

IRB GUIDANCE IS IRB REVIEW REQUIRED?

The first question one should consider when assessing the requirement for IRB review is whether the activity meets the regulatory definition of human research. Anyone unsure about IRB review requirements and whether their proposed activity constitutes “human research” requiring IRB review should contact the Office of Regulatory Affairs. The IRB staff will determine if the activity is human research. If an activity does not meet the regulatory definition of human research, the IRB will, upon request, issue a letter stating that the project does not require IRB review or approval.

DEFINING HUMAN RESEARCH

- Human Research** Any activity that:
- Meets the DHHS definition of “Research” and involves one or more “Human Subjects” as defined by DHHS regulations.
- OR**
- Meets the FDA definition of “Research” and involves one or more “Human Subjects” as defined by FDA regulations.

Health and Human Services Common Rule Definitions:

Research 45 CFR 46.102(d) defines research as a systematic investigation, including research development, and testing and evaluation, designed to develop or contribute to generalizable knowledge.

Human Subject 45 CFR 102(f) defines a human subject as an individual about whom an investigator conducting research obtains data through intervention or interaction with individual or identifiable private information.

Intervention or Interaction includes physical procedures performed on an individual, manipulation, communication or interpersonal contact with an individual or manipulation of an individual's environment.

Private information includes information that an individual can reasonably expect will not be made public, and information about behavior that an individual can reasonably expect will not be observed or recorded.

Identifiable means that the identity of the individual is or may be readily ascertained by the investigator or associated with the information.

Food and Drug Administration (FDA) Definitions:

Research: 21 CFR 50.3(c) defines research as an experiment that involves a test article and one or more human subjects that is subject to the IND or IDE regulations or which collects data to be submitted to or held for inspection by FDA.

Research is subject to the IND regulations when it involves any use of a

drug except for the use of a marketed drug in the course of medical practice (21 CFR §312.3)

Research is subject to the IDE regulations when it involves any use of a medical device to determine safety or effectiveness of that device. (21 CFR §812.2)

Human Subject: 21 CFR 50.3(e) defines human subject as an individual who is or becomes a participant in research, either as a recipient of a test article or as a control. In the case of research involving a medical device, a human subject also includes an individual on whose specimen a medical device is used.

Test Article: 21 CFR 50.3(j) defines test article as any drug (including a biological product for human use, medical device for human use, human food additive, color, adaptive, electronic product, or any other article subject to regulation under the jurisdiction of the FDA.

Student Projects

Generally, student research involving human subjects falls into one of two categories:

- **Research Practica**, the goal of which is to provide research training; and
- Directed or independent **Research Projects** (e.g., honors or graduate theses), which employ systematic data collection with the intent to contribute to generalizable knowledge.

Research practica **do not** require IRB review. Research projects do require prospective IRB review and approval.

Research Practicum - A course of study that involves the supervised practical application of previously studied theories of research method.

Frequently, schools offer courses that require students to undertake projects in which other people are interviewed, observed, or otherwise serve as participants. The purpose of these course projects is to train students and provide them with a closer view of social, educational, or psychological processes, and an opportunity to practice various research methods.

Provided such projects are not designed to develop or contribute to generalizable knowledge, these projects are not research and IRB review and approval are not required. For example:

- If a project involves the replication of an experiment with known results, then the project is not designed to develop or contribute to generalizable knowledge and the project is not research.
- If a project involves students using research methods (e.g., interview techniques or survey techniques), the results of those methods will be used to evaluate the students ability to apply these techniques, and the results will not be used to test a hypothesis, then the project is not designed to develop or contribute to generalizable knowledge and the project is not research.

Research practices that involve the testing or confirmation of a hypothesis may be research. If the project involves the collection of private identifiable data about living individuals or the collection of data about living individuals through interaction or intervention with those individuals, then before implementation the activity should be brought to the IRB for a determination of whether the activity is human research and requires IRB review.

Oral History

Oral History is a technique in which the researcher conducts a series of taped interviews with the participants in a particular historical event or period. Often, the intention is that these tapes become available to the public at a specified future time (frequently after a substantial delay) in order to convey historical insight.

In many cases, these interviews will be historical recollections of the character of a society or an institution rather than the interviewee's subjective perceptions. When such activities are designed to reconstruct the history of an event or period, then the project is not designed to develop or contribute to generalizable knowledge and the project is not research. Oral history that involves the testing or confirmation of a hypothesis may be research. Such activities should be brought to the IRB for a determination of whether the activity is human research.

Medical Case Reporting

For IRB purposes, a single case report is a retrospective analysis of one, two, or three clinical cases.

A single retrospective case report is a medical/educational activity and does not meet the Federal Policy for the Protection of Human Subjects definition of "research" which is "a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge."

Therefore the activity does not require review by the IRB. In general, the review of medical records for publication of "case reports" of typically three or fewer patients is NOT considered human research and does NOT typically require IRB review and approval because case reporting on a small series of patients does not involve the formulation of a research hypothesis that is subsequently investigated prospectively and systematically for publication or presentation. Reporting or publication is not typically envisioned when one interacts clinically with the subject.

Under HIPAA, a single case report is an activity to develop information to be shared for medical/educational purposes. Therefore, the use of protected health information to prepare a paper for publication of a single case report does not require IRB review for HIPAA purposes. If, however the investigator wishes to publish data with HIPAA identifiers a waiver of authorization is required.

When larger series of patients are being reported, investigators usually begin to ask specific research questions and formal systematic collection of data occurs, moving these activities closer to prospectively designed research. Researchers are advised to consult with the IRB when uncertainty exists about whether the activity meets the definition of human research.

