Quality Management Activity Guiding Questions Answer Key

Activity Title: The Case of an FDA Letter I

Activity Guiding Questions:

1. What is the nature of the citation?

   Clinical Investigator (CI) failed to personally conduct or supervise the clinical investigations [21 CFR 312.60].

2. According to the citation, what were the general responsibilities of the clinical investigator at the site?

   The general responsibilities of the clinical investigator included ensuring that the clinical trials were conducted according to the signed investigator statement, the investigational plan, and applicable regulations; protecting the rights, safety, and welfare of subjects under his/her care; and ensuring control of drugs under investigation [21 CFR 312.60]. By signing Form FDA 1572, he/she specifically agreed to personally conduct the clinical trial or to supervise those aspects of the trial that he/she not personally conduct.

3. Keeping Good Clinical Practices (GCP) Guidelines in mind could this citation have been prevented from happening? If so, how?
   Yes, it could have been prevented. The CI needed to adhere to GCP Guidelines and to the responsibilities he/she agreed to perform. By supervising adequately, the individuals to whom he/she delegated study tasks. Supervise adequately the conduct of Protocol and avoid the many of the violations noted in the citation.

4. At your tables, discuss and identify any violations cited in the excerpts identified in the citation.

   Failed to supervise and oversight of the protocol, violations include, but are not limited to, enrollment of subjects into the protocol when approval by the Columbia University Medical Center (CUMC) Institutional Review Board (IRB) had lapsed; failure to obtain informed consent from 28 of 50 enrolled subjects; and randomization and administration of investigational drug to 10 subjects before obtaining their informed consent to participate in the study.

5. As a group explain how this citation affect the safety of the participants.

   Failed to protect the rights, safety, and welfare of study subjects and to ensure the integrity of the study data. Lack of supervision and oversight over Protocol raised significant concerns about the adequacy of the protection of study subjects enrolled at the site in the studies mentioned in the study and also raised data integrity concerns generated for Protocol

6. What additional training needed to be provided to the clinical investigators?

   Re-education of investigators involved in Protocol, provide the instruction and oversight of the research staff delegated to recruiting and obtaining informed consent.

Notes Section:

Quality Management Guiding Questions Answer Key

Activity Title: The Case of an FDA Letter 2

Activity Guiding Questions:

1. What is the nature of the citation?

   Clinical investigator failed to obtain informed consent in accordance with the provision of 21 CFR part 50 [21 CFR 312.60 and 21 CFR 50.20].

2. According to the citation, what were the general responsibilities of the clinical investigator at the site?

   The clinical investigator's major responsibilities were to obtain informed consent of all participants in accordance with 21 CFR part 50. FDA's regulations at 21 CFR 50.20 state that, except as provided in 21 CFR 50.23 and 21 CFR 50.24, as an investigator may involve a human being as a participant in research covered by the regulations unless he/she has obtained the legally effective informed consent of the participant or the participant's legally authorized representative.

3. Keeping Good Clinical Practices (GCP) Guidelines in mind could this citation have been prevented from happening? If so, how?

   Yes, by complying with the general responsibilities of the clinical investigator, obtaining the informed consent from all participants who were enrolled in Protocol, taking full responsibility of providing instruction and oversight of the research staff delegated to recruiting and obtaining informed consent.

4. At your tables, discuss and identify any violations cited in the excerpts assigned to them. (Share ICH reference)

   The CI failed to obtain informed consent from participants and enrolled 10 participants into Protocol (a) (4) and gave the investigational drug before each signed the informed consent document.

5. As a group explain how this citation affect the safety of the participants.

   By failing to obtain informed consent prior to involving participants in research jeopardizes the safety and welfare of participants by denying them an opportunity to assess the risks and benefits of their participation in the clinical investigation.

Notes Section:

Quality Management Guiding Questions Answer Key

Activity Title: The Case of an FDA Letter 3

Activity Guiding Questions:

1. What is the nature of the citation?

   Clinical investigator failed to ensure that the investigation was in accordance with the investigational plan [21 CFR 312.60].

2. According to the citation, what were the general responsibilities of the clinical investigator at the site?

   The clinical investigator's major responsibilities are to ensure that the clinical studies are conducted in accordance with the investigational plan. The investigational plan for Protocol **(a)(4)** required the CI to administer the protocol-specified dose of investigational drug to each participant according to their assigned study arm, and to obtain study-related laboratory tests.

3. Keeping Good Clinical Practices (GCP) Guidelines in mind could this citation have been prevented from happening? If so, how?

   Yes, by complying with the general responsibilities of the clinical investigator, ensuring studies were conducted in accordance to the investigational plan, administer the protocol specify dose to each participant and obtain study-related laboratory tests and

4. At your tables, discuss and identify any violations cited in the excerpts assigned to them. (Share ICH reference)

   For Protocol **(a)(4)**, four participants were not dosed according to their protocol-specified study arm (standard dosing or stair-step dosing). The participant's dosing log information is not supported by the dosing log.

5. As a group explain how this citation affect the safety of the participants.

   By failing to administer investigational drug to participant according to the protocol-required dosing schedule compromises the validity and integrity of data generated at the CI site for Protocol **(a)(4)** and the safety, and welfare of the human participants of these studies.

Notes Section:

Quality Management Guiding Questions Answer Key

Activity Title: The Case of an FDA Letter 4

Activity Guiding Questions:

1. What is the nature of the citation?

   Clinical Investigator (CI) failed to assure that an IRB that complies with the requirements set forth in part 56 was responsible for the initial and continuing review and approval of the proposed clinical study [21 CFR 312.66].

2. According to the citation, what were the general responsibilities of the clinical investigator at the site?

   The clinical investigator is required to assure that an IRB complies with 21 CFR part 56 reviews and approves a proposed clinical investigation.

3. Keeping Good Clinical Practices (GCP) Guidelines in mind could this citation have been prevented from happening? If so, how?

   Yes, it could have been prevented. The CI needed to adhere to monitor the protocol for continuing IRB approval and ensure that no study-related procedures were performed without IRB approval or during a period in which IRB approval has lapsed. Develop a plan with details regarding how he/she was to ensure to monitor protocols for continuing IRB approval and how to ensure that no study – related procedures were performed without IRB approval or during a period in which IRB approval has lapsed.

4. At your tables, discuss and identify any violations cited in the excerpts identified in the citation.

   Failed to assure that an IRB that complies with 21 CFR part 56 reviewed and approved a proposed clinical study.) Impeded the IRB's ability to review the application to conduct Protocol **(a)(4)** and make a determination regarding the adequacy of that application. **Enrolled six participants** (Participants C42 through C47) into this protocol and gave them the investigational drug without

5. As a group explain how this citation affect the safety of the participants.

protecting the rights, safety, and welfare of subjects under your care; and ensuring control of drugs under investigation [21 CFR 312.60].
Failed to protect the rights, safety, and welfare of study subjects and to ensure the integrity of the study. Lack of supervision and oversight over Protocol raised significant concerns about the adequacy of the protection of study subjects enrolled at the site in the studies mentioned in the study and also raised data integrity concerns generated for Protocol

6. As a group explain how this citation affect the safety of the participants.

   The protection of the rights, safety, and welfare of subjects under the CI care; and assurance of control of drugs under investigation [21 CFR 312.60].

Notes Section: