# Mandatory Reporting Obligations Under the Regulations

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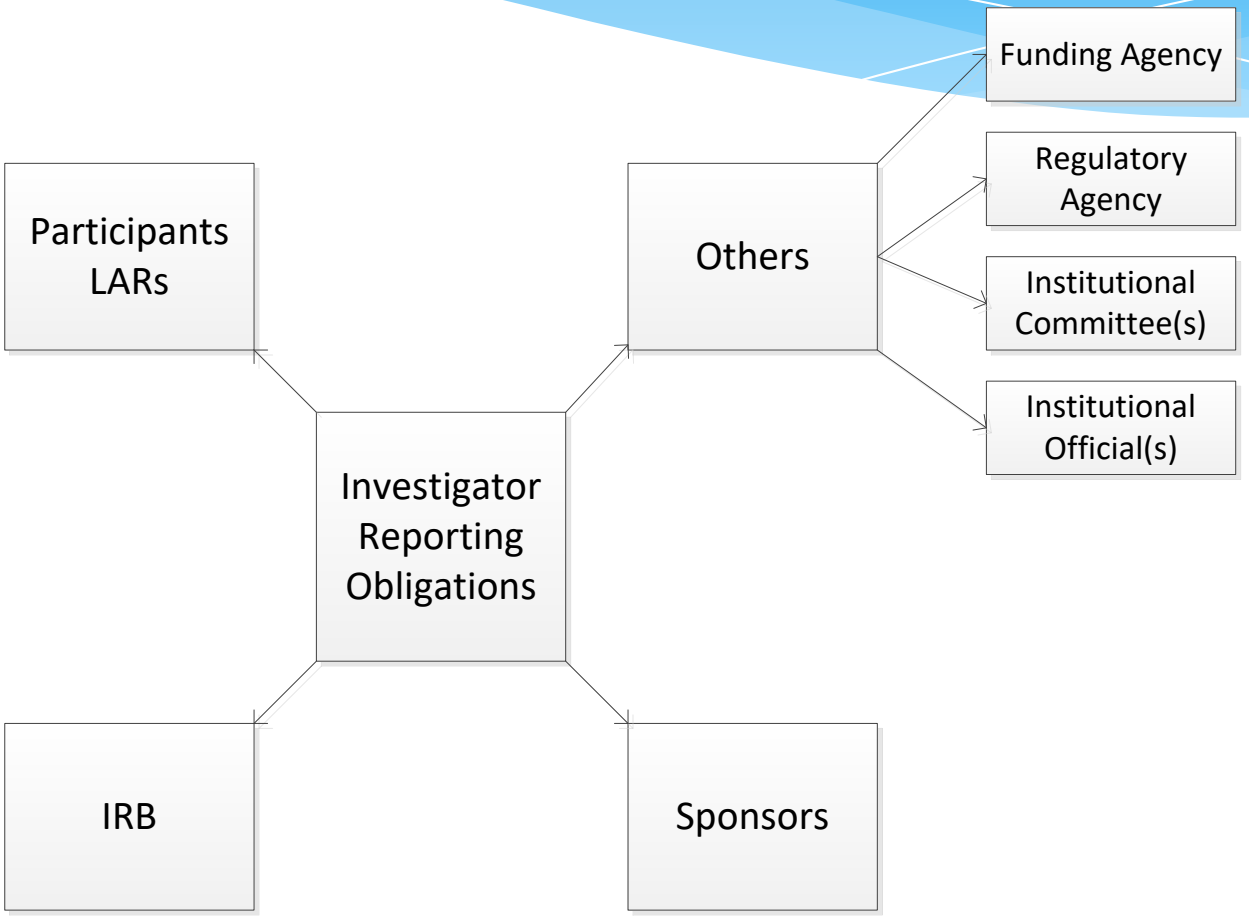
# Agenda

- Reporting Obligations Overview
- Regulations/Applicability
- What to Report
  - Unanticipated Problems (UPs)
  - Serious or Continuing (S/C) Noncompliance
- Protocol Deviations
- How to Analyze Information to Determine Whether Reportable
- Who Must Report, When & How

# Reporting Obligations



# Regulations

- Federal regulations require prompt reporting to the IRB, institutional officials (IOs), and
  - For federally funded research—the funding department or agency head & OHRP, and/or
  - For FDA regulated research—FDA of:
    - UPs involving risk to subjects or others;
    - Serious or continuing noncompliance with 45 CFR 46/FDA regulations or IRB requirements or determinations; and
    - Suspension or termination of IRB approval.

