U.S. FOOD & DRUG ADMINISTRATION

Office of New Drugs Standard Safety Tables & Figures for New Drug and Biologic Applications

CDR B. Nhi Beasley, Pharm.D.
Associate Director Biomedical Informatics (ADBMI)
Biomedical Informatics and Regulatory Review Science (BIRRS)
FDA/CDER/Office of New Drugs (OND)/Office of Drug Evaluation Science

Disclaimer

- The views and opinions expressed in this presentation are those of the presenter and do not represent official policy or position of the FDA
- I have no relevant financial or non-financial relationships to disclose.

Agenda

Standard Safety Tables and Figures (ST&F)
Manual of Policies and Procedures (MAPP)

Overview of the Standard Safety Tables & Figures
Integrated Guide (IG) and Targeted Analysis Guides (TAGs)

Frequently asked questions (FAQs)

CDER Manual of Policies and Procedures (MAPP)

- Federal directives
- Document internal polices and procedures
- Increase transparency
- https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/cder-manual-policies-procedures-mapp

ST&F MAPP Purpose and Policy

- Purpose
  - Describes good review practices for ST&F
    - Integrated Guide (IG) and Targeted Analysis Guides (TAGs)
  - Applicable submissions
    - New Drug Applications (NDAs), biologic license applications (BLAs), efficacy supplements, Over-The-Counter monographs
- Policy
  - ST&Fs are framework for display of clinical safety data in clinical reviews; can be modified
  - Generated for pivotal trial(s), pooled analyses
  - Applicant not required to submit safety analyses in these formats

