Guidance – Unanticipated Problems vs Adverse Events

The guidance is intended to help ensure that the review and reporting of unanticipated problems and adverse events occur in a timely, meaningful way so that human subjects can be better protected from avoidable harms while reducing unnecessary burden.

Unanticipated Problem (UP):

Any incident, experience or outcome that is:

1. ***Unexpected*** (nature, severity, or frequency): 1) given the description in the likely harms in the protocol, consent form, or other materials submitted to the IRB, and 2) the characteristics of the subject population;
2. ***Related***: Related to the subject's participation in the research; and
3. ***Greater risk of harm***: Suggests that the research places subjects or others at greater risk of physical, psychological, economic or social harms, than was previously known or recognized, even if no actual harm occurs.

Examples of UPs:

- Serious Adverse Events
- Change to the IRB-approved submission without prior IRB approval that increases the risk to subjects or others
- An event with implications for conduct or design of the research project
- Breach of privacy or confidentiality
- Receipt of wrong dose or contaminated study medication
- Complaint from subject or family member
- Lab or medication errors (that may involve risk to subjects)
- Disqualification or suspension of an investigator
- Change in the status of the subject that might affect their eligibility to remain in the study
- New information that suggests an unexpected change to the risk-benefit assessment or results in sponsor-imposed suspension of the study or enrollment due to a newly recognized risk
- Change in FDA labeling because of adverse consequences
- Withdrawal of investigational agent due to adverse events

See Prompt Reporting Flow

Adverse Event (AE):

An adverse event is any undesirable experience associated with human subject research; including any abnormal sign, symptom or disease, whether or not it is related to the subject's participation in the research.

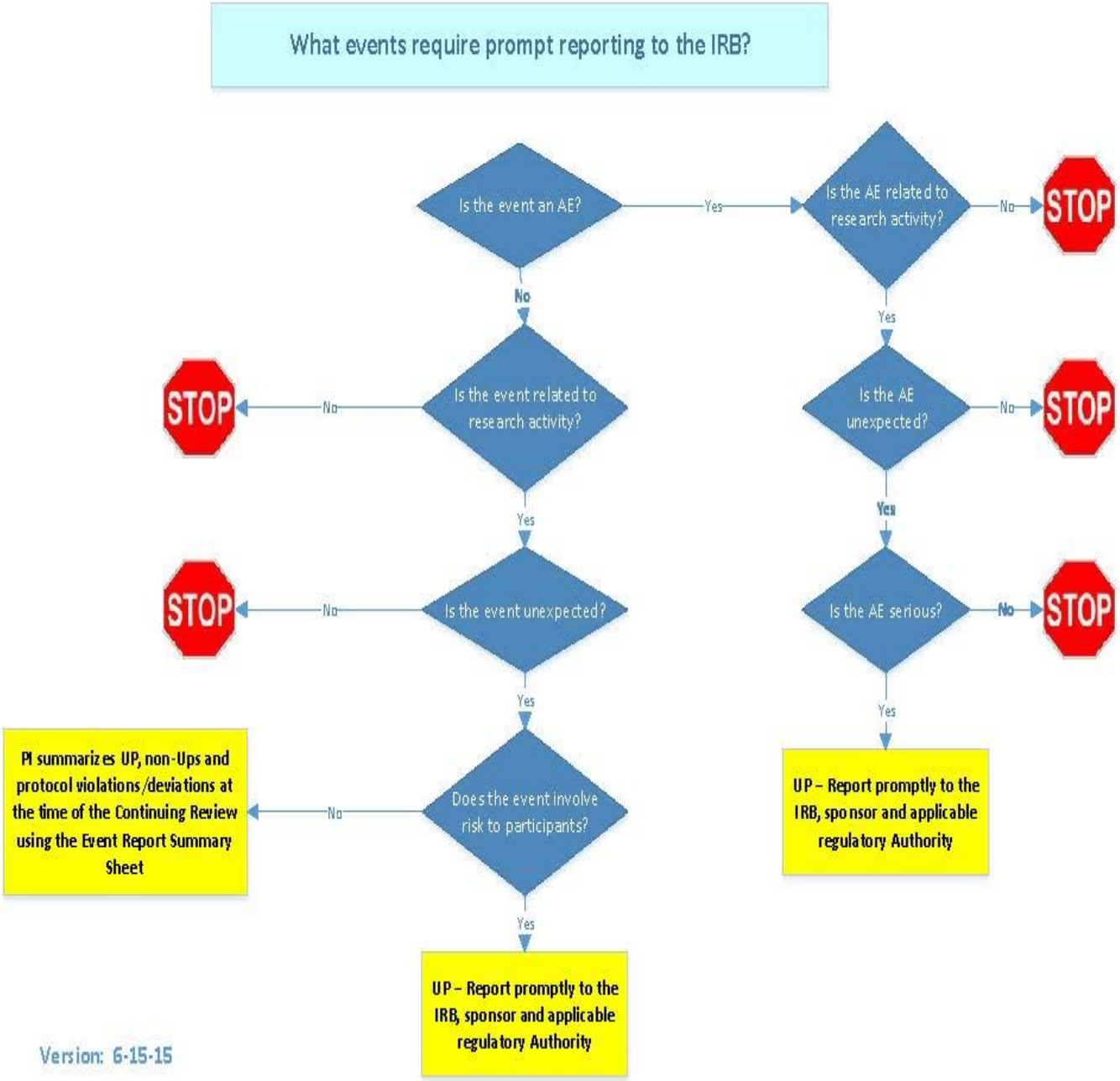
Examples:

