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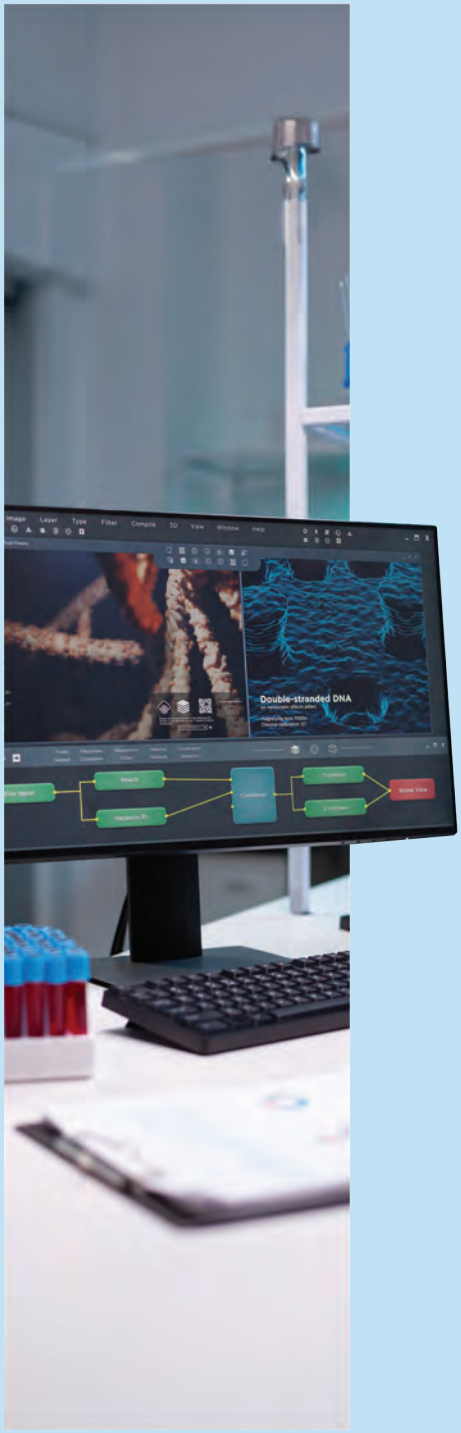

LEVERAGING AUTOMATION FOR CONTENT GENERATION OF PATIENT SAFETY NARRATIVES

Automation and artificial intelligence are indispensable assets for content authoring and content generation using patient datasets. Technological advances in automation offer significant advantages over the conventional medical writing process and achieve higher productivity, error free content and cost reduction. The current research focus on development and applicability for automation is used in safety narrative generation.

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Patient Safety Narratives

Patient safety narrative is a document which describes the reportable adverse events as per the safety narrative plan (SNP) during the study of an investigational drug. These narratives are a crucial part of clinical study report (CSR), which need to be submitted to the drug regulatory agencies during course of and after the completion of the clinical trial. Medical writers are responsible for authoring these narratives, which is generally a time-consuming process if done in the traditional way (manual writing) due to the reasons stated below.

Medical Writers need to go through large volumes of clinical and safety data from multiple sources for each patient and author the content accordingly. There is a need to update the narratives in case the underlying clinical or safety data of the patient undergoes changes during course of the trial. The number of narratives to be authored can range from a few hundreds to thousands for phase 2 and phase 3 studies which makes the authoring process effort intensive and time consuming.

Infosys has developed a solution for a leading pharma client which has proven to be highly efficient especially in scenarios where a large number of narratives need to generated for a study.

Infosys POV on the possible Solution/s

In order to envisage a solution that can assist in safety narrative generation, it is prudent to define the objectives first. Some of them could be:

- Achieve > 90% accuracy on paragraphs and 100% on tabular data
- Reduce ~1 hour spent on reviews and manual updates per narrative
- Reduce x days in overall narrative timeline

The first step towards automating the safety narrative generation process is to ensure that the clinical and safety data sets are readily available and are updated and reconciled in a timely fashion. It is also important to adhere to CDISC data standards (SDTM and aDAM).