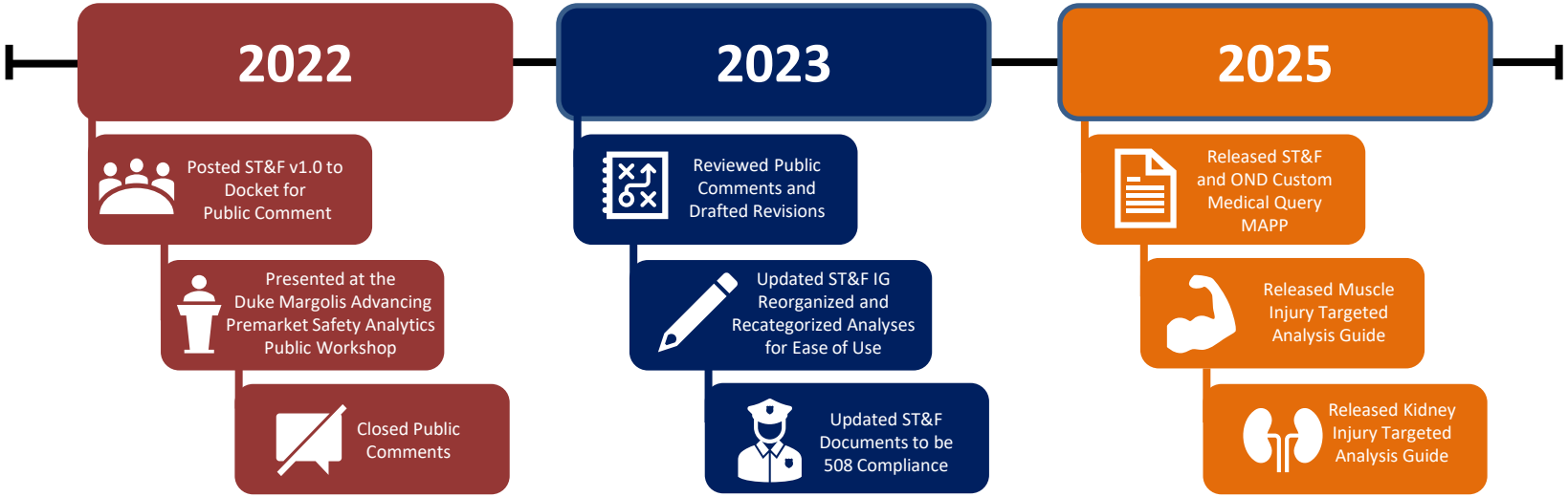
ST&F MAPP Review Practices

- Clinical Data Scientist (CDS) and cross-disciplinary review team
  - Determine analytical approach
  - Determine if customization needed
- CDS generates ST&F
- Evaluate data quality and clinical safety data presented in the ST&F
- Incorporate appropriate tables and figures into the review
- Generate additional analyses and if applicable, TAGs for identified potential safety signals

Why Standard Safety Tables & Figures?

- Clinical safety data generally required to support approval
- Uniform safety data presentation and visualization (e.g., color, lines, table layout)
- Improve quality of how clinical safety data displayed
- Streamline the review process

Timeline of ST&F Development



550
Docket Comments Reviewed

60
Total ST&F Tables

22
Total ST&F Figures

2
Targeted Analysis Guides Published

12
Public ST&F Presentations

5,000
Presentation Attendees

ST&F IG Organization

- **Core** (always generated, essential for safety review)
  - General
  - Adverse events (AE)
  - Subgroup analysis by baseline
  - Laboratory
  - Vital Signs
- **Expanded** (more in-depth look, allow for drill-down)
  - **AE, laboratory, and vital sign**
- **Optional** (alternative displays, generated upon request)

Standardized Tabular Display

To ensure standardization, all generated tables follow consistent formatting principles

Bolded column headers

Order of the treatment columns: drug arms followed by active control, and placebo

Subtext is indented

10 pt. Arial font for all table text (including headers)

Footnotes provide important definitions and context

Table 2. Demographics and Baseline Clinical Characteristics, Safety Population, Pooled Analysis (or Trial X)

Characteristic	Drug Name Dosage A N=XXX	Control N=XXX	Total Population N=XXX
Sex, n (%)			
Male	X (Y)	X (Y)	X (Y)
Female	X (Y)	X (Y)	X (Y)
Age, years			
Mean (SD)	X (Y.YY)	X (Y.YY)	X.X (Y.YY)
Median (min, max)	X (Y, Z)	X (Y, Z)	X (Y, Z)
Age groups (years), n (%)			
Group 1	X (Y)	X (Y)	X (Y)
Group 2	X (Y)	X (Y)	X (Y)
Race, n (%)			
American Indian or Alaska Native	X (Y)	X (Y)	X (Y)
Asian	X (Y)	X (Y)	X (Y)
Black or African American	X (Y)	X (Y)	X (Y)
Native Hawaiian or other Pacific Islander	X (Y)	X (Y)	X (Y)
White	X (Y)	X (Y)	X (Y)
Not reported	X (Y)	X (Y)	X (Y)
Other	X (Y)	X (Y)	X (Y)
Unknown	X (Y)	X (Y)	X (Y)
Ethnicity, n (%)			
Hispanic or Latino	X (Y)	X (Y)	X (Y)
Not Hispanic or Latino	X (Y)	X (Y)	X (Y)
Not reported	X (Y)	X (Y)	X (Y)
Unknown	X (Y)	X (Y)	X (Y)
Country of participation, n (%)			
Country A	X (Y)	X (Y)	X (Y)
Country B	X (Y)	X (Y)	X (Y)
Clinical baseline characteristics, n (%)			
Characteristic A	X (Y)	X (Y)	X (Y)
Characteristic B	X (Y)	X (Y)	X (Y)

Source: [include Applicant source, datasets and/or software tools used].
Note: Duration = [e.g., X-week double-blind treatment period or median and a range of pooled trial durations].
Abbreviations: n, number of subjects with given characteristic; N, number of subjects in treatment arm; SD, standard deviation.

