

Integrated Clinical Data with Oracle Life Sciences Applications

An Oracle White Paper
October 2006

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EXECUTIVE OVERVIEW

Even the largest pharmaceutical companies with extensive IT resources have struggled to produce an integrated eClinical solution. Forrester Research, in an article entitled 'Clinical Trials' EDC Endgame' states: "the market's desire for simplified integration and improved collaboration across the clinical trial process is driving EDC vendors to develop broader eClinical suites that combine EDC with data management, trial and site management, safety monitoring, and workflow capabilities."

This white paper discusses Oracle's integrated eClinical suite that is scalable for all companies. As Forrester states: "The firm's long history and the wide deployment of Oracle Clinical CDMS have become the thin end of the wedge for a broad eClinical suite."

INTRODUCTION

Data is central to the whole clinical development process. Clinical data is one of the most valuable assets to a pharmaceutical company. It serves as a basis for submission, approval, labeling and marketing of a compound. Without good clinical data - well organized, easily accessible, thoroughly documented data from well designed trials - the value of a drug may not be fully realized (1). Disparate databases from a variety of systems make it difficult to obtain an overall view of the data. One study has shown that the industry spends \$156 million annually to support data transfer between systems or organizations (2).

Major pharmaceutical companies have tried to develop in-house integrated solutions, but they seldom fulfill their original promise. These integrated internal systems bring risks such as failing to keep pace with technology and waiting years for full implementation before realizing the benefits.

CURRENT SYSTEM COMPLEXITY

Clinical Trial data can come from a variety of sources: subject-investigator interaction at sites, laboratories, and directly from subjects and partners (e.g. Contract Research Organizations - CROs). Data directly from subject-investigator interaction could be collected using Remote Data Capture (RDC) technology.

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These systems frequently have their own database and must be integrated with the central Clinical Data Management (CDM) system.

Safety, or adverse event data, can come from an equally diverse range of sources such as reports from clinicians, pharmacists, patients, literature, clinical trial data and registry. These events are collected in systems specifically designed to handle the reporting and tracking requirements for this data. Adverse event data from clinical trials must then be reconciled with the adverse event data in the CDM system.

Medications and adverse events recorded in the CDM and Safety systems must be coded against standard dictionaries or nomenclatures before reporting, examples include MedDRA for adverse events and WHO Drug for medications.

As a result, companies often have multiple systems to handle the core data and trial activities associated with clinical development. These systems are critical to every pharmaceutical company, and must be developed in-house or purchased. These systems will not be integrated unless the company invests significant resource in building bespoke interfaces. Figure 1 illustrates a classic clinical development architecture:

