FDA Regulations	HHS Regulations
56.101 Scope IRBs that review clinical investigations regulated by the FDA under sections 505(i), 507(d), and 520(g) of the act, as well as clinical investigations that support applications for research or marketing permits for products regulated by the FDA, including food and color additives, drugs for human use, medical devices for human use, biological products for human use, and electronic products.	46.101 Scope All research involving human subjects conducted or supported by HHS or conducted in an institution that agrees to assume responsibility for the research in accordance with 45 CFR 46 regardless of the source of funding.
56.102 and 50.3 Definitions Definitions for “Act”; “Application for research or marketing permit”; “Emergency use”; “Sponsor”; “Sponsor-investigator”; “Test article” do not have comparable terms defined in 45 CFR 46.	46.102 Definitions Definitions for “Department or agency head”; “Certification” do not have comparable terms defined in 21 CFR 50 or 56
FDA has defined “clinical investigation” to be synonymous with “research”. “Clinical investigation” means any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the FDA...or the results of which are intended to be later submitted to, or held for inspection by, the FDA as part of an application for a research or marketing permit.	HHS has defined “research” as a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. HHS has defined “Research subject to regulation” and similar terms as intending to encompass those research activities for which a federal department or agency has specific responsibility for regulating as a research activity, (for example, Investigational New Drug requirements administered by the FDA).
“Human subject” means an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy individual or a patient.	“Human subject” means a living individual about whom an investigator (whether professional or student) conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information.
“Institutional Review Board” means any board, committee, or other group formally designated by an institution to review, to approve the initiation or, and to conduct periodic review of, biomedical research involving human subjects. The primary purpose of such review is to assure the protection of the rights and welfare of the human subjects. The term has the same meaning as the phrase “institutional review committee” as used in section 520(g) of the act.	“IRB” means an institutional review board established in accord with and for the purposes expressed in this policy.
Definitions for “IRB approval”; “Minimal Risk”; “Institution”; “Legally authorized representative” are identical.	

FDA Regulations	HHS Regulations
56.103 Circumstances in which IRB review is required. Except as provided in 56.104 and 56.105, any clini cal investigation which must meet the requirements for prior submission to the FDA or considered in support of an application for a research or marketing permit must have been reviewed and approved by, and remained subject to continuing review by, an IRB meeting the requirements of this part. [In diverging from the assurance requirement, FDA stated its belief that it is inappropriate for it to adopt the assurance mechanism. The benefits of assurance from IRBs that are subject to FDA jurisdiction, but not otherwise to HHS jurisdiction, do not justify the increased administrative burdens that would result from an assurance system. FDA relies on its Bioresearch Monitoring Program, along with its educational efforts, to assure compliance with these regulations.]	46.103 Assuring compliance with this policy — research conducted or supported by any Federal Department or Agency Sections dealing with assurances and certifications (a), (b)(1)-(3), (c)-(f) are unique to the common rule and the HHS regulations.
56.104 Exemptions from IRB requirement a. Any investigation which commenced before 7/27/81, and was subject to requirements for IRB review under FDA regulations before that date, provided that the investigation remains subject to review of an IRB which meets the FDA requirements in effect before 7/27/81. b. Any investigation that commenced before 7/27/81 and was not otherwise subject to requirements for IRB review under FDA regulations before that date c. Emergency use of a test article, provided that such emergency use is reported to the IRB within 5 working days. Any subsequent use of the test article at the institution is subject to IRB review.	46.101(b) Exemptions from this policy a. Research conducted in established or commonly accepted educational settings... b. Research involving the use of educational tests... survey procedures, interview procedures or observation of public behavior... c. Research involving the use of educational tests (cognitive, diagnostic, aptitude achievement), survey procedures, interview procedures,...that is not exempt if the human subjects are elected or appointed....or if these sources are publicly available... d. Research and demonstration projects which are conducted by or subject to the approval of deparment or agency heads, and which are designed to study...public benefit or service programs...
Identical Exemption: Taste and food quality evaluations and consumer acceptance studies, if wholesome foods without additives are consumed or if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe....	

