Smarter Clinical Solutions

WHITE PAPER

Reconciling EDC and Safety Systems

The Problem

In clinical trials, details of Adverse Events (AEs) and Device Malfunctions (DMs) are captured by two separate systems. The Electronic Data Capture (EDC) system captures the AE/DMs for clinical research and the Safety system captures it for regulatory safety reporting.

This paper discusses the need for a robust reconciliation between these two systems. It starts by describing the problem and then describes an approach to achieve reconciliation.

When a patient in a clinical trial experiences an AE/DM, the site must report it to the sponsor company. There is then a regulatory requirement for the sponsor to report the issue to the appropriate regulatory authority. Both Clinical Research and Safety have reporting responsibilities. The AE/DM must be reported by both systems but only once from each system.

Safety is the primary responsibility of regulatory authorities and there are serious regulatory ramifications if this reporting requirement is not met. It is especially significant if the problem is “Serious” or reports a death.

To meet this regulatory requirement, a reliable reconciliation process is required to ensure that both EDC and Safety report exactly the same AE/DMs.

Case Study

A major device manufacture found that the serious AE/DMs being reported to the FDA from their EDC system did not match the reports coming from their in-house Incident reporting system. Their solution was to establish an IT project to build a reconciliation system. The result was that they had confidence that although coming from different systems, their clinical and regulatory reports were consistent.

Complications

1. When an AE or DM occurs in a clinical trial, the site can report it to the sponsor in one of three ways:
    a. Enter it into EDC and report it to the sponsor’s Safety group
        “Play safe and report it both ways”
    b. Enter it into EDC and expect the sponsor to manage things from there.
        “Why should I have to tell you something twice?”
    c. Report it to the sponsor’s Safety group
        This is most likely to happen if the patient experiences the AE/DM at a location other than the clinical trial site.

2. One fundamental matching issue between EDC and Safety is that whereas EDC is designed to capture well structured, source document validated and complete details of AE/DMs, most Safety systems have to capture much less well structured data. Essentially any report that comes in from a site by any means must be captured by Safety.

    For example: EDC might capture full Source Verified Details (SDV) of two separate AEs, “Severe Headache” and “Transient Ischemic Attack” with full demographic details, the report given to the

Safety team might me more like “Patient started by reporting a headache and then had a mild stroke” with only vague patient details.

Therefore, a convention IT systems match based upon primary keys is usually not possible. A more complex matching process is required.

3. To support coding against dictionaries, EDC is usually strict about creating one AE/DM for each separate issue. As in the above example. Whereas, Safety systems generally deal with cases where several issues are intentionally grouped into one Incident. Therefore, the Safety system and the matching process needs to allow for multiple AE/DMs linked to one Incident.

Requirements

Minimum Requirement

There is a minimal requirement that the Safety system identifies cases where the patient is in a clinical trial, otherwise even manual matching is virtually impossible.

Ideal Requirements

The ideal situation is if the Safety system already does or can be modified to capture:

- EDC Trial Number
- EDC Site Number
- EDC Patient Number
- List of EDC AE/DM Numbers

Key Codes

Reconciliation is easier if there is a system maintaining a master list of Trial Numbers and Site Numbers. If EDC and Safety use different numbering systems then a translation step will be required.

Basic Solution

The basic reconciliation process is to have the Medical Monitor maintain a simple set of MS Excel spreadsheets. If an AE or DM occurs in one of the monitor’s clinical trials, the monitor checks in the Safety system to confirm that it has also been reported there.

This solution is possible for small scale research but even then it is prone to error. Also, it will almost certainly not trap for incidents that were only reported to Safety.

Also, after an initial match, updates to EDC or Safety are unlikely to be noticed.

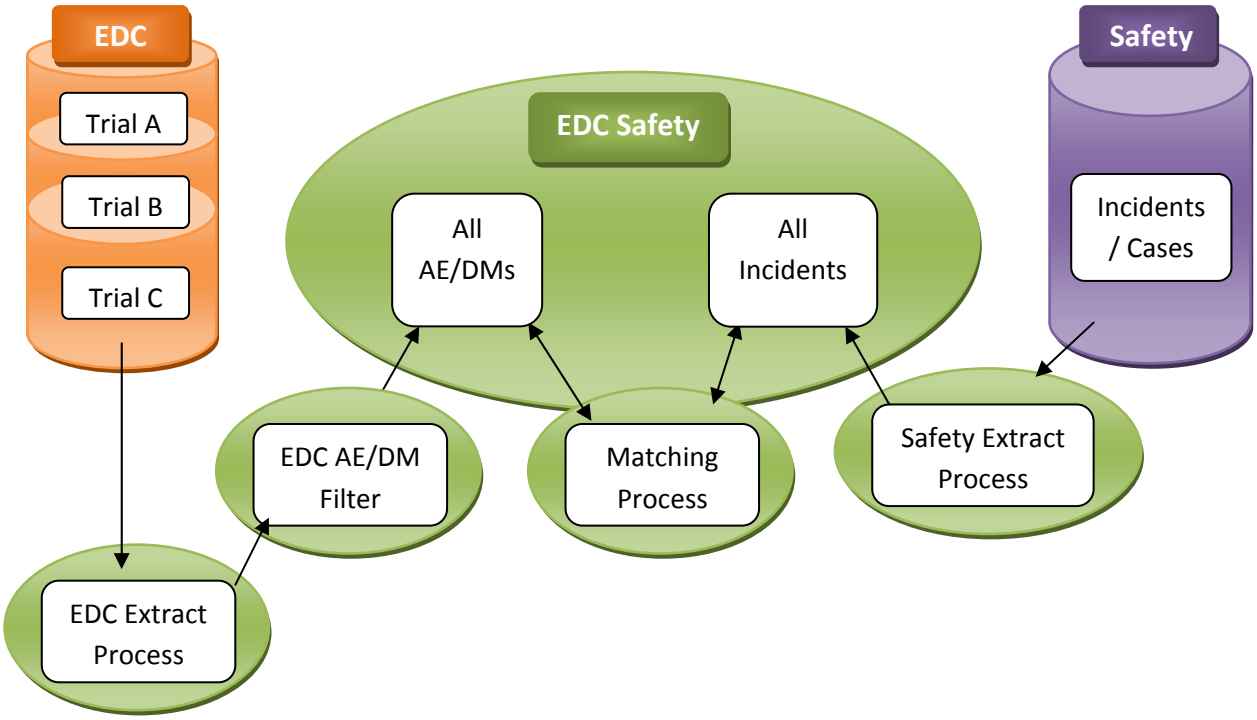
This solution is certainly far better than nothing but is far from the robust reconciliation required to meet regulatory requirements.

