

Personnel involved in recording, routing, and evaluating AEs include the study chair (a physician), data monitors, statisticians, as well as the Institutional Review Board (IRB), Data and Safety Monitoring Committee (DMC), and federal regulatory officials. To reveal one fine-grained detail of the process of AE reporting, this process may involve, “each night, an automated computer program e-mails the study chair, study statistician, and data monitor to notify them of any event that was reported the previous day and to report a cumulative summary of all events observed on that study” (155). Regarding the IRB, some clinical studies may require all AEs that are serious and unanticipated be reported to the IRB within 48 hours of the event (156).

The “point man” in this scenario is the clinical research associate (CRA). The CRA (157,158) manages patient recruitment strategies to ensure target patient numbers are met, ensures that SAEs are reported according to standard operating procedures (SOPs), for any amendments to the Clinical Study Protocol, arranges monitoring visits at appropriate time intervals and writes monitoring reports, including deviations and deficiencies, prepares follow-up letters to investigators, and tracks completed Case Report Forms (CRFs) sent to data management, track issued and resolved data queries. In filling out the CRFs, the CRA records the name of the AE, for example a seizure, vomiting, or anemia, when it occurred, when it was reported to the investigator, whether the AE was ongoing, the severity of the AE, whether the AE can be attributed to the study drug or medical device, whether the AE resulted in hospitalization, or if the AE was reported to the sponsor or to any regulatory agency (FDA; EMA), or if that particular AE was in the Consent Form (159).

a. The data manager’s tasks include documenting missing data

The data manager is an expert in computer systems, in capturing remote data, and in quality control. The data manager reports missing data and discrepancies to the principal investigator. As mentioned above, information on approved drugs, available from www.accessdata.fda.gov, extensively documents various types of missing data and discrepancies.

Data management also includes making certain that the names of adverse events, and the names of various medications, found on forms provided by various study sites are consistent with standard names found in appropriate dictionaries. These dictionaries

¹⁵⁵ Goldberg RM, Sargent DJ, Morton RF, Mahoney MR, Krook JE, O’Connell MJ. Early detection of toxicity and adjustment of ongoing clinical trials: the history and performance of the North Central Cancer Treatment Group’s real-time toxicity monitoring program. *J Clin Oncol.* 2002;20:4591–456.

¹⁵⁶ Columbia University and Columbia University Medical Center IRB Policy (April 13, 2004).

¹⁵⁷ American College of Radiology Imaging Network (ACRIN). Template for clinical study protocol.

¹⁵⁸ Young RC (2007) Data and Safety Monitoring Plan. Ensuring Patient Safety and the Integrity of Clinical Research (ver. 1.61) Fox Chase Cancer Center, Philadelphia, PA.

¹⁵⁹ London JW, Smalley KJ, Conner K, Smith JB. The automation of clinical trial serious adverse event reporting workflow. *Clin Trials.* 2009;6:446–454.