

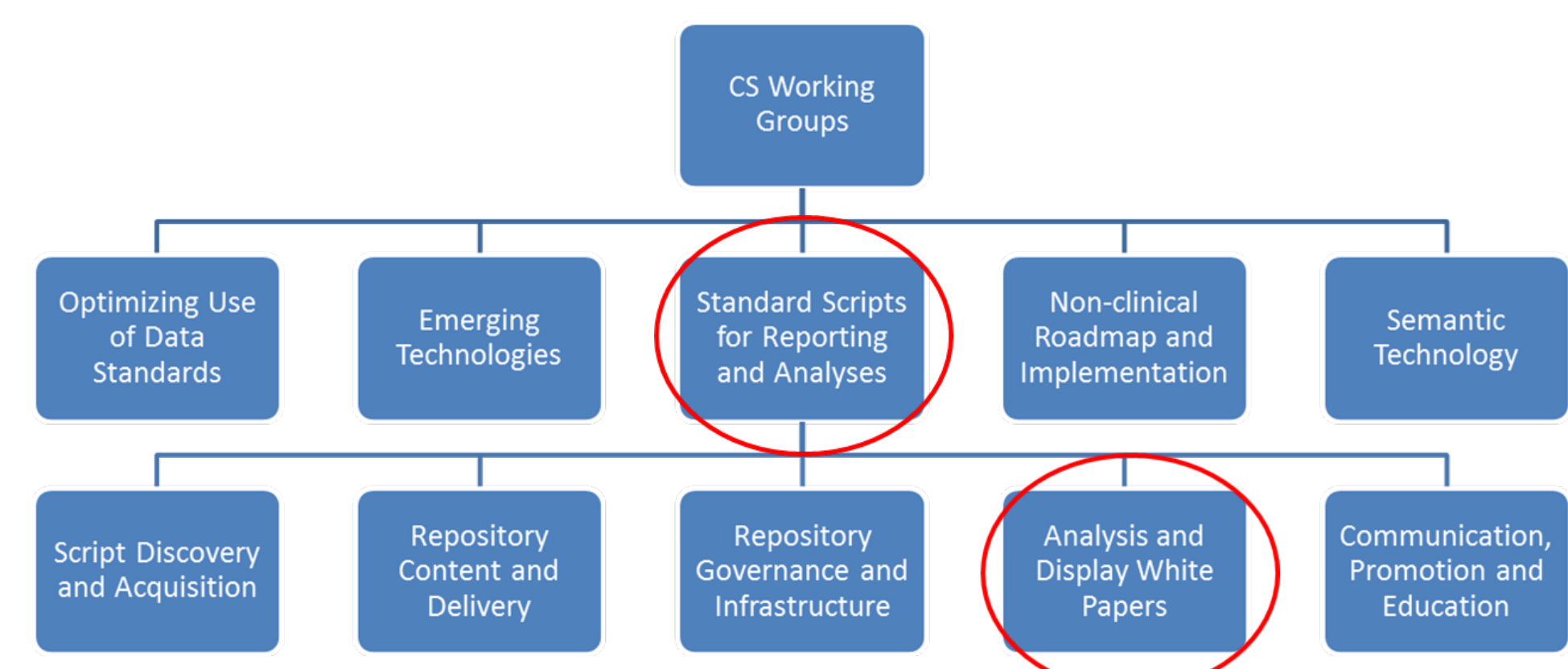
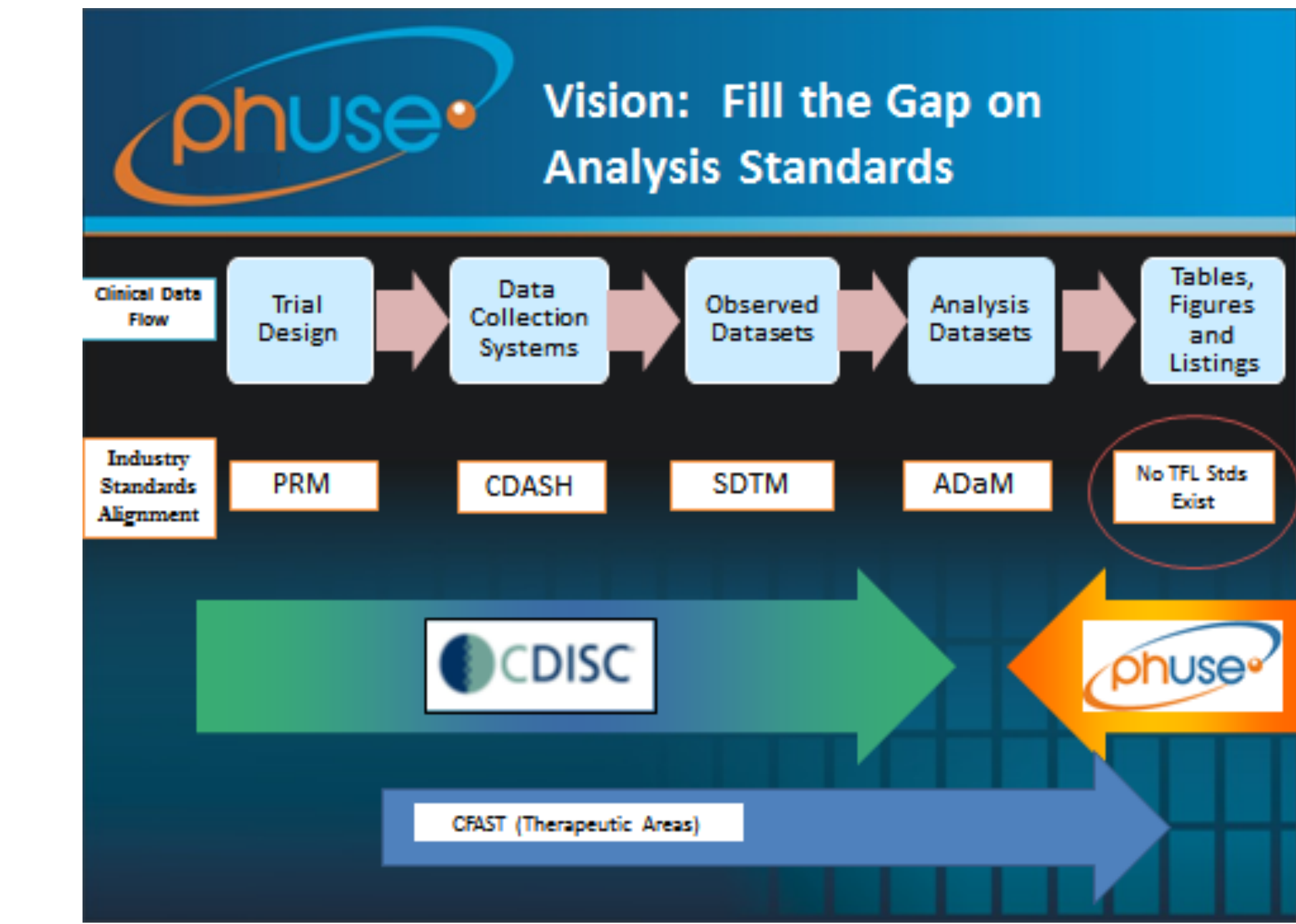
