

Answers to **Self-assessment Quiz**

Overview of Sponsor-Investigator Roles and Responsibilities in Clinical Investigations for Drugs and Biologics Orphan Products Grantees

1. The FDA's Office of Orphan Products Development (OOPD) is responsible for regulating orphan products under the Orphan Drugs Act. Which of the following are true statements?
 - A. OOPD is an office residing under the Center for Drugs Evaluation (CDER)
 - B. OOPD offers a Grant Program to encourage clinical research and development of products, which include drug and biologic products that are used in the diagnosis, prevention or treatment of rare diseases or conditions.
 - C. OOPD solicits applications for funding through the Orphan Products Grants Program through a Request for Applications (RFA)
 - D. Applicants receiving Grants (the Grantees) under OOPD's Grant Program are responsible for grant related issues and the clinician is responsible for the proper conduct of the clinical investigations and often play the dual role of the IND sponsor and a clinical investigator.
 - E. OOPD is the funding source for each Grant and also serves as sponsor of the clinical investigation.

Answer Choices:

- a. A and E only
- b. B, C, and D
- c. All of the above

Correct Answer: b.

2. Which of the following is false regarding the definition of a sponsor-Investigator:
- A. Is an individual that both initiates and conducts a clinical investigation.
 - B. Is a pharmaceutical company that both initiates and conducts a clinical investigation.

Answer Choices:

- a. A and B
- b. Only A
- c. Only B
- d. Neither A nor B

Correct Answer: b.

3. Which of the following are a Sponsor-Investigator's Responsibilities under FDA's regulations:
- A. Selecting qualified investigators
 - B. Obtaining signed investigator agreements
 - C. Obtaining financial disclosure from all clinical investigators
 - D. Ensuring that the clinical investigation is proceeding as per the investigation plan and protocol
 - E. Ensuring proper monitoring of the clinical investigation

Answer Choices:

- a. A and B
- b. A and C
- c. A, C, and D
- d. All of the above

Correct Answer: d.

4. Which of the following are not responsibilities of a Sponsor-Investigator under FDA's regulations:
- A. Selecting qualified monitors to monitor progress of the clinical investigation
 - B. Provide clinical investigators with the information they need to conduct the investigation
 - C. Protect the rights safety and welfare of subjects in the clinical investigation.
 - D. Obtain IRB approval prior to enrolling any subjects

E. Obtain and document informed consent signed and dated by subject or legally authorized representative (LAR)

Answer Choices:

- a. None of the above
- b. A and B
- c. B and D
- d. A, C, and D

Correct Answer: a.

5. Which of the following applies when a sponsor's responsibilities are transferred to a contract research organization (CRO):

- A. All transferred responsibilities need to be documented in writing
- B. The CRO that assumes the sponsor's responsibilities is subject to the same regulatory action as the sponsor
- C. Responsibilities that are not transferred to a CRO remain the responsibility of a sponsor.

Answer Choices:

- a. A and C
- b. A and B
- c. A, B, and C
- d. None of the above

Correct Answer: c.

6. The main purpose(s) of monitoring a study is/are to:

- A. Protect human subjects
- B. Ensure reliability of the data
- C. Ensure Regulatory Compliance of personnel with respect to protection of human subjects, adhering to the investigational plan and protocol and applicable regulations
- D. All of the above

Answer Choices:

- a. A
- b. A and C
- c. C
- d. A, B and C

Correct Answer: d.

7. Which of the following statements are true about a study Monitor and the Monitoring of a study:
- A. The monitor is an individual designated by a sponsor or contract research organization to oversee the progress of an investigation
 - B. The monitor must be qualified by training and experience to monitor the investigation
 - C. A sponsor-investigator is not required to ensure adequate monitoring of the investigation at his/her own site
 - D. The exact frequency of monitoring visits should be tailored to suit the complexity of each clinical investigation, and should be documented on a monitoring visit log

Answer Choices:

- a. A, B and C
- b. A, B and D
- c. C and D
- d. B, C, and D.

