CIMS GLOBAL & PHUSE NJ SDE

Implentation of Open-Source Package & Shiny in DMC Activity

July 2025

Telephone
908-557-9366

Address
285 Davidson Ave.
Suite 504
Somerset, NJ 08873
USA

Website
www.cims-global.com

©2025 CIMS Global. All rights reserved. This material is confidential and proprietary to CIMS Global and shall not be distributed, edited, or modified in any way without CIMS Global's advance written consent.

Bio

pzhang@cims-global.com

Peng Zhang, Ph.D.

Associate Director, Innovative Data Sciences

CIMS Global

- Specializes in adaptive trial design and statistical monitoring of clinical trials
- Leads internal development of R packages and R Shiny applications to support regulatory and data review workflows
- Has served as the unblinded independent statistician for 30+ DMC meetings across 10+ Phase II and III trials spanning multiple therapeutic areas.

Previous Presentations

- PHUSE 2025: *The Implementation of {teal} R Shiny Apps for DMC Activities [here]*
- BBSW Meetup 2025: *Innovative R/R-Shiny Approaches for Acing Data Review Meetings [here]*
- R/Pharma US 2024 Virtual Session: *Implementation of {teal} Shiny apps in DMC activity [here]*

©2025 CIMS Global. All rights reserved. This material is confidential and proprietary to CIMS Global and shall not be distributed, edited, or modified in any way without CIMS Global's advance written consent.

Introduction

- What open-source packages and apps can be Commonly Used For
  - Organization's Internal TFL review workflows
  - Regulatory submission support
  - Interactive dashboards for clinical data exploration (e.g., R Shiny apps)

- Potential Usage of Open-Source Tools for DMC Activities?
  - Reduce manual work and preparation time
  - Supports closed session review with interactive outputs
  - Improves efficiency and decision-making under tight timelines
  - Feasibility, benefits, and challenges will be discussed

CIMS

©2025 CIMS Global. All rights reserved. This material is confidential and proprietary to CIMS Global and shall not be distributed, edited, or modified in any way without CIMS Global's advance written consent.

phuse

DMC Meetings

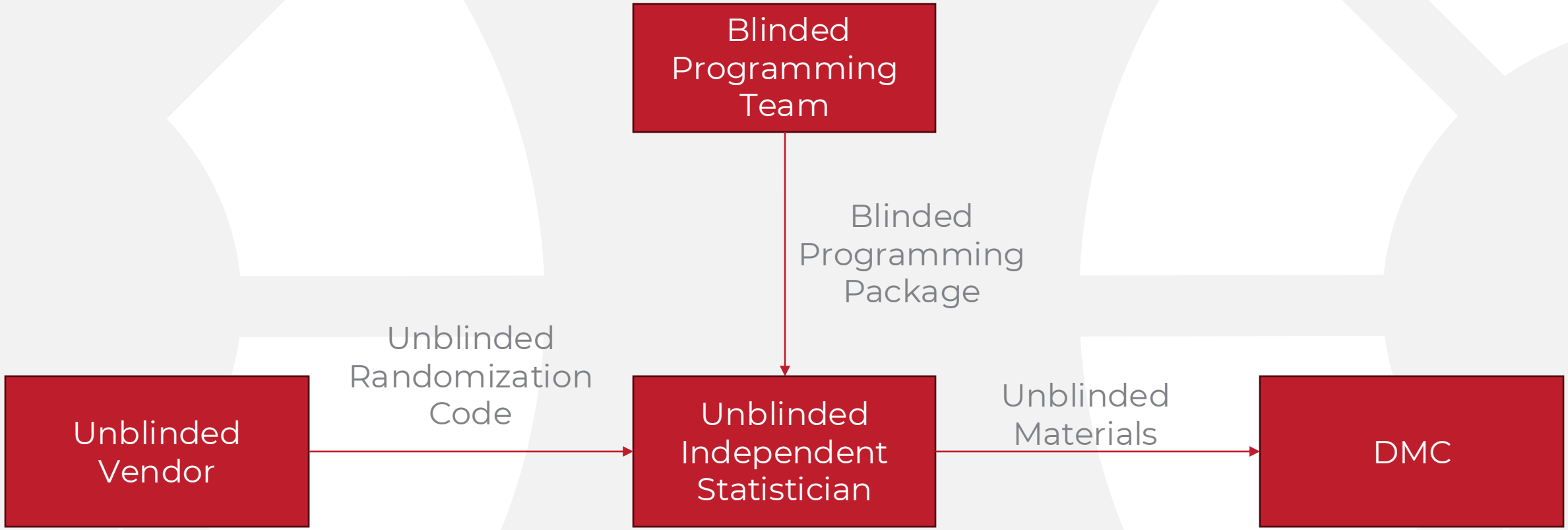
- Monitor the clinical trials
  - Safety
  - Efficacy
- Common format of DMC meetings includes an open session and a closed session.
- Open Session (30 mins to 1 hour)
  - Sponsor and DMC members
  - General study update, patient enrollment, safety concern, etc
  - Blinded format
- Closed Session (30 mins to 2 hours)
  - Unblinded Independent Statistician and DMC Members
  - Right after open session
  - Unblinded materials and draft recommendations for the study going forward.
- Re-join open session (10 to 30 mins)
  - DMC Recommendation to Sponsor
  - Further request

