

- **Classification of adverse events as induced by disease versus induced by the study drug.** Proper alignment of any given AE with the safety definitions might require an awareness of whether the AE was induced by the disease, induced by the study drug, or was produced by the simultaneous presence of both disease and study drug.
- **Classification of adverse events by considerations used by statisticians.** This further develops a topic detailed in an earlier chapter in this book, namely, intent to treat analysis and per protocol analysis.
- **Classification of adverse events as anticipated versus unanticipated.** An awareness of this classification can influence how AEs are reported to regulatory agencies.
- **Using raw data on adverse events to acquire cause-and-effect data on adverse drug reactions.** An awareness of this issue can also influence how AEs are reported to regulatory agencies. This introduces the Naranjo algorithm.
- **Paradoxical adverse drug reactions.** The paradoxical nature of some AEs may impair an investigator's ability to anticipate these AEs before embarking on a clinical trial, and may impact the way the paradoxical AEs are reported to regulatory agencies.
- **Monitoring and evaluating adverse events.** This material constitutes a shift in the chapter from issues that are medical or scientific, to issues relating to the processes of managing drug safety reporting. This introduces the job of the data manager, and a form called the Case Report Form.
- **Adverse events – capturing, transmitting, and evaluating data on adverse events.** This introduces the topic of transmitting and routing of reports of AEs, from any given clinical trial.
- **Forms for reporting of adverse events.** This reveals special forms for capturing AEs from individual patients, for use in clinical trials, or for use by the general public outside of any clinical trial.
- **Risk minimization tools.** This focuses mainly on *Dear Healthcare Professional* letters. Candid, unbiased accounts of risk minimization tools, such as *Dear Healthcare Professional* letters, consent forms, and package inserts, are available from published courtroom cases. Information about the content of these letters can be found on FDA's website at the location "Approved Risk Evaluation and Mitigation Strategies (REMS)."
- **Patient-reported outcomes.** Patient-reported outcomes encompass both safety and efficacy reporting.
- **Data and Safety Monitoring Committee.** This Committee plays a major role in regulated clinical trials. The Committee meets at regular intervals, reviews data on safety and efficacy, has the authority to unblind data, and recommends (but does not mandate) changes in the clinical trial. A typical recommendation is that of halting the clinical trial.