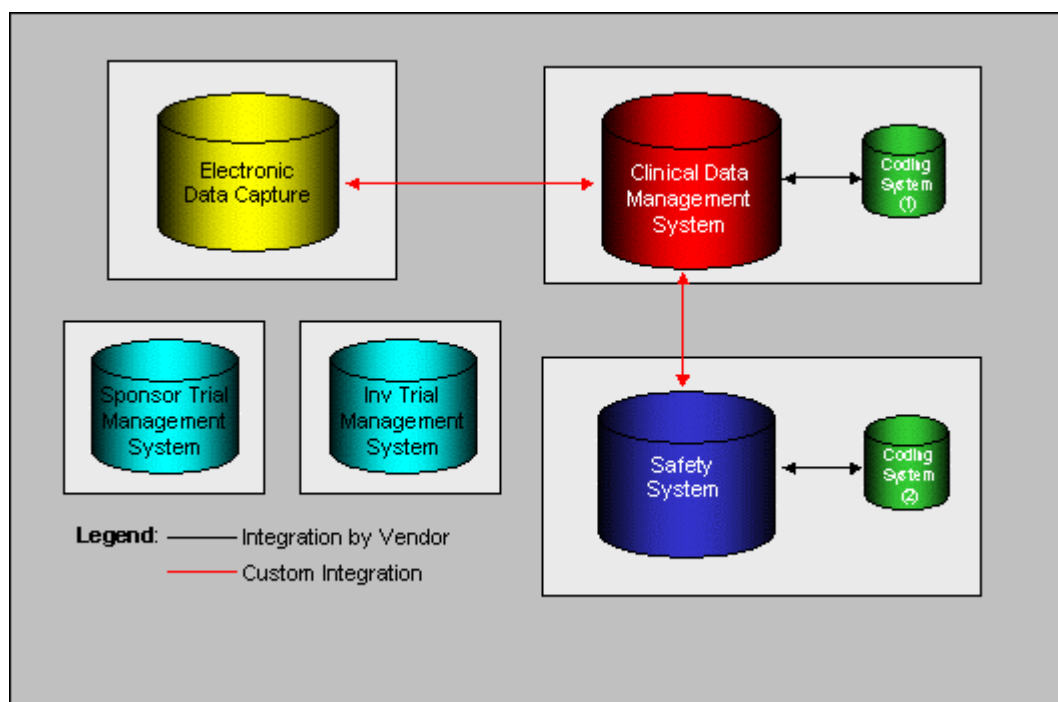


Figure 1: The architecture of core systems used in clinical development by a typical pharmaceutical company. The CDM and Safety systems both use coding systems. These are usually different systems, which software vendors have integrated as part of their products. The EDC data must integrate with the CDM system. Some EDC software vendors boast integration with CDM systems, but the integration is often incomplete and unsatisfactory. The clinical adverse events must be reconciled between the CDM and Safety systems. At best this is achieved by writing a custom interface between the systems, however typically paper printouts are produced from each database and the data is cross-referenced manually. Sponsors and Investigators have their own standalone systems to manage the clinical trail from their individual perspective.

Initially, the system architecture in Figure 1 looks simplistic and quite attractive from an integration perspective. However a closer look shows the costs and complexity associated with this architecture.

Dictionary Management

Standard terminologies used by the coding systems are updated on a regular basis. Handling multiple dictionary versions is a complicated process. Data must be traceable to the dictionary version it was coded against. One database could have five or more active versions of a dictionary that are being used for coding. Using two different coding systems doubles the complexity of handling multiple dictionary versions.

Industry best practices suggest clinical data should be coded the same way across all applications. If an adverse event of 'Pain in Head' is coded to 'Headache NOS' in the CDM system, then it should be coded the same way in the Safety system. This consistent coding is extremely difficult to achieve with two different coding systems.

Adverse Event Reconciliation

The clinical adverse events collected in the Safety system must be reconciled with the adverse events in the CDM system. Historically Safety systems and CDM systems were developed separately. Vendors did not consider the need for reconciliation of their data with other databases and is difficult to incorporate this functionality in mature systems. This has resulted in few Safety systems and CDM systems capable of automatically reconciling their data. Pharmaceutical companies usually produce a report of clinical adverse events from the Safety database and the CDM database, and then reconcile the data by hand. This introduces a time-consuming and error prone process that would not be needed given an integrated eClinical solution was in place.

EDC and CDM Integration

CDM systems have been used in clinical development for a number of years. Their function has been to collect and clean the data from clinical trials as quickly as possible. The data usually comes from two sources; paper CRFs (Case Report Forms) and electronic files from laboratories. The paper CRFs are hand entered into the database, whereas the laboratory data is batch loaded in a flat file format.

For years the industry has been trying to collect patient data electronically at the source, i.e. the investigator enters the patient data into an 'eCRF' rather than a paper CRF. This has been termed electronic data capture (EDC), remote data capture (RDC) or remote data entry (RDE). The goals are to speed the data collection and data cleaning cycle, thus reducing time and money spent on drug development.

A large number of software companies have built EDC solutions, as this was touted as the next revolution for pharmaceutical companies. These software

companies only produced EDC solutions and thus built their solutions as standalone systems. It was only later they realized that EDC systems must integrate with CDM systems. Future attempts by these software companies at integration have often proved to be insufficient and cumbersome.

ORACLE'S SUITE OF INTEGRATED SYSTEMS

The discussion above shows the complexity of using systems from different vendors for clinical development. Oracle has built the first fully integrated suite of applications for clinical development. The products can be deployed individually or together allowing for incremental growth for existing customers or a full eClinical suite for new customers. All the applications have been designed with integration in mind. Figure 2 shows the architecture of the Oracle Life Sciences Applications.