Standardized Figure Display

To ensure standardization, all generated figures follow consistent formatting principles

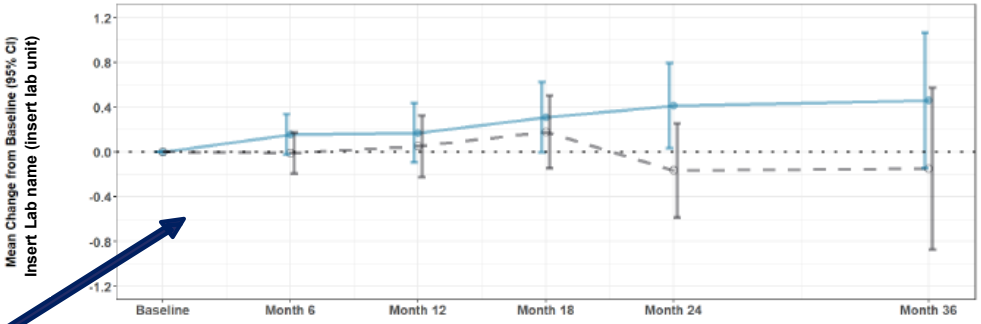
The y-axis is scaled appropriately

Standardized color selection and consistency across trials.

When the x-axis is used to represent time, labeled by **protocol specified visit** schedule

When displaying data over time, total "n's" are presented per time period at the bottom of the figure

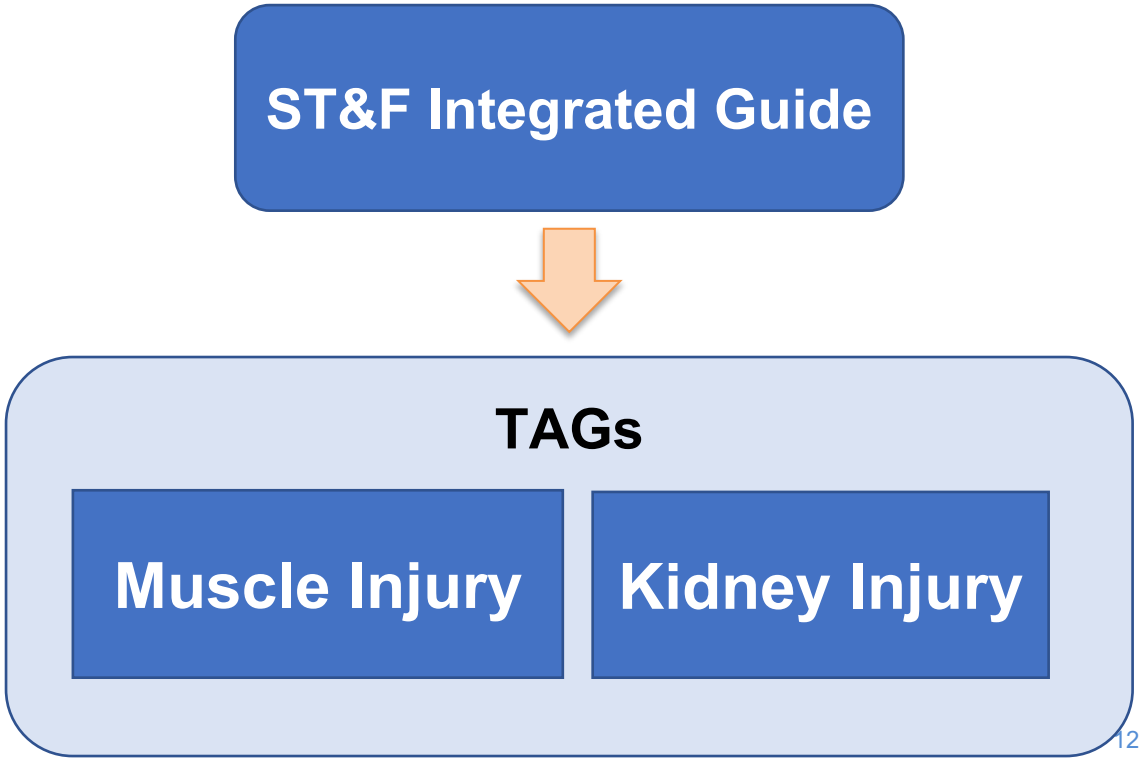
Figure 6. Mean General Chemistry Data Change From Baseline Over Time by Treatment Arm, Safety Population, Pooled Analyses (or Trial X)