# OHRP Applicability

- Non-exempt human subjects research that is:
  - Conducted or supported by HHS;
  - Conducted or supported by a non-HHS federal department/agency that has adopted the Common Rule (Common Rule Department/Agency); or
  - Covered by a Federalwide Assurance (FWA), regardless of funding source
    - ✓ Checked the box

**Terms of FWA**
http://www.hhs.gov/ohrp/assurances/forms/filasurt.html

# FDA Applicability

- Experiments that involve a test article and one or more human subjects and is either:
  - An IND or IDE regulated clinical trial or
  - Not an IND/IDE regulated clinical trial, but the results of which are to be submitted to, or held for inspection by, FDA to support research or marketing permits.

# Unanticipated Problems

# Unanticipated Problems (UPs)

- Any incident, experience, or outcome meeting the following criteria:
  - **Unexpected** (nature, severity, or frequency);
  - **Related or possibly related to research procedures**;
  - Suggests that the research places subjects or **others** at a **greater risk of harm** than previously known or recognized; &
  - Usually requires some action to address the incident, experience or outcome.

# UPs (cont'd)

- Places … others at a greater risk of harm than previously known/recognized
  - Family/friends of subjects
  - Research team members
  - Society at large
- Greater **risk** of harm
  - Actual harm not needed; simply exposing subjects/others to harm is sufficient
  - Not just limited to physical harm
    - ✓ Psychological
    - ✓ Economic
    - ✓ Social

# Serious or Continuing Noncompliance

# Noncompliance

- Any accidental or intentional failure to follow:
  - Common Rule/FDA regulations or
  - IRB requirements or determinations (e.g., following the protocol)
- Failure to follow includes:
  - Performing acts that violate the above;
  - Failing to act when required to do so.
- Includes noncompliance by institution's employee(s) or agent(s) involved in research
  - Research team members
  - IRB members/staff
  - Institutional Officials (IOs)
- CIRB SOPs (Section 10.3) definition of Noncompliance
  - A failure to meet the requirements of the applicable Federal regulations and/or the requirements of the CIRB.

# Serious Noncompliance

- Not defined in regulations; refer to CIRB SOPs
- CIRB SOPs (Section 10.3) definition:
  - Serious noncompliance:
    - Noncompliance that adversely affects the rights and welfare of study participants or results in any untoward medical occurrence that meets the criteria of "serious" or significantly impacts the integrity of study data.
    - Serious is defined as side effects that may require hospitalization or may be irreversible, long-term, life-threatening, or fatal. The CIRB may also consider as serious those events which, based on appropriate medical judgment, may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes above.

