

## eSafety Data Requirement and Screen Shots

### **I. Analysis Method Settings: Data Sets, AE Variables and Co-variates**

The following factors are typically analyzed in the ISS reports, and are available in eSafety to explore the exposure-safety relationship.

#### **1. Study Pool**

A study pool can be selected by

- i. Study ID
- ii. Study arm
- iii. Treatment regimen
- iv. Study length, size
- v. Clinical development phase

#### **2. Study Design**

The following study designs can be identified and re-grouped by dose level or treatment

- i. Parallel
- ii. Crossover
- iii. Sequential
- iv. Titration
- v. Extension
- vi. Adaptive

#### **3. Patient Subset**

Patient population can be defined by

- i. Demographic variables
- ii. Disease baseline
- iii. Special patient population
- iv. Laboratory results

#### **4. AE of Special Interest**

Specific AE can be identified by

- i. AE preferred term
- ii. Body system
- iii. Composite AE by combining multiple AE terms

## 5. AE Subset

A subset of AE's can be determined by

- i. Severity
- ii. Related to treatment or not
- iii. Time of AE occurrence
- iv. Duration of AE

## 6. Other Criteria

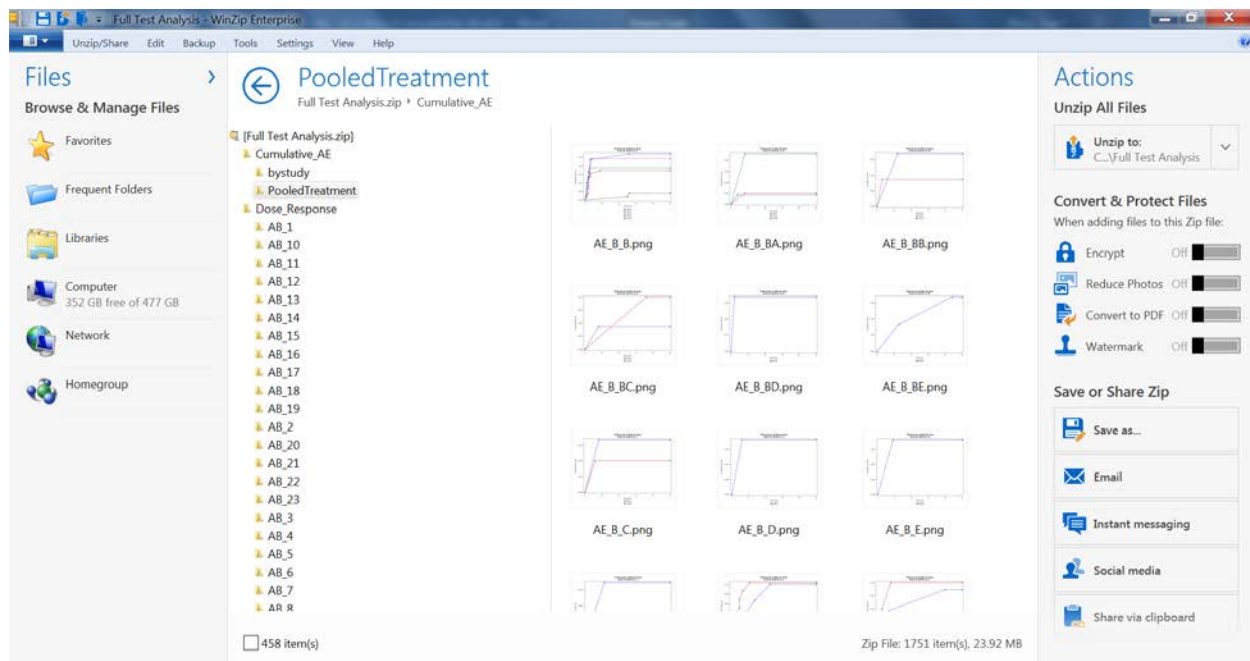
Additional inclusion and exclusion criteria for patient pool and AE

- i. Patient pool: can be subset by any variable listed in ADSL.xpt
- ii. AE: can be subset by any variable listed in ADAE.xpt

