Mastering Research Administration

A Complete Guide to the CRA®, CPRA®, and CFRA® Exams

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CHAPTER 13
Ethics in Human Research

Table of Contents

13.1. Introduction

Although scientific research has greatly advanced human knowledge, formal and universally accepted standards for the ethical treatment of human research participants did not exist until the mid-20th century. For example, when Louis Pasteur conducted vaccine experiments in the late 19th century, there were no systems of informed consent comparable to those required today. Likewise, when the Cold Spring Harbor eugenics studies conducted in the 1910s collected family pedigrees to "trace" traits such as "feeblemindedness" or "criminality" – leading to forced institutionalization and compulsory sterilization targeting poor people – there were no strong repercussions.

Major changes began after World War II, prompted by the egregious violations of human rights committed in the name of scientific research during that era. The Nuremberg Code, developed in 1947, was the first internationally recognized set of ethical principles for human experimentation. In the decades that followed, additional unethical studies—such as the Tuskegee Syphilis Study and research conducted on institutionalized individuals and prisoners—highlighted the need for stronger protections.

These events led to the development of more comprehensive frameworks, including the Declaration of Helsinki (first adopted in 1964) and the Belmont Report (1979), both of which significantly shaped modern research ethics.

Some pivotal milestones in human research ethics include:

- The Nuremberg Code (1947)
- The Helsinki Declaration (1964)
- The Belmont Report (1979)
- The Common Rule (1991)

13.2. The Nuremberg Code (1947)

The Nuremberg Code (1947) was developed in response to the World War II experiments conducted by the Nazis and had 10 principles.

1. Voluntary and informed consent of participants is absolutely essential.

2. Research must aim to produce valuable knowledge for the benefit of society and cannot be obtainable by other means.
3. Studies must be based on prior scientific evidence and sound design so that anticipated results justify conducting the research.
4. Unnecessary physical and psychological suffering must be avoided.
5. No study should be conducted when there is reason to expect death or disabling injury, except possibly when the investigators also serve as subjects.
6. Risks must never exceed the humanitarian importance of the problem being investigated.
7. Proper preparations and safeguards must be in place to protect participants.
8. Only scientifically qualified persons should conduct the research.
9. Participants must be free to withdraw at any time.
10. Researchers must stop the experiment if continuation is likely to result in injury, disability, or death.

13.3. The Helsinki Declaration (1964)

The Declaration of Helsinki was adopted by the World Medical Association in 1964 as a response to growing recognition that:

- The Nuremberg Code, while foundational, was written primarily for judging war crimes and was not tailored to medical professionals conducting therapeutic clinical research.
- Physicians needed guidance that emphasized professional duties, not just legal constraints.
- Rapid expansion of clinical trials, new pharmaceuticals, and medical technologies raised ethical challenges not addressed by earlier documents.
- There was a need to clarify issues such as research combined with clinical care, surrogate consent, and vulnerable groups.

Below is a summary of the Helsinki Declaration:

1. The well-being, rights, and interests of research participants must take precedence over the interests of science or society.
2. Research must be scientifically justified, based on sound evidence, a thorough understanding of existing knowledge, and appropriate preclinical studies.
3. An independent ethics committee must review and approve the research protocol before the study begins.
4. Risks must be minimized and proportionate to anticipated benefits for individuals or society.
5. Informed and voluntary consent is required; when participants have limited capacity to consent, additional safeguards must be in place.
6. Vulnerable populations require special protections, and may be included only when the research directly relates to their needs and cannot be conducted in non-vulnerable groups.
7. Participants' privacy, dignity, and confidentiality must be protected throughout the research process.
8. Research must be conducted with transparency, including trial registration and disclosure of funding sources, conflicts of interest, and institutional affiliations.
9. Use of placebos is restricted to situations where no proven intervention exists or when methodologically necessary and ethically justified.
10. Participants should have access to the best proven interventions after the study, reflecting a duty of post-trial care.

