WELCOME TO THE WEBINAR!

- The session will begin shortly
- Please mute your phone line to improve sound quality during the session
- Do not place your phone line on hold during the session
- **Remember to document this training**

REVIEW OF IMPAACT DEVIATION REPORTING PROCEDURES FOR SITE MONITORS

IMPAACT OPERATIONS CENTER
AND DATA MANAGEMENT CENTER

6 SEPTEMBER 2019

IMPAACT
International Maternal Pediatric
Adolescent AIDS Clinical Trials Network

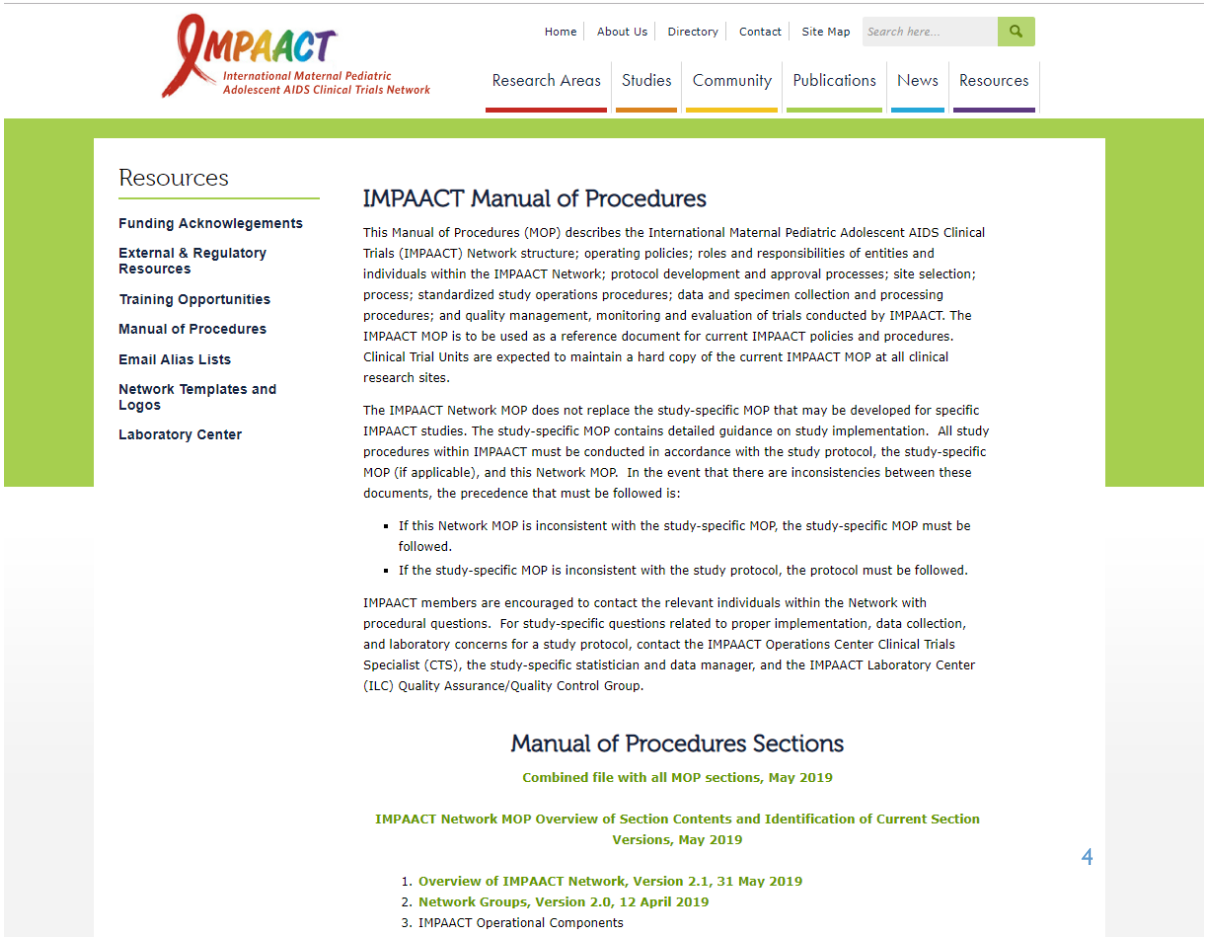
OVERVIEW OF TODAY'S DISCUSSION

