Chapter 48 - Bioresearch Monitoring

Subject	Implementation Date
SPONSORS, CONTRACT RESEARCH ORGANIZATIONS AND MONITORS	February 21, 2001
	Completion Date Continuing

Data Reporting	
Product Codes	Product/Assignment Codes
45Z, 46Z 57Z, 99Z 60Z, 61Z 68Z, 69Z 73Z, 74Z 94Z, 95Z	09810 Food Additives 41810 Therapeutics Products 42810 Blood and Blood Products 45810 Vaccines and Allergenic Products 48810 Human Drugs 68810 Veterinary Drugs 83810 Medical Devices and Radiological Health

Field Reporting Requirements

All establishment inspection reports (EIRs), complete with attachments, exhibits, and any post-inspectional correspondence are to be submitted promptly to the assigning Center. If an EIR contains serious findings that raise the possibility of one or more violations of the Federal Food Drug and Cosmetic Act (FFDCA) or other Federal statutes, a copy of the EIR should be forwarded to the District Compliance Branch at the time it is sent to the Center. When an FDA 483 is issued, a copy will be faxed to the Center contact identified in the assignment.

When the District becomes aware of any significant adverse inspectional, analytical, or other information which may affect the agency's new product approval decisions with respect to a firm, the District should immediately notify the responsible Center program office via electronic mail, fax, or by phone.

PART I - BACKGROUND

This compliance program is one of four agency-wide Bioresearch Monitoring Compliance Programs. Regulations that govern the proper conduct of clinical studies establish specific responsibilities of sponsors for ensuring (1) the proper conduct of clinical studies for submission to the Food & Drug Administration (FDA) and (2) the protection of the rights and welfare of subjects of clinical studies. The specific regulations are found in 21 CFR 312 (CBER and CDER), 21 CFR 812 (CDRH), and 21 CFR 511.1(b) (CVM). The specific responsibilities of sponsors of clinical studies include obligations to:

1) Obtain agency approval, where necessary, before studies begin.

2) Manufacture and label investigational products appropriately.

3) Initiate, withhold, or discontinue clinical trials as required.

4) Refrain from commercialization of investigational products.

5) Control the distribution and return of investigational products.

6) Select qualified investigators to conduct studies.

7) Disseminate appropriate information to investigators.

8) Select qualified persons to monitor the conduct of studies.

9) Adequately monitor clinical investigations.

10) Evaluate and report adverse experiences.

11) Maintain adequate records of studies.

12) Submit progress reports and the final results of studies.

Sponsors may transfer responsibility for any or all of these obligations to Contract Research Organizations (CROs). [Note: The medical device regulations (21 CFR 812) do not define or delineate responsibilities for CROs.] Under the regulations such transfers of responsibility are permitted by written agreement. Responsibilities that are not specified in a written agreement are not transferred. When operating under such

agreements, the CROs are subject to the same regulatory actions as sponsors for any failure to perform any of the obligations assumed.

Monitors are employed by sponsors or CROs to review the conduct of clinical studies to assure that clinical investigators abide by their obligations for the proper conduct of clinical trials.

A Sponsor-Investigator is an individual who both initiates and conducts an investigation, and under whose immediate direction the investigational article is administered, dispensed or implanted. The requirements applicable to a sponsor-investigator include both those applicable to an investigator and a sponsor. See CP 7348.811 for Clinical Investigators.

PART II - IMPLEMENTATION

A. Objective

The FFDCA requires the submission of reports of clinical investigations that have been conducted to show whether an investigational product is safe and effective for its intended use. Inspections under this program will be conducted to determine:

1. How sponsors assure the validity of data submitted to them by clinical investigators.

2. The adherence of sponsors, CROs, and monitors to applicable regulations.

B. Program Management Instructions

1. Coverage

a. Sponsors

This group consists of those individuals, organizations, or corporations that initiate clinical investigations and have been so identified by FDA through receipt of an investigational exemption, or application for research or marketing permit for an article. A sponsor is defined in the regulations at 21 CFR 312.3, 510.3(k), and 812.3(n).

b. Contract Research Organizations

This group consists of those organizations or corporations which have entered into a contractual agreement with a sponsor to perform one or more of the obligations of a sponsor (e.g., design of protocol, selection of investigators and study monitors, evaluation of reports, and preparation of materials to be submitted to FDA). In accord with 21 CFR 312.52 and 511.1(f), responsibility as well as authority may be transferred and thus the CRO becomes a regulated entity. [Note: The medical device regulations (21 CFR 812) do not contain provisions for CROs.]

c. Monitors

This group consists of those individuals who are selected by either a sponsor or CRO to oversee the clinical investigation. The monitor may be an employee of the sponsor or CRO, or a consultant.

