Paper TS04

Only Interactive Graphics Will Do

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ABSTRACT

The requirements for ongoing review of clinical trial data by physicians at pharmaceutical and biotechnology companies are growing faster than ever. Regulatory agencies are issuing guidelines on safety risk management at a time when withdrawal of medicines from the market has occurred for fears of safety. Traditional, periodic review of line listings and summary tables from data accumulating in an ongoing clinical trial is no longer sufficient for a physician.

The physicians not only require real-time access to (raw) clinical data as collected on the Case Report Form but also to the (derived) endpoints as-specified in the protocol or analysis plan. Integrating raw data from Oracle® Clinical with derived data from SAS datasets over SAS/Share® for interactive, drill-down capable graphics can be achieved with the Integrated Review application. The physicians may then review ongoing raw and derived data within a single, interactive, graphical application with little need to understand the underlying systems storing the disparate data.

INTRODUCTION

The medical review of ongoing clinical trials is required by international regulatory guidelines, for example ICH E2A, E2E and E6. During that review (amongst other tasks), the medical reviewer will be confirming that patients being recruited are of the type specified in the protocol and they will be monitoring patient safety, for example, looking for effects unlikely to be seen as a pattern by an investigator at a single site.

The obvious source for data to conduct medical review is the clinical data management system (CDMS). For many large pharmaceutical companies this means Oracle® Clinical or Clintrial™. For most drug indications, the data collected on the Case Report Form (CRF) only contains the “raw” data, so transformations and other algorithms are applied to produce the “derived” data used when summarizing in the Clinical Study Report e.g. time to first onset of an adverse event. In many companies, the CDMS stores this raw data whereas the derived data is handled by SAS and may never be stored back into the CDMS.

This leads to the questions:

- Which data source should be used for medical review?
- Can the medical review tools make it easy to cope with the volume and richness of the data?

TECHNICAL SOLUTION

Use both data sources – raw data from the CDMS and derived data from the SAS store, but most importantly, don’t force the medical reviewer to swap review tools just because the data source is different. Let them have the same graphical user interface (GUI) for both data sources.

In Figure 1 below, the reviewing tool accesses the raw data stored in the CDMS whereas in Figure 2 the reviewing tool accesses data files e.g. SAS or CDISC XML files, that have been extracted from the CDMS. This second scenario also permits accessing the derived data.

Figure 1 Reviewing Application uses Clinical Data Management System Directly

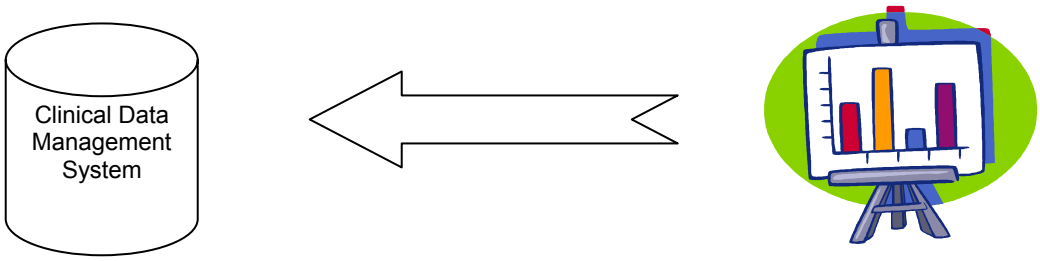
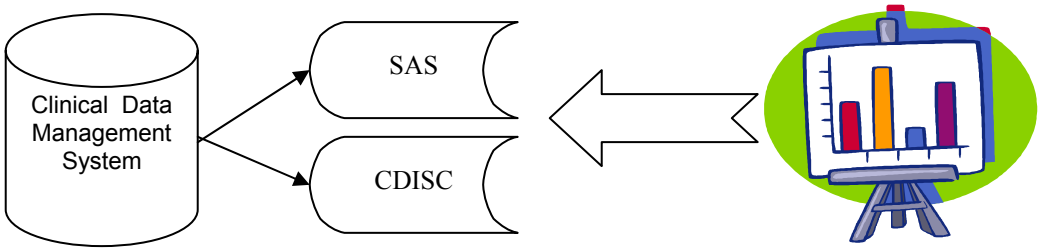