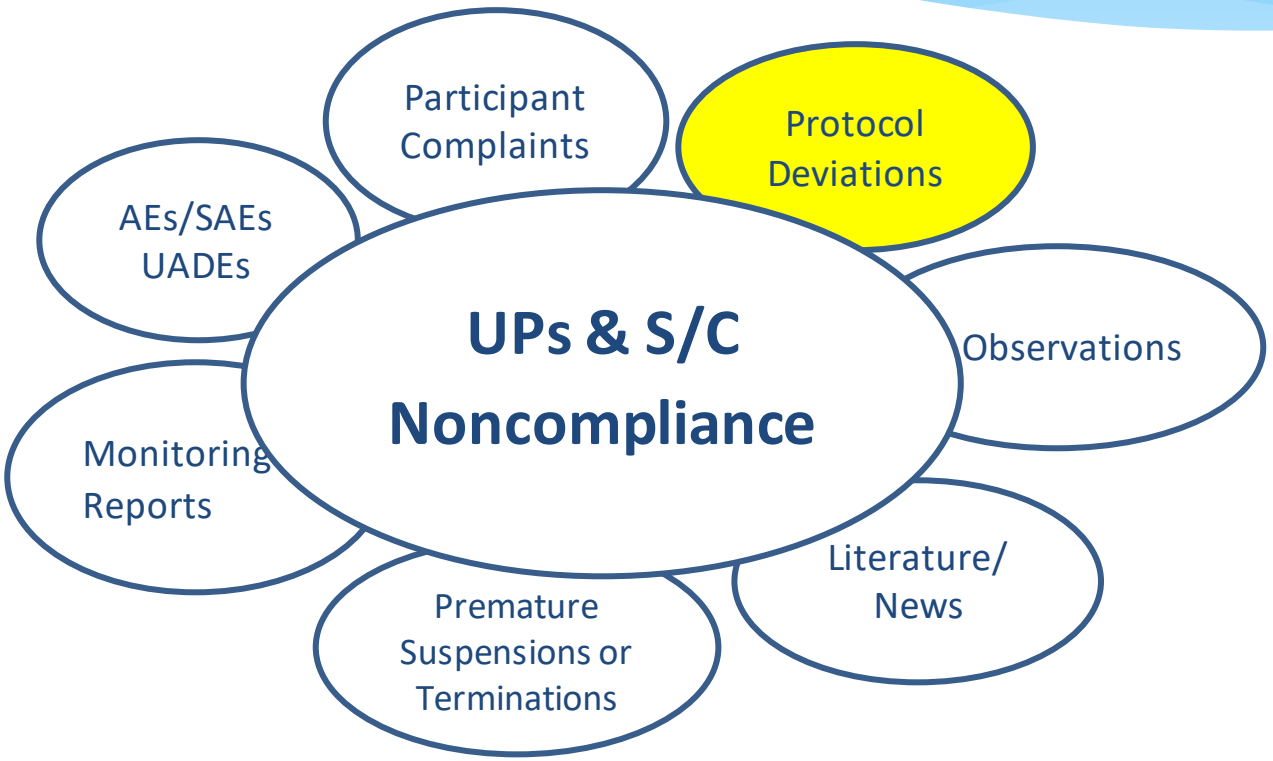
# OHRP - Serious Noncompliance

- Implementing more than minor protocol changes without IRB approval, except when necessary to prevent immediate hazard(s) to subjects;
- Conducting non-exempt human subjects research without IRB review and approval;
- Failing to obtain the legally effective informed consent of subjects, when required by the IRB, prior to involvement of subjects in non-exempt human subjects research activities.

# Continuing Noncompliance

- Not defined in regulations; refer to CIRB SOPs
- CIRB SOPs (Section 10.3) definition:
  - Continuing noncompliance
    - A systematic and habitual disregard of the requirements or decisions of the CIRB or of Federal regulations. Continuing noncompliance is an indication of a pattern that, if unaddressed, could jeopardize the rights and welfare of research participants or the integrity of the study data due to noncompliance with the protocol, Federal regulations, and/or the requirements of the CIRB.

# Possible Sources of UPs & S/C Noncompliance



# UP and Noncompliance Concepts

- Every event must be assessed as:
  - An isolated event; and
  - In the aggregate, if applicable;
  - To determine whether the isolated event or aggregate analysis of same or similar events, i.e., trend, meets:
    - ✓ UP Criteria;
    - ✓ Serious Noncompliance Criteria; or
    - ✓ Continuing Noncompliance Criteria