Automation can be achieved by adopting a combination of business rules driven approach and Generative AI. The solution involves the following steps:

Step 1: Ingest the safety narrative plan

A safety narrative plan (SNP) details out the criteria which determines the list of patients for which safety narratives should be generated. Some of the criteria includes death event, serious adverse event, permanent discontinuation from treatment or study or both, adverse events of special interest etc. The SNP also indicates the format in which the narrative should be rendered e.g. prose, tabular or hybrid.

As the first step, the solution should be able to ingest the SNP and auto-configure the rules based on which the list of patients can be generated for which narratives will be required. It should also provide a default outline for the narrative content.

This can be achieved by using leveraging machine learning techniques such as natural language processing (NLP).

Step 2: Finalize the narrative outline and configure business rule(s)

The content structure of a narrative can vary across studies depending on the reporting requirements, therapeutic area and decisions made by the authors and other stakeholders. Hence, it is important to ensure that the solution provides flexibility in defining the narrative outline

and configure what content should be generated using business rules whenever applicable. One of the ways to achieve this is by breaking down narrative content into smaller sections or content components which can be arranged in the desired sequence and configured as per the reporting requirements.

Content components are the building blocks which provide the outline for a narrative and determine how and what the content should be generated. Each content component is a self-contained and configurable template which can be used to generate specific section(s) of a safety narrative e.g. introduction, demography, medical history, concomitant medications, adverse event description etc. The template can have prose, tabular or hybrid layouts.

Configurations could include one or more business rules e.g. specific lab tests can be configured for adverse events which can be configured using the MedDRA dictionary. The period within which lab tests should be reported can also be configured with respect to the onset date of the adverse event.

The solution provides a simple user interface for defining the outline of the narrative content by choosing the content components in the desired sequence and configuring the underlying business rules for the content components thereafter.

In addition, the reference variables of the clinical and safety data sets can be explicitly configured for each content component, since variable names across SDTM and aDAM data sets across different studies might have slight variations.

Once the content components are configured, the system is ready to generate safety narratives.

Step 3: Refine the generated content using AI/ML

The generated content can be reviewed and further refined using natural language processing (NLP) and natural language generation (NLG) algorithms as illustrated below

Output Prior to NLP (generated in tabular format)
List of other adverse events

Onset Date	Investigator Term	MedDRA Preferred Term
16 Aug 2021	Gallbladder perforation	Ruptured gallbladder
16 Aug 2021	Nausea	Nausea