CIMS

©2025 CIMS Global. All rights reserved. This material is confidential and proprietary to CIMS Global and shall not be distributed, edited, or modified in any way without CIMS Global's advance written consent.

phuse

DMC Unblinded Materials Preparation



©2025 CIMS Global. All rights reserved. This material is confidential and proprietary to CIMS Global and shall not be distributed, edited, or modified in any way without CIMS Global's advance written consent.

Current Challenges

1. Time-consuming preparation of slides (open session, closed session)
    - Manual type-in numbers
    - Copy-paste information
2. Too many pages to review for unblinded materials :
    - 1k to 10k pages long
    - Limited time to review for DMC (1 week)
    - Table formats not intuitive for medical expert to understand
3. Inefficient static output:
    - Manually search for keywords, parameters, IDs
    - Ctrl+F
4. Insufficient information:
    - Subgroup analysis of given tables.
5. Delayed delivery for further request from DMC:
    - Multiple Parties
    - Several days or even 1 week
    - Pending study continuation

CIMS
©2025 CIMS Global. All rights reserved. This material is confidential and proprietary to CIMS Global and shall not be distributed, edited, or modified in any way without CIMS Global's advance written consent.

Open-Source Solution

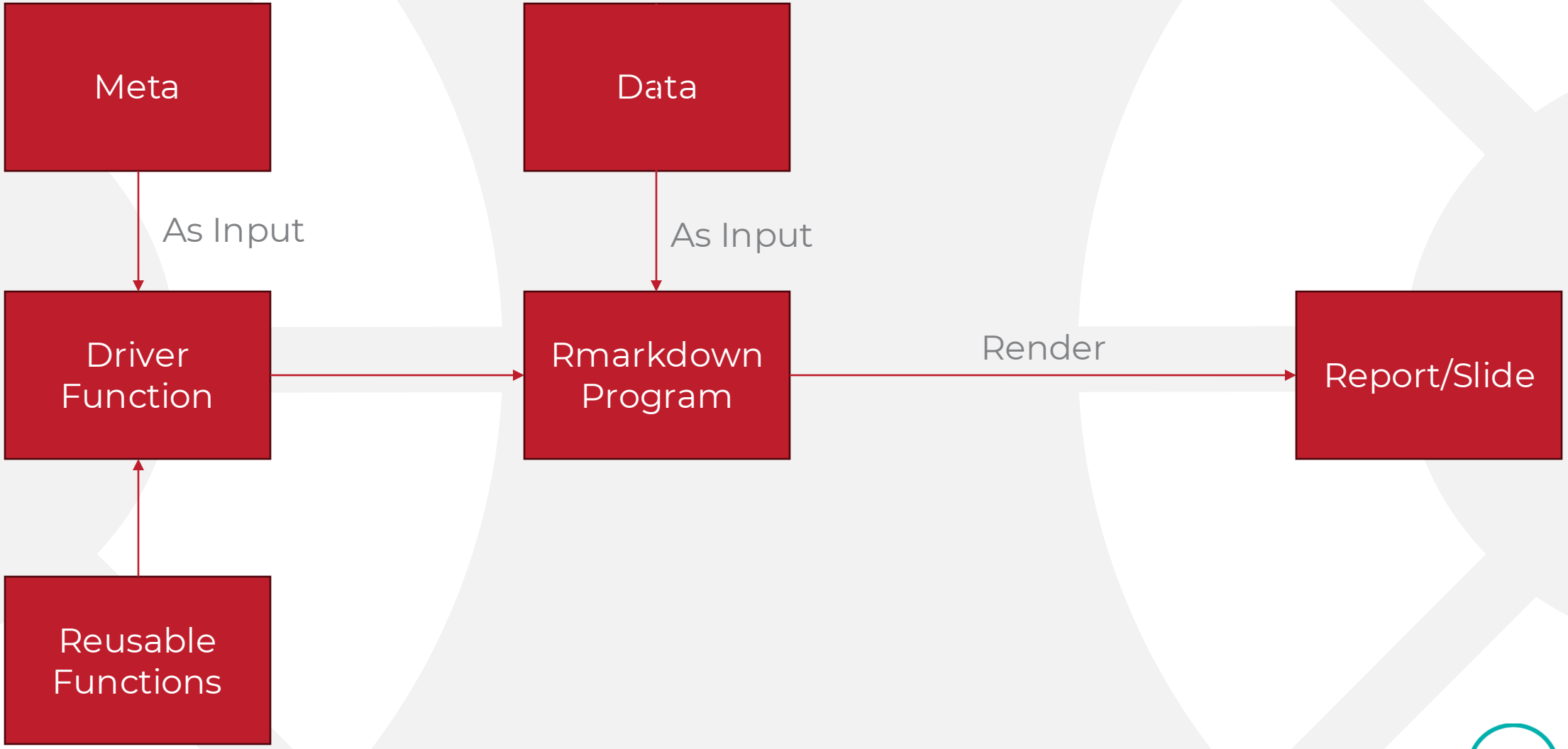
Challenges	Open-Source Solution
Manual processes of generating documents	• RMarkdown and reusable functions and template • Automated generation • Open/closed session slides, executive summary report • Inline tables, figures, and texts
Limited review time	• Shiny Dashboard • Real-time exploration • Listings and summary data in-session
Delayed follow-up requests through multiple parties	• Shiny Dashboard • Subgroup Analysis • Instant calculation using embedded statistical functions

©2025 CIMS Global. All rights reserved. This material is confidential and proprietary to CIMS Global and shall not be distributed, edited, or modified in any way without CIMS Global's advance written consent.

