

**Table 24.2** Example of questions for patients with poorly written questions (left) and adequately written questions (right)

	Poor Writing	Better Writing
Avoid double negatives	Is the patient currently not taking asthma medication? <input type="checkbox"/> Y <input type="checkbox"/> N	Is the patient currently taking asthma medication? <input type="checkbox"/> Y <input type="checkbox"/> N
Specify time points	How would you rate your pain? <input type="checkbox"/> severe <input type="checkbox"/> mild	How would you rate your pain since your last visit? <input type="checkbox"/> severe <input type="checkbox"/> mild
Avoid two questions in one sentence	Were answers 28–32 reviewed by the nutritionist and was the patient eligible? <input type="checkbox"/> Y <input type="checkbox"/> N	Were answers 28–32 reviewed by the nutritionist? <input type="checkbox"/> Y <input type="checkbox"/> N

## V. ADVERSE EVENTS – CAPTURING, TRANSMITTING, AND EVALUATING DATA ON ADVERSE EVENTS

Figures 24.2, 24.3, 24.4, and 24.5 illustrate the overall processes used for capturing, evaluating, and performing quality control of serious adverse events (SAEs). The processes used for AEs are somewhat different than for SAEs, in view of the fact that typical AEs are not submitted to regulatory agencies while, in contrast, SAEs may be submitted.

Thus, the big picture is revealed by the following small pictures. The arrows begin at the party that initiates the process of capturing events. The investigational site is the initiating party, in the first diagram, because this site is where the study subject experiences the AE, for example vomiting, fatigue, anorexia, or a seizure. In contrast, for the next diagram, follow-up is initiated by the sponsor's safety group, for example by the director of drug safety. The first two diagrams show the process where a contract research organization (CRO) is not involved, while the next two diagrams show the sponsor had hired a CRO to capture, store, and perform quality control work on adverse event data.

Title 21 of the Code of Federal Regulations (CFR) dictates the timeline of some of the reporting procedures (180):

*The sponsor shall notify FDA and all participating investigators...of...[a]ny adverse experience associated with the use of the drug that is both serious and unexpected; or [a]ny finding from tests in laboratory animals that suggest a significant risk for human subjects including reports of mutagenicity, teratogenicity, or carcinogenicity. Each notification shall be made as soon as possible and in no event later than 15 calendar days after the sponsor's initial receipt of the information. Each written notification may be submitted on FDA Form 3500A or in a narrative format... [t]he sponsor shall also notify FDA by telephone or by facsimile transmission of any unexpected fatal or life-threatening experience associated with the use of drug as soon as possible but in no event later than 7 calendar days after the sponsor's initial receipt of the information.*

<sup>180</sup> 21 CFR 312.32 (c) (April 1, 2006).