



An Update on the PhUSE Standard Analyses and Code Sharing Working Group

ASA Webinar

Hanming Tu and Mary Nilsson

02 May 2017

PhUSE

PhUSE stands for **P**harmaceutical **U**ser **S**oftware **E**xchange and is an independent, not-for-profit organization run by volunteers. Since its inception (2004), PhUSE has expanded from its roots as a conference for European Statistical Programmers, to a global membership organization and platform for the discussion of topics encompassing the work of Data Managers, Biostatisticians, Statistical Programmers and eClinical IT professionals.

- Hosts events
 - Annual conferences: EU since 2004; US starts 2018
 - Computational Science Symposiums: US since 2012; EU since 2016
 - Single Data Events: 4+ in US, 1+ in other regions per year
- Maintains a website: <http://phuse.eu>
- Publishes “PhUSE News”



Computational Science Collaboration

Mission:

*To provide an open, **transparent**, and collaborative forum in a **non-competitive** environment in which Academia, Regulators, Industry, and Technology providers can address computational science needs in support of product development and regulatory review, ultimately bringing safe and effective products to those who need them*

Collaboration with PhUSE started in 2012



**Computational Science
Working Groups**





Computational Science Working Groups



Working Group Information

Key site to know about: www.phuse.eu

Working Groups Button: Overview of active projects, new project ideas, call for volunteers, finalized work packages, draft work packages available for public review and comment

Conferences and Events Button: Slides from conferences, information on upcoming conferences

Wiki Button: Working group and project team updates, minutes, etc.



**Computational Science
Working Groups**





Computational Science Working Groups



Standard Analyses and Code Sharing Working Group Vision/Goals

- Leverage **crowd-sourcing** to improve the content and implementation of analyses for medical research, leading to better data interpretations and increased efficiency in the clinical drug development and review processes.
 - Establish and maintain a publicly available repository for storing program code to be used as analytical tools for medical research.
 - Where gaps exist, develop recommendations for analyses and displays in areas that could benefit from crowd-sourcing.
 - Where gaps exist, develop code for recommended analyses and displays that could benefit from crowd-sourcing (to reside in the repository).