The Declaration has been revised multiple times (notably in 1975, 1983, 1989, 1996, 2000, 2004, 2008, 2013, and 2024) to address emerging controversies such as the use of placebos when active treatments are available.

13.4. The Belmont Report (1979)

The Belmont Report (1979) was developed in response to mounting ethical concerns about human subjects research in the United States. Key drivers included:

- **The Tuskegee Syphilis Study scandal (1932–1972)** — the revelation that African American men with syphilis were deceived and denied treatment triggered national outrage.
- **Public distrust and congressional pressure** — hearings led by Senator Edward Kennedy called for federal reform.
- **Creation of the National Commission for the Protection of Human Subjects (1974)** — mandated by the National Research Act to establish ethical principles for research.
- **Need for a unified U.S. framework** — institutions sought consistent federal standards for institutional review boards (IRBs), informed consent, and vulnerable populations.

The Belmont report improved upon the previous codes of ethics (Nuremberg and Helsinki) by:

- Articulating three clear ethical principles
- Clarifying application to research oversight structures
- Focusing on vulnerable populations
- Setting a foundation for the U.S. regulatory system

13.4.1. Principles

The three principles of the Belmont Report were:

1. **Respect for persons**: People can make voluntary decisions to enter and quit the study. *This led to "written informed consent".*
2. **Beneficence**: Maximize benefit and minimize harm.
3. **Justice**: Those who receive the benefits should be the ones who bear the potential risks.

13.4.2. Application to Research Oversight Structures

The Belmont Report explicitly linked principles to operational requirements:

1. Informed consent
2. Risk–benefit assessment
3. Equitable selection of subjects

This went further than the Helsinki Declaration, which focused mainly on physician–researcher duties.

13.4.3. Focus on Vulnerable Populations

The Belmont Report addressed:

1. Diminished autonomy
2. Safeguards
3. Fairness in subject selection

The Declaration of Helsinki acknowledged vulnerability but did not structure protections around it.

13.4.4. Foundation for U.S. Regulatory System

The Belmont Report became the basis for:

- IRB requirements
- The Common Rule (45 CFR 46)
- Federal policy governing all federally funded research

Neither Nuremberg nor Helsinki had regulatory force in the U.S.

13.5. Comparing Nuremberg, Helsinki, and Belmont

Feature	Nuremberg Code	Helsinki Declaration	Belmont Report
Trigger	Nazi abuses	Medical research ethics concerns	Tuskegee + public policy crisis
Focus	Voluntary consent, avoiding harm	Physician duties, clinical research norms	Principles + operational rules
Structure	10 rules	Ethical guidance	3 principles + applications
Legal/Regulatory impact	Limited	Influential but not regulatory	Basis of U.S. federal regulations

13.6. Informed Consent

One of the major advances resulting from these codes of ethics was the development of **written informed consent**. Informed consent is not a single event or just a form to be signed. Informed consent is an educational process that takes place between the investigator and the prospective subject(s).

The basic elements of the consent process include full disclosure of the nature of the research and the subject's participation; adequate comprehension on the part of the potential subjects; and the subject's voluntary choice to participate. To this end, written informed consent must:

- **Be written at no more than an 8th-grade reading level**;
- **Clearly emphasize voluntariness**; and
- **Provide meaningful information about the procedure(s), risk(s)/benefit(s), and alternative methods**, including
    - Research: Purpose, Duration, Procedures
    - Risks
    - Benefits
    - Alternatives
    - Confidentiality
    - Compensation
    - Whom to Contact
    - Right to Refuse or Withdraw

13.7. Institutional Review Board

The Institutional Review Board (IRB) is a committee established by an institution to review and monitor research involving human participants, ensuring that studies meet ethical and regulatory standards. Its core mission is to protect the rights, welfare, and privacy of human subjects. Rooted in the ethical lessons of historical research abuses—such as the

Tuskegee syphilis study and Milgram obedience experiments—the IRB enforces principles from the Belmont Report (1979): respect for persons, beneficence, and justice.

