

# **How to Interpret the Federal Policy for the Protection of Human Subjects or "Common Rule" (Part A)**

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This Interpretive Guide to the Federal Policy for the Protection of Human Subjects or "Common Rule" was developed by a working group of individuals who attend the Human Subjects Research Subcommittee, Committee on Science, National Science and Technology Council. The document does not necessarily represent the position of any of their respective agencies.

## **Purpose**

The purpose of this document is to clarify and provide guidance on how to interpret selected aspects of the Federal Policy for the Protection of Human Subjects (Part A) sometimes called the Common Rule. The guidance is not intended to be exhaustive, but to help deal with a number of common concepts and issues often raised in the human subjects protection process. Thus it is intended to be used as a companion to the Common Rule itself. In addition, institutions must adhere to other laws and regulations applicable to their human subjects research including state law, foreign laws, and human subjects procedures of the Food and Drug Administration (FDA.)

## **Empowerment, Flexibility and Discretion of Institutions and IRBs.**

Trust in the honest, conscientious judgement of the human beings who serve on IRBs is pivotal to the entire system of protection of research subjects. Indeed, the system recognizes that there is no simple formula to apply to ethical decisions, and instead it vests the major responsibility of ethical decision making with the IRB. IRB actions are to be based on ethical principles (such as outlined in the Belmont Report.) They should fully recognize that ethical decisions involve a balance among such principles (such as respect for persons, beneficence, and justice) along with the importance of the knowledge that may reasonably be expected to result from proposed research (the requirement for which is itself grounded in the principle of beneficence.) In order to carry out its mandate, Institutions and IRBs are empowered with very wide discretion within the bounds of the Common Rule. Recognizing the very wide range of situations under which research may occur, above all else, the IRB should strive to do "the right thing" as it sees it. The regulations allow considerable flexibility to serve that purpose.

Institutions, IRBs and investigators all have a serious role to play. In the interest of promoting human subjects protection, it is important for institutions and IRBs to take a facilitative, collegial and educational posture with respect to investigators rather than a burdensome adversarial one. The IRB should encourage investigators to embrace ethical behavior by acting to facilitate ethical research and not be seen as an obstacle to the conduct of research. To that end, institutions and IRBs should promote education outreach efforts, and are encouraged to use their broad discretion to adopt creative administrative and other means to reduce administrative burden and maximize attention to the most important ethical issues.

## What is Research Under the Common Rule?

The Common Rule defines research as "... a systematic investigation including research development, testing and evaluation designed to develop or contribute to generalizable knowledge." Further, as described in the Belmont Report "...the term 'research' designates an activity designed to test an hypothesis, permit conclusions to be drawn, and thereby to develop or to contribute to generalizable knowledge.... Research is usually described in a formal protocol that sets forth an objective and a set of procedures to reach that objective."

Thus a key aspect of research is that there be a systematic design in advance, generally utilizing a scientific approach or protocol, for the definite purpose of contributing to generalizable knowledge. Research can include a wide variety of activities including: experiments, observational studies, surveys, tests, and recordings designed to contribute to generalizable knowledge. It generally does not include such operational activities as: medical care, quality assurance, quality improvement, certain aspects of public health practice such as routine outbreak investigations and disease monitoring, program evaluation, fiscal or program audits, journalism, history, biography, philosophy, "fact-finding" inquiries such as criminal, civil and congressional investigations, intelligence gathering, and simple data collection or data collection for other purposes. However, some of these activities may include or constitute research in the specific circumstance where there is clear advance intent to contribute to generalizable knowledge with a formal scientific protocol.

## Human Subject

This means a living individual about whom an investigator obtains 1) data through intervention or interaction or 2) identifiable private information. Intervention includes physical procedures and manipulations of the subject or the subjects environment for research purposes and interaction includes communication between the investigator and the subject. Private information includes information about behavior in which an individual can reasonably expect that no observation is taking place, or information for specific purposes (such as a medical record) that individuals can reasonably expect will not be made public. Private information must also be individually identifiable (i.e. the subject's identity is or may be readily ascertained by the investigator or the subject's identity readily associated with the information.)