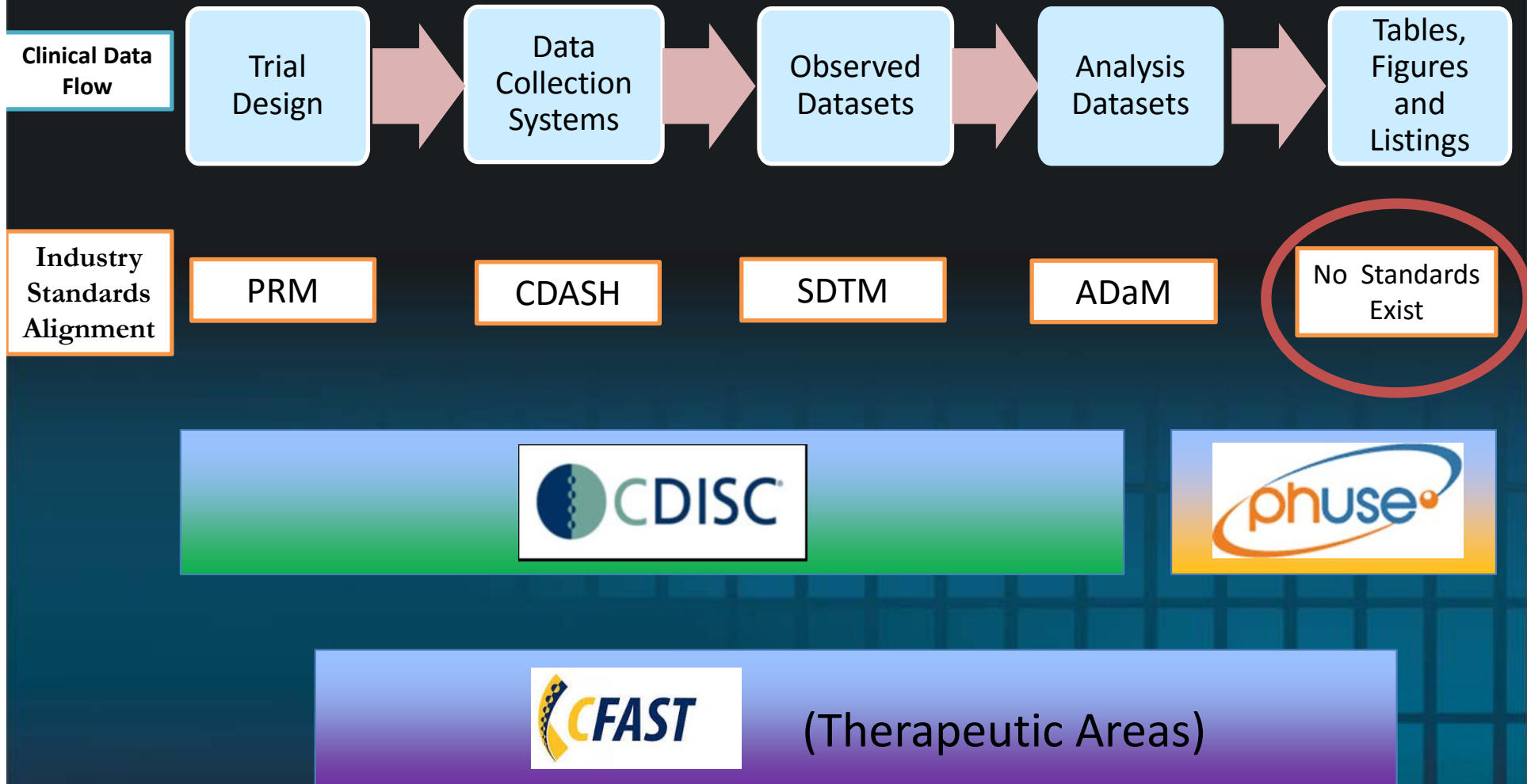


**Computational Science
Working Groups**



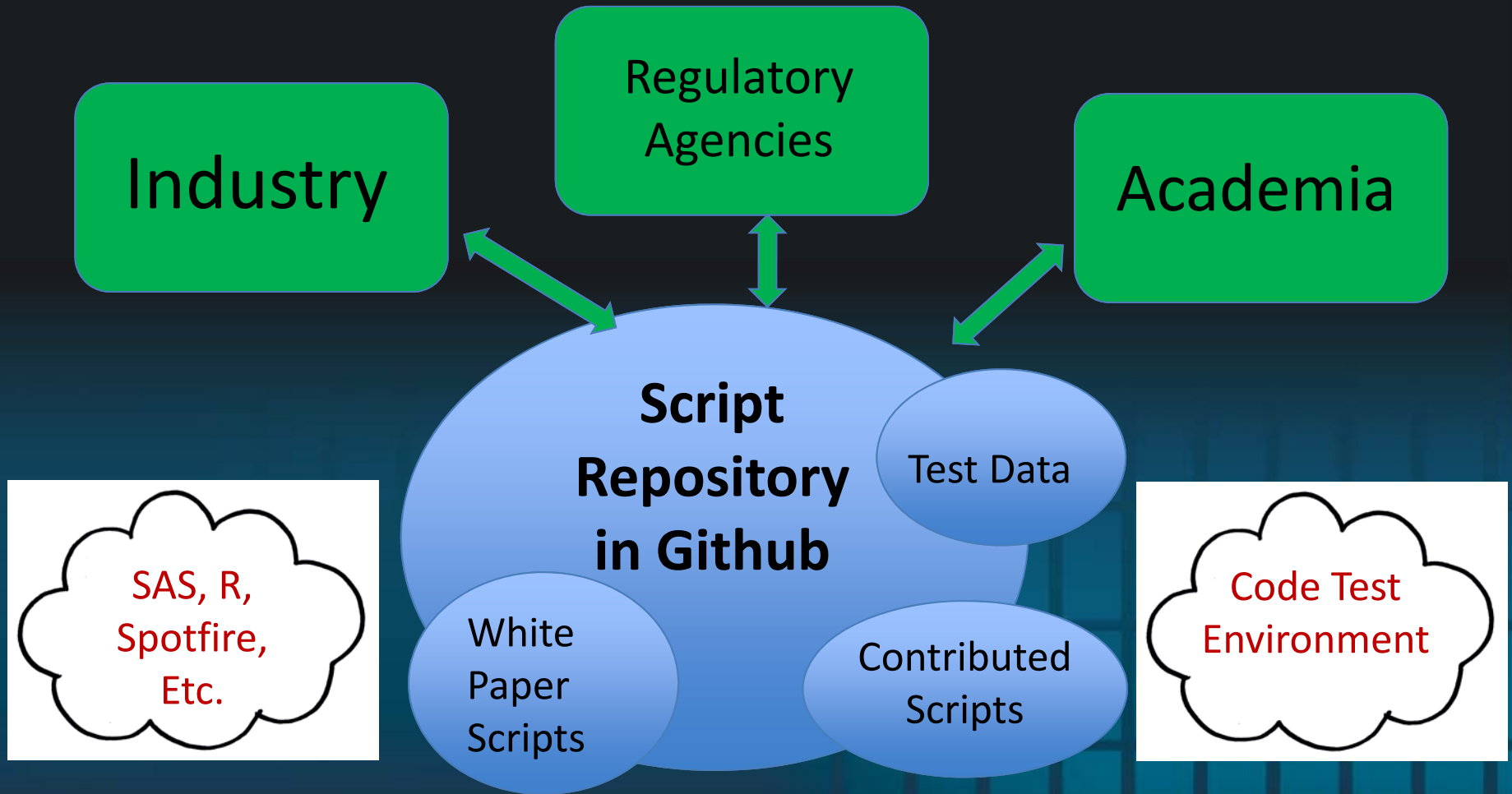


Vision: Fill the Gap on Analysis and Display Standards

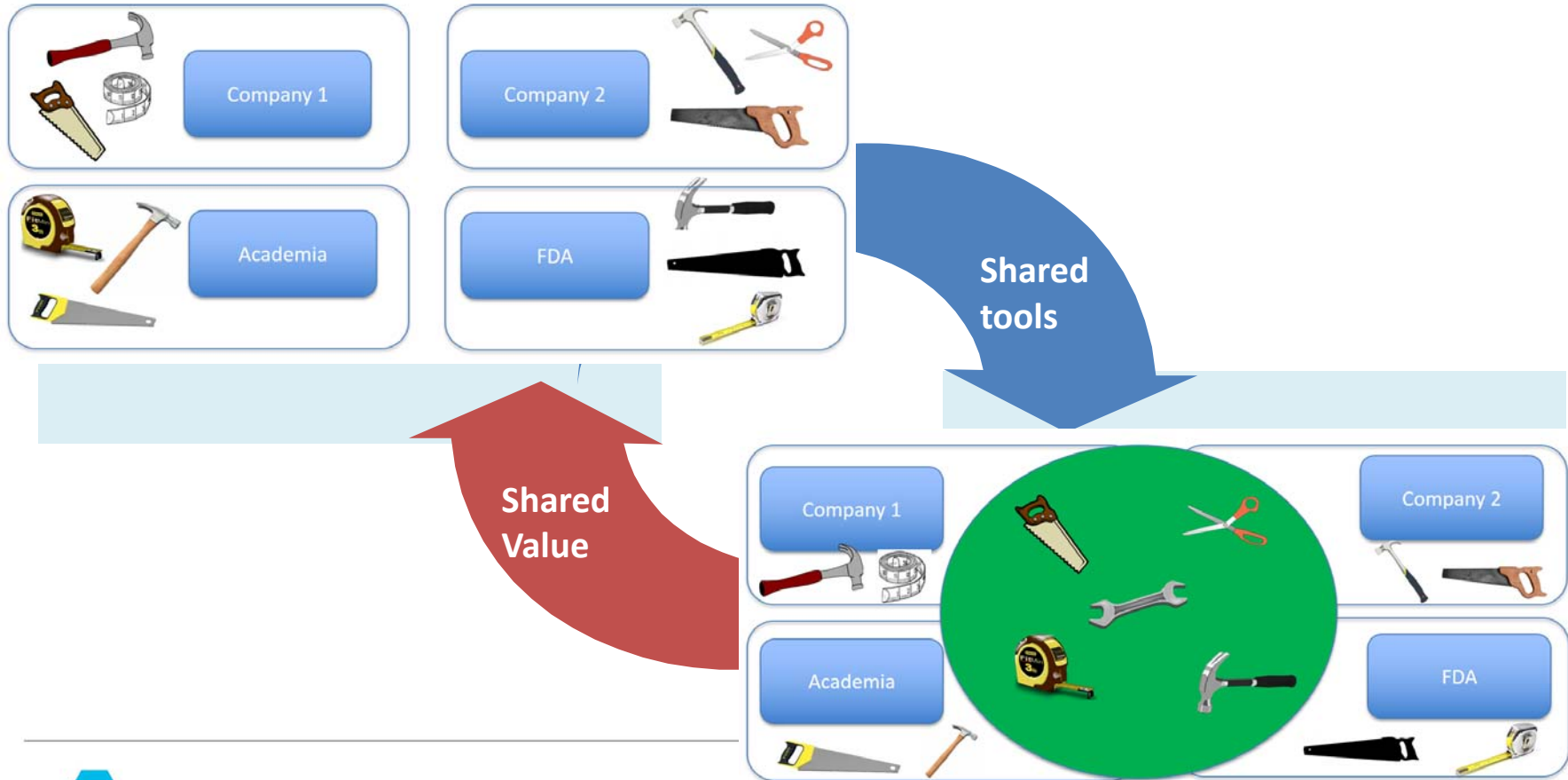




Vision: Script Repository (Shared Reusable Code Library)



Vision – From Everyone Building Their Own Tools to Shared Tools



**Computational Science
Working Groups**

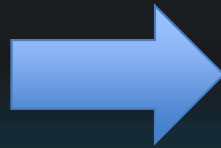




Focus Areas

- **Three Focus Areas, 6 active projects**

Script Repository
(4 projects)



Analyses and Display
White Papers
(ADW, Mary Nilsson)

Communication,
Promotion, Education
(CPE, Jared Slain and
Wendy Dobson)

Script Discovery and Acquisition (SDA,
Rebeka Revis, Alfredo Rojas)
Repository Content and Delivery (RCD,
Gustav Bernard, Andrew Miskell)
Repository Governance and
Infrastructure (RGI, Mike Carniello,
Hanming Tu)
Test Data Factory (TDF, Peter Schaefer)



Standard Analyses and Code Sharing Working Group Vision/Goals

- Why?
 - Better safety signal detection
 - Improve expertise in safety analytics
 - Ensure medical reviewers receive clinically relevant and meaningful analyses of patient safety for benefit-risk assessment
 - Assist in establishing analytical and statistical methods to reduce bias
 - Improved quality and efficiency
 - Reduce variability in analytical approaches
 - Have example code to facilitate implementation
 - Leverage crowd-sourcing in tool creation and maintenance



