

Qualification Process for Standard Scripts Hosted in the Open Source Repository

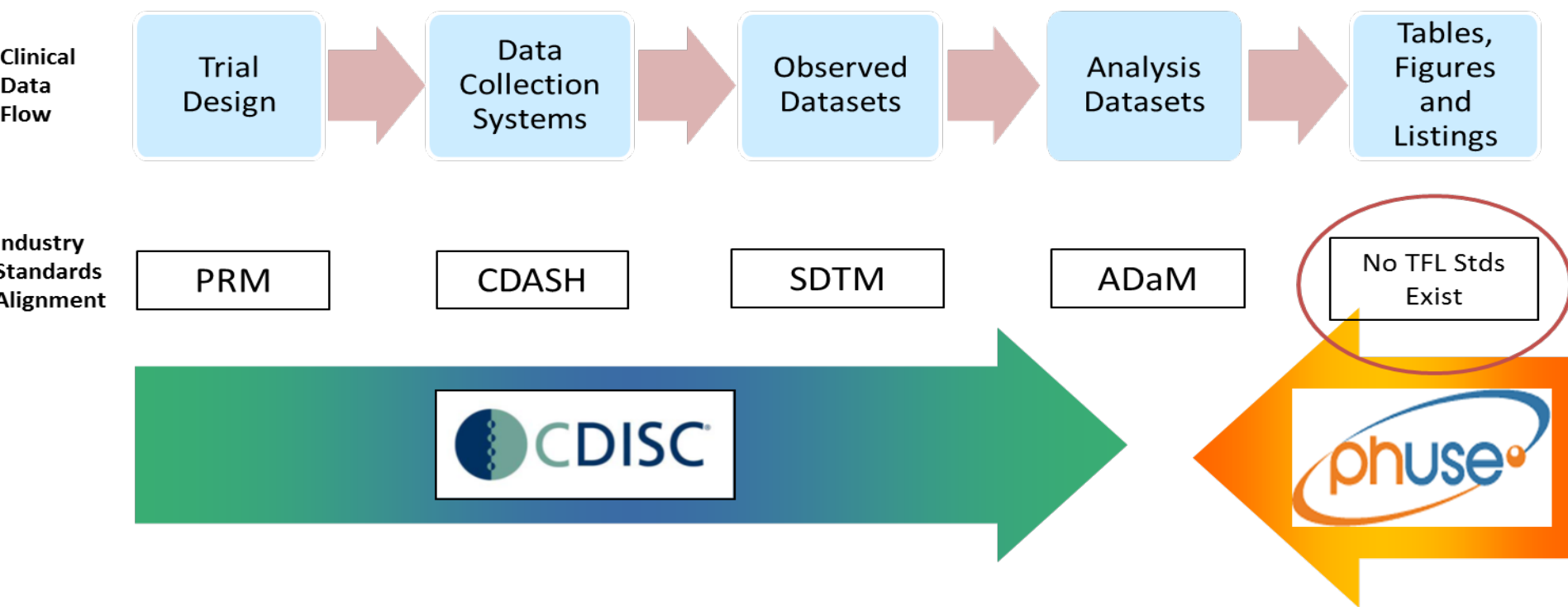
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ABSTRACT

Industry standards have evolved over time for data collection (CDASH), observed data (SDTM), and analysis datasets (ADaM). Using these standards as a foundation, a cross-industry working group within the PhUSE Computational Science Symposium (CSS) continues to establish standard analyses for data that are common across therapeutic areas, and a repository for SAS and R programs to analyze these data (laboratory measurements, vital signs, ECG, adverse events, demographics, medications, dispositions, hepatotoxicity, pharmacokinetics). Development of these standard tables and figures with associated scripts 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. The PhUSE CSS working group **Development of Standard Scripts for Analysis and Reporting** made substantial progress in 2014 to establish a code repository for standard analyses. The objective of this poster is to describe this cloud-based repository, and our process for qualifying these open source programs that support clinical trial research, reporting, and analysis.