- Key resources
- Definitions
- Protocol Deviations
- Reportable Protocol Deviations
  - Policy requirements for protocol deviations considered reportable by IMPAACT ("reportable deviations")
  - Procedures for reportable deviations
- Questions

KEY RESOURCES

IMPAACT Manual of Procedures, Section 12.4, Protocol Deviations

https://impaactnetwork.org/DocFiles/MOP/12_Implementation.pdf



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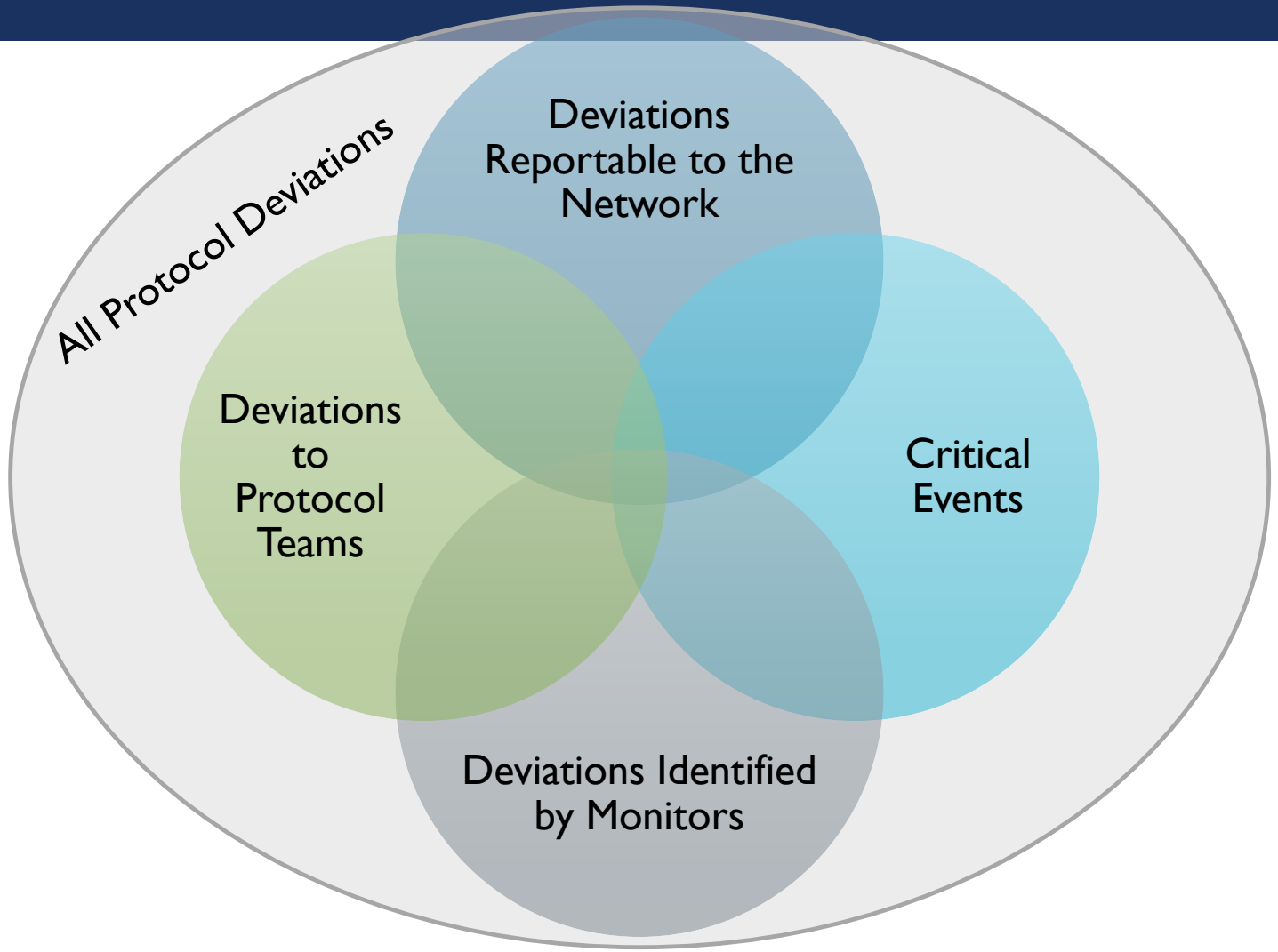
DEFINITIONS

