Application of SEND Data for Analysis

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A White Paper by the PhUSE Nonclinical Working Group.

To see an overview of the working group participants, go to
http://www.phusewiki.org/wiki/index.php?title=Application_of_SEND_Data_for_Analysis

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1. Introduction

SEND (Standard for Exchange of Nonclinical Data) is a tabulation of individual animal data from toxicology studies. As the implementation and exchange of SEND data is becoming more prevalent in the industry, focus is directed towards the usability and fitness for use of the SEND data. The usability of SEND data is essential in order to harvest the benefits of more efficient review and analysis.

While it is recognized that much of the nonclinical study analysis in current industry practice is performed on raw data extracts and the SEND datasets are created outside of this; SEND is being exchanged for a purpose. In this white paper a list of standard analyses that would be performed on the SEND package is identified to clarify the purpose of SEND data exchange.

The intent is that the definition of these analyses will make it possible for the industry to better assess SEND data quality through fitness for use.

2. Scientific background for SEND data review

This white paper will focus on using SEND tabulated data in facilitating the review of the study data, but not specifically how this review should be performed. This will be up to the scientific judgement of a toxicological reviewer. With that said, it is necessary to clarify a few principles behind a toxicologist's review of a nonclinical animal study.

The toxicology studies contribute to drug development by providing supporting information for setting a safe human dose and a risk-benefit profile for the compound. This is achieved through analysis of the animal data in order to

- Identify and characterize compound hazards
- Establish dose-response and exposure-response relationships
- Allow for informed assessment of risks to humans

At least three questions must be asked as part of a toxicological review of animal data:

1. Is there a real difference between control and treated groups?
2. Is the difference an effect of the experimental treatment?
3. Is the effect of treatment adverse?

In order to answer these questions and form a complete and accurate picture of the biological and toxicological relevance of the findings in a study, the toxicologist will review the data in several ways. This includes comparing treatment groups against each other, against controls and against historical control data, difference between sexes, looking at individual animals to identify outliers, susceptibility to toxicity, relevance for human healthy subject and patients ect. The use of statistical analysis is often an integral part of aiding the toxicologist in his or her review, but as the use of statistical methods is at the scientific discretion of the toxicologist it will not be discussed further in this white paper except for when SEND data can be compiled to facilitate such analysis.

The SEND data is divided into a set of domains which roughly corresponds to the defined endpoints that are measured in a toxicology study (e.g Body weights, food consumptions, clinical chemistry ect.). As part of

the toxicological review, endpoints are assessed individually (to answer question 1) as well as in conjunction with each other (to answer questions 2 and 3). This white paper will be centered on how SEND tabulated data can be utilized to aid in answering these three questions.

3. SEND domains

3.1 LB – Laboratory Test Results

4. References

1. http://www.cdisc.org/send. To download the SEND Implementation Guide: Find the box: SEND Product Downloads. Click “SEND Implementation Guide (IG) Version 3.0” to start the download.