**Computational Science
Working Groups**



Accomplishments: White Papers

- 6 Analysis/Display White Papers finalized
 - Vital Signs, ECGs, Labs - Central Tendency
 - *October 2013, Lead – Mary Nilsson*
 - Non-Compartmental Pharmacokinetics
 - *March 2014, Lead - Francois Vandenhende*
 - Demographics, Disposition, and Medications
 - *October 2014, Lead – Simin Baygani*
 - Vital Signs, ECGs, Labs – Outliers and Shifts
 - *September 2015, Lead – Wei Wang*
 - QT Studies
 - *March 2016, Lead – Christos Stylianou*
 - Adverse Events
 - *February 2017, Lead – Mary Nilsson, Nhi Beasley, Sheryl Treichel*

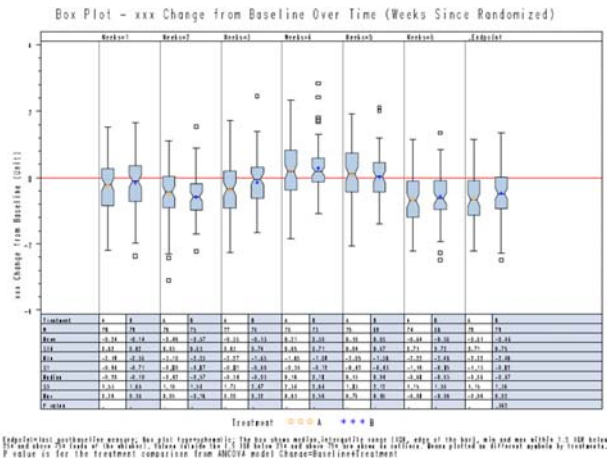
How to find final white papers: Go to www.phuse.eu, Click on Working Groups, Click on CS Deliverables Catalog



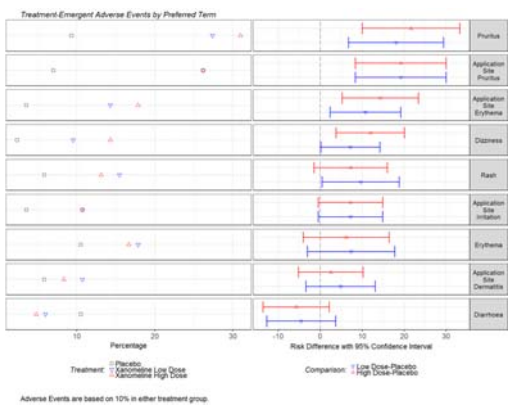
**Computational Science
Working Groups**



White Papers: Topics Covered



- Recommended analyses/displays for individual studies and integrated summaries (data common across TAs)
- Example SAP language
- Indicates which displays are most suited for interactive tools
- Discusses analytical and statistical topics/methods
 - P-values and CIs in safety
 - Events occurring after study drug stops
 - Alternative methods when percentages are biased



Computational Science Working Groups



Crowd-Sourcing Model – White Papers



**Computational Science
Working Groups**



Accomplishments: Repository

- MIT license chosen
 - <https://github.com/phuse-org/phuse-scripts/blob/master/LICENSE.md>
- Qualification guidelines developed
 - http://www.phusewiki.org/wiki/index.php?title=WG5_Project_02#Qualification_Process
- User-friendly front end developed
 - <https://github.com/phuse-org/phuse-scripts/wiki/Simple-Index>
- Repository has been updated to have a place to store scripts developed by other groups



**Computational Science
Working Groups**



Crowd-Sourcing Model - Repository



**Script Repository
in Github – Creation and
Governance Structure**



**Computational Science
Working Groups**



Accomplishments: Scripts Contributed

- Scripts contributed by other groups
 - FDA: <https://github.com/phuse-org/phuse-scripts/wiki/JumpStart-Scripts>
 - Non-clinical: <https://github.com/phuse-org/phuse-scripts/tree/master/contributed/Nonclinical>
 - Data Handle: <https://github.com/phuse-org/phuse-scripts/tree/master/lang/SAS/datahandle>
 - Spotfire Templates: <https://github.com/phuse-org/phuse-scripts/tree/master/contributed/Spotfire>



