Paper PP 27

Signal First: A Data-Driven Approach to Safety Prioritization Using SAS and Tableau

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1. ABSTRACT

In a transforming clinical research environment, resilient safety oversight requires both automation and precision. This paper presents a scalable framework that combines SAS and Tableau to prioritize safety signals in early-phase trials. SAS applies configurable rules—including Grade ≥3 AEs, SAEs, AESIs, lab shifts, and dose interruptions—to assign risk scores. These scores are visualized in interactive Tableau dashboards featuring AE timelines, lab shift plots, boxplots, and cross-domain views (AE, CM, VS, Dose, ECG). Each signal is linked to tailored plots, enabling reviewers to focus on high-risk subjects, patterns, and timepoints. By integrating robust analytics with visual intelligence, this system transforms static listings into proactive, scalable safety monitoring—delivering resilience and innovation in a changing world.

2. INTRODUCTION / BACKGROUND

Clinical research has evolved significantly over recent decades, driven by high-volume, multi-source data streams—from EDC systems and wearables to laboratory results—necessitating more sophisticated safety oversight in early-phase trials. Traditional static listings often hinder prompt detection of safety signals and fail to scale effectively across complex datasets (*Grindley, 2023; Quanticate, 2025*).

Pharmacovigilance extends beyond post-marketing activities; regulatory guidelines such as FDA 21 CFR 312 emphasize systematic, timely monitoring of safety data within pre-marketing stages (*Soterius, 2025*). Without real-time, data-driven methodologies, emerging safety issues—such as unexpected lab shifts or clustered AEs—may be overlooked until critical stages (*Soterius, 2025; Digi, 2025*).

SAS offers a validated environment for safety signal detection using rule-based scoring, standardizing datasets via CDISC SDTM/ADaM, and implementing disproportionality analyses for scalable signal identification (*Jha et al., 2025; Brinsfield & Olaleye, 2008*). Tableau and other visualization tools (e.g., Spotfire, R packages) enable interactive dashboards for real-time filtering, cross-domain exploration, and proactive insight generation (*Cloudbyz, 2023; Cougnaud et al., 2024; Effective Statistician, 2020*). This integrated approach converts manual reviews into an automated, scalable workflow, improving both efficiency and decision quality (*Cloudbyz, 2023; Jha et al., 2025*).

3. OBJECTIVES

Automate and prioritize safety signal detection:
Develop a configurable SAS-based rule engine to flag Grade ≥3 AEs, SAEs, AESIs, lab shifts, and dose interruptions, creating a prioritized, risk-scored output for reviewers (*Jha et al., 2025; Brinsfield & Olaleye, 2008*).

Integrate SAS and Tableau for scalable, visual safety monitoring:
Combine automated scoring from SAS with intuitive Tableau dashboards—integrating AE timelines, lab shift plots, boxplots, and cross-domain data visualizations—for real-time, interactive exploration (*Cloudbyz, 2023; Cougnaud et al., 2024*).

Enable proactive decision-making:
Equip stakeholders with timely, drill-down-enabled visualizations that highlight high-risk subjects and emerging patterns, enabling early interventions and informed safety decisions (*Quanticate, 2025; Effective Statistician, 2020*).

4. METHODOLOGY

4.1 Data Sources

Safety signal detection leveraged multiple clinical domains for comprehensive oversight:

- Adverse Events (AE) – severity grading, seriousness, AESI identification
- Concomitant Medications (CM) – medication patterns and administration routes
- Vital Signs (VS) – heart rate, blood pressure, temperature
- Dosing Records (Dose) – interruptions and deviations
- Electrocardiogram (ECG) – QTc prolongation and abnormalities
- Laboratory Data (LAB) – clinically significant shifts in key parameters
  (Jha et al., 2025; Digi, 2025; Soterius, 2025)

4.2 SAS Framework

A rule-based scoring system was implemented in SAS to quantify subject-level risk. Each rule assigns weighted points based on clinical significance:

