
# *Leveraging CDISC Standards for AE Narrative Automation*

Presented at CDISC Webinar
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# Let's Get on the Same Page

What is an AE Narrative

Regulatory agency submission deliverable

Summary of select events experienced by particular subjects during a clinical trial

with other information about those subjects' participation in the trial.

The criteria for including a subject/events are study specific.

Typical criteria include a serious AE, an AE of Special Interest, or an AE leading to discontinuation from the study.

What is the Goal of Automating

Generate a narrative for any study, based on a standard therapeutic area template,

as close to final product as possible

with the need for, at most, minimal further post generation manual entries or modifications (limited to medically subjective assessments).

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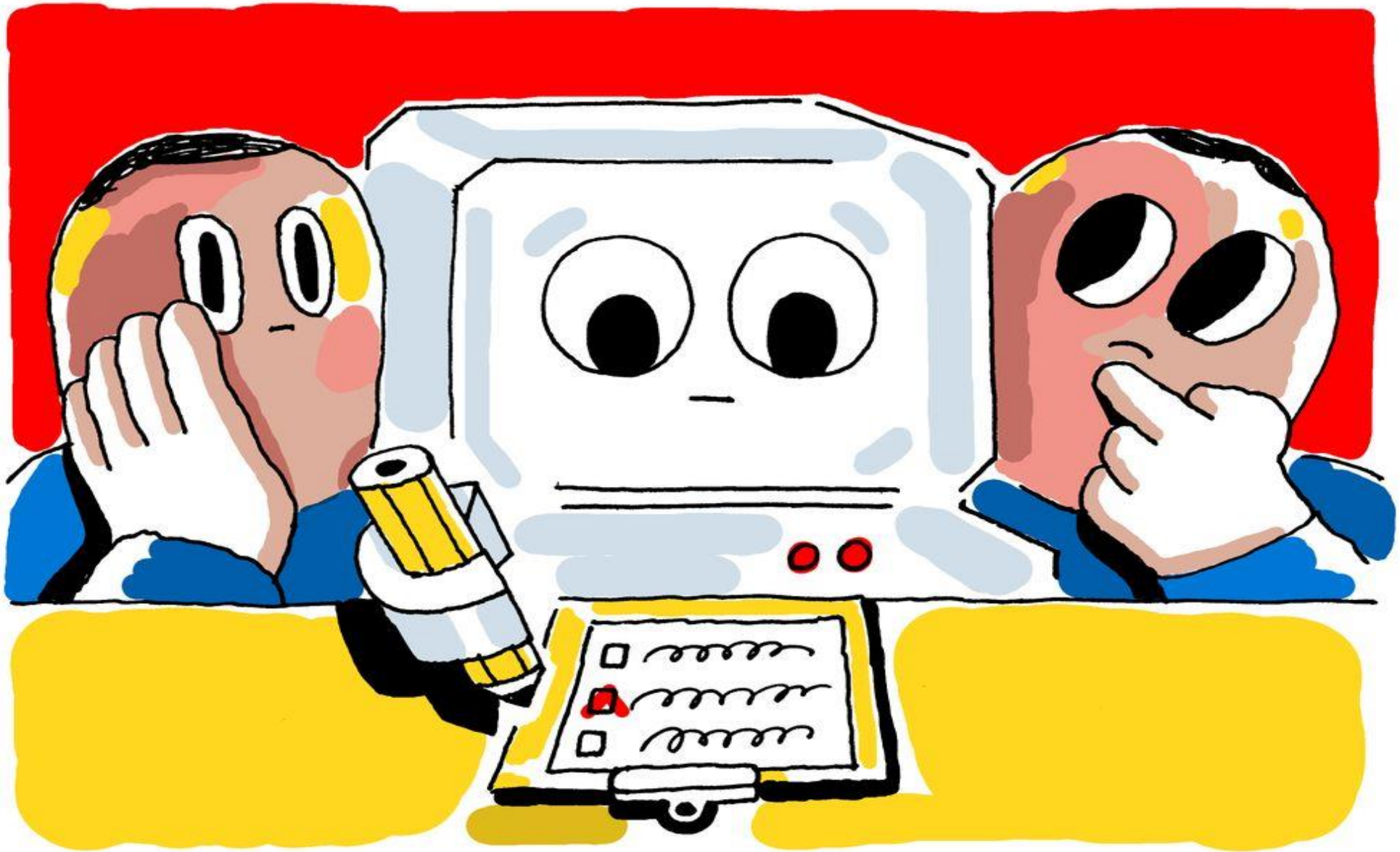
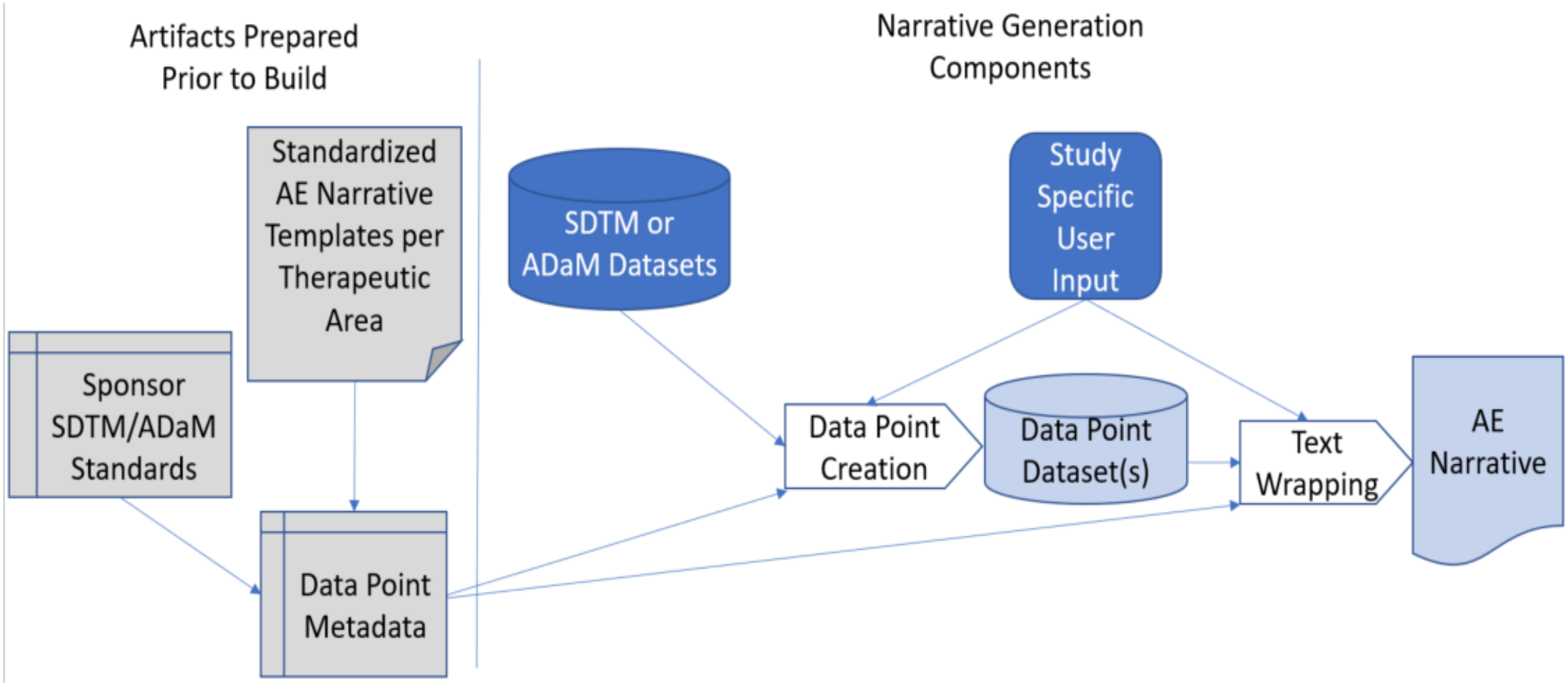
# So You Want Your Computer to Write Your Narrative



