

Table 2: Rules about the Conduct of Research

Core elements	What is it? How universal in reach?	How “hard” or “soft” is it? How obligatory? How precise are the requirements? Are there provisions for delegation?
Articulations of principles (often international)		
Nuremberg Code (1947)	Hortatory articulation of principles; 10 conditions that must be met for research on human subjects to be acceptable; stated universalistically	Subsequently reflected in Declaration of Human Rights, so “accepted in principle” by each of 51 signatories to Charter of United Nations; mostly no mechanisms for implementing provisions of code
Helsinki Rules (1964)	Hortatory articulation of principles; stated universalistically	World Health Organization, World Medical Society; “currently in use throughout the world” (according to US NIH; not clear what this means)
Belmont Report: Ethical Principles & Guidelines for the Protection of Human Subjects of Research (1979)	Hortatory articulation of principles by US national body; stated universalistically	Issued by the National Commission for the Protection of Human Subjects of Biomedical & Behavioral Research (in existence 1974-78)
Statutes, regulations, & guidance (national in origin but having effects beyond national boundaries)		
45 C.F.R. § 46, the Code of Federal Regulations Governing the Protection of Human Subjects in Research (Research Act of 1974)	Statute. Protection of human subjects in any research funded by DHHS; subsequently revised to apply to any US government funded research	The Code itself is “hard law” & so obligatory. Guidance issued episodically by the Office for Human Research Protections (OHRP) is “softer” & therefore not obligatory. Because the staff of the Institutional Review Boards of many entities treat the Guidance as obligatory, it is in practice obligatory for many individual researchers. This was preceded by the Public Health Service Policy on the Protection of Human Subjects (1966)
Federal Wide Assurance (FWA) (part of 45 CFR §46) (2005)	Clarifies that rules apply universally, including to international sites doing US government funded research	Hard law, reaching into other countries via funding mechanism (if funded by US government, must follow these regulations)
Research infrastructure, research practices (at varying levels)		
Research sponsor & research network conventions	Research sponsors & research networks have conventions that standardize some features of research – not the scientific core, but lab procedures, reporting conventions, & research & grants administration. Applies to entities receiving research monies or participating in research network activities; not confined by national borders.	Combined hard & soft law. Obligatory to comply with 45 CFR 46 (hard law), but additional prescriptions associated with collection of data, monitoring of study, etc. not always obligatory. Examples: sample SOPs often adopted by all or most research entities receiving funding from a particular sponsor; use of mandated third-party monitor; use of particular laboratories or data analysts.
Clinic, university, or research institute practices	Universities & other entities conducting research have conventions, which vary from one entity to another, about how to conduct ethics review, how to review grants proposals before submission (e.g. whose signatures must be affixed), etc. Also SOPs about laboratories, data processing, review of personnel’s qualifications, etc. Applies to all researchers affiliated with the clinic, university, or research institute & conducting research under its auspices.	Soft law in sense that no legal consequences, but can prohibit investigators from conducting research if do not meet requirements of entities like IRBs. IRB approval often required for submission of grants or for publication of research results
Research protocols	Recipe for conducting research, including instructions for selecting & recruiting research subjects, instructions about randomizing subjects to various arms of study, what to do with or to subjects at various points in the study, what data to collect & how to record it, what to do when adverse events occur. Applies to anyone engaged in activities associated with the particular protocol.	Soft law in sense that no legal consequences, but nevertheless obligatory; extremely specific; delegated enforcement by research monitors, committees to review serious adverse events, etc.