

# Safety Information and Unanticipated Problems Reporting

Quorum  
REVIEW IRB



# Objectives

This presentation will address the following issues:

- What events must be promptly reported to the Quorum Review Institutional Review Board (IRB/REB).
- When and how such events must be reported.
- Why it is important to promptly report certain reports to the Board.
- How to report serious events, major protocol deviations, and other unanticipated problems to the IRB/REB.

# Investigators confront a variety of events that may be reportable to the sponsor of the research or the IRB/REB

Unrelated adverse events

Major protocol deviations

Expected adverse events



Minor protocol deviations

Minor adverse events

New safety information

Significant adverse events

Unanticipated Problems

# Sponsors and IRB/REBs have different regulatory reporting requirements

## Sponsor

- Regulations require sponsors to monitor all adverse events (AEs) experienced by a study's participants.

## IRB/REB

- Regulations require an IRB/REB to develop procedures to ensure prompt reporting of “unanticipated problems involving risk to human subjects or others.”

# Sponsors monitor all adverse events experienced by a study's participants

- Sponsors monitor minor, serious, expected, unexpected, related and unrelated AEs.
- Sponsor perform data analysis and trending for the study
- Sometimes sponsors delegate data monitoring to a separate entity, such as a data safety monitoring board (“DSMB”).
- Sponsors must report their findings at least annually to the FDA

# Investigator reporting requirements to sponsors and IRB/REBs are different

## Investigator

- Investigators generally must report ***all adverse events*** to the sponsor of the clinical trial.
- The investigator's reporting requirements are set forth in regulation and the protocol for the study.

## IRB/REB

- Investigators must report ***all unanticipated problems involving risk*** to participants or others to the IRB/REB.

## “Unanticipated problem” is not defined by regulation

- The regulations do not provide a definition for “unanticipated problems involving risk to human subjects or others.”
- IRB/REBs must establish their own definition and procedures for investigators to report unanticipated problems

# Quorum's definition of an unanticipated problem

- An unanticipated problem is an event that adversely affects:
  - the risk/benefit ratio of the study;
  - the rights, safety or welfare of the participants; or
  - the integrity of the study
- “Unanticipated” is defined as:
  - not identified in nature, severity, or frequency in the relevant safety document(s) for the study product or is not identified as a possible risk in the study protocol or the informed consent form for the study.



