

Enhancing the ASAP Framework with an Interactive R Markdown Application: Seeing is Believing

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Enhance approaches for Aggregate Safety Analysis – FDA Recommendation

FDA's latest guidance in June 2021 on Sponsor Responsibilities for IND Safety Reporting insist on sponsors to document their plan for aggregate safety assessment.

Compliance requires enhanced approaches to meet health authority guidance.

Sponsor Responsibilities— Safety Reporting Requirements and Safety Assessment for IND and Bioavailability/Bioequivalence Studies Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 90 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to <https://www.regulations.gov>. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact (CDER) Paul Gouge, 301-796-2500, or (CBER) Office of Communication, Outreach and Development, 800-835-4709 or 240-402-8010.

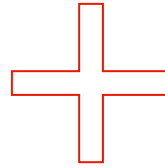
U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

June 2021
Drug Safety

The ASAP is a compound-specific strategic plan that harmonizes the safety surveillance and risk mitigation activities

PSAP

The Program Safety Analysis Plan (PSAP) provides an analytical strategy that will govern the data collection and analysis related to product safety in clinical trials.



PSS

The Product Safety Strategy (PSS) provides a broad descriptive overview of product safety across the product lifecycle. The strategy is inclusive of risk management, safety surveillance, and qualitative benefit risk assessment



ASAP*

Through combining the core functionality of the PSS and the PSAP, implementation of ASAP across clinical development programs will enable end-to-end management of all product safety topics. Our PSAP and PSS implementation efforts provide the building blocks to drive successful adoption of the ASAP across TAs

Adoption of ASAP enhances patient safety

The ASAP is an E2E process that enables teams to establish and access a product's safety profile with greater efficiency and enhance the identification of *unanticipated or rare* safety issues through leveraging aggregate safety data

Current State

No standardized approach to enable **early** integration of compound data across large, complex studies

Limited and varied access to pooled safety data across functions

Enhanced processes needed to support cross-functional SMT decision making

Inconsistency may drive differences in safety data collection, analysis, and presentation



Future State

Facilitates pro-active signal detection and reporting through systematic and standardized collection, analysis, and presentation of aggregate safety data

New tools to provide on-demand access to pooled safety data for cross-functional groups and accelerated response to HA queries

Structured processes enhance speed and precision of SMT decision making

Consistent product safety strategies to allow for harmonized surveillance and data analysis

Evolution of the ASAP

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Reimagining safety assessment process

Shift from statistical testing and confirming to learning and medical decision making within a quantitative framework

Key Aspects

- Earlier implementation
- Interdisciplinary involvement
- *Safety Topic of Interest*
- Adaptive nature
- Regulatory alignment

Impact

- Improved safety signal detection
- Enhance risk management
- Informed decision making

Challenges & Opportunities

Reporting involves enormous amounts of data, and keeps growing every day

- Large volume of static output becomes onerous
- Typical AE output is difficult to 'weed' through – multiple versions for subsets (e.g. AEs, SAEs, TEAEs, AESI etc.)

Resourcing needs may increase over the lifecycle due to the amount of data and output reviewed at the SMT

Can we gain efficiency, standardize and improve?

- Consistent data collection across studies in a program
 - ASAP template based upon standards
- Interdisciplinary and interactive approaches to safety data evaluation
- Enhanced systematic safety assessments combining quantitative and qualitative approaches

- Working group of key players (clinical, safety, programming, statistics, data management, project management)
- Develop output specifications document
 - What are we summarizing, what data is needed, what output is to be developed = requirements document + specifications document
- Design pooling algorithm(s): Living algorithms that change over time
- Pilot, Enhance and Maintain
 - Gather specifications (output, data needs)
 - Pilot initial set of output within R Markdown (very output centric)
 - R expert(s) develop the tool, validation through statistics and programming
 - Gather input into needs of the 'document' aspect of R Markdown
 - Demo the tool, provide continuous support – periodic checks for additional requirements

Demo



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Thank You