An adverse event occurs in one or more subjects.

1) Is the adverse event unexpected in nature, severity, or frequency?

   Yes
   
   2) Is the adverse event related or possibly related to participation in the research?

      Yes
      
      3) Does the adverse event suggest that the research place subjects or others at a greater risk of a physical or psychological harm than was previously known or recognized? NOTE: If the adverse event is serious, the answer is always ‘YES’.

      Yes
      
      Report the adverse event as an unanticipated problem under 45 CFR part 46

      No
      
      The adverse event is not an unanticipated problem and need not be reported under 45 CFR part 46

   No