It should also be noted that teaching, and soliciting colleagues' advice on clinical care of a specific patient or groups of patients during presentation of a case at departmental

conferences DOES NOT require IRB review. Generalized commentary by a clinician on the outcome of their clinical care of patients in accepted venues for discussion of clinical management is also not considered research requiring IRB review, if there is no prospective research plan and no formal, systematic and prospective collection of information. This type of communication may occur at hospital or practice meetings, in continuing education venues, or in editorials, where the comments are explicitly identified as personal experience and not formal clinical research.

In Vitro Device Studies

Unlike DHHS regulations, FDA regulations do not provide for exemption from IRB review when research involves existing specimens and the investigator records information without identifiers or linking codes. Nor do FDA regulations define “human subjects” with reference to the identifiability of the subject or of the subject’s private information (i.e., the donors of specimens/samples remain “human subjects” even when the specimens/samples are de-identified). Current FDA guidance indicates that IRB review is required for any IVD study involving human specimens/samples, even when the research involves no identifiers and the biological materials cannot be linked to any identifying information

Research involving cadavers, autopsy material or bio-specimens from now deceased individuals

While research with cadavers and autopsy materials that do not involve testing of in vitro devices does not meet the federal regulatory definitions of human research, the School of Medicine policies require submission to the IRB of research proposals involving cadavers or recognizable body parts. These research activities are reviewed to ensure that HIPAA privacy issues are addressed.

EXAMPLES OF ACTIVITIES THAT DO NOT MEET THE FEDERAL REGULATORY DEFINITIONS OF HUMAN RESEARCH

Activities that fit any of the categories below do not need IRB review.

1. Data collection for internal departmental, school, or other University administrative purposes.

Examples: teaching evaluations, customer service surveys.

Service surveys issued or completed by University personnel for the intent and purposes of improving services and programs of the University or for developing new services or programs for students, employees, or alumni, as long as the privacy of the subjects is protected, the confidentiality of individual responses are maintained, and survey participation is voluntary. This would include surveys by professional societies or University consortia. Note: If at a future date, an opportunity arose to contribute previously collected identifiable or coded survey data to a new study producing generalizable knowledge, IRB review may be required before the data could be released to the new project.

2. Information-gathering interviews and research where questions focus on processes, services, or policies and do not gather information about living individuals.

Example: canvassing librarians about inter-library loan policies or rising journal costs. Asking teacher what methods are in use at their schools or asking for aggregate information about their classes (e.g., class size or composition). Asking emergency room physicians what procedures are used for treating a particular disease.

3. Innovative therapies that do not involved investigational test articles (drugs or devices not approved by FDA) except when they involve "research" as defined by the above criteria. An innovative clinical practice is an intervention designed solely to enhance the well being of an individual patient or client. The purpose of an innovative clinical practice is to provide diagnosis, preventative treatment, or therapy to particular individuals. Note: When innovative therapies differ significantly from routine practice it should be viewed and treated as such with appropriate safeguards in place to protect the rights and welfare of the patients.

4. Quality improvement projects are not research unless designed to develop or contribute to generalizable knowledge. Quality improvement projects are not research when designed to improve or alter the quality of care or the efficiency of an institutional practice. Any individual who is unsure whether or not a proposed quality improvement project should be classified as research should contact the IRB for guidance. If the data is re-examined or re-analyzed and new information surfaces that would contribute to generalizable knowledge, an application must be submitted to the IRB.

5. Coded private information or biological specimens that were not collected for the currently proposed projects do not need IRB review as long as the investigator cannot link the coded data/specimens back to individual subjects. If the data/specimen provider has access to the identity of the subjects (e.g. subjects' names, addresses, etc.), the investigator must enter into an agreement with the data/specimen provider that states under no circumstances will the identity of the subjects be released to the investigator. Note: Investigators are not allowed to make this determination. These projects require verification from the IRB or the IRB liaison/designee. See OHRP Guidance: <http://www.hhs.gov/ohrp/humansubjects/guidance/cdebiol.pdf>

6. Research where Penn is not engaged in research does not require IRB review. Some examples of include: when an institution's employees or agents act as consultants on research but at no time obtain, receive, or possess identifiable private information, perform commercial services for the investigators, or inform prospective subjects about the availability of research. Note: the examples above are not an all inclusive listing. <http://www.hhs.gov/ohrp/humansubjects/assurance/engage.htm>

DETERMINATIONS

Investigators are not required to seek a determination of human research from the IRB when research activity falls outside the DHHS and FDA regulatory definitions of research. Investigators are encouraged to use the Research Determination Worksheet to guide the decision about whether an activity constitutes human research under DHHS or FDA regulations. If a determination is required by the funding agency or sponsor, investigators may submit, submit a request for written confirmation and the Research Determination Worksheet to the IRB and the IRB will provide a written response. IRB

staff are available to by telephone or email to provide guidance as to whether a project is human research as defined above.

REFERENCES

- US HHS Office of Human Research Protections (OHRP) Decision chart to assist in determining whether a project is human research.
www.hhs.gov/ohrp/humansubjects/guidance/decisioncharts.htm Select: Chart 1: Is an Activity Research Involving Human Subjects?
- Federal Policy for the Protection of Human Subjects (Common Rule)
<http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm>
- The Belmont Report
<http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.htm>
- Pritchard, Ivor A. *Searching for "Research Involving Human Subjects": What is Examined? What is Exempt? What is Exasperating*; IRB: Ethics and Human Research 23, no.3 (2001), 5-12