PharmaSUG 2016 - Paper PO16

"The car is in the shop but where are the mechanics?" The future of Standard Scripts for Analysis and Reporting

Dirk Spruck, Clinipace Worldwide, Marburg, Germany
Nina Worden, Santen, Emeryville, CA

ABSTRACT

The PhUSE/FDA Computational Science Standard Analyses Working Group has met its main goal: to establish a framework for standardizing analyses across the industry. Recent progress falls mainly in 3 areas:

1) The White Paper project has developed guidance on 9 data analysis topics, and has published 5 white papers.
2) The Infrastructure project has established a GitHub code repository.
3) The Content project has established implementation guidelines and a qualification process, and has published scripts that display standard measures of Central Tendency.

The focus for 2016, and moving forward, is to promote adoption of these standard analyses; to coordinate review of, finalize and publish white papers; and to increase the scope, quality and usability of the corresponding R and SAS scripts. A framework for collaboration enables standard analyses, but it is just a starting point. To fully realize the vision of standard industry analyses requires expertise and resources: a commitment by stakeholders. This poster will review the vision, summarize progress to date, and outline proposals to resource further advances.

INTRODUCTION

Since 2012 PhUSE has been organizing the Computational Science Symposium in Silver Spring, MD. The symposium is the annual face to face meeting of working groups, which continue to work on various topics throughout the year. The FDA has been participating in these working groups and at the 2016 conference it was announced that PhUSE and the agency are officially collaborating.

One of the working groups that emerged during the conference is the Analysis Standards working group, which is developing standards for the analysis of clinical trial data and a repository for analysis scripts. CDISC data standards cover the standardization all the way up to analysis data sets. However, the actual analysis and display of clinical data has not been standardized. It is the goal of the Computational Science (CS) Analysis Script working group to fill this gap of standardization.

While the working sub-groups of the analysis standards working group made impressive progress in recent years the 2015 – 2016 season was a time of consolidation and slower progress.

„YOU HAVE REACHED YOUR (FINAL) DESTINATION“

During the 2015 Computational Science Symposium Chris Hurley, Mary Nilsson, and Frank Senk displayed a poster titled “Standard Scripts for Analysis and Reporting ‘A vision within reach’”1. The poster displayed a race track with the achievements of the working group along the track. The main goal: to establish a framework for standardizing analyses across the industry has been met. And indeed in 2015 the vision of a repository of standard scripts that can be used by industry and regulators seemed to be within reach. Below is a summary of the progress made between the 2015 and 2016 conference:

White papers

The White Papers working group has been developing recommendations for standardized analysis displays on 9 analysis topics. The most recent paper on TQT studies was published right before the 2016 PhUSE/FDA Computational Science Symposium. Below is a list of all white papers currently published2:

- Analyses and Displays of Central Tendency (published 10Oct2013)
- Analyses and Displays of PK (published 25Mar2014)
- Analyses and Displays of Demographics, Disposition, and Medications (published 07Oct2014)
- Analyses and Displays of Outliers/Shifts from Normal to Abnormal (published 10Sep2015)
- White Paper TQT Studies (published 11Mar2016)

GitHub Code Repository

A code repository had been created in Google Code and was moved to GitHub in 2015 because of Google Code being discontinued. Along with the move the folders in the repository were restructured and a user friendly index page was generated.

Repository content

The script repository has been filled with scripts developed during Scriptathon events and with donated scripts from the FDA JumpStart program. Programming guidelines, qualification templates and guidelines were developed.

An important prerequisite for the acceptance of standard scripts in the repository is a certain level of trust. To achieve trust a qualification process for the scripts was developed in the 2015-2016 season. However the actual qualification of scripts has proved to be resource intensive. The qualification and documentation process has been started but because of the lack of dedicated resources its completion is currently not within reach.

THE ROAD AHEAD

The Standard Analysis working group will continue the development of recommendations for analysis and display of clinical trial data and publish white papers. The white papers are the basis for the standard scripts, which will be hosted in the script repository. The repository and the content will continuously be improved. The following bullets summarize the roadmap:

Develop Interface

- Build technology around the code library, e.g. a graphical user interface
- Increase usability and accessibility of standard scripts

Content and Qualification

- Add more scripts to library
- Qualify and document code
- Link to the Semantic Technologies' Analysis Results & Metadata project
- Establish common health authorities and industry scripts

Promotion, Acceptance, and Training

- Develop Training Material
- Promote analysis standards
- Create awareness and acceptance

CONCLUSION - "THE ENGINE STALLED"

The idea of having a code repository with standard scripts for industry and regulatory has been around for a few years now. The infrastructure and processes are in place and usability has been tested. An interface has been built for easy access and search of code. The FDA has provided some of their JumpStart scripts as part of the PhUSE / FDA collaboration. However, work still needs to be done to create packages around the scripts with qualification, documentation and training material. This last step is time consuming and resource intensive.

The main challenge to complete the vision of a comprehensive framework for cross industry standard analysis is the lack of resources. The framework is available, the concept proven. Processes are in place, and the library contains an initial set of scripts.

In order to realize the complete vision the standard working group proposes to:

- Secure monetary funding
- Get dedicated resources from sponsors
- Collaboration with academics

REFERENCES

1. Hurley, Chris; Nilsson, Mary; Senk, Frank, "Scripts for Analysis and Reporting 'A vision within reach'", *PhUSE Computational Science Symposium 2016*. Silver Spring, MD. Available at http://support.sas.com/resources/papers/proceedings09/TOC.html.
2. PhUSE Computational Science Working Groups deliverables catalog, 23March2016: Available at http://www.phuse.eu/CSS-deliverables.aspx

ACKNOWLEDGMENTS

The authors would like to thank the CS working group members for spending countless hours to develop and promote standards for the analysis of clinical trial data. Special thanks to Mary Nilsson and Hanming Tu for leading the standard analysis working group.

RECOMMENDED READING

- PhUSE Computational Science Working Groups: http://www.phusewiki.org/wiki/index.php?title=CSS_Working_Groups
- PhUSE Computational Science Working Groups deliverables catalog: http://www.phuse.eu/CSS-deliverables.aspx

CONTACT INFORMATION <HEADING 1>

Your comments and questions are valued and encouraged. Contact the author at:

Dirk Spruck
Clinipace Worldwide
Softwarecenter 3
35452 Marburg, Germany
dspruck@clinipace.com

Nina Worden
Santen