Title: Core Standard Operating Procedure for Event Reporting

I. Procedure Statement

To describe the reporting of adverse events, serious adverse events, and unanticipated problems.

II. Definitions

1. Adverse Event (AE): Any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject’s participation in the research, whether or not considered related to the subject’s participation in the research (Modified from the definition of adverse events in the 1996 International Conference on Harmonization E-6 Guidelines for Good Clinical Practice). Adverse events encompass both physical and psychological harms. (OHRP Guidance Document, “Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events”)

2. Serious Adverse Event (SAE): Any adverse event temporally associated with the subject’s participation in research that meets any of the following criteria:
   a. Results in death;
   b. Is life-threatening (places the subject at immediate risk of death from the event as it occurred);
   c. Requires inpatient hospitalization or prolongation of existing hospitalization;
   d. Results in a persistent or significant disability/incapacity;
   e. Results in a congenital anomaly/birth defect; or
   f. Any other adverse event that, based upon appropriate medical judgment, may jeopardize the subject’s health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition (examples of such events include allergic bronchospasm requiring intensive treatment in the emergency room or at home; blood dyscrasias; convulsions that do not result in inpatient hospitalization; or the development of drug dependency or drug abuse).

3. Unanticipated Problem (UP): Any incident, experience, or outcome that meets all of the following criteria:
   a. Is unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;
   b. Is related or possibly related to participation in the research (in this guidance document, possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and

   1. Suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than
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was previously known or recognized. (OHRP Guidance on Reviewing
and Reporting Unanticipated Problems Involving Risks to Subjects or
Others and Adverse Events).

III. Procedure/Content/Scope

This SOP will apply to all clinical trials research within MU Health including the School of Medicine, School of Health Professions, School of Nursing, and MU Healthcare. This SOP will outline the process of monitoring and reporting AEs, SAEs, and UPs to the sponsor and Institutional Review Board (IRB).

1. By definition, an AE may not rise to the level of a UP. Many AEs and SAEs require a report to the sponsor but not to the IRB (see IRB policy at http://research.missouri.edu/policies/by_department). The sponsor will outline the procedures for reporting and recording AEs, SAEs, and UPs in the protocol. All AEs, SAEs, and UPs must be recorded in the source documents. The investigator must keep a log, database, or other tracking system for all protocol-specific AE/SAE/UP reports occurring in the study to ensure that the requirements for an audit trail of documentation are fulfilled, and to allow for review of potential reportable trends. All clinical research staff must be aware of the safety reporting requirements of the sponsor, IRB, and the applicable regulatory authorities.

2. The Primary Investigator is responsible for:
   a. Review of source documentation in real time for any potential AEs, SAEs or UPs.
   b. Review of the log, database, or other tracking system for trends.
   c. Ensuring all sponsor-reportable events are submitted to the sponsor within the required period.
   d. Ensuring all IRB-reportable events are submitted to the IRB within the required period.
   e. Events that are reportable to the IRB are often different from those that require submission to the sponsor. Do not rely on the sponsor for a determination of whether an event requires submission to the IRB.

IV. REFERENCES:

2. Title 21 CFR Part 312, Investigational New Drug Application, Part 312.62, Investigator Record Keeping and Record Retention for Clinical Drug or Biological Trials.
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