Thus, simple observational studies of public behavior (including television and internet chat rooms) do not involve human subjects as defined, because there is no intervention or interaction and the behavior is not private. Also, studies based on data collected for non-research purposes do not constitute human subjects research unless individual identity is readily identifiable. Examples include: programmatic data such as service statistics, school attendance data, crime statistics, election returns, vital statistics, and pathologic specimens collected for therapeutic purposes (where such information does not readily identify individuals.) A number of the specific exemptions in the Common Rule (see below) further address some of these and similar situations.

## Exemptions

Survey and certain similar research - 101(b)(2). The Common Rule exempts such research except in situations where each of two things occurs: first the information would allow subjects to be identified (either directly or through identifiers linked to the subject) and second "any disclosure of the human subjects responses outside the research could reasonably place the subject at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability or reputation." Thus, survey

and similar research under formal human subjects protection is "covered" only when both privacy/confidentiality might be compromised through identification and the nature of the information disclosed is very sensitive. In determining whether there might be a reasonable risk or damage related to divulging the sensitive information etc., it is not enough that there be merely some hypothetically possible risk that can be construed. Rather the risks resulting from disclosure must be readily appreciable and significant.

Research involving the collection or study of existing data or specimens - 101(b)(4). "Existing" means existing at the time the research is conducted. Some Agencies interpret this to mean existing at the start of the research and some Agencies include as "existing" sources such as vital records routinely created on an ongoing basis without alteration, even though some may be created after the start of the research. This research is exempt if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified directly or through identifiers to the subjects. Thus the key point is how the data are recorded. The research would remain exempt if the investigator had access to identifiable information (such as medical records) but did not record identifiers. Moreover, consistent with the definition of human subject, identification need be readily ascertainable. Research would remain exempt for example if identity is linked only by legitimate encryption or other procedures that make it very difficult for investigators to identify individuals.

Public Benefit or Service Programs (101)(b)(5). This exemption to study, evaluate or otherwise examine public service or benefit programs is fairly broadly written. However, it is generally interpreted to be limited to research on the process or outcomes of service delivery (e.g. programmatic research or operations research.) DHHS, in fact interprets this exemption narrowly to apply primarily to entitlement and "entitlement-like" programs such as Social Security.

## **Waiver or Alteration of Informed Consent**

Section 116 (d) provides conditions for waiving or altering the informed consent procedure for research involving no more than minimal risk. A key condition is that "The research could not be practicably carried out without the waiver or alteration." The determination that the research could not be practicably carried out is not a matter of mere inconvenience to the research process. Rather, there need be a plausible concern that either the conduct or the findings of the research might be adversely affected by the consent process. An adverse effect might include a substantial delay or increase in cost. Examples of situations where waiver or alteration of informed consent may often be justified are minimal risk (and non-exempt) social science methods involving deception; and surveys and cultural anthropology where implementation of all or part of the informed consent process might offend or raise unwarranted suspicions among respondents - thereby adversely affecting the research. Certain medical record review research is another common example where consent may not be practicable. Section 117 (c) allows for waiver of a signed consent form under certain circumstances, but does not otherwise alter the consent requirements per se.

## **Informed Consent to Promote Communication**

Recognizing that communication is an imperfect human process, in the interest of better human subjects protection, it is important to recognize the informed consent process as a process of communication and not just a legal requirement. The consent form should not be confused with the informed consent process. In the interest of good communication, the process should promote: simple understandable language; emphasis on the required and most important information, and avoidance of "information overload," without large amounts of additional information of marginal use to the consent process. The

process should also promote good communication techniques such as active listening, individualizing and requesting restatement by the subject..