Risk Score Components

- Grade3_AE_Score
  Condition: Any AE with Grade ≥ 3
  Formula: Score = (Count of Grade ≥ 3 AEs) × 2
  Weight: 2 points per event
  (Jha et al., 2025)
- Serious_AE_Score
  Condition: AE marked as Serious = Yes
  Formula: Score = (Count of Serious AEs) × 3
  Weight: 3 points per event
  (Brinsfield & Olaleye, 2008)
- AESI_Score
  Condition: AE term matches AESI keyword
  Formula: Score = (Count of AESI AEs) × 2
  Weight: 2 points per event
  (Digi, 2025)
- LabShift_Score
  Condition: Clinically significant lab/vital shift (e.g., HR > 120 bpm, BP > 180/100, Temp

> 39 °C)
Formula: Score = (Count of abnormal shifts) × 1
Weight: 1 point per event
(Soterius, 2025)

- DoseInterrupt_Score
  Condition: Dose interruption = Yes
  Formula: Score = (Count of interruptions) × 2
  Weight: 2 points per event
  (Jha et al., 2025)

- ECG_Score
  Condition: QTc > 500 ms or other ECG abnormality
  Formula: Score = (Count of abnormal ECGs) × 2
  Weight: 2 points per event
  (Cougnaud et al., 2024)

- Total_Risk_Score
  Formula:
  Total_Risk_Score = Grade3_AE_Score + Serious_AE_Score + AESI_Score + LabShift_Score + DoseInterrupt_Score + ECG_Score

4.3 SAS Implementation

Import domain datasets (AE, CM, VS, Dose, ECG & LAB) from Excel

- Apply safety rules and calculate risk scores per subject
- Summarize and export RiskSummary.csv for Tableau visualization
  (Brinsfield & Olaleye, 2008; Jha et al., 2025)

4.4 Tableau Dashboards

Risk scores and clinical signals were visualized through interactive dashboards:

- AE Timelines – temporal patterns of adverse events
- Lab Shift Plots & Boxplots – distribution and outliers
- Cross-Domain Views – integrated AE, CM, VS, Dose, ECG for holistic review
  (Cloudbyz, 2023; Quanticate, 2025; Cougnaud et al., 2024)

4.5 Concomitant Medication (CM) Risk – Configurable

Although CM risk was excluded from the Total_Risk_Score, it was calculated for cross-domain insights:

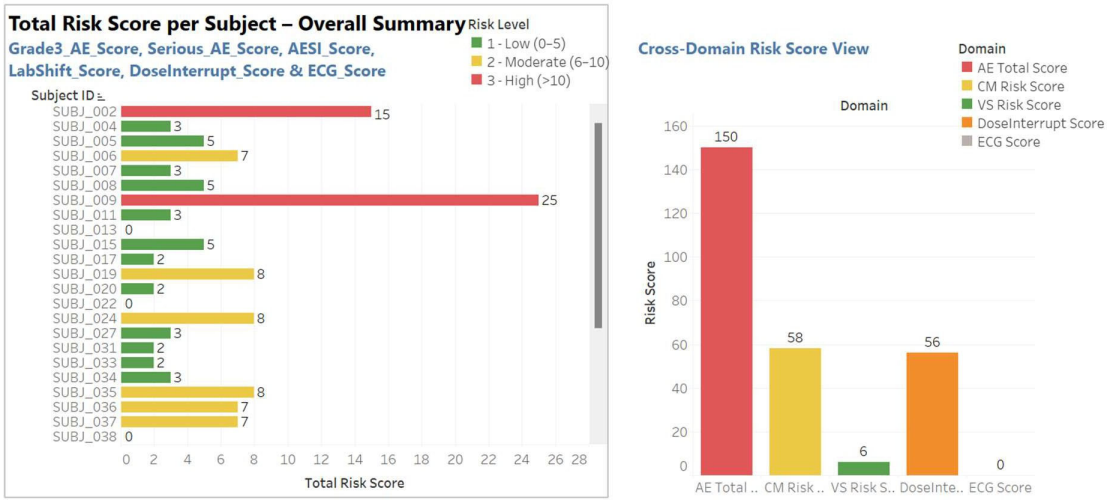
- High-Dose Events: ≥ 90th percentile dose → +2 points
- IV Route Events: Any IV administration → +2 points
- Polypharmacy Pressure: Distinct meds > 3 → +1 point per excess
  CM_Risk_Score = (HighDoseEvents × 2) + (IVEvents × 2) + (max(DistinctMeds − 3, 0) × 1)

5. RESULTS / VISUALS

Dynamic Visualizations for Risk Assessment and Pattern Recognition

To enable rapid identification of safety signals and cross-domain trends, we developed interactive Tableau dashboards that integrate multiple visual components. These dynamic visualizations provide a holistic view of adverse events (AEs), laboratory shifts, and cumulative risk scores across the study population.

