Strategies to Collaboratively Manage Protocol Deviations in Multi-site Clinical Trials- **Overview of Original Process**

Mitra Lewis, MS

Principal Clinical Study Manager at Emmes Company

Emmes

Celebrating 20 Years of
Research-Practice Partnerships

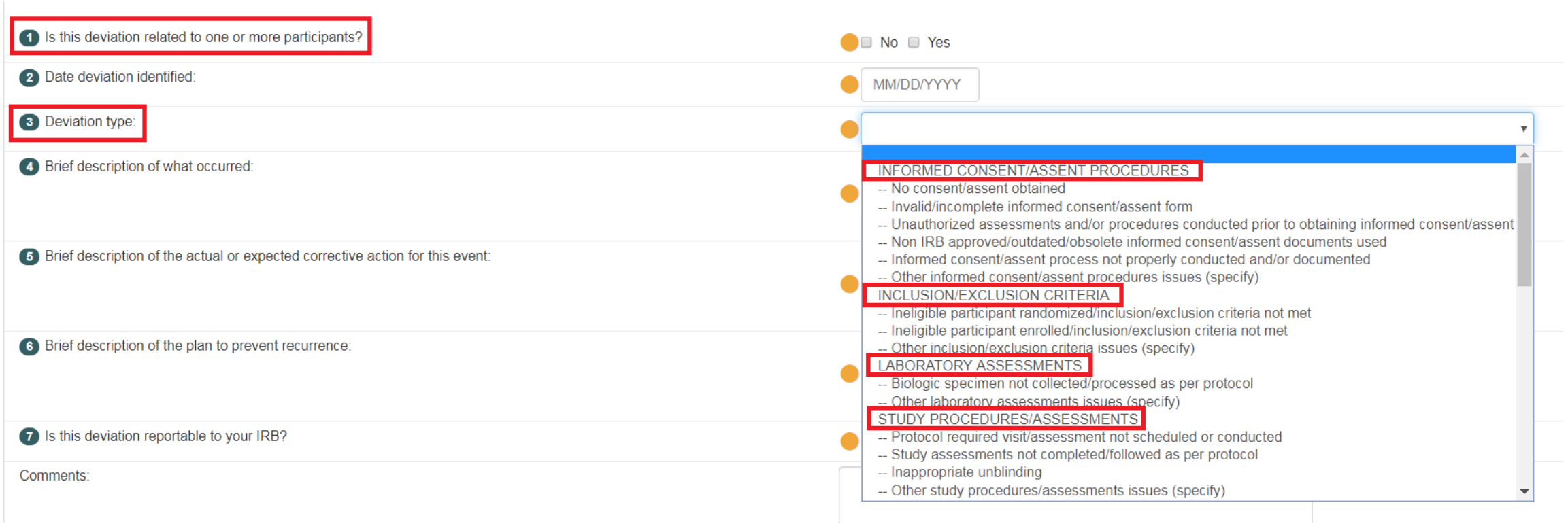
Reporting Protocol Deviations in EDC

- **Protocol Deviation and Protocol Deviation Review Forms**
  - document the occurrence of protocol deviations
  - must be completed any time a protocol deviation is discovered
- **Protocol Deviation Form**
  - captures detailed information about the protocol deviation
- **Protocol Deviation Review Form**
  - details the review of the protocol deviation by CCC staff

Emmes

Celebrating 20 Years of
Research-Practice Partnerships

Protocol Deviation eCRF Completed and Submitted by Site Staff



Emmes

Celebrating 20 Years of Research-Practice Partnerships

Major Protocol Deviations

No consent/assent obtained
Unauthorized assessments and/or procedures conducted prior to obtaining informed consent/assent
Ineligible participant randomized/inclusion/exclusion criteria not met
Ineligible participant enrolled/inclusion/exclusion criteria not met
Inappropriate unblinding
SAE not reported
Safety assessment (e.g., labs, ECG, clinical referral to care) not conducted per protocol
Stratification error
Medication dispensed to ineligible participant
Medication dispensed to incorrect participant
Medication dosing errors (protocol specified dose not dispensed)
Participant use of protocol prohibited medication
Breach of Confidentiality

Protocol Deviation Review eCRF

Completed by Protocol Specialist:	
1 What section of the protocol does this deviation refer to?	
2 Does the report of this deviation require site staff retraining?	No Yes
If "Yes", specify plan for retraining:	
3 Date deviation was discussed with Lead Investigative Team:	MM/DD/YYYY
4 Deviation is categorized as:	Major Minor
5 Deviation assessment by Protocol Specialist complete:	No Yes
Protocol Specialist reviewer:	(initials)
Protocol Specialist comments:	

Emmes

Celebrating 20 Years of Research-Practice Partnerships

Protocol Deviation Review eCRF contd.