Figure 2 Reviewing Application uses Extracts from Clinical Data Management System

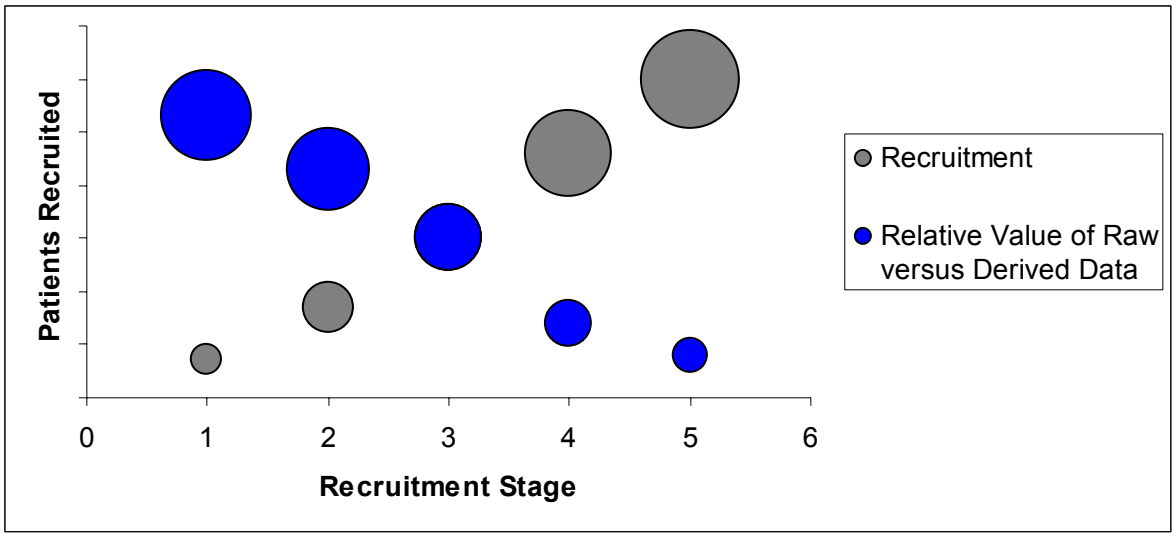


Regardless of which reviewing tool is being used, the above schematics reveal the pros and cons of the two approaches:

Access CDMS Directly	
PROS	CONS
• Real-time access to clinical data	• Data Management is often a separate function/department → less control over standardized structures of database design
	• CDMS often optimized for loading/data-entry → extraction & transformation may slow display-time for end-users
	• Physical distance between CDMS and reviewing tool could lead to slow performance
Access CDMS Extracts	
PROS	CONS
• Enforce standard data models (company or industry models) → easier to pool data across studies	• Extraction to data model requires a specification & User Acceptance Testing (UAT) stage → later in study recruitment before end-users can see even raw data

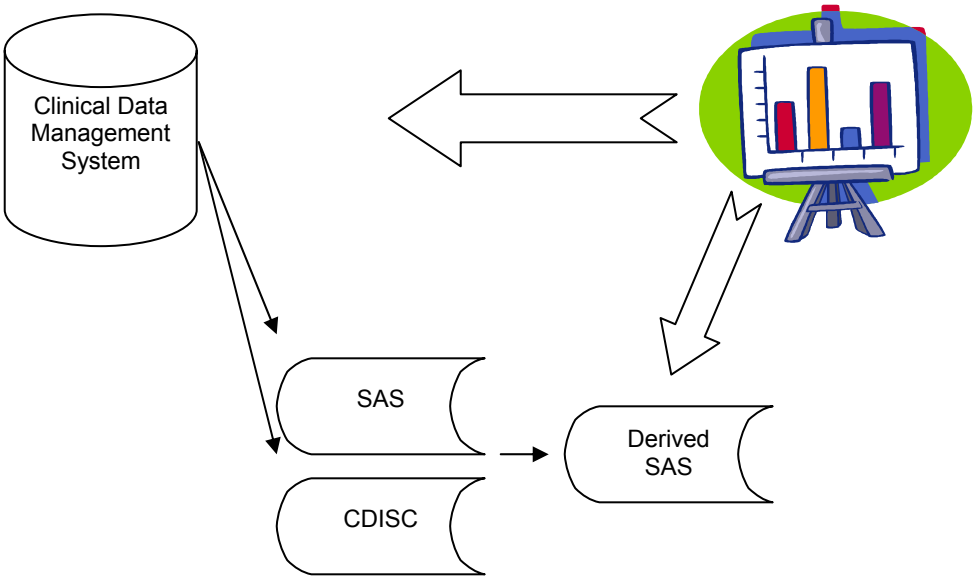
These pros and cons might lead some analysts to recommend that the medical review tool must use one or other approach, but not both. In fact, the following graphic reveals that the usefulness to the medical reviewer changes over time.

