Utilization of Ascentos™ and Transend™ for SEND Implementation of Pivotal Studies in Support of IND Submission

A. Licollari [1], E. Mihalcea [1], M. Schuster [2], P. Dugan [2], and M. Wasko [2].
[1] Nucro-Technics, Scarborough, ON, Canada; and [2] PDS, Mt. Arlington, NJ, USA.

INTRODUCTION

The **Standard for Exchange of Nonclinical Data (SEND)** is an implementation of the CDISC Standard Data Tabulation Model (SDTM) for nonclinical studies, which specifies a way to present nonclinical data in a consistent format. The SEND Implementation Guide (SENDIG) is a document that provides implementers with specifications for implementing SEND, including how to model various nonclinical endpoints, rules to doing so, and examples with sample data.

The objectives of the study were to utilize Ascentos to capture data during the conduct of toxicology studies and the TranSEND software for SEND implementation of pivotal studies in support of Investigational New Drug (IND) submission as well as to analyze the efficiency and accuracy of utilizing an electronic data capture system (Ascentos) along with software designed to create SEND datasets (TranSEND) when compared to paper and/or Excel based data capture systems.

Ascentos is a fully integrated Laboratory Information Management Solution (LIMS) that is designed to enhance preclinical laboratory workflow. It has the advantage of enabling one master protocol to become the foundation across all stages of the study, from General Toxicology to Pathology. This design ensures accelerated setup and synchronized conduct of the study. Ascentos is an integrated solution with bi-directional data access across the various modules. It also has unlimited glossaries and user definable activities to simplify data entry. Ascentos software is compatible with common systems and instrumentations.

TRANSEND is the all-encompassing web ware solution that effectively aggregates and translates data from multiple organizations and LIMS to produce one set of harmonized and validated SEND files, including define.xml and define.pdf, as required by the FDA. The TranSEND's operational flow is depicted in Figure 1.

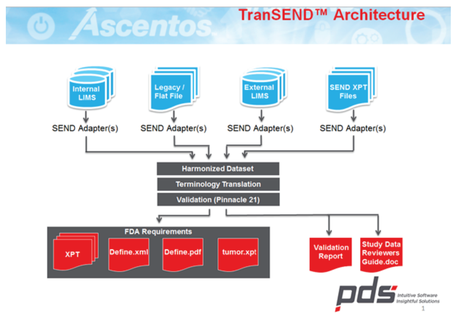

Figure 1 TranSEND's operational flow – An agnostic solution, TranSEND is able to receive data from all types of LIMS, Legacy Flat files and other XPT files from other sources. The TranSEND engine harmonizes the data, maps terms with Controlled Terminology and validates the dataset using the Pinnacle 21 Validator (the same validator the FDA uses). The FDA required files; XPT, Define.xml, Define.pdf, Validation reports and nonclinical Study Data Reviewers Guide (nSDRG) are all generated.

METHODOLOGY

Data from two 28-day repeated dose toxicity studies (rodent and non-rodent species) were generated at Nucro-Technics using electronic data capture system Ascentos V1.3 and then utilized TranSEND to create the SEND dataset. Several data sets such as plasma concentrations, pharmacokinetic parameters, electrocardiograms were prepared in excel format and uploaded to TranSEND prior to creating the export files. In addition in-life data utilizing data capture system that relied predominantly on paper and Excel were used to evaluate the efficiency and accuracy of the two methodologies and compared to determine the option that delivers the best scientific results. The standard CDISC SENDIG V.3.0 was used to generate the SEND files.

Validation of the SEND data sets against SENDIG V3.0 was accomplished with Pinnacle 21 Community Edition validator 2.1.1 (formerly OpenCDISC), which includes all of the FDA SEND published validation rules, version 2.1.

RESULTS

There were no errors in the Pinnacle 21 Community Edition Validator Report which had a total of 61,602 records in the rat study 330027 and 24,436 records for the dog study 330658. An example of the SEND export validation summary including protocol data, in-life data, microscopy is depicted in Figure 2.

Several warnings resulted from a small number of FDA SEND validation rules. The warnings were from permissible variables and were explained in the nSDRG which is generated for each study.

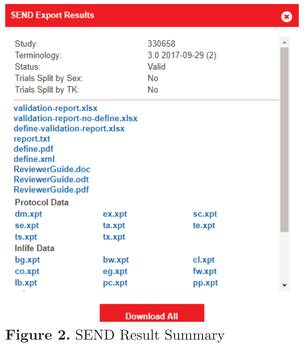

Figure 2. SEND Result Summary

DISCUSSION

This study evaluated the process of taking study data that was captured on paper or in Excel during the study and putting that data into the electronic format needed to include that data in the study report.

Studies have shown that manual data entry in scientific studies has an error rate of a low of 0.5% for some fields and as high as 6.4% in others. Fields in text formats were significantly more error-prone than those with direct measurements or involving numerical figures.1

Studies of single data entry (SE), where one individual enters the data, show error rates can be quite variable and have been reported to be as low as 10 and as high as 124 per 10,000 fields. In a study where two professional data managers conducted SE and consistency checks, error rates were lower, at 13 and 15 errors per 10,000 fields.2

28-day repeated dose studies can have a little as 25,000 pieces of data and as much as 45,000 pieces of data, depending on the number of animals, clinical observations, clinical laboratory tests and microscopic pathology readings. Using a conservative 30,000 pieces of data, the error rate of 14 errors per 10,000 fields shown by the professional data managers could still result in as many as 42 errors when data is manually entered into an electronic format from paper or Excel.

With the electronic data capture system, Ascentos, the assumption is that the data entered into the system is accurate (just as we would assume the data written on paper or originally entered into Excel is accurate). Using a validated system, there is no chance of human error in transcribing the raw data from the LIMS to the study report.

The manual creation of the SEND datasets, creates another opportunity for human error in manual data transcription. Assuming the same amount of data and error rate as above, it is reasonable to believe that the manual creation of the SEND dataset will result in another approximately 42 errors.

Efficiency of Using an Electronic Data Capture System (LIMS – Laboratory Information Management System) & electronic SEND dataset creation versus manual processes – typical 28 day tox study

Utilizing Manual Processes (in man hours)	Activity	Utilizing Ascentos & TranSEND (in man hours)	
+ 42	In study data collection (assumes 30,000 data points at 5 seconds savings)	0	Ascentos
176	Prepare data for report	8	
(100% QC) 160	QC data in report	(10% QC) 16	TranSEND
176	SEND dataset creation	40	
(100%) 160	SEND dataset QC	(10% QC) 16	
714	Total	80	

CONCLUSIONS

In conclusion, in this experimental work, we demonstrated that TranSEND is a suitable software for SEND implementation of pivotal studies in support of Investigational New Drug (IND) submission. In addition, utilization of the Ascentos LIMS (Laboratory Information Management System) to capture data during the study and the TranSEND software tool to create the SEND dataset for the legacy 28 day study increases remarkably the accuracy and data preparation efficiency when compared to manual data entry from paper or Excel.

REFERENCES

1 – Hong MDH, Yao HHI, Pedersen JS, et. al. Error rates in a clinical data repository: lessons from the transition to electronic data transfer – a descriptive study. BMJ Open 2013;3:e002406. Doi:10.1136/bmjopen-2012-002406

2- Monika M. Wahl, MPH, David V. Parks, BSEE, MBA, Robert C. Skeate, MD, Steven Goldin, MD, PhD.; Reducing Electronic Transcription Errors: J Am Med Inform Assoc. 2008;15:386-389. DOI10.1197/jamia.M2381