Correct Answer: b.

8. Which of the following is true regarding Data Safety Monitoring Boards (DSMB):
- A. DSMB is a group that reviews data from a clinical investigation
 - B. DSMB advise the sponsor on the continuing safety of subjects
 - C. DSMB evaluates data for continuing validity and scientific merit

Answer Choices:

- a. A, B and C
- b. A and B
- c. C and B
- d. None of the above.

Correct Answer: a.

9. Which of the following is not an Investigator Responsibility:

- A. Conduct clinical investigation according to signed investigator statement, investigational plan and applicable regulations
- B. Protect the rights safety and welfare of subjects in the clinical investigation
- C. Follow the protocol and investigational plan
- D. Select Qualified Clinical Investigators and Obtain financial disclosure from all clinical investigations

Answer Choices:

- a. D only
- b. C only
- c. B only
- d. A only

Correct Answer: a.

10. True or False: Records and reports that are to be maintained by a sponsor-investigator may include all the following:

- Case Histories
- Test product accountability
- Correspondence with the IRB
- Monitoring reports
- All correspondence with the FDA,
- Correspondence with other investigators, sponsors and monitors (if available)

Answer Choices:

- a. True
- b. False

Correct Answer: a.

11. Case histories record all observations and other data pertinent to the investigation on each individual administered the investigational product or employed as a control in the investigation. Case histories include all of the following, except:
- A. Case report forms
 - B. Supporting data including, for example, signed and dated consent forms and medical records including, for example, progress notes of the physician, the individual's hospital chart(s), and the nurses' notes i.e., source records.
 - C. Informed consent obtained from each subject prior to participation in the investigation
 - D. Code of Federal Regulations

Answer Choices:

- a. A and D
- b. B and D
- c. C and D
- d. D only

Correct Answer: d.

12. True or False: Documenting protocol deviations are a part of an investigator's responsibilities for adequately maintaining records and reports. The documentation of protocol deviations should include:
- a. Reasons for the protocol deviations
 - b. Prior approval and authorization from the sponsor, IRB, and FDA, for any changes or deviations from the investigational plan.

Answer Choices:

- a. True
- b. False

Correct Answer: a.

13. Which of the following are true statements with regard to FDA's Bioresearch Monitoring (BIMO) Inspections:

- A. During a BIMO inspection one may observe what items and data and procedures the FDA considers important in the conduct of a clinical investigation and how they can impact the "quality of the data."
- B. The objectives of a BIMO inspection are to protect human research subjects from undue hazard or risk while participating in a clinical investigation and to ensure the quality and integrity of data submitted in support of product marketing applications.
- C. FDA BIMO inspections evaluate data integrity and data validity

Answer Choices:

- a. A and C
- b. B and C
- c. C and A
- d. A, B and C

Correct Answer: d.

14. Which of the following cannot be the subject of an FDA BIMO inspection using a compliance program:

- A. Clinical coordinators
- B. Sponsor-Investigators
- C. Monitors
- D. Contract Research Organizations
- E. Institutional Review Boards

Answer Choices:

- a. A
- b. B
- c. C
- d. D
- e. E

Correct Answer: a.

15. FDA on-site inspection may be routine a inspection or may follow-up on specific causes or concerns. Which of the following is a true statement:

- A. A routine BIMO inspection is a general inspection that may focus on data submitted in support of a marketing application, are usually pre-announced and the inspection sites may be chosen randomly due to the nature of the clinical investigation being conducted.
- B. A directed or for-cause inspection follows-up on specific causes or concerns that the FDA may have, the inspections may be unannounced and could be conducted because of a complaint received by FDA or because of specific questions about the data integrity.

Answer Choices:

- a. Only A
- b. A and B
- c. Neither A nor B
- d. Only B

Correct Answer: b.