# Automation Big Picture



# Intended Take-aways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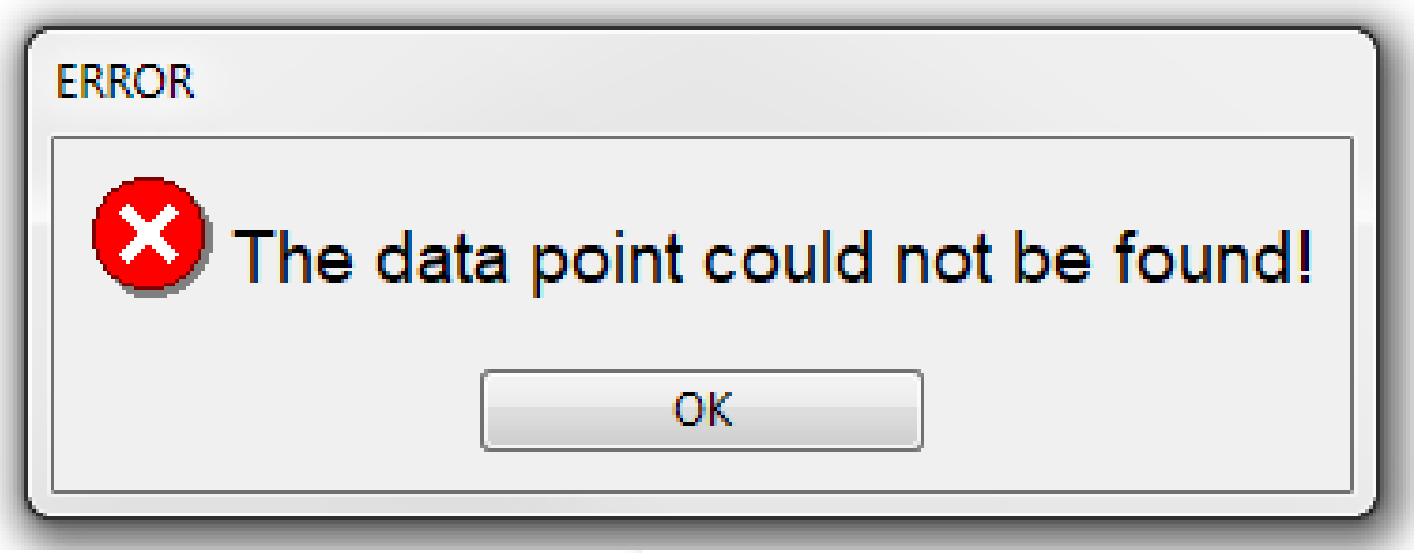
# Use SDTM or ADaM?


- Can be dependent on:
  - How fully developed are sponsor defined SDTM versus ADaM standards
  - The timing of when the sponsor develops their ADaM datasets relative to when it is desired to be able to generate the narrative
  - How much derived data (only present in ADaM) is desired to be included in the narrative

