Welcome to the Meeting

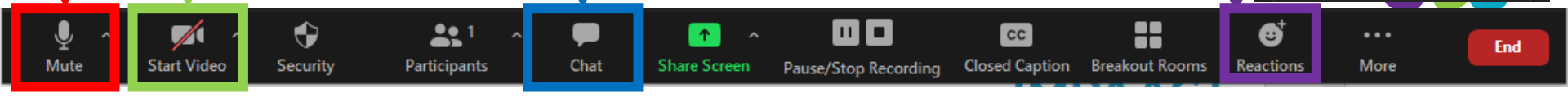
The session will begin shortly. While you wait, follow these steps to set up your Zoom and locate the interactive tools we will use today.

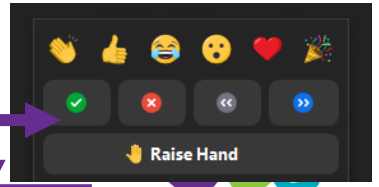
3. Open the chat panel – say “hi” and type your name and site

1. Please mute your line

2. You may use video if you would like

4. The ‘reactions’ feature can be used to raise your hand or provide other feedback





When lines are muted, please type questions into the chat box.

Reminder: document this training!

Site IoRs are responsible for ensuring that study staff are adequately trained to serve their designated site- and study-specific functions.

Per the **DAIDS Site Clinical Operations and Research Essentials (SCORE)** Manual, all sites must establish and follow a standard operating procedure for personnel training and certification documentation.

IoRs are responsible for documenting that each study staff member completed study-specific training corresponding to his or her designated roles and responsibilities. This documentation must be on file at the site and available for inspection/monitoring at any time.

Reminder: document this training!

- Ops Center will provide an email documenting that the training was conducted.
- **Sites are responsible for documenting individual staff attendance.**
- An example sign-in log is shown here, but any format consistent with site SOPs may be used.

IMPAACT Processes for Reportable Protocol Deviations

Wednesday, 23 August 2023

Training Led by: IMPAACT Operations Center Staff
Training Content: see attached slides
Training Participants: as recorded below

Printed Name	Signature	Role

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IMPAACT Network Reportable Protocol Deviations

IMPAACT Operations Center and DMC Deviation Groups:
O'Landa Johnson, Nicole Macagna, and Katie McCarthy, FHI 360
Mattie Bartlett, Marlene Cooper, Carrie Fry, Chelsea Krotje, and Stephanie Popson, Frontier Science

August 2023

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Overview

- This presentation provides a refresher on the IMPAACT reportable protocol deviation (PD) policies and procedures, with a focus on recent updates to the Cross-Network Protocol Deviation Reporting Guide.

Topics of Discussion

- Key Resources
- Definitions
- Processes and Considerations for Reportable Protocol Deviations

Key Resources

IMPAACT Manual of Procedures (MOP)

- Section 12, Study Implementation, Subsection 12.5 – Protocol Deviations
  - www.impaactnetwork.org/resources/manual-procedures
  - IMPAACT policies and guidelines pertaining to documentation and reporting of PDs
  - Procedures and options for reporting reportable PDs
  - Definitions and classifications of PDs

Operations Center Protocol Deviations Team

- IMPAACT.Deviation@fstrf.org

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Key Resources

IMPAACT Website

- www.impaactnetwork.org/resources/manual-procedures
- Guidance documents and training materials related to PDs

Cross-Network Protocol Deviation Reporting Guide

- Link to be available on HANC website
- Definitions and classifications of PDs
- Procedures for reporting reportable PDs via eCRF

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HIV/AIDS Network Coordination (HANC) Cross-Network Protocol Deviation Reporting Guide

- Guide is to be utilized by the NIAID HIV/AIDS Clinical Trials Networks
- Standardizes definitions and classifications for protocol deviations
- Provides definitions and examples of protocol deviations
- Describes the process for reporting reportable deviations via the Cross-Network Protocol Deviation eCRF

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Updates to Cross-Network Protocol Deviation Reporting Guide

- Sites must report PDs within 5 days of awareness (previously 10 days)
- Updates have been made to some of the categories and examples of reportable PDs
- Sites are no longer required to document corrective and preventive actions (CAPAs) in PD reporting forms; sites will be asked to submit CAPA documentation upon request by Network reviewers and/or study teams