Source: [include Applicant source, datasets and/or software tools used].
Note: Duration = [e.g., X-week double-blind treatment period or median and a range of pooled trial durations].
Note: If a timepoint is reached where there are only a few subjects remaining in the trial (e.g., less than 5%), consideration should be made to truncate this graph as the results would not be considered a reliable indicator of the true mean.
Note: Subjects with both baseline and postbaseline data available are included in the mean change from baseline calculations at each visit. The number of subjects reflects only those included in the mean change from baseline calculations, rather than the total number of subjects.
Note: The vertical bars shown on the plotted lines indicate the 95% confidence interval of the mean change at the corresponding time points.
Note: Only central laboratory data were used for the plot.
Abbreviations: CI, confidence interval.

Targeted Analysis Guides (TAGs)

TAGs
- Available by request
- Therapeutic area-specific tables and figures
- More in-depth analyses



Kidney Injury IG versus Targeted Analysis Guide

Integrated Guide

Kidney Injury Screening Analyses

1. AEs
2. Lab studies (estimated Glomerular Filtration Rate, serum creatinine)
   - Mean change from baseline over time
   - Exceeding specified thresholds
   - Last On-Treatment Values

Kidney Injury Guide

Kidney Injury Screening Analyses

Kidney Injury TAG*

1. AEs by Medically Important Outcomes, Action taken with study drug
2. More lab studies
   - Exceeding last known value
   - % change from baseline
3. Time to Event
4. Subject level analyses

*Produced upon request by reviewer

FREQUENTLY ASKED QUESTIONS AND ANSWERS

Question 1: Where is ST&F IG located?

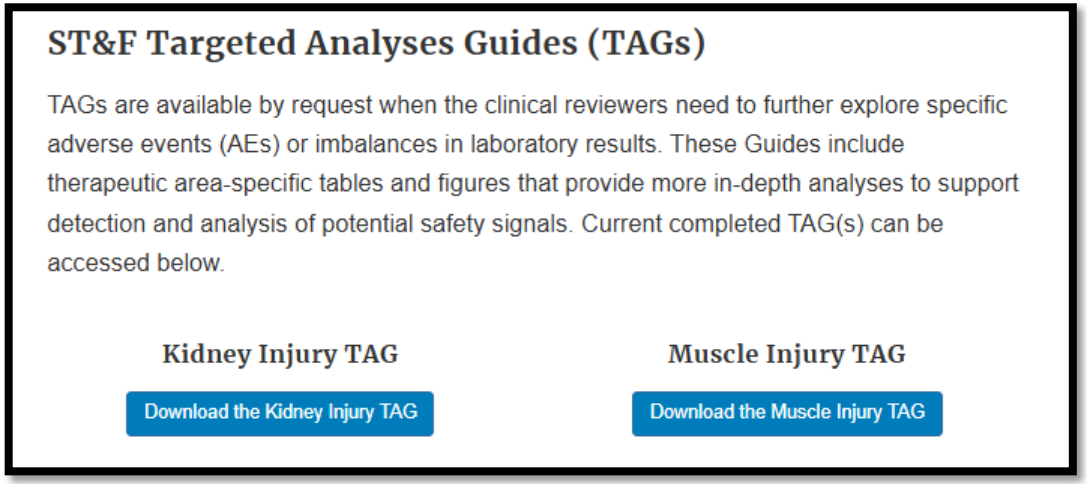
- Version 2 posted on June 13, 2025 on FDA external website https://www.fda.gov/drugs/development-resources/standard-safety-tables-and-figures-stfs

Question 2: How often will ST&F be updated?

