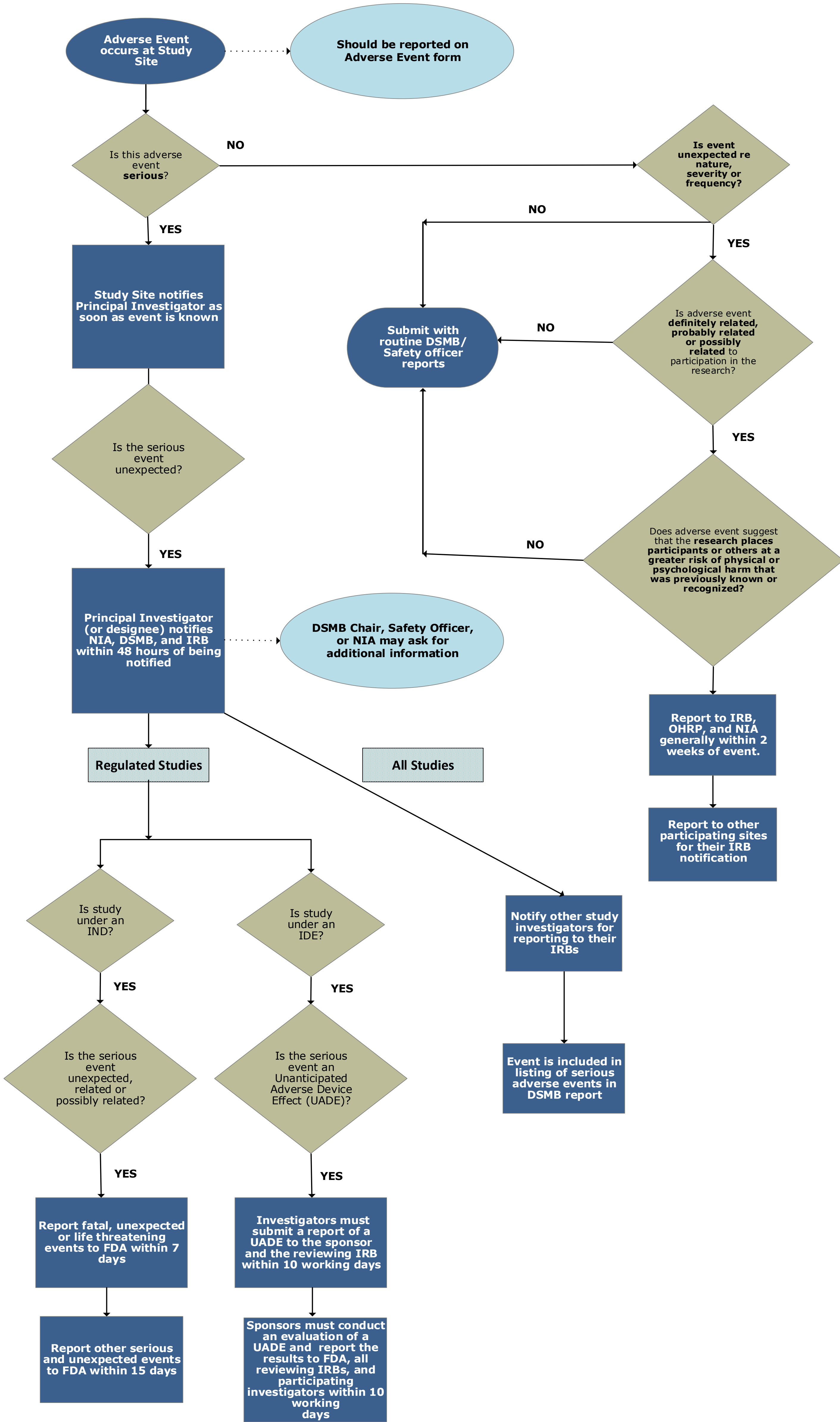


Serious Adverse Event/Unanticipated Problem Decision Tree for Principal Investigators



"Serious Adverse Event/Unanticipated Problem Decision Tree for Principal Investigators"

"Adverse Event occurs at Study Site" is next to "Should be reported on Adverse Event form" and leads to "Is this adverse event serious?".

If "Is this adverse event serious?" is "YES", then "Study Site notifies PI as soon as event is known", which leads to "Is the serious event unexpected?".

If "Is the serious event unexpected?" is "YES", then "Principal Investigator (or designee) notifies NIA, DSMB, and IRB within 48 hours of being notified", which is next to "DSMB Chair, Safety Officer, or NIA may ask for additional information" and leads to "Regulated Studies" and "All Studies".

"Regulated Studies" leads to "Is the study under an IND?". If "YES", then leads to "Is the serious event unexpected, related or possibly related?". If "YES", then "Report fatal, unexpected, or life threatening events to FDA within 7 days" or "Report other serious and unexpected events to FDA within 15 days".

"Regulated Studies" leads to "Is the study under an IDE?". If "YES", then leads to "Is the serious event an Unexpected Adverse Device Effect (UAE)?" . If "YES", then "Investigators must submit a report of a UAE to the sponsor and the reviewing IRB within 10 working days" and "Sponsor must conduct an evaluation of a UAE and report the results to FDA, all reviewing IRBs, and participating investigators within 10 working days".

"All Studies" leads to "Notify other study investigators for reporting to their IRBs" and "Event is included in listing of serious adverse events in DSMB report".

If "Is this adverse event serious?" is "NO", then leads to "Is event unexpected re nature, severity or frequency?".

If "Is event unexpected re nature, severity or frequency?" is "YES", then leads to "Is adverse event definitely related, probably related or possibly related to participation in the research?". If "YES", then lead to "Does adverse event suggest that the research places participants or others at a greater risk of physical or psychological harm that was previously known or recognized?".

If "Does adverse event suggest that the research places participants or others at a greater risk of physical or psychological harm that was previously known or recognized?" is "YES", then "Report to IRB, OHRP, and NIA generally within 2 weeks of event." and "Report to other participating sites for their IRB notification".

If "Does adverse event suggest that the research places participants or others at a greater risk of physical or psychological harm that was previously known or recognized?" is "NO", then "Submit with routine DSMB/Safety officer reports".

If "Is adverse event definitely related, probably related, or possibly related to participation in the research?" is "NO", then "Submit with routine DSMB/Safety officer reports".

If "Is event unexpected re nature, severity or frequency?" is "NO", then
"Submit with routine DSMB/Safety officer reports".