SUMMARY OF STANDARDIZATION



PhUSE WHITE PAPER SUMMARY

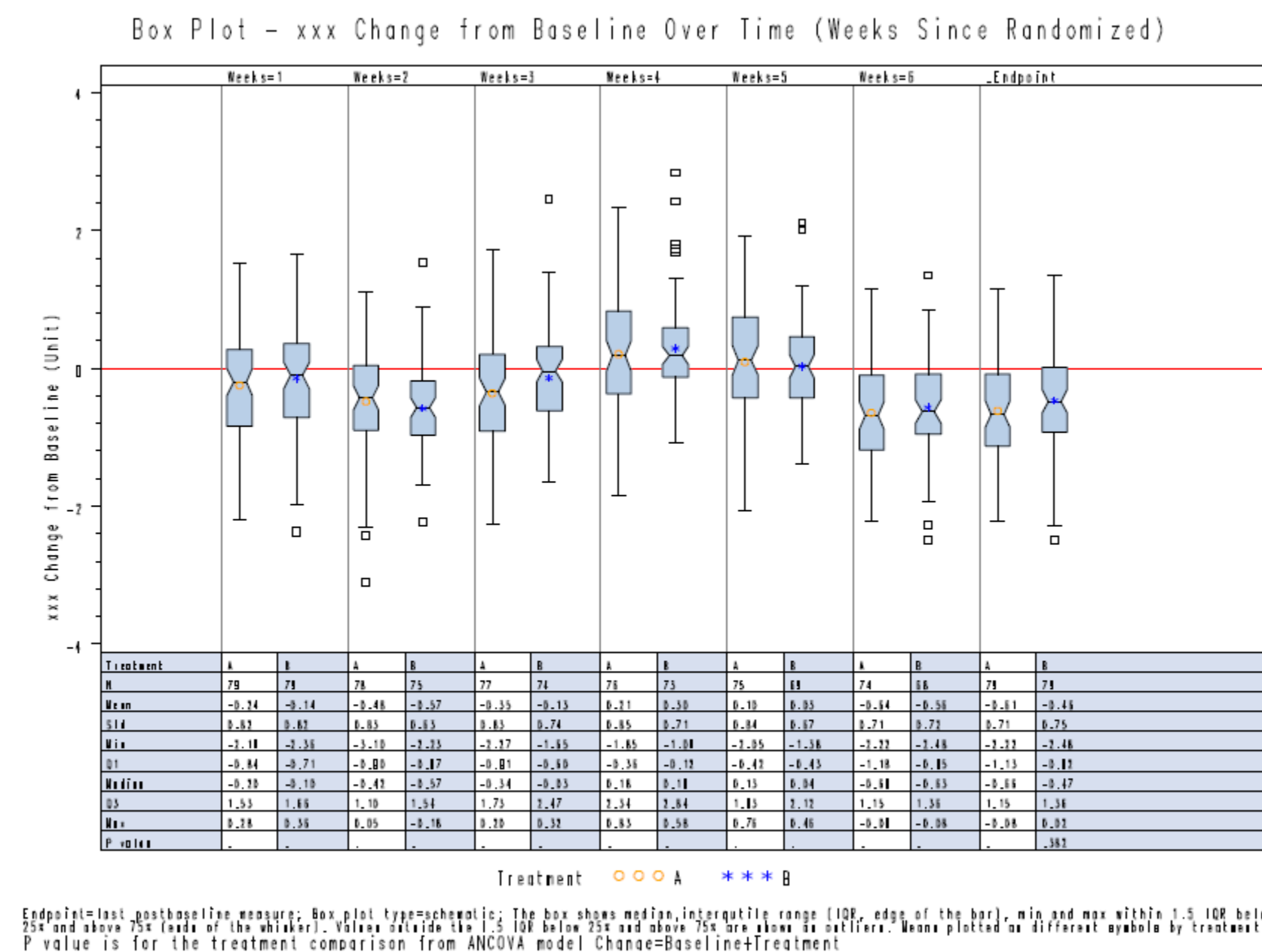
- Nine white papers at various stages
 - ECGs, Vitals, Labs – Central Tendency
 - **Finalized** October 2013
 - ECGs, Vitals, Labs – Outlier/Shifts
 - Draft 3 Review ongoing – Target Q2 2015
 - Adverse Events
 - Draft 1 Review ongoing – Target Q1 2015
 - Demographics, Disposition, Medications
 - **Finalized** October 2014
 - Hepatotoxicity
 - In progress – Call for volunteers
 - Pharmacokinetics
 - **Finalized** March 2014
 - QT Studies
 - In progress – Volunteers needed
 - Questionnaire
 - In progress – Volunteers needed
 - Events of Special Interest
 - In progress – Volunteers needed

