Paper 242-25

A Standard Reporting System for Phase 1 Clinical Trials
A SAS® Based Application "*Clin Pharm World*"

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ABSTRACT

The Parke-Davis Clinical Pharmacology standard reporting system, called *Clin Pharm World* (*CP World*), is a SAS based multi-platform application that runs on a Windows NT workstation and a Unix host. It makes extensive use of Base SAS, SAS/CONNECT® and SAS Dynamic Data Exchange (DDE) technology. It also utilizes Visual Basic (VB) macros that run under Microsoft Excel. The Unix portion of the application uses SAS SQL PASSTHROUGH to extract data from an Oracle database, and performs the intensive data manipulation. The Windows NT portion of the application serves as the interface between the user and the Unix host. Additionally, Windows NT performs a data output 'step' using SAS DDE technology. The VB portion of the application is invoked with SAS DDE and allows great flexibility and customization for table formatting. The final output is stored in Excel and accessed, via the Parke-Davis intranet by our clients (i.e., clinical scientists, physicians and medical writers).

INTRODUCTION

BACKGROUND

Historically, clinical databases were stored on a mainframe computer, using a SAS based data entry and management system. The reporting programs were also mainframe SAS, and the output tables were "classic" SAS, using data _null_ formatted output. With the change to an Oracle Clinical database in 1997 and migration from mainframe to a Unix and Windows NT environment, an opportunity arose to develop a new standard reporting application that employed the latest technology such as SAS/CONNECT and SAS DDE.

GIPMS AND CIDS

The Parke-Davis Clinical Reporting Systems (CRS) department, which is responsible for reporting clinical trial results for all drug development phases and all therapy areas, has adopted a strategy that is based upon standard program requirements, specifications, and output programs. The standard program requirements and specifications are called GIPMs (Global Integrated Program Modules), and the standard programs are being delivered via a system called CIDS (Clinical Information Delivery System). The goal of this strategy is to be able to produce like-program output across all therapy areas and to significantly reduce the time that is currently being spent redeveloping programs common to all studies, regardless of therapy areas. For more details, refer to the SUGI 24 poster presentation of Brucken, Harper and Makowski [1].

CLINICAL PHARMACOLOGY

The Parke-Davis Clinical Pharmacology Department (Clin Pharm) conducts phase one clinical trials on healthy volunteers to assess the safety, pharmacodynamics, pharmacokenetics, bioavailability, and bioequivalence of new chemical compounds. The CRS group (membership consists of the authors) on the Clin Pharm team, is responsible for presenting the data obtained from those trials in both listing and summary tables. Clinical scientists, writers and medical experts rely on these tables to review the clinical trial data and make critical business, medical and scientific decisions on whether a new compound warrants further development.

Phase one trials have unique features when compared to phase two and three trials.
These features include:

- The first time that a study drug is tested in humans
- Typically a short study duration (a few weeks) with only a few doses of a study medication being given
- A small number of healthy volunteers (typically 12-24)
- A dependence on both listing and summary tables to report the results

The focus of the GIPM/CIDS initiative is to initially provide standardized summary tables (e.g., Summaries of Adverse Events, Prior Medications, Vital Signs, etc.). Because of the nature of phase one studies (i.e., first time in humans, etc.), reviewers are focused upon the details of each individual who participated. Hence, the need for custom listing tables, an element not currently provided by CIDS.

CLIN PHARM WORLD APPLICATION

OVERVIEW

The new application, *Clin Pharm World* (*CP World*), has four major components (see the flowchart at the end of the paper). The 'GetStudy' and 'GetProgram' components reside on a Windows NT sever and act as a user interface. The user selects a study by typing the compound investigation number (CI) and protocol number (PROT). Next, the user selects which programs to run based on the desired tables. The application then performs a remote submit to switch work from SAS running on Windows NT to SAS running on Unix. The next component, 'GetData', resides on the Unix host. It dynamically extracts data from the Oracle Clinical database using SAS SQL PASSTHROUGH. It also performs some data pre-processing such as deriving

common data sets used by multiple table programs. The fourth component consists of the individual programs. They reside on the Windows NT server and are remote submitted to Unix for more table specific data processing. Then the data is downloaded to the Windows NT workstation for output to Excel. Each program uses an output engine based on SAS DDE to create tables on pre-formatted Microsoft Excel worksheets that serve as output templates.

FEATURES IN DETAIL

The central point of the *CP World* application is a SAS program called CPWorld.sas. This program, housed on a Windows NT server, acts as a submission system to allow CRS programmers the capability to selectively choose and conditionally execute the tables they require. Once it is launched via an icon created on the tool bar within SAS, it brings up a window for the user to enter a study. Once the study is entered, the application brings up the second window for the user to select which programs to run based on the data collected in a particular study.

Based upon the tables requested, *CP World* will evaluate and furnish only the necessary data required to provide the desired report(s). For instance, if the user requires a listing of adverse events, *CP World* will acquire (from Oracle Clinical) the dosing regimen, subject demographics, adverse event, dosing, and comment data sets.

