Waiver of Informed Consent

Waiver or alteration of consent: Common Rule

§46.116(d) An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth in this section, or waive the requirements to obtain informed consent provided the IRB finds and documents that:

1. the research involves no more than minimal risk to the subjects;
2. the waiver or alteration will not adversely affect the rights and welfare of the subjects;
3. the research could not practicably be carried out without the waiver or alteration; and
4. whenever appropriate, the subjects will be provided with additional pertinent information after participation.

Waiver or alteration of consent: FDA-Regulated Research

The FDA's IRB regulations do not permit waiver of consent for FDA-regulated research with the narrow exception of emergency research meeting the requirements of 21 CFR 50.23 and 21 CFR 50.24.

Although the FDA's regulations to do not permit waiver of consent, in July 2017 the FDA released a new guidance entitled IRB Waiver or Alteration of Informed Consent for Clinical Investigations Involving No More Than Minimal Risk to Human Subjects. This guidance allows IRBs to waive or alter the informed consent requirements using the Common Rule criteria (above) until the FDA is able to harmonize its regulations with those of the Common Rule for waiver of consent.

State of California Definition of Medical Experiment

If the study falls under the State of California Definition of a medical experiment, the waiver cannot be granted.

A "medical experiment" is defined in the California Health and Safety Code Section 24174, as:

(a) The severance or penetration or damaging of tissues of a human subject or the use of a drug or device, as defined in Section 109920 or 109925, electromagnetic radiation, heat or cold, or a biological substance or organism, in or upon a human subject in the practice or research of medicine in a manner not reasonably related to maintaining or improving the health of the subject or otherwise directly benefiting the subject.

(b) The investigational use of a drug or device as provided in Sections 111590 and 111595.

(c) Withholding medical treatment from a human subject for any purpose other than maintenance or improvement of the health of the subject.

Important Tips

- Each of the 4 elements of §46.116(d) should be explained and justified.
- An explanation for why the research is not greater than minimal risk is generally not difficult.
- In explaining why the research will not adversely affect the rights or welfare, it is important to recognize the right of individuals to determine whether or not to participate in research.
  - It is important to address why a waiver would not adversely impact the subjects.
  - Breach of confidentiality is frequently the principle risk for research involving a waiver request. It is therefore, appropriate to discuss the protections in place to protect subject confidentiality.
- Providing a compelling argument for why the research could not be practicably carried out is the most difficult. Practicable means possible, it does not mean convenient. If a subject is available to consent then it is usually (but not always) possible to obtain their consent.
  - For example, if the subject comes to clinic on a regular basis, it would be practicable to obtain their consent, even for a retrospective review of records. It is important to show that the research could not wait for the time it would take to wait for all subjects to come to clinic (i.e., it was possible to obtain consent but the research would not be practicable).
  - Examples where it might not be practicable to obtain consent: 1) retrospective research where subjects are lost to follow up or no longer seen regularly in clinic or seen at a variety of locations at infrequent intervals or 2) a prospective observational epidemiology study involving a entire practice or inpatient unit where there is a need for 100% participation to ascertain the rate of infection.
  - Example where it would be practicable: records will be reviewed and then subjects will be asked to complete a questionnaire. Consent should be obtained prior to records review and not just prior to the questionnaire.
- Generally the requirement to provide feedback to participants is not applicable, particularly for a retrospective review of records. However, for some types of research it may be appropriate to make the study results available to the individual subjects or to the broader community from which the subjects were drawn. This could be in the form of newsletters or fliers in a doctors office to inform those who were subjects.
- If the research involves individually identifiable health information, then the investigator must also request a waiver of Written Authorization. See Waiver of HIPAA for more information.

