



d-wise™

Accelerate to the Speed of Life

Customised Narratives using JMP Clinical

PhUSE Connect 2019

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What is an AE Narrative?

AE Narrative

- A brief summary of specific events experienced by patients
- Included in a regulatory submission as an appendix to the Clinical Study Report
- VERY time-consuming to create manually
- No specifics on content from regulators

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

Demography
Exposure
Adverse Events
Medical History
Concomitant
Medications
Disposition

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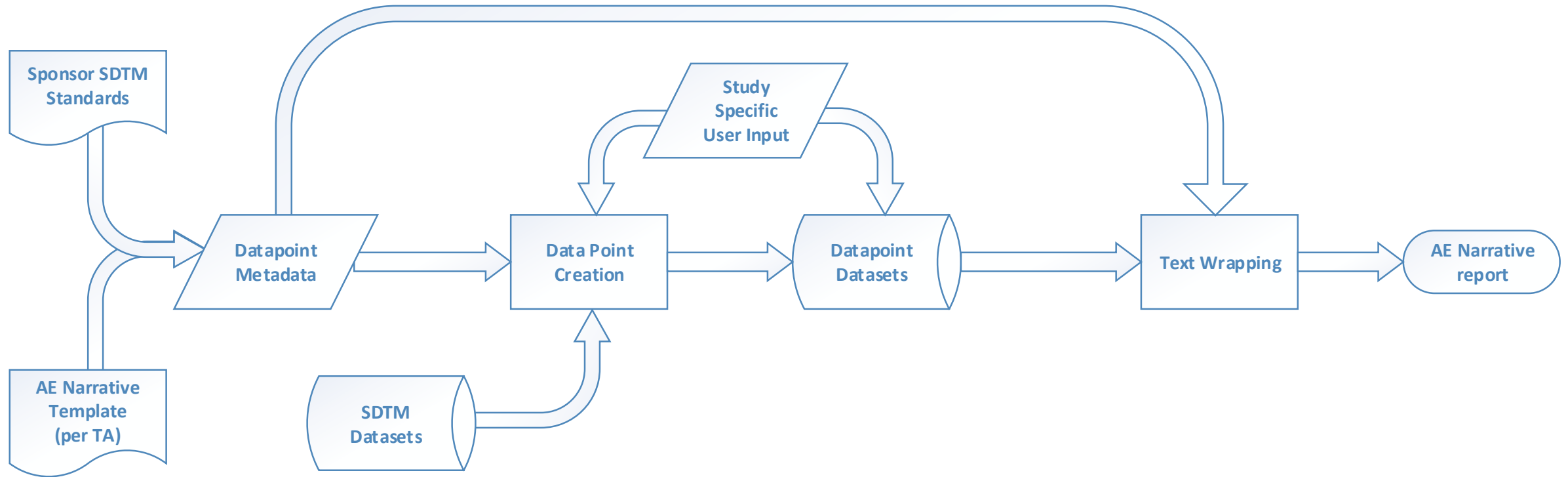
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What did the sponsor want?

- Automated AE Narrative generation that took account of therapeutic area (TA) differences
- JMP Clinical
 - What is it?

How does automated AE narrative generation work?



How did we do it?

- Review TA templates
- Identify Datapoint metadata
- Customise JMP Clinical UI
- Generate Datapoint datasets
- Use SAS ODS to generate output with text wrapping
- Data Point Validation

TA Template

✓ The data points

✓ A description of the data points

✓ The text to be wrapped around those data points

✓ Any conditions which should result in alternate text

At the time the subject experienced <<(AEDECOD) AE Preferred term>> he/she was also experiencing <<(NEARAES1) List of comma-separated concurrent AEs sorted by onset date, SOC, and PT – each followed by AE severity in parenthesis>>

{If no concurrent events, replace with: At the time the subject experienced <<(AEDECOD) AE Preferred term>> he/she was not experiencing any other adverse events.}

Datapoint Metadata

- Metadata for the data points referenced in the TA Template
- Critical for deriving datapoints that are a combination of multiple values

Variable 	Label 	Dataset(s) use 	Level (HEADER, USUBJID, EVENT, or REPORT) 	Notes 	Narrative Template Excerpt 	Verbiage to Build Code 
NEARAES1	Formatted list of all non-serious AEs occurring at same time as narrative AE	AE	EVENT	If any of the AESTDTC and/or AEENDTC used are partial the imputed (first day of month and/or day of the month) date is used. List concurrent non-serious AEs, sorted by onset date, SOC, and PT, followed by <AESEV> in parenthesis If any comparison event with the same preferred term and grade/severity occurs more than once only the first one (chronologically) is included in the NEARAES1 data point. All non-serious AEs that are concurrent to the topic AE should be listed even if that non-serious AE is also a topic AE (but, of course, the exact same topic AE of itself should not be listed)	At the time the subject experienced <<enter event>>(AEDECOD), he was also experiencing non-serious AEs including << List concurrent AE, sorted by onset date, SOC, and PT, followed by AE severity in parenthesis. (NEARAES1).	At the time the subject experienced <<AEDECOD>>, he was also experiencing non-serious AEs including <<NEARAES1>>.

