4 Human Research Privacy

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This chapter provides an overview of the ethical guidelines and United States regulations governing the privacy and confidentiality of individually identifiable information in human subject research. The chapter is organized into three parts:

- Ethical codes governing research,
- Major regulations, and
- Practical issues that come up in applying the regulations.

In addition, please see below for some basic definitions related to human subject research privacy.

Basic Definitions

The privacy professional should have an understanding of the following basic terms related to research privacy: Research, Human Subjects, Privacy and Confidentiality. It is important to know and understand how to differentiate between a research situation involving human subjects and a health care situation involving patients in order to know which regulations apply to the situation. In addition, while the terms “privacy” and “confidentiality” are sometimes used in casual conversation to mean the same thing, it is important to distinguish between them for research purposes. The National Science
Foundation provides the following useful definitions:\[3\]:

**Research.** The Common Rule and HIPAA define “research” as “a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.”\[4\] Note that in this definition, “research” is not limited to human subject research. FDA regulations do not define the term “research,” but instead define the term “clinical investigation” as “any experiment that involves a test article [regulated by the FDA] and one or more human subjects...”\[5\] A test article includes, but is not limited to, drugs, devices, or biologicals.

**Human Subject.** The Common Rule defines a “human subject” as “a living individual about whom an investigator...conducting research obtains...[d]ata through intervention or interaction with the individual or,...[i]dentifiable private information.” It also defines three primary types of human subject research activities:

- **“Intervention”** means physical procedures and manipulations of the subjects or their environment (such as a blood draw),

- **“Interaction”** means communication or interpersonal contact between an investigator and a subject, and

- **“Private information”** means information about behavior in which the individual can expect no observation or recording is taking place, and information provided for a specific purpose by an individual with a reasonable expectation that it will not be made public (such as a medical record).\[6\]

The FDA defines a “human subject” as “an individual who is or becomes a participant in research, either as a recipient of the test article [or] as a control. A subject may be either a healthy human or a patient.”\[7\] While not stated, one can infer that FDA studies are, by definition, interventions.

HIPAA does not define “human subject,” but its requirements related to research apply only to protected health information (PHI), which is health information that can reasonably identify an individual (and will be discussed more fully below).\[8\] Of note, while the Common Rule definition of “human subject” refers to living individuals, and the FDA definition implies that participants are alive, in general, HIPAA also applies to the PHI of deceased...
individuals.\[9] (There are, however, some provisions that provide some flexibility for the PHI of deceased individuals used in research which also will be discussed more fully below).

**Privacy** “refers to persons; and to their interest in controlling the access of others to themselves.”

**Confidentiality** “refers to data; and to the agreements that are made about ways in which information is restricted to certain people.”

**Ethical Codes Governing Research**

Three ethical codes: the Nuremberg Code, the Belmont Report and the Declaration of Helsinki provide an historical context and an ethical framework from which to understand the specific U.S. regulations that apply to research privacy. These codes were written, primarily, to address research activities that were deemed to pose serious harm to the human subjects involved and to standardize the protections of human subjects going forward. The focus, then, was to protect the individuals with only a minor concern over the confidentiality of the data involved.

The codes address broad themes related to the ethical conduct of research, such as:

- Obtaining individual consent of research participants,
- Respect for human subjects,
- Social justice,
- Good science,
- The limitation of risks and harm to subjects, and making sure that risks taken are commensurate with the potential benefit of research,
- Both the investigator’s and the participant’s ability to end an individual’s participation in a trial, and
- An investigator’s ability to end a trial.
Written before today’s widespread concern about privacy and confidentiality, neither the Nuremberg Code nor the Belmont Report explicitly reference privacy or confidentiality. However, we can understand in today’s information-based society how the concepts of obtaining informed consent from research participants, and making sure that risks taken in research are commensurate to the potential benefit of the research, do relate to privacy and confidentiality. In particular, we understand the importance of informing research participants about how their individually identifiable information will be collected, used, disclosed and protected, and obtaining their consent to use their information. In addition, the design of research studies must take into account, and provide adequate protections against, the financial, reputational or other risks of individually identifiable information being breached or inappropriately used or disclosed.

The Declaration of Helsinki, while first developed in 1964, is a code for the ethical conduct of research and has been updated to reflect the privacy and confidentiality concerns related to the conduct of research in today’s society. Brief summaries of the three codes are found below.

**Nuremberg Code**

In 1947, the Counsel for War Crimes included as part of their verdict in the trial of doctors who were involved in Nazi human experimentation the *Directives for Human Experimentation*, which is known as “The Nuremberg Code.”[10] The code covers ten points, three of which include the following concepts that are relevant to a discussion of privacy:

- Consent,
- Avoiding all unnecessary physical and mental suffering and injury, and
- Ensuring that the degree of risk to be taken never exceeds that determined by the humanitarian importance of the problem to be solved by the experiment.