Automated Report

©2025 CIMS Global. All rights reserved. This material is confidential and proprietary to CIMS Global and shall not be distributed, edited, or modified in any way without CIMS Global's advance written consent.

Flow



©2025 CIMS Global. All rights reserved. This material is confidential and proprietary to CIMS Global and shall not be distributed, edited, or modified in any way without CIMS Global's advance written consent.

How Automation Drives Efficiency in DMC Preparation

1. Standardized Inputs
   - Use ADAM datasets as a consistent data source
   - Updates before each meeting
2. Reusable Internal Functions
   - {cimstfl} simplifies generation of TFLs with input parameters
   - {stat2mw} creates templated descriptions from outputs
   - Functions reduce code duplication and improve consistency
3. R Markdown Automation
   - Generates open and closed session slides, executive summaries, and inline tables
   - Removes need for manual formatting or copy-pasting
4. Fast, Reproducible Outputs
   - Same code used across meetings or studies
   - Fewer QC cycles and easier validation
   - Enables faster turnaround and supports in-meeting review
   - Traceable between data and values in the documents

CIMS

©2025 CIMS Global. All rights reserved. This material is confidential and proprietary to CIMS Global and shall not be distributed, edited, or modified in any way without CIMS Global's advance written consent.

phuse

Example Output

Population at Screening (cont.)

Category	A: Drug X (N=134)	B: Placebo (N=134)	Total (N=268)
Sex			
N	134	134	268
F	79 (59.0%)	82 (61.2%)	161 (60.1%)
M	55 (41.0%)	52 (38.8%)	107 (39.9%)
Race			
N	134	134	268
ASIAN	68 (50.7%)	67 (50.0%)	135 (50.4%)
BLACK OR AFRICAN AMERICAN	31 (23.1%)	28 (20.9%)	59 (22.0%)
WHITE	27 (20.1%)	26 (19.4%)	53 (19.8%)

footnote of t_b_dm_01 line 1
footnote of t_b_dm_01 line 2

CIMS
shall not be distributed, edited, or modified in any way without CIMS Global's advance written consent.