Protocol deviation	Any departure from an IRB-approved protocol
<u>Reportable</u> protocol deviation	Deviations that require additional reporting by the IoR or designee as described in Section 12.4.3. Defined by IMPAACT as deviations that result in: • Significant increased risk to the study participants or others • Significant non-compliance with IRB-approved protocol requirements • Significant non-compliance with Good Clinical Practices or Good Clinical Laboratory Practices and all applicable regulations

DEVIATIONS, VIOLATIONS, CRITICAL EVENTS… OH MY!



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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

- Deviations may or may not render a participant ineligible 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

PROTOCOL DEVIATIONS

- All protocol deviations must be adequately documented in study records consistent with DAIDS SOPs for source and essential documentation, including
  - Description of the deviation
  - Reasons why it occurred
  - Corrective and preventive actions taken in response
- Deviations must also be reported to site IRBs/ECs and other regulatory entities, following their polices and procedures

https://www.niaid.nih.gov/research/daids-clinical-site-implementation-operations

CORRECTIVE ACTIONS

- Action taken to correct (when possible) or otherwise address a protocol deviation.
- Corrective actions are commonly specified in consultation with the relevant protocol team and/or IMPAACT leadership.

EXAMPLES OF CORRECTIVE ACTIONS

- Documenting the deviation
- Notifying the affected participant(s), protocol team, and/or IRB
- Re-consenting the participant(s)
- Completing missed procedures
- Repeating laboratory tests
- Completing additional participant monitoring or management procedures
- Destroying specimens collected in error

PREVENTIVE ACTIONS

- Action taken to prevent recurrence of a deviation.
- Preventive actions are commonly specified in consultation with the relevant protocol team and/or IMPAACT leadership.

EXAMPLES OF PREVENTIVE ACTIONS

- Discussing the deviation with relevant study staff, refresher training of study staff
- Reviewing and/or revising SOPs or other study implementation materials
- Developing new study implementation materials
- Implementing additional communication, QC/QA, or oversight/supervisory procedures
- Changing day-to-day workflow
- Changing general participant management or laboratory procedures

