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One at a Time; Producing Patient Profiles and Narratives

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ABSTRACT

Patient profiles can take many forms depending on the purpose for which they are going to be used. For data cleansing, it can be a data dump for each patient so that any data anomalies can be discovered. For medical review, the narrative type of profile would best. All of this can be done with Base SAS® and macros to create the listings, formatted profiles, and narratives. An alternative is with a data visualization tool, JMP® Clinical. Patient profiles are customizable and can display data from any combination of the core safety CDISC domains. A configurable patient narrative can be created for each subject who experienced a serious adverse event during the clinical trial.

INTRODUCTION

A patient profile is a listing of data gathered on an individual subject who participates in a clinical trial. It may include all, most or just a selected portion of the data. It may be expressed in narrative English, collated or just a simple data dump. A patient profile can be the key to identifying why a subject took a concomitant medication, the effects of an unrelated surgical intervention or the sequence of adverse events which culminated in a serious adverse event. Or it can simplify the task of verifying all of the dosing records for an individual subject. These different usages require a certain amount of customized programming.

The first type of patient profile is the data dump. With this type of profile, it is important to see each and every field that is collected on the Case Report Form (CRF). Once the data is clean and data standards have been applied, the best method for medical review, discovery of subject abnormalities or preparation for the Clinical Study Report (CSR), the narrative type of profile would best. Clinical reviewers are interested in how the whole patient looks, but not quite interested in each field that is collected on the CRF. All of the patient profiles can easily be created with Base SAS® and macros. Another way to create the patient profile is with a data visualization tool, JMP Clinical®. Along with the visual display of JMP Clinical, a configurable patient narrative can be created for each subject who experienced a serious adverse event during the clinical trial. Reviewers and medical writers enjoy the speed of this programmed process, using the write-ups as a starting point for the final patient narratives compiled in the CSR required by the FDA.

MEETING CUSTOMER NEEDS

The key to successful patient profile programming is to identify and recognize the requirements of your customer. Patient profiles are generally created for three different categories of customers:

1) Clinical Research Associate or CRA
2) Medical Writer
3) Clinical Safety Scientist/Physician.

The CRA is, first and foremost, interested in the accuracy of the data. The medical writer wants the highlights in order to write his/ her patient profile report and the physician wants all the relevant data in order to make accurate clinical judgments about the subject.

PATIENT PROFILE USERS

CRA

The CRA (or data manager or statistical programmer) has a primary purpose of recording and reporting all of the clinical trial data accurately. They need all of the data from all of the domains that are reported in the trial without regard to interpretation, meaning or severity. For example, a list of all adverse events, sorted by order of occurrence or report is helpful to a CRA. The CRA patient profile is a simple listing of every record for that particular subject in every domain. Subject based domains have a single line, event based domains are sorted by the sequence identifier and output as is. No frills, no interpretation needed.

The CRA is just interested in the data and finding the data without any difficulty. For the CRA, we pass the data from every domain through a program which appends every record for that identified subject into a unified dataset or a one line note identifying there is no adverse event records for that subject. Note that this may produce long lines of data. Often it is necessary to pre-compress long character variables and delete redundant variables.

MEDICAL WRITER

The medical writer may be required to write a patient profile or summary of each subject for the clinical study report. In order to complete this task, they need all significant events and an ability to place them in both chronological order and/or the time frame of the study. Thus, all dosing, subject visits, epoch changes, serious adverse events, physician reports and significant laboratory results are needed. When working with a medical writer, they are always asked to define the requirements for each of those categories. The significant laboratory results are the most interesting. Either a list of specific labs with (or without) specific values or just any abnormal lab value can be requested. In general, a little customization here goes a long way.

After a clinical trial closes the medical writers are asked to produce a patient narrative, often for each subject, or for specific subjects. The dates which are required for this narrative includes the dates of informed consent, randomization, first dosing, dosing changes, final dosing and last contact. This information is in both trial time reference (i.e. second dosing on day 13) and calendar date format. In addition, any significant event which occurs during the course of the trial which affects the general health of the individual subject, their progress during the trial, their likelihood of completing the trial or their outcome or result from the trial is possibly a significant event. The medical writer will be judging what is significant and crafting that information into an English language narrative. Domains which certainly will be reported include DM for demographic information, SV for the identification of subject visits, EX for dosing values and DS for epoch changes. Other domains which may provide significant information include (but are not limited to): AE for significant (frequently either serious or area of interest adverse events), CM for any concomitant medications which were employed to treat serious AEs, SU for important substance usages, MH for medical histories, IE for inclusion or exclusion criteria which received a waiver, LB for lab results which were out of normal range or were of special interest, SG for any surgeries, especially ones which either related to AEs or caused dosing delays. Your medical writer may have other domains of interest.