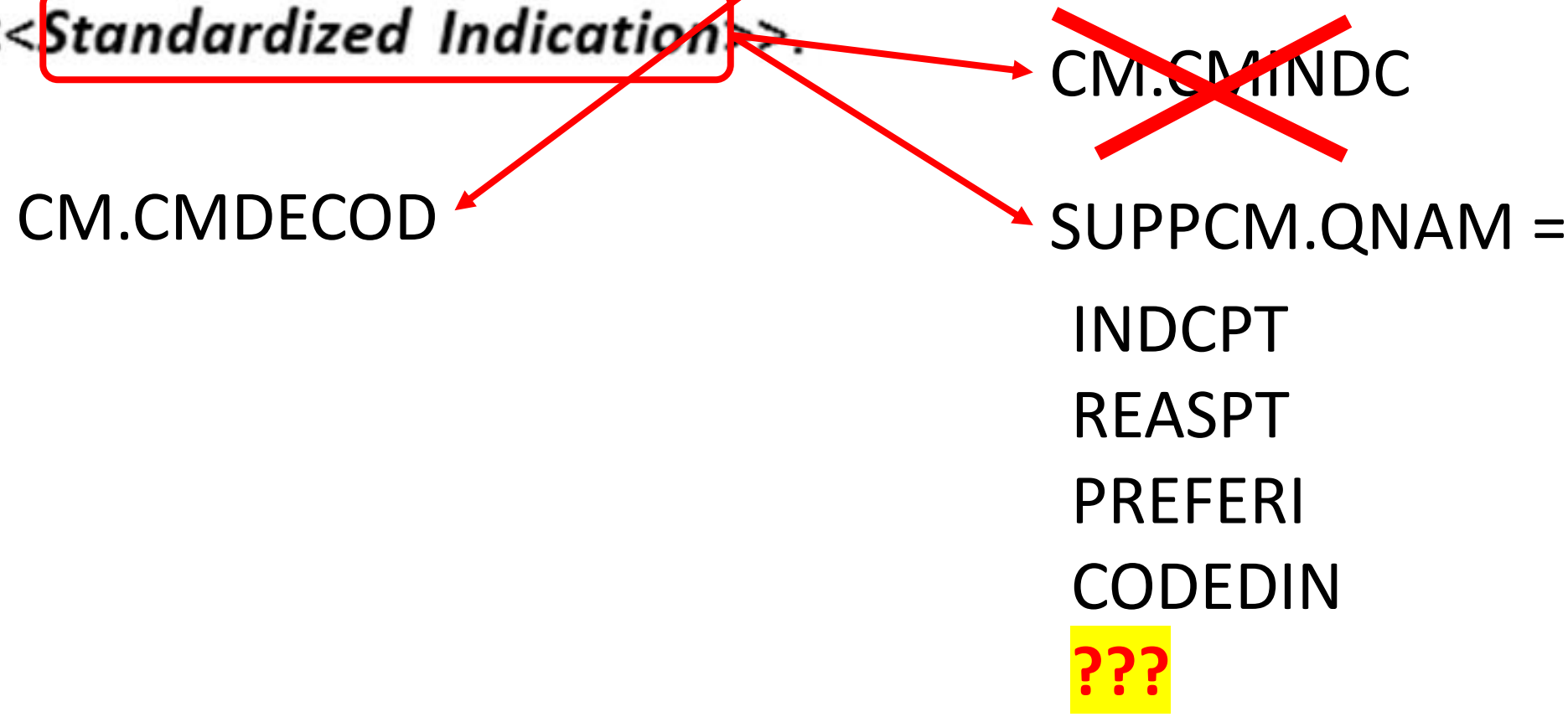
Maybe start with SDTM datasets, then
switch the source to ADaM datasets once available to take advantage of derived flag variables

# Source Data – Standardization is Critical



# Examples of Impact of Lack of Standardization

At the time of the AE, the following concomitant medications were ongoing: <<***Standardized Medication Name***>> for <<***Standardized Indication***>>.



# Examples of Impact of Lack of Standardization

The subject completed the study on <<***Completion Date***>>.

*Or*

The subject did not complete the study due to <<***Reason for Non-completion***>>.

**DS.DSDECOD =**
**where DS.EPOCH =**

| **DSDECOD** | **EPOCH** |
|---|---|
| COMPLETED | TREATMENT |
| COMPLETED | STUDY TREATMENT |
| ~~COMPLETED~~ | ~~RUN IN TREATMENT~~ |
| COMPLETED | FOLLOW UP |
| ~~COMPLETED RUN IN~~ | ~~TREATMENT~~ |
| COMPLETED STUDY ACCORDING TO PROTOCOL | STUDY |
| ~~COMPLETED~~ | ~~STUDY WASHOUT~~ |

# Impact of Standards Versions

# Implications for Sponsor Standards Development

- Priority needs to be given to developing standards for any piece of data which will be used by an automated tool


  - This includes standardizing mapping to:
    - ✓Domains
    - ✓Variables
    - ✓Controlled Terminology
    - ✓SUPPQUALs (subset of Controlled Terminology)

# Why solid sponsor defined SDTM/ADaM standards are critical

# Narrative Templates

✓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 coma separated concurrent AEs sorted by onset date, SOC, and PT – each followed by AE severity in parentheses*>>

{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.}

# From Template to Output

## Template Sentence

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

{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.}

## Output Sentence

At the time the subject experienced traumatic liver injury she was also experiencing angina pectoris (Grade 2), plural effusion (Grade 2), and pulmonary oedema (Grade 3).