Final White Papers: www.phuse.eu
Draft White Papers: www.phusewiki.org

EXAMPLE DISPLAYS FROM THE WHITE PAPERS

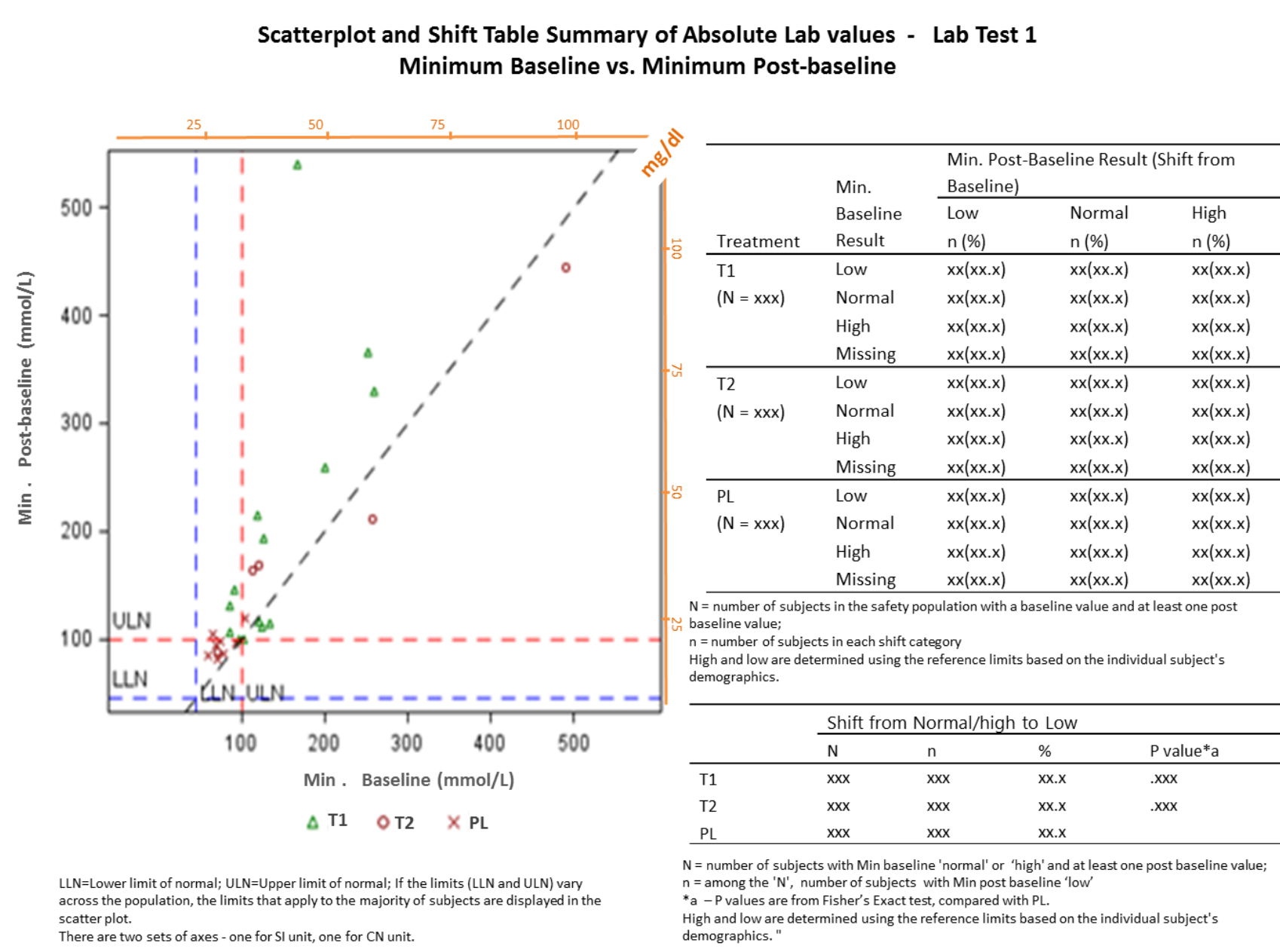
Mean Changes–Boxplots

- Visualize changes over time, and changes from baseline
- Assess the impact of outliers (out-of-range values in red)
- Easy to see treatment differences
- Summary table complements box plot



Outliers/Shifts

- Outliers/shifts analysis for safety measures
- Min. & Max. Baseline vs. Post-baseline comparisons
- Scatter plot of patient-level values
- Shift table summaries
- Treatment-emergent High/Low table