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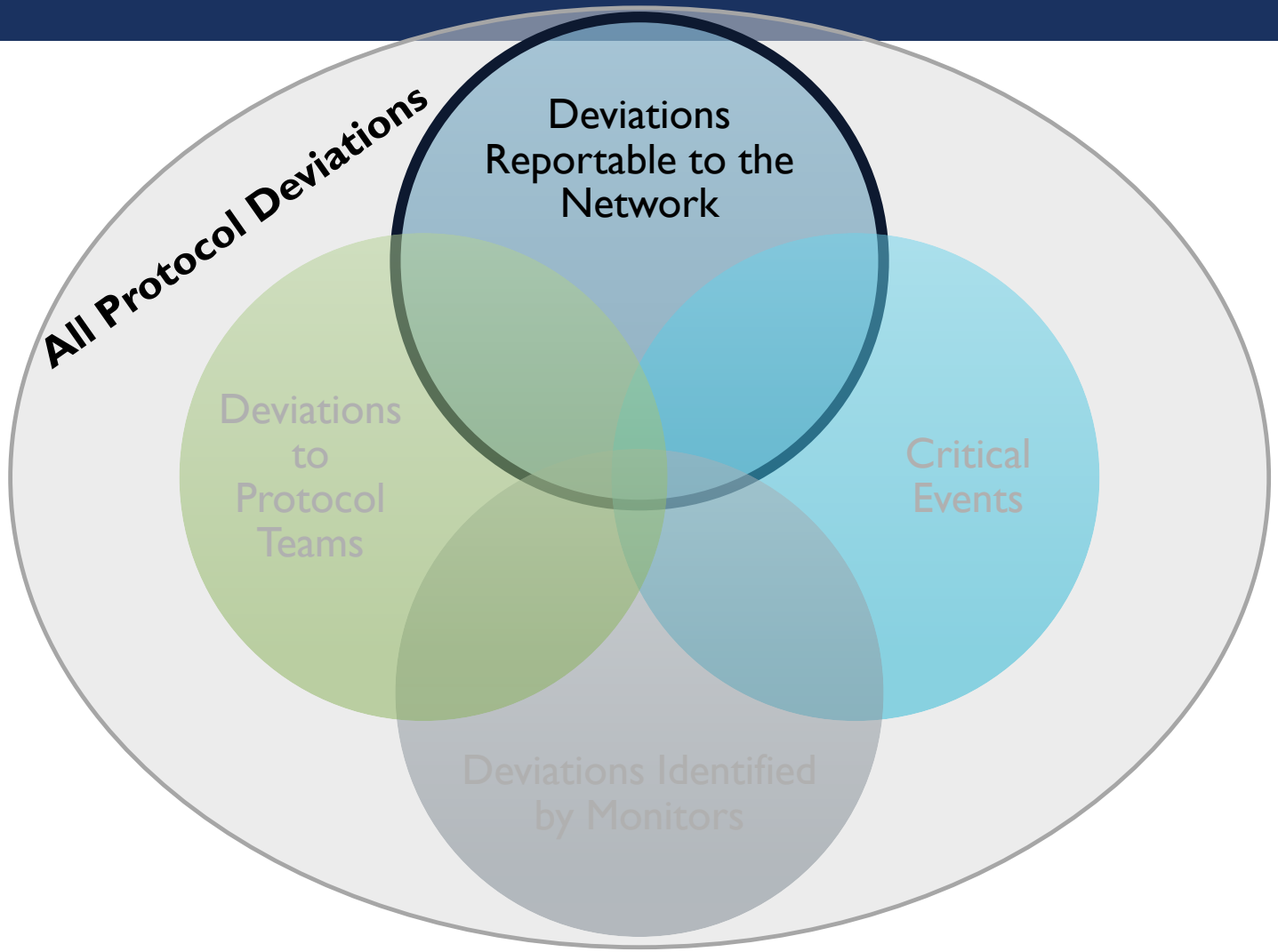