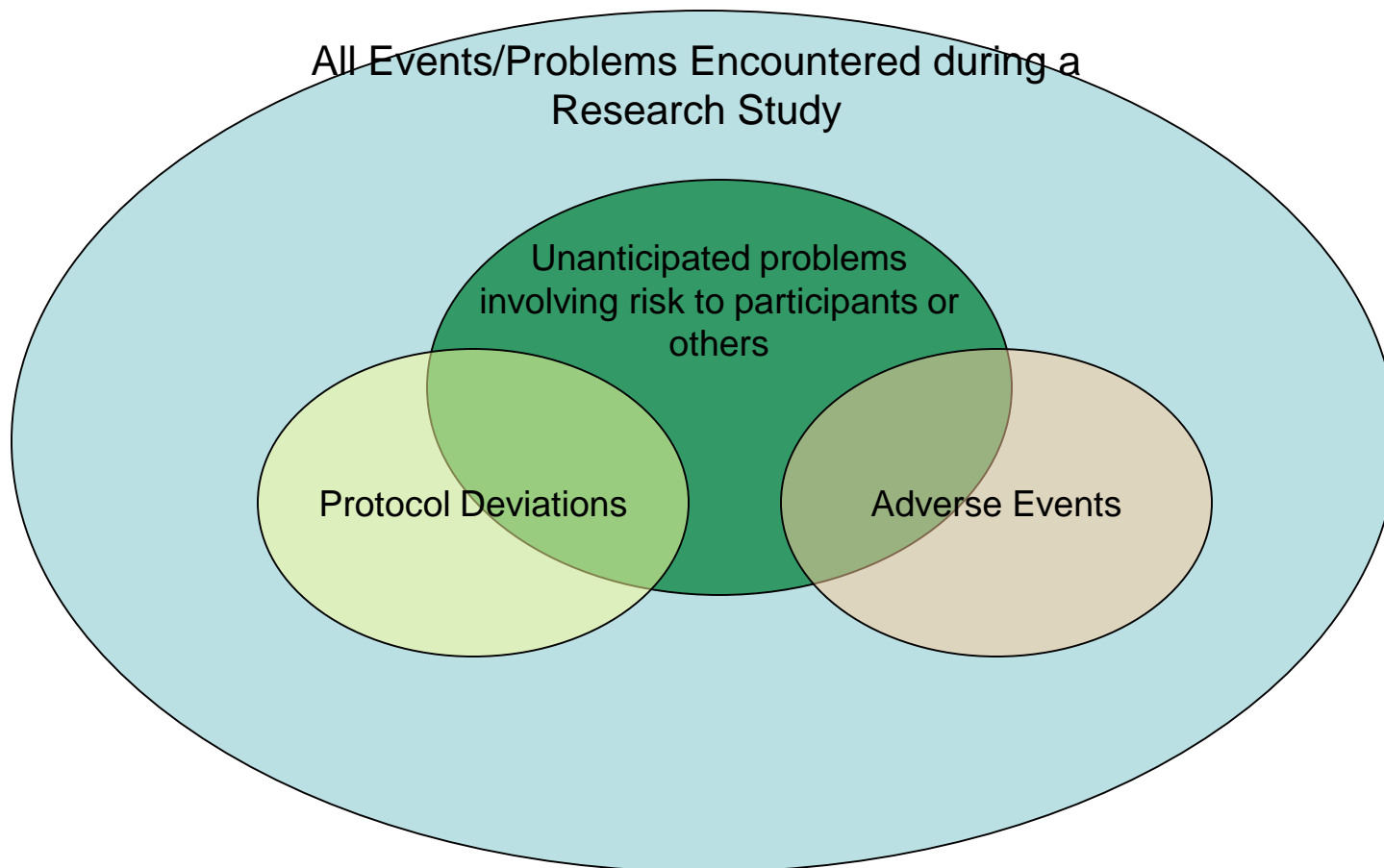
## Prompt reporting of unanticipated problems allows the IRB/REB to decide whether:

- The risk/benefit ratio of the study is still acceptable given the new information
- Modifications should be made to the study to minimize risk to participants
- Participants should be informed of new information, potential risks, or other findings
- The study should be suspended or terminated

## Quorum's policy regarding reportable events

- Quorum's position is that only unanticipated problems involving risk to subjects or others are reportable events that must be reported promptly to the IRB/REB.
- A reportable event must be reported ***within 10 business days*** of the investigator becoming aware of the event.
- Reportable events must be reported using Quorum's report forms.

# Report only unanticipated problems involving risk to participants or others



## What events to report

- Serious Adverse Events
- Major Protocol Deviations/Violations
- Other reportable events as defined by Quorum

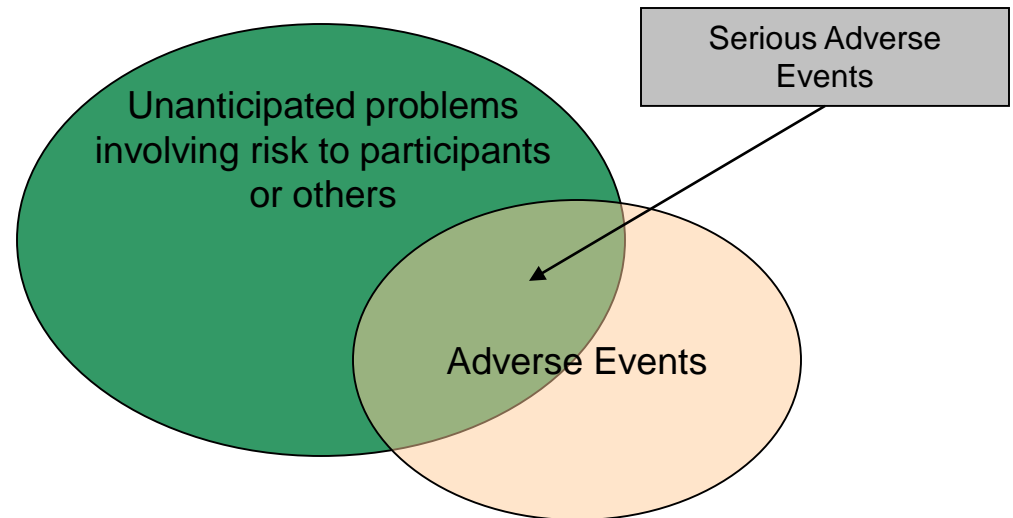
## What events to report...a closer look