Visual 1.1



5.1. Total Risk Score per Subject – Overall Summary – Visual 1.1

The visualization aggregates multiple safety components into a Total Risk Score for each subject, including:

- Grade 3 AE Score
- Serious AE Score
- AESI Score
- Lab Shift Score
- Dose Interrupt Score
- ECG Score

Each subject's cumulative score is displayed as a horizontal bar, color-coded by risk level:

- Green: Low (1–5)
- Yellow: Moderate (6–10)
- Red: High (> 10)

Insights:

- Subject SUBJ_009 has the highest risk score (25), followed by SUBJ_002 (15), both in the high-risk category.

Reviewer Benefit:

- Prioritization: Immediately identify high-risk subjects for detailed evaluation.
- Efficiency: Consolidates multiple safety domains into a single metric, reducing manual effort.
- Transparency: Provides clear thresholds for risk categorization, aiding regulatory decision-making.

5.2. Cross-Domain Risk Score View – Visual 1.1

This bar chart summarizes cumulative risk contributions across domains:

- AE Total Score: 150 (dominant contributor)
- CM Risk Score: 58
- Dose Interrupt Score: 56
- VS Risk Score: 6
- ECG Score: Minimal contribution

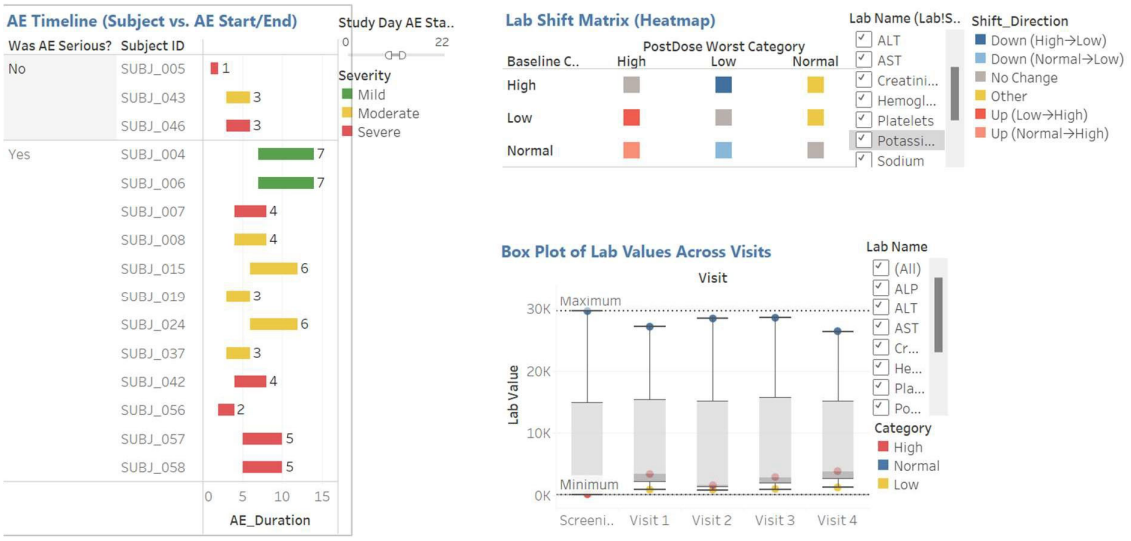
Insights:

- Adverse Events (AE) are the primary driver of overall risk, followed by Concomitant Medications (CM) and Dose Interruptions.
- Vital Signs (VS) and ECG show negligible impact, suggesting lower associated safety concerns.