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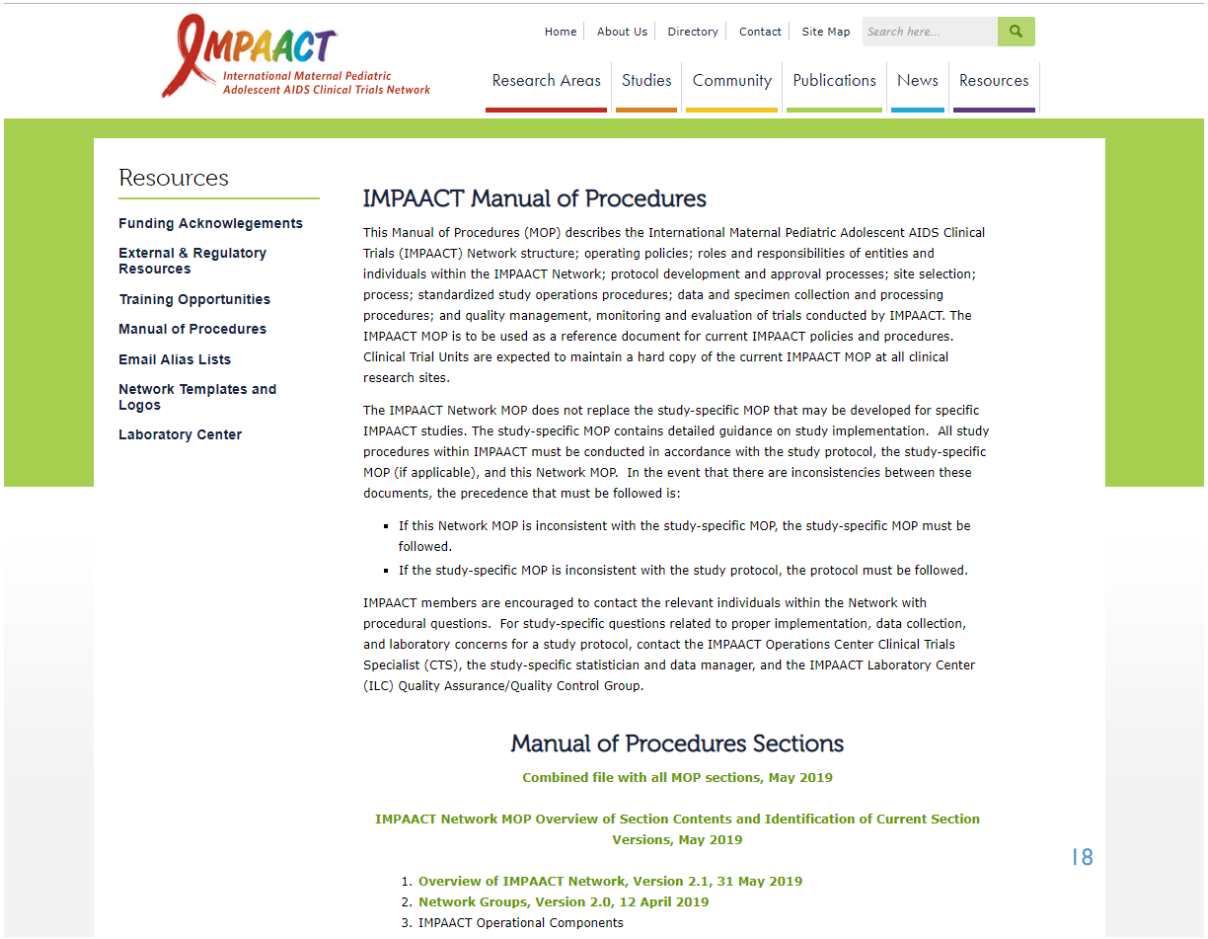

REPORTABLE PROTOCOL DEVIATIONS

Protocol deviations are reportable to the IMPAACT Network if they result in

- Significant increased risk to participants or others
- Significant non-compliance with IRB-approved protocol requirements
- Significant non-compliance with GCP or GCLP and all applicable regulations

REPORTABLE PROTOCOL DEVIATIONS: PARTICIPANT NON-COMPLIANCE

- Participant non-compliance (e.g., participant misses study visits or does not take study drug) is considered a protocol deviation but is not 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

QUESTIONS?
OR NOT SURE ABOUT REPORTABILITY?

If a site has questions about a deviation, they can email the protocol Clinical Trials Specialist or the Deviation Group: IMPAACT.deviation@fstrf.org

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SITES SHOULD REPORT ANY REPORTABLE PROTOCOL DEVIATIONS

A. Within 10 working days of site awareness
B. Within 3 working days of site awareness
C. As soon as all of the information is known

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IF A SITE IOR DETERMINES A PREVIOUSLY REPORTED DEVIATION IS NOT REPORTABLE, WHAT STEPS SHOULD BE FOLLOWED?