FDA Regulations	HHS Regulations
56.105 Waiver of IRB requirement. On the application of a sponsor or sponsor-investigator, the FDA may waive any of the requirements contained in these regulations, including the requirement for IRB review, for specific research activities or for classes of research activities, otherwise covered by these regulations.	No comparable provision.
56.107 and 46.107 IRB Membership requirements are identical	
56.109 and 46.109 “IRB review of research” are virtually identical with the following exceptions: * 46.109(c) refers to the criteria in .117 for waiving the requirement for a signed consent form — .117(c)(1) is not included in FDA's regulations because FDA does not regulate research in which “the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality.” * 56.109(c) and (e) contain additional language related to FDA's emergency research rule; HHS published identical criteria for emergency research in a Secretarial announcement of waiver of the applicability of 45 CFR 46, 10/2/96.	
56.110 and 46.110 “Expedited Review procedures for certain kinds of research involving no more than minimal risk, and for minor changes in approved research” are virtually identical, except: * 56.110 refers to the FDA and 46.110 refers to the Secretary, HHS, or the department or agency head * 56.110(d) states “The FDA may restrict, suspend, or terminate an institution's or IRB's use of the expedited review procedure **when necessary to protect the rights or welfare of subjects**.” 46.110(d) states that “The department or agency head may restrict, suspend, terminate, **or choose not to authorize** an institution's or IRB's use of the expedited review procedures.”	
56.111 and 46.111 “Criteria for IRB approval of Research” are virtually identical except 56.111 contains references to sections in part 50 and 46.111 contains references to sections in part 46.	
56.112 and 46.112 “Review by institution” are identical.	
56.113 and 46.113 “Suspension or termination of IRB approval of research” are virtually identical except 56.113 refers to FDA and 46.113 refers to the department or agency head.	

FDA Regulations	HHS Regulations
56.114 Cooperative research In complying with these regulations, institutions involved in **multi-institutional studies** may use joint review, reliance upon the review of another qualified IRB, or similar arrangements aimed at avoidance of duplication of effort.	46.114 Cooperative research Cooperative research projects are those projects covered by this policy which involve more than one institution. In the conduct of cooperative research projects, each institution is responsible for safeguarding the rights and welfare of human subjects and for complying with this policy. With the approval of the department or agency head, an institution participating in a **cooperative project** may enter into a joint review arrangement, rely upon the review of another qualified IRB, or make similar arrangements for avoiding duplication of effort.
56.115 and 46.115 “IRB Records” are virtually identical except * The list of IRB members required by 56.115(a)(5) is cross-referenced in 46.115(a)(5) to 46.103(b)(3) * 56.115(b) refers to FDA rather than the department or agency * 56.115(c) states that “The FDA may refuse to consider a clinical investigation...if the institution or the IRB that reviewed the investigation refuses to allow an inspection under this section.” Part 46 does not contain a comparable requirement.	
56.120 Lesser administrative actions The agency may 1. Withhold approval of new studies; 2. Direct that no new subjects be added to ongoing studies; 3. Terminate ongoing studies when doing so would not endanger the subjects; or 4. When the apparent noncompliance creates a significant threat to the rights and welfare of human subjects, notify relevant State and Federal regulatory agencies and other parties with a direct interest in the agency's action of the deficiencies in the operation of the IRB. The parent institution is presumed to be responsible for the operation of an IRB, and FDA will ordinarily direct any administrative action against the institution. However, depending on the evidence of responsibility for deficiencies, determined during the investigation, FDA may restrict its administrative actions to the IRB or to a component of the parent institution determined to be responsible for formal designation of the IRB.	46.123 Early termination of research support; Evaluation of applications and proposals. 1. The department or agency head may require that...support for any project be terminated or suspended...when the department or agency head finds an institution has materially failed to comply with the terms of this policy. 2. In making decisions about supporting or approving applications or proposals...the department or agency head may take into account...factors such as whether the applicant has been subject to a termination or suspension under...this section and whether the applicant or the person or persons who would direct or has directed the scientific and technical aspects of an activity has, in the judgment of the department...materially failed to discharge responsibility for the protection of the rights and welfare of human subjects (whether or not the research was subject to federal regulation).