Reviewer Benefit:

- Domain-Level Focus: Allocate resources to domains with the highest risk impact.
- Pattern Recognition: Highlight systemic issues (e.g., AE-dominated risk).
- Strategic Decision-Making: Supports targeted investigations and mitigation strategies.

Visual 1.2



5.3 AE Timeline (Subject vs. AE Start/End) –Visual 1.2

This visualization plots AE duration for each subject, categorized by seriousness and severity:

- Severity: Mild, Moderate, Severe (color-coded)
- Seriousness: Yes/No grouping
- Duration: Represented by bar length (study days)

Insights:
Subjects with serious AEs show distinct patterns in both duration and severity:

- SUBJ_004 and SUBJ_006 experienced Mild severity AEs lasting 7 days, indicating prolonged but less severe impact.
- SUBJ_015 and SUBJ_024 had Moderate severity AEs with durations of 6 days, suggesting higher clinical concern despite slightly shorter duration.
- SUBJ_057 and SUBJ_058 exhibited Severe AEs lasting 5 days, highlighting acute but intense safety events that require immediate attention.
  Non-serious AEs generally cluster around shorter durations, but span Mild to Severe severity, indicating that even non-serious events can present significant variability in intensity.

Reviewer Benefit:
These dynamic AE timelines provide critical insights for safety evaluation by enabling:

- Pattern Recognition: Severity does not always correlate with duration—shorter events can still be severe, while mild events may persist longer.
- Risk Stratification: Quickly identify and prioritize subjects with severe or prolonged AEs for deeper investigation.
- Temporal Context: Clarify AE onset and persistence, supporting linkage to dosing schedules or other interventions.
- Integrated Assessment: Correlate AE patterns with lab shifts and cumulative risk scores for a holistic safety view.

5.4 Box Plot of Lab Values Across Visits – Visual 1.2

The box plot displays lab value distributions across visits (Screening, Visit 1–4), showing:

- Median, IQR, and Outliers
- Category Color Coding: High, Normal, Low

Insights:

- Stable medians across visits suggest overall consistency.
- Outliers indicate subjects requiring closer monitoring.
- Shifts toward High or Low categories across visits may reveal emerging safety signals.

Reviewer Benefit:

- Trend Analysis: Detect longitudinal changes in lab values.

- Outlier Detection: Identify subjects deviating from normal ranges.
- Risk Correlation: Link abnormal lab trends with AE timelines and risk scores.

5.5 Lab Shift Matrix (Heatmap) – Visual 1.2

This heatmap compares baseline vs. post-dose worst category for key lab parameters (ALT, AST, Creatinine, Hemoglobin, Platelets, Potassium, Sodium):

- Shift Directions: Up (Low → High; Normal → High), Down (High → Low; High → Normal), No Change, Other
- Color Coding: Indicates direction and severity of shift

Insights:

- Upward shifts in ALT/AST may indicate hepatic concerns.
- Downward shifts in platelets or hemoglobin could signal hematologic risks.

Reviewer Benefit:

- Rapid Detection: Quickly spot clinically significant lab changes.
- Integrated View: Correlate lab shifts with AE timelines and risk scores.
- Decision Support: Prioritize subjects for further investigation based on combined signals.

5.6 Overall Impact

These dynamic Tableau visualizations transform raw data into actionable insights by:

- Enabling quick pattern recognition across subjects and domains.
- Integrating multi-domain safety signals for holistic risk assessment.
- Improving reviewer efficiency, reducing manual interpretation time, and enhancing decision-making accuracy.

6. DISCUSSION

Highlighting Reviewer Capabilities: Identifying High-Risk Subjects and Timepoints

The integration of dynamic visualizations with risk scoring enables reviewers to move beyond static listings and adopt a proactive approach to safety oversight. By leveraging interactive dashboards:

- High-Risk Subject Identification: Instantly pinpoint subjects with elevated cumulative risk scores (e.g., > 10), as well as those exhibiting severe or prolonged AEs.
- Critical Timepoint Detection: AE timelines and lab trend visualizations identify periods of heightened vulnerability, such as clusters of severe AEs or significant lab shifts post-dose.
- Cross-Domain Correlation: Combining AE, lab, and ECG data in a unified view supports comprehensive signal detection, reducing the likelihood of missed safety concerns.

