Recommendations for Populating Control Type (TCNTRL) with CDISC SEND Controlled Terminology

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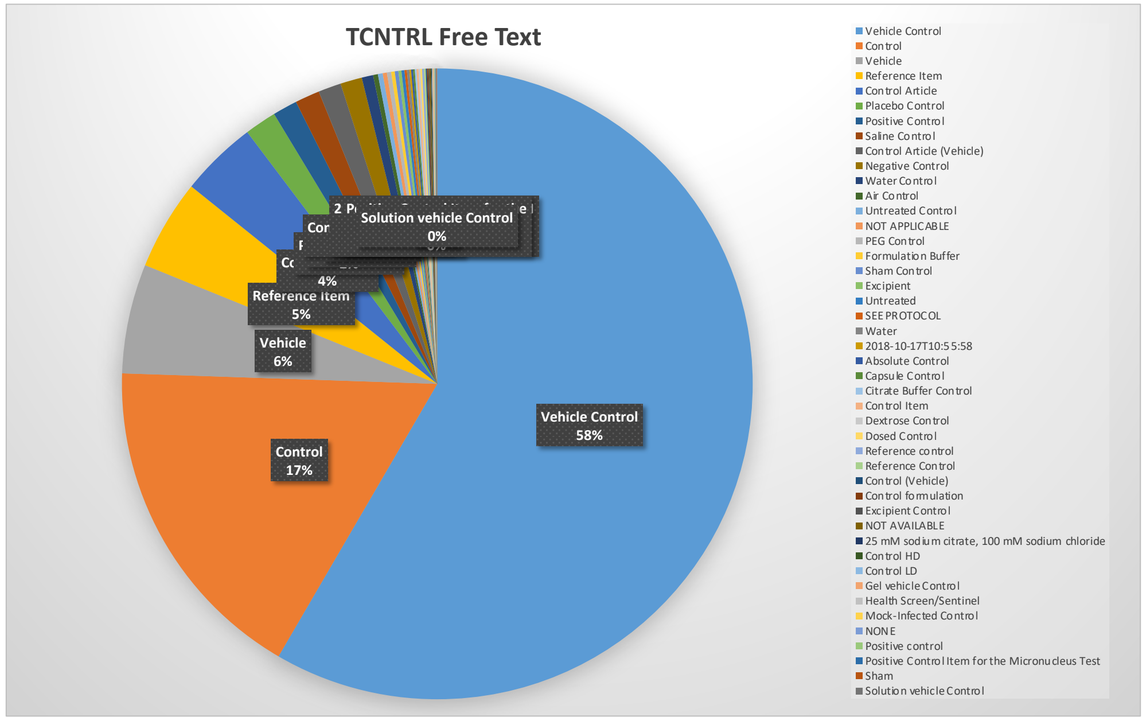
Abstract

Toxicologists need to determine if findings are treatment related or normal background findings. When SEND data sets are used in queries for background findings, it is important to accurately categorize the different control group types. SEND Trial Set (TX) domain includes Control Type (TCNTRL) parameter as free text, leading to ambiguous terms not adequately differentiating the various types of control groups. In order to utilize TCNTRL in cross-study searches to confidently identify vehicle/negative control animals, it is necessary to limit the variation of the TCNTRL terms. This poster recommends Controlled Terminology for TCNTRL parameter to increase the accuracy and value of SEND data. Based on the result from the publication '*Leveraging the Value of CDISC SEND Data Sets for Cross-Study Analysis: Incidence of Microscopic Findings in Control Animals*', it will increase the number of vehicle/negative control group records usability by approximately 38%, showing the importance of implementing Controlled Terminology for TCNTRL.

Background

In the manuscript Leveraging the Value of CDISC SEND Datasets for Cross-Study Analysis: Incidence of Microscopic Findings for Control Animals, data from the FDA CDER SEND dataset repository was analyzed to identify vehicle/negative control animals. The TCNTRL variable was populated over 90% of the time in >1,800 sponsor-submitted SEND datasets, TCNTRL was entered as free text including the use of synonyms and ambiguous terms.