1.1 Population at Screening

Table 2

Category	A: Drug X (N=134)	B: Placebo (N=134)	Total (N=268)
Age			
N	134	134	268
Mean (SD)	33.8 (6.6)	35.4 (7.9)	34.6 (7.3)
Median	33.0	35.0	34.0
Q1 - Q3	28.0 - 39.0	30.0 - 40.0	29.0 - 39.0
(Min, Max)	(21.0, 50.0)	(21.0, 62.0)	(21.0, 62.0)
Sex			
N	134	134	268
F	79 (59.0%)	82 (61.2%)	161 (60.1%)
M	55 (41.0%)	52 (38.8%)	107 (39.9%)
Ethnicity			
N	134	134	268
HISPANIC OR LATINO	15 (11.2%)	18 (13.4%)	33 (12.3%)
NOT HISPANIC OR LATINO	104 (77.6%)	103 (76.9%)	207 (77.2%)
NOT REPORTED	6 (4.5%)	10 (7.5%)	16 (6.0%)
UNKNOWN	9 (6.7%)	3 (2.2%)	12 (4.5%)

footnote of t_b_dm_01 line 1
footnote of t_b_dm_01 line 2

- The participants were divided into two groups: the A: Drug X group (134) and the B: Placebo group (134).
- The mean (SD) of Age was 34.6 (7.3) with a median of 34 (range 21 to 62).
  In the A: Drug X group, the mean (SD) age was 33.8 (6.6) with a median of 33 (range 21 to 50).
  In the B: Placebo group, the mean (SD) age was 35.4 (7.9) with a median of 35 (range 21 to 62).

CIMS ©2025 CI shall not b

Notes

- Pending internal R package repo update for {rtables} of using 0.6.10
- {rtables} split `tt_to_flextable()` starting from 0.6.11 to {rtables.officer}
- {autoslider.core} requires rtables >=0.6.12
- Currently borrowing idea from {autoslider.core} for internal development
- Consider combination in the later stage

CIMS

©2025 CIMS Global. All rights reserved. This material is confidential and proprietary to CIMS Global and shall not be distributed, edited, or modified in any way without CIMS Global's advance written consent.

Interactive Dashboard

©2025 CIMS Global. All rights reserved. This material is confidential and proprietary to CIMS Global and shall not be distributed, edited, or modified in any way without CIMS Global's advance written consent.

Experience

- Previously using {teal} structure
  - {teal.modules.clinical} and {teal.modules.general}
- Key Component [1]
  - {teal.data}: Combine ADaM dataset
  - {teal.slice}: Filter panel
  - {teal.reporter}: Generate instant report
- Currently shift to internal building of Shiny Apps for DMC Activity
  - Statistical function validation through internal controlled package
  - More flexibility in the customization
    - Parameter Panel
    - Download button and formats
    - Study-specific outputs
    - Data Connection
  - Still keep {teal.slice}, {teal.data} for the effective/efficient data filtering

[1] **PHUSE 2025**: *The Implementation of {teal} R Shiny Apps for DMC Activities [here]*

©2025 CIMS Global. All rights reserved. This material is confidential and proprietary to CIMS Global and shall not be distributed, edited, or modified in any way without CIMS Global's advance written consent.