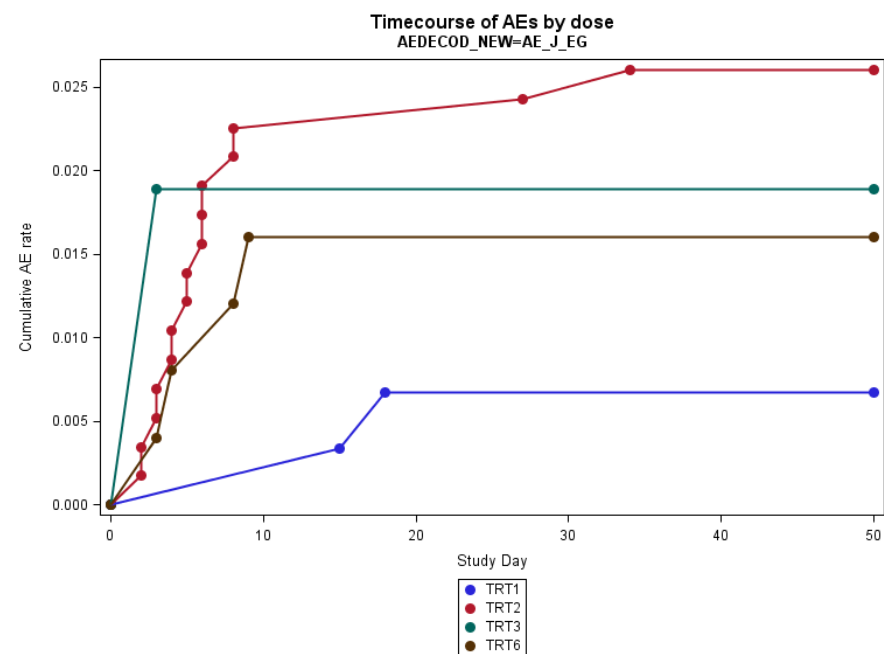
## II. Analyses Outputs

### 1. Cumulative AE Rate

The cumulative rates of all AEs are available in the “/Cumulative AE” folder and further organized into “/pooled treatment” (which shows pooled study results) and “/bystudy” (which shows individual study results).

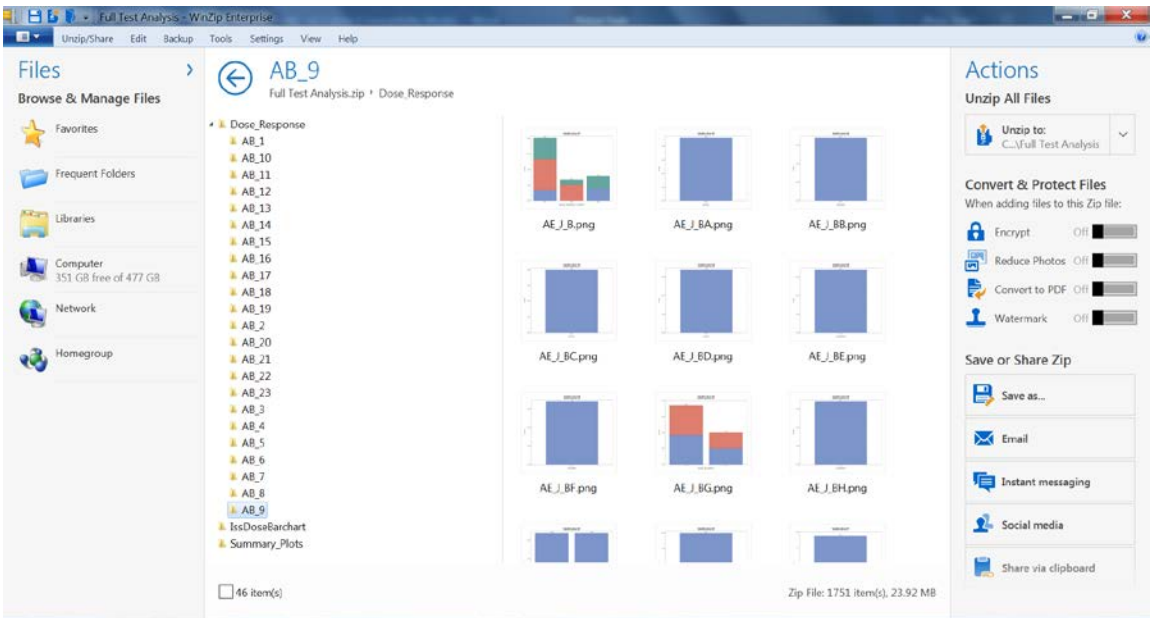


The cumulative rate of an AE term is plotted as a function of time of the first occurrence in each subject. An example is shown below