## **Minimal Risk**

As defined in the Common Rule this "... means that the probability and magnitude of the harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests." More specifically it means the risks encountered inherent to the daily lives of the population or class of research subjects involved and the additional of risk added by the research. Thus, a treadmill test of low intensity might be minimal risk for the population in general, but more than minimal risk for research conducted with a group of cardiac patients. Likewise, measuring blood levels of a drug with serious side effects among a group of patients already receiving it for therapy might be considered minimal risk, whereas administering the same drug solely for research purposes and measuring it among the healthy population could be more than minimal risk. This standard should not be interpreted to mean that additional highly risky or potentially harmful interventions are considered minimal risk for certain severely ill patients simply because such patients are subject to such interventions as part of their treatment. Many non-exempt surveys may be considered minimal risk since they do not exceed the harm or discomfort of certain psychological examinations or tests or those ordinarily encountered in daily life.

## **Expedited Review**

In order to qualify for expedited review, research must be 1) both on the list of expedited review procedures published in the Federal Register and be found by the reviewer to be of minimal risk, or 2) involve only minor changes in approved research. Expedited review per se does not mean any decrease in human subjects protection required in the conduct of the research itself.

## **Timing of IRB Review in Relation to Funding**

Covered research may not be supported without certification that the research has been reviewed and approved by the IRB. The Common Rule itself does not actually require IRB approval prior to agency review and/or funding, but some Agencies may. In addition Sections 118 and 119 provide for activities funded without definite plans for human subjects research. In any case, IRB approval must precede the actual conduct of the covered human subjects research.

## **Multiple Site Research**

Section 114 addresses cooperative research. Each institution is responsible for safeguarding subjects rights and following appropriate procedures. However, institutions may rely on the review of another qualified IRB. It is recognized that the types of research, the levels of risk and the kinds of sites where cooperative research takes place vary widely and the need for considerable adaptability is recognized. For example, the mere fact that research occurs at a certain place (such as a health department, school or supermarket) does not mean that "place" would be considered a research institution. If a site is only opening its doors to researchers or data abstractors, or is merely providing data, it is not considered a research institution. While it is not necessary that every site or every institution provide its own IRB review (an IRB may be "remote" from the site of the actual research,) it is important that the IRB review and oversight that is conducted is explicitly considered competent and cognizant of the conditions and

situations in the sites under its purview. One specific mechanism is a cooperative amendment to assurances of institutions participating in cooperative research, which can be agreed to by those institutions, and approved by the sponsoring agency to document the terms of reliance on another institution's IRB.

## **Continuing Review**

IRBs must conduct continuing review of covered research at least annually. IRBs have considerable latitude in what the review entails. The key concept is that the review be substantive and meaningful. In some cases it may involve a complete review of the entire protocol by the full IRB together with any additional changes, events and findings. It may also include observations of the research or the consent process. In other instances, IRBs may adopt more expeditious procedures, for example relying on findings of a principal reviewer or on research progress reports. The IRB may consider a biomedical or other intervention study closed when all active participation of the subjects has ended and the investigator is no longer accessing private identifiable information. Once a study is closed, it is a good idea to have reasonable ongoing procedures in place as appropriate and practicable, to protect confidentiality and to provide feedback of relevant emerging information to subjects.

## **Promoting Ethical Behavior in Areas Exempt from the Common Rule**

Even though certain classes of research are exempt under the Common Rule, they should not be considered exempt from common ethical standards. For example, a certain survey may be exempt, but it is common courtesy and otherwise generally reasonable to ask permission and provide some simple information to respondents. Likewise, research on existing specimens might not record identifiers and thus be exempt, but researchers ought still to take care to protect individual privacy. The interest in promoting ethical behavior outside the common rule is not intended as a mandate for more structured procedures, but rather to advance a cultural norm of ethical behavior for research and non-research activities alike, to be exercised with discretion by institutions and individuals.

## **Promoting More Active Oversight of Higher Risk Research**

As with any undertaking, a sense of priority is important in dealing with human subjects research and institutions are encouraged to exercise more active oversight beyond the minimum requirement of the Common Rule for certain higher risk research, as appropriate.

More active oversight could include such activities as special educational outreach to investigators and other appropriate stake holders, site visits and observations of research activities, research participant interviews as appropriate, ongoing IRB briefings of research progress, timely monitoring and evaluation of untoward events, and data monitoring and safety boards.

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