Table 1. Brief History of Research Ethics Violations and Formation of IRB Regulations

Year	Event	Significance
1932-1972	Tuskegee Syphilis Study	Study done by the U.S. Public Health Service with 300 indigent African American sharecroppers who had syphilis, with the goal of tracing the natural progression of the disease. Subjects did not understand their disease and were simply told they had "bad blood." They were recruited by African American nurses and subjected to procedures, including spinal taps, done solely for research. Once penicillin was available to treat syphilis the subjects were not offered treatment and the study continued. In addition to the research violations, the federal government's involvement continues to seed distrust among African Americans but did lead to future research regulations.
1948	The Nuremberg Code	Document formed in response to Nazi physicians' treatment of prisoners during the Holocaust; basic elements of research participation include voluntary and informed consent, benefits outweigh the risks, and right to voluntary withdrawal from the study.
1950s	Willowbrook Hepatitis Studies	Series of studies done to understand hepatitis transmission among severely cognitively impaired children admitted to an extended care facility. Healthy children were intentionally infected with hepatitis by feeding them a solution made from the feces of children with hepatitis.
1951	Henrietta Lacks	Lacks, a poor African American, was being treated at Johns Hopkins Hospital for cervical cancer. A physician removed some of her cancer cells and found they proliferated quickly in the lab. The "HeLa" cell line was used without Lacks or her family's knowledge by researchers for decades to test the effects of radiation and poisons, study the human genome and how viruses work, and help develop the polio vaccine.[8] However, no one consented to the collection and future use of these cells.
1962	Thalidomide Experience	Thalidomide, a drug used in the 1950s to treat nausea during pregnancy, was still investigational yet that was not disclosed. The drug caused severe birth defects. The Food, Drug, and Cosmetic Act was amended to require informed consent prior to giving investigational medications.
1963	Food and Drug Administration	Food and Drug administration instituted to regulate clinical trials of medications, biological products, and medical devices; to oversee protection of human participants; to assure the quality and safety of medical products.
1964	Declaration of Helsinki	Document that built on the Nuremberg Code; describes standards of ethical research. Has been revised multiple times since.
1966	*New England Journal of Medicine* Article	Classic article[9] describing 22 recently published respected studies where the study was unethical due to lack of informed consent or undue risk to the subjects.

1970s	San Antonio Contraception Study	Study done at an indigent clinic that evaluated the efficacy of various contraception medications. Subjects were randomized to either an active medication or a placebo, yet women in the placebo group were not informed they were no longer receiving contraception. Many unplanned pregnancies resulted.
1974	National Research Act	Establishes the modern IRB system for regulating research, including criteria an IRB must follow to approve research. Regulations found in Title 45, Part 46 of the Code of Federal Regulations become known as "45 CFR 46".
1979	Belmont Report	Report from the Commission for Protection of Human Subjects; clarifies three ethical principles that apply to all research: respect for persons, beneficence, and justice.
1981	Protection of Human Subjects Law	Formed the basis of clinical research laws; emphasized importance of balancing risks and benefits in research; stressed the importance of following strict protocols.
1991	Common Rule	Federal Policy for the Protection of Human Subjects; added protection for vulnerable subjects and outlined role of IRBs and informed consent.
2018	Updates to Common Rule	Common Rule updated with new exemption categories, requirements for informed consent, and details about disclosing private information and biospecimens.

Sources:[3,6,8,9]