**Computational Science
Working Groups**



Accomplishments: Scripts Developed

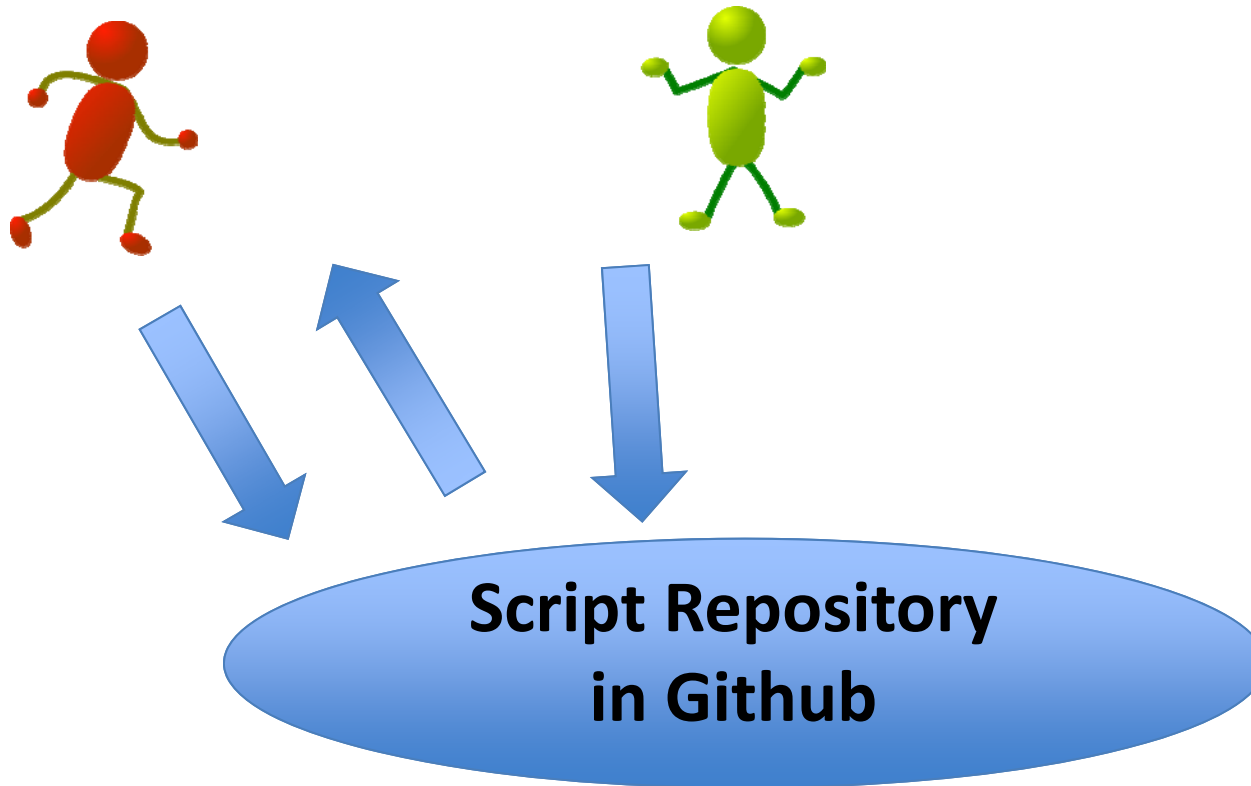
- Scripts developed by volunteers
 - 6 Scriptathons (plus additional work by project members) resulting in several scripts at various stages
 - Focused on creating scripts associated with the displays in the white papers, starting with ADaM data
 - The specifications for the scripts include assumptions and required ADaM variables
 - Starting with CDISC pilot data
 - Scripts developed based on white paper
 - Central Tendency package Qualification Completed: 6 Recommended displays in CT White Paper



**Computational Science
Working Groups**



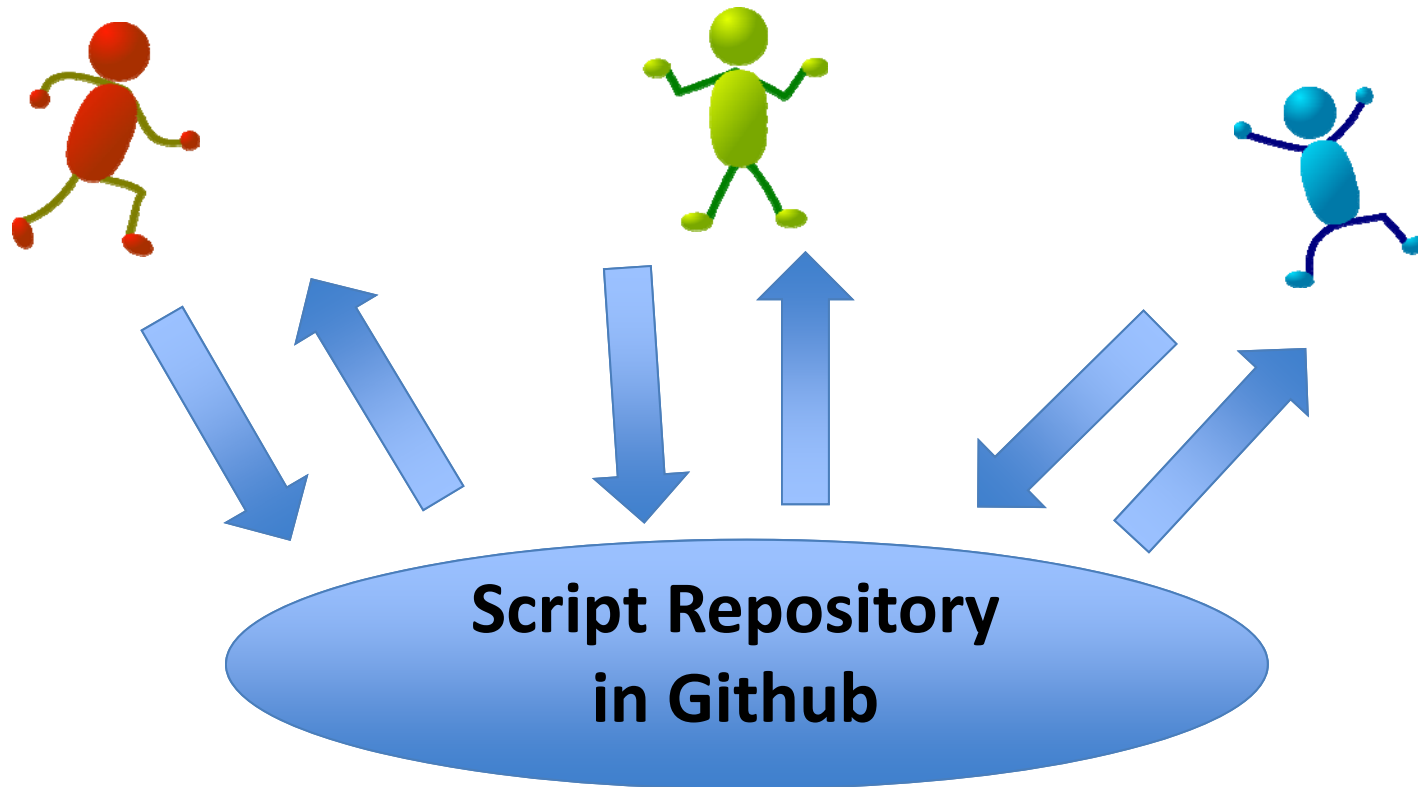
Crowd-Sourcing Model – Repository Content