Benefits of Combining Analytics and Visualization:

- Holistic Safety Assessment: Analytics quantify risk; visualization contextualizes it, enabling intuitive interpretation of complex data.
- Rapid Signal Detection: Heatmaps, timelines, and box plots convert raw data into actionable insights, accelerating decisions.
- Enhanced Communication: Visual summaries facilitate clear, transparent discussions among clinical teams and regulatory bodies.

Scalability Across Studies and Therapeutic Areas: The framework is study-agnostic, allowing:

- Adaptability: Applicable across early-phase and late-phase trials, regardless of therapeutic area.
- Consistency: Standardized risk scoring and visualization templates ensure uniform safety monitoring across programs.
- Efficiency: Reduces manual effort in generating listings and supports real-time updates as new data become available.

Reviewer Efficiency and Signal Traceability:

- Efficiency Gains: Interactive dashboards minimize time spent navigating static tables, enabling focus on interpretation rather than data extraction.
- Traceability: Drill-down capabilities allow reviewers to trace signals back to individual subjects, events, and timepoints, ensuring transparency and audit readiness.
- Prioritization: Facilitates targeted review of high-risk subjects and domains, optimizing resource allocation.

7. CONCLUSION

Summary of Impact

This approach transforms traditional static listings into dynamic, integrated safety oversight tools, enabling:

- Faster pattern recognition across subjects and domains.
- Improved risk stratification for timely interventions.
- Comprehensive signal detection, reducing missed safety concerns.

Future Directions

- Expansion to Later-Phase Trials: Scaling the framework to Phase III and post-marketing studies for broader applicability.
- Integration of Machine Learning Models: Incorporating predictive analytics to anticipate emerging safety signals and automate risk scoring.
- Real-Time Monitoring: Leveraging live data feeds for continuous safety surveillance and adaptive decision-making.

8. REFERENCES

- Brinsfield, E., & Olaleye, D. (2008). *Automated Drug Safety Signal Detection with Guided Analysis*. SAS Institute. https://www.lexjansen.com/pharmasug/2008/sas/SA12.pdf
- Cloudbyz. (2023, March 27). *Leveraging Tableau for Real-Time Signal Management Solution for Drug Safety and Efficacy*. https://www.cloudbyz.com/resources/pharmacovigilance/leveraging-tableau-for-real-time-signal-management-solution-for-drug-safety-and-efficacy/
- Cougnaud, L., Faes, M., Van Krunckelsven, D., et al. (2024, July 10). *Interactive medical and safety monitoring in clinical trials with clinDataReview: a validated and open source reporting tool*. *Frontiers in Medicine*. https://doi.org/10.3389/fmed.2024.1356323
- Digi. (2025, April 28). *Safety Signal Detection in Pharmacovigilance: Comprehensive Methods and Best Practices*. https://www.clinicalstudies.in/safety-signal-detection-in-pharmacovigilance-comprehensive-methods-and-best-practices/
- Effective Statistician (Schacht, A.). (2020). *The Future of Safety Analyses: Interactivity, Visualizations and the FDA*. https://theeffectivestatistician.com/the-future-of-safety-analyses-interactivity-visualizations-and-the-fda/
- Grindley, D. (2023, February 23). *Adopting Data Analytics and Visualizations to Ensure Patient Safety and Improve Data Quality*. *Contract Pharma*. https://www.contractpharma.com/exclusives/adopting-data-analytics-and-visualizations-to-ensure-patient-safety-and-improve-data-quality/
- Jha, S. K. (2025, November). *SAS in pharmacovigilance and clinical trial safety analysis*. *International Journal of Advance Research Publication Review*, 2(11). https://ijarpr.com/uploads/V2ISSUE11/IJARPR0886.pdf
- Quanticate. (2025, April 29). *The Role of Clinical Trial Data Visualisation in Modern Drug Development*. https://www.quanticate.com/blog/clinical-trial-data-visualisation
- Soterius. (2025, July 12). *Early Signal Detection in Clinical Drug Trials*. https://soterius.com/blogs/signal-detection-in-early-phase-clinical-drug-trials/

9. CONTACT INFORMATION

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