In practice, the IRB reviews research protocols to assess risk–benefit balance, adequacy of informed consent, participant selection, and data confidentiality. It operates under federal regulations 45 CFR 46 and must consist of 5 diverse members, including at least one member who is not otherwise affiliated (employment or contractual relationship) with the university or institution, at least one non-scientist, and at least one scientist. In the United States, the IRB has a Federal Wide Assurance Number (FWA#).

Single IRB (sIRB): The 2018 amendment of the Common Rule simplified some human protection procedures by requesting only a single IRB (sIRB) for multi-site projects.

13.8. Levels of IRB Review

Human research studies have different levels of risk. For example, a study of blood samples that are already collected and anonymized may have a low risk, whereas brain surgery studies on humans that are alive may carry a higher risk. As such, IRB reviews are divided into three main categories.

Only the IRB, IRB Chair, or their designee can decide the risk category.

1. **Full-board review**: complete processing by the full IRB, or a minimum quorum thereof;
2. **Expedited review**: processing by a single IRB member is possible; or
3. **Exempt**: reviewed by the IRB chair to be exempt from either 1. or 2. above based on the 8 exemption categories listed in 2 CFR 46.104(d), see table below.

EIGHT EXEMPTION CATEGORIES FOR IRB REVIEW		
1.	***Educational Practices***	Research in established or commonly accepted educational settings. Involves normal educational practices like teaching methods, curricula, or classroom management.

EIGHT EXEMPTION CATEGORIES FOR IRB REVIEW CONT'D

2.	***Educational Tests, Surveys, Interviews, or Public Observation***	Research using educational tests, surveys, interviews, or observation of public behavior. Identifiable information must not place participants at risk**.**
3.	***Benign Behavioral Interventions***	Research involving minimal-risk behavioral interventions with adult participants who can provide consent. Interventions must be brief, harmless, and unlikely to cause stress or discomfort.
4.	***Secondary Research for Which Consent Is Not Required***	Research using existing data, documents, records, or biospecimens. Must be publicly available or recorded in a way that participants cannot be identified.
5.	***Public Benefit or Service Programs***	Research and demonstration projects conducted or approved by a federal agency that evaluate public benefit or service programs.
6.	***Taste and Food Quality Evaluation***	Studies of taste, food quality, or consumer acceptance where food is safe for consumption.
7.	***Storage or Maintenance of Identifiable Information/Biospecimens***	Long-term storage of identifiable data or specimens for future research. Data must be secured and limited to research purposes.
8.	***Research Involving Coded Private Information or Biospecimens***	Research where the investigator cannot readily identify participants. Often used in genetics or retrospective data studies.

13.9. Summary

Human research ethics developed in response to historical abuses, including Nazi experiments, the Tuskegee Syphilis Study, and other unethical studies, leading to key milestones such as the Nuremberg Code, the Belmont Report, and the Common Rule. These frameworks emphasize respect for persons, beneficence, and justice, operationalized through informed consent and Institutional Review Board (IRB) oversight. The IRB reviews research to ensure ethical compliance, appropriate risk–benefit balance, and participant protection, with full-board, expedited, or exempt review options based on study risk. Together, these mechanisms safeguard human participants and maintain accountability in scientific practice.

13.10. Practice Questions

1. The study of "how to arrange reproduction in human populations to increase what is regarded as desirable characteristics" is most closely related to:
    a. Eugenics
    b. Optogenetics
    c. Genomics
    d. Proteomics

2. Which of the following events led to deeper conversations about bioethics in research?
    a. The eugenics movement
    b. The Tuskegee syphilis experiment
    c. The Milgram obedience experiments
    d. All of the above

3. Which one directly contributed to the Nuremberg Code of Ethics?
    a. Tuskegee syphilis experiment
    b. World War II atrocities
    c. Stanford prison experiment
    d. The Belmont Report

4. Which of the following was NOT included in the Nuremberg Code of Ethics?
    a. The study participant should receive adequate information about what may occur during the study.
    b. The study participant is free to join the study and has the right to exit the study at any time.
    c. The researcher must be qualified.
    d. Written informed consent must be obtained from the study participant.

