Paper AD07

Customised AE Narratives using JMP Clinical

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ABSTRACT

Medical Writers create AE Narrative reports of adverse events of interest as part of a regulatory submission – a lengthy task! JMP Clinical provides a tool to automate this process, however it cannot easily take account of different needs for different therapeutic areas (TAs). This case study will present how we took the basic report and customised it to meet the needs of a group of Medical Writers preparing AE Narratives for Respiratory, Vaccines and Oncology studies. The end result was a tool that allowed for user customisation; was adaptable for different TAs and different studies within those TAs; and allowed the user to create a report in minutes rather than weeks!

INTRODUCTION

This case-study describes a project d-wise undertook to help a sponsor automate their AE Narrative generation process, with the aim of cutting timelines and reducing costs

An AE Narrative Report consists of brief summaries of specific events experienced by patients during the course of a clinical trial (see Figure 1). Typically serious adverse events (SAE), but can also include other events of interest, such as events with high severity, or events that lead to subject discontinuation.

Regulatory agencies do not specify the layout of the report – there could be no 'one size fits all template' as each sponsor structures their studies and data differently. Industry guidance exists and most companies define templates for their therapeutic areas (TA) of interest.

The reports are *very* time consuming to create manually – the medical writer must sift through data from multiple sources and construct the report… It can take weeks for a large study. Not anyone's idea of a fun time!

Our sponsor wanted a tool that automated the AE Narrative generation process, while also taking into account the different needs of key TAs. For example, oncology studies collect different data points to respiratory studies, and the narratives will also be different. They also wanted the output report to be as close to final as possible – the medical writers should have to perform minimal manual editing.

They already had JMP Clinical - a tool that allows GUI-based visualisation of trial data and has built in functionality to auto-generate narratives. However, our client wanted more control over the output, such as defining specific text to wrap around datapoints, and to ensure that the output matched their different TA templates.

Subject: 101005
Randomized Arm: Placebo
Investigator Name: 101A
Drugs and Doses on Day of Event: On Treatment

Serious Adverse Event (coded term [reported term]): INTESTINAL PERFORATION [INTESTINAL PERFORATION]

Subject 101005 was a 67-year-old white female. Her medical history included loss of consciousness associated with sah (1988), and hypertension prior to sah (start date unknown). The subject completed the trial on 10JUN1988 (Day 67).

On 17APR1988 (Day 13) the subject experienced a intestinal perforation (severe) which was considered a serious adverse event (SAE). Though the event was considered serious, no reasons were provided on the case report form. The subject was on treatment when the event occurred. Trial medication had an action of not applicable as a result of the event. It is not known from the case report form if therapeutic measures were administered to treat the event.

Adverse events that occurred within a +/- 3-day window of the onset of the SAE included vasoconstriction (moderate). Concomitant medications taken at the onset of the SAE included: acetaminophen, gentamicin, morphine, phenobarbital, ranitidine, and vancomycin.

The investigator considered the AE to be not related to study medication. The event ended on 19APR1988 (Day 15) with a final outcome of recovered/resolved.

Figure 1: Sample of an AE Narrative report

HOW DOES AUTOMATION WORK?

Sponsor SDTM standards and the AE Narrative template defined by the medical writers drive the definition of data point metadata. This metadata fully describes each datapoint that appears in the report – the source domain(s), variable name, derivation rules, date imputation rules, and conditions (e.g. if AE start date is after treatment start).

Datapoint creation programs then use the metadata and study specific user input to generate SAS datasets containing the datapoints needed. The study specific user input can be filters on subject, demography or adverse event data, AEs of interest for the study. This gives an extra layer of flexibility for the users.

A further program then takes the datapoints, wraps text around them to create human readable text, and outputs in RTF/Word format.

WHAT DID WE DO?

The first stage of the project was to review the TA templates from the client to identify the datapoints needed, the wrapping text to use, the conditions to be met for the data to be reported, and alternate text (if needed) when no data was present.

E.g. when producing a list of concurrent AEs – what text to present if no concurrent AEs were present.

Datapoint metadata worksheets were created for each TA. These are critically important when deriving datapoints that are a combination of multiple values. As part of the metadata effort, we also documented the date imputation rules to be used, and developed and validated a macro to automate the imputation.