Completed by Protocol Monitor:	
6 Deviation requires review by Protocol Monitor:	● No ○ Yes
7 Corrective action for this deviation was completed and documented on-site as described:	○ No ○ Yes
If "No", specify reason:	
8 Deviation was reported to the IRB as required:	○ No ○ Yes
If "No", specify reason:	
9 Preventive action plan related to this event was completed and documented on-site as described:	○ No ○ Yes
10 Review by Protocol Monitor is complete:	○ No ○ Yes
Protocol Monitor reviewer:	(initials)
Protocol Monitor comments:	

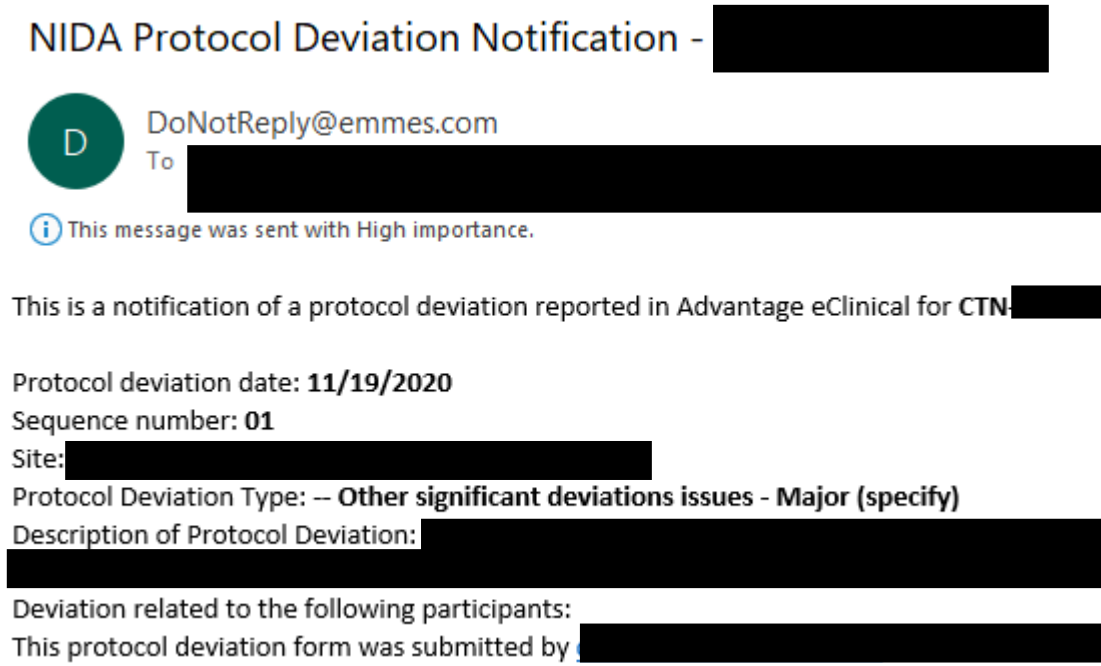
Emmes

Celebrating 20 Years of
Research-Practice Partnerships

NATIONAL DRUG ABUSE TREATMENT CLINICAL TRIALS NETWORK

Automated Emails and Listings

- Immediate email when protocol deviation is entered in EDC
  - Sent to members of Clinical Coordinating Center, Data and Statistics Center, and Investigative Team
- Weekly email with links to listing
  - Newly reported (last 7 days) protocol deviations
  - Cumulative list of protocol deviations



NIDA Protocol Deviation Notification - [redacted]

D DoNotReply@emmes.com
To [redacted]

This message was sent with High importance.

This is a notification of a protocol deviation reported in Advantage eClinical for **CTN-**[redacted]

Protocol deviation date: **11/19/2020**
Sequence number: **01**
Site: [redacted]
Protocol Deviation Type: -- **Other significant deviations issues - Major (specify)**
Description of Protocol Deviation: [redacted]
Deviation related to the following participants:
This protocol deviation form was submitted by [redacted]

Emmes

Celebrating 20 Years of
Research-Practice Partnerships

Processing Events as Confirmed Protocol Deviations

Event Occurs

If Clearly Identified as a Protocol Deviation

- Site reports protocol deviation in EDC
- CCC reviews protocol deviation in EDC
- CCC reviews PD with the Investigative Team
- CCC completes review of protocol deviation in EDC

Processing Events as Potential Protocol Deviations

Event Occurs

If Unclear Whether Event is a Protocol Deviation

- CCC leads discussion with the Investigative Team
- CCC communicates decision to the site(s)
- If determined to be a protocol deviation, site reports in EDC
- CCC reviews PD in eClinical
- CCC reviews PD with the Investigative Team