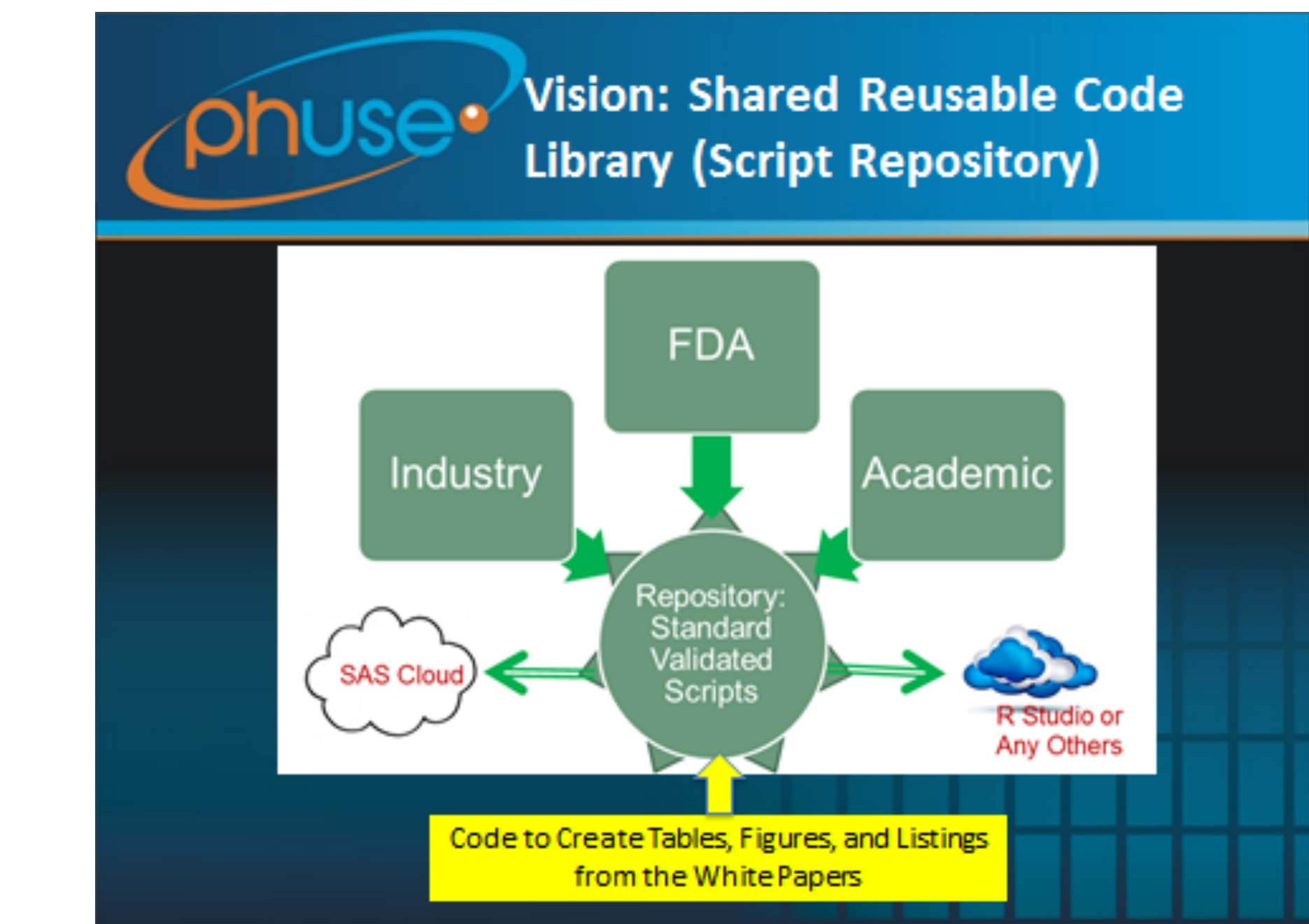
Standard Analyses and Displays for Common Data in Clinical Trials – Socialize the Deliverables!

