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

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

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

NO → 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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