- ***Serious Adverse Events***
- Major Protocol Deviations/Violations
- Other reportable events as defined by Quorum

# Quorum's Definition of a Serious Adverse Event (SAE)

A Serious Adverse Event\* (SAE) is an adverse event that, in the investigator's judgment is:

- Serious,
- Unanticipated, and
- At least possibly related to study procedures or the study drug product



\*Quorum's definition of an SAE is not the same as the definition used by sponsors and within the clinical research industry. IND safety reports, CIOMS reports, and MedWatch reports do not automatically meet Quorum's reporting requirements for an SAE. Only those that reveal an unanticipated problem involving risk to participants or others should be reported.

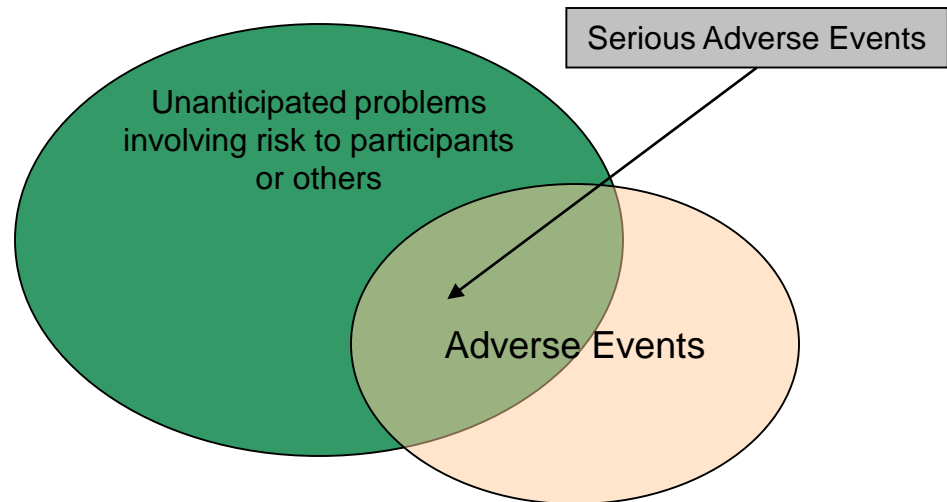
# What makes an SAE serious?

In the investigator's judgment it...

- Results in death
- Is life threatening (places the participant at immediate risk of death)
- Results in persistent or significant disability/incapacity (a substantial disruption of the participant's ability to conduct normal life functions)
- Results in, or prolongs inpatient hospitalization
- Is a congenital anomaly/birth defect, or
- Jeopardizes the participant or requires intervention to prevent one of the other outcomes listed here

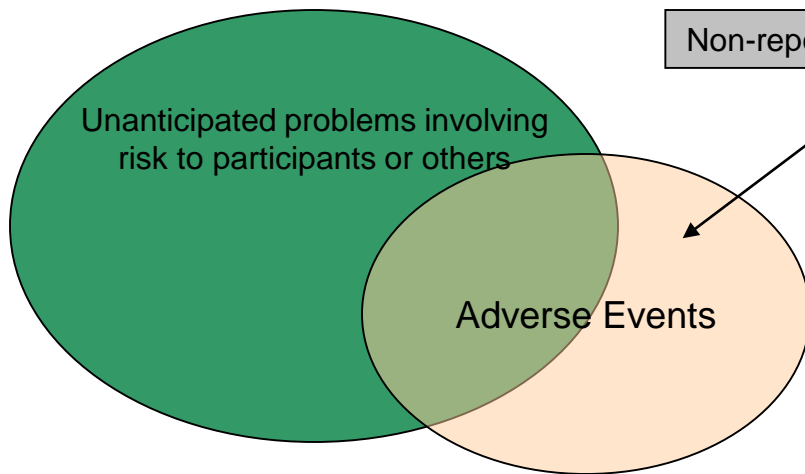
# Quorum's policy on reporting SAEs to the IRB / REB

- An investigator should report to the IRB / REB all serious adverse events that occur at his or her site.