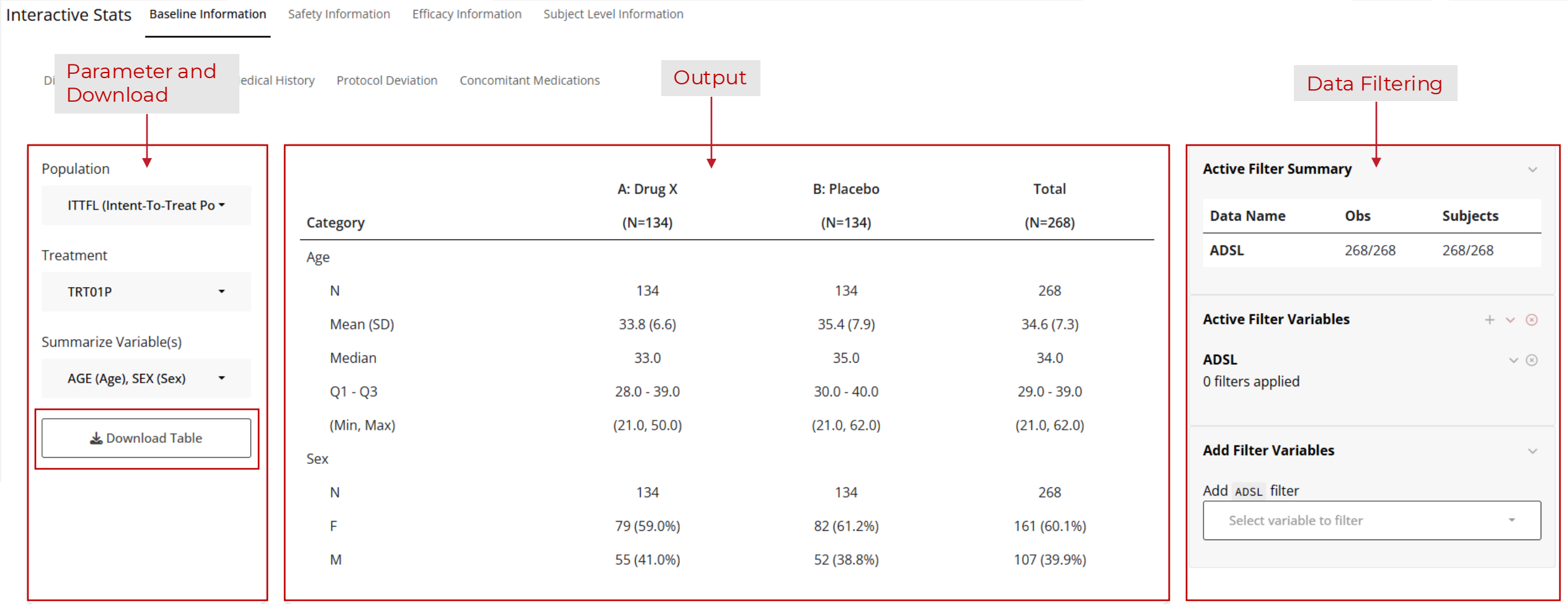
{teal} vs self-developed R Shiny Apps

Feature	Teal Modules	Self-Developed R Shiny Apps
Available Modules	Direct use	Development for R Shiny UI, Server, statistical functions
Preparation Time	Short, use {teal} codes	Long, build from scratch
Study-specific outputs	Build new teal modules by using teal developer guide	Build Shiny modules with general Shiny Knowledge
Layout Flexibility	Limited change for the parameter panel	Customizable layout for DMC Usage
Statistical Function	Source code of teal modules	Self-developed package with validation
Effective UI components	{teal} structure	Self-developed panel + {teal.slice}, {teal.data}
Portable Output	Combined Report but less formatted	Formatted .docx output

CIMS
©2025 CIMS Global. All rights reserved. This material is confidential and proprietary to CIMS Global and shall not be distributed, edited, or modified in any way without CIMS Global's advance written consent.
phuse

