PhUSE Computational Science Symposium (CSS) White Paper on *Analyses and Displays Associated with Adverse Events*

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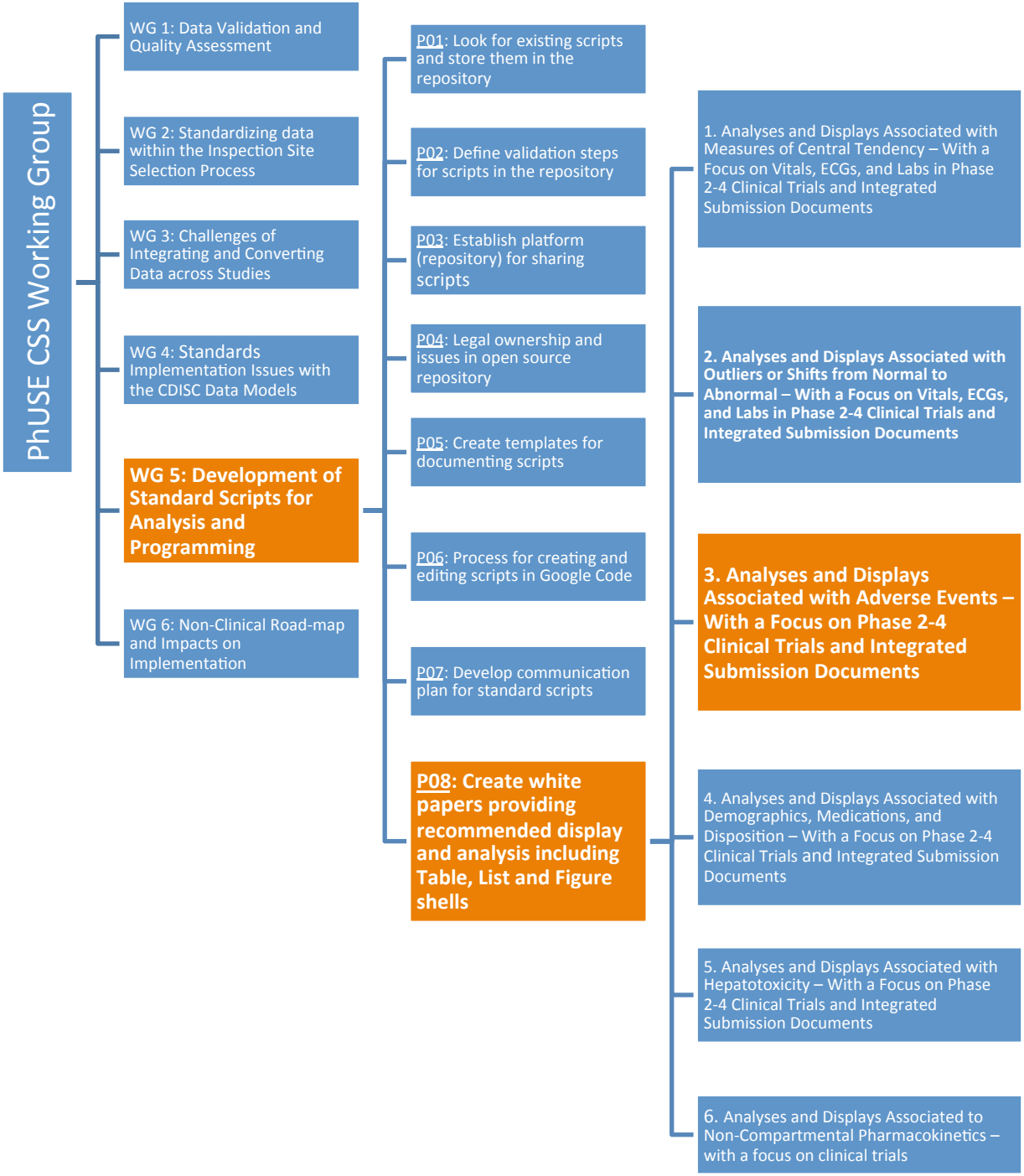
Introduction

- Industry standards have evolved for data collection (CDASH), observed data (SDTM), and analysis datasets (ADaM) leading to the recognized need for developing standard tables and figures for common assessments across clinical trials and across therapeutic areas