**Belmont Report**

In 1979, following the discovery of ethical lapses in medical research in the U.S., such as the 1932–1972 Tuskegee syphilis study (where African-American
men with syphilis were not informed of their diagnosis and were denied medically appropriate treatment)[11], the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, published Ethical Principles and Guidelines for the Protection of Human Subjects of Research, [12] which is known as the “Belmont Report,” based on the conference center where it was in part developed.[13]

The Belmont Report identified the difference between medical practice and research, and determined that where research is taking place, three basic ethical principles need to be followed to protect human subjects:

- **Respect for Persons.** This principle relates to the individual autonomy of each person, notes that some individuals have “diminished autonomy,” and that those with diminished autonomy must be adequately protected.

- **Beneficence.** This principle relates to doing no harm, maximizing possible benefits, and minimizing possible harms.

- **Justice.** This principle relates to the selection of research participants to assure that research does not inappropriately take advantage of disadvantaged populations.

The report expanded upon these ethical principles, and applied them in three areas:

- Informed consent,
- Assessment of risk and benefits, and
- Selection of subjects.

Practical concepts that are identified in the report that relate to a discussion of privacy in research include the notion of requiring informed consent from research participants, and that the informed consent process provide participants with sufficient information about the study so that they can “understand clearly the range of risk and the voluntary nature of participation.”[14] Furthermore, the report identifies that a review committee should determine whether the risks to participants in a study are justified.

**Declaration of Helsinki**
A third ethical code governing research is the World Medical Association Declaration of Helsinki, Ethical Principles for Medical Research Involving Human Subjects. The Declaration of Helsinki was adopted by the World Medical Association (WMA) in Helsinki, Finland in 1964, and has been amended at subsequent WMA General Assemblies through 2008. The WMA is an international association of physicians, and the Declaration of Helsinki states that it applies to physicians engaged in research regardless of the legal or regulatory frameworks that may apply in the jurisdictions where their research is carried out.

The current version of the Declaration of Helsinki is comprised of 35 paragraphs, including the following three that directly relate to privacy:

- “It is the duty of physicians who participate in medical research to protect the life, health, dignity, integrity, right to self-determination, privacy, and confidentiality of personal information of research subjects.”

- “Every precaution must be taken to protect the privacy of research subjects and the confidentiality of their personal information and to minimize the impact of the study on their physical, mental and social integrity.”

- “For medical research using identifiable human material or data, physicians must normally seek consent for the collection, analysis, storage and/or reuse. There may be situations where consent would be impossible or impractical to obtain for such research, or would pose a threat to the validity of the research. In such situations, the research may be done only after consideration and approval of a research ethics committee.”

**Major Regulations**

The four principal United States regulations governing the privacy and confidentiality of individually identifiable information in research discussed below are:

- *Protection of Human Subjects*, also known as the Common Rule (45 C.F.R. 46, Subpart A)
• FDA regulations on the Protection of Human Subjects and Institutional Review Boards (21 C.F.R. 50 and 56),

• HIPAA Privacy Rule (45 C.F.R. 160 and 164), and

• Public Health Service Act Certificates of Confidentiality (301(d), 42 U.S.C. 241(d)).

Regulatory “Who’s Who”

All four regulations are overseen by offices or operating divisions of the Department of Health and Human Services (HHS) as noted in the chart below.

Common Rule

The Protection of Human Subjects regulation was first published in 1974, and was updated in 1981 in response to the Belmont Report.[19] The regulation contains Subparts A through E as follows:

• Subpart A: Basic HHS Policy for Protection of Human Research Subjects,

• Subpart B: Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research,
Subpart C: Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects,

Subpart D: Additional Protections for Children Involved as Subjects in Research, and

Subpart E: Registration of Institutional Review Boards.

In 1983 the President’s Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research issued “Implementing Human Research Regulations: The Adequacy and Uniformity of Federal Rules and of Their Implementation” (the Commission Report), which concluded that 45 C.F.R. 46, Subpart A is the benchmark policy for federal agencies.[20] In 1991, Subpart A was adopted by 16 federal agencies and became known as the Common Rule.[21] Today, the Common Rule applies to 18 agencies, one of which is HHS.[22] Subparts B through E are not part of the Common Rule.[23]

Applicability

The Common Rule “applies to all research involving human subjects conducted, supported or otherwise subject to regulation by any federal department or agency”[24] that has adopted the Common Rule. The Common Rule addresses requirements to protect human subjects in general, with only a subsection of the rule addressing privacy and confidentiality requirements. In addition, the Common Rule “requires compliance with pertinent federal laws or regulations which provide additional protections for human subjects.”[25] Each institution engaged in research that is subject to federal regulation must provide a written assurance of compliance with the Common Rule, which may be filed centrally with the HHS Office for Human Research Protections (OHRP).[26]

Institutional Review Boards

The Common Rule requires human subject research to be reviewed by Institutional Review Boards (IRB). IRBs must perform both an initial review of proposed research and then conduct continuing reviews not less than once a year. The rule establishes the following criteria that must be met in order for an IRB to approve research:[27]
- Risks to subjects are minimized,
- Risks to subjects are reasonable in relation to anticipated benefits,
- Selection of subjects is equitable,
- Informed consent is sought from each prospective subject or their legally authorized representative,
- Informed consent is appropriately documented,
- When appropriate, the research plan makes adequate provisions for monitoring data to ensure the safety of subjects,
- When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data, and
- When some or all of the subjects are likely to be vulnerable to coercion or undue influence, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