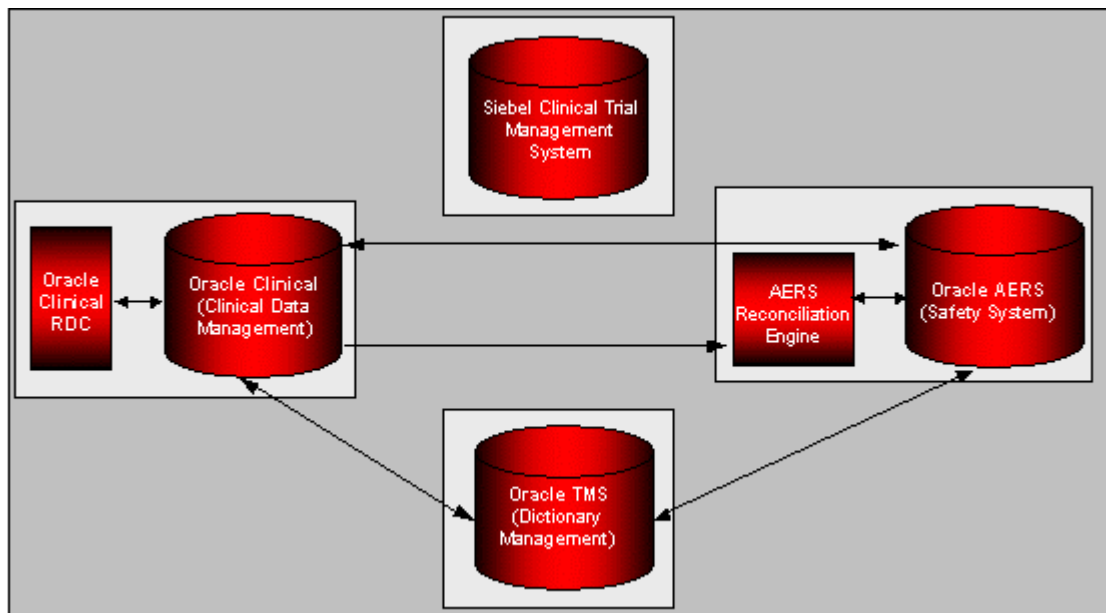


Figure 2: Oracle Life Sciences applications integrated architecture. Clinical trials are setup and operationally managed by the Sponsor/CRO from Oracle-Siebel Clinical Trial Management System. TMS is the central coding system for both CDM and Safety systems, thus providing consistent coding. Oracle AERS pulls AEs and metadata from Oracle Clinical thus reducing reconciliation effort. The AERS reconciliation engine compares the CDM and Safety databases and flags any differences in a report, thus reducing reconciliation time and effort. Oracle Clinical RDC is a different front end on Oracle Clinical. Data entered through Oracle Clinical RDC goes directly into the same tables as data entered from Oracle Clinical. Oracle Clinical and RDC also use the same data definitions, screen layouts and edit checks.

Oracle Clinical – Clinical Data Management

Oracle Clinical provides the life science industry the most integrated Clinical Data Management (CDM) and Remote Data Capture (RDC) application on the market while also providing 'Best of Breed' CDM & RDC applications. Oracle Clinical was built based on hundreds of companies all having extensive experience in conducting clinical trials thus giving Oracle Clinical an essential industry perspective. In the commercial software marketplace for Clinical Data Management

solutions, most vendor offerings consist of separate applications for the design, analysis and workflow processes of Clinical Data Management and the data collection and ease of use characteristics of Remote Data Capture. Oracle Clinical/RDC provides a single application architecture for both CDM and RDC. Oracle Clinical/RDC provides additional functionality in key areas such as integration, data collection, localization, reporting, and especially ease of use.

Oracle TMS - Dictionary Management

Oracle Thesaurus Management System (TMS) was specifically designed to handle the complexities of MedDRA. These complexities include the multi-axial hierarchy of the dictionary, and six monthly updates requiring version control. However, TMS can now handle any dictionary or thesaurus, and some companies are using TMS to manage more than 100 dictionaries.

