OHRP 45 CFR part 46 Frequently Asked Questions (FAQs)



**Question 1:** What is the historical basis for the current human research regulations, 45 CFR part 46?

**Answer:** The history of contemporary human subjects protections began in 1947 with the Nuremberg Code, developed for the Nuremberg Military Tribunal as standards by which to judge the human experimentation conducted by the Nazis. The Code captures many of what are now taken to be the basic principles governing the ethical conduct of research involving human subjects.

Similar recommendations were made by the World Medical Association in its Declaration of Helsinki: Recommendations Guiding Medical Doctors in Biomedical Research Involving Human Subjects, first adopted in 1964 and subsequently revised many times.

Basic regulations governing the protection of human subjects in research supported or conducted by HHS (then the Department of Health, Education and Welfare) were first published in 1974. In the United States, a series of highly publicized abuses in research led to the enactment of the 1974 National Research Act (Public Law 93-348), which created the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. One of the charges to the National Commission was to identify the basic ethical principles that should underlie the conduct of biomedical and behavioral research involving human subjects and to develop guidelines to assure that such research is conducted in accordance with those principles. In 1978, the Commission published "Ethical Principles and Guidelines for the Protection of Human Subjects of Research," also known as the Belmont Report , named after the Belmont Conference Center where the Commission met when drafting the report. The Belmont Report identifies three fundamental ethical principles for all human subjects research—respect for persons, beneficence, and justice.

Based on the Belmont Report and other work of the National Commission, HHS revised and expanded its regulations for the protection of human subjects in the late 1970s and early 1980s. The HHS regulations are codified at 45 CFR part 46, subparts A through D. The statutory authority for the HHS regulations derives from 5 U.S.C. 301; 42 U.S.C. 300v-1(b); and 42 U.S.C. 289.

The regulations found at 45 CFR part 46 are based in large part on the Belmont Report and were written to offer basic protections to human subjects involved in both biomedical and behavioral research conducted or supported by HHS. In 1991, 14 other Federal departments and agencies joined HHS in adopting a uniform set of rules for the protection of human subjects, identical to subpart A of 45 CFR part 46 of the HHS regulations. This uniform set of regulations is the Federal Policy for the Protection of Human Subjects, informally known as the "Common Rule." In 1995 the Central Intelligence Agency was required by Executive Order to comply with all subparts of the HHS regulations.

**Question 2:** What human research issues are addressed in 45 CFR part 46?

**Answer:** HHS regulations at 45 CFR part 46 stipulate substantive and procedural requirements for investigators and institutions engaged in HHS-supported or -conducted research. Specifically, in addition to providing definitions and information about application of the regulations, specific sections of the regulations address the following topics:

- Assuring compliance with the regulations (46.103)
- Institutional Review Board (IRB) membership (46.107)
- IRB functions and operations (46.108)
- IRB review of research (46.109)
- Expedited review procedures for certain kinds of research involving no more than minimal risk, and for minor changes in approved research (46.110)
- Criteria for IRB approval of research, including minimizing risk, ensuring confidentiality, and protecting vulnerable populations, (46.111)
- Review by institution (46.112)
- Suspension or termination of IRB approval of research (46.113)
- Cooperative research (46.114)
- IRB records (46.115)
- General requirements for informed consent (46.116)
- Documentation of informed consent (46.117)
- Applications and proposals lacking definite plans for involvement of human subjects (46.118)
- Research undertaken without the intention of involving human subjects (46.119)
- Evaluation and disposition of applications and proposals for research to be conducted or supported by a Federal Department or Agency (46.120)
- Use of Federal funds (46.122)
- Early termination of research support: Evaluation of applications and

proposals (46.123)
- Conditions (46.124)

Additional protections for specific populations have been adopted by HHS (and other departments and agencies to a lesser extent), as follows:

- 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

**Question 3:** How can I find out if the 45 CFR 46 human subject research regulations apply to my research?

**Answer:** HHS regulations at 45 CFR 46.103(a) require that each institution engaged in human subjects research that is supported or conducted by HHS provide the Office on Human Research Protections with a satisfactory Assurance of Compliance to comply with the regulations, unless the research is exempt under 45 CFR 46.101(b). The assurance identifies policies and procedures for the institution and describes the activities to which the regulations apply. You should check your institution's Terms of Assurance to find out whether the regulations apply to your research. In addition, you might want to consult OHRP's decision charts at http://www.hhs.gov/ohrp/humansubjects/guidance/decisioncharts.htm.