**Computational Science
Working Groups**



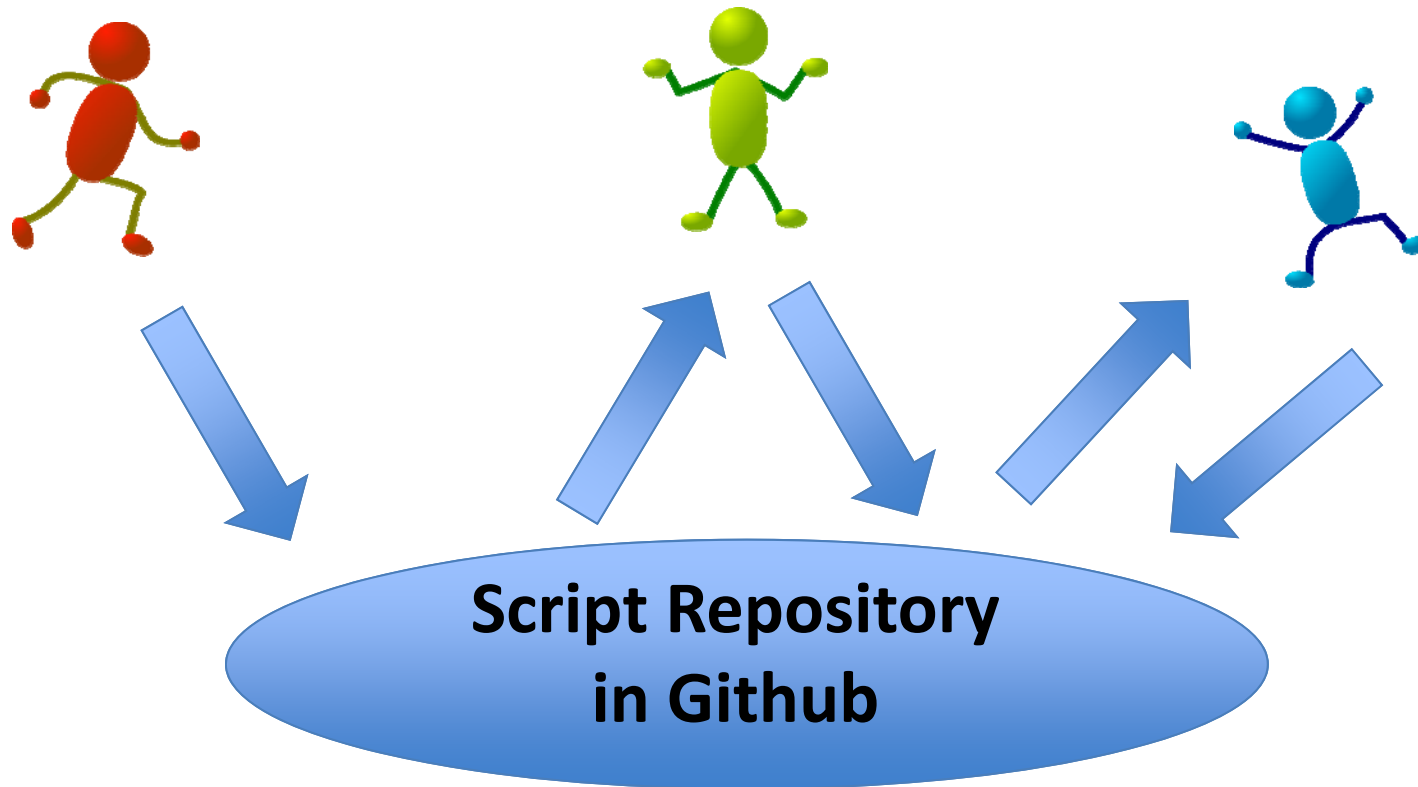
Crowd-Sourcing Model - Vision



**Computational Science
Working Groups**



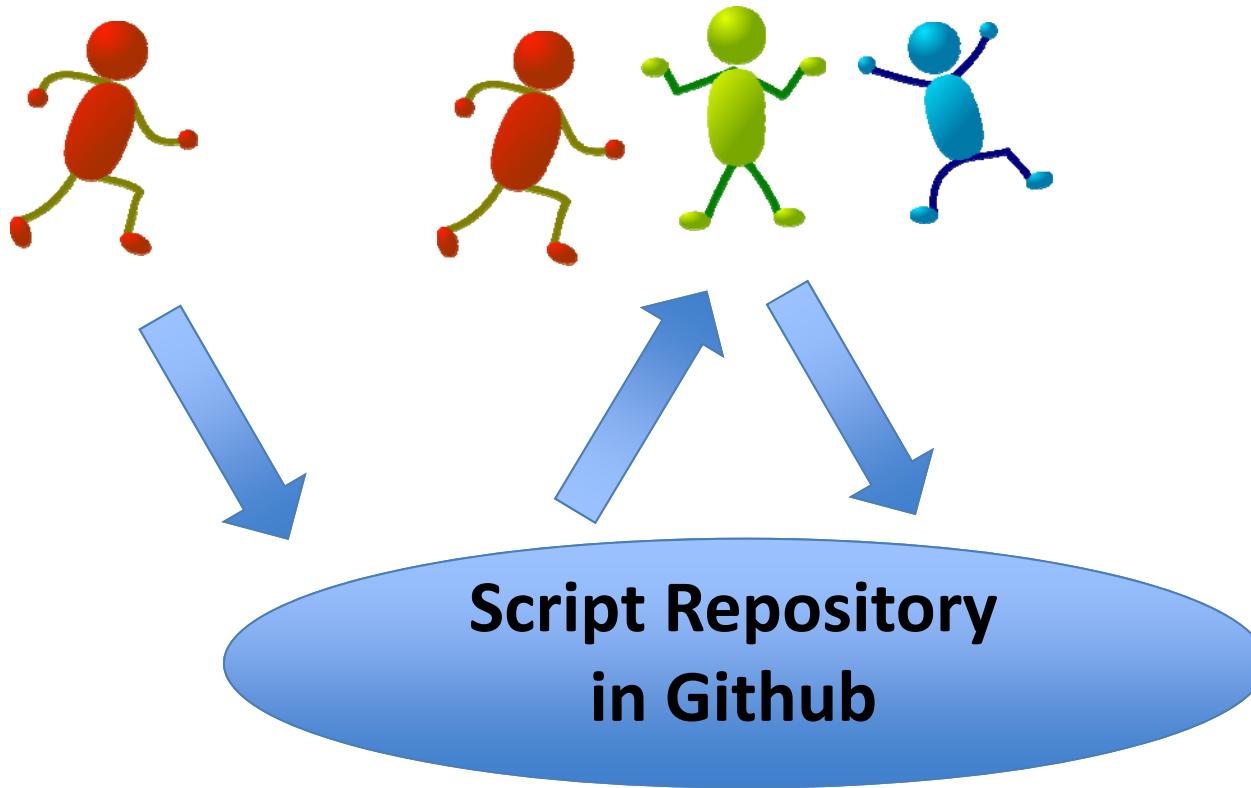
Crowd-Sourcing Model - Vision



**Computational Science
Working Groups**



Crowd-Sourcing Model - Vision



**Computational Science
Working Groups**



Working Group Next Steps

- Next Steps by Project Team
 - Analysis and Display White Papers (ADW) - Mary
 - Communication, Promotion, Education (CPE) - Mary
 - Script Discovery and Acquisition (SDA) – Hanming
 - Repository Content and Delivery (RCD) – Hanming
 - Repository Governance and Infrastructure (RGI) – Hanming
 - Test Data Factory (TDF) - Hanming



**Computational Science
Working Groups**



White Papers














- Analysis and Display White Papers (ADW)
 - Project Description:
 - Provide recommended Tables, Figures, and Listings for clinical trial study reports and submission documents for measurements that are common across clinical trials and across therapeutic areas.
 - Project Lead: Mary Nilsson
 - Project Next Steps:
 - Work on AE white paper follow-ups (consolidated terms, gender-/pediatric-specific lists)
 - Work on 4 new white papers
 - Work on updating 3 white papers



**Computational Science
Working Groups**



Analysis and Display White Papers Project Team

	Version 1		Version 2	
	Public Review	Published	Public Review	Published
Vital Signs, Labs, ECG – Central Tendency		Oct 2013 	Q4 2017 	
Non-Compartmental PK		March 2014 		
Demographics, Disposition, Medications		Oct 2014 	Q3 2017 	
Vital Signs, Labs, ECG – Outliers / Shifts		Sept 2015 	Q4 2017 	
QT/QTc Studies		March 2016 		
Adverse Events		Feb 2017 		
Treatment-Emergent Definitions	Q3 2017 			
Hepatotoxicity	Q3 2017 			
Questionnaires	Q4 2017 			
Events of Special Interest	Q4 2017 			

Communication, Promotion, Education

- Communication, Promotion, Education (CPE)
 - Project Description:
 - Conceptualize Efficient Ways to Communicate Working Group Progress and Results
 - Project Leads: Jared Slain, Wendy Dobson
 - Project Next Steps:
 - Keep project page on PhUSE Wiki updated
 - Find people already going to events to present/promote working group (Help if you can!)
 - Create an educational series on analytical and statistical methods from the white papers