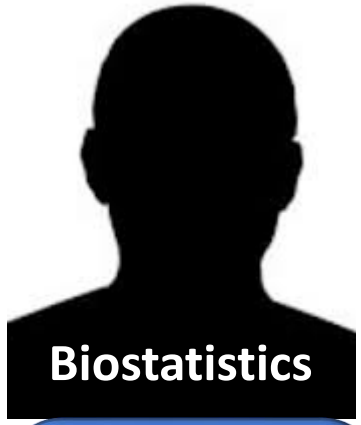
# Who Defines the Templates

**Clinical Development**

responsible for writing the narratives

**Automation Development**

to ensure all specifications have been covered



**Biostatistics**

to advise on logic rules

# Rules to be Defined


Examples:

Date imputation rules

Logic for selecting events/interventions:

- “during”
- “prior”
- “after”
- “at baseline”
- “ongoing”

# Factors Determining Contents


Study Specific

Type of data collected in a study

E.g., hospitalizations, autopsy, substance use, tumor response…

Study design

E.g., single dose/multi dose, has follow-up, open label/blinded…

Clinical events of interest

E.g., signs and symptoms, vital signs, abnormal labs…

Disease under study

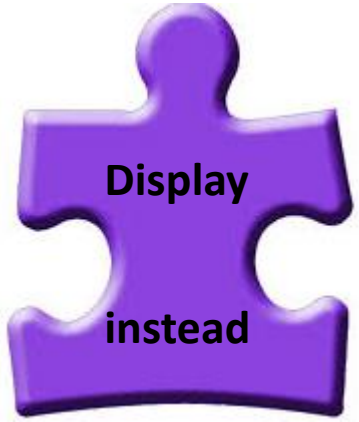
E.g., background medications, diagnosis differences…

# Why AE narrative templates need to be air tight

# Study Specific Information


e.g., to select subjects discontinuing within x number of days after last dose

Tell it: The value of x.




e.g., to display “last drug prior to”

Tell it: When you see EXTRT of MIR99 display instead Miracle Drug 99.


e.g., to display “all disease under study medications”

Tell it: What’s the value of CMCAT to use to find these?