**Question 4:** How does HHS ensure that regulatory requirements for human research are met?

**Answer:** HHS employs many approaches to facilitate compliance with the regulations. First, through a system of IRB registration and assurances, HHS regulations require institutions to commit to compliance with 45 CFR part 46 before initiating participation in HHS-conducted or -supported research involving human subjects. On behalf of the Secretary, HHS, the Office on Human Research Protections (OHRP) approves the terms of these written institutional assurances, which constitute binding commitments.

In essence, OHRP holds accountable and depends on institutional officials, committees, researchers, and other agents of the institution to comply with the institution's assurance and the regulations.

In carrying out its oversight responsibility, OHRP's Division of Compliance Oversight monitors compliance through not-for-cause compliance oversight surveillance activities and for-cause compliance oversight evaluations of allegations or indications of noncompliance with the regulations. OHRP has the authority under Title IV of the Public Health Service Act (42 USC 281 et seq.) to investigate complaints about human subject protections in HHS-conducted or -funded research, as well as any other research covered by the institution's Assurance of Compliance. OHRP also promotes compliance through its Division

of Policy and Assurances, which provides policy and guidance documents pertaining to the regulatory requirements in 45 CFR 46.

In addition, through its Division of Education and Development, OHRP provides a multifaceted education program—including national conferences, research community forums, and a quality improvement program—all of which enhance understanding of the regulations and what is necessary for compliance.

**Question 5:** Do the human research regulations apply to non-U.S. institutions?

**Answer:** Yes, whenever non-U.S. institutions are engaged in non-exempt HHS-supported or –conducted human subjects research, the regulations apply. Please see: http://www.hhs.gov/ohrp/humansubjects/assurance/filasurt.htm#sectionb .

**Question 6:** How does 45 CFR part 46 relate to the Common Rule and human subjects regulations used by non-HHS agencies?

**Answer:** The current U.S. system of protection for human research subjects is heavily influenced by the Belmont Report , written in 1979 by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. The Belmont Report outlines the basic ethical principles in research involving human subjects. In 1981, with this report as foundational background, HHS and the Food and Drug Administration revised, and made as compatible as possible under their respective statutory authorities, their existing human subjects regulations.

The Federal Policy for the Protection of Human Subjects or the "Common Rule" was published in 1991 and codified in separate regulations by 15 Federal departments and agencies, as listed below. The HHS regulations, 45 CFR part 46, include four subparts: subpart A, also known as the Federal Policy or the "Common Rule"; subpart B, additional protections for pregnant women, human fetuses, and neonates; subpart C, additional protections for prisoners; and subpart D, additional protections for children. Each agency includes in its chapter of the Code of Federal Regulations [CFR] section numbers and language that are identical to those of the HHS codification at 45 CFR part 46, subpart A. For all participating departments and agencies the Common Rule outlines the basic provisions for IRBs, informed consent, and Assurances of Compliance. The list below displays the agencies and departments that have signed onto the Common Rule and their CFR numbers.

- Agency for International Development (22 CFR part 225)
- Consumer Product Safety Commission (16 CFR part 1028)
- Department of Agriculture (7 CFR part 1c)
- Department of Commerce (15 CFR part 27)
- Department of Defense (32 CFR part 219)
- Department of Education (34 CFR part 97 subpart A)
- Department of Energy (10 CFR part 745)
- Department of Health and Human Services (45 CFR part 46 subpart A)
- Department of Housing and Urban Development (24 CFR part 60)

- Department of Justice (28 CFR part 46)
- Department of Veterans Affairs (38 CFR part 16)
- Department of Transportation (49 CFR part 11)
- Environmental Protection Agency (40 CFR part 26)
- National Aeronautics and Space Administration (14 CFR part 1230)
- National Science Foundation (45 CFR part 690)

In addition, the Central Intelligence Agency must comply with all subparts of 45 CFR part 46 under Executive Order 12333.

Several non-HHS federal departments and agencies have additional regulations in place for research involving special populations or for human subjects research in general. Investigators are encouraged to review the regulations of the funding agency to determine whether additional regulations apply. Also, many agencies have not adopted subparts B, C, or D and grantees of those agencies are not necessarily bound by them. Grantees should consult their funding agency for guidance.

**Question 7:** How do subparts B, C, and D of the HHS human research regulations at 45 CFR part 46 relate to subpart A?

**Answer:** Subparts B (additional protections for pregnant women, human fetuses, and neonates); C (additional protections for prisoners); and D (additional protections for children) are regulations that supplement subpart A by providing additional protections for vulnerable subject populations. Investigators conducting HHS-supported research in these populations must comply with all of the requirements of subpart A as well as the requirements of the relevant subpart. Institutions may further choose to apply subparts B-D to all research regardless of whether it is HHS-supported. Therefore, investigators should contact their relevant institutional officials to determine which subparts apply to their specific research project.