Figure 3 The Changing Importance of Raw Data with Increasing Patient Recruitment



At the start of the trial, a company physician needs to review the raw data to ensure the correct type of patients are being enrolled, so immediacy of data is paramount. This contrasts with later in the trial when a sufficient quantity of patients has been recruited to enable ongoing review of a large safety database. The medical reviewer thus needs a tool that will read CDMS when raw data is needed but can read SAS data when derived data is needed.

Figure 4 Reviewing Application uses Clinical Data Management System Directly plus Extracts

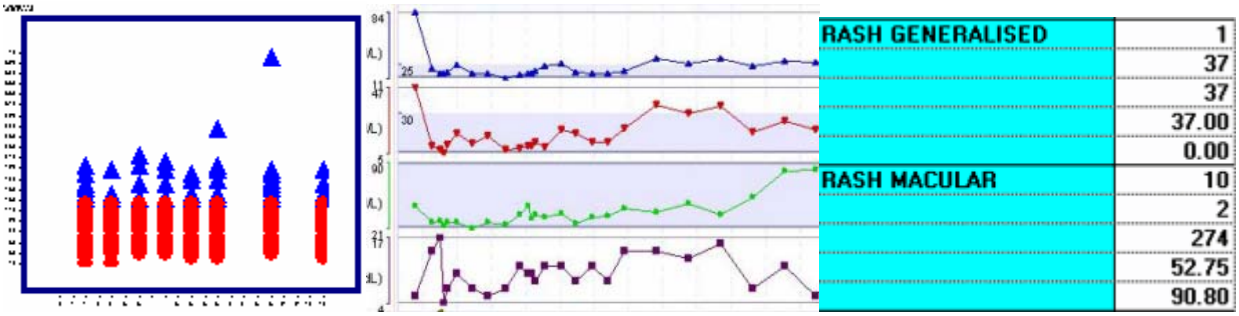


For reading the derived SAS data, we chose SAS/Share ODBC as the communication method. For Oracle® Clinical or Clintrial™ we can choose an application that understands the metadata associated with the database design. Integrated Review® from Integrated Clinical Systems Inc. supports these (and other) access methods.

IMPLEMENTATION

Integrated Review® is available as a Windows client application with a traditional Microsoft style GUI. The client application connects to a variety of database server architectures to retrieve the data requested by the graphs being used by the reviewer. Installing the client application as close as possible to the CDMS minimizes the time between request and the update of the interactive graph. This can be achieved by installing Integrated Review on a Citrix® server in the same data centre as the CDMS. Furthermore, ensuring the derived SAS data is available at that same data centre keeps retrieval time to a minimum.

In Figure 4 the connection to the CDMS is via a proprietary protocol whereas the connection to the derived SAS datasets is via SAS/Share. The medical reviewer is thus able to run interactive graphs, tables and listings based on the raw data from the CDMS at the start of the study and then once the SAS datasets become available run reports based on the derived data too.



The end-user can choose to run reports at any time and if there are points of potential interest the end-user can drill down to reveal more data. For example, drill down from a barchart of adverse events to discover which patients have reported a specific event then easily review their laboratory data in another window.

CONCLUSION

SAS/Share in conjunction with Integrated Review® can be used to bring together raw and derived data so that a medical reviewer can perform interactive review of clinical trial data without the need to fully understand the underlying systems storing the disparate data.

REFERENCES

CONTACT INFORMATION

Your comments and questions are valued and encouraged. Contact the author by email (masked to minimize spam) at:

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