Adverse Event Reporting: Trials and Tribulations

Joanne R. Less, Ph.D.
Director, IDE and HDE Programs
ODE, CDRH, FDA

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I. Definitions and Reporting Requirements
   - Who's Responsible?
   - To Whom?
   - Timeframes?

II. Problems in Reporting

III. Other Reportable Events

“Anticipated” Adverse Events

- No definition in IDE regulation; Those that are prospectively identified in the IP in the IDE
- Reported by sponsor to FDA, CIs, and IRBs in progress reports (Section 812.150(b)(5))

“Anticipated” AEs

- Reports used by FDA to monitor study -- assess risk/benefit relationship as study progresses
- If R/B profile changes or new AEs are detected, may need to modify informed consent document, protocol, etc.

Unanticipated Adverse Device Effect (UADE)

Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in IP

UADE (Cont'd)

Or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of the subjects. (Section 812.3(s))

Reporting Requirements UADEs

- CI reports to sponsor & reviewing IRB w/in 10 days of learning of the effect (Section 812.150(a)(1))
- Sponsor must "immediately" conduct evaluation of the effect to determine if the UADE presents an "unreasonable risk to subjects" (Section 812.46(b))

Reporting Requirements UADEs

Sponsor determines if study (and any other related studies) should:

- **Continue; report evaluation to FDA, all IRBs, and all CIs w/in 10 days of being notified of the effect**
- **Terminate: report to FDA w/in 5 days of making the determination and not later than 15 days of learning of the effect**

Reporting Requirements UADEs

- If the sponsor terminates the study, sponsor may not restart w/out FDA & IRB approval
- Sponsor submits IDE supplement with results of evaluation. FDA decides if study should restart and if any other modifications are needed.

Problems in Reporting

- Understanding what needs to be reported and when
  - (e.g., a death in a resuscitation trial - is it an AE or a UADE?)
- Adequately evaluating AEs and UADEs
- Over-reporting;Under-reporting
- Where to report

Other Reportable Events

1) Failure to obtain IC

- CI IRB and Sponsor (5 days)
- Sponsor FDA (5 days)
- Include any corrective action plan

2) Emergency use

- CI Sponsor & IRB (5 days)
- Sponsor FDA (5 days)

Other Reportable Events

3) Withdrawal of IRB approval

- Study not conducted in accordance with IRB requirements or is associated with unexpected serious harm to subjects
- IRB CI, Institution, & FDA (“promptly”) (Section 56.113)
- CI Sponsor FDA & all IRBs (5 days) (Section 812.150)

Other Reportable Events (Cont'd)

4) Protocol deviations

- Should be approved by FDA if deviation effects R, S, or W of patient
- If occurs w/out FDA approval, report "promptly"

5) SR determinations

- Sponsor FDA (5 days)

Summary

- To minimize the risks to subjects involved in clinical trials, meaningful review and prompt reporting of adverse events is critical
- All parties need to do their part

*IDE Staff (301) 594-1190