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ABSTRACT

The “Analysis and Display White Papers” project team, which is part of the “Development of Standard Scripts for Analysis and Programming” Computational Science Working Group, is providing recommendations for analyses, tables, figures, and listings for data that are common across therapeutic areas (laboratory measurements, vital signs, electrocardiograms, adverse events, demographics, medications, disposition, hepatotoxicity, pharmacokinetics). Nine white papers are at various stages of development, including 4 that have been finalized. The white papers include recommendations on statistical analyses, including mock figures, tables, and listings. Work is ongoing to include ADaM specifications. This Project Team provides an organized process for sharing improved methodologies (including visual analytics) that can lead to earlier safety signal detection, better characterization of product safety profiles, and improved efficiency. This poster will provide an update of this effort. We encourage all medical researchers to utilize the recommendations, and to help advertise this effort to their respective organizations!

THE BIG PICTURE



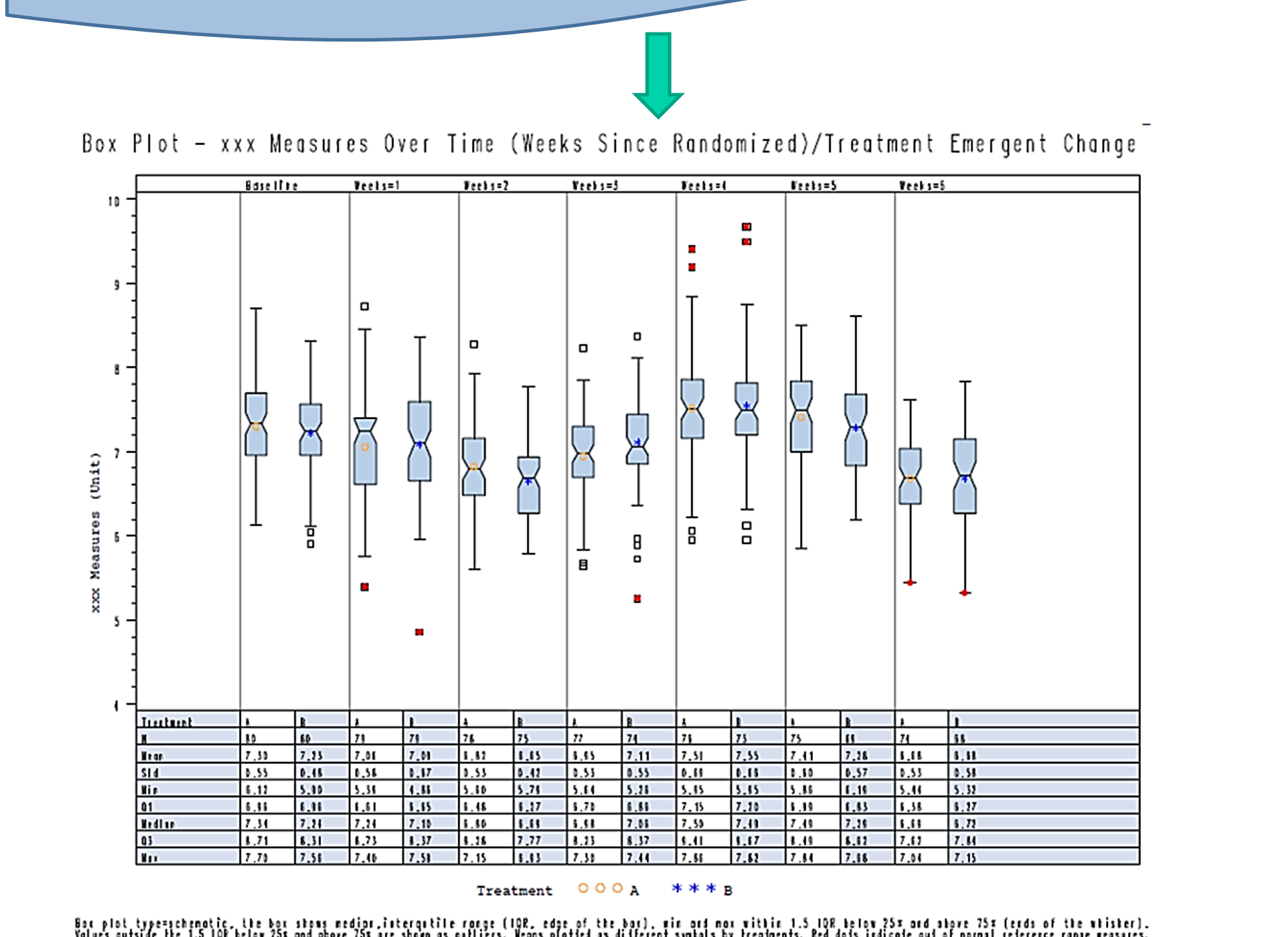
PROJECTS OVERVIEW

	Version 1				Version 2			
	Begin	Internal Review	Public Review	Published	Begin	Internal Review	Public Review	Published
Vital Signs, Labs, ECG – Central Tendency	2012		4 drafts 2012-3	Oct 2013	Jan 2016	Feb or March 2016	NA	March 2016
Vital Signs, Labs, ECG – Outliers / Shifts	2014		2 drafts 2014	Sep 2015	2018			
Demographics, Disposition, Medications	2013		2 drafts 2014	Oct 2014	2017			
Non-Compartmental PK	2012		2 drafts 2013-4	Mar 2014	2017			
Adverse Events	2014		Oct 2014; March or April 2016					
TQT Studies	2014		Aug 2015	March or April 2016				
Hepatotoxicity	2014		March or April 2016					
Questionnaire	Jan 2016							=Final
Events of Special Interest	2017							=In Progress

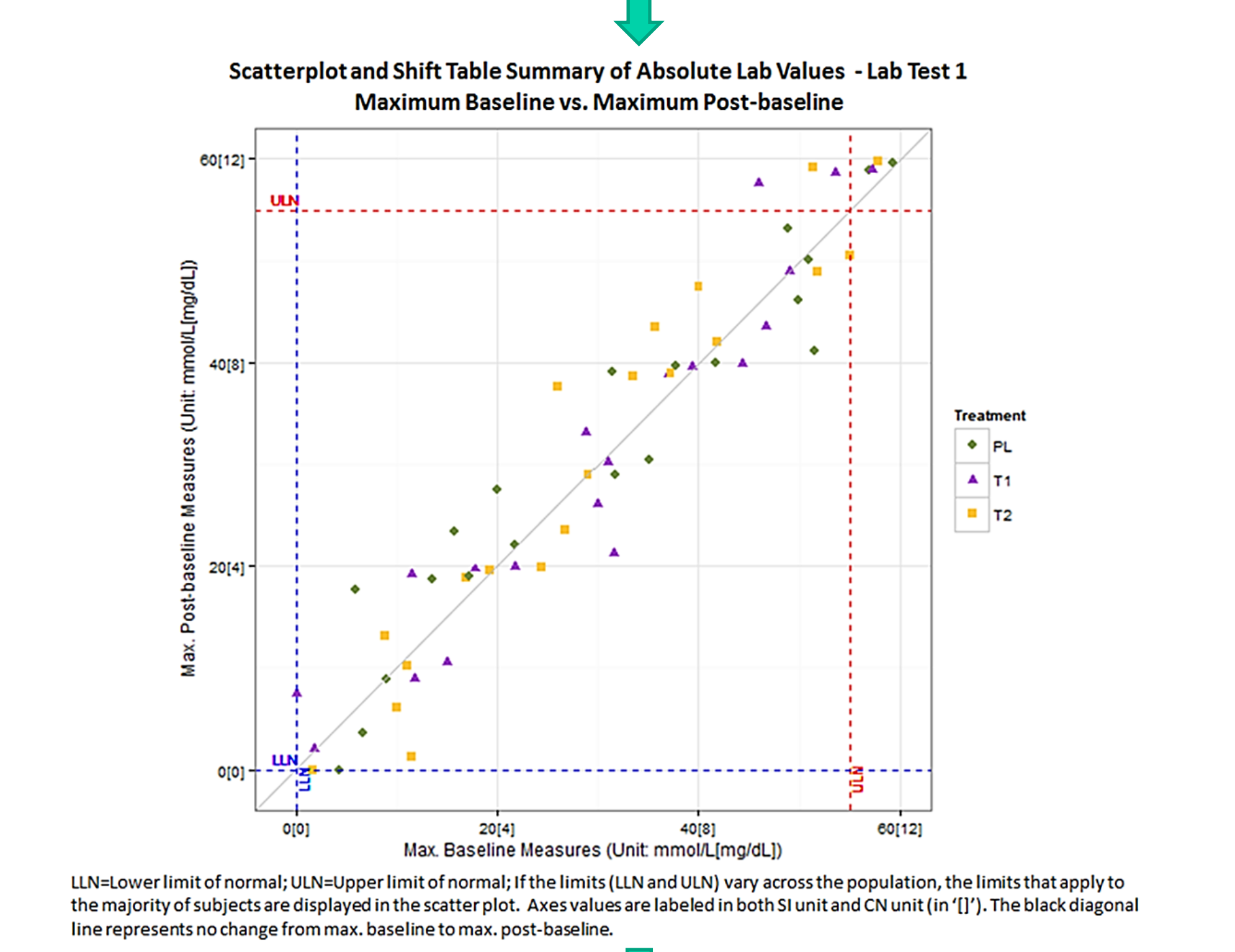
FINAL WHITE PAPERS READY TO SOCIALIZE!