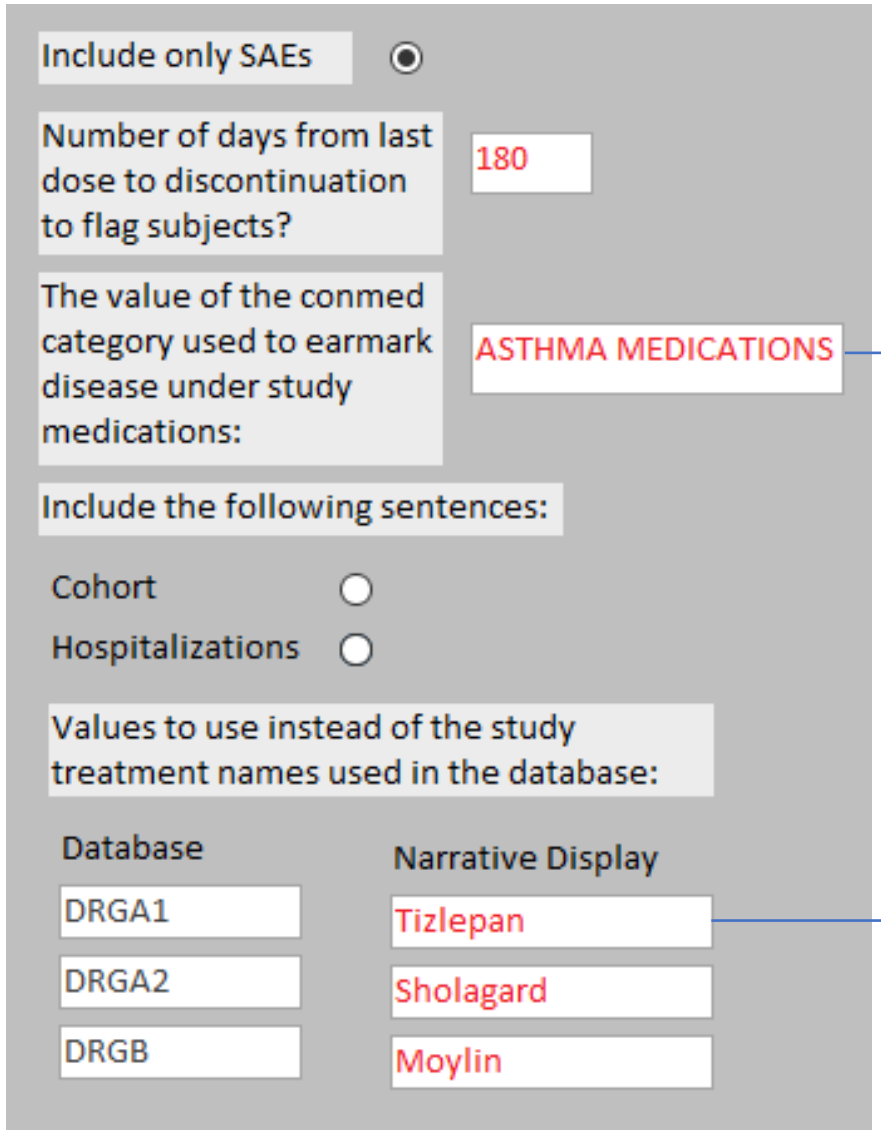

e.g., whether to display a statement about the cohort

---or---

which criteria to use to select subjects/events

Tell it

# From Study Specific Input to Output




The subject was taking the following disease under study medications at the start of the study: albeuteral and fluticasone proprionate.

The subject discontinued the study due to AE within 180 days of her last dose of Tizlepan (25 mg).

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# Why enabling study specific input is necessary

# What is Data Point Metadata?

- Metadata for the data points around which text is wrapped in the narrative

> 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 parentheses*>>.

- Conceptually similar to CDISC SDTMIG metadata:

**DM – Specification for the Demographics Domain Model**

**dm.xpt, Demographics — Version 3.2. One record per subject, Tabulation**

| Variable Name | Variable Label | Type | Controlled Terms, Codelist or Format | Role | CDISC Notes | Core |
|---|---|---|---|---|---|---|
| STUDYID | Study Identifier | Char | | Identifier | Unique identifier for a study. | Req |
| DOMAIN | Domain Abbreviation | Char | DM | Identifier | Two-character abbreviation for the domain. | Req |
| USUBJID | Unique Subject Identifier | Char | | Identifier | Identifier used to uniquely identify a subject across all studies for all applications or submissions involving the product. This must be a unique number, and could be a compound identifier formed by concatenating STUDYID-SITEID-SUBJID. | Req |
| SUBJID | Subject Identifier for the Study | Char | | Topic | Subject identifier, which must be unique within the study. Often the ID of the subject as recorded on a CRF. | Req |
| RFSTDTC | Subject Reference Start Date/Time | Char | ISO 8601 | Record Qualifier | Reference Start Date/time for the subject in ISO 8601 character format. Usually equivalent to date/time when subject was first exposed to study treatment. Required for all randomized subjects; will be null for all subjects who did not meet the milestone the date requires, such as screen failures or unassigned subjects. | Exp |
| RFENDTC | Subject Reference End Date/Time | Char | ISO 8601 | Record Qualifier | Reference End Date/time for the subject in ISO 8601 character format. Usually equivalent to the date/time when subject was determined to have ended the trial, and often equivalent to date/time of last exposure to study treatment. Required for all randomized subjects; null for screen failures or unassigned subjects. | Exp |
| RFXSTDTC | Date/Time of First Study Treatment | Char | ISO 8601 | Record Qualifier | First date of exposure to any protocol-specified treatment or therapy, equal to the earliest value of EXSTDTC. | Exp |
| RFXENDTC | Date/Time of Last Study Treatment | Char | ISO 8601 | Record Qualifier | Last date of exposure to any protocol-specified treatment or therapy, equal to the latest value of EXENDTC (or the latest value of EXSTDTC if EXENDTC was not collected or is missing). | Exp |