IRB Response to the Waiver Request

IRBs should consider the following points when determining whether research could not practicably be carried out without the waiver or alteration. Put another way, it would not be practicable to perform the research (as it has been defined in the protocol by its specific aims and objectives) if consent was required. The emphasis being that it is impracticable to perform the research, and not just impracticable to obtain consent. The following concepts may help an IRB determine whether the research could not be practicably carried out without the waiver of consent:

- **Scientific validity** would be compromised if consent was required. Examples of this might include the following:
The sample size required is so large (e.g., population-based studies, epidemiology trials) that including only those samples/records/data for which consent can be obtained would prohibit conclusions to be drawn or bias the sample such that conclusions would be skewed.

The subjects for whom records would be reviewed are no longer followed and may be lost to follow-up. For example the proportion of individuals likely to have relocated or died may be a significant percentage of the subject population and the research results may not be meaningful and lose statistical power.

The disclosure of the study purpose as part of the consent process would bias the research subjects so that the results will not be meaningful.

Ethical concerns would be raised if consent were required. For example:

- There is a risk of creating additional threats to privacy by having to link otherwise de-identified data with nominal identifiers in order to contact individuals to seek consent.
- There is a risk of inflicting psychological, social or other harm by contacting individuals or families.
- The disclosure of the study purpose as part of the consent process would bias the research subjects so that the results will not be meaningful.
- There is a scientifically and ethically justifiable rationale why the research could not be conducted with a population from whom consent can be obtained.
- Practicability should not be determined solely by considerations of convenience, cost, or speed.

Research Involving Prospective Enrollment of Subjects

Research that involves an intervention or interaction with a living individual or their identifiable data that will be created after the date of IRB submission is considered to be prospective. The IRB requires a thorough rationale for a waiver of consent for prospective research. Typical justifications for a waiver of consent for prospective research include Pragmatic, Ethical and Epidemiological justifications. Often, the justification for waiver involves several reasons rather than just a single reason.

Pragmatic Reasons:

- Too Many Sites to Cover. If a study involves subjects who could be seen at any of a number of CHOP sites, it could be impossible for the study team travel to all of the sites.
- Time of Patient Visits. Patients come to the ED 24 hours a day, 7 days a week. Often the study budget won't support this level of coverage.
- Inability to Identify Subjects Ahead of Time. Often, study subjects can not be identified ahead of time (like an ED patient or an emergency admission) and therefore, the study staff can't plan for coverage to obtain consent.
- Too many Subjects: If the study involves 100's or 1000's of subjects, it might be physically impossible to obtain consent.

Ethical Reasons:

If the research involves subjects who are gravely ill, it might not be appropriate to approach families during the course of hospitalization. If after discharge, there is a possibility that the child has died, calling the family to request consent could precipitate an emotional burden.

Epidemiological Reasons:

Probably the most important rationale is the impact of loss of subjects on the scientific validity of the study.

- Bias. Subjects who refuse to consent usually differ systematically from those that do. If enough subjects will be lost because they could not be approached in time or because they did not wish to consent, the study results will be biased. If elimination of subjects who do not consent will have an impact on study validity, then this argument should be carefully developed and explained.
- Willingness to Participate Depends on Outcome. Parents whose child has a favorable outcome may be more willing to participate in a study than those whose child did not. This can seriously bias the study results.
- Impact on Study Power. Many diseases of interest to pediatricians are relatively rare and loss of even a few subjects could affect the power of the study and therefore the validity.

Research Limited to Use of Existing Records or Specimen

The IRB's most frequent request for waivers is for research involving existing medical records or specimens. The investigator must request a Waiver of Consent and a Waiver of HIPAA Authorization. If children are subjects, Waiver of Assent. The criteria for waiver of assent and consent are the same.

The basis for both waivers (consent and HIPAA) include the requirements for the research to be no greater than minimal risk and that it not be practicable to conduct the research without the waiver.

What are existing records or biospecimens?

The terms existing, retrospective and prospective are frequently misused by investigators. This confusion leads to the potential for research non-compliance.

- Existing means that the records/biospecimens are already available as of the date of submission to the IRB.
- Retrospective means reviewing records or using specimens that are existing.
- Prospective means that the records or specimens don't exist yet as of the date of IRB submission. Reviewing data from medical charts after the information has been recorded is still prospective review from the IRB's perspective.
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