5. Which of the following was first developed partly in response to increased need to address ethics of clinical trials, which had become common internationally?
    a. The Nuremberg Code (1947)
    b. The Helsinki Declaration (1964)

c. The Belmont Report (1979)
d. The Common Rule

6. Obtaining "written informed consents" was established as a foundational principle of human studies following the:
    a. Nuremberg Code of Ethics (1947)
    b. The Helsinki Declaration (1964)
    c. The Belmont Report (1979)
    d. International Ethical Guidelines for Biomedical Research (1982)

7. The National Research Act led to the publication of:
    a. Nuremberg Code of Ethics
    b. The Helsinki Declaration
    c. The Belmont Report
    d. International Ethical Guidelines for Biomedical Research

8. Which of the following most proximately influenced the passage of the National Research Act?
    a. The eugenics movement and the resulting controversies
    b. The Tuskegee Syphilis Experiment
    c. The World War II atrocities
    d. The use of Henrietta Lacks tissues to create immortal HeLa cells

9. Which one is NOT one of the three Belmont Report principles?
    a. Respect for persons
    b. Beneficence
    c. Justice
    d. Researcher competence

10. Making sure that "those who receive the benefits of research are the same as those who bear the burden" is most closely related to:
    a. Respect for persons
    b. Beneficence
    c. Justice
    d. Equanimity

11. “Maximize benefits and minimize risks” is most closely related to:
    a. Respect for persons
    b. Beneficence
    c. Justice
    d. Minimalistic medicine

12. “Informed Consent” was developed to ensure:
    a. Respect for persons
    b. Beneficence
    c. Justice
    d. Abiding by the DATA Act

13. Which one is NOT correct about informed consents? They must:
    a. Be written at an 8th-grade level.
    b. Include information about the procedures, risk/benefit, and alternative methods.
    c. Emphasize voluntariness.
    d. State the education level of the principal investigators.

14. IRBs must have at least _____ voting members.
    a. 5
    b. 7
    c. 9
    d. 11

15. Institutions receive their federal-wide assurance number (FWA#) and register their IRB with:
    a. OHRP
    b. OLAW
    c. OSHA
    d. OFAC

16. Federal-wide assurance has to be renewed every ___ year(s).
    a. 1
    b. 2
    c. 3
    d. 5

17. Standards for the composition of IRBs, IRB record keeping, and expedited review procedures were set by:
    a. The Helsinki Declaration (1964)
    b. The Belmont Report (1974)
    c. International Ethical Guidelines for Biomedical Research (1982)
    d. The Common Rule (1991)

18. The Common Rule is codified in Title ____ of Code of Federal Regulations.
    a. 2
    b. 12
    c. 45
    d. 50

19. Which of the following is not a requirement for university IRB membership?
    a. At least one member who is not otherwise affiliated (employment or contractual relationship) with the university
    b. At least one non-scientist
    c. At least one scientist
    d. At least one member from the project to be discussed

20. The main distinguishing feature of research as opposed to patient care is:
    a. Contribution to generalizable knowledge
    b. Quality of care offered to patients
    c. Liability
    d. Respect for patient's decision

21. All of these are characteristics of human subjects research EXCEPT one:
    a. A systematic investigation, contributing to generalizable knowledge
    b. Working with data from living individuals
    c. Obtaining data through interacting with the individual, or from identifiable data or biospecimens
    d. Quantitative analysis of data using statistical models

22. Which one is NOT considered human subjects research?
    a. Collecting survey data from a random sample of the US population for alcohol consumption
    b. Conducting immunological studies on personally identifiable biological specimens
    c. Studying immune markers in blood samples from 500 individuals who passed away due to Covid-19
    d. A Phase 1 randomized trial of a new cancer treatment

23. Which one is NOT a type of IRB review?
    a. Exempt
    b. Discretionary
    c. Expedited
    d. Full-Board

24. How many IRB exemption categories are there?
    a. 3
    b. 5
    c. 8
    d. 12

25. If a research study falls in an exemption category, it:
    a. Needs full IRB approval.
    b. Needs IRB approval by only 3 members.
    c. Needs IRB approval by only 3 members and should be complete within 7 days.
    d. Does not need full IRB approval but needs to be reviewed by a member of the IRB.

