JOURNAL OF CLINICAL RESEARCH BEST PRACTICES

Vol. 7, No. 1, January 2011 "Can You Handle the Truth?"

Writing Notes to File at the Study Site

By Tatjana Markovic

When something unusual happens in a clinical study, it is common to document the incident with a note to file in the regulatory binder or other study files. Incidents can include decisions made, instructions from the study sponsor, problems experienced, and other matters that are important to remember if one is to understand what happened during the study.

The ICH guideline for Good Clinical Practice (E6 2.10), adopted by FDA as guidance, applies to all study documentation, including notes:

> All clinical trial information should be recorded, handled and stored in a way that allows its accurate reporting, interpretation and verification.

The question to ask when writing a note is: "What are the chances that a data query, site monitor, auditor or FDA investigator will ask a question and find this note useful in understanding what happened in the study?" For example, if a subject is seven feet tall and weighs 150 pounds, it might be useful to write a note saying, "Yes, subject 123 really is that tall and thin." The FDA investigator may arrive five years after the study is complete, so written documentation is essential.

Well-written notes save time, provide clarity, establish accountability, and enable reconstruction of events that can later seem puzzling. They avoid frustration, wasted time, unusable data, unhappy sponsors, and FDA 483 observations. In the absence of adequate documentation, the incident might be interpreted in the worst possible way.

Notes are an important component of robust quality programs that also include root cause investigations and corrective and preventive action (CAPA) plans. They help assure sponsors and regulators that conscientious efforts have been taken to address the issue and minimize reoccurrence to secure data quality and subject safety. CAPA documentation is normally confidential and kept separate from study documentation, so notes in the study files should include a brief statement about how the problem was addressed.

Consider the following actual note (disguised to protect the guilty):

> Subject NBI was not dosed.
>
> Jane Dint
>
> 11/21/10

This note raises more questions than it answers:

- What was the date of the study visit?
- Why was the subject not given the drug?
- Was not dosing the subject a protocol deviation?
- Did the investigator authorize not giving the drug?
- What was the subject's status?
- What was the treatment arm?
- Was there something significant about the study drug?

Consider the following revised note:

> At visit on 20 NOV 2010, subject NBI did not receive dose of SureCure20, 10 mg, due to subject's febrile state (102° F). Dr. Cardio instructed no dosing per phone instructions at that time. Willa Gain referred subject to his primary care physician for treatment. Scheduled visit for 27 NOV 2010, still in visit window.
>
> Jane Did
>
> 21 NOV 2010

The revised note provides the information needed to understand why the subject was not dosed. When the subject appears the following week for his or her visit while the study coordinator is vacationing in Hawaii, the back-up coordinator will know how to proceed.

The incident above appears to have been handled correctly and required no further action. However, notes about incidents that expose issues with procedures, training or other elements important for proper study conduct require more information, including the following sections:

- Basic information, including date, author and subject of note
- What happened? (who, what, where, when, how, why)
- Why is the incident important?
- What has been or will be done to address this incident?
- What will be done to prevent or mitigate similar incidents in the future? (CAPA plan)
- Where the note is to be filed

The following note illustrates the proper contents of a note documenting an issue:

> **Date:** 20 DEC 2010
>
> **To:** T12485 Study File
>
> **CC:** Quality Assurance File
>
> **From:** Everett Kawshon, Quality Assurance
>
> **Re:** Obsolete Informed Consent Form Used
>
> **Incident:** Myron Dox used version 7 of the informed consent form with subject NAC on 7 DEC 2010, instead of the correct version 9. Subject gave consent.
>
> **Implications:** The use of an obsolete consent form makes consent invalid. However, changes to the form were not material to subject safety.
>
> **CAPA Plan:** Consent will be re-obtained with the correct version at subject's next visit. After investigation, it was determined that obsolete printed forms had not been removed from the file. Remaining unused copies of the form have been removed and destroyed. Consent forms used for other subjects in the study have been reviewed and found to be correct. A spot check of other studies revealed no other problems. Procedures for ensuring use of correct version of consent form will be reviewed and revised, as appropriate.

Once a note is filed, it should not be changed, other than making minor corrections with the usual signature and date. If additional or revised information arrives later, create a new note that refers to the first note.

Notes are useful in many circumstances, but they can be misused:

- Incidents documented elsewhere do not need a redundant note that provides no additional, useful information.

- Incidents that are interesting but not important do not need documentation in a note.
- Documenting a problem in a note only begins to address the problem. The note must also describe a plan to correct or mitigate the problem and a plan to prevent or mitigate future occurrences.

Conclusion

The old saying, "If it's not documented, it didn't happen," has a corollary: "If it's not documented right, bad things might happen." The bad things inadequate notes can cause include frustration, wasted time, unusable data, unhappy sponsors, and FDA 483 observations. Complete and accurate notes to file are especially important because they document unusual incidents that are likely to raise future questions.

Author

Tatjana Markovic is a Quality Assurance Technical Associate at Cetero Research. Contact her at 1.636.757.2276 or tatjana.markovic@cetero.com.