Emmes

Celebrating 20 Years of
Research-Practice Partnerships

Cleaning and Reporting Protocol Deviations

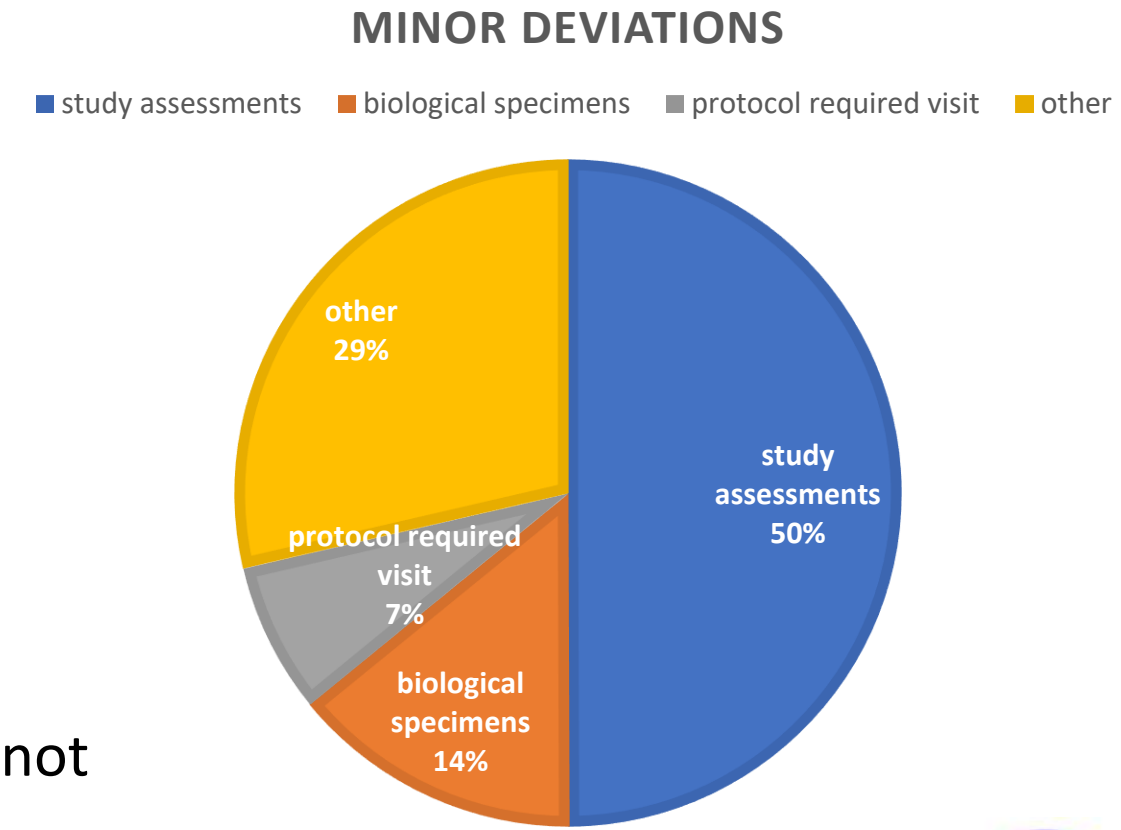
Date of Protocol Deviation and Protocol Deviation number	Deviation Type	Participant ID (located within the PDV form)	Deviation Description	Resolution Corrective Action	Action Required by the Site
2019-04-21 1st Protocol Deviation of the day	STUDY MEDICATION MANAGEMENT: Medication dispensed to incorrect participant	02340000680012	Due to a staff outage I was by myself. I was running a study visit when another subject came in. This subject was running late and had not called to let me know. The subject was in a big hurry to leave. I was in a hurry and mistakenly selected a card from an incorrect medication box. I gave the incorrect card to the MC who then dispensed to the participant.		1. Provide a revised description of the deviation only. A) Do **not** include why the deviation occurred. B) Include the participant ID number (0012) of the card that was inadvertently dispensed. 2. Complete the resolution corrective action.

Emmes

Celebrating 20 Years of
Research-Practice Partnerships

Protocol Deviations of a Completed Trial

- ~1,000 protocol deviations
  - 5% major deviations
  - 95% minor deviations
- Minor deviations
  - 50% study assessments not completed/followed as per protocol
  - 14% biologic specimen not collected/processed as per protocol
  - 7% protocol required visit/assessment not scheduled or conducted



Emmes

Celebrating 20 Years of Research-Practice Partnerships

Purpose

- report and document deviations from the protocol
- clarify results during statistical analyses
- present to regulatory bodies (e.g., DSMB) for monitoring of safety/integrity of the study
- inform potential protocol amendments
- identify issues that warrant re-training/clarification/process updates

Perception

- punishing/blaming site staff
- poorly conducted study
- poorly managed study

Emmes

Celebrating 20 Years of
Research-Practice Partnerships