Recommended Solution

To achieve a reliable reconciliation, a fully validated IT application is required. The overall architecture is relatively simple.

- Extract new and updated AE/DMs from EDC
- Filter the EDC extract for AE/DMs that belong in the Safety system.
- Extract new and updated Incidents from the Safety system
- Automatically match AE/DMs with Incidents
- Manual match AE/DMs with Incidents
- A process to add missing Incidents to EDC
- A process to add missing AE/DMs to Safety

Overall Architecture



"All AE/DMs" Data Items	"All Incidents" Data Items
EDC Data Extract Items Study Number Site Number Patient Number Date of Birth Gender AE/DM Number Start Date Description	Safety Extract Data Items Incident Number Study Number Site Number Patient Number Date of Birth Gender List of AE/DM Numbers Start Date Description
Additional "All AE/DMs" Data Items Status Incident Number Match Date Matched By Matching Comments Tracking Comments	Additional "All Incidents" Data Items Status List of matched AE/DM Numbers Match Date Matched By Matching Comments Tracking Comments

"All AE/DMs" Status Values	"All Incidents" Status Values
Status **New –** new in EDC **Auto-Match** – matched to an Incident using the automatic process **Manual-Match** – matched to an Incident manually **Waiting for an Incident** – an incident needs to be created in the Safety system **Updated** – an update has been made to the AE/DM in EDC	**Status** **New –** new in Safety **Auto-Match** – matched to an AE/DM using the automatic process **Manual-Match** – matched to an AE/DM manually **Waiting for an AE/DM** – an AE/DM needs to be created in the EDC system **Updated** – an update has been made to the Incident in the Safety system

EDC Extract

This is an extract of new or updated data from EDC. The extract can work in one of two ways:

If the reconciliation system can be designed to handle duplicate data coming from EDC, then every night, the extract can run and collect all new or updated data from the past seven days. The duplicates would then be ignored. It relies upon manual intervention of the system is down for more than seven days however it is relatively simple.

To avoid the need to handle duplicates. Each extract can store the date and time it ran. The next time it runs it will start from the date time of the previous run. This reduces processing but requires maintaining a table of runs. There are also complications around EDC activity while the extract is actually running.

AE/DM Manual Filter

EDC systems typically capture any unexpected experience of a patient, good or bad. For example, a "Mild Headache" would be captured in EDC. However, these minor AEs do not normally require tracking in the

Safety system. Therefore, a manual process is required to have a Safety/Medical expert review the AE/DMs to decide if they belong in Safety.

Automated Matching

Automatic matching is possible if both systems capture the Study Number, Site Number, Patient Number and AE/DM numbers. To provide additional confirmation of the automated match, additional matching can be done using the patient's gender, date of birth and Start Date. Finally a manual review can check the descriptions for compatibility.

Manual Matching

Manual matching is then required to start from an unmatched:-

- EDC AE/DM and list possible Incidents that are possible matches based upon the information available from each system.
- Safety Incidents and list possible AE/DMs that are possible matches based upon the information available from each system.

- For example, list possible matches based on Trial, Site, Gender, Date of Birth and Start Date.

Then a medical expert has to study the descriptions of the Incidents to identify a match. If there is not a suitable match then the "Missing Incident or AE/DM" process should be followed.

If a match is found then there are two possibilities.

1. If the pair should have matched automatically but there was a problem with the matching fields.
    - For example, if the Safety system captures AE Numbers but in this case the AE Number was missing from the Incident.

    Then a request should be sent to the Safety system requesting them to update the Incident. The miss-match should then be left open until the updated Incident comes through the system.

2. If the pair could not have matched automatically due to limitations on the data available from each system.
    - For example, if the Safety System does not capture AE Numbers.

    Then the manual match should be accepted and closed.

Missing Incidents

A process is required to send details of unmatched AE/DMs to the Safety team to investigate as possible Incidents. The Safety team should contact the Site and confirm that the AE/DM is also a Safety Incident based upon the company's SOPs and guidelines.

If so, the Safety team should create it in Safety system and eventually it will come through to the Reconciliation system and close out the miss-match.

Missing AE/DMs

A process is required to send details of unmatched Incidents to the site monitor. The monitor should contact the Site and confirm that the Incident is also an AE/DM based upon the company's EDC data management plan and guidelines. If required, the site should then enter it into EDC.

After the site enters it into EDC, it will come through to the Reconciliation system and close out the miss-match.

Conclusion

With a robust, reliable reconciliation system in place, patient problems should be reported once and only once from both EDC and Safety. Regulatory requirements will be met and the sponsor will not be harmed by double counting of problems.