Algorithm for Determining Whether an Adverse Event is an Unanticipated Problem

An adverse event occurs in one or more subjects.

1. Is the adverse event unexpected in nature, severity, or frequency?
   - Consider disease progression and predisposing risk factors
   - Is the event covered in the protocol related documents (consent form, protocol, investigator’s brochure)?

   NO

   YES

2. Is the adverse event related or possibly related to participation in the research?
   - Consider if related to underlying disease, disorder or condition of subject
   - If there is not adequate information available for the local investigator to assess this aspect the answer is NO.

   NO

   YES

3. Does the adverse event suggest that the research places subjects or others at a greater risk of physical, psychological, economic or social harm than was previously known or recognized?
   
   NOTE: If the adverse event is serious, the answer is always “YES.”
   - A serious event is one that is life threatening or results in: death, inpatient hospitalization, prolongation of existing hospitalization, persistent or significant disability/incapacity, congenital anomaly/birth defect, or may jeopardize the subject’s health and may require medical or surgical intervention to prevent one of the outcomes above.
   - If event is not serious consider if there is a trend that would warrant a change in the protocol related documents

YES

STOP

The adverse event is not an unanticipated problem and need not be reported under 45 CFR part 56

YES

Report the adverse event as an unanticipated problem.

What action will be taken?
- Consent revisions
- Protocol revisions
- Other corrective action

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