45 C.F.R. Part 46, Subpart A (commonly referred to as the "Common Rule") is the federal regulation that governs the protection of human research subjects. The Common Rule was published in 1991 by the U.S. Department of Health and Human Services, and it was subsequently codified by the departments and agencies listed below:

The following departments and agencies have codified the Common Rule in regulation:

> Department of Agriculture,[1] Department of Energy,[2] National Aeronautics and Space Administration,[3] Department of Commerce,[4] Consumer Product Safety Commission,[5] Agency for International Development,[6] Department of Housing and Urban Development,[7] Department of Justice,[8] Department of Defense,[9] Department of Education,[10] Department of Veterans Affairs,[11] Environmental Protection Agency,[12] Department of Health and Human Services,[13] the National Science Foundation,[14] Department of Transportation.[15]

The following departments and agencies comply with all subparts of 45 C.F.R. Part 46, including the special protections for pregnant women, prisoners, and children, although they have not adopted it via regulation:

> Central Intelligence Agency,[16] Department of Homeland Security,[17] and the Social Security Administration[18]

This regulation requires institutions that conduct research involving human subjects to submit research proposals for approval by institutional review boards, obtain informed consent from human subjects, and to provide assurance of their compliance with the Common Rule to the department or agency that is supporting their research.

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[1] 7 C.F.R. pt. 1c
[2] 10 C.F.R. pt. 745
[3] 14 C.F.R. pt. 1230
[4] 15 C.F.R. pt. 27
[5] 16 C.F.R. pt. 1028
[6] 22 C.F.R. pt. 225
[7] 24 C.F.R. pt. 60
[8] 28 C.F.R. pt. 46
[9] 32 C.F.R. pt. 219
[10] 34 C.F.R. pt. 97
[11] 38 C.F.R. pt. 16
[12] 40 C.F.R. pt. 26
[13] 45 C.F.R. pt. 47, s. A
[14] 45 C.F.R. pt. 690
[15] 49 C.F.R. pt. 11
[16] Exec. Order No. 12333, 46 Fed. Reg. 59941 (Dec. 4, 1981) (directing the Central Intelligence Agency to follow regulations promulgated by the Department of Health and Human Services for human experimentation).
[17] Pub. L. No. 108-458, 118 Stat. 3869 (directing the Department of Homeland Security to follow the Common Rule).
[18] Pub. L. No. 103-296, 108 Stat. 1476 (the Social Security Administration must follow regulations promulgated by the Department of Health and Human Services that existed before the Administration was established as an independent agency, unless the Administrator has taken action indicating otherwise).

45 CFR Part 46 Subpart A

1) Applicability of the Common Rule

Federal funds cannot be used for research involving human subjects if the requirements of the Common Rule have not been satisfied.[19] The department or agency head may impose additional requirements on research for the purpose of protecting human subjects.[20]

a. Definitions[21]

Research, for the purposes of this summary, means a systematic investigation designed to contribute to the generalized knowledge.[22] *Research subject to regulation* includes research activities that a federal agency has specific authority to regulate.[23]

The term *human subject* refers to a person from whom a researcher obtains:

1) Data through *intervention*, which means a physical procedure or manipulation of the individual or the individual's environment, or through interaction;[24] or
2) *Private information*, such that the person may be identified by use of the data, and expects that the data will not be made public in an identifiable format.[25]

IRB means an institutional review board created to carry out the Common Rule.[26]

Minimal risk is the notion that the probability and severity of the harm expected as a result of the research is not greater than the harm generally encountered during daily life or routine examinations.[27]

b. Research Subject to the Common Rule[28]

The Common Rule applies to any research conducted or supported by a federal agency that has codified the regulation, except if the research falls into one of the categories of exceptions listed below. Further, if the research is not conducted or supported by the federal agency or department but is considered research subject to regulation,[29] an *IRB* must review and approve the research as required by the Common Rule.