2. Procedure

a. Inspection Teams

In certain instances inspections will be conducted with Center personnel participating as team members.

1) A field investigator will serve as team leader and is responsible for the cooperative conduct of the inspection. Responsibilities of the team leader are explained in the Investigations Operations Manual (IOM) 502.4.

2) Center personnel will serve as scientific or technical support to the team leader and shall participate in the inspection by:

a) Attending pre-inspection conferences when and if scheduled.

b) Participating in the entire on-site inspection as permitted by agency priorities.

c) Providing support, as agreed upon with the team leader, in the preparation of specific sections of the inspection report where the Center participant's expertise is especially useful.

Any difficulties among participants in the inspection should be discussed with District management and, if not resolved, immediately referred to the HFC-130 contact for this program.

b. Specific

1) If a sponsor has contracted out all or part of their responsibilities, notify the Center contact of this fact and continue the inspection. The Center will decide whether to follow up with an inspection at the CRO or monitor and issue any additional assignments.

2) Whether a sponsor or CRO monitor is used, a monitor inspection will cover monitor's obligations for overseeing the investigation as instructed in Part III.

PART III – INSPECTIONAL

A. General Instructions

1. All inspections of sponsors, CROs, and monitors are to be conducted **without** prior notification unless otherwise instructed by the assigning Center.

2. Each inspection will consist of a comparison of the practices and procedures of sponsors, CROs, and monitors to the commitments made in the application for investigational exemption (including 510(k)), and applicable regulations and guidelines as instructed by the report formats in the attachments. Use the firm's copy of the application to compare with actual practices.

   DEVICES ONLY: Requests for inspections from CDRH normally involve Significant Risk (SR) devices that require full compliance with the Investigational Device Exemption (IDE) requirements. In addition to covering the identified SR device, the investigator should **determine** whether the sponsor/monitor is involved in clinical investigations of Non-significant Risk (NSR) devices, which require compliance with the abbreviated IDE requirements of 21 CFR 812.5, 812.7, 812.46, 812.140(b)(4) and (5), 812.150(b)(1) through (3) and (5) through (10). When appropriate, the investigator should choose at least one (1), but no more then three (3), NSR device investigations to **determine** the level of compliance with the abbreviated requirements.

   Determine whether the sponsor/monitor is involved in any clinical studies involving the humanitarian use of a device described in 21 CFR Part 814 Subpart H. **Determine** whether the sponsor has submitted any Humanitarian Device Applications Exemptions. Review distribution records for humanitarian use devices at the sponsor site to ensure compliance with exemption criterion (<4000 patients/year), proper accountability, confirmation of institutional review board (IRB) approval prior to distribution, and prompt notification to CDRH's Office of Device Evaluation of the withdrawal of approval by an IRB.

3. If significant violative practices are encountered, the assigning Center should be notified and will provide guidance on continuing the inspection.

4. If access to records or copying records is refused, or if actions by the inspected party take the form of a partial refusal, call attention to 301(e) and 505(k)(2) of the Act. If this does not resolve the issue, proceed with the

inspection and at the earliest opportunity notify the Bioresearch Monitoring Program Coordinator (HFC-230) and the contact for the assigning Center. IOM Section 514 provides general guidance on dealing with refusal to permit inspection.

5. Issue a Form FDA 483, Inspectional Observations, at the conclusion of the inspection when deviations from regulations are observed. **Deviations from guidance documents should not be listed on the FDA 483.** However, they should be discussed with management and **documented** in the EIR.

B. Establishment Inspections

1. Organization and Personnel

a. **Determine** the overall organization of the clinical research activities and monitoring of the selected studies.

b. **Obtain** relevant organizational charts that document structure and responsibilities for all activities involving investigational products.