When coding for a medical writer patient profile, start with the physician profile (below) and reduce the input as needed to achieve a result which provides adequate information. In many environments, the medical writer only produces a profile for serious adverse event subject or those who die during the course of a trial. If that is the case, this information is provided once very prominently and once in temporal sequence.

PHYSICIAN

For a physician overseeing the clinical trial, the customization rises to another level. The starting point is that we attempt to provide the equivalent of a briefing that they would receive from another physician as if the physician was going to assume the responsibility for the care of that individual. With this in mind, three sections are prepared: an English language introductory section, a brief baseline section and a schedule of events. Each is programmed and generated differently.

METHODS OF PRODUCING PATIENT PROFILES

BASE SAS CODE USING MACROS

Base SAS has been used for many years to produce the patient profiles. Macros have been created and either embedded within the programs or set up in an AUTOCALL library for the programmers to use when needed. The easiest way to create the programs is to format the data into records with the same variable name and type and then print off the information. This can be done in many ways by using PROC PRINT, PROC REPORT, DATA _NULL_ and the Output Delivery System (ODS) for creation of listings, HTML, PDF or RTF files. Each domain that is read in will be keyed with the unique subject identifier (USUBJID), the event and or the finding. They will all be printed out together by domain with a header record for each page with the study identifier, unique subject identifier and other pertinent information that will identify the subject and some of the demographic data.

ENTERPRISE GUIDE

As with the Base SAS code, Enterprise Guide (EG) can be used to create a project that will produce the patient profile. The tasks within EG are used to manipulate the data into the format needed for the production of the profile. EG is a point and click way to create the profiles in a graphical user interface. Generally, a job flow is created to determine the steps needed to manipulate the data. Then the tasks are used to produce the output. Using ODS, the profiles are created for the various users.

JMP CLINICAL

JMP Clinical is designed for medical reviewers, medical writers, data monitors and biostatisticians engaged in analyzing safety data from clinical trials. JMP Clinical lets you generate patient profiles for an individual or group of subjects, by selecting subjects from a Hy's Law graph, box plots or shift plots, etc. Reviewers and medical writers can also record and save unstructured text about any subject or group, noting, among other things, cases of death, serious adverse events and reasons for discontinuation. Patient profiles display data from any combination of the core safety domains. Once the reports are tailored, they can be printed in PDF or RTF, making for straightforward communication of findings among review groups.

JMP Clinical can also compose a configurable patient narrative for each subject who experienced a serious adverse event during the clinical trial. Reviewers and medical writers enjoy the speed of this programmed process, using the write-ups as a starting point for the final patient narratives compiled in the Clinical Study Report (CSR) required by the FDA.

CONCLUSION

There are many people in the clinical world who use the Patient profiles. There are many ways in which these users require the data to be presented. From the data dump for the CRA to the narratives that are used by others, patient profiles have become an integral part of the data cleansing and review for the clinical trials data.

CONTACT INFORMATION

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APPENDIX A

EXAMPLES OF PATIENT PROFILES

NARRATIVE:

Subject 12-071 is a 55 year old white female not of Hispanic ancestry on Treatment Sequence A-1-1, who signed
IC on 22 March 2011. She is 164 cm in height and 73 kg in weight.
Physical Examination: minor heart murmur.
Medical History: Sporadic Asthma (- - 1989), AMI (27 Mar 2003),
Baseline:
Baseline Vitals were: BP 130-85, Pulse 55, Respiration 12/min, Temp 98.6 F
Baseline Lab Results (in standard units)
Hematology: Na 140 K 5.0   CO2 25 Cl 103   Glucose 92   Ca 9.5
BUN 17   Creatinine 1.0   HGB 12.5   HCT 44
Chemistry: AST 25 ALT 14 Billirubin 14.5   Albumin 4.0
Urinalysis: Ketones Neg   SpecGrv 1.010   pH 6.0   UProt Neg   UGluc Neg

Schedule of Events

Brf Desc	Date	Cat	Event Description	Note
IC	04FEB2008	DS	Signed Informed Consent	
Random	11FEB2008	DS	Subject Randomized	
Baseline	12FEB2008	SV	Baseline Visit – Run-in Dosing	RI Started
		all	*visits*	*would be listed here*	
SAE	01MAR2008	AE	Appendicitis	SAE, unrelated
Surg Intv	01MAR2008	SG	Appendix Surgically removed	unrelated
Conmed	02MAR2008	CM	Percacet 7.5mg QID	approved
Exposure	03MAR2008	EX	2 week Dose-Delay	approved
Exposure	17MAR2008	EX	Visit 3 Dosing	Dosing A
Dose Cg	24MAR2008	DS	Completed Stage One	Dosing 1
			. . . continued . . .	