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[19] 45 C.F.R. § 46.122
[20] 45 C.F.R. § 46.124
[21] 45 C.F.R. § 46.102
[22] 45 C.F.R. § 46.102(d)
[23] 45 C.F.R. § 46.102(e)
[24] 45 C.F.R. § 46.102(f)
[25] 45 C.F.R. § 46.102(f)
[26] 45 C.F.R. § 46.102(g)
[27] 45 C.F.R. § 46.102(i)
[28] 45 C.F.R. § 46.101
[29] 45 C.F.R. § 46.102(e)

For research proposals involving human subjects submitted to the department or agency from its own officers and employees, the department or agency may use the appropriate experts and consultants to evaluate the proposal, and must take into consideration risks to the subjects, the level of protection against these risks, and any potential benefits from the research to the subject and to society.[30]

Compliance with the Common Rule does not alter other existing obligations that may exist under foreign[31], federal,[32] state, or local[33] law that provide additional protection for human subjects.

If the research occurs in a foreign country, the head of an agency or department may approve the use of foreign policies and procedures instead of the Common Rule if the procedures afford at least the same amount of protection for human subjects.[34]

The head of an agency or department may waive some or all of the requirements in the Common Rule for specific types of research.[35]

c. **Research Not Subject to the Common Rule**[36]

Unless otherwise required by the head of an agency or department, the Common Rule does not apply to:

- Research in an established education setting on a topic such as the effectiveness of a particular curricula;[37]
- Research concerning the use of tests or procedures to evaluate public behavior; [38] however, the Common Rule applies to this type of research if:
    - The research seeks identifying information and disclosure of such information would potentially harm the subject or expose them to criminal or civil liability;[39]
    - The research involves a candidate or public official;[40] or
    - A federal statute mandates that identifying information be kept confidential.[41]

[30] 45 C.F.R. § 46.120
[31] 45 C.F.R. § 46.101(g)
[32] 45 C.F.R. § 46.101(e)
[33] 45 C.F.R. § 46.101(f)
[34] 45 C.F.R. § 46.101(h)
[35] 45 C.F.R. § 46.101(h)
[36] 45 C.F.R. § 46.101
[37] 45 C.F.R. § 46.101(b)(1)
[38] 45 C.F.R. § 46.101(b)(2)
[39] 45 C.F.R. § 46.101(b)(2)
[40] 45 C.F.R. § 46.101(b)(3)(i)

- Research with existing and publically-available data, and the researcher does not use the information in a way that allows the subject to be identified;[42]
- Research that evaluates public benefit or service programs;[43] or
- Consumer studies of the taste and quality of food if the foods are consumed without additives or the additives do not exceed the levels that have been approved by the appropriate agency.[44]

d. Research Without Definite Plans for Human Subject Involvement

If an application or proposal, usually involving a grant or contact, may involve human subjects but there are no definite plans to do so, the application does not need to be reviewed by the IRB before an award is made. However, human subjects may not be involved in any project until the project has been approved by the IRB, and certification is submitted to the department or agency by the institution.[45]

If research is undertaken without the intention of involving human subjects, but the inclusion of human subjects is later proposed, the proposal must be approved by the IRB, certification must be submitted to the department or agency, and the department or agency must approve the proposed change.[46]

2) *Assuring Compliance with the Common Rule*[47]

Researchers must provide a written assurance that their research activities will comply with the Common Rule to the appropriate department or agency.[48] The assurance must include:

- A statement regarding the researcher's commitment to protecting the human subjects;[49]
- Designation of an IRB, with accompanying information regarding IRB meeting space and support for the IRB in carrying out its responsibilities;[50]
- A list of IRB members and their qualifications, as well as documentation regarding any relationship between the research institution under review and the IRB member;[51]
    - Any changes in IRB membership must be reported to the agency;[52]