✉***Think Isolated Event Analysis***
✉***As Well As Trend Analysis!***

# Protocol Deviations

# Protocol Deviations (PDs)

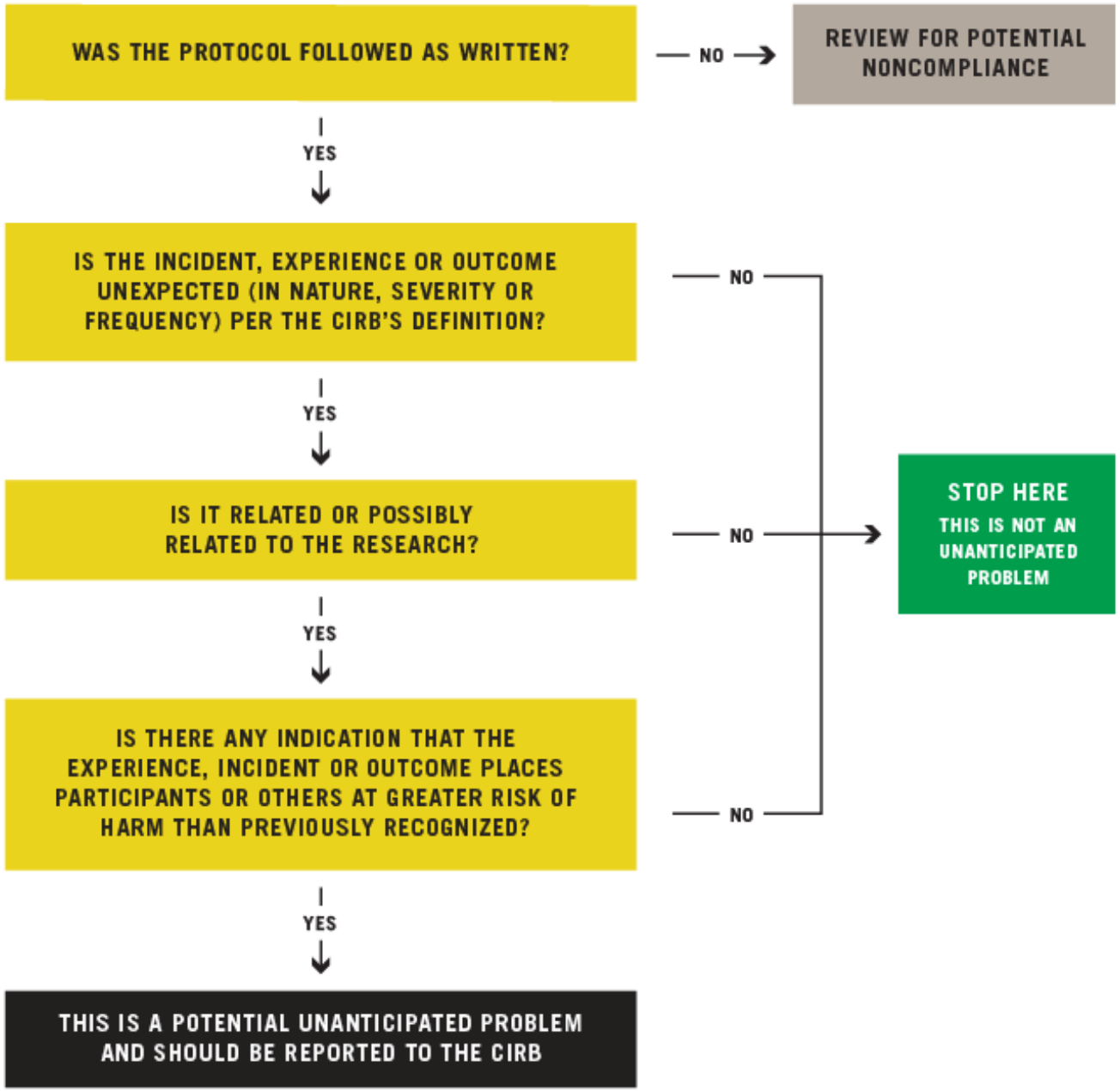
- Expected/future PDs are not reviewed by the CIRB
- PDs reported to the CIRB fall into one of the two categories:
  - Potential Unanticipated Problems (UP) or
  - Potential Serious or Continuing Noncompliance (SCNC)

# How to Analyze PDs to Determine Whether PD Constitutes a Reportable Event

# Using the CIRB's Algorithm to Determine Whether a PD is a UP

* While reviewing the algorithm to determine if a PD is an UP keep in mind:
  * The CIRB defines "unexpected" as incidents, experiences, or outcomes that occur while the CIRB-approved protocol *is followed as written*
  * Unexpected events are those that are NOT included in the CIRB-approved protocol, informed consent document, or Investigator's Brochure
  * If all answers are "Yes" or if the PI and research team are uncertain, the incident should be reported to the CIRB as a potential UP