Introductory Section

The programming for the first section depends on your company having a line feeder macro. Your company may
reference this macro in a different way, but most have a macro which will parse long character strings into 40 (or 50)
character long, whole word substrings, suitable for fitting lines on a page. This macro is employed because many of
the transcriptions of variables will be of unpredictable or different lengths. For example, the variable DM.SEX is
employed to generate the text "man", "woman", "male", "female", "girl" or "boy". These terms vary in length between 3
letters and 6 letters. Instead of leaving an 8 character long blank in the text, it is preferable to allow the line feeder
macro to adjust the length of the text for the whole line. Thus, the whole text is created in one character string of
length up to 256 characters, or possibly multiple strings if your narrative can exceed this amount. The example text
above:

"Subject 12-071 is a 55 year old white female not of Hispanic ancestry on Treatment Sequence A-1-1, who signed IC on 22 March 2011. She is 164 cm in height and 73 kg in weight. Physical Examination: minor heart murmur.
Medical History: Sporadic Asthma (- - 1989), AMI (27 Mar 2003), "

was created employing the following variables: DM.SUBJID, DM.AGE, DM.RACE, DM.ETHNIC, DM.ARMCD, DS.DECOD, DS.DSSTDTC, SC.SCTESTCD, SC.SCSTRESN, PE.PEMODIFY, MH.MHDECOD, and MH.MHSTDTC. For each of these variables a format or other decoding scheme (such as for dates) is applied and the output text included into two string variables (the second for medical history alone.). These variables are then cut into appropriate page width strings and listed. This strategy is frequently called a drop-in text approach.

Baseline Section

The baseline vitals and labs are gathered from the LB and VS domains. Often, baseline questionnaire results (from QS) or EG (eeg) are also included in trials where that is appropriate. The variables required include: LB.LBCAT, LB.LBTESTCD, LB.LBORRES, LB.LBSTRESN, LB.LBSTRESC, LB.LBBLFL, LB.LBNRIND, VS.VSTESTCD, VS.VSORRES, VS.VSORRESU, and VS.VSNRIND. Dates/ visit names of baseline tests or verbatim names of tests may also be helpful. The compact version of the baseline section is demonstrated; a more verbose version (one line per test, date of test, original result and standardized result) is available upon request

Schedule of Events

Often, grouping elements together by date of occurrence provides insight into the causative chain. While not suggesting that a patient profile should even suggest a causative chain a physician examining a profile should receive the relevant information in order to make their own judgments about causative chains. In order to accomplish this task four tasks must be completed: first, the appropriate events must be gleaned from each domain, second, these events should be put into a standard format, third, the events should all be sorted by start date/time and fourth, all events are brought into a single table. Of these the first is easily the most difficult.

Here are several suggestions for records which are appropriate. All DS and SV records, unless there are more than twenty subject visits should be included. This provides a good sense of when within the trial events occur. Any EX record, unless the dosing is a daily occurrence and the study lasts more than three weeks. Any IE. Any SAE and any other AE with the same SOC as any SAE. Any CM taken for an AE. Any SG and any CM, dose-delay EX, AE, LB, EG, CO or DS which relates to it. Any abnormal lab and the first normal lab (of the same test) afterwards. Any SU which changes, is proscribed, or could contribute to being proscribed. Any pre-selected (by the protocol) LB, EG, QS or VS reassessment or comment (CO) on the same should be included. Any outcome measure (from the protocol) should also be included. Anything from any other domain which alters the course of treatment, the degree of success of the trial or the safety or efficacy of the medication should also be considered appropriate to include. Anything which marks a stage of completion of the trial is also appropriate.

On every page of the profile I include the following info in the header or footer: a subjid, the trial identifier, the site identifier, a generation date (when I am creating the profile), blinded/unblended status and a treatment code. When creating a portrait-based profile, I restrict myself to five columns: a brief description of the type of record (8-10 character), the start date (and time, if needed,) the domain id (two letters), an event description and a note. If I can switch to a landscape based profile then I will add a second note column and a longer description field. For records from each domain I select the terms for each of these fields. Note fields may be –SCAT or --ORRES + --ORRESU. The brief description is often a fuller version of the domain name. The event description, the longest field will be –DECOD or –TERM or both.

Once all records are in a standard format and then placed in a single dataset they are sorted by the date (and time) and the domain name. This puts AEs typically on top of a number of related records and keeps the others in a reasonable order. The records are now prepared to printed out which can be done through your favorite choice of output (proc print, ODS, data _null_, etc.) Be prepared for feedback and to re-create your profile at least once for each new physician you send patient profiles to.