26. Exemption category #1 is for studies that are for:
    a. Routine educational studies.
    b. Secondary research with identifiable personal information.
    c. Taste/food quality evaluation and consumer acceptance.
    d. Federal demonstration projects of public benefit

27. Who determines that a study is exempt from the IRB review?
    a. The PI
    b. The department chair (or designee)
    c. The IRB chair (or designee)
    d. The awarding agency

28. Groups that are more protected and their studies CANNOT be considered exempt from IRB review include:
    a. Prisoners
    b. Mentally impaired
    c. Pregnant women
    d. All of the above

29. Which study is more likely to be exempt from IRB review?
    a. Phase 3 clinical trial of a new vaccine
    b. Research on comparison of instructional techniques
    c. A prospective study of 20,000 people to determine cancer risk factors, if only questionnaire data is collected
    d. A prospective study of 20,000 people to determine cancer risk factors, if questionnaire data and biological specimens are collected

30. The 2018 amendment of the Common Rule simplified some human protection procedures by:
    a. Requesting only a single IRB (sIRB) for multi-site projects
    b. Eliminating continuing review requirement for studies that are approved via expedited review
    c. Removing public health surveillance from the list of what is considered research
    d. All of the above

13.11. Answers to Practice Questions

1. A "Eu" means good. Eugenics is historically defined as the study and practice of improving the genetic quality of a human population by selective breeding or other means intended to encourage desirable traits and discourage undesirable ones. Some of the research studies on eugenics led to abuses in human research, including issues related to consent, autonomy, and equity.

2. D Eugenics raised moral issues about who decides "desirable" traits. The Tuskegee syphilis experiments exposed grave abuses in human subject research and lack of informed consent. Milgram obedience experiments raised concerns about psychological harm and deception. Collectively, they shaped modern bioethics.

3. B The Nuremberg Code (1947) was developed in response to Nazi human experimentation uncovered after WWII. The Code articulated principles like voluntary consent and welfare of participants. Tuskegee — occurred later (1932–1972) and influenced U.S. policy (Belmont Report), not the Nuremberg Code. The Stanford prison experiment — 1971, much later and influential for psychology ethics. The Belmont Report — published in 1979 as a U.S. response to domestic abuses.

4. D The Nuremberg Code requires voluntary informed consent and that participants be adequately informed — but it does not strictly require that consent be written in all cases. It emphasizes voluntary, informed agreement. Documentation format was not specified in the Code itself. Adequate information about what may occur is a central Nuremberg requirement. Freedom to join and to withdraw is explicit in the Code. That researchers must be qualified is part of ensuring scientifically valid and ethical conduct.

5. B The Declaration of Helsinki was developed by the World Medical Association specifically to provide ethical guidance for clinical research involving human subjects, at a time when clinical trials were expanding internationally. It built on—but went beyond—the Nuremberg Code by addressing issues such as informed consent in clinical settings, physician-researcher obligations, and vulnerable populations.

6. C Informed consent was developed as a result of human rights abuses in medical research and treatment, particularly Nazi medical experiments after World War II, leading to the Nuremberg Code. The concept was also shaped by legal cases like Schloendorff v. Society of New York Hospital (1914) and Salgo v. Leland Stanford Jr. University Board of Trustees (1957), as well as scandals such as the Tuskegee Syphilis Study in the United States. The Belmont Report established written informed consent as a foundational principle for human research, largely as a response to historical unethical studies like the Tuskegee Syphilis Study.

7. C The National Research Act (1974) established the National Commission for the Protection of Human Subjects, which authored the Belmont Report in 1979, outlining ethical principles and guidelines for research with human subjects. The Helsinki Declaration is an earlier international declaration (1964). International Ethical Guidelines is later international guidance (1980s onward).