Vital Signs, Labs, ECGs – Central Tendency and Outliers/Shifts

- Recommendations include boxplots, scatterplots, and shift tables
- Boxplots include an overlay of values outside of reference limits (colored)
- White papers include discussion on handling measurements after study drug is discontinued



Box plot (approximately, the box shows median, interquartile range (IQR), edge of the box, size and any values 1.5 IQR below box and above 1.5 IQR of the whisker). Values outside the 1.5 IQR below box and above 1.5 IQR are shown as outliers. Lines plotted in different colors by treatments. Red dots indicate set of exact reference range present.



LLN=Lower limit of normal; ULN=Upper limit of normal; If the limits (LLN and ULN) vary across the population, the limits that apply to the majority of subjects are displayed in the scatter plot. Axes values are labeled in both SI unit and CN unit (in '[]'). The black diagonal line represents no change from max. baseline to max. post-baseline.

Scatterplot and Shift Table Summary of Absolute Lab Values - Lab Test 1
Maximum Baseline vs. Maximum Post-baseline

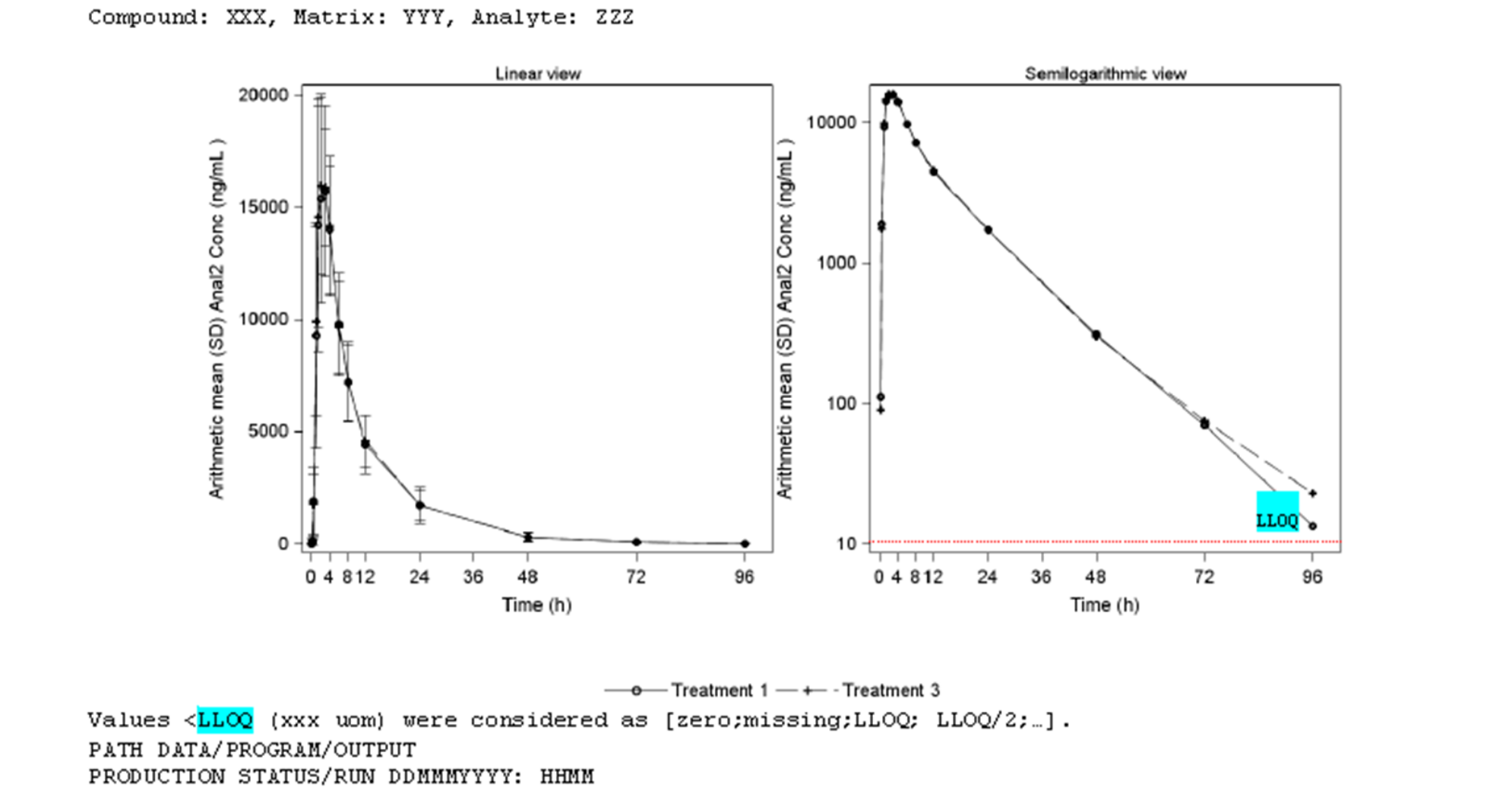
Treatment	Max. Baseline Result	Max. Post-baseline Result (Shift from Baseline)			
		Low	Normal	High	Missing
T1 (N = xxx)	Low	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
	Normal	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
	High	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
	Missing	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
T2 (N = xxx)	Low	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
	Normal	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
	High	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
	Missing	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
PL (N = xxx)	Low	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
	Normal	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
	High	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
	Missing	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)

N = number of subjects in the analysis population; n = number of subjects in each shift category; High and low are determined using the reference limits based on the individual subject's demographics.
*a – P values are from Fisher's Exact test, compared with PL

Pharmacokinetics:
Non-compartmental Analysis (NCA)

- Recommendations for calculating PK Parameters
 - PK definitions and formulas
 - Management of source data
 - Missing sampling data, concentrations <LLOQ, outliers, baseline adjustment for endogenous compounds, actual vs. planned time points, reporting of missing PK parameters
- Recommendations for TFLs

Mean PK Concentration-time Profiles



Values <LLOQ (xxx.x) were considered as [zero/missing/LLOQ/2].
PATH DATA/PROGRAM/OUTPUT
PRODUCTION STATUS/RUN DDDDDDDDD: HHHH