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Protocol Deviations

Protocol Deviation: any change, divergence, or departure from the study design or procedures defined in the DAIDS approved, Good Clinical Practice (GCP) compliant protocol (ICH E3)

Protocol deviations may include:

- Administrative inconsistencies or minor study implementation errors (e.g., visit or procedure performed outside of window)
- Departure from specified treatment, examination, data collection, or reporting procedures
- Violation of inclusion/exclusion criteria

Protocol deviations may be incurred by:

- Study participants, protocol team members, investigators of record (IoRs), sub-investigators, coordinators, study medical staff, supervisory or oversight staff, etc.

Protocol Deviations

- Deviations may or may not render a participant ineligible for study participation and may be considered significant or serious when they increase potential risk to participants or affect the integrity of study data.

- An isolated deviation may not be significant by itself, but significance may increase with numerous deviations of the same nature.

Examples of Protocol Deviations

- Hair collection for study drug levels was missed in error for a participant who was off treatment/on study
- Infant's washout PK sampling was obtained within the specified window but it was not possible to perform a physical exam within the window
- Procedures required to be performed within 48 hours of birth were performed between 49 and 50 hours of birth

Examples of Protocol Deviations

- Visit non-compliance (for example, a study visit is conducted outside of the required timeframe or a procedure is missed) and there are no safety concerns
- Incorrect execution of the consent form (for example, participant did not date their signature)
- Participant declines to complete scheduled research activities

Types of Protocol Deviations

Reportable: a subset of protocol deviations that may significantly impact the completeness, accuracy, and/or reliability of key study data or that may significantly affect a participant's rights, safety, or well-being. Reportable PDs require additional reporting by the IoR or designee.

Reportable PDs are no longer categorized as major or critical

Not Reportable: any PD that does not meet the definition of a reportable PD.

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Participant Non-Compliance

- Participant non-compliance (e.g., missed visits, missed doses of study drug) is a protocol deviation but is not typically considered a reportable protocol deviation.

- Participant non-compliance should be documented and reported per usual site procedures and any applicable protocol requirements but should not be reported to the Network.

Examples of Reportable Protocol Deviations

- Enrollment of an ineligible participant
- Failure to obtain informed consent or assent from the participant, legal guardian, or other legally authorized representative prior to performing protocol-specified procedures
- Performing procedures not specified in the IRB/EC approved protocol and not otherwise clinically indicated for the participant

Examples of Reportable Protocol Deviations

- Knowingly reporting an inaccurate laboratory result
- Failure to follow protocol-specified procedures for participant safety monitoring, management, or reporting (including failure to report expedited adverse events within three reporting days)
- Breach of participant confidentiality

Protocol Deviations Procedures

- All protocol deviations must be recorded in the participant's research record and include:
  - A description of the deviation
  - Reasons why it occurred
- See the Source Documentation Requirements section of the DAIDS Site Clinical Operations and Research Essentials Manual (SCORE) for further guidance.
- Deviations must also be reported to site IRBs/ECs and other regulatory entities, following local policies and procedures.

Procedures for **Reportable** Protocol Deviations

- All reportable PDs must be reported by site investigators within **5 reporting days** of awareness

Reporting timeframe shortened from 10 days to 5 days

- Entered either via eCRF or into the Protocol Deviation Reporting System (PDRS) on the Frontier Science portal
- Once entered, a copy of the PD report and any supplemental documentation (e.g., IRB/EC correspondence, lab reports) should be emailed to IMPAACT.Deviation@fstrf.org

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Protocol Deviation Reporting System

- A help file is available on the Frontier Science Portal to assist users with entering reportable protocol deviations through the system:

https://www.frontierscience.org/apps/cfmx/apps/common/Portal/index.cfm?event=item.help.show

DEV10009: Protocol Deviation (Cross-Network) eCRF

Page: **DEV10009: Protocol Deviation (Cross-Network)**

INSTRUCTIONS:
- **This form should only be keyed for participants enrolled on study.**
- Refer to the network MOP or SOP for the definition of reportable protocol deviations.
- Report the range of dates when a protocol deviation occurred.

Date of site awareness: ...

Deviation start date: ...

Deviation stop date: ...