Applying the Familiar

- R Shiny Dashboard Structure Inspired by {teal}



Module Development

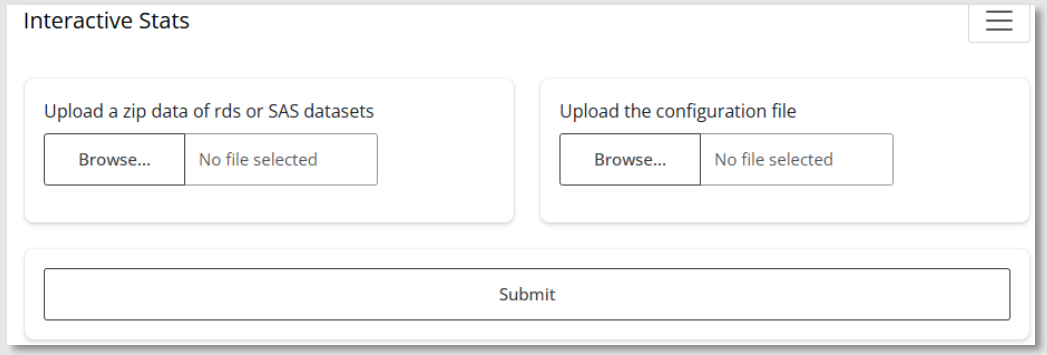
- Common Review in DMC Meetings

Baseline/Study	Safety	Subject-level listing	Efficacy
• Disposition • Demographic • Protocol Deviations • Medical History • Concomitant Medication	• Adverse Event • Lab Results • Vital Signs • Exposure	• Demographic • Adverse Event • Lab Results • Exposure • Medical History, • Concomitant Medication • Vital Sign	• Time to Event • KM Plot

©2025 CIMS Global. All rights reserved. This material is confidential and proprietary to CIMS Global and shall not be distributed, edited, or modified in any way without CIMS Global's advance written consent.

Connection to Data (General Solution)

1. Upload/Connection to ADaM Data



2. Configuration file specifies datasets and variables used by the app modules

Description	Variable	Value
Baseline Module	check_mod_baseline	Y
Baseline Analysis: Planned Treatment Variable	base_trt	TRT01P
Baseline Analysis: Planned Treatment Variable choices	base_trt_option	TRT01P|TRT01A
Disposition	check_disp	Y
Disposition: Reason of Study Discontinuation	disp_anal_var	DSTRREAS
Demographic	check_dm	Y
Demographic: Variables	dm_anal_var	AGE|SEX|COUNTRY|RACE
Protocol Deviation	check_pd	Y
Protocol Deviation: Primary protocol deviation variable	pd_anal_var	DVDECOD
Medical History	check_mh	Y
Medical History: Level 1 variable options	mh_anal_var_option_1	MHBODSYS|MHCAT
Medical History: Level 1 variable	mh_anal_var_1	MHBODSYS
Medical History: Level 2 variable options	mh_anal_var_option_2	MHTERM|MHDECOD
Medical History: Level 2 variable	mh_anal_var_2	MHDECOD

©2025 CIMS Global. All rights reserved. This material is confidential and proprietary to CIMS Global and shall not be distributed, edited, or modified in any way without CIMS Global's advance written consent.

Alternative Solution: Customization for each study

- Clinical Data Scientist to build Shiny Apps in workspace
  - Posit Workbench, RStudio server
- Enable your workplace connect to the R shiny server
  - R Shiny Server
  - API
- Deploy Shinyapps from workplace to clouds
- Configure connection between data and application
- GxP compliance and configuration
  - E.g., Role-based access control
  - Security
  - Talk with QA and IT.

CIMS

©2025 CIMS Global. All rights reserved. This material is confidential and proprietary to CIMS Global and shall not be distributed, edited, or modified in any way without CIMS Global's advance written consent.

Frequent Useful Features in DMC Dashboards

- Subgroup Filter for baseline covariates between two groups
- AE rate between treatment groups for targeted AE Term or category
- Lab value summary/figures
  - Selected Parameter
  - Selected Visit
- Listing to find
  - SAE
  - AE Leading to treatment discontinuation
  - SAE Leading to treatment discontinuations
  - Abnormal lab values
- Portable Word Format Results

©2025 CIMS Global. All rights reserved. This material is confidential and proprietary to CIMS Global and shall not be distributed, edited, or modified in any way without CIMS Global's advance written consent.

Example Lab Figures

Adverse Event Summary | Adverse Event | Lab Value | **Lab Value Figure** | Vital Sign | Vital Sign Figure

Population

SAFFL (Safety Populatior

Treatment

TRT01A

Summarize Variable

AVAL (Analysis Value)