# Investigators do not need to report minor, expected, or unrelated adverse events to the IRB/REB



Non-reportable Adverse Events

Examples of adverse events not considered reportable:

- A minor headache, even if probably caused by the study drug
- A worsening of the underlying disease condition, if such worsening was expected
- A MedWatch report that, in the PI's judgment, reports a risk that is probably not related to the PI's study

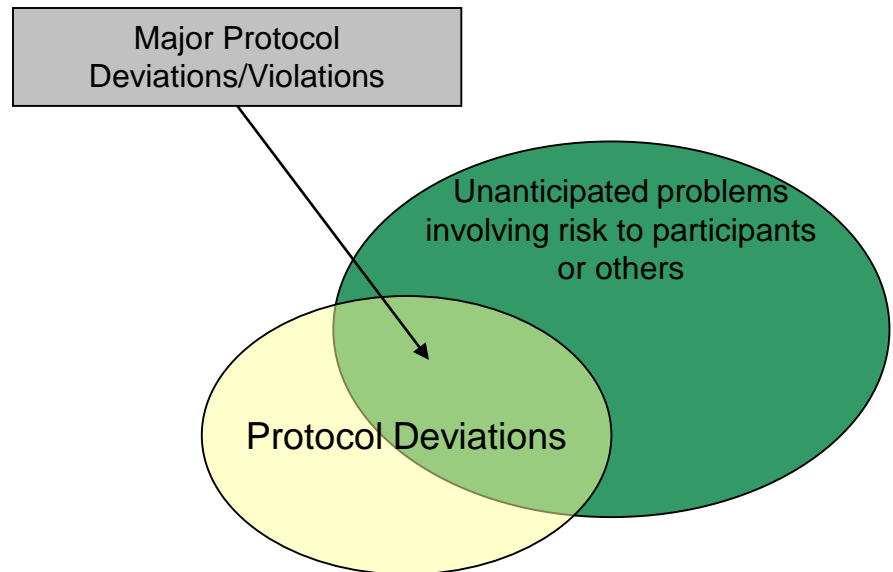
## What events to report...a closer look

- Serious Adverse Events
- ***Major Protocol Deviations/Violations***
- Other reportable events as defined by Quorum

# Quorum's Definition of a Major Protocol Deviation/Violation

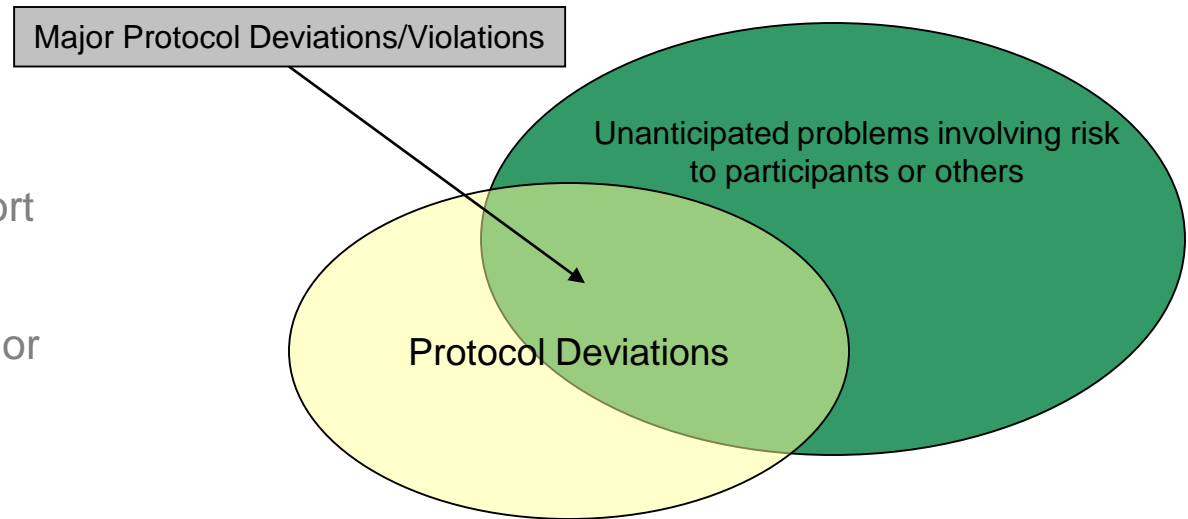
A Major Protocol Deviation/Violation, is a deviation or violation that adversely affects:

- risk/benefit ratio of the study;
- the safety, rights or welfare of participants or others; or
- the integrity of the study.