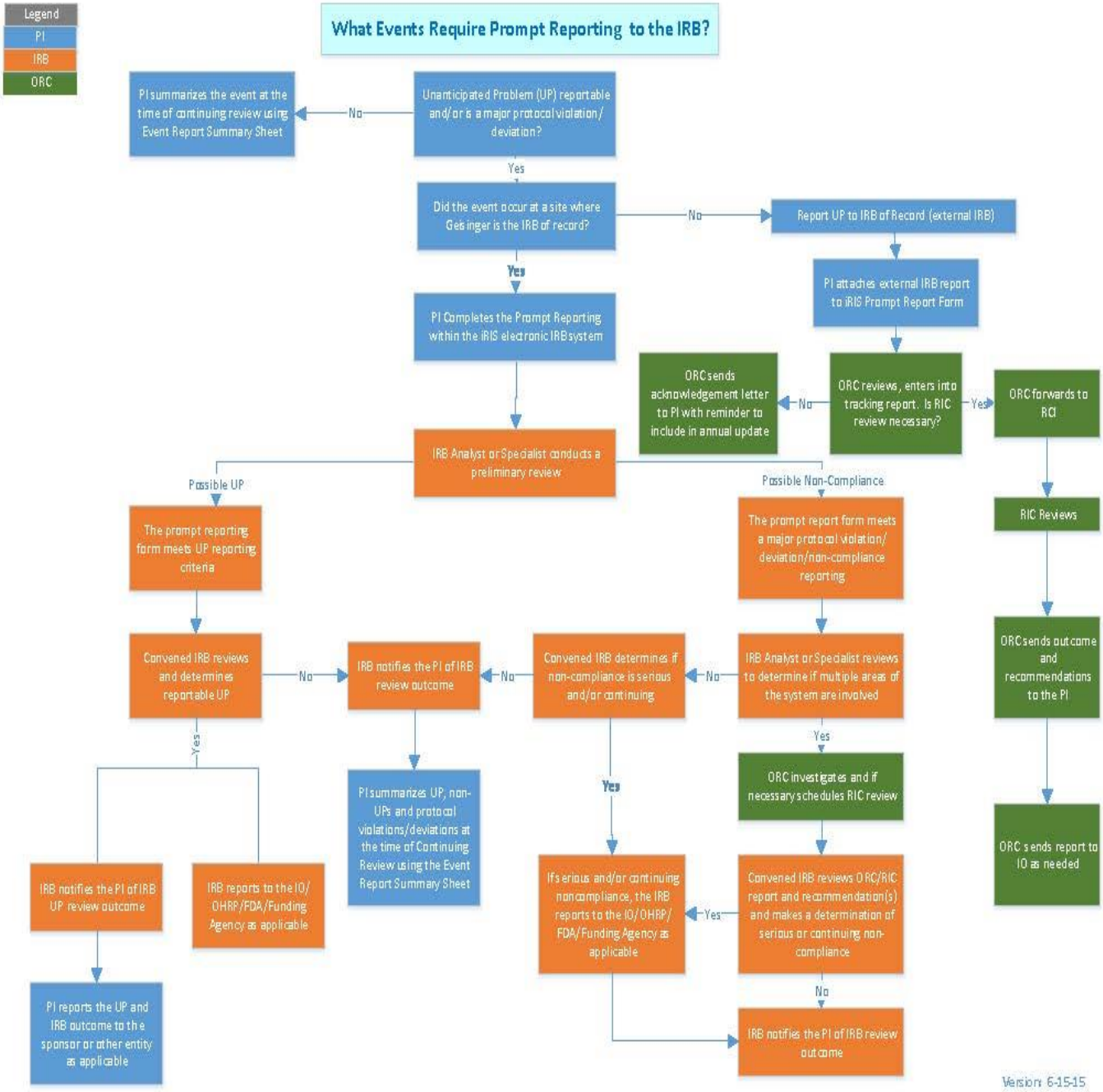
- Upper respiratory infection
- Broken wrist
- Nightmares
- UTI
- Flu
- Headache