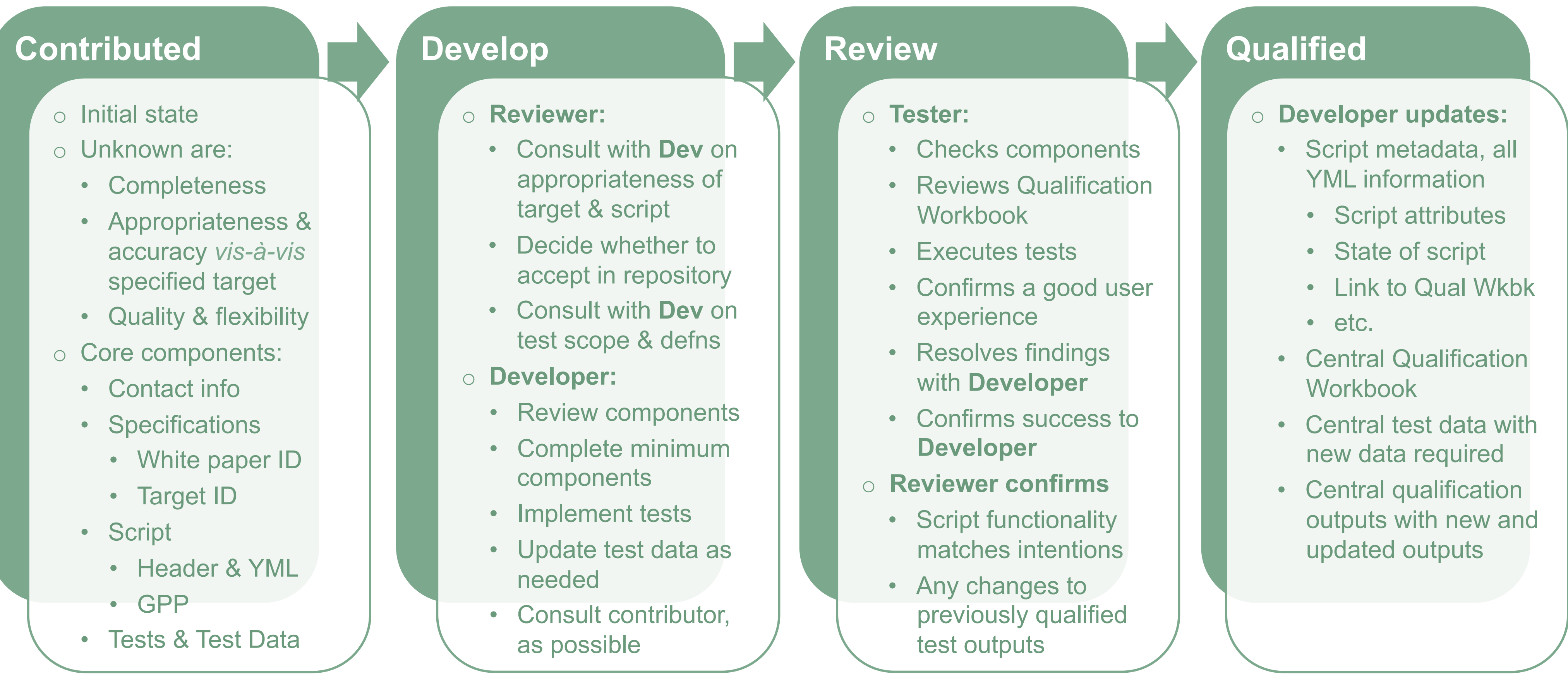
Qualification of Scripts in our Repository