Demographics, Disposition, Medications

- Demographics should include age, age categories, sex, race, and weight
- Disposition reasons discussed
 - Recommends listings for non-specific reasons
- Collection of concomitant medication information discussed
 - WHO Drug Dictionary and ATC categories may be helpful

Disposition

Title (optional; add more if needed)
<Insert population (for example, Safety Population (N = xxx))>
<Insert study ID(s) or description of database utilized
Study Phase or phases (if needed)>

	Treatment A (N=xxx)	Treatment B (N=xxx)	Total (N=xxx)
Subject Disposition	n (%)	n (%)	n (%)
Completed the study	xx(xx.x)	xx(xx.x)	xx(xx.x)
Discontinued	xx(xx.x)	xx(xx.x)	xx(xx.x)
Death or Adverse Event	xx(xx.x)	xx(xx.x)	xx(xx.x)
Death	xx(xx.x)	xx(xx.x)	xx(xx.x)
Adverse Event	xx(xx.x)	xx(xx.x)	xx(xx.x)
Lack of Efficacy-Related Reasons	xx(xx.x)	xx(xx.x)	xx(xx.x)
Lack of Efficacy	xx(xx.x)	xx(xx.x)	xx(xx.x)
Progressive Disease	xx(xx.x)	xx(xx.x)	xx(xx.x)
Disease Relapse	xx(xx.x)	xx(xx.x)	xx(xx.x)
Other Reasons	xx(xx.x)	xx(xx.x)	xx(xx.x)
Lost to Follow-up	xx(xx.x)	xx(xx.x)	xx(xx.x)
Non-compliance with Study Drug	xx(xx.x)	xx(xx.x)	xx(xx.x)
Pregnancy	xx(xx.x)	xx(xx.x)	xx(xx.x)
Protocol Violation	xx(xx.x)	xx(xx.x)	xx(xx.x)
Physician Decision	xx(xx.x)	xx(xx.x)	xx(xx.x)
Withdrawal by Subject	xx(xx.x)	xx(xx.x)	xx(xx.x)
Withdrawal by Parent/Guardian	xx(xx.x)	xx(xx.x)	xx(xx.x)
Recovery	xx(xx.x)	xx(xx.x)	xx(xx.x)
Technical Problems	xx(xx.x)	xx(xx.x)	xx(xx.x)
Other	xx(xx.x)	xx(xx.x)	xx(xx.x)

Abbreviations: N = total number of subjects in the population; n = number of subjects the specified category.
% = Percentage of patients with N as the denominator.

HOW TO FIND WHITE PAPERS

- Final White Papers
 - Go to www.phuse.eu
 - Click on CS Working Groups
 - Click on CS Deliverables Catalogue
 - Direct link: www.phuse.eu/CS-deliverables.aspx
- Draft White papers
 - Go to www.phusewiki.org
 - Click on CSS Working Groups
 - Click on Development of Standard Scripts for ...
 - Click on the P08-ADW link
 - Go to the Project Plan Section - Each white paper has its own wiki page with links to drafts

WE NEED YOU TO SOCIALIZE THE DELIVERABLES!

- Use the recommendations in the final white papers!
 - Forward to any existing standards groups
 - Link to white papers from Statistical Analysis Plans
- Participate in white paper reviews
- Recruit for white paper reviews
- Advertise! Advertise! Advertise!
- Subscribe to 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)

Abbreviations:

- ADaM = Analysis Data Model
- ADW = Analysis and Display White Papers (Project Team)
- ATC = Anatomical Therapeutic Chemical
- CDASH = Clinical Data Acquisition Standards Harmonization
- CSR = Clinical Study Report
- CS = Computational Science
- PK = Pharmacokinetics
- PRM = Protocol Representation Model
- SDTM = Study Data Tabulation Model
- TFL = Tables, Figures, and Listings
- WHO = World Health Organization