JMP Clinical UI

Adverse Events Narrative

Options

General

* AE Narrative Template
Default

☐ Include subject-level table of contents

☐ Use subject identifier for study in lieu of unique subject identifier, if available

Adverse Events

☒ Include serious adverse events only

Event Type
All event types

☐ Ignore available treatment emergent flags

Offset for End of Dosing
0

Number of days around Adverse Event start date for reported related events
3

☒ Include the reported event term in the header only when different than the coded term

Exposure

☐ Include exposure (EX) in the narrative

☐ Treatment end date is equivalent to the start date

☒ All study treatments are to be taken at least once per day

☒ A 0 dose for placebo or vehicle indicates a dose interruption

Concomitant Medications

Number of days prior to Adverse Event start date for reporting concomitant medications
0

Concomitant medications are reported using:
☒ Reported name of drug
☐ Standardized medication name

☐ Include concomitant medication indication in narrative

How did we do it?

- ~~• Review TA templates~~
- ~~• Identify Datapoint metadata~~
- ~~• Customise JMP Clinical UI~~
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- Data Point Validation

What challenges did we face?

- Misinterpretation of datapoint metadata
- Much variation in application of CDISC standards
 - SDTM SUPP Domains primer

SDTM SUPP Domains – a primer

SUBJID	AESEQ	AEDECOD	AESER	AESHOSP
20016160006	11	Diarrhoea	N	
20016160006	12	Diarrhoea	N	
20016160006	13	Diarrhoea	Y	Y
20016160006	14	Dry mouth	N	
20016160006	15	Dyspnoea	N	
20016160006	16	Enteritis	N	
20016160006	17	Fatigue	N	
20016160006	18	Gastrointestinal mucosa hyperaemia	N	
20016160006	19	Gastrointestinal oedema	N	
20016160006	20	Hypoalbuminaemia	N	

SUBJID	IDVARVAL	QNAM	QLABEL	QVAL
20016160006	13	AEDICT	Dictionary Name	MedDRA
20016160006	13	AEVER	Dictionary Version	20.0
20016160006	13	AEADMDTC	Hospitalization Admission Date	2017-07-25
20016160006	13	AEDISDTC	Hospitalization Discharge Date	2017-08-02
20016160006	13	AETRTEM	Treatment Emergent Flag	Y
20016160006	13	AEEXBA	AE Occur Before or After Dosing	NA
20016160006	13	AEACNCRF	CRF Action Taken with Study Treatment	DOSE NOT CHANGED
20016160006	13	DLT	Dose-limiting Toxicities	YES
20016160006	13	AETRRT	AE Required Treatment	CONCOMITANT MEDICATION

What challenges did we face?

- Much variation in application of CDISC standards
 - Dose Adjustment
 - reduced, interrupted, not received, or increased dose
 - DDBDYS, DOINC, DORED, DORRD, DOSDEL, DOSDELAY, DOSERD1, DOSINC, DOSINT, DOSRED, DOSREDYN, DOSYN, DSINCYN, EXINTRP, FULDOSE
 - Primary Cause of Death
 - CADEATH, PRDEATH, DSPRDTH
 - Secondary Cause of Death
 - SECDEATH, DSSECDTH
 - Autopsy performed?
 - 1, Y, YES, PERFORMED
 - Action Taken (with Study Med due to AE)
 - ACN<trt id>, ACNMED, AEACN<n>, AEACNC, AEACNC<n>, AEACNCRF
 - Or, in a different dataset as CAN<trt id>, ACNIP<n>, ACNMEDI
 - Causality
 - AECAAD, AECAAD<n>, AEREL<n>, AERELCRF, AEREL<trt id>, AERELP, AERELT, REL<trt id>
 - AE Description
 - Over 100 different values for QNAM

What was the end result?

- A happy sponsor with a working tool that allows users to generate an AE Narrative Report in a matter of minutes.
- They estimate that they have saved >\$1,000,000 p.a.

Key Takeaways

Automation and customisation AE Narratives is definitely possible
BUT, it requires:

- Data consistency
- Good collaboration between developers and users
- Time!

Questions..?