PROCESSING EFFICIENCIES

Because *CP World* creates access to the required data only once, significant processing efficiencies are gained if the user also needs other tables that utilize the same data (e.g., an adverse event summary, a demographics listing and summary, or a listing of subject medication dosing). In previous Clin Pharm applications (both mainframe and Unix based), data were extracted each time a program was executed.

CP World also creates "derived" data sets to further accelerate and streamline reporting. When the adverse event (AE) data set is processed, additional data sets including AEs with dose or treatment, TESS (Treatment Emergent Signs and Symptoms) only, and Associated AEs are also created.

MODULAR DESIGN

CP World is developed with a modular design approach. The first module is the extract engine using data extract methodology. Remote submissions are made to a Unix server where the availability of variables and the possible names of Oracle views are assessed. This is to accommodate data base/study variations. Dynamic data set creation is initiated by querying SAS dictionary tables for varying ORACLE data base structures such as different view names for the same data or the same view name containing different variables. All known variations are built into the system. The application also provides a utility to check on database deviations from what has been accounted for in the system. If, for example, a study collects data that are not accommodated in the initial application, the utility will output a warning message in the log.   Additionally, derived fields such as CI, protocol, and adverse event body system and

preferred terms are also created in the data extract engines.

The second module deals with data manipulation. The vast majority of data processing in *CP World* is performed on the Unix server. Once the data are "table ready", a download is made to the desktop for 'export' to Microsoft Excel via output engines based on SAS DDE technology.

The last module is the output engine. The output engines also have built-in features to create tables dynamically based on database variations and/or user desired flexibility. For example, if information on smoking is not collected for a given study, the output engine will hide the smoking status column on the Excel demographic listing table. Excel commands, such as hiding a column, are issued by calling preprogrammed Excel macros written in Excel Visual Basic. The user can also specify at the time of report execution whether the summary of subject characteristics should be reflected in a single composite summary or broken out by regimen. In listings of ECGs, vital signs, and physical examination results, the user can selectively choose to include dosing information.

AN EXAMPLE

When a database for a particular study is released, the CRS analyst will place a copy of the therapy approved Excel specifications in their personal work area (e.g., c:\c_data\Excel). Once there, the analyst will rename it from ClinicSpecs.xls to the protocol number that is being worked on. For example, a study for CI-1004 (1004-12) would have an Excel workbook named 1004012.xls.

From this point, the user invokes *CP World* from a Windows NT workstation by either pressing a pre-programmed 'button' or submitting the CPWorld.sas program. The following screen appears after submitting *CP World*.
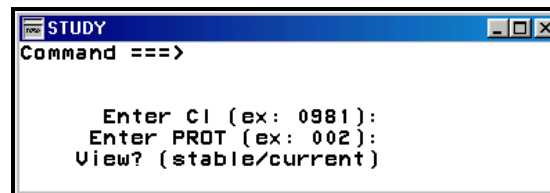
From there, the user enters the Clinical Investigation Number (Enter CI), protocol number (Enter PROT) and the Oracle/Clinical view (stable or current).

If the user makes an entry error, an error message automatically appears and asks that the data be re-entered. Next, a menu selection appears where the user will type 1 in the place of 0 for the table(s) that he/she wants.

The entries at the bottom of the screen allow the user a degree of report flexibility. For instance, the user can tell the system that when it summarizes adverse events by body system to sort the output by a specific treatment group or regimen (sRegId).

The other options on the bottom of the screen provide the aforementioned capability to summarize demographics by treatment and include dosing information on various reports.

THE FUTURE

The future of *Clin Pharm World* includes continual enhancements and process improvements. In the near term the targeted changes include:

- Integration with CIDS
- Conversion to SAS 8 to take advantage of the new outputting features. Since the *Clin Pharm World* system was developed in a very modular format, conversion should be straightforward and fast.
- Continuing to add new programs to the menu selection (e.g., visual acuity, etc.)
- Evaluation of other products such as SAS QC, which may be useful in better illustrating clinical trial results
- Modifications to allow the execution of programs against derived data sets (e.g., Integrated Safety Summary, etc.)

REFERENCES:

1. Brucken, Harper, and Makowski. (1998) "Developing Standardized Requirements, Specifications and Programs for Clinical Trials Reports", Proceedings of the Twenty-Fourth Annual SAS User Group International Conference, 24.

ACKNOWLEDGEMENTS:

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FLOWCHART

CP World Application

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┌─────────────────────────┐        ┌─────────────────────────┐
│   GetStudy  (On NT)      │        │    GetProg (On NT)      │
│─────────────────────────│───────▶│─────────────────────────│
│   Enter study selection  │        │   Select programs based on│
│   by CI, Prot and View   │        │   data collected in a study│
└─────────────────────────┘        └─────────────────────────┘
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Behind the Scene: Opens connection to the Unix
Server, sends macro variables created in GetStudy
and GetProg, sets options and libnames

GetData (On Unix)

Finds appropriate data view names, checks for
existing variables, and extracts initial data sets

Create Derived Data Set: takes base AE data set
and creates data sets for TESS AE, Associated
TESS AE, DosePt, and Regimen data set

Table Specific Manipulation (Remote Submit to
Unix and DDE on NT)

All data manipulation required to produce specified
output table resides here. Opens Excel and outputs
data