A. Notify the IRB/EC, as appropriate, per their policies and procedures for reporting protocol deviations.

B. Remove or inactivate the case report form submitted to the IMPAACT Data Management Center.

C. Document the deviation in study records, including a description of the deviation, reasons why it occurred and corrective and prevention actions taken in response.

D. Discuss the deviation with the protocol team and protocol CTSs.

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D. Discuss the deviation with the protocol team and protocol CTSs.

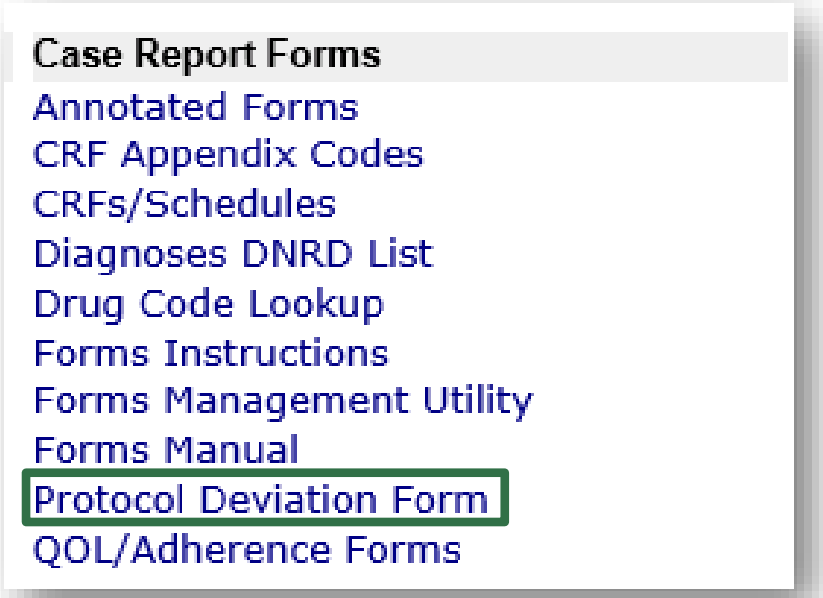
PROCEDURES FOR REPORTABLE PROTOCOL DEVIATIONS

- Report within 10 working days of site awareness
- Complete and enter a protocol deviation case report form (CRF) into the database **AND** email a copy of the completed CRF to IMPAACT.deviation@fstrf.org
- Email any additional supplemental documents (e.g., IRB correspondence) with the completed CRF
- See network MOP for exceptions for deviations involving >25 participants or not involving specific participants

