Abstract

The Epilepsy Branch (EP) of the National Institute of Neurological and Communicative Disorders and Stroke (NINDS), National Institutes of Health, currently employs microprocessors to coordinate and monitor clinical trials data. Computerized case report forms are used by nurse clinicians and data technologists on site to record specified patient information on floppy disks. The disks are then copied and sent to a registered nurse at the EP who intensively monitors the data. The computerized case report forms must have clinical data that would identify abnormalities or possible trends leading to complications. The data collected must be adequate for a reliable analysis at the completion of the study and support further investigations. The forms were designed to be flexible and generalized for all antiepileptic drug clinical trials and require only minor changes to accommodate the specific needs of individual trials.

Introduction

The Epilepsy Branch (EP) of the National Institute of Neurological and Communicative Disorders and Stroke sponsors studies in the United States to evaluate promising new antiepileptic drugs. The purpose of these studies is to determine the dosing and efficacy of new antiepileptic medications in the control of seizure disorders. The study of one new antiepileptic drug usually involves 60 to 80 patients at two or more separate contracting research centers. It is the function of the EP within the scope of these trials to coordinate the activities of the trials, monitor the data and analyze the results.

System Description

In order to efficiently coordinate and monitor clinical trials data, the EP has implemented a microprocessor-based data collection and reporting system. Each contracting center is provided with a computer system consisting of a Digital VP-155 video display terminal, PDP 11/50 central processing unit with disk drives and a LAMBDA printer.

Case Report Forms

Because of the voluminous amount of data required in these studies, data collection for the clinical trial of antiepileptic drugs requires a structured, microprocessor system of case report forms. The form selector image in Figure 1 displays the series of forms which the user must access repeatedly during the study.

Figure 1

Since these studies deal with human subjects, the system must be flexible to accommodate deviations from the protocol, such as a delayed visit date. The forms also need to be generalized to be utilized in various antiepileptic drug studies that are similarly designed and implemented.

The computerized case report forms are an integral part of the study. They must contain adequate data for a reliable analysis at the completion of the study and support further investigations. The forms must also contain clinical data that would identify abnormalities or possible trends leading to complications. An example of a computerized case report form is shown in Figure 2.

The computerized case report forms are developed by a team at the Epilepsy Branch consisting of the project officer, a statistician, a physician, a registered nurse and a computer specialist. The project officer and statistician determine which data items must be collected according to contract and analytic considerations. The physician and the registered nurse ensure that all medically relevant information necessary for monitoring safety as well as efficacy is available. The
The system in use by the FP has been designed with a high priority assigned to flexibility and ease of modification. Since these trials all involve the same target disorder, a set of generalised form images useful for studies in epilepsy have been developed. However, because each trial is somewhat unique due to the characteristics of the drug being evaluated, nature of the particular seizure disorder, and specification of research protocol, customisation for each trial is usually required.

Form Editor

Customisation of the various form images is readily accomplished with use of the form editor. The form editor is a software tool that can manipulate the text and fields of a form image. The visual attributes are assigned values (such as reverse video, blinking, or underline) by simple keystroke commands. Rearrangement of the contents of the image to suit design requirements or changes is a matter of simple editing functions. The fields (positions where the user enters data) of a form image are defined using FORM-L-like picture descriptions. By properly assigning these designators, the form designer can ensure that only data of the proper type is entered in a particular field. For example, the user will receive an automatic error message if any non-numeric entry is attempted in a field defined "DOC".

Other facilities available within the form editor are the assignment of default values, association of "Help" messages, justification and application program interaction parameters.

Default values are a convenience to the user when a list of usually standard responses must be verified. When default values are provided, the user need perform data entry only when the observed value deviates from the expected condition. Defaults are particularly useful for checklists.

This system includes the capability of presenting a single line of help information that has been uniquely defined for a particular field. Depending upon circumstances, the help message might be used to assist the user in determining the format of a given entry, display the normal range of values associated with a field, or define explicitly the data being solicited.

The form editor can specify left or right justification for a field. In left justification, data entry starts at the left most portion of the field and characters are added toward the right. In other words, the action is similar to that of a typewriter. Left justification is appropriate for many types of data entry.