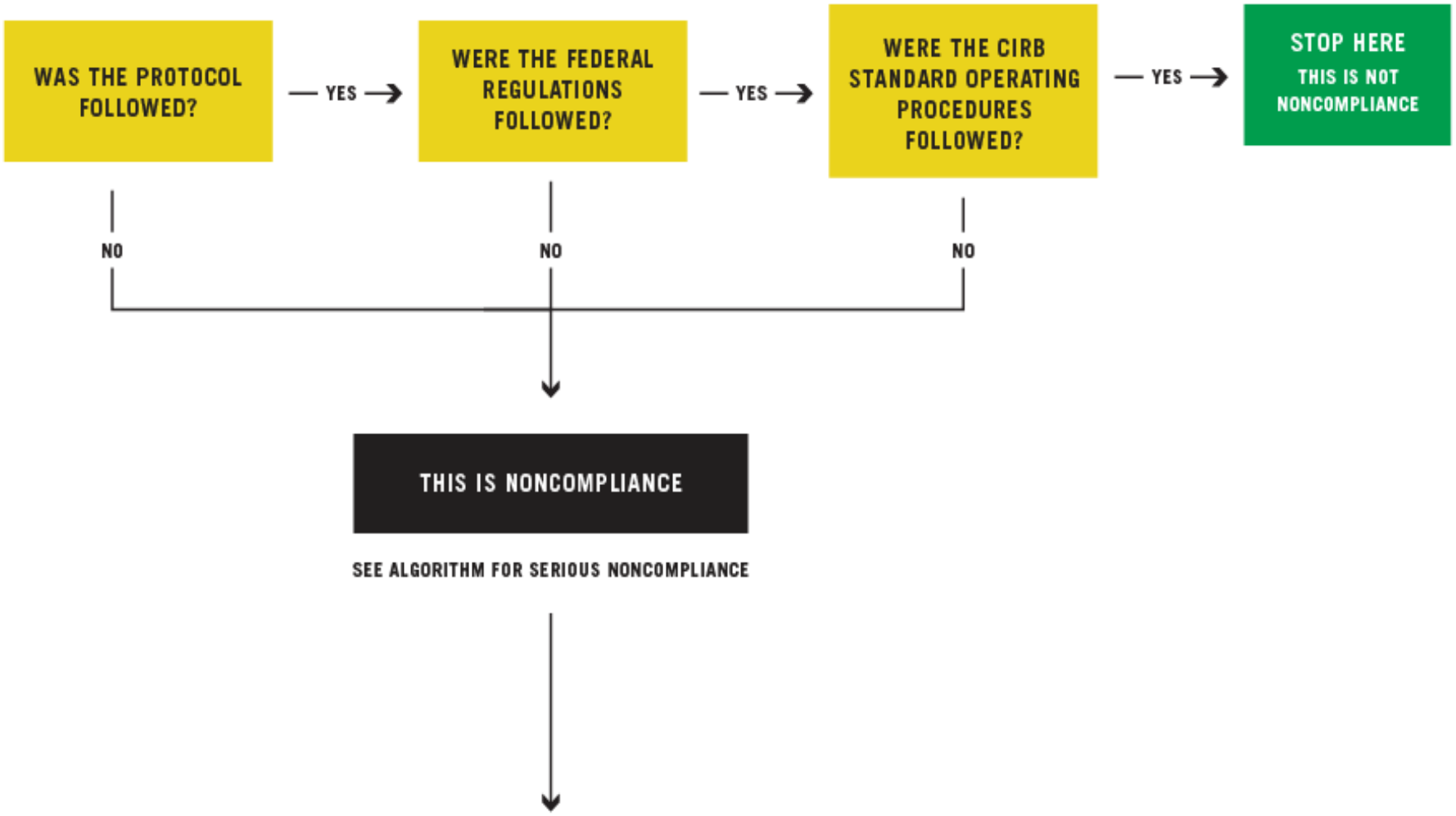
# CIRB's Algorithm to Determine Whether an Event is a UP