Upon installation, TMS is integrated with both Oracle Clinical and Oracle AERS. However the open APIs (Application Programmable Interfaces) allow for easy integration with other systems. The integration ensures that you are coding in a consistent manner across all your systems, because all your data will be coded against the same dictionaries, and coding decisions will be applied across all your systems and databases.

Oracle AERS - Adverse Event Reconciliation

The recent Vioxx tragedy has spurred Congress and the FDA to impose further safety mandates upon the drug industry. Oracle AERS is one of the leading adverse event tracking and reporting systems with over 60 customers using the system to record adverse events encountered in clinical trials and post-marketing settings. Oracle AERS gives pharmaceutical companies the power to store and monitor all serious adverse events so that safety concerns can be addressed before a drug reaches the market. It is the only Safety system that is fully integrated with the leading CDM System – Oracle Clinical.

Oracle AERS pulls adverse event information from the Oracle Clinical database to Oracle AERS, therefore preventing duplicate effort and possible database discrepancies. If the details of a clinical adverse event reach the Safety department before the data has been entered into Oracle Clinical, then the users can pick the patient and investigator information directly from the Oracle Clinical database, thus reducing possible discrepancies.

It is still possible for discrepancies to appear between the two databases if, for instance, an adverse event is updated in one database and not the other. The AERS Reconciliation engine identifies any differences between the AERS database and the CDM database. Any differences will be shown on the Reconciliation Report and entries will be made in the Oracle AERS Discrepancy Database.

As with TMS, Oracle AERS has an open API architecture allowing for integration with other CDM systems as well.

Oracle Clinical RDC - EDC & CDM Integration

Oracle Remote Data Capture (RDC) is built upon the same data model as Oracle Clinical. This brings many benefits as the same data entry screens and edit checks are used by Oracle Clinical and Oracle RDC. Mixed mode trials become simple, as the data entered through RDC is stored in the same tables as the data entered through Oracle Clinical. There is no duplication of effort because the study only needs to be defined once in Oracle Clinical and then available to both applications. Oracle RDC can leverage all the power of a CDM back end and a fast setup of trials is possible by using the Oracle Clinical Global Library. CRFs designed in Oracle Clinical can be made available in RDC instantly via the tight integration between Oracle Clinical and Oracle RDC. Deploying Oracle RDC as your remote data capture product will result in reduced training time for environments already using Oracle Clinical. Via the Oracle RDC and Oracle Clinical integration, lab data can be captured and surfaced in Oracle Clinical and displayed in the RDC interface.

Oracle-Siebel - Clinical Trial Management System

Clinical trials are increasingly global in nature, conducted concurrently across multiple geographies. Making trial information accessible to the right people at the right time with the right level of detail becomes ever more critical. Siebel Clinical Trial Management System enables global clinical organizations to maintain a centralized trial management database while providing a user with the most relevant and appropriate information based on their specific roles and responsibilities. Thus, real-time trial information is available not only to clinical research associates managing individual sites, but also to regional managers responsible for geographic areas as well as global trial managers managing global trials. Armed with the most current and relevant data, clinical users are able to spot problems earlier and take corrective actions sooner, thus reducing overall trial costs.

Identifying the investigators with the right subject demographics is a critical first step. Investigators with outstanding track record on meeting enrollment and performance target bring tremendous value to clinical organizations. Competition to secure the service and loyalty of these prized investigators has intensified in the past few years. Leading clinical organizations have started applying the CRM paradigm to manage interactions with their investigators. Using Siebel Clinical Trial Management System as a centralized repository for all investigators, customers can collect and track all relevant information about their investigators, from personal profiles to disease specialties, from past trial experiences to current trial performance. By analyzing the comprehensive investigator data, clinical organizations are able to identify the investigators most suitable for a trial.

Furthermore, Siebel Clinical Trial Management System can be used to provide personalized services to investigators by facilitating communications to the study team and by providing timely and accurate payments to investigators. The results are improved relationships with investigators, faster enrollment, better trial quality, and lower trial costs.