1) **Identify** all departments, functions, and key individuals responsible for areas of sponsor activities such as protocol development, selection of investigators, statistical analysis, clinical supplies, monitoring, and quality assurance.

2) **Determine** who has the authority to review and approve study reports and data listings.

3) **Determine** who is responsible for final evaluations and decisions in the review of adverse experiences.

c. **Obtain** a list of outside services and contractors (CROs, laboratories, IRBs) and **document** the services they provide and who is responsible for their selection and oversight.

1) When a sponsor transfers responsibility for their obligations to a CRO:

a) **Determine** if the transfer of responsibilities was submitted to the agency as required by 21 CFR 312.23(a)(1)(viii), 314.50(d)(5)(x), 511.1(b)(4)(vi), and 514.1(a)(8)(viii).

b) **Document** any instance where transfer of responsibilities was not reported to the agency.

c) **Obtain** a copy of any written agreement transferring responsibilities.

2) If a CRO is contracted to collect adverse experience reports from clinical investigators, **determine** who at the sponsoring firm is responsible for obtaining these reports and submitting them to FDA.

d. **Obtain** a list of all monitors (for the studies being inspected) along with their job descriptions and qualifications.

2. Selection and Monitoring of Clinical Investigators

a. **Obtain** a list of all investigators and **determine** if there is a FDA 1572 (21 CFR 312.53(c)(I)) or a signed investigator agreement (21 CFR 812.20(b)(4)&(5)) for each clinical investigator identified.

b. Regulations require that the sponsor select clinical investigators qualified by training and experience (21 CFR 312.53(a), 511.1(b)(7)(I), and 812.43(a)). **Determine** the sponsor's criteria for selecting clinical investigators.

c. **Determine** if the sponsor provided the investigator all necessary information prior to initiation of the clinical trial. This may include clinical protocols or investigational plans, labeling, investigator brochures, previous study experience, etc.

d. **Determine** if the sponsor identified any clinical investigators who did not comply with FDA regulations. Did the sponsor secure prompt compliance? **Obtain** evidence of prompt correction or termination by the sponsor.

e. **Identify** any clinical investigators whose studies were terminated and the circumstances. **Review** monitoring reports for those clinical investigators and **determine** if those instances were promptly reported to FDA as required by 21 CFR 312.56(b) and 812.43(c)(3).

f. Identify any non-compliant clinical investigator not brought into compliance and not terminated by the sponsor. **Determine** the reason they were not terminated.

3. Selection of Monitors

a. **Review** the criteria for selecting monitors and **determine** if monitors meet those criteria.

b. **Determine** how the sponsor allocates responsibilities when more than one individual is responsible for monitoring functions, e.g., a medical monitor may have the responsibility for medical aspects of the study (and may be a physician) while other monitors may assess regulatory compliance.

4. Monitoring Procedures and Activities

a. Procedures

1) **Review** the procedures, frequency, scope, and process the sponsor uses to monitor the progress of the clinical investigations. (Device regulations (21 CFR 812.25(e)) require written monitoring procedures as part of the investigational plan.)

2) **Obtain** a copy of the sponsor's written procedures (SOPs and guidelines) for monitoring and **determine** if the procedures were followed for the selected study. In the absence of written procedures, conduct interviews of the monitors as feasible and **determine** how monitoring was conducted.

b. Activities

1) **Review** pre-trial and periodic site-visit reports.

2) **Determine** if the sponsor assured, through documentation, that the clinical investigation was conducted in accordance with protocols submitted to FDA.

3) **Determine** if responsibilities of the clinical investigators were carried out according to the FDA regulatory requirements (21 CFR 312.60, 312.61, 312.62, 312.64, 312.66, 312.68, 812.46, 812.100, and 812.110).

c. Review of Subject Records

1) **Compare** individual subject records, supporting documents and source documents with case report forms (CRFs) prepared by the clinical investigator for submission to the sponsor.

2) **Determine** if, when, and by whom CRFs are verified against supporting documents (hospital records, office charts, laboratory reports, etc.) at the study site.

3) **Determine** if all CRFs are verified. If a representative sample was selected, **determine** how the size and composition of the sample was selected.

4) **Determine** if a form is used for data verification and **obtain** a copy. **Obtain** a copy of any written procedures (SOPs and guidelines) for data verification.