# Quorum's policy on reporting Major Protocol Deviations

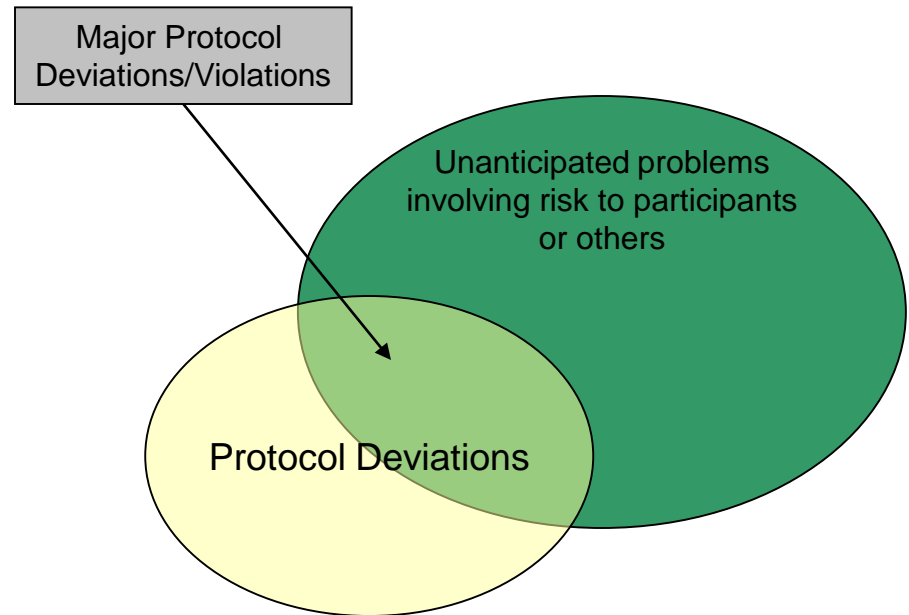
An investigator should report to the IRB/REB all Major Protocol Deviations/ Violations that occur at his or her site.



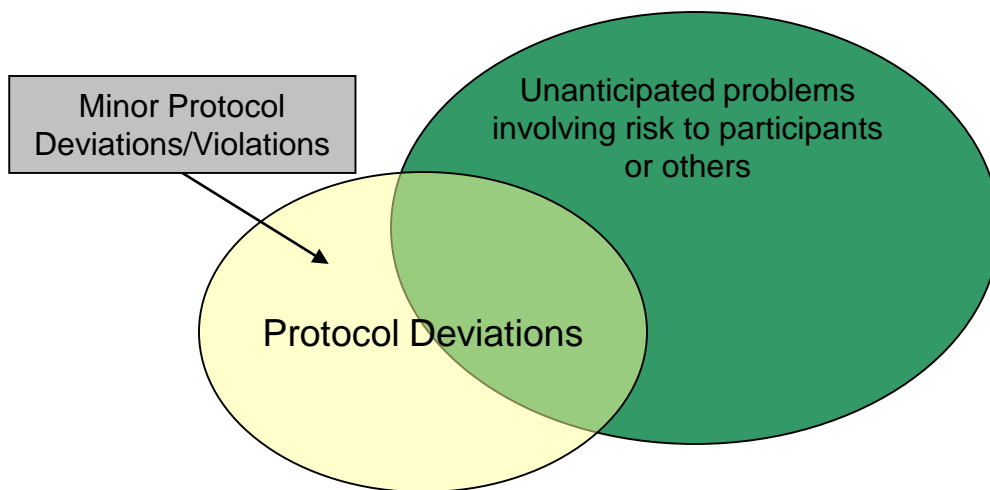
# Report only Major Protocol Deviations/Violations to the IRB/REB

Examples of Major Protocol Deviations/Violations:

- Failure to obtain informed consent
- Study procedures initiated before informed consent
- Omitting study procedure(s) required by approved protocol
- Drug dispensing/dosing error
- Failure to securely control the study product
- Deviation necessary to eliminate an apparent immediate hazard to a participant



# Don't report minor protocol deviations/violations to the IRB/REB



Examples of possible minor protocol deviations/violations:

