Baylor University
OFFICE OF THE VICE PROVOST FOR RESEARCH

Research Compliance Institutional Review Board Guidance	Version Date: 11/01/23 IRB-G-15

Guidance on Enrollment and Accrual of Research Study Participants

PURPOSE

Investigators may not enroll more participants than the number specified in the IRB application and protocol currently approved by the IRB unless an amendment to increase enrollment has been approved. Enrollment above the IRB-approved number (i.e., over-enrollment) is not allowed and may result in noncompliance actions. The purpose of this guidance is to define when a human subject is considered "enrolled" so a researcher knows when to: close a study to enrollment; request an increase in enrollment numbers; submit a reportable event form for unapproved over-enrollment (F-14); and accurately fill out the enrollment section of the F-09 Continuing Review Form or F-12 Research Closure Form.

BACKGROUND

The number of participants in a study directly relates to the Belmont Report concept of Justice, whether 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 state the total number of participants to be enrolled in the study when seeking IRB approval.

The IRB reviews participant enrollment and accrual into research studies as part of its oversight of human subjects research. There are several reasons for this oversight:

1. All participants in human subjects research are considered to be at some level of risk, even if that level is minimal. Because the IRB is charged with the protection of human subjects in research, the number of participants exposed to such risks must be monitored.
2. If a study plans to accrue more than the number of subjects initially proposed, the IRB is required to evaluate the incremental risk posed to additional subjects. While this is especially important for moderate-to-high risk research, the same considerations apply to research that places subjects at lower levels of risk.
3. If a study is not able to accrue sufficient numbers of subjects, it is less likely that the research will contribute to generalizable knowledge. Under those conditions, it may not be reasonable to expose subjects to any level of risk/inconvenience, even if it is minimal.

DEFINITIONS

Recognizing that enrollment of participants is a process, the IRB has adopted the following definitions to clarify the point at which a participant is considered to be enrolled in research.

Enrolled Participant: Individual who is eligible for participation (i.e., meets the inclusion criteria for the study), has given informed consent, and participated in some or all of the study procedures (excluding screening procedures where applicable).

Screened Participant: Individual who has given informed consent and participated in screening procedures to determine eligibility.

Screen Failure: Individual who has given informed consent and participated only in screening procedures to determine eligibility but was determined to be ineligible to take part in the study. Screen failures are not considered to have enrolled in the study.

Withdrawals: Individual who has given informed consent and participated in some study procedures, but who withdrew or was withdrawn from the study. There are two 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 did take part in some study procedures but did not communicate any reasons or intention to withdraw (e.g., the enrolled participant does not show up for study sessions or they complete initial components and then "disappear," etc.).

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.

EXAMPLE OF COMPLETED ENROLLMENT TABLE FOR F-08 CONTINUING REVIEW FORM

Enrollment

2.	**Anticipated, IRB-approved enrollment number**: 150

Instructions: Complete #3 **or** #4 – not both. For #3, please fill out each box – put "0" instead of leaving blank.

Total Numbers enrolled since the beginning of the study			
3.	a.	Adult participants (or LARs) who gave consent (do not include parents/guardians of minor participants)	115
	b.	Minor participants (under 18) who gave assent (if applicable)	
	c.	Screen failures after consent/assent (Consented but did not meet inclusion/exclusion criteria)	10
	d.	Passed screening and continued in the research	105
	e.	Withdrew or were withdrawn by PI	5
	f.	Completed the research	75
	g.	Currently active (enrolled but has not completed all research procedures)	25
(A+B)-C=D & D-E-F=G **If E+F+G is more than IRB approved enrollment number**, please explain:			
4.		**If your research was granted a waiver of consent,** enter the number of individuals whose data, samples, etc. was collected.	

The IRB approved enrollment number for the study is 150 participants. So far, the study team has enrolled 115 participants with 10 screen fails, bringing their total enrollment number to 105 (115-10= 105) Therefore, the current enrollment is 105 which means that 105 of the 150 "spots" have been taken. The study team may enroll (consent and pass screening) an additional 45 participants (150-105= 45). If enrollment is anticipated to go above 150, an amendment needs to be reviewed and approved by the IRB ***prior to enrolling more subjects.***

As noted above, investigators conducting 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 and cannot be "replaced" by enrolling more than the original approved number. 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. Suggestion: if using an electronic survey software, set up the parameters to not allow responses after 500 responses has been reached.

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. 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 and 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 pass screening to 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.

Example D

An investigator is conducting a research study on the impact of range of motion resistance training on markers of skeletal muscle damage in college students. Participants are asked to complete 26 visits over the course of 10 weeks. The investigator has approval to enroll a total of 50 participants. 100 hundred individuals are contacted via email and asked if they would be interested in enrolling in the study. 70 individuals agree to participate and give informed consent, 5 fail screening, and 45 participants complete the study activities, and 20 were withdrew or were withdrawn by the PI. So far, the study team has enrolled 70 individuals with 5 screen fails resulting in a total 65 total participants being enrolled (45 participants who completed the study activities and 20 who withdrew or were withdrawn) resulting in over enrollment of 15 more participants than the study team was approved to enroll.

REFERENCES

45 CFR 46 Part A
OHRP, Guidance on Continuing Review (2010)