Siebel Clinical Trial Management System Document Tracking provides clinical research associates with an efficient alternative to track regulatory and other study documents during various stages of the trial spanning from site initiation to site closeout and at various levels from site to country to protocol. Workflows and alerts available as part of Siebel Clinical Trial Management System allow relevant users to be notified for specific interventions such as document review or renewal.

Siebel Clinical Trial Management System activity management provides clinical research associates with a powerful tool to actively maintain contacts with sites, and to manage issues through to resolution. Using Siebel Clinical Trial Management System trip report tool, clinical research associates can schedule site visits based on investigators availability, site enrollment, or completed work. Pre-built visit report templates help drive consistent business processes based on regulatory mandates and companies' standard operation procedures.

Siebel Clinical Trial Management System also provides an easy and efficient way to create and submit visit reports. Using various productivity tools within Siebel Clinical Trial Management System, several leading pharmaceutical, biotechnology, medical devices, and contract research organizations have reported improved process efficiencies, thus significantly improving clinical research associates' productivity.

ORACLE'S BROAD eClinical SUITE

Oracle has delivered to the marketplace the most integrated suite of applications for clinical research and development. Oracle took many of the core applications used by companies conducting clinical trials and made them fully integrated. There are still a variety of other applications that companies use to support the clinical trials process. These applications still require integration with the core clinical applications.

To facilitate the integration of this disparate data, Oracle has developed the Life Sciences Data Hub (LSH). In basic terms, this is a validated data warehouse designed specifically for the Pharmaceuticals industry. LSH brings data together from a variety of applications into one central location facilitating analysis and reporting.

LSH has knowledge of the Oracle Life Sciences Applications and can be taught the knowledge of any other database supporting the clinical development process.

Consolidating clinical data into one central location is advantageous when it comes to both analysis and reporting.

Forrester Research states: “Pharma firms looking beyond data capture are thinking about eClinical technology as a platform investment, not a point solution.” This same research organization has acknowledged Oracle’s eClinical Suite as the leader in the market as far as the breadth of the eClinical suite and coherence of suite architecture. The dream of an integrated eClinical Suite is now a reality. Oracle’s eClinical Suite is currently available and being used by the world’s largest pharmaceutical companies running the largest clinical trials.

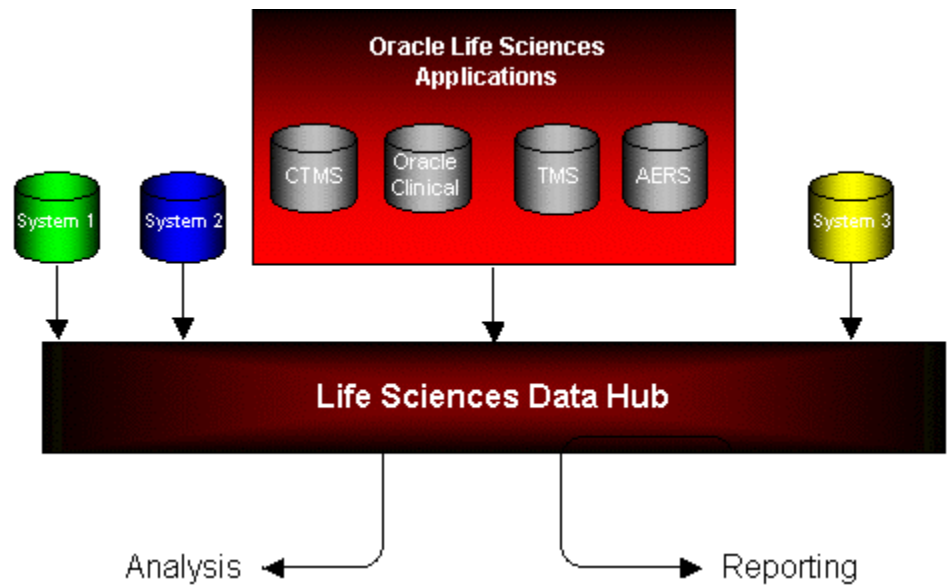


Figure 3: The Life Sciences Data Hub (LSH) will take data from all applications supporting the clinical trials process and consolidate the data for reporting and analysis.



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