FDA Regulations	HHS Regulations
56.121 Disqualification of an IRB or an institution ...The Commissioner may disqualify an IRB or the parent institution if the Commissioner determines that: 1. The IRB has refused or repeatedly failed to comply with any of the regulations set forth in this part, and 2. The noncompliance adversely affects the rights or welfare of the human subjects in a clinical investigation....	46.120 Evaluation and disposition of applications and proposals for research to be conducted or supported by a Federal Department or Agency The department or agency head will evaluate all applications and proposals involving human subjects.... This evaluation will take into consideration the risks to the subjects, the adequacy of protection against these risks, the potential benefits of the research to the subjects and others, and the importance of the knowledge gained or to be gained. On the basis of this evaluation, the department or agency head may approve or disapprove the application or proposal, or enter into negotiations to develop an approvable one. 46.122 Use of Federal Funds Federal Funds administered by a department or agency may not be expended for research involving human subjects unless the requirements of this policy have been satisfied.
56.122 Public disclosure of information regarding revocation A determination that the FDA has disqualified an institution and the administrative record regarding that determination are disclosable to the public under part 20. 56.123 Reinstatement of an IRB or an institution An IRB or an institution may be reinstated if the Commissioner determines...that the IRB or institution has provided adequate assurance that it will operate in compliance with the standards set forth in this part....	No comparable provisions.

FDA Regulations	HHS Regulations
56.124 Actions alternative or additional to disqualification Disqualification of an IRB...is independent of...other proceedings or actions authorized by the Act. The FDA may, at any time, through the Department of Justice institute any appropriate judicial proceedings (civil or criminal) and any other appropriate regulatory action, in addition to or in lieu of, and before, at the time of or after disqualification. The agency may also refer pertinent matters to another Federal, State, or local government agency for any action that that agency determines to be appropriate.	46.124 Conditions With respect to any research project...the department...head may impose additional conditions prior to or at the time of approval when in the judgment of the department or agency head additional conditions are necessary for the protection of human subjects.
50.20 and 46.116 General requirements for informed consent are virtually identical.	
50.25 and 46.116(a) Elements of informed consent are virtually identical except: * 50.25(a)(5) requires the confidentiality statement to note “the possibility that the FDA may inspect the records.” * 46.116(c) and (d) state the conditions under which the IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent, or waive the requirement to obtain informed consent [the conditions could not apply in FDA regulated research]	
50.27 and 46.117 Documentation of informed consent are virtually identical except: * 46.117(c)(1) is not included in FDA's comparative section contained in 56.109(c). 46.117(c)(1) allows the IRB to waive the requirement for the investigator to obtain a signed consent form if it finds that the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality.	
50.23(a)-(c) Exception from general requirements Describes an exception from the general requirements for obtaining informed consent in circumstances that are life-threatening; informed consent cannot be obtained from the subject; time is not sufficient to obtain consent from the subject's legal representative; and there is available no alternative method of approved or generally recognized therapy that provides an equal or greater likelihood of saving the life of the subject.	No comparable provisions

FDA Regulations	HHS Regulations
50.23(d) Waiver of informed consent for military personnel Describes the criteria and standards that the President is to apply in making a determination that informed consent is not feasible or is contrary to the best interests of the individual in military exigencies in accordance with the Strom Thurmond Defense Authorization Act for FY 1999	No comparable provision.

1. In 1991 FDA's regulations were harmonized with the common rule to the extent permitted by statute.
2. Differences in the rules are due to differences in the statutory (1) scope or (2) requirements.
3. FDA has additional IRB requirements contained in parts 312, 812, and 814. For example, 812.2(b)(ii) states that research is considered to have an approved application for an IDE, unless FDA has notified the sponsor to the contrary, if IRB approval of the investigation is obtained after presenting the reviewing IRB with a brief explanation of why the device is not a significant risk, and maintains such approval, (iii) and ensures informed consent is obtained in accordance with part 50.
4. HHS has special subparts relating to vulnerable populations, e.g., children, prisoners, pregnant women, etc. FDA does not have comparable provisions for these populations.
5. The HHS regulations require assurances and certifications from the grantee institution. FDA regulations generally require assurances of compliance from either or both the sponsor of the research and the clinical investigator.

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