Adverse Event Reporting

Jodie Riley, M.ISM

Adverse Events

- Adverse Events (AEs) are ". . . any **untoward** medical occurrence in a subject that was not previously identified which does not necessarily have a causal relationship to the study drug…"
- Events existing prior to randomization should not be reported as AEs, unless there is a change in severity.
- Pre-existing conditions that are discovered after randomization are not adverse events. These should be documented as medical history.
- Abnormal lab values collected after randomization that are considered to be clinically significant by the site investigator are adverse events.

Serious Adverse Events

Serious Adverse Events (SAEs):

- Are Fatal
- Are Life-threatening
- Result in hospitalization/prolonging of hospitalization – excluding optional, pre-planned surgery
- Result in disability/congenital anomaly
- Require intervention to prevent permanent impairment or damage

Reporting AEs

- Reported on Form 104 – Adverse Event Case Report Form (CRF)
- One AE per CRF
- Report diagnosis, not symptoms
  - Fever, cough, chest pain, crackles = pneumonia
- Avoid abbreviations/colloquialisms

Reporting AEs

- Death, surgery, intubation, etc. are NOT adverse events. They are outcomes of adverse events.
- All AEs will be coded using MedDRA.

- A new feature of WebDCU™ will auto-populate the Lowest Level Term when 3 or more letters are entered into the name field .

Reporting Requirements for AEs

- AE reporting – from Randomization through Day 6 or Hospital Discharge, whichever comes first
- SAE reporting – from Randomization through End of Study

Data Entry Timelines for AEs

- Non-serious AEs must be entered and **submitted** into WebDCU™ within 5 days of data collection.

- SAEs must be entered and **submitted** into WebDCU™ within **24 hours** of discovery.

Reporting SAEs

SAEs require additional information to be submitted on the AE CRF:

- Detailed description of the event
- Relevant tests/laboratory data
- Relevant history and pre-existing conditions
- Concomitant medications

SAE Narratives

- Narratives assist the Independent Medical Safety Monitor (IMSM) in reviewing the event.
- Narratives are pre-populated into the MedWatch form, if expedited reporting is required.
- Remove any protected health information (PHI) from the narrative
  - i.e., subject, physician or institution name

IMSM Review Process

- Site enters data and submits AE CRF into WebDCU™
- Automatic e-mail notifications to Site Manager (SM) and Internal Quality Reviewer (IQR)
- If SAE and data is sufficient, automatic e-mail notification sent to the IMSM
- IMSM blindly reviews the event and indicates whether it is serious, unexpected and study intervention-related
- SM closes review process

MedWatch Reports

- FDA requires expedited reporting for AEs that are serious, unexpected and study intervention-related.

- If the IMSM determines that the SAE is serious, unexpected and study intervention-related, WebDCU™ generates a pre-populated MedWatch form and sends an automatic e-mail notification to the Site Manager.

MedWatch Reports

- Site staff completes MedWatch
- SM submits MedWatch to FDA
- SM notifies sites of MedWatch posting to WebDCU™

MedWatch Reporting Requirements

- Fatal or life-threatening SAEs:
  - Initial report due within 7 days of discovery
  - Complete report due within 15 days of discovery

- Non-fatal and non life-threatening SAEs:
  - Initial report due within 15 days of discovery

- Follow-Up Reporting
  - PI responsible for obtaining any follow-up information and submitting that data into WebDCU™ as soon as it becomes available