

ISSUES WITH STANDARDIZATION OF SOFTWARE DEVELOPMENT IN PHARMACEUTICAL MANAGEMENT

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ABSTRACT

Reliability and continued use of software components are ongoing issues in pharmaceutical industry. There has been little done to standardize Data Management development processes. The primary goals for Global Integrated DataBase(GIDB) is to reduce or eliminate problems of data definition discrepancies during data management support for clinical trials. Once the work on the front-end is streamlined and structured, the back-end will follow. But the primary benefit of establishment of more effective Data Management, is the ability to attract more business due to having methods to support clinical Data Management.

Keywords: Pharmaceutical Data Management, software reusability, contract research, global database

INTRODUCTION

Software development is still plagued by a low degree of reusability, inconsistency in data definitions, and lack of comprehensive standardization of processes(2, 9, 11). Delivering quality in systems eliminates rework. It is estimated that US organizations loose \$85 billion revenue due to system downtime(3). Reliability has to be integrated into the application development process and built into the business plan.

Many traditional engineering disciplines have scientifically mastered its methods and approaches including modular reusability, deriving the creativity of new designs from existing knowledge repositories. Chemical engineering is an example of a field where standardization and scientific models set the pace for new development.

Creativity in software development results in non-standard approaches to software development rather than reusing the existing software modules. To enforce comprehensive standard development processes Computer-Aided Software Engineering(7) and Case Based Reasoning (CBR) (4, 6, 10) methodology, which enforce and promote software reusability, have been brought to developers.

Reusability and standardization do not come with the purchase of the latest technologies. To achieve this goal many companies re-define established processes, re-write Standard Operating Procedures (SOP) and Working Instructions (WI), and establish internal cultures that promote software reuse. Many pharmaceutical companies this can be noticed in Drug Research and Development Business Units and, more specifically, in Data Management (DM) areas where the most intensive software development takes place.

DATA MANAGEMENT IN PHARMACEUTICAL INDUSTRY

With the help of the latest industry software products, large pharmaceutical companies are successfully applying and using standardization in their day-to-day work. However, smaller drug producers and pharmaceutical Contract Research Organizations (CRO), are still lagging behind. DM's primary responsibility is to support data management for clinical trials conducted during drug research. DM is also delegated with the responsibility to prepare the largest portion of documentation being furnished to the FDA during the approval submissions. There may be several groups in a DM department, and once a DM project has started, the work is passed on from one group to another. Therefore, all groups have to work in close cooperation in order to achieve the ultimate deliverables.

Many pharmaceutical companies have offices in different countries, with networks connected to their development sites. Most utilize industry-specific software application packages which are designed to help DM professionals do their work (1, 5, 8). These packages are geared for a client-server network architecture including web-based features and capabilities(Fig. 1).

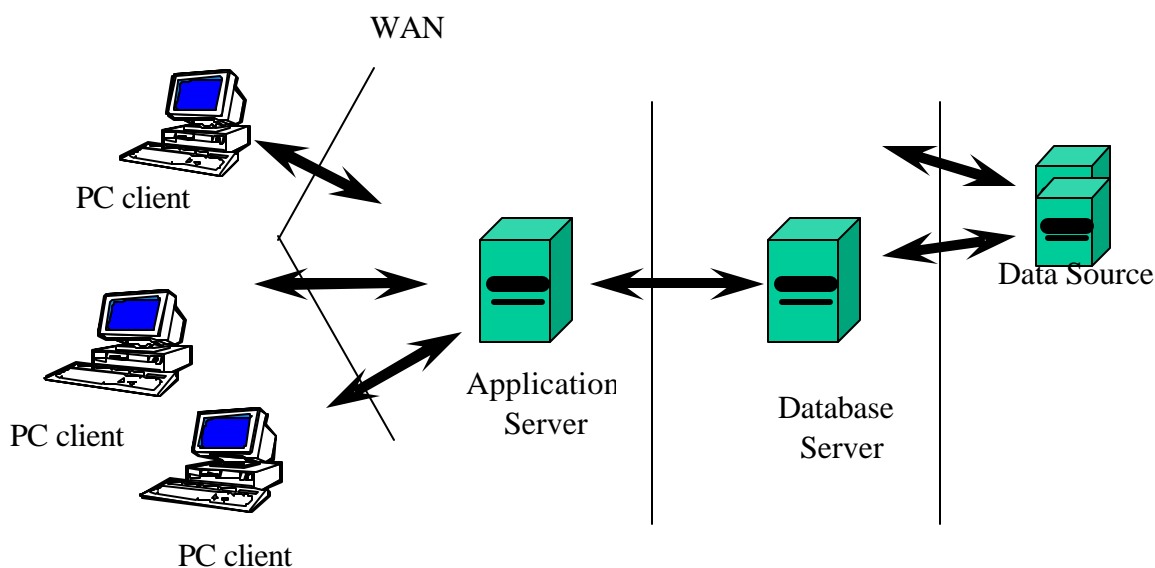


Fig. 1 Client Server Architecture

With the help of software development tools, such an establishment can be initialized, implemented, and promoted at any company. However, there has been little done to standardize DM development processes in many pharmaceutical CROs. They still lack the comprehensive development methodologies geared for software reuse. Using the experience and knowledge accumulated by DM, such companies' DMs can evolve in the direction of totalitarian standardization of their internal processes.