Roles

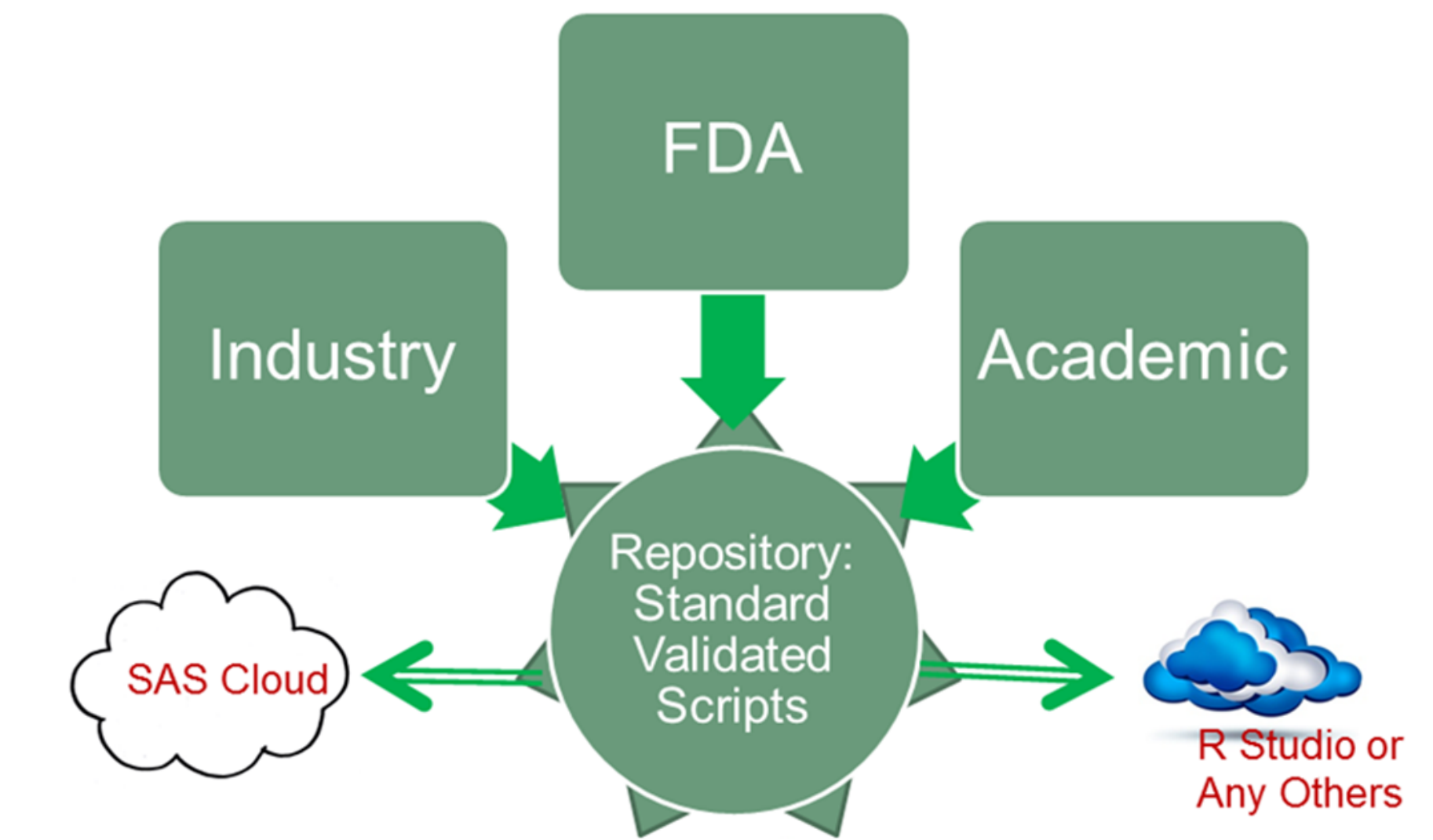
- **Contributor:** Anyone with skill & interest
- **Developer:** A volunteer familiar with our objectives
- **Tester:** A volunteer familiar with our objectives
- **Reviewer:** Contributors to our white papers

States

- **Contributed:** Script received from any source
- **Develop:** A volunteer is progressing the script
- **Review:** A volunteer is reviewing the script
- **Qualified:** Successful review, ready for public use



SCRIPT REPOSITORY – THE VISION



SCRIPT REPOSITORY

- PhUSE Repository:
 - <http://code.phuse.com>, or
 - <https://code.google.com/p/phuse-scripts/>
- Google Code to host the script repository
 - MIT open-source license
 - Process guidelines under development
 - **24 SAS and 3 R scripts** contributed by 2015
- Established the basic structure and process
 - ✓ Folder structure and naming conventions
 - ✓ Required metadata and recommended programming style for scripts
 - ✓ Roles and responsibilities
 - ✓ Tasks and duties
 - ✓ Process of tracking issues
 - ✓ Test data and validation documentation

CONCLUSIONS

- Industry standards have evolved over time for collected (CDASH), observed (SDTM), and analysis data (ADaM).
- Shared learning of improved methodologies can lead to earlier safety signal detection and better safety profiles.
- Our working group volunteers are delivering standard data displays based on industry input and review.
- We have established an open-source repository for sharing SAS and R scripts across the industry.
- We now aim to deliver standard scripts that can be used across the industry to deliver standard displays & analyses.
- We welcome new members! Contact information on www.phusewiki.org.