16. FDA BIMO inspections are classified based on the results of the inspectional findings or observations. Which of the inspectional classifications listed below would result in a regulatory action such as an FDA Warning Letter or proceed directly to a Disqualification proceeding due to serious concerns with data integrity, data quality, and or protection of human subjects.

- A. NAI classification
- B. VAI classification
- C. OAI classification
- D. OIG classification

Correct Answer: c.

17. True or False: During a routine BIMO inspection FDA may inspect all of the following study records:

- A. Standard Operating Procedures
- B. Protocols - the original and any subsequent amendments
- C. Documentation of IRB submissions and approval
- D. Signed investigator agreements - Form FDA 1572s
- E. Financial disclosure statements by the clinical investigator
- F. Correspondence between the sponsor and the IRB, the FDA and the clinical investigator
- G. Test article storage, distribution, and accountability documentations
- H. Monitoring plans, monitoring visit logs, and monitoring reports.
- I. Training records

- J. Case report forms
- K. Adverse event reports.
- L. Data line-listings submitted to the FDA
- M. Business financial and expenditure records
- N. Advertising and promotional accounts and expenditures

Answer Choices:

- a. True
- b. False

Correct Answer: b.

18. In general, when an FDA inspector conducts a data audit during a clinical investigator inspection; the FDA inspector is:
- A. Determining if the data is consistent, accurate, and complete
 - B. Comparing data on case report forms vs. data on case histories vs. data submitted to the FDA
 - C. Evaluating corrective actions taken for any protocol deviations
 - D. Verify that the test-article was properly dispensed and accounted

Answer Choices:

- a. A and D only
- b. B and D only
- c. C and D only
- d. All of the above

Correct Answer: d.

19. If writing a response to Form FDA 483 observations, the sponsor- investigator should consider which of the following actions:

- A. Assess the validity and significance of each violation
- B. Disagree with observations that are not accurate
- C. Submit additional supporting documentation, if available.
- D. Suggest corrective actions or action plans for valid violations

Answer Choices:

- a. None of the above
- b. C and D only
- c. A and C only
- d. C only
- e. All of the above

Correct Answer: e.

20. According to FDA's regulations, it is the sponsor's responsibility to obtain a signed statement from the clinical investigator stating all of the following except:

- A. To conduct the trial in accordance with GCP and applicable regulatory requirements
- B. To comply with procedures for data recording/reporting
- C. To permit monitoring of the ongoing investigation.
- D. To conduct the study under an active investigational new drug (IND) application.
- E. To delegate the responsibility of conducting or supervising the clinical investigation

Answer Choices:

- a. A and D
- b. B only
- c. C and D
- d. D only
- e. E only

Correct Answer: corrected answer: e

21. True or False: Sponsors are required to report fatal or life threatening adverse experiences associated with the use of an investigational agent within 7 working days to FDA.

Answer Choices:

- a. True
- b. False

Correct Answer: a

22. True or False: FDA regulations require sponsors to notify FDA and all participating investigators of any serious and unanticipated adverse effects within x number of days after first learning about the adverse effects. In such a situation, what is the value of x?

Answer Choices:

- a. 10 days
- b. 15 days
- c. Immediately
- d. 21 days
- e. 7 days

Correct Answer: b.

23. True or False: A sponsor of a clinical study using an investigational test product is not required to make a safety report for any adverse experience associated with the use of the drug until the time of submitting the annual report.

Answer Choices:

- a. True
- b. False

Correct Answer: b.

24. True or False: All protocol changes, even those to avoid imminent hazards to the study subject, should not be implemented by a clinical investigator without the explicit written agreement of the study sponsor.

Answer Choices:

- a. True
- b. False

Correct Answer: b.

