Introduction

This paper is a progress report which describes how a clinical information system was developed and approved at SYNTEX Corporation. The system is intended to make medical research data available to monitors of clinical studies. The theme presented here is how this was accomplished at SYNTEX using not only SAS/AF, but also the sample menu system software provided with SAS/AF. By modifying the sample menu system software, it was possible to develop a Clinical Data Review System prototype, and to gain approval for further development. This was accomplished with a minimum of programming time and effort. The rationale for using SAS/AF software at SYNTEX is that it provides the programming leverage to serve numerous end users of clinical data. During the coming year, the system will evolve into a full-scale production version.

Background

The goal of a Clinical Data Review System is to enable people with little or no computing experience to review medical research data in an interactive computing environment. At SYNTEX, there is a need for up-to-date information on large amounts of drug safety and laboratory data collected during the course of clinical trials. With such information readily available, a study monitor could identify patients at risk, and recommend early termination and/or alternative treatments if necessary.

At SYNTEX, monitors currently review individual case report forms and standardized data listings, communicate with the trial investigators, and perform interim study analyses. These tools are time-intensive, and restrict the number and complexity of the monitors’ questions. Monitors need quicker access to the data.

An interactive environment would be well-suited for this type of task because of the short turn-around time between the formulation of a clinical data question and its answer. Interactive access to large amounts of clinical data would allow a study monitor the flexibility to ask more questions about the data. The monitor could gain a better "feel" for the data being collected in any given study.

Prior to the SAS/AF based Clinical Data Review System, there was no efficient way for many monitors to access the clinical data base. Providing such access would have involved a prohibitive amount of programming resources. A new approach to data processing was required.

The Bioanalysis Department, the major SAS user at SYNTEX, had an idea. By using SAS/AF to develop a prototype, the feasibility of such a system could be demonstrated to upper management. This would be done with a minimum of strain on the department's programming resources. If such a demonstration succeeded, the department would probably get the go ahead for development of a full-scale Clinical Data Review System.

The SAS/AF sample menu system would be an essential component of the prototype Clinical Data Review System. By modifying and adding to the SAS/AF sample menu system it would be possible to develop a prototype Clinical Data Review System with a minimum of programming time and effort.

How The Prototype Review System Was Built

The development of the prototype Clinical Data Review System consisted of five steps: copying the SAS/AF sample menu system software, creating a TSO CLIST to execute the system, extracting data from the clinical information data base, developing SAS programs to subset and reshape the extracted data, and modifying the sample menu system.

1. Copying the SAS/AF sample menu system.

SAS/AF documentation includes useful information on copying AF programs. After old and new libraries are allocated, a simple PROC BUILD statement with appropriate CATALOG and MERGE references creates a new copy of the SAS/AF menu system. In order to do this, it is necessary to know where the original menu system resides in one's computer system and to have information about the space needed to allocate the copy for the library.

2. Copying the CLIST to execute the SAS/AF sample menu system.

At SYNTEX, SAS/AF runs under TSO
and a CLIST to execute the menu system needed to be built. SAS Institute provided a CLIST to accompany the sample menu system and at SYNTEx this CLIST was copied using ISPF and subsequently modified.

3. Clinical Data Extraction

Input data for the menu system was retrieved from an IDMS Data Base using special procedures written at SYNTEx. The data was then input to a SAS program in order to create a SAS Dataset.

4. Reshaping SAS Datasets for Input

To use the SAS/AF sample menu system with relatively few modifications, it was necessary in some instances to reshape the clinical data extracted from the data base. For example, one of the users of the menu system wanted to display the ages of patients in terms of ranges. A simple SAS program was needed to prepare extracted data to meet this special requirement. In general, there was an unavoidable need to write special front-end SAS programs for all clinical studies. As will be seen below, future development of the menu system will shift the burden of meeting special user-defined requirements from programs developed outside the menu system to general purpose tools existing within the menu system.

5. Modifying the SAS/AF sample menu system.

The prototype Clinical Data Review System at SYNTEx had to meet some specific user requirements. Some of these could be met by deliberately reshaping input data, as mentioned in section 4 above. Nevertheless, it was also necessary to go beyond the capabilities of the sample software provided by SAS Institute.

Three categories of software changes evolved as the system developed. First, it was necessary to make some textual changes to menus and also to the automated titles which initiate the menu system. The other two kinds of changes were more substantial. These involved changing the form in which user-requested data is displayed, and also making graphic capabilities more powerful.

For example, to make data listed at the terminal more readable, it was decided to use PROC FSPRINT. This made it possible for users to select and to track output variables of special interest.

