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What Screening Is Permitted Prior to Informed Consent?

Michael R. Hamrell

Ethics and Good Clinical Practice (GCP) requires that informed consent be obtained before any study-specific procedures are performed and before a subject enters a clinical trial. Before investing everyone's time in the informed consent process, it would be convenient to know whether a potential subject is eligible for the trial. However, the necessary eligibility assessments may require the potential subject's informed consent before those assessments are conducted. How are we to deal with this Catch-22?

According to an FDA Information Sheet:

> For some studies, the use of screening tests to assess whether prospective subjects are appropriate candidates for inclusion in studies is an appropriate pre-entry activity. While an investigator may discuss availability of studies and the possibility of entry into a study with a prospective subject without first obtaining consent, informed consent must be obtained prior to initiation of any clinical procedures that are performed solely for the purpose of determining eligibility for research, including withdrawal from medication (wash-out). When wash-out is done in anticipation of or in preparation for the research, it is part of the research.
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> Procedures that are to be performed as part of the practice of medicine and which would be done whether or not study entry was contemplated, such as for diagnosis or treatment of a disease or medical condition, may be performed and the results subsequently used for determining study eligibility without first obtaining consent. On the other hand, informed consent must be obtained prior to initiation of any clinical screening procedures that is performed solely for the purpose of determining eligibility for research.[1]

This guidance clearly prohibits study-specific, health-related procedures prior to informed consent. Is consent required prior to interviewing a potential subject for the purpose of determining study eligibility? The information sheet is ambiguous on this point. Taking a medical history is a health-related activity performed in clinics, so it may be a "clinical procedure." The information sheet appears to assume it is by saying that "an investigator may discuss availability of studies and the possibility of entry into a study" without explicitly permitting interview questions.

There is no explicit regulatory restriction, but asking intrusive personal medical questions prior to consent is probably out of bounds. Unfortunately, there is no generally accepted definition of "intrusive." As a broad guideline, questions that establish general eligibility are acceptable, but a complete medical history is not. Questions about sensitive topics such as psychiatric conditions and sexually transmitted diseases are relatively likely to require prior informed consent. Deciding where to draw the line requires an IRB's expertise on local community standards.

The FDA considers clinical procedures used as part of the screening process to be part of subject recruitment and selection and thus subject to IRB review and oversight.[1,2] An IRB can waive the requirement for informed consent if a procedure presents no more than minimal risk, is standard-of-care for a regular visit, and does not require informed consent outside the research context.[3] For example, informed consent is not normally required to

take vital signs or draw blood during a regular visit to the clinic. Similarly, it is common in medical practice for physicians to ask questions about their patients' health.

Washing out a medication for screening purposes is specifically prohibited prior to consent, but what about fasting prior to a blood draw? There are no explicit rules, but the general consensus among IRBs is that it is not permitted. It is tempting but probably unethical to finesse the rules by telling a potential subject, "We may need to draw some blood. You can save yourself a second trip if you fast before coming in." (However, an argument can be made that, for some people, the risk of fasting is less than the risk of traveling to the clinic a second time.)

Information derived from standard of care in a medical practice can be used for assessing a potential subject without first obtaining informed consent. If a test or procedure would be performed in the normal course of medical practice and in the absence of a clinical trial, then it likely is standard of care and can be used for screening purposes. For example, it is common in physician's offices to measure the blood pressure of every patient (potential study subject or not), when they first enter an examination room. It is perfectly acceptable to use these readings to identify potential subjects for a hypertension study. There is no requirement to repeat the measurement in the screening process.

In contrast, a study may require a cardiac stress test within the previous three months. If a patient normally has an annual cardiac stress test, and the last stress test was six months ago, standard of care requires waiting six months for the next test. Administering a stress test now is not standard of care and therefore requires informed consent, even if it did not present more than minimal risk. If the patient has recently experienced unusual symptoms, an extra stress test may be standard of care, but there is also an extra burden on the physician to justify such a convenient requirement.

HIPAA authorizations are often bundled into consent forms, but informed consent and HIPAA authorization are separate matters, with different rules. For example, potential subjects can verbally agree to answer questions and provide private information during the screening process, but they cannot give verbal informed consent to be in the study. They also must be informed of what will happen to the information, how it will be used, and what happens to the information if they choose not to join the study.[4]

If a study requires screening tests that go beyond standard of care and are not eligible for an IRB waiver, a general, nonspecific, IRB-approved consent form can be used for just the screening procedures. A sample consent form is at http://www.firstclinical.com/journal/2007/Screening_Consent_Form.doc

The consistency of the screening process can be improved with a prepared interview script. The script serves the additional function of providing a list of questions for the IRB to review for intrusiveness.

A standard operating procedure (SOP) about what screening activities require what type of consent (or waiver) can avoid confusion.[5]

Site monitors can detect noncompliance with GCP requirements for consent prior to screening activities by reviewing the process used to recruit and screen subjects and the timing of assessments relative to consent. For example, subjects are unlikely to "walk in cold" for screening and be fasting and off their usual medications. Any convenient deviation in the timing of regular standard of care procedures should be well-justified in the subject's medical records.

In summary, any study-related clinical procedure or interview question that is not standard of care is a candidate for prior informed consent. Different IRBs draw the line in different

places, so consultation with the relevant IRB is helpful. A general-purpose screening consent form can often resolve any ambiguities.

References

1. Guidance for Institutional Review Boards and Clinical Investigators: Screening Tests Prior to Study Enrollment. FDA Information Sheets. http://www.fda.gov/oc/ohrt/irbs/toc4.html#screening
2. Guidance for Institutional Review Boards and Clinical Investigators: Recruiting study subjects. FDA Information Sheets. http://www.fda.gov/oc/ohrt/irbs/toc4.html#recruiting
3. 21 CFR §56.109 (c)(1)
4. 21 CFR §50.27 (a)
5. Hamrell, Michael R. & Wagman, Bruce. Standard Operating Procedures in Clinical Research: A Beginner's Guide. Qual Assur J, 5:93-97, 2001.

Author

Michael R. Hamrell, Ph.D. is President of MORIAH Consultants, a regulatory and clinical research consulting firm. Contact him at 1.714.970.0790 or michael@moriahconsultants.com.