- The PhUSE Development of Standard Scripts for Analysis and Programming Working Group is leading an effort to create several white papers providing recommended analyses and displays for common safety measurements, and has developed a Script Repository as a place to store shared code

- The FDA Safety Reviewer Guidance includes discussion sections on safety review of deaths, other serious adverse events, dropouts and other significant adverse events, adverse events associated with dropouts, common adverse events, and also additional adverse event analyses and explorations

- This poster will cover the recommended tables and figures associated with this safety review as outlined in the draft white paper titled "Analyses and Displays Associated with Adverse Events – Focus on Adverse Events in Phase 2-4 Clinical Trials and Integrated Submission Documents".


PhUSE CSS Working Group
WG 1: Data Validation and Quality Assessment
WG 2: Standardizing data within the Inspection Site Selection Process
WG 3: Challenges of Integrating and Converting Data across Studies
WG 4: Standards Implementation Issues with the CDISC Data Models
WG 5: Development of Standard Scripts for Analysis and Programming
WG 6: Non-Clinical Road-map and Impacts on Implementation
P01: Look for existing scripts and store them in the repository
P02: Define validation steps for scripts in the repository
P03: Establish platform (repository) for sharing scripts
P04: Legal ownership and issues in open source repository
P05: Create templates for documenting scripts
P06: Process for creating and editing scripts in Google Code
P07: Develop communication plan for standard scripts
P08: Create white papers providing recommended display and analysis including Table, List and Figure shells
1. Analyses and Displays Associated with Measures of Central Tendency – With a Focus on Vitals, ECGs, and Labs in Phase 2-4 Clinical Trials and Integrated Submission Documents
2. Analyses and Displays Associated with Outliers or Shifts from Normal to Abnormal – With a Focus on Vitals, ECGs, and Labs in Phase 2-4 Clinical Trials and Integrated Submission Documents
3. Analyses and Displays Associated with Adverse Events – With a Focus on Phase 2-4 Clinical Trials and Integrated Submission Documents
4. Analyses and Displays Associated with Demographics, Medications, and Disposition – With a Focus on Phase 2-4 Clinical Trials and Integrated Submission Documents
5. Analyses and Displays Associated with Hepatotoxicity – With a Focus on Phase 2-4 Clinical Trials and Integrated Submission Documents
6. Analyses and Displays Associated to Non-Compartmental Pharmacokinetics – with a focus on clinical trials

White Paper Status: Preliminary Draft

1. Analyses and Displays Associated with Adverse Events – Focus on Adverse Events in Phase 2-4 Clinical Trials and Integrated Submission Documents

Version 1.0
Created xx XXXX 201x

A White Paper by the PhUSE Computational Science Symposium Development of Standard Scripts for Analysis and Programming Working Group

This white paper does not necessarily reflect the opinion of the institutions of those who have contributed.

Examples of Discussed Topics

- General Considerations
  - Which treatment comparison statistics to include: P-values, Percent Differences, Confidence Intervals, Odds Ratio, and/or Relative Risk
  - Whether or not to incorporate AE grades in tables
    - Eg., CTCAE grades 1-5, mild/moderate/severe

Recommended Tables, Figures

Treatment Emergent Adverse Events in Descending Order of Preferred Term with Treatment Comparison Statistics

Preferred Term	Treatment A n (%)	Treatment B n (%)	Total n (%)	Comparison Statistics (TBD)
Number of subjects reporting treatment emergent adverse events	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx
Preferred term 1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx
Preferred term 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx
Preferred term n	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx

Page x of y

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Recommended Tables, Figures

Treatment Emergent Adverse Events in Descending Order of Preferred Term within System Organ Class with Treatment Comparison Statistics

