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Creating Standard Analyses and Displays for Common Safety Assessments in Clinical Study Reports

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ABSTRACT

The PhUSE Computational Science Symposium (CSS) Development of Standard Scripts for Analysis and Reporting Working Group is providing recommendations for analyses, tables, and figures for data that is common across therapeutic areas (laboratory measurements, vital signs, electrocardiograms, adverse events, demographics, medications, disposition, hepatotoxicity, pharmacokinetics). This paper provides an update of this effort, and instructions for how to participate in the development and review process.

INTRODUCTION

Industry standards have evolved over time for data collection (CDASH), observed data (SDTM), and analysis datasets (ADaM). Although substantial progress has been made, additional standardization can improve product development. Development of standard tables and figures with associated analyses will lead to improved product life-cycle evaluation by ensuring reviewers receive the desired analyses for the evaluation of patient safety. More importantly, having an organized process for shared learning of improved methodologies can lead to earlier safety signal detection and better characterization of the safety profile of our products. A cross-industry working group (the PhUSE Computational Science Symposium Development of Standard Scripts for Analysis and Reporting Working Group) is providing recommendations for analyses, tables, and figures for data that is common across therapeutic areas (laboratory measurements, vital signs, electrocardiograms, adverse events, demographics, medications, disposition, hepatotoxicity, pharmacokinetics). This poster will provide an update of this effort, and instructions for how to participate in the development and review process.

WORKING GROUP DESCRIPTION

The goal of the Working Group is to produce recommendations and establish a platform for the collaborative development of programs to be used as analytical tools for clinical trial research, reporting, and analysis. This includes:

- Identification of areas that can benefit from a standard set of analyses
- Development of recommendations for analyses, tables and figures within a topic area
- Creation of a process and guidelines for documentation and management of scripts (programs)
- Incorporation of data standards whenever feasible

There are two main areas of focus - the creation of white papers outlining recommendations for analysis and reporting of different types of safety data, and the development of scripts (programs) for generating the data displays shown in the white papers. This paper focuses on the creation of white papers portion of the project. A separate paper focuses on the development of scripts.

The leadership of the Working Group and contact information can be found in the CSS Working Groups section of the PhUSE Wiki: http://www.phusewiki.org/wiki/index.php?title=Standard_Scripts

WHITE PAPERS

The following white papers have been finalized, or are in progress:

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 Summary Documents *(finalized in October 2013)*

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 Summary Documents *(third draft targeted for public comment in September 2014)*
3. Analyses and Displays Associated with Adverse Events – With a Focus on Phase 2-4 Clinical Trials and Integrated Summary Documents *(first draft targeted for public comment in September 2014)*
4. Analyses and Displays Associated with Demographics, Disposition, and Medications – With a Focus on Phase 2-4 Clinical Trials and Integrated Summary Documents *(final white paper targeted for October 2014)*
5. Analyses and Displays Associated with Hepatotoxicity – With a Focus on Phase 2-4 Clinical Trials and Integrated Summary Documents *(first draft targeted for public comment by the end of 2014)*
6. Analyses and Displays Associated with Non-Compartmental Pharmacokinetics – With a Focus on Clinical Trials *(finalized in March 2014)*
7. Analyses and Displays Associated with QT Studies *(first draft targeted for public comment by the end of 2014)*

The scope of the white papers includes information that would normally be included in a Statistical Analysis Plan, plus any associated table, listing and figure shells, and detailed information that might be required for performing the analysis. However, actual implementation details, such as page layouts, margin requirements and variables to be used will not be addressed. Recommendations for difficult or potentially controversial decisions related to analyses or displays will be provided where possible; when a decision cannot be reached, a description of the issues that have been considered will be included.

Final white papers can be found in the publications section of the PhUSE website: http://www.phuse.eu/publications.aspx.

Drafts can be viewed in the CSS Working Groups section of the PhUSE Wiki: http://www.phusewiki.org/wiki/index.php?title=WG5_Project_08.

HOW TO PARTICIPATE

If you are interested in joining the Development of Standard Scripts for Analysis and Reporting Working Group, you can contact the Working Group leadership and/or add yourself to the Development of Standard Scripts listbox mailing list. For instructions on how to add yourself to a listbox mailing list, go to www.phusewiki.org and click on "Join a Working Group", join a mailing list section. Choose “CSS-WG-Standard-Scripts”.

If you are interested in joining the White Papers Project within the Development of Standard Scripts Working Group, follow the same instructions above, except choose the following listbox mailing list: CSS-WG-Standard-Scripts-WhitePapers.

If you are not interesting in joining the Working Group, but you would like to be alerted when a white paper has been finalized or ready for broad review, follow the same instructions above, except choose the following listbox mailing list: CSS-WG-SS-WhitePaperReviewers.

When a white paper has been finalized, or when a white paper is ready for broad review, please help spread the word within your organization and across your contacts. Thanks!

CONCLUSION

This paper is intended to serve as an update on the progress made by the Standard Scripts Working Group in developing white papers outlining recommendations for analysis and reporting of various types of clinical trial safety data. We encourage broad participation in these efforts!

REFERENCES

PhUSE home page: www.phuse.eu
PhUSE Wiki home page: www.phusewiki.org
PhUSE Publications (where final white papers reside): http://www.phuse.eu/publications.aspx
PhUSE CSS Standard Scripts Working Group Wiki page:
http://www.phusewiki.org/wiki/index.php?title=Standard_Scripts
PhUSE CSS Standard Scripts White Papers Project Wiki page (where draft white papers reside):
http://www.phusewiki.org/wiki/index.php?title=WG5_Project_08

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RECOMMENDED READING

PhUSE White Papers Project Wiki Page: http://www.phusewiki.org/wiki/index.php?title=WG5_Project_08
The following FDA guidance: Reviewer Guidance Conducting a Clinical Safety Review of A New Product Application and Preparing a Report on the Review

CONTACT INFORMATION

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