DATA MANAGEMENT ARCHITECTURE

Most pharmaceutical companies use clinical application packages for their DM work. Although these packages provide comprehensive support for DM, they have very different internal architectures, interfaces, and functionality. Such dissimilarities require different approaches taken by DM units of the companies toward standardization. We looked at two industry standard packages that consists of several highly integrated modules, each module capable of running independently of the others. These modules actually represent DM's functions performed during clinical trials. For example, their Design, Manage, Resolve, or Retrieve imply much about what kind of DM work is being accomplished by these modules.

There are logical and physical objects used to implement and manage a clinical study database. Logical levels of granularity are an item, a panel, a protocol (owner), a page section, page template, and the study book. The physical objects are an item and table. The logical objects are needed in order to design the software interface used during entering of clinical data. But all logical objects are created only after the database physical objects are implemented. The physical objects nominate a protocol to be an owner of the lower level objects, panel and an item and, are created first. The logical objects do not constitute the database itself and can be modified without any impact on the underlined database. Such an independence of logical and physical layers together with logically oriented de-normalization of the database itself provides a very flexible, robust, and easy to work with structure of clinical software package.

There are other independent objects that are instance-shared, rather than owned by a protocol. Two of these objects, for example, are code lists and coding thesauruses, which are implemented to enhance data collection and eliminate data entry errors. However, it does not have a central repository or global library where all data definitions are stored. Instead, all data definitions are owned by a protocol which claimed the ownership on everything it internally stored. With such internal structure, each protocol has to have all data definitions within itself and, therefore, much data redundancy and inconsistencies among data can be expected. How may standardization of data collection be possible if the application tool itself does not directly support it?

GLOBAL INTEGRATED DATABASE (GIDB)

The primary goal for GIDB is to reduce or eliminate problems of data definition discrepancies during data management support for clinical trials conducted in different countries. For instance, in the US, patients' height/weight data is collected in inches/pounds, while in European countries such measurements are represented in centimeters/kilograms. If integrated without a special pre-processing, such databases may deliver much confusion. In order to enforce the GIDB standards and cascade them down on the sites Global Project Data Managers must ensure that the DM be conducted in consistent and standard ways.

A single project might include clinical studies in different phases for several years. Since every project had its own test drug, it is possible to identify most of the clinical measurements necessary by identifying potential data points from the inception of the project. Although data items might vary and collected measurements change, the core data points should always be consistent in every study. Therefore, it is logical to create a central repository for a project

where all core and some auxiliary data definitions are stored so all project studies could reuse them.

For some companies, solution to more efficient software development would not be possible without concentrating on all DM activities and efforts toward standard practices. During database build, DB programmers ensure that database object names matched SAS object names which are used by SAS programmers once databases are downloaded and converted to SAS data sets. For SAS programmers no additional mapping and other modifications are necessary. Once SAS part of DM had been accomplished, the data are passed to the statistical programmers.

It can be seen that each of the links in a DM chain benefited from reusability and established common rules in data processing. With DM processes structured and integrated the company can successfully meets the FDA's requirements about quality of data gathered with low Acceptable Data Error rate.

TO LEARN, ADOPT AND IMPLEMENT

These processes and practices clearly demonstrate a significant effort toward standardization on the front-end development. DM activities are integrated in the highly cooperative process and such a well-defined structured approach shows significant benefits of reuse.

Many clients require total compliance with their internal data management standards, and dictate which development strategies should be used. For instance, some clients require the company to create a client domain and conduct all DM software development there. During development, no object can be copied down from another domain. This may cause tremendous overhead of the same or similar data definitions. Similarly, in some packages, there is no project level protocols defining core data objects for studies and database development occurs without relying on any standards other than those required by clients. On the other hand, some other clients do not have specific development requirements and the reuse of pre-defined data definitions becomes possible, especially when it is already encouraged. All these objects may be identified, for example, in specifically created domain, and therefore, clients will not have to worry about any references to their rivals. Of course, the other DM components have to be 'in sync'.

CONCLUSION

The Global Librarian has to use the experience accumulated within the company and identify the objects which will become the first core library objects. Simultaneously, the CRF designs need to be standardized and a naming convention schema should be established to serve as guidance for any new objects. Once the work on the front-end is streamlined and structured, the back-end will follow. Various methods of standardizing DM support can be used as well. Once all DM practices are established, the speed and quality of the overall software development will increase. Although many pharmaceutical CRO companies have more than one set of internal DM practices, they can still well benefit from redesigning their current approaches to the software development. Since many of them have all the necessary components, the human and technological, they will likely succeed in identifying standard system development requirements and implementing the software engineering orientation established for the global data

management. Using accumulated knowledge from the industry experience, pharmaceutical CROs can speed up the Drug Research and Development, which will help bring a better medication to all clients.

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