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[41] 45 C.F.R. § 46.101(b)(3)(i)
[42] 45 C.F.R. § 46.101(b)(4)
[43] 45 C.F.R. § 46.101(b)(5)
[44] 45 C.F.R. § 46.101(b)(6)
[45] 45 C.F.R. § 46.118
[46] 45 C.F.R. § 46.119
[47] 45 C.F.R. § 46.103
[48] 45 C.F.R. § 46.103(a)
[49] 45 C.F.R. § 46.103(b)(1)
[50] 45 C.F.R. § 46.103(b)(2)
[51] 45 C.F.R. § 46.103(b)(3)
[52] 45 C.F.R. § 46.103(b)(3)

- Written procedures which the IRB will follow that govern:
    - The review of the proposed research and subsequent reporting of the IRB's findings;
    - Information regarding whether the project requires review more than annually or whether the project needs verification from an individual other than the investigator; and
    - Reporting to the IRB any changes to the research if the changes are made before IRB approval; changes may only be made after IRB approval to remove sources of potential harm to the human subjects.[53]
- Written procedures governing reporting to the IRB and any other department or agency officials the following:
    - Unanticipated risk to the subjects or noncompliance with the Common Rule or IRB requirements; and
    - Any change in the status of IRB approval, including suspension or termination.[54]

The assurance must be completed and submitted by an individual with authority to act on behalf of the research institution, and must be submitted according to the department of agency's procedures.[55] The assurance will be reviewed by appropriate department or agency staff; the staff will consider in reviewing the assurance the adequacy of the proposed IRB in relation to the intended scope of the proposed research, including the need for continuing review.[56]

The department or agency may approve the assurance, disapprove the assurance, condition the assurance, or begin negotiations with the institution to facilitate approval.[57] Each institution must certify that each proposal and application for research covered by the assurance and the Common Rule has been approved by an IRB according to department or agency policy.[58] If an institution does not have an approved assurance for the research, applicants have 30 days after receiving a request for certification to submit a certification that the research has been approved by an IRB, or else the application will be sent back to the institution.[59]

3) *IRB Procedures*

a. Membership[60]

[53] 45 C.F.R. § 46.103(b)(4)
[54] 45 C.F.R. § 46.103(b)(5)
[55] 45 C.F.R. § 46.103(c)
[56] 45 C.F.R. § 46.103(d)
[57] 45 C.F.R. § 46.103(e)
[58] 45 C.F.R. § 46.103(f)
[59] 45 C.F.R. § 46.103(f)
[60] 45 C.F.R. § 46.107

IRBs should consist of at least five members who are of diverse backgrounds, both professionally and with regard to race, gender, and culture.[61] The IRB members must have the requisite experience and competence to review the proposed research projects that come before it, including how laws and standards of professional conduct apply to the research.[62] If an IRB reviews research that involves vulnerable human subjects such as pregnant women or prisoners, the IRB should consider including a member of the vulnerable population or a person who has experience working with the population.[63]

In selecting the composition of an IRB, efforts should be made to avoid creating an IRB that represents only one gender.[64] An IRB cannot be composed of members that represent only one profession.[65] At least one member must have a background in science, and at least one member must have background in something other than science.[66]

At least one member must not be affiliated with the institution whose research is being reviewed, nor be related to someone affiliated with the institution.[67] An IRB member may not have a conflict of interest.[68] The IRB can consult with individuals with special expertise relating to the area of research that they are reviewing, but this consultant may not vote.[69]

b. Functions and Operations[70]

Each IRB must follow the written procedures set forth in the assurance and, except in the case of expedited review, review of the research must occur at meetings where a majority of the IRB members are present, including at least one member with a background in a field other than science; approval requires a majority of those present at the meeting.[71]

i. Review of Research[72]

IRBs may approve, disapprove, or require modifications to research proposals.[73] The IRB must provide written documentation of its decision to the institution; if the IRB disapproves the

