# CDISC Standards Can Benefit Medical Writers in Authoring Adverse Event Narratives

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## Introduction

The analysis of adverse events (AEs) is an important component for understanding the safety profile of any new therapy under investigation. An AE is any unfavorable experience that occurs during the course of a clinical trial that may or may not be due to the particular treatment being administered. Of particular importance, serious adverse events (SAEs) are AEs that result in death, are life threatening, require inpatient hospitalization or prolongation of hospitalization, result in disability or permanent damage, or are congenital anomalies or birth defects.

When a clinical trial subject has an SAE or other significant adverse event, such as those leading to the discontinuation of the study, a narrative is written for the clinical study report. These AE narratives summarize the details surrounding the event to enable understanding of the circumstances that may have led to the occurrence and its subsequent management.  Such details may include the dose of study drug at the time of the event, the duration of the dose prior to the event, concomitant medications taken at the time of the event and used to treat the event, and other AEs that may have recently occurred. Other details include demography, medical history, lab results, the severity of the event and whether the event was related to study medication.

Narratives are written from the original SAE report faxed from the clinical site in combination with data listings that are generated as part of the study deliverables. Information contained in the typical narrative requires the medical writer to review these many disparate data sources. This is time consuming and, true for any manual effort, can require additional review and quality control. Too often, these narratives are written when the full data becomes available, which may become a rate-limiting factor in completing the study report.

CDISC standards make it possible to automate the generation of AE narratives and to develop a flexible tool that is available to everyone.

## Methods

A SAS program generates AE narratives that are written to an RTF file. This file type can be viewed and edited in Microsoft Word or other word-processing packages. The program summarizes the contents of ADSL and several SDTM domains: demographics (DM), adverse events (AE), medical history (MH), disposition (DS), concomitant medications (CM), exposure (EX), ECG test results (EG, not shown), laboratory test results (LB) and vital signs (VS, not shown). Various options permit the users to tailor the narrative content or presentation to their specific needs. Once generated, the narratives can be further nuanced with additional details from the SAE report or additional study domains.

Data from a clinical trial of aneurysmal subarachnoid hemorrhage (Haley et al., 1993) provides illustration. Narratives were generated using JMP® Clinical.

## Results

Of the 902 subjects treated with nicardipine or placebo, 310 subjects experienced 683 SAEs. Using our program, 683 narratives were generated in less than one minute. A sample narrative that includes laboratory measurements is presented below.

## Conclusions

- Allowing a program to generate narratives initially can give the writer an idea of common themes, and for therapeutic areas where multiple SAEs per subject are the norm, can significantly hasten the writing process.
- Our program allows medical writers and clinicians to focus on the science, rather than spending time flipping through multiple listings to generate a narrative from scratch.
- Writing can be performed in stages prior to database lock as subjects complete the study.  The medical writer can edit or add additional detail to the narrative from additional sources.  Using the Compare Documents functionality of Microsoft Word, these edited narratives can be compared to those generated on the final locked database to highlight any data changes that should be incorporated into the final narratives.
- Using a program to generate the initial draft reduces errors and time spent in quality control.  Further, it can provide a more complete picture of the circumstances surrounding the SAE.
- CDISC standards make it possible to develop a flexible tool that is available to everyone. Understanding data formats, requirements and relationships within and between domains is critical for the development of easy-to-use and powerful software.
- Automatic generation of adverse event narratives illustrate the power and benefits of adopting CDISC standards to the masses, even among skeptics to the CDISC mission.

## Reference

Haley EC, Kassell NF & Torner JC.  (1993). A randomized controlled trial of high-doseintravenous nicardipine in aneurysmal subarachnoid hemorrhage. *J  Neurosurg* 78: 537-47.

## This narrative was written by a program. CDISC standards made it possible.

**Subject: 101004**
**Randomized Arm: NIC .15**
**Investigator: 101A**
**Drug and Dose at Event Onset: 30 mg/h of NIC .15**

### Serious Adverse Event (coded term [reported term]): COMA [COMA]

Subject 101004 was a 48-year-old white female. Her medical history included focal deficit (1988), headache (1988), loss of consciousness (1988), vomiting (1988), other medical condition (1977) and allergies (start date unknown). She began dosing with 30 mg/h of nic .15 on 28JAN1988 (Day 1). The subject discontinued the trial on 31JAN1988 (Day 4) due to death.

On 28JAN1988 (Day 1) the subject experienced a coma (severe) which was considered a serious adverse event (SAE). Though the event was considered serious, no reasons were provided on the case report form. At the time of the event, the subject was taking 30 mg/h of nic .15 and had been at this dose for 1 day. The SAE occurred on the first day of dosing with any study medication. Trial medication had an action of drug withdrawn 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 brain oedema (mild), hydrocephalus (severe), hyperglycaemia (mild), hypotension (severe), intracranial pressure increased (severe), subarachnoid haemorrhage (severe) and vasoconstriction (severe). Concomitant medications taken at the onset of the SAE included docusate sodium (stool softner), phenobarbital (sedative), potassium supplements (fluids) and ranitidine (decrease acidity).

The subject had the following abnormal lab tests at baseline: high creatine kinase [411 U/L, range = (15 - 195)], high chloride [112 mmol/L, range = (97 - 107)], high leukocytes [21 U/L, range = (3 - 20)], low partial pressure carbon dioxide [2394 Pa, range = (4655 - 5985)] and high partial pressure oxygen [31654 Pa, range = (9975 - 13965)]. The subject had no on-study lab tests with results different than baseline on or prior to the start day of the event. On the closest lab test day subsequent to the start of the event , the subject had the following on-study lab tests with results different than baseline: low blood urea nitrogen [2.142 mmol/L, range = (2.499 - 7.497) , BL = normal], low carbon dioxide [91.308 mg/dL, range = (100.004 - 130.44) , BL = normal], low creatinine [0.053040001768 mmol/L, range = (0.05746 - 0.10608) , BL = normal] and normal leukocytes [11 U/L, range = (3 - 20) , BL = high].

The investigator considered the AE to be related to study medication. The final outcome of the event was reported as recovered/resolved on 31JAN1988 (Day 4).

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