POLICY AND PROCEDURES

OFFICE OF NEW DRUGS

Good Review Practices: Standard Safety Tables and Figures

Table of Contents

PURPOSE

- This Manual of Policies and Procedures (MAPP) and its referenced documents describe good review practices for the Office of New Drugs (OND) within the Center for Drug Evaluation and Research (CDER) regarding the use of the Standard Safety Tables and Figures (ST&Fs), which are composed of the Integrated Guide (IG) and Targeted Analysis Guides (TAGs) for Clinical review staff in OND.

- The practices and procedures in this MAPP apply to new drug applications (NDAs), biologics license applications (BLAs) submitted under section 351(a) of the Public Health Service Act (PHS Act), and efficacy supplements to those applications.[1]

- The procedures in this MAPP are intended to improve the quality and consistency of the display of clinical safety data, not interpretation of these data in OND reviews of marketing applications.

[1] The MAPP also applies to over-the-counter (OTC) monograph order requests (OMORs) in cases where clinical safety data from clinical trials are submitted for FDA to make a determination as to whether the drug is generally recognized as safe and effective (GRASE) under section 201(p)(1) of the Federal Food Drug and Cosmetic (FD&C) Act. An OMOR refers to a request for FDA to issue an administrative order under section 505G(b)(5) of the FD&C Act (21 U.S.C. 355h(b)(5)).

BACKGROUND

- Applications for FDA approval of a new drug[2] generally require submission of clinical safety data to support a determination that the proposed product is safe and effective for its proposed use(s).[3]

- OND Clinical reviewers use ST&Fs to identify and assess potential safety findings in marketing applications and present clinical safety data in their reviews.

- Using ST&Fs results in more streamlined and efficient review of marketing applications. Implementation of ST&Fs is expected to improve the quality of clinical safety data review in marketing applications and consistency in presentation of clinical safety data in FDA reviews.

- The ST&F Working Group developed the ST&Fs to: (1) establish a standard set of clinical safety analytic tables and figures; and (2) create an IG containing instructions to support clinical reviewers in their use of the ST&F outputs for their review of clinical safety data.

- TAGs contain additional analyses to further investigate safety signals identified during initial clinical safety review or for certain adverse events of special interest (AESI).

POLICY

- ST&Fs serve as a framework for the display of clinical safety data in FDA reviews. These displays are example analyses and should be modified and customized based on the specific study design(s), safety issues, and new issues that arise during the safety evaluation.

- ST&Fs are typically generated for the following:

  – Pivotal or registration trials

  – Any other individual trial of interest to the OND clinical reviewer including those that differ substantially from the pivotal trial in key design characteristics (e.g., lead-in period, enrichment, population, duration, cross-over design)

  – Pooled analyses (if appropriate)

[2] For the purposes of this MAPP, all references to *drugs* include both human prescription and nonprescription drug products and biological products regulated by CDER, unless otherwise specified.
[3] Refer to section 505(b)(1)(A)(i) and (d) of the FD&C Act and 21 CFR 314.50(d)(5), 314.54(a)(1)(ii), and section 351(a)(2) of the PHS Act and 21 CFR 601.2(a).

- Additional targeted analyses (e.g., TAGs, custom targeted analysis) may be needed to further assess potential safety signal(s) identified during the clinical safety review.

- Applicants are not required to submit or display safety analyses following the format and methodologies described in the ST&Fs.

RESPONSIBILITIES

- OND/Office of Drug Evaluation Science (ODES)/Division of Biomedical Informatics, Research, and Biomarker Development (DBIRBD)/Biomedical Informatics and Regulatory Review Science (BIRRS) team (including Associate Director for Biomedical Informatics (ADBMI)) is responsible for:

  – Providing program oversight for ST&Fs development and policies.

  – Supporting the ST&F Working Group, including member recruitment.

  – Supporting the clinical review team in their review of clinical safety data and safety signal exploration.

- ST&F Working Group is responsible for:

  – Developing content for ST&F.

  – Creating instructions for OND Clinical Data Science (CDS) staff to generate the ST&Fs package for a specific marketing application.

  – Reviewing the ST&F templates annually and updating them as appropriate.

- OND CDS team is responsible for:

  – Initiating discussions with the clinical and statistical reviewers to align on the approach to clinical safety data analysis.

  – Generating the ST&Fs package for OND clinical reviewers based on instructions outlined in the IG and in alignment with the agreed-upon approach to analysis.

  – Generating TAGs and custom analyses targeting potential safety issues identified by the clinical review team.

  – Sharing the ST&Fs with the clinical review team.

- OND Clinical review team is responsible for:

  - Assessing clinical safety data information submitted in the marketing application.

  - Collaborating with the CDS, statistical review team, and ADBMI to determine the preferred approach to performing the clinical safety analyses.

  - Interpreting and summarizing the clinical safety data submitted in the marketing application and presented in the ST&Fs package.

  - Requesting custom analyses and TAGs from statistical reviewers or CDS team to further explore safety signals, where applicable.

- Office of Biostatistics (OB) statistical review team is responsible for:

  - Contributing to discussions about the appropriate approach to analysis for the ST&Fs for the specific marketing application review, given the clinical questions of interest and the trial design(s).

  - Contributing to interpretation of clinical safety results (e.g., understanding of statistical uncertainty and potential impact of missing data).

  - Conducting custom analyses to further assess identified signals or AESIs, where applicable.

PROCEDURES

1. Prior to generating the ST&F package, the OND CDS team and the cross-disciplinary review team (e.g., clinical, statistical, and ADBMI) work together to:

   a. Determine the analytical approach to summarize the clinical safety data to be presented in the ST&Fs.

   b. Determine the need for customization based on the specific trial design(s) and any previously identified review issues following the instructions contained within the ST&F IG.

2. The OND Clinical review team, in collaboration with the OB statistical review team and ADBMI, evaluates the clinical safety data submitted in the marketing application and presented in the ST&F package and incorporates appropriate tables and figures into the review.

3. The OND CDS and clinical review teams discuss the need for any custom analyses (e.g., TAGs) targeting potential safety issues identified during the review, and the CDS team generates the custom analyses according to the formatting principles outlined in the ST&F IG.

REFERENCES

- CDER Standard Safety Tables and Figures (Site to be launched in coordination with the publication of this MAPP).
- FDA BIRRS Team site (https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/biomedical-informatics-and-regulatory-review-science-birrs)

EFFECTIVE DATE

- This MAPP is effective upon date of publication.

CHANGE CONTROL TABLE

Effective Date	Revision Number	Revisions
06/13/2025	Initial	N/A