Sometimes, however, data entered in a left-justified manner might require the user to insert leading zeros or blanks for padding purposes. For this reason, right-justification is also available under the form editor. When a field is defined as right-justified, characters are entered at the right-most portion of a field. As each succeeding character is entered, the previously entered characters are moved one space toward the left.

To communicate with the application program, the form editor provides capabilities for assigning form names, field names, and certain attributes for controlling various aspects of access to particular fields.

The application program communicates with the form image via an intermediate form driver. From the programming point of view, all communication with a field is accomplished by accessing the field name. In a FORTRAN program, for example, the application program can move the cursor to the
position a field occupies on the screen, wait for the user to complete the entry, and transfer the content to a program variable with a single subroutine call. Since field names are the only item of interest to an application program, a form designer can completely redesign a form without any need to modify the applications software.

In the particular application developed at the FP, additions or deletions of case report forms to existing systems is simplified by use of standardized modules. Generally, each application module usually consists of about 20 case report forms. Data entry for each form is controlled by a single software module. Since a user cannot complete more than one form at a time, each of these modules is assigned to the same overlay region. These modules are the only program units that contain form dependent information. Support for various generalized functions, (e.g. file control, footnoting, computational routines) are contained in standardized modules in other overlay regions.

Consequently, modification of the basic system to handle a particular trial is a straightforward matter. Even sudden protocol changes that arise unexpectedly can be easily incorporated.

**Training**

Because of the ongoing changes in the computerized case report forms and the diversity of patients and staff at the various clinical centers, it is imperative that thorough training techniques be utilized to ensure uniformity of the study. Before the study begins, the monitoring team at the FP trains the nurse clinicians and data technicians from the clinical research centers in the use of the microprocessor system.

Personnel from all clinical centers researching the same drug are trained simultaneously at the FR in Bethesda, Maryland. Each trainee has access to an individual computer system identical to the system they will be using on site. By having a separate system, each trainee can progress at his or her own rate and save all previously entered data.

The training begins at a rudimentary level, since the majority of trainees have no previous computer experience. An operation manual for the automated data entry system, PRDATA, is given to all trainees prior to the training period. This technical report and users guide has detailed steps for assembling the hardware, starting the system, accessing and utilizing individual case report forms, and trouble shooting. The trainees are asked to familiarize themselves with this manual.

The trainees are first given a demonstration of hardware assembly. They must then assemble their own systems repeatedly until they are comfortable with the procedure.

Xeroxed case report forms with hypothetical patient data are given to the trainees. Referring to the operation manual for assistance, the trainees enter data identical to that on the xeroxed forms. They are allowed to work at their own pace and ask for assistance from FP personnel when needed.

When the trainees have mastered these tasks they are given a hypothetical patient case report and a hard copy of blank case report forms. They are to decipher the information given in the case report and transfer the data to the appropriate blanks on the case report forms. This information is then entered in the computer and each completed case report form is printed. The nurse from the FP then checks the printed form and makes written corrections. The trainees must then access the incorrect forms on the computer and make the needed corrections.

The training session for each group involved in the study of the same antiepileptic drug is three days long. This in-depth training period helps to ensure consistency and conformity among the clinical centers. All personnel become better acquainted, aiding in communication which becomes paramount during the study. Coordination between the clinical centers through a comprehensive training session results in a more controlled reliable clinical trial.

**Summary**

The team at the FP must be alert to the requirements of executing a safe and accurate clinical trial. These requirements are incorporated into a microprocessing system to assist in the thorough and effective transfer of data from the clinical centers to the FP. The computerized case report forms, where clinical data is entered, were developed by the FP team. These forms can easily be modified to meet particular needs of a study by the use of the form editor.

The clinical center personnel must enter accurate patient data on the computerized case report forms for a reliable study. Extensive training techniques are utilized by the FP team to ensure that thorough and appropriate data is entered. The use of computerized case report forms has proven to be an excellent tool in the execution and analysis of clinical trials.

2. PRDATA, Technical Report and Users Guide: Moore, Penny; Palesch, Yuko; Swisher, Kathleen; NIC, NIMEC, CMHC, FP, TR; November 1969.

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