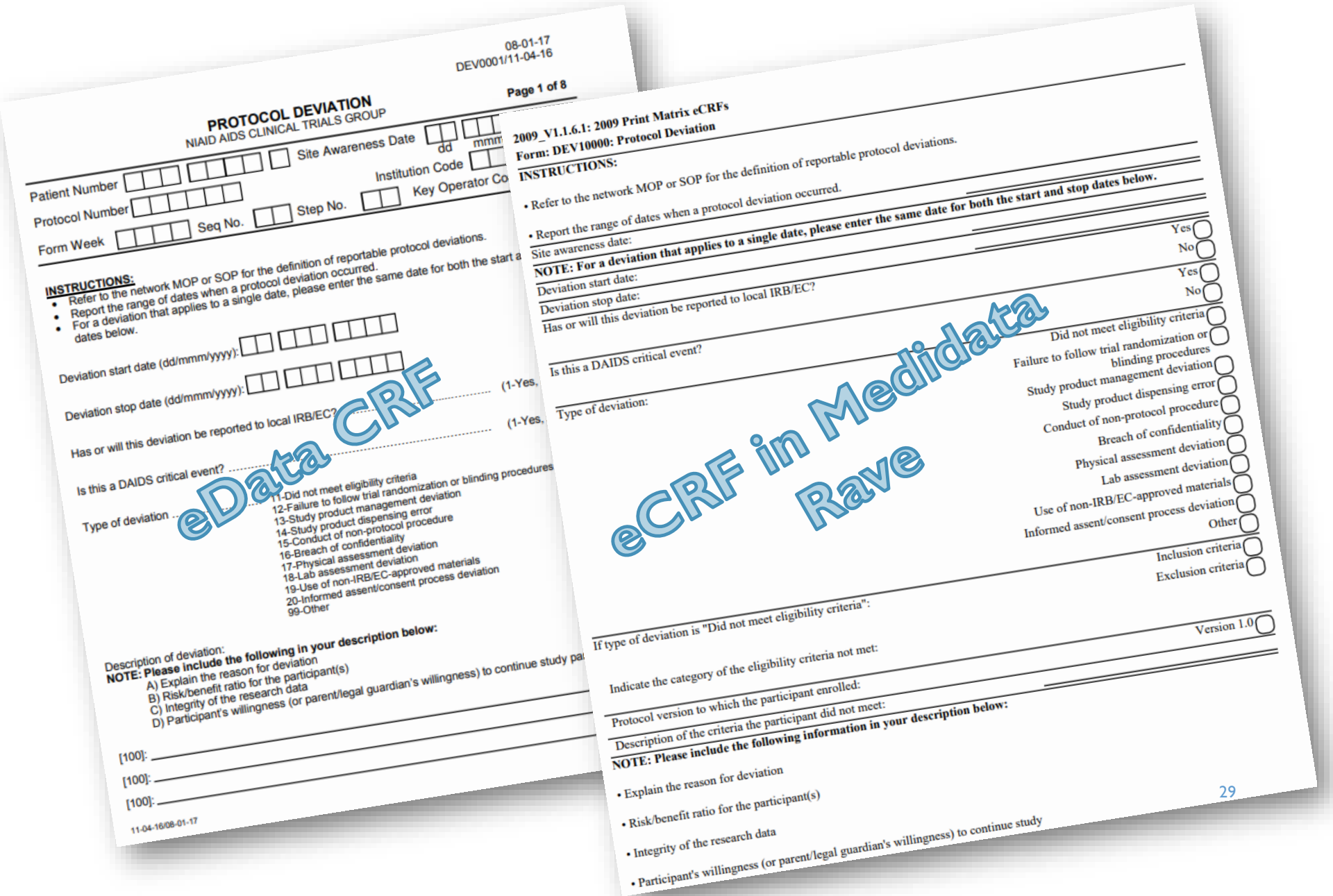
WHERE IS THE CRF LOCATED?

www.frontierscience.org

eData Studies:



Medidata Rave Studies:


PROTOCOL DEVIATION
NIAID AIDS CLINICAL TRIALS GROUP
08-01-17
DEV0001/11-04-16
Page 1 of 8
Patient Number
Site Awareness Date
Protocol Number
Institution Code
Form Week
Seq No.
Step No.
INSTRUCTIONS:
Refer to the network MOP or SOP for the definition of reportable protocol deviations.
Report the range of dates when a protocol deviation occurred.
For a deviation that applies to a single date, please enter the same date for both the start a
dates below.
Deviation start date (dd/mmm/yyyy):
Deviation stop date (dd/mmm/yyyy):
Has or will this deviation be reported to local IRB/EC?
Is this a DAIDS critical event?
Type of deviation
11-Did not meet eligibility criteria
12-Failure to follow trial randomization or blinding procedures
13-Study product management deviation
14-Study product dispensing error
15-Conduct of non-protocol procedure
16-Breach of confidentiality
17-Physical assessment deviation
18-Lab assessment deviation
19-Use of non-IRB/EC-approved materials
20-Informed assent/consent process deviation
99-Other
Description of deviation:
NOTE: Please include the following in your description below:
A) Explain the reason for deviation
B) Risk/benefit ratio for the participant(s)
C) Integrity of the research data
D) Participant's willingness (or parent/legal guardian's willingness) to continue study pa
[100]:
[100]:
[100]:
11-04-16/08-01-17
eData CRF
2009_V1.1.6.1: 2009 Print Matrix eCRFs
Form: DEV10000: Protocol Deviation
INSTRUCTIONS:
• Refer to the network MOP or SOP for the definition of reportable protocol deviations.
• Report the range of dates when a protocol deviation occurred.
Site awareness date:
NOTE: For a deviation that applies to a single date, please enter the same date for both the start and stop dates below.
Deviation start date:
Deviation stop date:
Has or will this deviation be reported to local IRB/EC?
Yes
No
Is this a DAIDS critical event?
Yes
No
Type of deviation:
Did not meet eligibility criteria
Failure to follow trial randomization or blinding procedures
Study product management deviation
Study product dispensing error
Conduct of non-protocol procedure
Breach of confidentiality
Physical assessment deviation
Lab assessment deviation
Use of non-IRB/EC-approved materials
Informed assent/consent process deviation
Other
If type of deviation is "Did not meet eligibility criteria":
Inclusion criteria
Exclusion criteria
Indicate the category of the eligibility criteria not met:
Protocol version to which the participant enrolled:
Version 1.0
Description of the criteria the participant did not meet:
NOTE: Please include the following information in your description below:
• Explain the reason for deviation
• Risk/benefit ratio for the participant(s)
• Integrity of the research data
• Participant's willingness (or parent/legal guardian's willingness) to continue study
eCRF in Medidata Rave
29