The text wrapping portion of the process was changed from the default JMP Clinical method. JMP Clinical uses Java

Velocity templates, however our client wanted to use SAS ODS as they felt it would be easier to maintain in the longer term.

Once the primary programming was complete and narrative reports were able to be generated, we performed a thorough validation effort to ensure that the reports were accurately reflecting the study data.

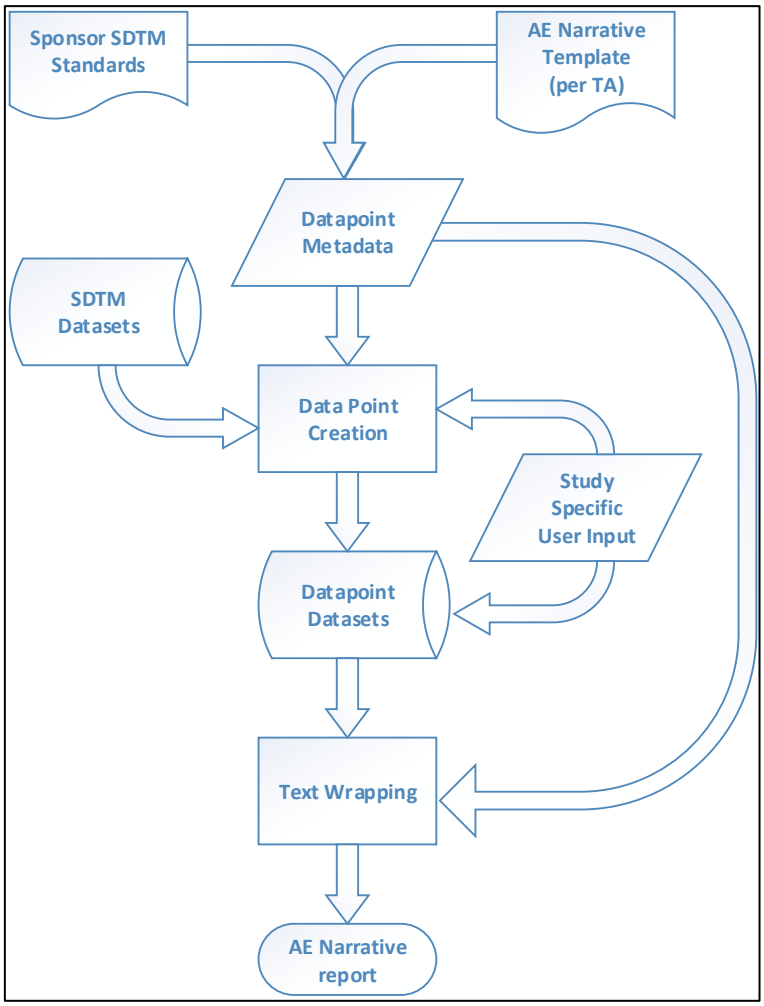

Figure 2: Automated AE Narrative Process Flow

WHAT CHALLENGES DID WE HAVE?

During the validation effort it became apparent that the datapoint metadata didn't always accurately capture the derivation requirements e.g. which order to present a list of events or concomitant medications.

There were also misunderstandings between programmers and medical writers over some terms, like 'last visit'. Does that mean 'most recent visit', or 'last visit in the study'?

The biggest challenge however, was inconsistent use of CDISC standards. To be clear – the data was all compliant with CDISC standards – just inconsistent between studies. The most common issue was a wide variety in QNAM values used in SUPPxx domains.

The problem this caused was in taking extra time to find the data needed – it would be easy to think that a particular

piece of data wasn't collected because, for example, there were no records where QNAM='PRDEATH' when looking for 'primary cause of death'. It because common to perform frequency counts of QNAM and QLABEL values in each SUPPxx domain of interest, to get a feel of what data was actually present.

CONCLUSION

By the end of the project, we had created a tool that could create an AE Narrative Report for four different TAs in a matter of minutes rather than weeks. The client were very happy with the tool, and estimate they have saved over $1,000,000 per year.

Creating customised, automated AE Narratives is definitely possible, but it requires data consistency, good collaboration between developers and users, and time – this project took approximately a year to complete.

CONTACT INFORMATION

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