5) **Determine** how the sponsor assures that IRB approval is obtained prior to the enrollment of subjects in the study.

6) **Determine** how the sponsor assures that informed consent is obtained from all subjects in the study.

7) **Determine** how the sponsor handles serious deviations from the approved protocol or FDA regulations. If serious deviations occurred, **obtain** evidence that the sponsor obtained prompt compliance or terminated the clinical investigator's participation in the investigation and reported it to FDA.

8) **Determine** if the sponsor makes corrections to CRFs and if the sponsor obtains confirmation or verification from the clinical investigator.

9) If sponsor-generated, site-specific data tabulations are provided by the assigning Center, **compare** the tabulations with CRFs and source documents.

d. Quality Assurance (QA)

Clinical trial quality assurance units (QAUs) are not required by regulation. However, many sponsors have clinical QAUs that perform independent audits/data verifications to determine compliance with

clinical trial SOPs and FDA regulations. QAUs should be independent of, and separate from, routine monitoring or quality control functions. Findings that are the product of a written program of QA will not be inspected without prior concurrence of the assigning FDA headquarters unit. Refer to Compliance Policy Guide 7151.02 for additional guidance in this matter.

1) **Determine** if the firm conducts QA inspections and audits.

2) **Determine** how the QAU is organized and operates.

3) **Obtain** a copy of any written procedures (SOPs and guidelines) for QA audits and operation of the QAU.

4) Describe the separation of functions between the QAU and monitoring of clinical trials.

5) Sponsors are required to submit a list of audited studies (21 CFR 314.50(d)(5)(xi)). If the assigning Center provides the list, **compare** the list with the sponsor's records.

5. Adverse Experience/Effects Reporting

a. Regulations require that FDA be promptly notified of unanticipated adverse experiences/effects with the use of investigational articles.

1) Drugs/biologics 312.32(c) and (d) - Telephone within 7 calendar days if fatal or life threatening; written reports within 15 calendar days if both serious and unexpected.

2) Veterinary drugs 511.1(b)(8)(ii) - Promptly investigate and report any findings associated with use of the new animal drug that may suggest significant hazards.

3) Devices 812.150(b)(1) – Within 10 working days of unanticipated adverse device effects.

b. **Determine** if adverse experiences reported from clinical sites were relayed to FDA as required by regulation.

c. **Determine** the sponsor's method or system for tracking adverse reactions and for relaying information of adverse experiences to participating investigators.

d. **Obtain** copies of any notification to investigators relating to adverse experiences.

6. Data Collection and Handling

a. Study Tabulations

1) Sponsors are required to submit in an NDA/PMA analyses of all clinical studies pertinent to the proposed drug/device use (21 CFR 314.50(d)(5)(ii-iv) and 814.20(b)(3)).

a) **Obtain** a list of all clinical studies contained in the application(s) referenced in the inspection assignment.

b) **Identify** any studies not included in the NDA/PMA and **document** the reason they were not included.

b. Investigator Tabulations

1) Sponsors are required to obtain from each clinical investigator a signed agreement (form FDA 1572 for human drugs and biologics and an investigator agreement for devices) prior to initiation of the clinical trial (21 CFR 312.60 and 812.43 (a)).

a) **Review** all signed agreements submitted to the associated IND/IDE.

b) **Identify** any clinical investigators with signed agreements not included in the NDA/PMA and **document** the reason they were not included.

c. Data Tabulations

1) FDA regulations require that sponsors submit data tabulations on each subject in each clinical trial in an NDA/PMA (21 CFR 314.50(f)(1) and 814.20(b)(6)(ii)).

a) **Determine** if the number of subjects in the studies performed under an IND/IDE is the same as the number reported in the NDA/PMA.

- **Determine** the number of subjects listed in each of the clinical trials and compare the number of subjects in the tabulations to the corresponding CRFs submitted to the sponsor.

- **Document** any subjects not included in the NDA/PMA and the reason they were not included.

d. Data Collection and Handling Procedures

1) **Review** the sponsor's written procedures (SOPs and guidelines) to assure the integrity of safety and efficacy data collected from clinical investigators (domestic and international).

2) **Verify** that the procedures were followed and **document** any deviations.