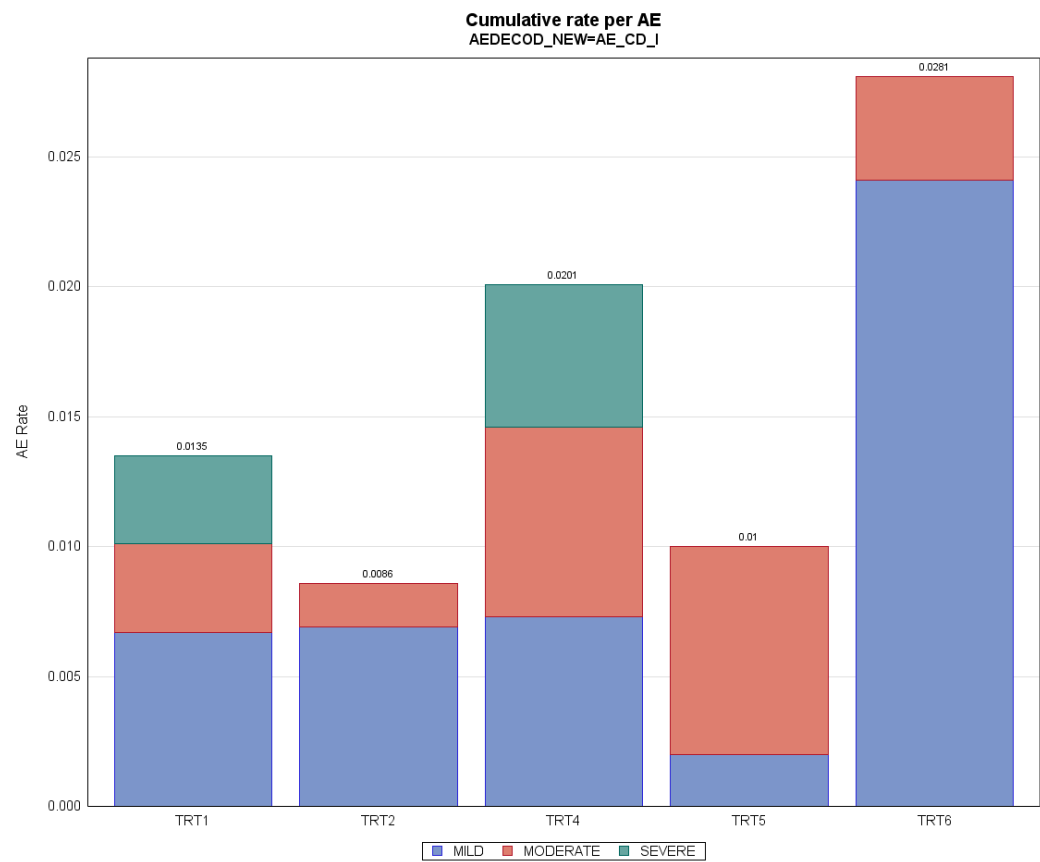


2. Dose Response of AE

The dose response of each AE term is available under the “/Dose Response” folder, and further organized by the body system folders

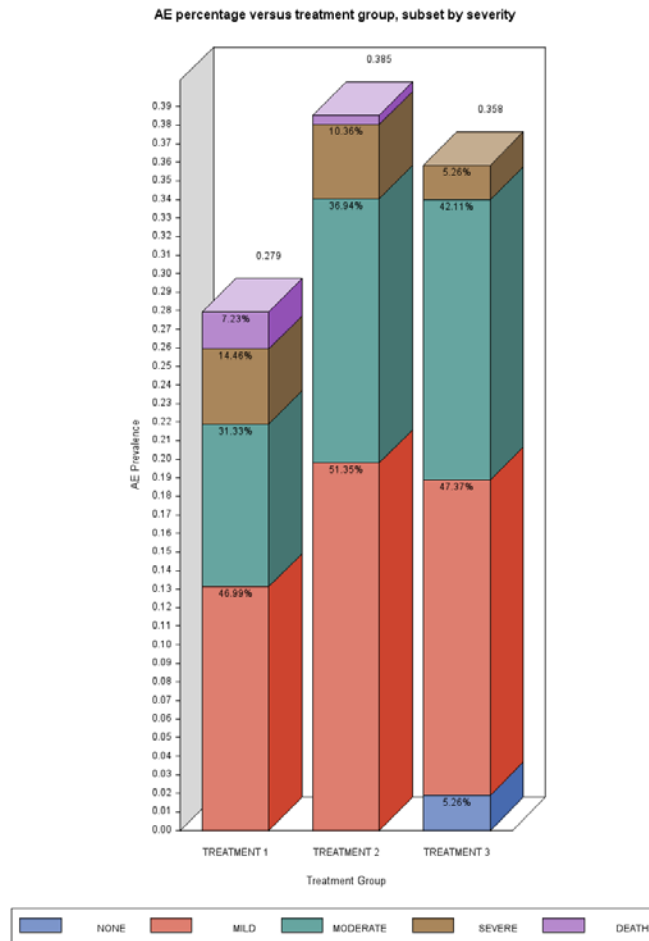


The AE rate is plotted per dose and color coded by severity. An example is shown below