In addition, all graphic procedures were converted over to SAS/GRAPH. After this conversion, changes to the software consisted of color enhancements and also BY-group processing capabilities for user-selected graphs. In addition, the G100 option was added to some of the graphs in order to present data in the required form.

Several other changes of this kind were made to the sample system. Although relatively simple in nature, these changes, taken together, produced a greatly enhanced menu system which enabled the SYNTEx users to form a very positive impression of SAS/AF as applied to the review of clinical information. Relatively little programming time was needed to accomplish this result. Two purposes were served by following the course of modifying existing software. First, a system was developed quickly, which would be demonstrated to users and to management. This helped to educate these groups of people about the capabilities of the SAS/AF product. Second, programming staff with no previous experience in SAS/AF were able to learn quickly how to use the SAS/AF system, indeed more quickly than if an entirely new menu system had been built from scratch. Developing the Clinical Data Review System beyond the prototype stage will require more sophisticated SAS/AF techniques, and can build on a good foundation.

Future Directions

Following the approval of the prototype Clinical Data Review System, work has begun on developing a full-scale production version. Some of its requirements are already apparent. These fall into two main categories: refining the system’s computer-based training and help facilities, and enhancing its programming capabilities.

1. Computer-based Training

One of the outstanding features of SAS/AF software is its built-in help facilities which range from global help for the entire system, to specific help for a single field on one screen. The sample menu system’s help screens were intended to be all-purpose in nature, and of course in some cases are not appropriate to applications at SYNTEx. For example, the sample menu system’s help facilities are often directed toward teaching users about SAS. In the production version Clinical Data Review System, however, users are more likely to need help about medical research data and how to monitor it.

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As a result, a top priority for the production version system is to develop help facilities and computer-based training which will be oriented specifically to needs at SYNTEX. This is especially important for new users who are totally unfamiliar with computers and programming. The Clinical Data Review System must be designed and built in the closest possible coordination with the user community.

2. Enhancing programming capabilities

The sample menu system, provided with SAS/AF software, could not possibly anticipate many of the specific data processing requirements inherent in clinical data monitoring. Many of these requirements have to do with the ways in which the data is stored on the clinical data base. For example, clinical data is entered from many different forms, and there are many problems associated with being able to synchronize data from these forms. The same data may have different SAS variable names, depending on which form is being referenced.

Such differences can cause obvious problems in processing the data. Plotting a variable from one point to another is impossible if the variable’s names differ from form to form. This illustrates a problem which is inherent in the clinical data itself and which exceeds the capabilities of the sample menu system. New program screens need to be developed which will be geared specifically to the data base environment at SYNTEX and to the specific analytical requirements of our users.

What the sample menu system does teach us, however, is that it is highly desirable, wherever possible, to create generalized programs. In a similar way, the Clinical Data Review System will strive to serve as many different users as possible and with as few separate processing paths as possible. After all, one of the attractive characteristics of SAS/AF is its leverage. That is, instead of a many-to-many programmer/user relationship, SAS/AF permits a one-to-many relationship. Such a relationship can only be achieved through a conscious design effort as was done in the sample system. What is important, therefore, is not to copy the code of the sample menu system, but rather its spirit and its intent.

There are numerous other features of the production version which will be added. These include providing hard-copy graphics output, and developing an interactive link between the Clinical Data Review System and the clinical data base. Such refinements are under consideration is rather astonishing considering that a year or so ago, prior to the release of SAS/AF, even a much less sophisticated system would have consumed an unreasonable share of the Bioanalysis Department’s resources.

Summary and Conclusions

Prior to the release of SAS/AF, the possibility that a Clinical Data Review System could be developed by the Bioanalysis Department was remote. At that time, clinical data monitors were relying on tedious and resource-intensive methods for reviewing medical research data. This was creating a potentially serious problem, affecting more than the resources of the monitoring staff. As pharmaceutical compounds become more complex, so too does their analysis. Drug safety and efficacy, always of considerable importance, must be determined in an increasingly complex environment.

At the same time, the manpower resources of the Bioanalysis Department were not available to provide an expanding staff of medical research monitors with the help they would need to determine safety and efficacy of a growing number of compounds. SAS/AF solved the contradiction between the growth of user requirements on the one hand, and the limitation of programming resources on the other. By using a slightly modified version of the SAS/AF sample menu system, it was possible to build a prototype review system. The prototype system served two purposes simultaneously. First, it showed the medical monitoring staff that they had a way to access and analyze important data quickly in a new environment.

Second, the prototype demonstrated to management that the Bioanalysis Department could meet the needs of many users without straining its own resources. SAS/AF provided the leverage necessary to satisfy both needs simultaneously.

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