

Overview of 21 CFR Part 312, 21 CFR Part 812, and ICH (E6) Requirements

The following table provides a generalization of similar sections that appear in each of the 21 CFR Parts 312 and 812 regulations and the ICH (E6) guideline. The source documents should be referenced for specifics about the section and differences at a detail level. Sections which only apply to a specific document are so noted in the table.

| Section | Generalization of Requirements |
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| <i>General Provisions</i> | Regulations apply when test articles are subject to the (USA) Federal Food, Drug, and Cosmetic Act. Test articles must be identified as an investigational product. Various rules apply to promotional materials and charging for the article. Definitions help to ensure consistent interpretation of the regulations. |
| <i>Regulatory and IRB/IEC Responsibilities</i> | Regulatory agencies have certain obligations regarding the study, such as maintaining the confidentiality of some Sponsor information. Regulatory agencies may also put a hold on a study, terminate a study, and provide processes for resolving disputes. Regulations provide requirements for how an IRB/IEC is organized and their specific oversight responsibilities. The Investigator and Sponsor must ensure that required information is provided to these organizations. |
| <i>Obtaining Study Approval</i> | Studies involving test articles, which are covered under the application and scope of the regulations, must be approved. Requests for approval (i.e., IDE/IND) contain specific information, such as a cover sheet, description of the test article, and manufacturing information. The Study Protocol (Investigational Plan) is included with the application. Requests may be made to waive certain requirements, withdraw an application, and the application and supporting documents can be amended during the conduct of the study. Drug studies have some specific requirements depending if the study is a Phase 1, 2, or 3 study. |
| <i>Transfer of Sponsor Obligations</i> | Written agreements should be in place to define GCP responsibilities that the Study Sponsor transfers to another party. |
| <i>Conflicts of Interest</i> | The Investigator is required to provide a disclosure of financial information for review to ensure that there are no potential conflicts of interests with their participation in the study. |
| <i>Developing the Study Protocol and Cress</i> | A Study Protocol, which documents how the study will be conducted, is submitted with the application for study approval. The Study Protocol will identify the purpose of the study, describe the study design, and among other items, will include assessments of safety and efficacy, describe quality control, data handling, and record keeping requirements. CRFs are included to identify the data to be collected. When required, changes or amendments are made to the Study Protocol. In addition to the Study Protocol, a Report of Prior Investigations may be required. |

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| <i>Selecting and Managing Investigators</i> | Investigators, who qualify based on training and experience, are selected, and identified in the Study Protocol. Records are obtained to document the Investigator's qualifications and their agreement and commitment to participating in the study. Information and the appropriate training regarding the study (e.g., Investigator's Brochure) and test articles is developed and provided to the Investigator. The Investigator's compliance to the requirements of the study is monitored and corrective actions taken, as necessary, to establish compliance. |
| <i>Approvals to Start the Study</i> | Studies, which are subject to regulations, cannot be started until approvals to conduct the study are received. |
| <i>Managing the Test Articles</i> | Upon regulatory approval, the test articles can be distributed to the Investigator. The test articles can only be dispensed to subjects enrolled in the study. Records must be maintained that account for test articles distributed, dispensed, and dispositioned at the end of the study. |
| <i>Collecting Clinical Data</i> | The study can start once appropriate approvals are received. Participating study Investigators conduct the study according to the Study Protocol and applicable regulations. When appropriate, subjects are screened for potential enrollment in the study. Subjects must provide Informed Consent before they can be enrolled in the study. Any randomization and or blinding of test articles is performed as required and the Sponsor notified in cases where unbinding of the test article is required. At the Investigational Site, clinical observations are either transcribed onto CRFs from source medical records, or entered directly into an EDC system. Data may also be provided from laboratories and other sources (X-rays, etc.). The Investigator completes reports as required. Processes to change data are communicated to the Investigator. |
| <i>Reporting and Addressing Safety Issues</i> | The Study Protocol, and/or other documents, such as the Investigator Brochure, will describe events that are considered safety issues (e.g., unanticipated and serious adverse events). Safety issues are reported to the appropriate organizations (i.e., Study Sponsor, IRB, and/or regulatory agency) within stated time frames. The Investigator is required to provide appropriate medical follow-up. The Sponsor will monitor the resolution of safety issues, and take appropriate actions as necessary, which may include terminating the study. |
| <i>Processing Clinical Data</i> | Data collected by the Investigator are reviewed and processed by appropriately trained and experienced persons for eventual reporting and analysis. Included are quality assurance and control activities, the entering into computer systems (where EDC systems are not used), generating of data queries, and data clean and lock processes. Processing may include a medical review of the data. |
| <i>Managing the Study</i> | Study activities are managed to ensure compliance to study requirements and regulatory requirements. In addition to monitoring, quality assurance audits are performed. Compliance issues must be identified and resolved. These, in addition to safety issues, may result in the termination of the study or an individual Investigational Site. Various progress and other types of reports are produced and provided to the appropriate organizations. Reports are either the Investigator's or Sponsor's responsibility. |

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| <i>Monitoring Investigational Sites</i> | Appropriately trained and experienced persons are used to monitor the Investigational Sites to evaluate their compliance with study and applicable regulatory requirements. |
| <i>Storing and Retaining Records</i> | Essential study documents are generated and required to be on file before, during, and upon the completion (termination) of the study. Retention requirements define how long these documents are retained. Ownership of the documents may be transferred, in writing, to another party. |
| <i>Preparing for Inspections</i> | Essential study documents and records must be made available for inspection by regulatory agencies. |
| <i>Non-Study Use of the Test Article</i> | Various processes must be followed when the test article is used for treatment and emergency use. |
| <i>Public Disclosure of Data and Information</i> | There are some information regarding the submission for approval and the study that the FDA may publicly disclose. |
| <i>Contact Information</i> | Information regarding contacting the FDA is provided. |
| 21 CFR Part 312 Requirements Only | |
| <i>Foreign Clinical Studies Not Conducted Under an IND</i> | Various requirements must be met for the FDA to accept foreign studies not conducted under an IND. |
| <i>Use of the Drug for Laboratory Research Animals or In Vitro Tests</i> | The investigation drug may be distributed for use in laboratory research animals and in vitro tests; however, certain labeling and distribution requirements apply. |
| ICH (E6) Requirements Only | |
| <i>Compensation</i> | Compensation to Investigators and subjects must meet appropriate regulatory requirements and the financial aspects of the study must be documented. |
| <i>Multi-Center Studies</i> | The Sponsor must ensure that various requirements, such as the documenting of coordinating Investigator responsibilities and communication between Investigators, are met. |
| <i>Generating Clinical Reports</i> | Clinical reports will conform to standards, as required. |