219857323104584c509f&mc=true&node=pt21.1.56&rgn=div5>

Continuing Review Guidance, 2010, Office for Human Research Protections

<https://www.hhs.gov/ohrp/regulations-and-policy/guidance/guidance-on-continuing-review-2010/index.html>

IRB Continuing Review after Clinical Investigation Approval, February 2012, Food and Drug Administration

<https://www.fda.gov/regulatory-information/search-fda-guidance-documents/irb-continuing-review-after-clinical-investigation-approval>

Document History

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