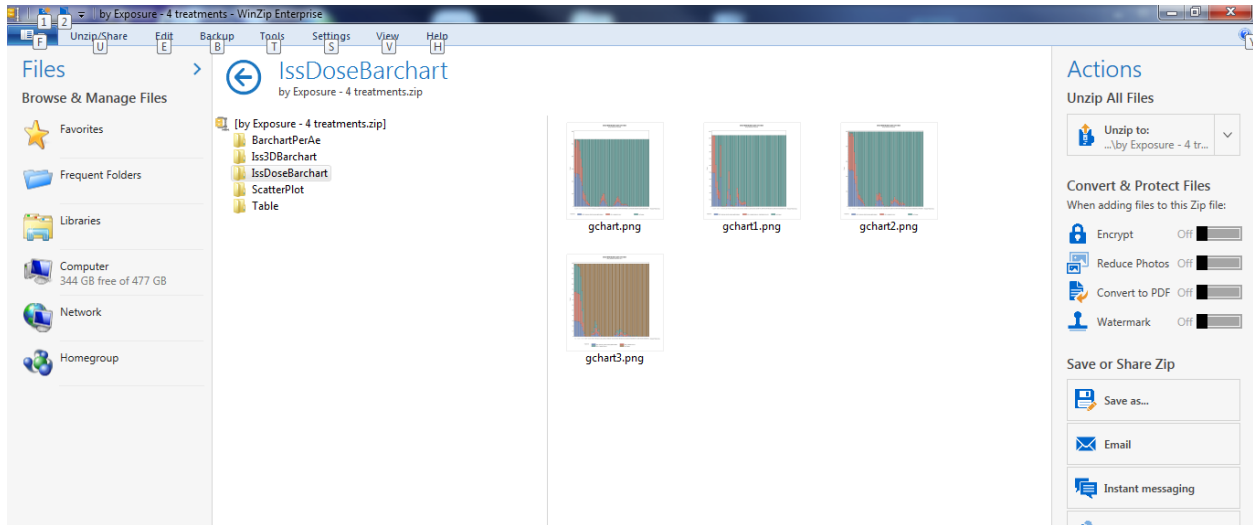
### 3. Total AE Prevalence

The total AE Prevalence is available in the “/Summary\_Plots” folder. The total AE rate is plotted per dose and color coded by severity. An example is shown below

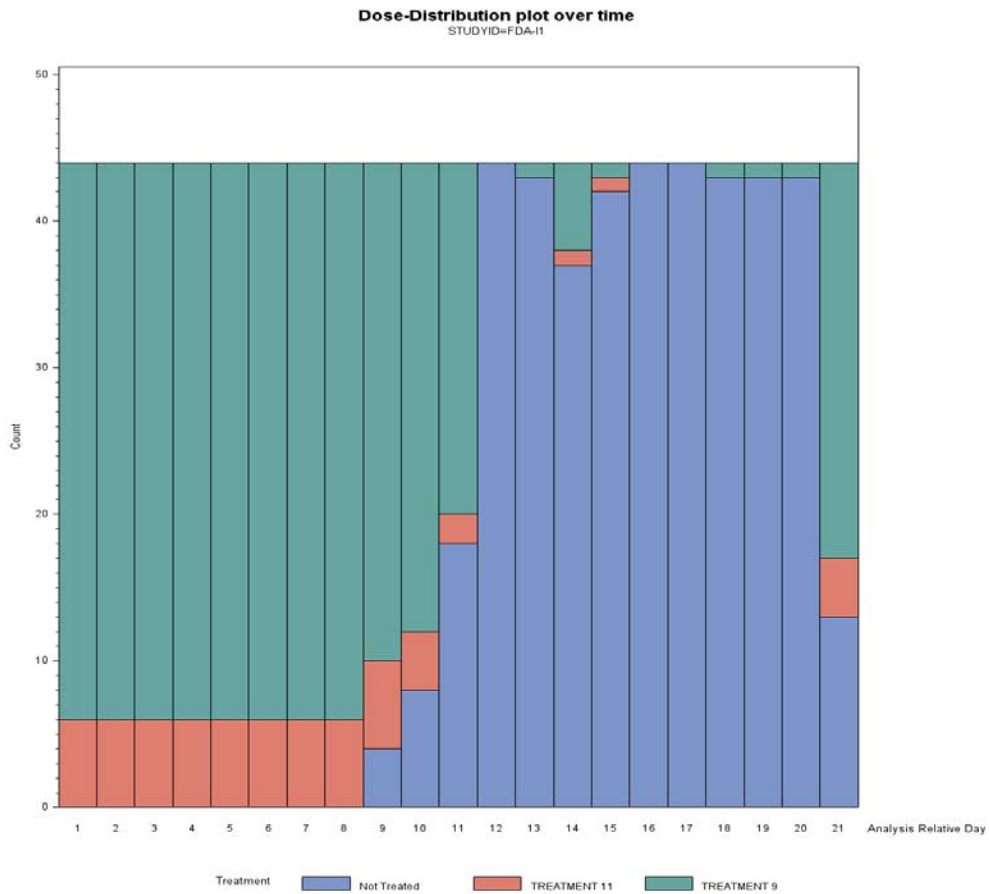


#### 4. The dosing records

The dosing record as a function of study time is available in the “/IssDoseBarChart” folder.