7. Record Retention

a. Refer to 21 CFR 312.57, 511.1(b)(7)(ii), and 812.140(d)

8. Automated Entry of Clinical Data

In August 1997, the Agency's regulation on electronic signatures and electronic recordkeeping became effective. The Regulation, at 21 CFR Part 11, describes the technical and procedural requirements that must be met if a firm chooses to maintain records electronically and/or use electronic signatures. Part 11 works in conjunction with other FDA regulations and laws that require recordkeeping. Those regulations and laws ("predicate rules') establish requirements for record content, signing, and retention. Certain older electronic systems may not have been in full compliance with Part 11 by August 1997 and modification to these so called "legacy systems" may take more time. Part 11 does not grandfather legacy systems and FDA expects that firms using legacy systems are taking steps to achieve full compliance with Part 11.

If a firm is keeping electronic records or using electronic signatures, **determine** if they are in compliance with 21 CFR Part 11. **Determine** the depth of part 11 coverage on a case by case basis, in light of initial findings and program resources. At a minimum, ensure that: (1) the firm has prepared a corrective action plan for achieving full compliance with part 11 requirements, and is making progress toward completing that plan in a timely manner; (2) accurate and complete electronic and human readable copies of electronic records, suitable for review, are made available; and, (3) employees are held accountable and responsible for actions taken under their electronic signatures. If initial findings indicate the firm's electronic records and/or electronic signatures may not be trustworthy and reliable, or

when electronic recordkeeping systems inhibit meaningful FDA inspection, a more detailed evaluation may be warranted. Districts should consult with center compliance officers and the Office of Enforcement (HFC-240) in assessing the need for and potential in depth review of, more detailed part 11 coverage. When substantial and significant part 11 deviations exist, FDA will not accept use of electronic records and electronic signatures to meet the requirements of the applicable predicate rule. See Compliance Policy Guide (CPG), Sec. 160.850.

The following are basic questions to be evaluated during an inspection of electronic recordkeeping practices and the use of electronic signatures by sponsors, CROs, and monitors.

Primary raw data collection should be **reviewed** to **determine** when changes were made and by whom. Concentrate on any original data entries and changes that can be made by anyone other than the clinical investigator.

a. Software

1) Who designed and developed the software?

2) Can it be modified, or has it been modified? If so, by whom?

3) If the clinical investigator can modify it, how would the sponsor be aware of any changes?

4) Has the software been validated? Who validated the software? What was the process used to validate the software? How was the validation process documented?

5) Are error logs maintained (for errors in software and systems) and do they identify corrections made?

b. Data Collection

1) Who is authorized to access the system and enter data or change data?

2) Are original data entered directly into an electronic record at the time of collection or are data transcribed from paper records into an electronic record?

3) Is there an audit trail to record:

a) changes to electronic records,

b) who made the change, and

c) when the change was made?

4) Are there edit checks and data logic checks for acceptable ranges of values?

5) How are the data transmitted from the clinical investigator to the sponsor or CRO?

c. Computerized System Security

1) How is system access managed, e.g., access privileges, authorization/deauthorization procedures, physical access controls? Are there records describing the names of authorized personnel, their titles, and a description of their access privileges?

2) What methods are used to access computerized systems, e.g., identification code/password combinations, tokens, biometric signatures, electronic signatures, digital signatures?

3) How are the data secured in case of disasters, e.g., power failure? Are there contingency plans and backup files?

4) Are there controls in place to prevent, detect, and mitigate effects of computer viruses on study data and software?

5) Are controls in place to prevent data from being altered, browsed, queried, or reported via external software applications that do not enter through the protective system software?

d. Procedures

Are there written procedures for software validation, data collection, and computerized system security?

9. Test Article

a. Integrity

1) Describe the procedures the sponsor uses to ensure the integrity of the test article from manufacturing to receipt by the clinical investigator:

a) **Determine** if the test article met required release specifications by review of the Certificate of Analysis.

b) **Determine** where the test article was stored and if the conditions of storage were appropriate.

c) **Determine** how the sponsor verifies article integrity during shipment to the clinical investigator.

2) **Determine** if test article was properly labeled (See 312.6, 511.1(b)(1), and 812.5).