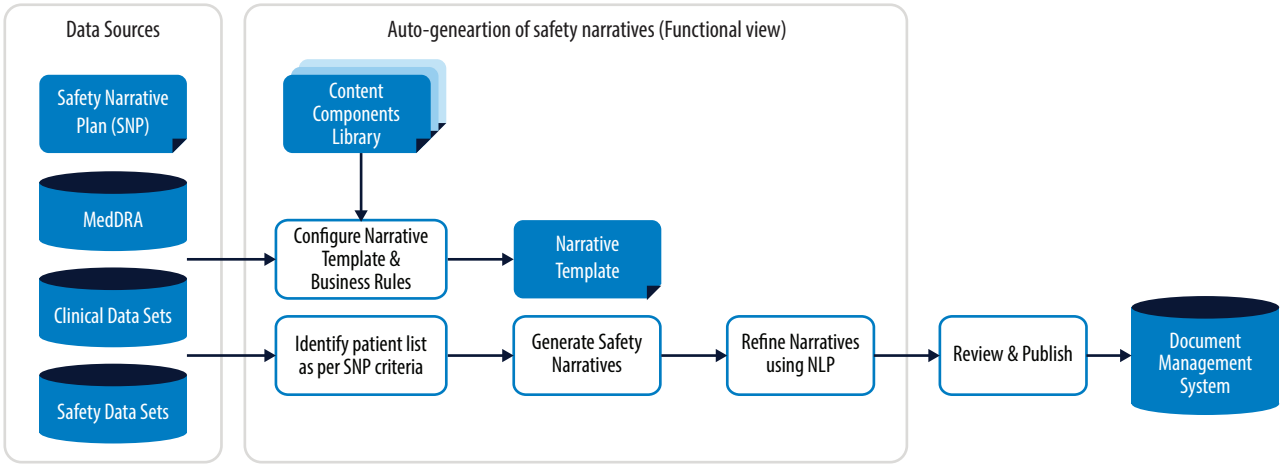
NLP output

The patient also experienced adverse events of Ruptured gallbladder and Nausea on 16 Aug 2021.

NLP and NLG techniques can also be used to summarize long paragraphs if needed.

The functional architecture diagram below depicts the workflow as described in the above-mentioned section.

Figure 1: Functional Architecture



Conclusion

Automation of safety narrative generation can help achieve up to 60% higher productivity and drastically reduce turnaround times especially for phase 2 and phase 3 studies having large patient populations.

Similar automation strategies can also be leveraged to generate other sections of a clinical study report In addition, Generative AI can be used to bring in content review effectiveness, which in turn can further optimize the overall content authoring process.

For illustration purposes. below is a sample safety narrative document with the content components and underlying business rules overlayed. Please note that the data in the sample narrative is hypothetical.

[Begin: Narrative Title]

DEATH NARRATIVE

[End: Narrative Title]

[Begin: Narrative Introduction]

Subject ID Number: 1001001

Treatment Group: No Subject Drug

Serious Adverse Event Reaction (AER) Case Number: 2020010001

Other SAE case(s) available for this subject that did not meet narrative criteria: None Available

MedDRA Preferred Term:	***Investigator Term:***
Serious Adverse Event(s):	
Choking	*Choking Secondary to Seizure*

Drug Permanently Discontinued Due to the Event(s): Not Applicable

Cause of Death: Choking on Food due to a Seizure

[End: Narrative Introduction]

[Begin: Demography & Dosing]

This 55-year-old Hispanic female subject in the United States received first dose of blinded therapy intramuscularly for the treatment of acute repetitive seizure (ARS) on 12 Jul 2020. Subsequently the subject entered in the open-label phase of the study in Aug 2020, but the open label diazepam was never administered.

[End: Demography & Dosing]

[Begin: Adverse Event Description, Business Rule: Include safety case description if available]

On 12 Sep 2020 the subject experienced a fatal choking secondary to a seizure. The caregiver informed the site that the subject was alone at home and choked following a seizure. Per the subject's husband the cause of death was choking on food due to a seizure. No treatment was given. Emergency Medical Technicians (EMTs) performed LPR but the subject was pronounced dead at her home; she was not taken to the hospital and was then taken by coroner. An autopsy was not performed. Action taken with study drug was not applicable. Illnesses present at the onset of choking secondary to seizure and other relevant medical history included seizure since 1976.

[End: Adverse Event Description]

[Begin: Concomitant Medications, Business Rule: report concomitant medications 2 weeks prior to the onset of adverse event]

Concomitant therapy taken within 2 weeks before the onset of choking secondary to seizure included pregabalin (Lyrica®) 75 mg every night, via oral route, for convulsion since 31 Aug 2020, valproic acid (Divalproex®) 2500 mg since 1 Sep 2020 by oral route for seizures (frequency reported as five times daily) and levetiracetam 1500 mg since 1 Sep 2020 by oral route (frequency reported as twice daily).

[End: Concomitant Medications]

[Begin: Causality Statement]

In the opinion of the investigator, there was not a reasonable possibility that the reported event of choking was related to the study medication diazepam.

[End: Causality Statement]

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