25. Which of the following is true?

- A. Certificates of Confidentiality (CoC) affirmative prohibit CoC holders (sponsors, sponsor-investigators, or their representatives) from disclosing identifiable and sensitive information, unless specific exceptions are applicable.
- B. CoCs are mandatory for all federally funded human research subject research that involves identifiable and sensitive information unless specific exceptions are applicable.
- C. For non-federally funded research, CoCs are not required but are issued at FDA's discretion, if requested, for human research subject research that involves identifiable and sensitive information, unless specific exceptions are applicable.
- D. The protections afforded by mandatory and discretionary CoCs issued by FDA are identical and the statutory responsibilities are the same, and applicable for studies of a product subject to FDA's jurisdiction and subject to FDA's regulatory authority.
- E. The disclosure prohibitions shall not apply to disclosure or use that is-
 - (i) required by Federal, State, or local laws, except with the consent of the individual to whom the information, document, or biospecimen pertains
 - (ii) necessary for the medical treatment of the individual to whom the information, document, or biospecimen pertains and made with the consent of such individual
 - (iii) made with the consent of the individual to whom the information, document, or biospecimen pertains, or
 - (iv) made for the purposes of other scientific research that follows applicable Federal regulations governing the protection of human subjects in research.

Answer Choices:

- a. A and B
- b. C and D
- c. A and E
- d. A, B, C, only
- e. All the above

Correct answer: e = All the above.

26. True or False:

ClinicalTrials.gov is a registry and results information database of publicly and privately supported clinical studies of human participants conducted only in the U.S.

Answer Choices:

- a. True
- b. False

Correct Answer = b

27. Which of the following is a true statement:

- A. The National Institutes of Health (NIH) leads the implementation responsibilities of ClinicalTrials.gov by:
 - Developing and maintaining the ClinicalTrials.gov data bank
- B. HHS Funding Agency (FDA, NIH, AHRQ) has the following responsibility:
 - Verifying compliance with the clinical trial information submission requirements for applicable clinical trials (ACTs) for which the grantee is the responsible party before releasing remaining funding or funding future grants
- C. FDA is responsible for enforcing the following requirements:
 - Informed consent statement regarding ClinicalTrials.gov (21 CFR 50.25(c))
 - Certification of Compliance (Form FDA 3674)
 - Registration and submission of results information

Answer Choices:

a = A & C only

b = C only

c = B & C only

d = All of the above

Answer = d

28. True or false

- A. For a clinical trial, including applicable clinical trial, the Primary Completion Date is defined as the date that the final subject was examined or received an intervention for the purposes of final collection of data for the primary outcome, whether the clinical trial concluded according to the pre-specified protocol or was terminated.

Answers:

- a. True
- b. False

Answer = a

29. Which of the following statement is false:

- A. There can only be one Responsible Party: The Responsible Party is the sponsor of the clinical trial. The Principal Investigator (PI) cannot serve as the Responsible Party in an applicable clinical trial.
- B. Clinical Trial summary results information for all ACTs must be submitted to ClinicalTrials.gov

Answers:

- a. = A only
- b. = B only
- c. = A & B

Answer = c

30. Which statement is true?

- A. Willfully and knowingly submitting false Certification of Compliance (Form FDA 3674) is a criminal offense.
- B. FDA OOPD should not be listed as either the “collaborator” or the “sponsor” of the clinical trial in CT.gov.
- C. Possible legal consequence for failure to comply with ClinicalTrials.gov requirements include:
 - Notice of Noncompliance letters
 - civil monetary penalties
 - Remaining grant funding or future grant funding may not be released to the grantee if required clinical trial information for ACTs has not been submitted and verified.

Answers:

- a = A only
- b = B only
- c = C only
- d = All of the above

Answer = d

31. Which of the following Offices at FDA would serve as good contacts for questions regarding sponsor-investigator roles and responsibilities in clinical investigations for drugs and biologics orphan product grantees:

- A. Office of Orphan Products Development (OOPD)
- B. Office of Clinical Policy (OCLiP)
- C. Center for Drug Evaluation and Research (CDER) Office of Scientific Investigations (OSI)
- D. Center for Biologics Evaluation and Research (CBER) Division of Inspections and Surveillance

Answers:

- a. A only
- b. A & B
- c. A, C and D only
- d. All of the above

Answer = d