- Study visit(s) or study procedure(s) conducted out of timeframe
- Failure to initial every page of a consent form
- Participant failure to return study diaries
- Other protocol deviations/violations that only affect logistical or administrative aspects of the study

## What events to report...a closer look

- Serious adverse events
- Major protocol deviations
- ***Other reportable events as defined by Quorum***

# Additional reportable events

- Adverse Audit or Enforcement Action(s)
  - Adverse audit results from a sponsor audit
  - FDA Form 483 or Warning Letter
  - Suspension, restriction, reprimand, etc. regarding a medical license
- Recalls / Withdrawals / Clinical Holds
  - Early Study termination
  - Regulatory Agency or Sponsor marketing withdrawal
  - FDA partial or complete clinical hold
  - FDA Public Health Advisory
- Participants complaints regarding an alleged breach of the rights, safety, or welfare of the participants or others, or integrity of the study.
- Reports, publications, or interim results or findings
- Incarceration of a participant
- Breach of confidentiality (e.g., loss of study records, breach of a secured database, disclosure of PHI not covered by HIPAA authorization)
- Research personnel misconduct
- New or updated product information safety information (e.g., revised Investigator Brochure, device manual, or product label/package insert)
- Data Safety Monitoring Board report



# Must an investigator report other events to the IRB/REB?

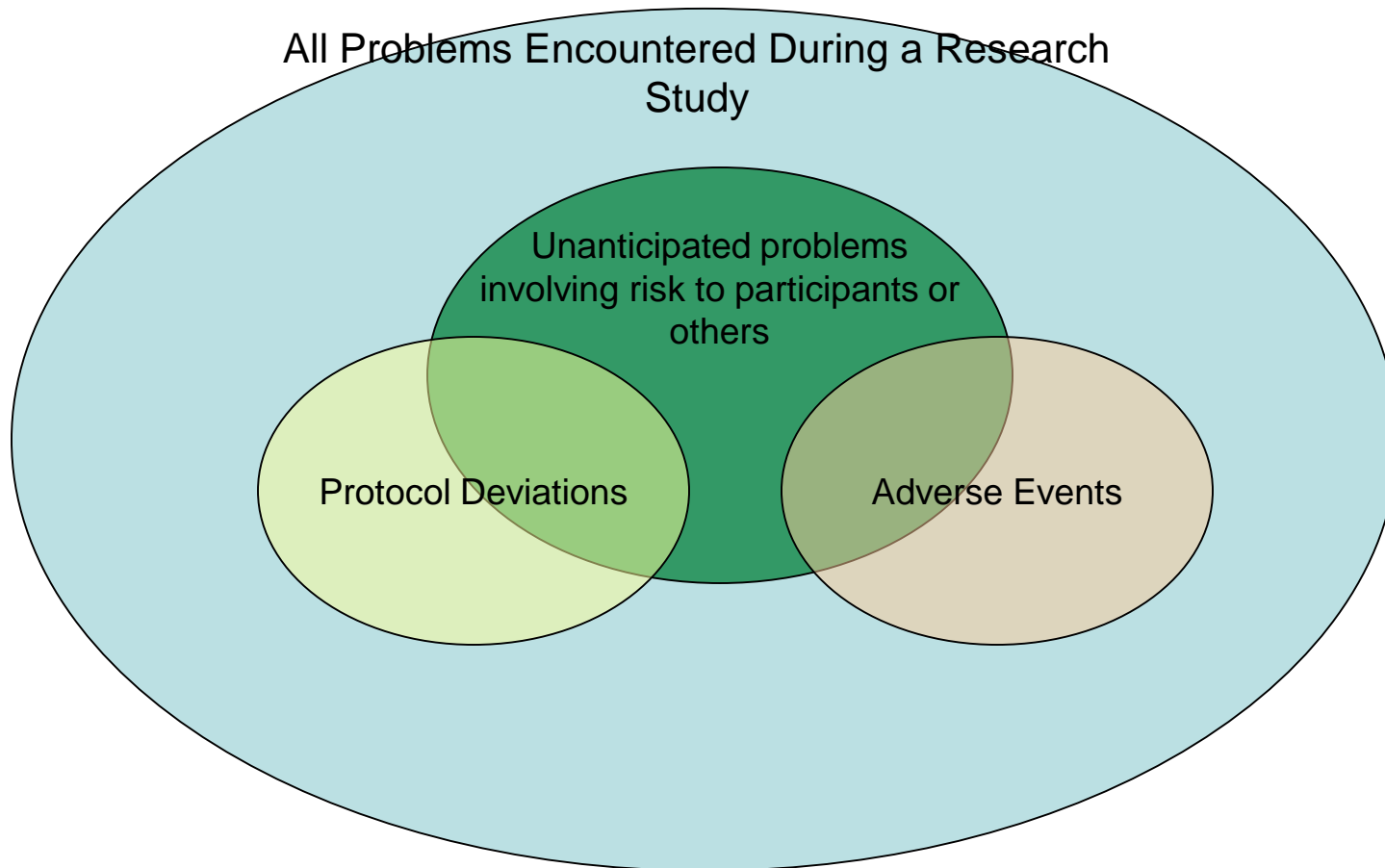
- An investigator should maintain records (such as logs or line listings) of all adverse events, protocol deviations, etc., according to instructions from the sponsor or site monitor
- At the time of periodic site review, the investigator should report to the IRB/REB whether the investigator believes the study or consent form should be modified in light of these events
- Do not submit logs or line listings of non-reportable adverse events, minor protocol deviations/violations, etc., to the IRB/REB.