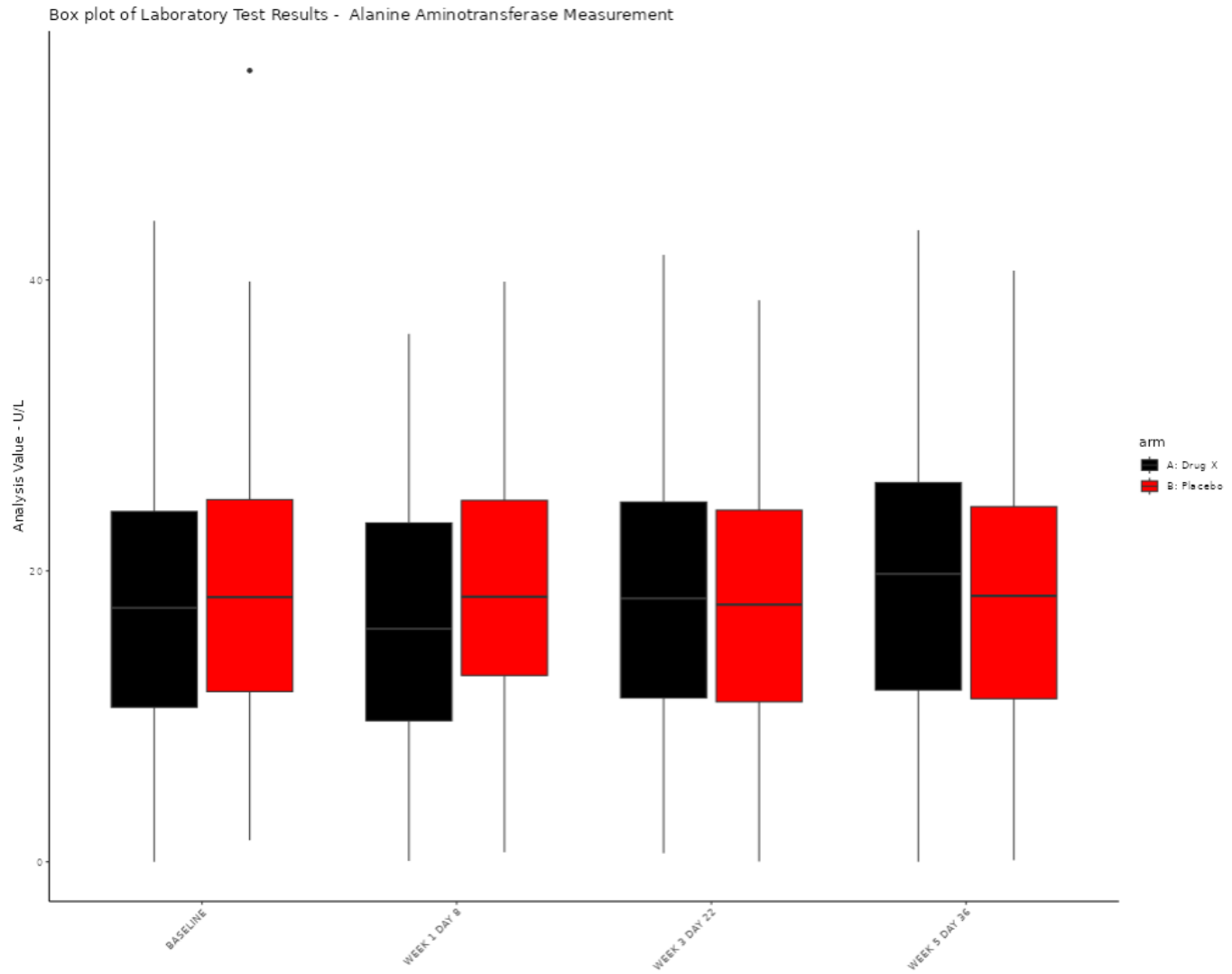
Parameter Variable

PARAM (Parameter)

Parameter Value(s)

Alanine Aminotransfera

Download Plot



Active Filter Summary

Data Name	Obs	Subjects
ADSL	268/268	268/268
ADLB	3216/5628	268/268

Active Filter Variables

ADSL
0 filters applied

ADLB
1 filter applied

AVISIT Analysis Visit
4 levels selected

BASELINE (804), WEEK 1 DAY 8 (804), WEEK

1 filter applied across datasets

Add Filter Variables

Add `ADSL` filter

Select variable to filter

Add `ADLB` filter

Select variable to filter

Example AE Listing

Interactive Stats | Baseline Information | Safety Information | Efficacy Information | Subject Level Information

Demographics | Adverse Event | Lab Value | Vital Sign | Medical History | Concomitant Medication

