

Engagement in Research for Pragmatic Clinical Trials

Determining which individuals or groups are engaged in research can be particularly complex in pragmatic clinical trials (PCTs). Nevertheless, doing so is essential to protecting those engaged according to their particular role (i.e., research subject, study team member, or service provider) and in ensuring compliance with federal research regulations. This document provides considerations for investigators designing and conducting PCTs as well as institutional review boards (IRBs) overseeing them. The Office for Human Research Protections (OHRP), the overarching federal oversight body for research with human subjects, issued guidance on the general topic of engagement in 2008*, but it was not directed at PCTs in particular. Given the complexities in this context, more specific guidance from OHRP would be welcome.

Key Questions

- Which individuals/groups are included in the research?
- Are these individuals/groups research subjects, study team members, or service providers?
- Why does it matter how the individuals/groups are categorized for the research?

Addressing these questions involves considering three categories of individuals in relationship to the research activity: research subjects, study team members, and service providers.

Research Subjects

It is generally easy to identify the subjects in a research study. The Department of Health and Human Services (DHHS) regulations provide the following definition of a human subject:

“a living individual about whom an investigator conducting research obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.” [45 CFR 46.102(e)]

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In most studies, determining who is a research subject is obvious; it is the person being exposed to the research activity (e.g., drug, device, procedure, survey, data collection). But in some studies, identifying the research subject is more complex. Consider a study that randomly assigns individuals to two different approaches aimed at reducing opioid use following surgery: these individuals are research subjects. But if the study also includes a medical record review of surgeons to document their opioid-prescribing practices, it might not be clear whether the surgeons are also subjects.

Why does it matter?

For research subjects, the IRB must determine that there are adequate protections and whether written/oral consent is required or a waiver of consent is justified under the regulations.

Study Team Members

Study team members are best understood to be the individuals who design and conduct the research. Study team members may include the principal investigator, sub-investigators/co-investigators, and other identified study team members (e.g., research nurse, research coordinator, data manager). Institutions have varying definitions of the activities that make someone a study team member, such as intervening or interacting with subjects for research purposes and/or obtaining the informed consent of a subject.

Why does it matter?

When individuals/groups are identified as study team members, their site is considered “engaged in research,” which means that the site would be required to obtain a [Federalwide Assurance \(FWA\)](#) if the study is federally funded, and their study staff would be required to complete human subjects research training as mandated by their institution.

Service Providers

In some studies, service providers may be used to conduct specific aspects of the study intervention. For example, if part of the intervention includes acupuncture treatment, the researchers may contract with community acupuncturists to perform these services. OHRP guidance for determining whether an individual/group participating in the research is a service provider defines the conditions that must exist in order for a site to be considered a service provider and NOT “engaged” in research:

Institutions whose employees or agents perform commercial or other services for investigators provided that all of the following conditions also are met:

- (a) the services performed do not merit professional recognition or publication privileges;
- (b) the services performed are typically performed by those institutions for non-research purposes; and

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- (c) the institution's employees or agents do not administer any study intervention being tested or evaluated under the protocol.*

To fall clearly within the category of a service provider, the individuals/groups must be providing the same service they provide for clinical care, without altering care for the study. This means they would not be providing research protocol-driven care but rather the same care/services they ordinarily provide.

In addition, OHRP guidance states that the service providers must not administer the study interventions being tested or evaluated under the protocol and they must not enroll subjects or obtain their informed consent for the research.

If the level of involvement falls outside the aforementioned conditions, the persons conducting these activities should be classified instead as study team members, which raises the issues of site requirements for an FWA and human subjects research training as described above.

Why does it matter?

If the services provided by individuals/groups included in the research (e.g., acupuncturists) are limited to the same services they typically provide off-study, and they have no role in obtaining informed consent, then the site is not considered "engaged in research," it does not need an FWA, and the service providers do not need to complete and document human subjects research training. But if the site is considered "engaged in research," then the institution and the individuals/groups need to comply with the requirements described above. Therefore, investigators should review the OHRP guidance on this issue*, which provides detailed scenarios under which institutions, individuals, and groups are considered engaged in research, or not engaged in research, in order to ensure that the proposed research is designed and planned appropriately.

* Details on OHRP guidance are at [Engagement of Institutions in Human Subjects Research \(2008\)](#).