Preferred Term	Treatment A n (%)	Treatment B n (%)	Total n (%)	Comparison Statistics (TBD)
Number of subjects reporting treatment emergent adverse events	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx
System Organ Class 1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx
Preferred term 1.1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx
Preferred term 1.2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx
Preferred term 1.n	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx
System Organ Class 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx
Preferred term 2.1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx
Preferred term 2.2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx
Preferred term 2.n	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx
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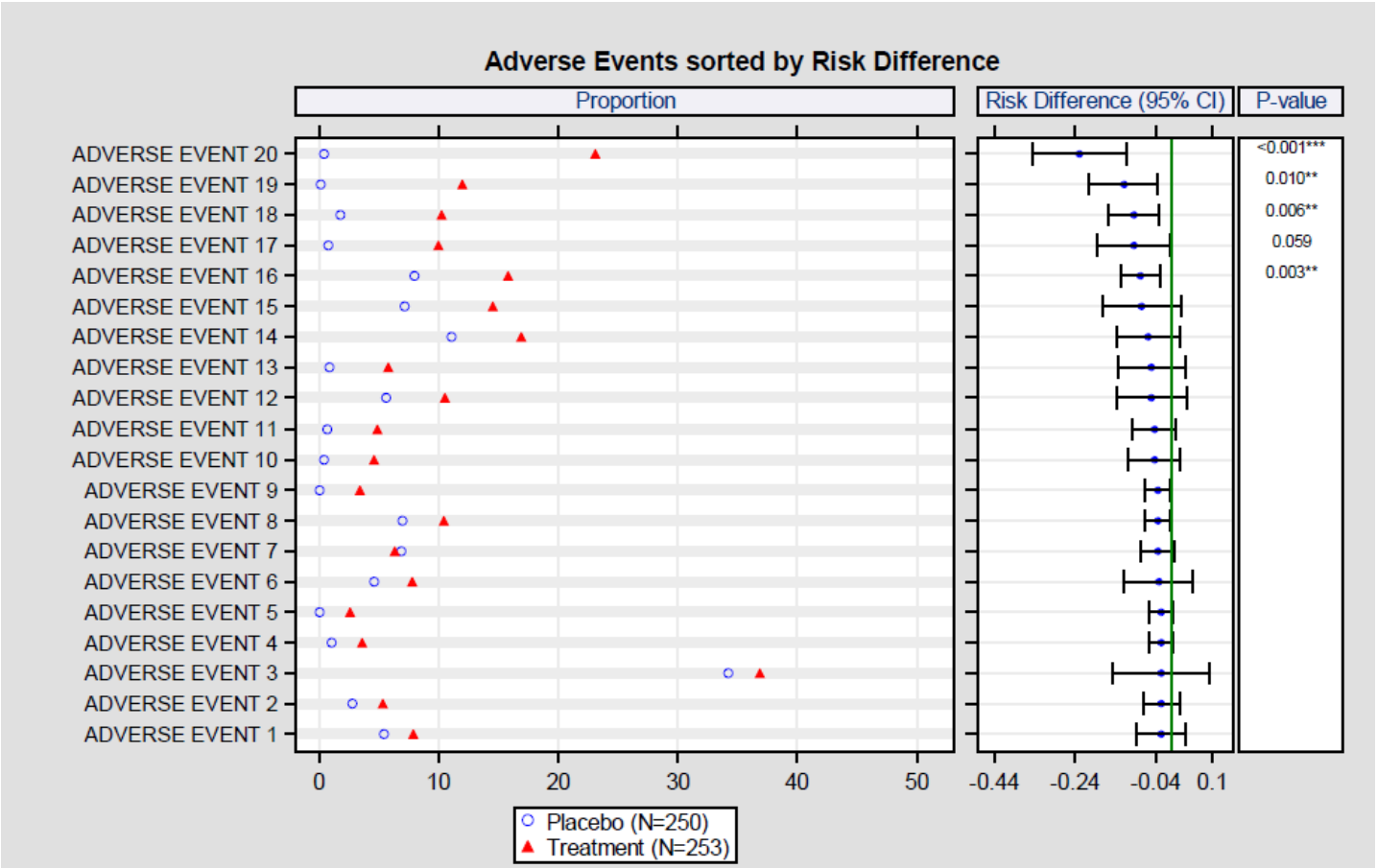
Recommended Tables, Figures



First 20 AEs that having highest risk in the Treated group comparing to Placebo group.
***, **, * statistically significant at 0.001, 0.01, and 0.05 level, respectively.
P-value from fishers exact test.

Conclusion

- White Paper is currently in preliminary draft form
- Next Steps include:
  - Collect feedback
  - Other displays for consideration
- This white paper provides guidance and foundation for the work in the Script-a-thon.

Acknowledgements

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Further Information

www.phusewiki.org