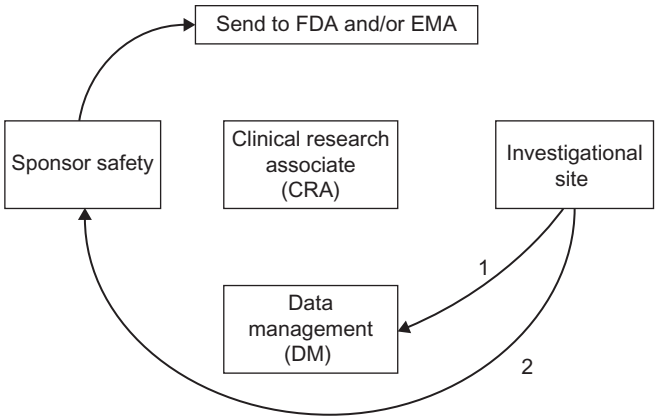

Figure 24.2 Initial report of SAE (situation where there is no CRO). One paper trail for processing adverse events starts at the investigational site, and then continues to data management. Another paper trail begins at the investigational site, and proceeds to the sponsor's drug safety group, and then to regulatory agencies

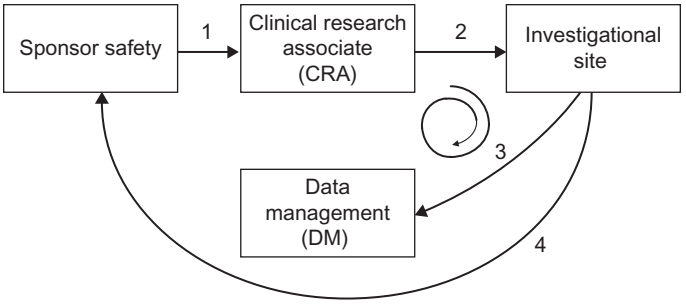

Figure 24.3 Follow-up to report of SAE (situation where there is no CRO). Follow-up of an SAE involves getting missing data, rationale according to the investigator's assessment, and information on resolution of the SAE. After the sponsor initiates follow-up, the next few subsequent steps are shown above. Following these steps, what occurs is a reiterative process, involving three parties, the CRA, the investigational site, and data management personnel, until the Case Report Form is completely filled in. The reiterative process is indicated by the spiral

The CFR also dictates the requirement for following up reports of adverse events. In short, if an adverse event was found initially not to be serious enough to report, but upon follow-up was determined to be serious enough to report, then the investigator must report it (181):

> *The sponsor shall promptly investigate all safety information received by it…[f]ollowup information to a safety report shall be submitted as soon as the relevant information is available.*

[181] 21 CFR 312.32 (d) (April 1, 2006).