

## Guidance for Question IV.2: Number of Subjects

### ***Ethical aspects***

Careful thought should go into how many subjects will be recruited to participate in a research project: Asking for more than are needed to test a hypothesis or demonstrate a principle wastes resources. Asking for fewer than needed can lead to a Type 2 error; expose subjects to unnecessary risks; and waste resources.

### ***Numbers of Subjects (Question IV.2a)***

It is important to distinguish the following numbers:

- N1: number of subjects approved by the IRB ..... *This is usually the number requested*
- N2: number of persons who consent to participate ..... *This is the number who enroll*
- N3: number of subjects who finish the research procedures
- N4: number of useful subjects' records ..... *May be the same as N3, but not necessarily*
- N5: number of useful subjects' records needed for analysis ..... *The number you're really interested in*

IRB reviewers have noted that investigators confuse **N1 and N3** and **N1 and N5**.

N1 should be greater than N2, N3, N4, or N5.

Furthermore,  $N2 \geq N3 \geq N4 \geq N5$

**Dropouts.** Subjects who consent to participate (*enrolled* subjects) but do not finish all the procedures (N2-N3) are called *dropouts* and  $(N2-N3)/N2$  is the *dropout rate*. The investigator should be prepared to explain a high dropout rate because it might indicate that research subjects are experiencing unanticipated side effects.

**Screen failures** refers to persons who initially consent to participate and then are found on further, specialized, testing to be ineligible to participate in the research. Screen failures occur frequently in clinical research where eligibility cannot be readily determine from a person's medial history; they are relatively rare in SBE research. Screen failures are counted as part of the number approved by the IRB (N1) and number who consent to participate (N2). Screen failure rates can be quite high, eg, 90%, for certain rare presentations of a disease or condition,

**Note regarding SONA.** Psychology students who enroll in a project through SONA are **not** considered research subjects until and unless they formally consent to participate.

**Researcher's responsibilities.** The researcher is responsible for:

1. Determining N5 before submitting the application (See next section)
2. Keeping track of N2 and N3

## ***How is the number determined? (Question IV.2b)***

An investigator must consider several factors when determining the number of subjects to be recruited for a research study:

**Type of research.** Quantitative research and qualitative research employ very different approaches to determining how many research subjects should be recruited. As a rule of thumb, the investigator should look to methods that are generally accepted within the field of inquiry.

**Level of risk.** In general, the higher the risk level the higher the expectation of rigor in justifying the number of subjects to be recruited.

**Quantitative research.** A *complex* quantitative protocol should contain a robust sample size calculation based on the following:

1. anticipated effect size (probably the most difficult part of the calculation);
2. alpha level (probability of making a type 1 error, usually set at 5%);
3. beta level (probability of making a type 2 error, usually set at 20%);
4. number of subjects who might be expected to drop out of the study (a 20% drop out rate is common); and
5. the statistical test that will be used.

Methods used to calculate sample size based on these considerations are often incorporated into statistical packages or are available at various online sites ([here](#), [here](#), and [here](#)). (There are other ways to calculate sample size that do not rely on alpha, beta, P value, and effect size; use them if they make sense to you.)

*Simple research designs* often allow for less rigorous methods of calculating sample size, especially if the risk level is minimal. Reference to the relevant literature or to one's own experience may suffice.

**Qualitative research.** In contrast to quantitative research, sample size determinations in qualitative research are far less formulaic. One concept that is frequently discussed is *redundancy*: stop collecting data when no new themes emerge from the study. However, this approach is not particularly useful prospectively. A more useful, but less analytic approach is to look to similar published work in the field as a starting point.

**Dropouts.** It is prudent to expect that a fraction of consented subjects will either drop out or their data will not be usable. Therefore, an investigator should consider requesting approval to enroll more subjects than the sample size calculation indicates. A 20% overage is usually acceptable. (Be very careful discarding data as "not usable". It is best to specify criteria for not accepting data at the beginning.)

## ***What's the big deal about enrolling more subjects for a minimal risk study?***

Enrolling more subjects than approved by the IRB raises red flags:

1. The investigator is not paying attention to how the protocol is being conducted. This can become a noncompliance matter because in the original application you certify that you would:
  - a) conduct the research as described; and
  - b) request approval from the IRB for changes to the protocol including changes to sample size
2. If subjects are being compensated, then the funding agency (which may be CMU) will ask where the additional money is coming from?

### ***Need more subjects?***

Not requesting approval for enough subjects on the initial application is not unusual. Some of the more common reasons are:

1. Persons consent, then do not show up to participate. These people count against the number approved to participate, N1.  
Note: Enrolling to participate in a research project through SONA **does not** qualify as consenting to participate.
2. Persons consent, then drop out before completing the entire protocol.
3. Persons consent, then experience unpleasant side effects during testing and drop out.
4. The number needed to demonstrate a statistically significant difference between groups was underestimated.

The IRB will consider a request to increase the number of subjects approved for a study. (Submit a protocol change request.) If the protocol involves more than minimal risk, then the request should be amply justified, and it may have to be considered at a convened meeting.

***Under no circumstances should an investigator increase number of subjects beyond what was originally approved without IRB approval.***