[61] 45 C.F.R. § 46.107(a)
[62] 45 C.F.R. § 46.107(a)
[63] 45 C.F.R. § 46.107(a)
[64] 45 C.F.R. § 46.107(b)
[65] 45 C.F.R. § 46.107(b)
[66] 45 C.F.R. § 46.107(c)
[67] 45 C.F.R. § 46.107(d)
[68] 45 C.F.R. § 46.107(e)
[69] 45 C.F.R. § 46.107(e)
[70] 45 C.F.R. § 46.108
[71] 45 C.F.R. § 46.108
[72] 45 C.F.R. § 46.109
[73] 45 C.F.R. § 46.109(a)

research proposal, the IRB must include in writing the reasons for the disapproval, and the institution must be given a chance to respond.[74]

IRBs must require information to be provided to subjects to facilitate informed consent as defined in the Common Rule; IRBs may require additional information to be provided to research subjects if the information would contribute to the protection of their rights and welfare.[75] An IRB may require documentation of compliance with the informed consent policy or waive the documentation requirement.[76]

The IRB must review the research on a continuing basis at least once a year, and riskier research should be reviewed on more than an annual basis; the IRB or a third party may observe the consent process and the research.[77]

ii. Criteria for Approval[78]

Research may only be approved by IRB if all of the following conditions are met:

- Risks to the subjects are minimized, and if possible, risks should be minimized by using procedures that are already being performed on the human subjects for purposes of diagnosis or treatment;[79]
- Risks to the subjects are considered reasonable in light of the potential benefits, both to the subject and to society with regard to the knowledge that may be gained from the research;[80]
- The subjects are selected for the research in an "equitable" manner, in light of the research's purpose, the research's setting, and the involvement of vulnerable populations such as children, pregnant women, prisoners, and individuals who are disadvantaged economically or educationally;[81]
- Informed consent is secured from each subject, or the subject's representative who is legally authorized to give informed consent;[82]
- If appropriate, the research proposal includes provisions regarding monitoring of the collection of data to guarantee the subjects' safety;[83]
- If appropriate, the research proposal includes provisions regarding data confidentiality to protect the subjects' privacy.[84]

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[74] 45 C.F.R. § 46.109(d)
[75] 45 C.F.R. § 46.109(b)
[76] 45 C.F.R. § 46.109(c)
[77] 45 C.F.R. § 46.109(e)
[78] 45 C.F.R. § 46.111
[79] 45 C.F.R. § 46.111(a)(1)
[80] 45 C.F.R. § 46.111(a)(2)
[81] 45 C.F.R. § 46.111(a)(3)
[82] 45 C.F.R. § 46.111(a)(4)
[83] 45 C.F.R. § 46.111(a)(5)

Additional precautions should be taken if the research subjects belong to a vulnerable population.[85]

iii. Expedited Review[86]

Expedited IRB review is available for:

- Research that appears on a list published by the Secretary in the Federal Register, which, in consultation with other agencies, outlines categories of research that may take advantage of expedited review, and the research does not create more than a *minimal risk*; [87] and/or
- Research that has been approved in the last year, with minor changes[88]

In an expedited review situation, an IRB chairperson or an experienced IRB reviewer may act on behalf of the IRB to review the research, and may take any IRB action other than to disapprove of the research; research disapproval may only occur through the non-expedited review procedure.[89]

All members of an IRB must be kept informed about research that has been approved under expedited review.[90]

The head of a department or agency may restrict the use of expedited review procedures.[91]

iv. Suspension or Termination of IRB Approval[92]

An IRB may suspend or terminate approval of research if the research is not being conducted in a manner consistent with the requirements set out by the IRB, or if the research has the potential to produce unexpected and serious harm to the subjects.[93] An IRB must include a statement explaining the reasons for suspension or termination of approval, and the suspension or termination must be reported to the investigator, the institution officials, and the head of the department or agency.[94]

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[84] 45 C.F.R. § 46.111(a)(5)
[85] 45 C.F.R. § 46.111(b)(5)
[86] 45 C.F.R. § 46.110
[87] 45 C.F.R. § 46.110(a)-(b)
[88] 45 C.F.R. § 46.110(b)
[89] 45 C.F.R. § 46.110(b)
[90] 45 C.F.R. § 46.110(c)
[91] 45 C.F.R. § 46.110(d)
[92] 45 C.F.R. § 46.113
[93] 45 C.F.R. § 46.113
[94] 45 C.F.R. § 46.113

c. Records[95]

