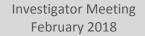
Adverse Event Reporting

Jodie Riley, M.ISM



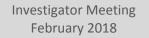




Adverse Events

- Adverse Events (AEs) are "... any <u>untoward</u> 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

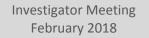
- Reported on Form 104 Adverse Event Case Report Form (CRF)
- One AE per CRF
- Report diagnosis, not symptoms
 - Fever, cough, chest pain, crackles = pneumonia
- Avoid abbreviations/colloquialisms



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 .



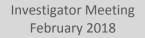




Reporting Requirements for AEs

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





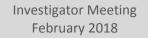


Data Entry Timelines for AEs

Non-serious AEs must be entered and <u>submitted</u> into WebDCU[™] within 5 days of data collection.

 SAEs must be entered and <u>submitted</u> 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



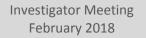


MedWatch Reports

• FDA requires expedited reporting for AEs that are serious, unexpected <u>and</u> 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