# Data Point Metadata Purpose

**Enable Possible Metadata Driven**

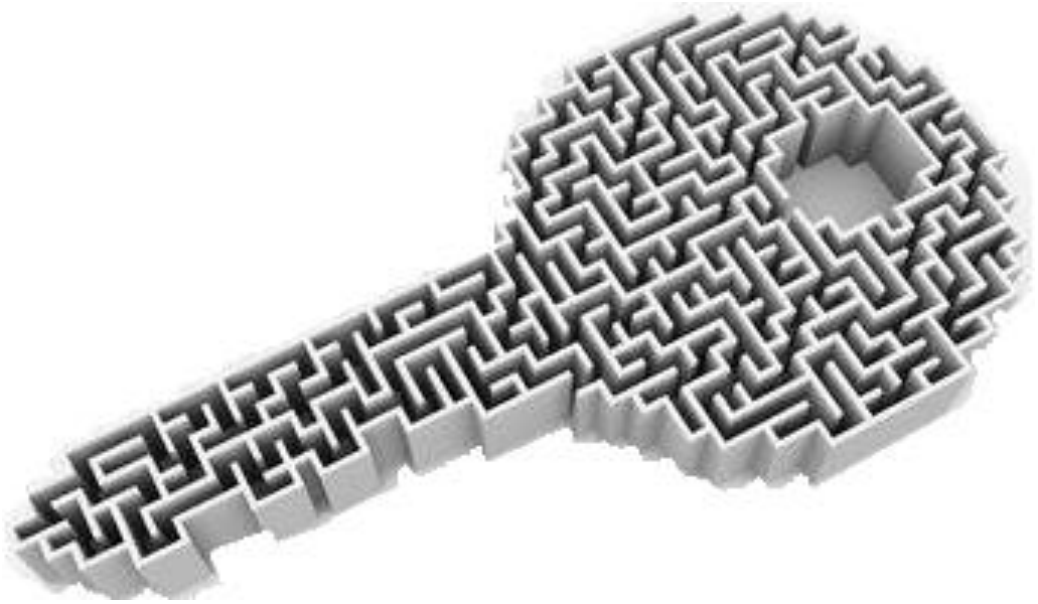
creation of data points (at least shells)

**Facilitate Troubleshooting, Maintenance, and/or Enhancement**

of the automation

**Provide Traceability**

back to the source (SDTM/ADaM) data



**Facilitate Validation**

of the data points

**Build in Consistency**

of conventions across TA

**Establish Assumptions**

of the (SDTM/ADaM) source data

# Why datapoint metadata is an automation development linchpin

# Keys to a Successful Automation Method

- ☑ correctly pulls in the data as intended
- ☑ can generate multiple versions of narrative templates
- ☑ can accept study specific user entry to control the data and display
- ☑ missing data and/or source data which fails to meet standards does not cause malfunction
- ☑ produces helpful error messages identifying issues with the source data
- ☑ provides a user-friendly user interface
- ☑ Can be run by the clinical group responsible for writing the AE Narrative without any programmer intervention

# What to look for in an implementation method

# Take-aways


Why solid sponsor defined SDTM/ADaM standards are critical
Why AE narrative templates need to be air tight
Why enabling study specific input is necessary
Why datapoint metadata is an automation development linchpin
What to look for in an implementation method