An IRB must maintain documentation of:

- All research proposals and accompanying documentation, including reports submitted by the investigators and reports of injured subjects;[96]
- Minutes of IRB meetings, including attendance and vote information;[97]
- Information relating to continuing reviews;[98]
- Correspondence between investigators and IRB members;[99]
- A list of IRB members and their qualifications;[100]
- The IRB's written procedures;[101] and
- Information relating to any new findings that must be provided to subjects because of their potential likelihood to affect the subject's provision of informed consent.[102]

Records must be maintained for at least three years, and if the record pertains to research, it must be maintained for at least three years after the research is completed.[103] Authorized representatives from the department or agency must be able to inspect and copy the records.[104]

4) *Informed Consent Requirement*

a. General Requirements[105]

Informed consent generally must be secured from each subject, or the subject's representative who is legally authorized to give informed consent; each subject must be given adequate opportunity to decide whether to participate in the research or not. [106] The information provided to the subject or the subject's representative must be in a language that they understand. Informed consent cannot waive the subject's rights, nor can it absolve a researcher from possibile negligence liability.[107]

In order to secure informed consent, researchers must provide the subjects with the following:

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[95] 45 C.F.R. § 46.115
[96] 45 C.F.R. § 46.115(a)(1)
[97] 45 C.F.R. § 46.115(a)(2)
[98] 45 C.F.R. § 46.115(a)(3)
[99] 45 C.F.R. § 46.115(a)(4)
[100] 45 C.F.R. § 46.115(a)(5)
[101] 45 C.F.R. § 46.115(a)(6)
[102] 45 C.F.R. § 46.115(a)(7)
[103] 45 C.F.R. § 46.115(b)
[104] 45 C.F.R. § 46.115(b)
[105] 45 C.F.R. § 46.116
[106] 45 C.F.R. § 46.116
[107] 45 C.F.R. § 46.116

- Information regarding the research, including its purpose, its duration, its procedures, and whether any of those procedures are experimental;[108]
- Information regarding any potential risks or discomforts to the subject associated with the research;[109]
- Information regarding potential benefits to the subject or to others that are associated with the research;[110]
- Disclosure of information relating to any other treatments or procedures that are available and could potentially benefit the subject;[111]
- Information regarding the extent to which information will be kept confidential;[112]
- If the research involves more than a minimal risk, information must be included if there will be compensation or medical treatment available should injury occur;[113]
- Information regarding who the subject may contact for more information about the research, and whom the researchers should contact in the event that the subject is injured;[114] and
- A statement informing the subject that participation is voluntary and that participation can be discontinued at any time without penalty or loss of something that the subject was entitled to otherwise.[115]

If appropriate, one or more of the following additional pieces of information may be given to the subjects in order to secure informed consent:

- Information regarding potential unforeseen risks of the treatment or procedure, either to the subject, or to an embryo or unborn fetus should the subject become pregnant;[116]
- Information regarding circumstances that may result in termination of the subject's participation by the investigator, regardless of their consent;[117]
- Information regarding potential costs the subject may incur from participating in the research;[118]
- Procedures the subject should follow to withdraw from the research, and any consequences that may ensue from the withdrawal;[119]

[108] 45 C.F.R. § 46.116(a)(1)
[109] 45 C.F.R. § 46.116(a)(2)
[110] 45 C.F.R. § 46.116(a)(3)
[111] 45 C.F.R. § 46.116(a)(4)
[112] 45 C.F.R. § 46.116(a)(5)
[113] 45 C.F.R. § 46.116(a)(6)
[114] 45 C.F.R. § 46.116(a)(7)
[115] 45 C.F.R. § 46.116(a)(8)
[116] 45 C.F.R. § 46.116(b)(1)
[117] 45 C.F.R. § 46.116(b)(2)
[118] 45 C.F.R. § 46.116(b)(3)
[119] 45 C.F.R. § 46.116(b)(4)

- Notification to the subject that any new developments that occur during the course of the research that may affect the subject's willingness to participate will be provided to the subject;[120] and/or
- The approximate number of subjects involved in the research[121]

The requirement of informed consent can be altered or waived in the following circumstances, provided that the IRB documents their findings:

- The research is conducted or subject to approval by a local or state government official,[122] and cannot reasonably be carried out without alteration to the informed consent requirement,[123] and the research evaluates public benefit programs; or
- The research does not pose more than a minimal risk to the subjects and cannot reasonably be carried out without alteration to the informed consent requirement; the research may not adversely affect the subjects' rights and welfare, and if appropriate, the subjects will be provided with relevant information after their participation.[124]

Informed consent requirements do not preempt other applicable laws, including state or local laws that require additional disclosure to secure informed consent.[125] The informed consent requirements do not limit a physician's authority to provide medical care in an emergency if the physician is authorized to do so under applicable law.[126]

b. Documentation Requirements[127]

Informed consent should be secured via a written consent form that has been approved by the IRB and signed by the subject, or the subject's representative with legal authority to do so.[128] A copy of the written consent should be provided to the subject.[129] The written consent form should either be:

- A written consent form that includes all of the required elements of informed consent; the subject or the subject's representative must have ample opportunity to read the form before it is signed;[130] or
- A written consent form that states that the required elements of informed consent were provided orally to the subject or the subject's representative. The IRB must first approve a written summary of the information provided orally to the subject, and a witness must

[120] 45 C.F.R. § 46.116(b)(5)
[121] 45 C.F.R. § 46.116(b)(6)
[122] 45 C.F.R. § 46.116(c)(1)
[123] 45 C.F.R. § 46.116(c)(2)
[124] 45 C.F.R. § 46.116(d)
[125] 45 C.F.R. § 46.116(e)
[126] 45 C.F.R. § 46.116(f)
[127] 45 C.F.R. § 46.117
[128] 45 C.F.R. § 46.117(a)
[129] 45 C.F.R. § 46.117(a)
[130] 45 C.F.R. § 46.117(b)(1)

be present when the information is provided; the witness must sign both the short consent form and the summary. A copy of the summary and the short form must be provided to the subject.[131]

The documentation of informed consent requirement may be waived by the IRB, though they may require the investigator to provide a written statement about the research to the subject, under the following circumstances:

- The informed consent documentation would be the only documentation linking the subject to participation in the research, potentially resulting in a confidentiality breach. In this situation, the subject may chose not to have documentation linking them to participation;[132] or
- The research does not pose more than a minimal risk to the subject, and written consent would not normally be required outside of a research context.[133]

5) *Other Provisions*

a. Research Involving More than One Institution

If a proposed research project involves more than one research institution, the institutions may enter into an arrangement that allows for joint review, or enter into a comparable arrangement that prevents duplication of IRB effort, provided that the head of a department or agency approves of the arrangement.[134]

b. Early Termination of Support by Department or Agency

The department or agency head may terminate or suspend support for a project in accordance with the applicable procedures if it finds that the institution materially failed to comply with the Common Rule.[135]

When deciding whether to support or approve an application or proposal, the department or agency head may also consider whether the applicant has had support terminated or suspended previously, or whether individuals in charge of scientific and technical aspects of the research have not protected the rights and welfare of human subjects, even if the research was not subject to the Common Rule.[136]

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[131] 45 C.F.R. § 46.117(b)(2)
[132] 45 C.F.R. § 46.117(b)(c)(1)
[133] 45 C.F.R. § 46.117(b)(c)(2)
[134] 45 C.F.R. § 46.114
[135] 45 CFR § 46.122(a)
[136] 45 CFR § 46.122(b)