If the event happens during the conduct of a human research study, it is an AE. Adverse events must be reported to the IRB ONLY when the event is related to participation in the research (i.e., investigational product or research procedures), the event is serious and unexpected, and might affect the IRB's prior risk-benefit assessment.

See Adverse Event Decision Tree

Adverse Event Decision Tree




Legend
PI
IRB
ORC
What Events Require Prompt Reporting to the IRB?
Unanticipated Problem (UP) reportable and/or is a major protocol violation/ deviation?
No
PI summarizes the event at the time of continuing review using Event Report Summary Sheet
Yes
Did the event occur at a site where Geisinger is the IRB of record?
No
Report UP to IRB of Record (external IRB)
PI attaches external IRB report to iRIS Prompt Report Form
Yes
PI Completes the Prompt Reporting within the iRIS electronic IRB system
ORC reviews, enters into tracking report. Is RIC review necessary?
No
ORC sends acknowledgement letter to PI with reminder to include in annual update
Yes
ORC forwards to RCI
IRB Analyst or Specialist conducts a preliminary review
Possible UP
Possible Non-Compliance
RIC Reviews
The prompt reporting form meets UP reporting criteria
The prompt report form meets a major protocol violation/ deviation/non-compliance reporting
ORC sends outcome and recommendations to the PI
Convened IRB reviews and determines reportable UP
No
IRB notifies the PI of IRB review outcome
No
Convened IRB determines if non-compliance is serious and/or continuing
No
IRB Analyst or Specialist reviews to determine if multiple areas of the system are involved
Yes
ORC investigates and if necessary schedules RIC review
ORC sends report to IO as needed
Yes
PI summarizes UP, non-UPs and protocol violations/deviations at the time of Continuing Review using the Event Report Summary Sheet
Yes
If serious and/or continuing noncompliance, the IRB reports to the IO/OHRP/ FDA/Funding Agency as applicable
Yes
Convened IRB reviews ORC/RIC report and recommendation(s) and makes a determination of serious or continuing non-compliance
IRB notifies the PI of IRB UP review outcome
IRB reports to the IO/ OHRP/FDA/Funding Agency as applicable
PI reports the UP and IRB outcome to the sponsor or other entity as applicable
No
IRB notifies the PI of IRB review outcome
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