HHS Reporting Requirements and Adverse Events

Michael A. Carome, M.D.
Director, Division of Compliance Oversight
Office for Human Research Protections

Title 45
Code of Federal Regulations
Part 46

Protection of Human Subjects
(Last revised June 18, 1991)

Educational Objectives

- **To understand the reporting requirements under HHS regulations for the protection of human subjects (45 CFR Part 46)**
  - ***What? To Whom? When? How?***
- **To provide an overview of OHRP's process for evaluating the reports it receives from institutions**

What adverse event reporting requirements are stipulated by HHS regulations for the protection of human subjects?

What adverse event reporting requirements are stipulated by HHS regulations for the protection of human subjects?

NONE

What Events Need to be Reported Under 45 CFR Part 46?

- Any unanticipated problems involving risks to subjects or others.
- Any serious or continuing noncompliance with 45 CFR Part 46 or the requirements or determinations of the IRB.
- Any suspension or termination of IRB approval.

[45 CFR 46.103(b)(5)]

Where do adverse events fit into the HHS reporting requirements? (1)

- The HHS regulations at 45 CFR Part 46 do not reference “adverse events.”
- OHRP expects that certain adverse events (AEs) will be determined by investigators and/or the IRB to be unanticipated problems involving risks to subjects; it is these AEs that must be reported in accordance with the HHS regulations.

Where do adverse events fit into the HHS reporting requirements? (2)

- To ensure compliance with 45 CFR 46.103(a) and 103(b)(5), investigators should report unanticipated serious AEs to the IRB.

Where do adverse events fit into the HHS reporting requirements? (3)

- **The IRB, in reviewing such AEs should (i) carefully assess the relationship of the AE to the research interventions and interactions; (ii) determine whether the AE represents an unanticipated problem; (iii) follow written procedures for ensuring that any AE determined to be an unanticipated problem is reported per HHS regulations; and (iv) determine whether the research or informed consent document require modification.**

Where do adverse events fit into the HHS reporting requirements? (4)

- Any adverse event or group of adverse events that results in suspension or termination of IRB approval of the research must also be promptly reported.

Adverse Events versus Unanticipated Problems Involving Risks to Subjects

- Not all adverse events are unanticipated problems involving risks to subjects or others.
- Not all unanticipated problems involving risks to subjects are adverse events.

To Whom Must the Events Referenced Under 45 CFR 46.103(b)(5) be Reported?

- The IRB
- Appropriate institutional officials
- The head of the supporting Department or Agency.
- OHRP

[45 CFR 46.103(a) and 46.103(b)(5)]

What is the Required Time Frame for Reporting Under 45 CFR 46.103(b)(5)?

- Promptly

What is the Required Time Frame for Reporting Under 45 CFR 46.103(b)(5)?

How should reporting to OHRP be accomplished?

- Submit to Division of Compliance Oversight
- Regular mail, express mail, facsimile, and e-mail
- Include the following information:
  - Project title, PI name, HHS or other Federal support
  - A detailed description of the incident
  - A description of the any corrective actions or modifications to the research required by the IRB or the institution.
- Be aware that such reports are subject to release under the Federal Freedom of Information Act.

What does OHRP do with the reports it receives from institutions? (1)

- Log into a database and review.
- Where human subjects may be at risk of harm as a result of the events, assess whether the institution, IRB, and investigators are taking appropriate action.
- Assess the adequacy of the IRB's/institution's evaluation of the matter.

What does OHRP do with the reports it receives from institutions? (2)

- Assess the adequacy of the corrective actions taken or proposed:
  - Investigator/project specific
  - Systemic
- Share with other relevant agencies.
- Issue written response.