8. B Public exposure of the Tuskegee study (particularly in 1972) and the resulting outrage were direct catalysts for Congress to pass the National Research Act to strengthen protections for human research participants.

9. D The Belmont Report's three core principles are: respect for persons, beneficence, and justice. Researcher competence, while important, is not one of the three named Belmont principles.

10. C Justice in research ethics concerns fair distribution of benefits and burdens. The quoted idea reflects distributive justice — ensuring vulnerable populations are not unfairly burdened while others reap benefits.

11. B Beneficence requires researchers to promote welfare, balancing benefits against risks and minimizing harm.

12. A Informed consent operationalizes respect for persons by protecting autonomy — letting individuals make voluntary, informed decisions about participation.

13. D Informed consent forms must be understandable (commonly recommended around an 8th-grade reading level), include procedures, risks/benefits, alternatives, and emphasize voluntariness. They do not have to state the PI's education level.

14. A Federal regulations (45 CFR 46.107) require IRBs to have at least 5 voting members to ensure diversity of perspectives.

15. A The Office for Human Research Protections (OHRP) within HHS administers Federal wide Assurances (FWAs) and maintains IRB registration for HHS-funded human subject's research. OLAW (Office of Animal Laboratory Welfare) handles animal welfare (not human IRB registration). OSHA (Occupational Safety and Health Administration) — occupational safety, unrelated**.** OFAC (Office of Foreign Assets Control) — financial sanctions office, unrelated.

16. D A Federal-wide Assurance (FWA) must be renewed every five years. Institutions must renew their FWA by its expiration date, even if no changes have occurred, to maintain its active status. Updates must be submitted within 90 days of a change to the institution's legal name, Human Protections Administrator, or Signatory Official.

17. D The Common Rule (codified in 1991, revised later) sets baseline federal requirements for IRB membership, records, and review types (exempt, expedited, full-board).

18. C Protections for human subjects are codified in 45 CFR 46 (Common Rule and related regulations).

19. D IRBs require diversity: at least one unaffiliated (community) member, at least one non-scientist, and at least one scientist. However, having a member from the specific project would be a conflict of interest and is not permitted for the review of that project.

20. A Human subjects research is defined by a systematic investigation aimed at generalizable knowledge and involves living individuals (direct interaction or identifiable data/specimens). The other choices – high quality of care, liability, and respect for patient's decisions – are features of both clinical care and clinical research.

21. D Quantitative analysis is a method, not a defining characteristic — qualitative studies or non-statistical analyses can also be research with human subjects

22. C Federal human subjects regulations apply to living individuals. Research using samples from deceased persons generally does not fall under the human subjects definition (though institutional policies or other laws may still apply).

23. B IRB review types are Exempt, Expedited, and Full-Board. “Discretionary” is not a formal review category.

24. B Under the revised Common Rule (2018), there are 8 categories of research that may be exempt from full IRB review (with specific conditions).

25. D Exempt research is not subject to continuing IRB oversight in the same way as non-exempt research, but an IRB official (chair or designee) must determine and document that the activity meets exemption criteria. It’s not simply PI-declared.

26. A Exemption Category 1 typically covers research conducted in established educational settings involving normal educational practices (e.g., curriculum, classroom management) where risk is minimal. Secondary research with identifiable info is a different exemption category (often category 4). Taste/food quality is another specific exemption category (often category 3). Federal demonstration projects are separate.

27. C Only IRB-authorized personnel (often the IRB chair or a designated reviewer) can make an official exemption determination; the PI cannot unilaterally declare exemption.

28. D Vulnerable populations such as prisoners, mentally impaired persons, and pregnant women require additional protections and generally cannot be included in exempt research categories due to higher risk and need for safeguards.

29. B Educational research that compares instructional techniques in normal educational settings and poses minimal risk commonly qualifies for exemption (Category 1). Large prospective cohort studies collecting only questionnaires might be eligible for exemption depending on identifiability, but collecting biological specimens (d) or large population studies (c) may raise identifiability/privacy issues that preclude exemption — b is the clearest minimal-risk educational example.

30. D