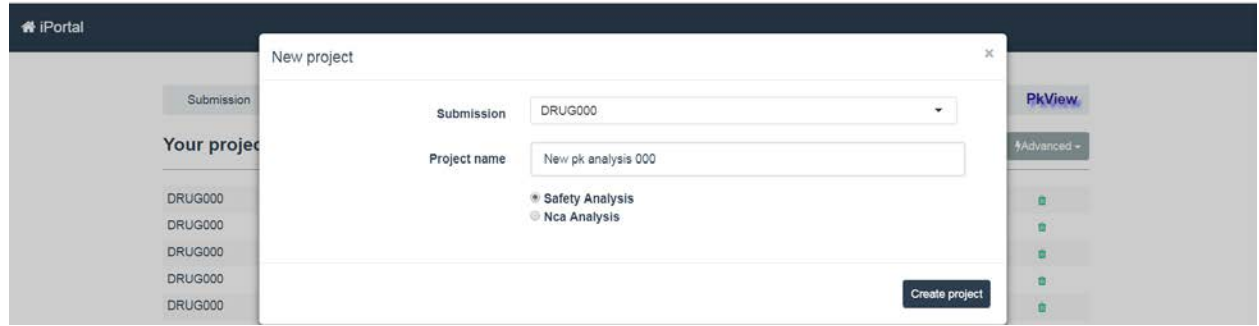
An example of the dosing record plot is shown below:



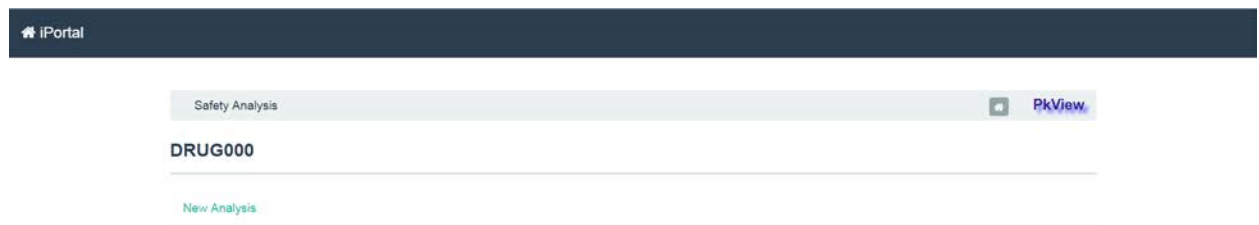
### III. User Interface

a. Steps to create a new safety analysis project –

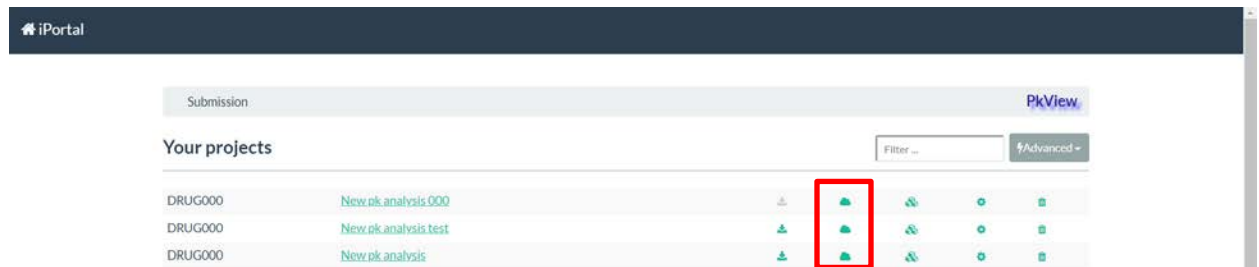
- On the homepage select 'Advanced' tab and click 'New Project'.
- On the 'New Project' screen, select the drug name and enter the project name.
- Select 'Safety Analysis' option and click 'Create Project'.



- The project gets created and the 'Safety Analysis' screen appears



- Once the project is created, the user can directly navigate to safety analysis screen from the homepage by clicking on the 'Safety Analysis' icon.



b. Required data files and variables

The user interface will initially load the required variables for the exposure safety analysis based on CDISC ADAM data standard terminology. The three required ADAM data files: ADAE.xpt, ADSL.xpt, and ADVS.xpt. An example of the starting screen of eSafety is shown below.

