CLINICAL TRIAL MANAGEMENT USING THE SAS SYSTEM

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SUMMARY

We have designed and used a system to manage clinical trials of investigational drugs using a CMS data base, an INQUIRE data base, and a series of SAS programs. This system will generate listings of subject status and number; side effects sorted by organ system, date, or study; the number of subjects in each study for various time periods; and projected visit dates.

INTRODUCTION

Management of clinical trials of investigational drugs is often problematical. Typically, such clinical trials involve hundreds of subjects who have been entered into the trial in a staggered sequence. Thus, while some subjects are approaching the end of their participation in the trial, some are just beginning their participation.

Accurate and efficient management of the trial requires day-to-day access to information regarding the status of subjects entered into the trial. This includes the number of subjects entered, completed, discontinued for drug unrelated reasons, and terminated for either drug-related adverse experiences or for lack of drug efficacy. The type, severity, and date of adverse experiences are also needed for internal project management and for ethical reasons (such as the possible need for early termination of the trial).

In the beginning, we tabulated such information manually for ongoing studies in a large clinical project, and found the process quite tedious. We then automated this process to increase the accuracy of recorded information, make the information available for status reports, and increase the overall efficiency of project management.

DATA BASES

Two data bases are utilized in this system. The primary data base is a CMS file (STATUS1 DATA). This file contains information on subject status and side effects. It has a logical record length of 132 characters. Variables are study number, investigator name, subject number, status in study (ongoing, completed, discontinued, terminated for lack of efficacy, or terminated for toxicity), and an open comment field. Included in the status variables are a "continuation" code for subjects terminated for lack of drug efficacy who were continued in the study after the addition of a second drug, and a visit number at which the discontinuation or termination occurred.

Reports of adverse experiences must be entered at the beginning of the comment field, with the affected organ system listed first, followed by the date of occurrence (in DATE7 format, with 31DEC99 for unknown dates) followed by a brief description of the adverse experience. Other key words which may be entered anywhere in the comment field are:

1) names of the second drug (DRUG2A or DRUG2B) added to the regimen of terminated subjects described above.

2) a notation regarding any notification that may have been made to the human subjects Institutional Review Board (IRB) or the FDA (Form 1639) of any serious adverse experiences.

The second data base is an INQUIRE system (INQUIRE DATA). Information regarding each subject-visit is entered into this system by field personnel.

PROGRAMS

Eight SAS programs are available. The programs are as follows:

STATUS1 inputs data from STATUS1 DATA, and sorts by study, investigator, and subject number, and prints out all variables.

STATUS2 inputs data from STATUS1 DATA, and sums subject status by study, by study by investigator, and for all studies combined.

STATUS3 inputs data from STATUS1 DATA, and tabulates the reason for termination (i.e., efficacy failure or toxicity) by investigator by study. For subjects who have been terminated for efficacy failure and have had a second drug added, it tabulates the number of subjects taking a second drug (DRUG2A and DRUG2B).

STATUS4 inputs data from STATUS1 DATA, and pulls off data on adverse experience dates and organ systems involved. Three separate sections are printed, sorted by organ system, by study by investigator, and by date. Adverse experiences reported to an IRB or to the FDA on Form 1639 are also listed.

STATUS5 inputs data from STATUS1 DATA, and, when the exact date is not yet available, lists adverse experiences with the date 31DEC99, a code for unknown date.

STATUS6 inputs data from INQUIRE DATA and outputs to an SAS data set using PROC INQSAS.

STATUS7 inputs data from the SAS data set generated in STATUS6, and counts the number of subject-visit by each time period by study by investigator. These data are listed using PROC MEANS and are shown graphically using PROC CHART.
STATUS8 inputs data from the SAS data set generated in STATUS6, and, using a visit schedule, projects visits which are due to occur by a given date (e.g. OLAPR84) but are not yet in the data base. These projected visits are merged with the STATUS DATA set to delete subjects who have been discontinued or terminated from the study. These visits are then listed by investigator by study by projected visit date.

DISCUSSION

We have presented here a method for automating status type reports for clinical trials of investigational drugs. We have used this system for management of a large project involving a number of multi-center studies. Status reports are generated in far less time than by previous manual methods, and far more accurately. The ability to generate such reports with little manual effort has allowed us to generate these reports more frequently, so that we can better track the status of the studies and maintain tighter control.

We think that this system may prove useful to others involved in the management of clinical trials.


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