3) **Determine** if the test article was recalled, withdrawn, or returned.

b. Accountability

1) **Determine** whether the sponsor maintains accounting records for use of the test article including:

a) Names and addresses of clinical investigators receiving test articles (report names and addresses). See 312.57, 511.1(b)(3), and 812.140(b)(2).

b) Shipment date(s), quantity, batch or code mark, or other identification number for test article shipped. See regulations above.

c) Final disposition of the test article. See 312.59, 511.1(b)(7)(ii), and 812.140(b)(2).

d) Final disposition of food-producing animals treated with the test article (511.1(b)(5).

A detailed audit should be performed when serious violations are suspected.

2) **Determine** whether the sponsor's records are sufficient to reconcile test article usage (compare the amount shipped to the investigators to the amount used and returned or disposed of).

3) **Determine** whether all unused or reusable supplies of the test article were returned to the sponsor when either the investigator(s) discontinued or completed participation in the clinical investigation, or the investigation was terminated.

4) If the test article was not returned to the sponsor, **describe** the method of disposition and **determine** if adequate records were maintained.

5) **Determine** how the sponsor controls and monitors the use of devices that are not single-use products, such as lithotripters or excimer lasers.

6) **Determine** if the sponsor is charging for the test article and **document** the fees charged.

10. Sample Collection

    a. Samples may be obtained at the direction of the assigning Center.

    b. During the inspection, if collection appears warranted, contact the assigning Center for further instructions.

11. Establishment Inspection Reports (EIRs)

    Information contained in EIRs may be used in support of approval or denial of a pre-marketing application. The EIR must **document** all findings that could significantly impact the decision-making process.

    a. Full Reporting

        1) A full report will be prepared and submitted in the following situations:

            a) The initial inspection of a firm.

            b) All inspections that may result in an OAI classification.

            c) Any assignment specifically requesting a full report.

        2) The EIR should contain the headings described in IOM 593.3, in addition to the headings outlined in Part III, B. The report must always include sufficient information and documentation to support the recommended classification.

    b. Abbreviated Reporting

        1) An abbreviated report may be submitted in all but the above situations. An abbreviated report does not mean that an abbreviated inspection can be conducted. Abbreviated reports must contain sufficient narrative and accompanying documentation to support the inspectional findings. The specific headings appearing under Part III, Inspection Procedures should be fully addressed during the inspection. **The EIR should be clearly identified as an abbreviated report**.

2) The report should include all the headings described in IOM section 593.1 and include:

   a) Reason for inspection

   b) Prior inspectional history

   c) Updated history of business

   d) Administrative procedures

   e) Persons interviewed and individual responsibilities

   f) Areas covered during the inspection

   g) Discussion with management

PART IV - ANALYTICAL

If sample analysis is required at a field laboratory, contact Division of Field Science (DFS) at 301-443-7103.

PART V - REGULATORY / ADMINISTRATIVE STRATEGY

A. District EIR Classification Authority

The District is encouraged to review and initially classify EIRs under this compliance program.

B. Center EIR Classification Authority

The Center has the **final** classification authority for all Bioresearch Monitoring Program inspection reports. The Center will provide to the District copies of all final classifications, including any reason for changes from the initial classification.

C. EIR Classifications

The following guidance is to be used in conjunction with the instructions in FMD-86 for initial District and Center classification of EIRs generated under this compliance program:

1. NAI - No objectionable conditions or practices were found during an inspection (or the objectionable conditions found do not justify further regulatory action).

2. VAI - Objectionable conditions or practices were found, but the agency is not prepared to take or recommend any administrative or regulatory action.

3. OAI - Regulatory and/or administrative actions will be recommended.

D. Regulatory/administrative follow up will be in accordance with 21 CFR 312, 511, and 812. FDA can invoke other legal sanctions under the FFDCA or Title 18 of the United States Code where appropriate.

E. The following are available to address violations of regulations:

1. Warning and Untitled Letters

2. Re-inspection

3. Termination of an exemption (IND, IDE, INAD)

4. Refusal to approve or license

5. Withdrawal of approval (PMA, NDA, NADA)

6. Determination of not substantially equivalent or recission of a 510(k) for devices

7. Implementation of the Application Integrity Policy

8. Initiation of stock recovery - see Regulatory Procedures Manual Part 5, 5-00-10

9. Seizure of test articles

10. Injunction

11. Prosecution under the FFDCA and other Federal statutes, i.e., 18 U.S.C. 2, 371, 1001, and 1341.

12. Referral of pertinent matters with headquarters' concurrence to other Federal, state, and local agencies for such action as that agency deems appropriate.