While the rule makes IRBs directly responsible for assuring that human subject research studies adequately protect the privacy of subjects and the confidentiality of data, the rule does not provide any additional detail on the standards that an IRB should follow in order to do so. Typically, an IRB will require information on what personally identifiable information will be collected, used and disclosed as part of the study, and how that information will be safeguarded, as part of a human subject research study’s application for approval. In addition, at least for organizations that are subject to HIPAA, IRBs will expect applicants to comply with HIPAA and to follow the organization’s HIPAA policies and procedures for both privacy and security, which are discussed more fully below.

It should be noted that the Common Rule also confers on IRBs the authority to suspend or terminate their approval of research.[28] Therefore, if a human subject research study fails to appropriately protect privacy and confidentiality, the IRB may halt the study.

**General Requirements for Informed Consent**

The Common Rule also establishes requirements for the process of obtaining,
the content, the documentation, and the waiver of informed consent.\[29\]

In general, the Common Rule requires that investigators provide subjects with “sufficient opportunity to consider whether or not to participate” in the study, and that consent is obtained under circumstances that “minimize the possibility of coercion or undue influence.”\[30\] The Common Rule also requires that the informed consent use language understandable to the subject, and specifies that the informed consent may not waive the subject’s legal rights or “release the investigator, sponsor, institution or its agents from liability for negligence.”\[31\]

The Common Rule establishes the following basic elements that must be part of an informed consent:\[32\]

- A statement that the study involves research, its purpose, the duration of subject’s participation, a description of procedures to be followed, and identification of experimental procedures,
- A description of reasonably foreseeable risks or discomforts,
- A description of benefits to subject or others,
- A disclosure of alternative treatments available, if any,
- “A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained,”
- If the research involves more than minimal risk, an explanation of any compensation and medical treatment that are available for injuries,
- A contact for questions and to report injury, and
- A statement that participation is voluntary, and that the subject may discontinue participation in the study with no loss of benefits to which the subject is otherwise entitled.

The Common Rule also establishes the following additional elements of informed consent:\[33\]

- A statement that a particular treatment or procedure that is part of the study may involve unforeseeable risks to the subject,
• Circumstances under which the investigator may terminate the subject’s participation,

• Additional costs to the subject that may result from participation,

• Consequences of subject’s decision to withdraw from research and procedures for orderly termination by the subject,

• A statement that significant new findings developed during the research that may relate to the subject’s willingness to participate in the study will be provided to the subject, and

• The approximate number of subjects in the study.

Of note is that while the IRB must determine in its review of a human subject research study that there are “adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data,” the Common Rule only requires that the informed consent form provided to subjects include information about “the extent, if any, to which confidentiality of records identifying the subject will be maintained.” Thus the Common Rule requires that the study tell subjects who or what institutions will have access to their personal information, but doesn’t require a study to outline for subjects specifically what information or types of information about the subject will be collected, used or disclosed, or how the information will be protected, though such additional information may be provided. As discussed in the section on HIPAA below, for research being conducted by organizations covered by HIPAA, the HIPAA authorization will require more explicit communication regarding information to be used or disclosed for research purposes.

**IRB Alterations or Waivers**

The Common Rule allows an IRB to alter requirements of the informed consent procedure or content or to waive obtaining informed consent if the:

• Research involves no more than minimal risk to the subjects,

• Waiver will not adversely affect the rights and welfare of the subjects,

• Research could not practicably be carried out without the waiver or alteration, and
• Whenever appropriate, subjects will be given pertinent information after participation.

The Common Rule also provides for the waiver or alteration of informed consent for public benefit programs research.[35]

**Documentation of Informed Consent**

The Common Rule specifies that informed consent must be documented by a written consent form approved by the IRB and signed by the subject or their legal representative.[36] The informed consent form also may be read to the subject, and then signed, as long as the subject has had the chance to read the form.[37] Alternatively, the required elements of an informed consent may be presented orally to a subject, and a short form written consent signed by the subject. In this case, a written summary of the oral presentation must be approved by the IRB, and the presentation must be witnessed. The presenter must sign the written summary of the oral presentation; the witness must sign the written summary and the short form consent, and the subject must also be provided a copy of the written summary.[38] In instances where an IRB has not waived the requirement to obtain informed consent, the IRB may nonetheless waive the requirement that the investigator obtain signed consent if either:

• The “only record linking subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality.”[39] In this case, each subject should be asked whether they wish to have documentation linking them to the study and the subject’s wishes should govern.

• The “research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.”[40]

**Common Rule Privacy Summary**

The Common Rule’s privacy requirements can be summarized in the following four points:

• The IRB must determine whether there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data,
• The informed consent form must state the extent, if any, to which confidentiality of records identifying the subject will be maintained,

• The IRB may waive or alter the process or content requirements for informed consent, and

• Documentation of informed consent may be waived in limited, minimal risk situations.