The Development of a Real-Time Protocol Deviation Notification, Tracking and Resolution Process in Multi-Site Substance Use Treatment Clinical Trials

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Protocol Deviations

Definition: A protocol deviation/violation is generally an unplanned excursion from the protocol that is not implemented or intended as a systematic change (BIMO, 2015)

- **Major:**
  - Inadequate or delinquent informed consent
  - Accidental distribution of incorrect study medication or dose
  - Ineligible participant enrolled
  - Unreported Serious Adverse Events (SAEs)

- **Minor:**
  - Missed assessment/lab test
  - Missed or out of window study visit
Multi-site behavioral and pharmacological substance abuse treatment interventions across a nearly 250 settings with diverse patient populations.

The Emmes Clinical Coordinating Center (CCC) supports the CTN in its general operations and developed a process designed for rapid reporting, notification, and resolution of protocol deviations...
Protocol Deviation (PD) Occurs

- Site staff enters PD in Advantage EDC (EDC)
- EDC sends email notifications simultaneously

  - Lead team reviews the PD within 7 days; often on the weekly operations teleconference call

  - Lead Node (LN)
  - DSC
  - CCC
  - Other pharma partners

  - LT to follow-up on site call (group or indiv)
  - CCC Protocol Spec. reviews eCRF in EDC
  - Site monitor reviews in EDC on next visit

Communication
Protocol Deviation

Date of deviation: 08/21/2014
Protocol deviation number: 1st Protocol Deviation of the day

1. ✔ Date deviation identified:
2. ✔ Deviation type:
   If "Other", specify:
3. ✔ Brief description of what occurred:
4. ✔ Brief description of the actual or expected corrective action for this event:
5. ✔ Brief description of the plan to prevent recurrence:
6. ✔ Is this deviation reportable to your IRB?
   ✔ If "Yes", will the IRB be notified at the time of continuing review?
     ✔ If "Yes", date of planned submission:
     ☐ If "No", date of actual submission:
   ☐ If "No"
Protocol Deviation Types

- Informed Consent Procedures
- Inclusion/Exclusion Criteria
- Laboratory Assessments
- Study Procedures/Assessments
- Adverse Event
- Randomization Procedures
- Study Medication Management
- Study Behavioral Intervention
- Other Significant Deviations
Protocol Deviation Types

**ADVERSE EVENT**
- AE not reported - SAE not reported
- AE/SAE reported out of protocol specified reporting timeframe
- AE/SAE not elicited, observed and/or documented as per protocol
- Safety assessment (e.g. labs, ECG, clinical referral to care) not conducted per protocol
- Other: specify
Protocol Deviation Review

Protocol Deviation Review

Protocol:  
Participant:  
Form: Protocol Deviation Review

Date of deviation: 08/21/2014
Protocol deviation number: 1st Protocol Deviation of the day

Completed by Protocol Specialist:

1. ✔ What section of the protocol does this deviation refer to?
   8.1.1 Informed Consent (Phase 1)

2. ✔ Does the report of this deviation require site staff retraining?
   If "Yes", specify plan for retraining:
   ✔ No ☐ Yes

3. ✔ Deviation was discussed with Lead Investigative Team on:
   01/08/2015 (mm/dd/yyyy)

4. ☐ Deviation is categorized as:
   ☐ Major ☑ Minor

5. ✔ Deviation assessment by Protocol Specialist complete:
   ☐ No ✔ Yes

Protocol Specialist reviewer:
DB (initials)
Completed by Protocol Monitor:

6. Corrective action for this deviation was completed and documented on-site as described:
   If "No", specify reason:
   - Yes

7. Deviation was reported to the IRB as required:
   If "No", specify reason:
   - Yes

8. Preventive action plan related to this event was completed and documented on-site as described:

9. Review by Protocol Monitor is complete:
   - Yes
   Protocol Monitor reviewer:
   - SS (initials)

The site's IRB does not require this protocol deviation to be submitted until the annual review.
**Cumulative report generated weekly**

*Allows patterns, systemic errors, to be detected*

<table>
<thead>
<tr>
<th>PD Type</th>
<th>PD Description</th>
<th>PD Resolution</th>
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</thead>
<tbody>
<tr>
<td>STUDY ASSESSMENTS: Other</td>
<td>The participant's Week 16 visit was completed 1 day out of Window.</td>
<td>Research staff will continue to attempt to have participant's complete their weekly visits as scheduled within their visit window.</td>
</tr>
<tr>
<td>STUDY ASSESSMENTS: Other</td>
<td>Participant week 3 visit was completed 3 days outside of the visit window due to participant needing to reschedule.</td>
<td>Encourage participants to complete visits on time, have reminder calls</td>
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</tbody>
</table>
Advantages:

- Real time attention to PDs
- Group discussion/consensus
- Immediate training reduces similar issues from reoccurring but if it's protocol wide then protocol needs amendment (e.g., tight windows)
- This is a metric for site performance- helps identify a need for retraining
Questions, comments? Contact...

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Thank you!