PART VI - REFERENCES AND CONTACTS

A. References

1. FFDCA - Sections 501(i), 505(i) and 505(k)(2)

2. Regulations in 21 CFR Parts 11, 50, 56, 312, 314, 511, 514, 809, 812, and 814.

3. SPECIFIC FORMS

   a. FDA Form 1571 - Investigational New Drug Application (See 21 CFR 312.40)

   b. FDA Form 1572 - Statement of Investigator, (See 21 CFR 312.53(c))

   c. Notice of claimed investigational exemption for a new animal drug, (See 21 CFR 511.1(b)(4)).

4. ICH Good Clinical Practice Consolidated Guideline, May 1997.

5. Guideline for the Monitoring of Clinical Investigations, January 1988.

6. Good Target Animal Study Practices: Clinical Investigators and Monitors, May 1997.

B. Program Contacts

When technical questions arise on a specific assignment, or when additional information or guidance is required, contact the assigning Center. Operational questions should be addressed to HFC-130.

1. Office of the Associate Commissioner for Regulatory Affairs

   a. Office of Enforcement, Division of Compliance Policy: Dr. James F. McCormack, HFC-230, 301-827-0425, FAX 301-827-0482.

   b. Office of Regional Operations, Division of Emergency and Investigational Operations: Dr. Thaddeus Sze, HFC-130, 301-827-5649, FAX 301-443-6919.

2. Center for Drug Evaluation and Research (CDER), Division of Scientific Investigations:

   a. Good Clinical Practice Branch I – Dr. John Martin, HFD-46, 301-594-1032, FAX 301-827-5290.

   b. Good Clinical Practice Branch II – Dr. Antoine El Hage, HFD-47, 301-594-1032, FAX 301-827-5290.

3. Center for Biologics Evaluation and Research (CBER)

   Division of Inspections and Surviellance – Mr. Joseph Salewski, HFM- 664, 301-827-6221, FAX 301-827-6748.

4. Center for Veterinary Medicine (CVM)

   Bioresearch Monitoring Staff: Ms. Dorothy Pocurull, HFV-234, 301-827-6664, FAX 301-827-1498.

5. Center for Devices and Radiological Health (CDRH)

   Division of Bioresearch Monitoring: Ms. Barbara Crowl, HFZ-311, 301-594-4720, FAX 301-594-4731.

6. Center for Food Safety and Applied Nutrition (CFSAN)

   Division of Product Policy: Dr. John Welsh, HFS-207, 202-418-3057, FAX 202-418-3126.

PART VII – HEADQUARTER'S RESPONSIBILITIES

A. Office of Regulatory Affairs

1. Division of Compliance Policy

   a. Coordinates compliance policy and guidance development.

   b. Coordinates responses to inquiries regarding agency interpretation of regulations and policy.

   c. Serves as the liaison with other Federal agencies and foreign governments with whom FDA has Memoranda of Agreement or Memoranda of Understanding.

   d. Resolves issues involving compliance or enforcement policy.

   e. Advises and concurs with Centers on recommended administrative and regulatory actions.

   f. Coordinates modifications and future issuance of this compliance program.

2. Division of Emergency and Investigational Operations

   a. Provides inspection quality assurance, training of field personnel, and operational guidance.

   b. Maintains liaison with Centers and Field Offices and resolves operational questions.

   c. Coordinates and schedules joint Center and multi-District inspections.

3. Division of Field Science

   a. Assigns laboratories for sample analysis and responds to method inquiries (DFS).

B. Centers

1. Identify the sponsors or CROs to be inspected (including applications for investigational exemptions, and applications for research or marketing

permits to be covered), and forward inspection assignments and background data, e.g., protocols, correspondence, and reviewers' concerns, to the field.

2. Review and make final classifications of EIRs. Conduct follow-up regulatory/administrative actions. Provide the field copies of all correspondence between the sponsor or CRO and FDA. Provide technical guidance and support to the field as needed.