Recommendation:

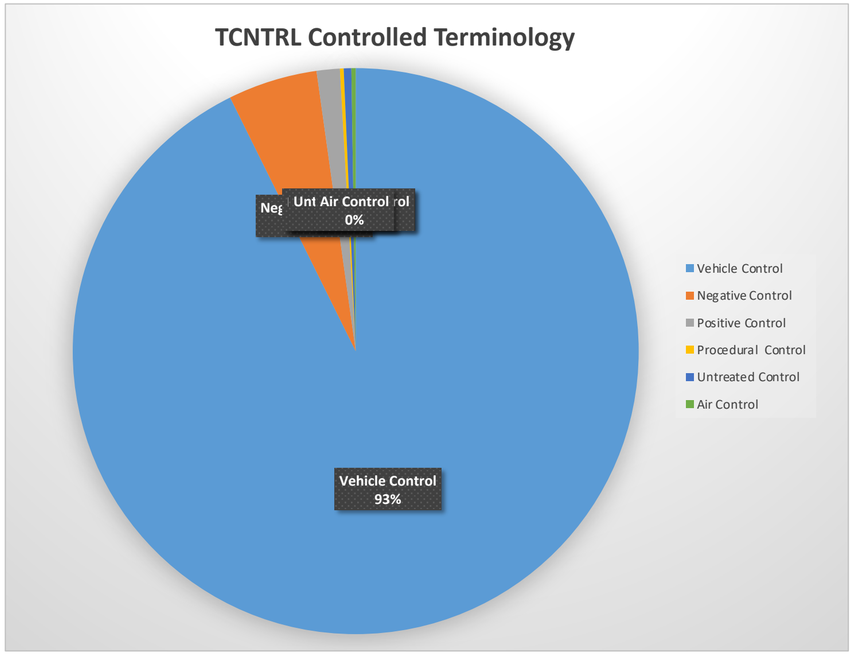
Implementing controlled terminology for TCNTRL (for SEND IG3.0 & 3.1), increases the number of vehicle/negative control group records usable for analysis by approximately 38%. This increase in properly classified records shows the importance of implementing controlled terminology for TCNTRL to distinguish vehicle/ negative control animals from positive control animals when evaluating background control findings. Currently, the CDISC Controlled Terminology team is developing a Codelist for Control Type (CNTRL) that is in alignment with our recommendations.

Overview

- **July 2020:** PHUSE Working Group project "Harmonization of SEND Implementation to Enable Historical Control Data Analysis" as a collaboration between BioCelerate and the PHUSE CSS's Nonclinical Topics Working Group to address SEND harmonization issues.
- **September 2020:** PHUSE CSS 2020, the Nonclinical Topics Working Group evaluated the proposal of using controlled terminology for the control type (TCNTRL) variable and concluded:
  - ❖ Use of CT is a straightforward solution
  - ❖ Exceptional value for historical control use cases, cross-study analyses or individual study analysis
  - ❖ High priority
- **August 2021:** *The Recommendations for Populating Control Type (TCNTRL) with CDISC SEND Controlled Terminology white paper* was published on the PHUSE website:https://phuse.s3.eu-central-1.amazonaws.com/Deliverables/Nonclinical+Topics/WP-058.pdf

Scope

Recommendations for TCNTRL controlled terminology are intended to harmonize and define control types for parallel design toxicology studies. Other types of study design (e.g., crossover, dose escalation, factorial and Latin square) are out of scope since the designs generally do not include animals that only received vehicle/negative control material. Parallel study design is the most common type of toxicology study design; therefore, the ability to accurately search on control type will create larger datasets for defining background control findings.



Conclusion

Industry is encouraged to adopt the proposed approach to populate TCNTRL using controlled terminology being developed by CDISC. The controlled terminology and definitions will increase the accuracy and value of SEND data to determine background control findings versus treatment effects. This will help in identification of historical control findings to enable identification of compound-related effects and also improve individual study or cross-study analysis.

Acknowledgements

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