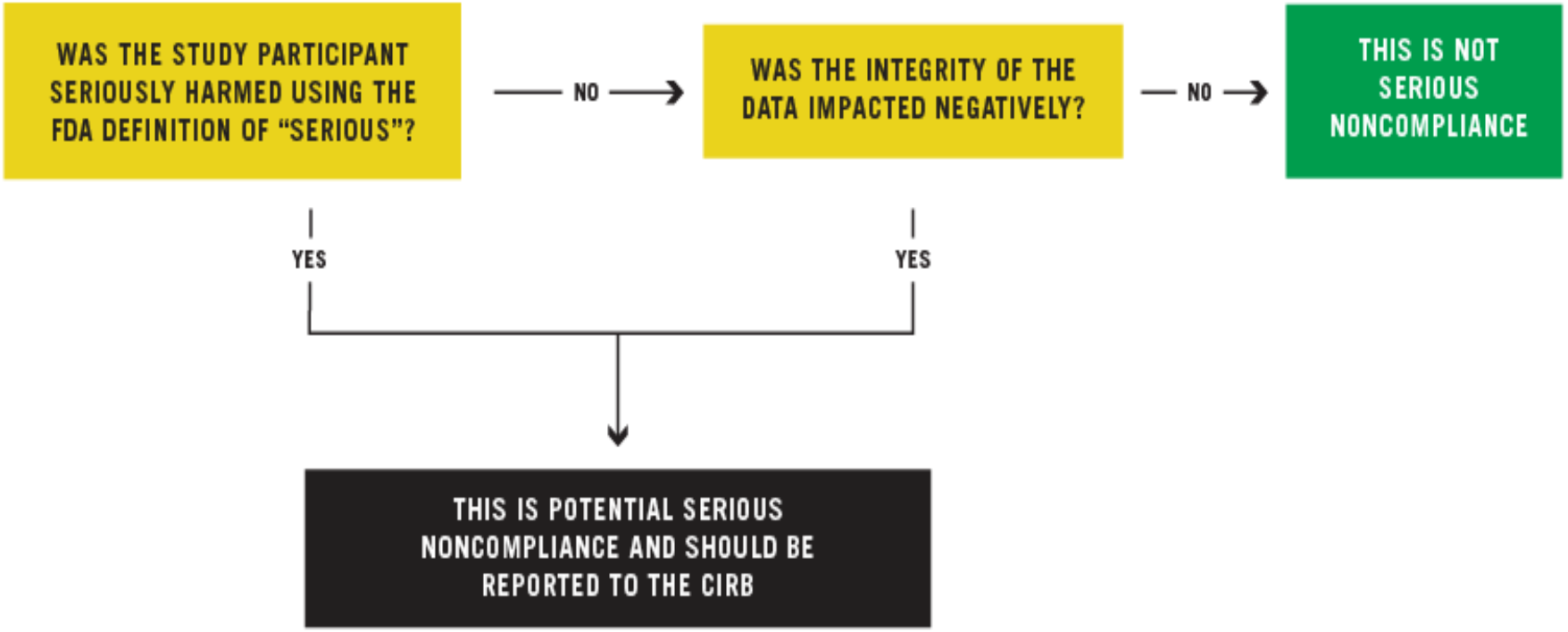
# Using the CIRB's Algorithm to Determine Whether an Event is Serious and/or Continuing Noncompliance

- While reviewing the algorithm to determine if an event is SCNC keep in mind:
  - The CIRB defines "serious" as:
    - Noncompliance that adversely affects the rights and welfare of study participants or results in any untoward medical occurrence that meets the criteria of "serious" or significantly impacts the integrity of study data
    - Side effects that may require hospitalization or may be irreversible, long-term, life-threatening, or fatal
  - There are two algorithms associated with this determination on the following slides

# CIRB's Algorithm to Determine Whether an Event is Noncompliance (step 1)



# CIRB's Algorithm to Determine Whether an Event is Serious Noncompliance (step 2)



# Who Must Report, When & How

# Who Must Report?

- If the incident is determined by the PI to be a potential UP and/or potential SCNC, it should be reported to the CIRB by the PI or designee.
- If it is uncertain whether or not to report an incident, proceed with reporting to the CIRB.
- If the CIRB determines the event is not serious noncompliance, similar incidents in the future do not need to be reported to the CIRB. They are still noncompliant, but not reportable noncompliant.

# When to Report?

- Promptly
  - Not defined by regulations, rather by institutional policy

CIRB Policy

- Locally Occurring Unanticipated Problems:
  - PI notifies the CIRB within 7 days of its receipt of the information related to serious adverse events that meets the criteria of an UP.
  - PI notifies the CIRB within 14 days of its receipt of information related to other potential UP. (i.e. those not related to SAEs)
- SCNC must be reported promptly

# How to Report?

- Determine if the incident is a potential UP or SCNC utilizing the CIRB' algorithms located on the CIRB's website
  - Algorithm to Assess a Potential Unanticipated Problem
  - Algorithm to Assess Potential Noncompliance
- If it is determined by the PI that event is potentially a UP and/or SCNC, utilize the CIRB's worksheet located in IRBManager.
  - Unanticipated Problem And/Or Noncompliance Reporting Worksheet
- CIRB's Quickguide is available on the CIRB's website and outlines the submission process step-by-step
  - Completing the Unanticipated Problem and/or the Noncompliance Reporting Worksheet

# ??? Questions ???