## What if the Sponsor instructs investigators to submit all AEs to the IRB/REB?

- If Quorum receives a report about an event that is not reportable under our policies, Quorum will generally issue an acknowledgment of receipt to the site with a reminder that Quorum does not require reporting of such events.

Review:

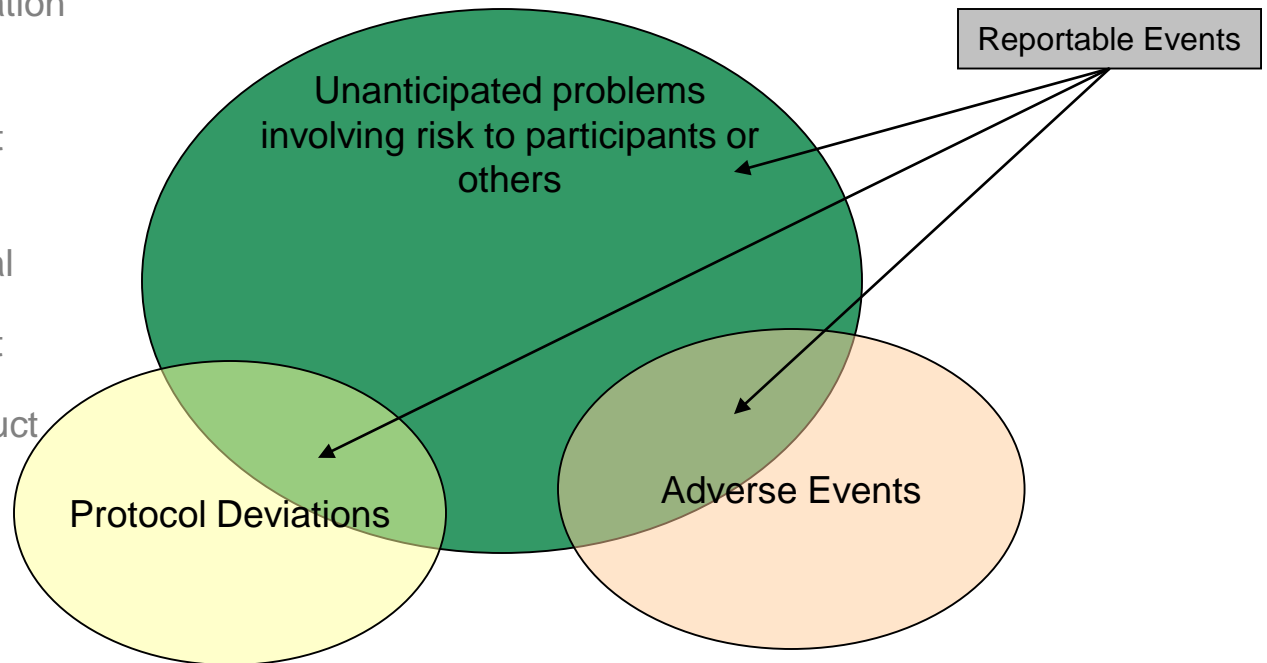
Report only unanticipated problems



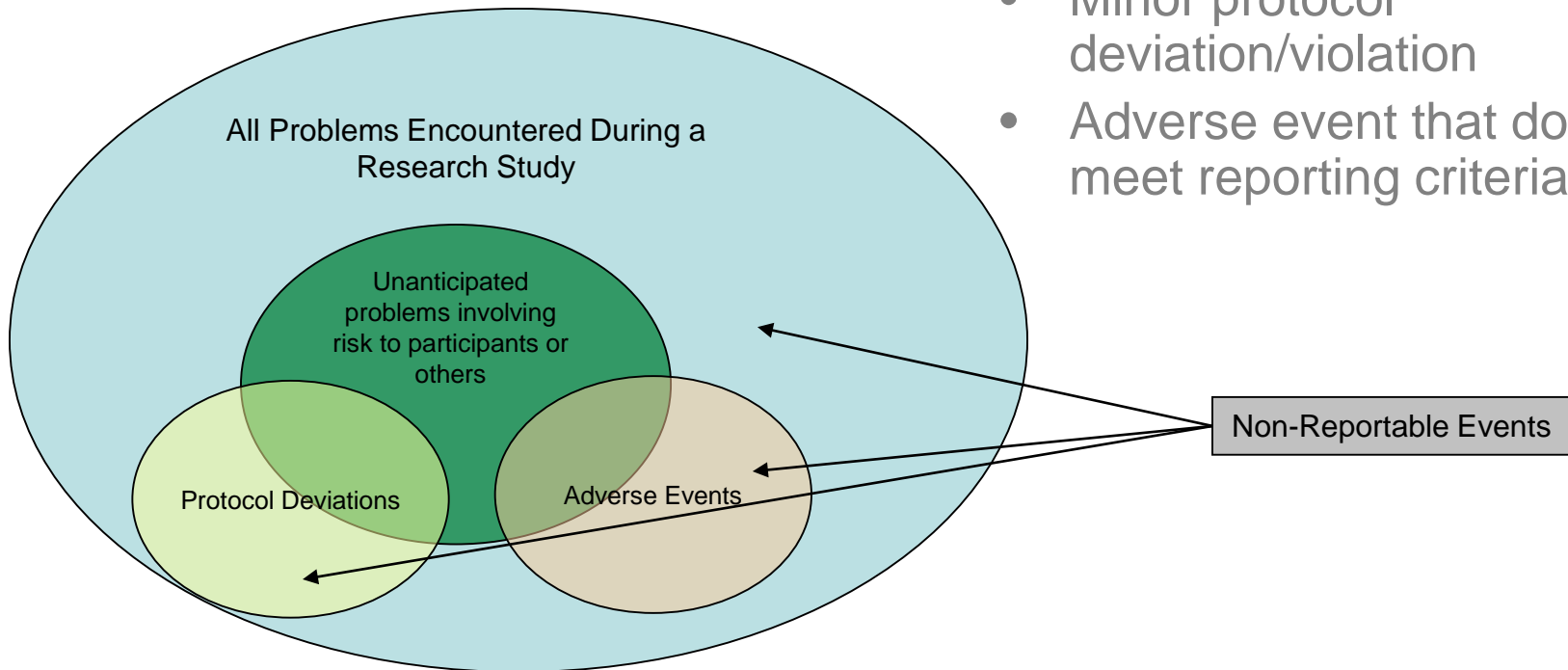
# Review: Examples of unanticipated problems involving risk to participants or others that should be reported

**Do** report these types of events:

- Serious Adverse Event
- Major Protocol Deviation/Violation
- Complaints
- Participant incarceration
- Adverse Audit or Enforcement Action(s)
- Breach of confidentiality
- Recalls / Withdrawals / Clinical Holds
- New or updated study product safety information
- Research personnel misconduct



# Review: Examples of non-reportable events



***Do not*** report these types of events:

- Minor protocol deviation/violation
- Adverse event that does not meet reporting criteria

# Use one form to report all reportable events

- **Safety Information and Unanticipated Problem Report** for SAEs, major protocol deviations/violations, unanticipated events or other reportable events reported by the Sponsor to the investigator (MedWatch Reports, IND Safety Reports, etc.)

## For more information...

Please link to Quorum's website for more guidance on safety reporting and to find Quorum's reporting forms:

<http://www.quorumreview.com/sites/safety/>