**Computational Science
Working Groups**



Repository Projects

- Script Discovery and Acquisition (SDA)
 - Project Description:
 - Discover, acquire and review scripts to be stored in the repository with adequate metadata to describe the scripts
 - Project Leads: Rebeka Revis, Alfredo Rojas
 - Project Next Steps:
 - Review selected scripts contributed by the FDA
 - Create script metadata files
 - Capture the codes behind Interactive display of the data in Spotfire or R Shiny



**Computational Science
Working Groups**



Repository Projects

- Repository Content and Delivery (RCD)
 - Project Description:
 - Develop and enhance scripts under a defined qualification process to ensure the usability and quality of the standard scripts
 - Project Leads: Gustav Bernard, Andrew Miskell
 - Project Next Steps:
 - Package CT scripts including linking to whitepaper, spec and qualification docs
 - Finish the shift outlier package including spec and metadata
 - Create a R group to develop R scripts for CT package



**Computational Science
Working Groups**



Repository Projects

- Repository Governance and Infrastructure (RGI)
 - Project Description:
 - Establish the basic structure and management of the repository.
 - Define and enforce existence of required metadata for scripts
 - Manage users and projects in the repository
 - Project Leads: Mike Carniello, Hanming Tu
 - Project Next Steps:
 - Create a test environment (R and SAS)
 - Expand the YML metadata usage
 - Continue maintaining and administering the repository
 - Crowd-source a shared interactive tool for safety data



**Computational Science
Working Groups**



Repository Projects

- Test Data Factory (TDF)
 - Project Description:
 - Provide test data formatted in SDTM and ADaM that support a more systematic and comprehensive testing of these concepts and scripts.
 - Project Leads: Peter Schaefer
 - Project Next Steps:
 - Determine test dataset requirements
 - Implement scripts that create ‘simulated’ SDTM and/or ADaM test data sets
 - Publicize the test data sets



**Computational Science
Working Groups**



Working Group Needs

- More project team members
- Increased participation in white paper reviews – Help recruit!
- Use/reference recommendations in existing final white papers!
 - Forward to any existing standards groups
 - Link to white papers from Statistical Analysis Plans
- Participate in re-usable code development
 - Write, Test, Qualify, Review, Improve
- Keep eyes open for existing scripts that need a public home
- Advertise! Advertise! Advertise!



**Computational Science
Working Groups**



How to Participate

- Sign up for the PhUSE working group mailings
 - From phusewiki.org, click “Join a Working Group Now”
 - Standard Scripts Groups
 - CSS-WG-Standard-Scripts (Entire Working Group)
 - CSS-WG-Standard-Scripts-WhitePapers (White Paper Project Team)
 - CSS-WG-Standard-Scripts-Platform (Script Repository)
 - CSS-WG-SS-WhitePaperReviewers (Notified when a white paper is ready for review)
- See wiki pages for each of the projects (www.phusewiki.org)



**Computational Science
Working Groups**



Potential Opportunities for Collaboration

- Establish liaisons between PhUSE and ASA efforts
 - The Standard Analyses and Code Sharing Working Group is particularly suited for a collaboration with the ASA
 - PhUSE already has an official collaboration with CDISC ([Memorandum of Understanding](#))
- Help each other with communication
- Co-sponsor educational forums



Important Links

- Working Group:
 - Main Page: http://www.phusewiki.org/wiki/index.php?title=Standard_Scripts
 - Projects:
 - [P01 - SDA](#): Script discovery and acquisition (Rebeka M Revis; Alfredo Rojas)
 - [P02 - RCD](#): Repository content and delivery (Gustav Bernard; Andrew Miskell; FDA Liaison: Mat Soukup)
 - [P03 - RGI](#): Repository governance and infrastructure: (Mike Carniello and Hanming Tu)
 - [P07 - CPE](#): Communication, Promotion and Education (Jared Slain and Wendy Dobson)
 - [P08 - ADW](#): Analysis and Display White papers (Mary Nilsson)
 - [P09 - TDF](#): Test Data Factory (Peter Schaefer)
- Repository:
 - Github: <https://github.com/phuse-org/phuse-scripts>
- Publications:
 - [Analyses and Displays of Central Tendency 10Oct2013](#)
 - [Analyses and Displays of PK 25Mar2014](#)
 - [Analyses and Displays of Demographics, Disposition, and Medications 07Oct2014](#)
 - [Analyses and Displays of Outliers/Shifts from Normal to Abnormal 10Sep2015](#)
 - [Analyses and Displays Associated with ThoroughQT/QTc Studies 11Mar2016](#)
 - [Analyses and Displays Associated with Adverse Events 03Feb2017](#)
- Index Pages:
 - Simple Index: <https://github.com/phuse-org/phuse-scripts/wiki/Simple-Index>.
 - Standard Index: <https://github.com/phuse-org/phuse-scripts/wiki/Standard-Script-Index>
 - Mirrored Index: http://www.phusewiki.org/wiki/index.php?title=Standard_Script_Index
 - FDA JumpStart: <https://github.com/phuse-org/phuse-scripts/wiki/JumpStart-Scripts>



**Computational Science
Working Groups**



**The premier community for people
working in the biometric area**



 ***phuse.eu***

 ***@PhUSETwitta***

 ***/PhUSE***

 ***phusewiki.org***