The screenshot shows the eSafety application interface for configuring an analysis. The title bar indicates 'DRUG dummy - Analysis (1).xml'. The main content area is divided into three sections: ADAE-Adverse Events, ADSL-Subject Level, and ADVS-Vital Signs. Each section contains dropdown menus for selecting variables and dates. The ADAE section includes fields for Subject ID (USUBJID), Body system or organ class (AEBODSYS), Severity/Intensity (AESEV), Dictionary Derived Term (AEDECOD), Analysis E Start Day (ASTDY), Analysis Start Date (ASTDT), Treatment (TRTA), Analysis Start Day (ASTDY), Study Identifier (STUDYID), Serious Event (AESER), Severity/Intensity (Choose...), and adverse period (Choose...). The ADSL section includes fields for Treatment (ARM), Treatment Start Date (TRTSDT), and Last Visit Date (LSTVSTD). The ADVS section includes a field for Analysis Relative Day (ADY). Each section has a 'View Data' button.

Here is the definition of each required field:

ADAE:

Variable name	Standard CDISC ADAM Terms
Subject ID	USUBJID
Body system or organ class	AEBODSYS
Severity/Intensity	AESEV
Dictionary derived terms	AEDECOD
Analysis E start day (optional, alternative to 'analysis start day')	AESTDY
Analysis start date (optional, alternative to 'analysis start day')	ASTDT
Treatment	TRTA
Analysis start day	ASTDY
Study identifier	STUDYID
Serious event	AESER
Severity/intensity (optional, alternative to standard 'Severity/intensity' term)	ASEV
Adverse period (optional)	APERIOD

ADSL:



Variable name	Standard CDISC ADAM Terms
Treatment	ARM
Last visit date	TRTED, RFENDT, LSTDTALL, DISCDTC, SFFUPDT, LSTCONDT, ARFENDT
Treatment start date	TRTSDT

ADVS:

Variable name	Standard CDISC ADAM Terms
Analysis relative day	ADY

### c. Treatment names from ADAE and ADSL

The treatment terms under the treatment variables in ADSL must match the terms under the treatment variable selected for ADAE, so that the two files can be merged. Some studies may have different treatments throughout the trial and the treatment names in the sequential periods are typically defined by TRT001A, TRT002A, TRT003A, etc., respectively in ADSL.

The screenshot shows the iPortal interface with the following sections:

- Top Navigation:** iPortal, Disease Progression, Code Library, Manuals, Tools. User is logged in as Yue.
- ADSL - Subject Level:**
  - Treatment:** ARM - ARM (selected)
  - Treatment Start Date:** TRTSDT - TRTSDT (selected)
  - Last Visit Date:** LSTVSTDT - LSTVSTDT (selected)
- ADVS- Vital Sign:**
  - Analysis Relative Day:** ADY - Analysis Relative Day (selected)
- ADSL Variables:**
  - ☒ TRT01A, ☐ AGE, ☐ SEX, ☐ WEIGHT
  - ☒ TRT02A, ☐ ARM, ☐ STUDYID
  - ☒ TRT03A, ☐ LSTVSTDT, ☐ TRTSDT
  - ☒ TRT04A, ☐ RACE, ☐ USUBJID
- Additional Options:** (button)


#### d. Study Pool


All treatments in all studies listed in the ISS datasets are automatically grouped and ranked by the dose level. For example, in the screen shots below, all treatments from various studies are grouped accordingly and ranked by the dose level. The user can select or deselect study and arm, or re-rank the dose level.

For special study designs with multiple treatments per ARM, such as titration, safety extension, cross over, or sequential studies, different treatment periods from different studies can be combined by specifying the combination of “Study Pool” described in this session and “Treatment names from ADAE and ADSL” described in the previous session.

The screenshot shows the 'Options' screen in the iPortal. It features a table with columns for 'Selected studies', 'StudyId', 'ARM', 'TRTP', 'Study Duration', 'Revised TRTP', 'Numeric Dose', and 'Order'. The table lists 12 rows of study data. Each row has a checkbox in the 'Selected studies' column. The 'Study Duration' column contains numeric values, and the 'Revised TRTP' column contains text input fields. The 'Numeric Dose' and 'Order' columns contain numeric input fields. There are 'Clear All' and 'Select All' buttons in the 'Selected studies' column, and a 'Reset to 0' button in the 'Order' column.