QUESTIONS TO BE ADDRESSED

- Site awareness date (i.e., the date any one at your site – clinic, lab, data – first became aware of the event)
- Deviation start and stop dates
- Has or will this deviation be reported to local IRB/EC? (Yes/No)
- Has or will this deviation be reported to DAIDS as a critical event? (Yes/No)

TYPE OF DEVIATION

- Did not meet eligibility criteria
- Failure to follow trial randomization or blinding procedures
- Study product management deviation
- Study product dispensing error
- Conduct of non-protocol procedure
- Breach of confidentiality
- Physical assessment deviation
- Lab assessment deviation
- Use of non-IRB/EC-approved materials
- Informed assent/consent process deviation
- Other

DESCRIPTION OF DEVIATION

- Explain the reason for deviation
- Risk/benefit ratio for the participant(s)
- Integrity of the research data
- Participant's willingness (or parent/legal guardian's willingness) to continue study participation

CORRECTIVE ACTIONS AND PREVENTIVE ACTIONS

- As discussed earlier!

GENERAL INSTRUCTIONS

- Sites should enter the form in eData or Medidata Rave, as applicable, AND
- Email PDF of completed CRF and supplemental materials to: IMPAACT.deviation@fstrf.org
- Ops and DMC communicate frequently regarding deviations reported:
  - Expectation that data reported to both Ops and DMC will match
  - If there are inconsistencies, they will be queried

CHANGING OR DELETING A FORM

eData

- Online Correct
- Delete Form 

Medidata Rave

- Change data and save
- Inactivate form 

QUESTIONS ON PROTOCOL DEVIATION FORMS

- Contact the Protocol Data Manager for questions on using eData or Medidata Rave to submit or modify a form
- Contact the protocol Clinical Trials Specialists or the Deviation Group regarding questions about what to report: IMPAACT.deviation@fstrf.org

PROCEDURES FOR REPORTABLE PROTOCOL DEVIATIONS

- Sites will receive a confirmation message within 24-48 hours of emailing
- If the deviation is reportable:
  - The deviation report will be sent by the Operations Center to Network Leadership
  - The Operations Center will follow-up with the site on any further clarifications and next steps

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
  - However, the site Investigator of Record (IoR) retains responsibility for final determination of reportability
  - The Operations Center will ask the site to reply with the site IoR's determination

AS A REMINDER…

- All protocol deviations must be adequately documented in study records consistent with DAIDS SOPs for source and essential documentation, including
  - Description of the deviation
  - Reasons why it occurred
  - Corrective and preventive actions taken in response

- Deviations must also be reported to site IRBs/ECs and other regulatory entities, following their polices and procedures

QUESTIONS?