The ST&F will be reviewed annually and updated as required. Updates will be released on the external website and announced by FDA.

Question 3: When will the TAGs be released?

Muscle Injury and *Kidney Injury* TAGs were released at the time of ST&F v2.0 release. Additional TAGs will be released in the future.



Question 4: How can I be kept informed of future releases of the ST&F?

https://www.fda.gov/drugs/development-approval-process-drugs/cder-small-business-industry-assistance-sbia

Question 5: Are sponsors required to submit safety tables and figures following the format and methodologies within the ST&F?

No. The intent of ST&F is to foster transparency and collaboration, outlining OND's approach to safety analysis.

Question 6: Can tables and figures within the ST&F be customized?

Yes. The ST&F serve as a framework for example scenarios, and all analyses can be customized as needed.

Question 7: How is causality incorporated into the ST&F?

AE relatedness to drug as assessed by the investigator has been removed from the ST&F adverse event tables. It was not the intent of the ST&F to promote display of investigator assessment of causality.

Question 8: Do the ST&F laboratory analyses report data using U.S. conventional or SI units?

The ST&F by default use US conventional units as it is intended for FDA review. The decision of whether to use US conventional or SI units is out of scope for the ST&F. Sponsors should refer to the Technical Conformance Guide on approaches for electronic data submission.

https://www.fda.gov/regulatory-information/search-fda-guidance-documents/study-data-technical-conformance-guide-technical-specifications-document

Question 9: Do the analyses in ST&F include both scheduled and unscheduled laboratory data in safety analyses?

In general, data from all visits (scheduled and unscheduled) should be considered in the overall safety evaluation. The method for handling local laboratory measures and unscheduled visits is out of scope for the ST&F and should be addressed during the planning of pivotal trials and outlined in the Statistical Analysis Plan.

Questions 10: How are differences in pediatric normal reference ranges addressed in the ST&F?

The ST&F currently reflect abnormality criteria for adults only. However, the FDA is working to incorporate pediatric criteria for laboratories and vital signs in future updates.

Concluding Remarks

- The ST&F MAPP describes good review practices, and outlines the policies, procedures, and responsibilities for OND reviewers that use ST&F.
- Standard Safety Tables and Figures
  - Provide uniform, standard safety data presentation
  - Can be customized
  - Foster consistency and improve efficiency

Acknowledgement: ST&F Working Group

Current Members

- Yang Veronica Pei (Project co-lead)
- B. Nhi Beasley (Project co-lead)
- Frank Anania
- Bryant Chen
- Ling Cao
- Paul (Skip) Hayashi
- Rhonda Hearns-Stewart
- Salman Hosain Linda Jeng
- Maria Matilde Kam
- Gregory Levin
- Jinzhong Liu
- Susan Mayo
- DeAngelo McKinley
- Abhilasha Nair
- Mahtab Niyyati
- Frank Pucino
- Vanitha Sekar
- Jeff Siegel
- Christopher Smith
- Mat Soukup
- Qunshu (Elena) Zhang
- Jizu Zhi

Previous Members

- Sarita Boyd
- Anne Bunner
- Michelle Carey
- Chenoa Conley
- Sarah Connelly
- Susan Duke
- Justin Earp
- Jeffry Florian
- Rachel Glasser
- Ramya Gopinath
- Matthew Guerra
- Kerry Joe Lee
- Vaishali Popat
- Scott Proestel
- Alan Shapiro
- Kim Shimy
- James Smith
- Larissa Stabinski
- Robert Temple
- Ellis Unger
- Preeti Venkataraman
- Douglas Warfield
- Ellen Wertheimer


FDA
U.S. FOOD & DRUG
ADMINISTRATION