Selected studies	StudyId	ARM	TRTP	Study Duration	Revised TRTP	Numeric Dose	Order
<input checked="" type="checkbox"/>	FDA-I20	ARM_18	TREATMENT 1	27	TREATMENT 1	0	1
<input checked="" type="checkbox"/>	FDA-I6	ARM_17		50			
<input checked="" type="checkbox"/>	FDA-I14	ARM_40	TREATMENT 10	32	TREATMENT 10	0	2
<input checked="" type="checkbox"/>	FDA-I14	ARM_43		32			
<input checked="" type="checkbox"/>	FDA-I2	ARM_41		43			
<input checked="" type="checkbox"/>	FDA-I7			29			
<input checked="" type="checkbox"/>	FDA-I1	ARM_32	TREATMENT 11	18	TREATMENT 11	0	3
<input checked="" type="checkbox"/>	FDA-I1	ARM_35		18			
<input checked="" type="checkbox"/>	FDA-I1	ARM_36		18			
<input checked="" type="checkbox"/>	FDA-I5	ARM_29		11			

iPortal    Disease Progression    Code Library    Manuals    Tools ▾										Logged In as Yue	Search in AskOCP 
<input checked="" type="checkbox"/>	FDA-I10	ARM_2	TREATMENT 12	13	TREATMENT 12	0	4				
<input checked="" type="checkbox"/>	FDA-I11	ARM_2		10							
<input checked="" type="checkbox"/>	FDA-I19	ARM_11		9							
<input checked="" type="checkbox"/>	FDA-I19	ARM_12		9							
<input checked="" type="checkbox"/>	FDA-I19	ARM_13		9							
<input checked="" type="checkbox"/>	FDA-I19	ARM_14		9							
<input checked="" type="checkbox"/>	FDA-I19	ARM_5		9							
<input checked="" type="checkbox"/>	FDA-I19	ARM_7		9							
<input checked="" type="checkbox"/>	FDA-I3	ARM_15		45							
<input checked="" type="checkbox"/>	FDA-I3	ARM_16		45							
<input checked="" type="checkbox"/>	FDA-I3	ARM_27		45							
<input checked="" type="checkbox"/>	FDA-I3	ARM_28		45							
<input checked="" type="checkbox"/>	FDA-I3	ARM_37		45							
<input checked="" type="checkbox"/>	FDA-I3	ARM_38		45							
<input checked="" type="checkbox"/>	FDA-I9	ARM_42		9							
<input checked="" type="checkbox"/>	FDA-I3	ARM_15	TREATMENT 13	45	TREATMENT 13	0	5				
<input checked="" type="checkbox"/>	FDA-I3	ARM_16		45							

iPortal    Disease Progression    Code Library    Manuals    Tools ▾										Logged In as Yue	Search in AskOCP 
<input checked="" type="checkbox"/>	FDA-I17	ARM_21	TREATMENT 18	3	TREATMENT 18	0	10				
<input checked="" type="checkbox"/>	FDA-I17	ARM_22		3							
<input checked="" type="checkbox"/>	FDA-I9	ARM_39		9							
<input checked="" type="checkbox"/>	FDA-I17	ARM_29	TREATMENT 19	3	TREATMENT 19	0	11				
<input checked="" type="checkbox"/>	FDA-I16	ARM_2	TREATMENT 2	50	TREATMENT 2	0	12				
<input checked="" type="checkbox"/>	FDA-I20	ARM_46		27							
<input checked="" type="checkbox"/>	FDA-I6	ARM_2		50							
<input checked="" type="checkbox"/>	FDA-I20	ARM_47	TREATMENT 3	27	TREATMENT 3	0	13				
<input checked="" type="checkbox"/>	FDA-I8	ARM_3	TREATMENT 4	28	TREATMENT 4	0	14				
<input checked="" type="checkbox"/>	FDA-I8	ARM_4		28							
<input checked="" type="checkbox"/>	FDA-I8	ARM_25	TREATMENT 5	28	TREATMENT 5	0	15				
<input checked="" type="checkbox"/>	FDA-I16	ARM_26	TREATMENT 6	50	TREATMENT 6	0	16				
<input checked="" type="checkbox"/>	FDA-I13	ARM_23	TREATMENT 7	15	TREATMENT 7	0	17				
<input checked="" type="checkbox"/>	FDA-I15	ARM_44		26							
<input checked="" type="checkbox"/>	FDA-I18	ARM_10		21							
<input checked="" type="checkbox"/>	FDA-I18	ARM_11		21							
<input checked="" type="checkbox"/>	FDA-I18	ARM_6		21							