Patient ID
AB12345-BRA-1-id-134

System Organ Class
cl B/ cl B.2, cl D/ cl D.1, cl

SAE
Y

Toxicity Grade
2, 3

Relationship to Study Drug
N

Treatment	Subject ID	AGE	SEX	System Organ Class/ Preferred Term	Start Day/End Day	Duration of AE (days)	Toxicity Grade	SAE	Relationship to Study Drug	Action Taken	Outco
A: Drug X	AB12345-BRA-1-id-134	47	M	cl A/ cl A.1	2020-02-29(321)/ 2022-01-27(469)	149.00	2	Y	N	DOSE NOT CHANGED	RECO
A: Drug X	AB12345-BRA-1-id-134	47	M	cl A/ cl A.1	2020-02-29(393)/ 2022-01-27(435)	43.00	2	Y	N	DRUG WITHDRAWN	RECO

Active Filter Summary

Data Name	Obs	Subjects
ADSL	268/268	268/268
ADAE	1231/1231	245/245

Active Filter Variables

ADSL
0 filters applied

ADAE
0 filters applied

Add Filter Variables

©2025 CIMS Global. All rights reserved. This material is confidential and proprietary to CIMS Global and shall not be distributed, edited, or modified in any way without CIMS Global's advance written consent.

Portable .docx Outputs

Baseline Demographic Table

Category	A: Drug X (N=134)	B: Placebo (N=134)	Total (N=268)
Age			
N	134	134	268
Mean (SD)	33.8 (6.6)	35.4 (7.9)	34.6 (7.3)
Median	33.0	35.0	34.0
Q1 - Q3	28.0 - 39.0	30.0 - 40.0	29.0 - 39.0
(Min, Max)	(21.0, 50.0)	(21.0, 62.0)	(21.0, 62.0)
Sex			
N	134	134	268
F	79 (59.0%)	82 (61.2%)	161 (60.1%)
M	55 (41.0%)	52 (38.8%)	107 (39.9%)
Race			
N	134	134	268
ASIAN	68 (50.7%)	67 (50.0%)	135 (50.4%)
BLACK OR AFRICAN AMERICAN	31 (23.1%)	28 (20.9%)	59 (22.0%)
WHITE	27 (20.1%)	26 (19.4%)	53 (19.8%)
AMERICAN INDIAN OR ALASKA NATIVE	8 (6.0%)	11 (8.2%)	19 (7.1%)
MULTIPLE	0	1 (0.7%)	1 (0.4%)
NATIVE HAWAIIAN OR OTHER PACIFIC ISLANDER	0	1 (0.7%)	1 (0.4%)
OTHER	0	0	0
UNKNOWN	0	0	0

Data cutoff date:
Program Location:
Output Location:
Dataset Location:

©2025 CIMS Global. All rights reserved. This material is confidential and proprietary to CIMS Global and shall not be distributed, edited, or modified in any way without CIMS Global's advance written consent.

Challenges

- Agreement from Sponsor and DMC
  - What to be displayed
  - Who can use
- Validation
  - Consistency to the results in TFLs.
  - Responsibility
- Challenges of developing/using open-source tools
  - GxP Compliance for Statistical Computation Environment
  - External R Package Management
  - Internal R Package Development Lifecycle
  - Shiny Production Lifecycle
  - Statistical Validity

CIMS
©2025 CIMS Global. All rights reserved. This material is confidential and proprietary to CIMS Global and shall not be distributed, edited, or modified in any way without CIMS Global's advance written consent.
phuse

Summary

- To develop useful tools
  - Identify the pain-point from previous/current practice.
  - Learn the capability of available open-source packages
  - Identify potential usage to resolve the pain point
  - Borrow development experience from packages with high quality
- Automated Generation of the report
  - Time-saving document preparation
  - Reproducible
  - Fast Turnaround
  - Traceable between data and outputs
- Interactive Shiny Dashboard
  - Efficient review of tables and listings
  - Instant calculation & visualization for the questions in the meeting
  - Portable outputs used for meeting minutes

CIMS
©2025 CIMS Global. All rights reserved. This material is confidential and proprietary to CIMS Global and shall not be distributed, edited, or modified in any way without CIMS Global's advance written consent.

Thank You!

We welcome any questions or thoughts that you may have.

pzhang@cims-global.com
CIMS Global, NJ
www.cims-global.com

©2025 CIMS Global. All rights reserved. This material is confidential and proprietary to CIMS Global and shall not be distributed, edited, or modified in any way without CIMS Global's advance written consent.