Has this deviation been reported or will it be reported to the IRB/EC? ○ Yes ○ No

Is this deviation related to a local, national, regional, or global disruptive event (e.g., COVID-19 pandemic, natural disaster, geopolitical conflict)? ○ Yes ○ No

Deviation category:

#	Indicate the category of the eligibility criteria not met	Protocol version to which the participant enrolled	Description of the criteria the participant did not meet
1	_	_	_

Add a new Log line Inactivate

Provide a description of the deviation [1900]:

Provide a brief summary of the deviation [200]:

Procedures for **Reportable** Protocol Deviations

- The Operations Center deviations team and/or study CRMs will contact the site with questions or to request clarifications.

- If the deviation is considered reportable:
  - The Operations Center will send the deviation report to Network Leadership and a subset of protocol team members.

Procedures for **Reportable** Protocol Deviations

If the Operations Center assesses the deviation as not reportable:

- The Operations Center will communicate this assessment to the site.
- The Operations Center will ask the site to reply with the site IoR's determination of reportability.
  - If deemed reportable, the PD will undergo Network distribution.
  - If deemed not reportable, the site will be instructed to remove the deviation report from the study database.

The Sponsor retains the final decision on whether a protocol deviation is considered reportable.

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eCRF vs. PDRS Reporting

- PDs that affect one participant should be reported via eCRF and PDs that affect more than one participant should be reported via the PDRS.
- PDs that occurred at the study or site level (i.e., those that do not involve specific participants) should be reported using the PDRS.
- Both systems feed information into the relevant study databases for monitoring and analysis purposes.
- Reportable deviations submitted through either system will be handled in a similar manner through the DMC and Operations Center for reporting to Network reviewers.

Sites should only submit a deviation through <u>one</u> of the mechanisms (not both)

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Key Reminders

- Individual missed visits or evaluations generally do not meet the IMPAACT Network definition of a reportable deviation.

- Trends of multiple missed visits or evaluations, that are due to reasons other than participant non-compliance, generally do meet the Network definition of a reportable deviation.
  - Reporting would likely be done through the PDRS.
  - Trends can be across the site or across the study.

A Note on Trends

What is considered a trend for reporting purposes? Would two or three missed evaluations be considered a trend?

- There is no specific definition of trend for reporting purposes. Sites and teams need to consider the impact of the missed evaluations on participant safety and data integrity.

Key Reminders

- A trend of multiple missed visits over the course of several weeks because of a site shutdown would generally be reportable.

- A trend of multiple missed laboratory evaluations over the course of several weeks because a site could only conduct virtual visits would generally be reportable.

Key Reminders

- An individual participant choosing not to come to the site due to potential COVID-19 risk would generally not be reportable.

- An individual missed visit because of operational disruption at a site (e.g., site was closed for a short time and visit could not be re-scheduled within the window) would generally not be reportable.


Quiz time

Reportable or Not?

1. In a PK study, a participant is reminded over the phone to switch her study drug to morning dosing beginning 3 days before her visit. She confirms her understanding. However, when she comes to the clinic for the PK visit, she reports that her last dose of study drug was last night.

Not reportable because the deviation is due to participant non-compliance

Reportable or Not?

2. During a monitoring visit, an informed consent form is identified as having an incorrect year in the date of signature.

Likely not reportable because it is an administrative error not otherwise associated with increased risk to the participant

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Reportable or Not?

3. During a monitoring visit, an informed consent form is identified as not signed by the participant.

Likely reportable because of the significance of the omission with respect to GCP compliance and potential risk to the participant

Reportable or Not?

4. Three participants did not have a screening HIV RNA assay performed within the time period specified in the study inclusion criteria.

Likely reportable because of the significance of the error with respect to eligibility, potential risks to the participants, and potential impacts on data integrity, and because this is a trend

Reportable or Not?

5. For a study in which the protocol-specified window for the Labor and Delivery (L/D) visit is 3 days after delivery, all participants at the site were scheduled for their L/D visit 5 days after delivery.

Likely reportable because of the significance of the error with respect to data integrity (and potential risk to the participants) and because this is a trend

Reportable or Not?

6. Hair collection for study drug levels was missed for one participant.

Likely not reportable because the deviation only involved one missed collection from one participant

THANKS!

Any questions?

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