iPortal	Disease Progression	Code Library	Manuals	Tools -	Logged in as Yue				Search in AskOCP	
<input checked="" type="checkbox"/>	FDA-I3	ARM_15	TREATMENT 13	45	TREATMENT 13	0	5			
<input checked="" type="checkbox"/>	FDA-I3	ARM_16		45						
<input checked="" type="checkbox"/>	FDA-I3	ARM_27		45						
<input checked="" type="checkbox"/>	FDA-I3	ARM_28		45						
<input checked="" type="checkbox"/>	FDA-I3	ARM_38		45						
<input checked="" type="checkbox"/>	FDA-I19	ARM_29	TREATMENT 14	9	TREATMENT 14	0	6			
<input checked="" type="checkbox"/>	FDA-I3	ARM_15		45						
<input checked="" type="checkbox"/>	FDA-I3	ARM_37		45						
<input checked="" type="checkbox"/>	FDA-I3	ARM_38		45						
<input checked="" type="checkbox"/>	FDA-I14	ARM_40	TREATMENT 15	32	TREATMENT 15	0	7			
<input checked="" type="checkbox"/>	FDA-I2	ARM_41		43						
<input checked="" type="checkbox"/>	FDA-I7			29						
<input checked="" type="checkbox"/>	FDA-I14	ARM_40	TREATMENT 16	32	TREATMENT 16	0	8			
<input checked="" type="checkbox"/>	FDA-I14	ARM_43		32						
<input checked="" type="checkbox"/>	FDA-I2	ARM_41		43						
<input checked="" type="checkbox"/>	FDA-I7			29						
<input checked="" type="checkbox"/>	FDA-I2	ARM_41	TREATMENT 17	43	TREATMENT 17	0	9			

iPortal	Disease Progression	Code Library	Manuals	Tools -	Logged in as Yue				Search in AskOCP	
<input checked="" type="checkbox"/>	FDA-I18	ARM_11		21						
<input checked="" type="checkbox"/>	FDA-I18	ARM_6		21						
<input checked="" type="checkbox"/>	FDA-I18	ARM_8		21						
<input checked="" type="checkbox"/>	FDA-I4	ARM_2		21						
<input checked="" type="checkbox"/>	FDA-I18	ARM_29	TREATMENT 8	21	TREATMENT 8	0	18			
<input checked="" type="checkbox"/>	FDA-I11	ARM_48	TREATMENT 9	18	TREATMENT 9	0	19			
<input checked="" type="checkbox"/>	FDA-I11	ARM_49		18						
<input checked="" type="checkbox"/>	FDA-I11	ARM_50		18						
<input checked="" type="checkbox"/>	FDA-I11	ARM_51		18						
<input checked="" type="checkbox"/>	FDA-I11	ARM_52		18						
<input checked="" type="checkbox"/>	FDA-I11	ARM_53		18						
<input checked="" type="checkbox"/>	FDA-I12	ARM_1		15						
<input checked="" type="checkbox"/>	FDA-I13	ARM_24		15						
<input checked="" type="checkbox"/>	FDA-I15	ARM_45		26						
<input checked="" type="checkbox"/>	FDA-I5	ARM_2		11						

e. Inclusion/Exclusion Criteria for Patient subset and AE of interest

Inclusion and exclusion criteria can be applied to narrow down patient subset or AE of interest. In the example below:

Patient subset

- Include only severity = moderate and severe
- Include only Age > 40 y
- Exclude study = FDA-I1 and FDA-I10AE of interest

[iPortal](#) [Disease Progression](#) [Code Library](#) [Manuals](#) [Tools -](#)

ADAE- Adverse Events Count

View Data

Inclusions

AESEV

=

☐ DEATH ☐ LIFE-THREATENING ☐ MILD ☒ MODERATE ☒ SEVERE

Choose...

Choose...

Choose...

Exclusions

Choose...

Choose...

Choose...

Choose...

ADSL- Total Subjects Count

View Data

Inclusions

AGE

>

☐ 17 ☐ 18 ☐ 19 ☐ 20 ☐ 21 ☐ 22 ☐ 23 ☐ 24 ☐ 25 ☐ 26 ☐ 27 ☐ 28 ☐ 29 ☐ 30 ☐ 31 ☐ 32 ☐ 33 ☐ 34 ☐ 35 ☐ 36 ☐ 37 ☐ 38 ☐ 39 ☒ 40 ☐ 41 ☐ 42 ☐ 43 ☐ 44 ☐ 45 ☐ 46 ☐ 47 ☐ 48 ☐ 49 ☐ 50 ☐ 51 ☐ 52 ☐ 53 ☐ 54 ☐ 55 ☐ 56 ☐ 57 ☐ 58 ☐ 59 ☐ 60 ☐ 61 ☐ 62 ☐ 63 ☐ 64

Choose...

Choose...

Choose...

Exclusions

STUDYID

=

☒ FDA-I1 ☒ FDA-I10 ☐ FDA-I11 ☐ FDA-I12 ☐ FDA-I13 ☐ FDA-I14 ☐ FDA-I15 ☐ FDA-I16 ☐ FDA-I17 ☐ FDA-I18 ☐ FDA-I19 ☐ FDA-I2 ☐ FDA-I20 ☐ FDA-I3 ☐ FDA-I4 ☐ FDA-I5 ☐ FDA-I6 ☐ FDA-I7 ☐ FDA-I8 ☐ FDA-I9

Choose...

Choose...

Choose...