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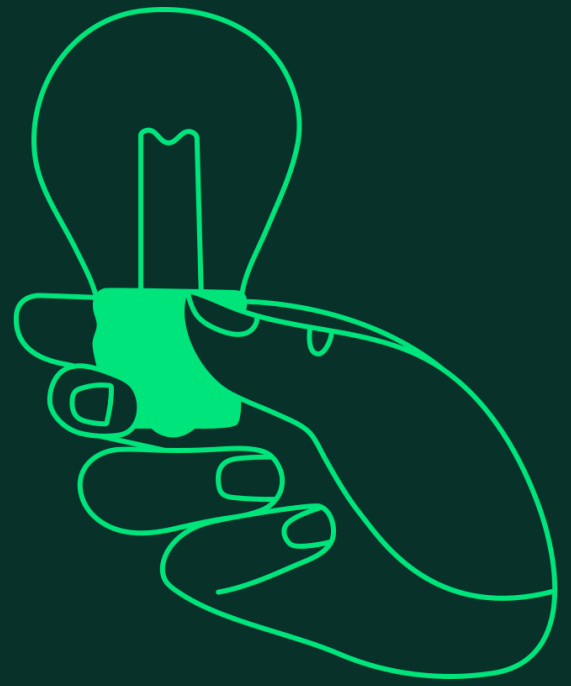
Quantitative Evolution of Drug Safety: Adapting Inventions to Innovations



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On Behalf of
PSI/EFSPI Benefit Risk SIG: Safety Implementation WG

Life forward

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Current Practices in Safety Analyses and Reporting in drug development

Practice	Primary Purpose	Typical Use	How Routine Today
Static Tables, Listings & Narratives (TLFs)	Regulatory-compliant safety reporting (AEs, SAEs, labs, vitals, ECGs)	CSRs, DSURs/PSURs, IB updates, DSMB packages	Universal / Standard of Care
Cumulative AE & SAE Line Listings	Ongoing medical review of individual cases	Routine safety physician review during trial conduct	Universal / Very Frequent
Aggregate AE Summary Tables (by SOC/PT, severity, seriousness)	Identify overall safety patterns	Regular internal reviews; all submissions	Universal / Very Frequent
Lab/Vitals/ECG Shift Tables & Outlier Listings	Detect clinically relevant abnormalities	Periodic safety review and reporting	Universal / Frequent
Patient Profiles (static PDFs)	Case-level deep dives	Triggered reviews, DSMB discussions	Very Common

Current Practices in Safety Analyses and Reporting in drug development (2)

Practice	Primary Purpose	Typical Use	How Routine Today
Interactive Safety Dashboards (e.g., JReview, Spotfire, R Shiny apps)	Faster internal signal exploration & drill-down	Internal safety team workflows	Moderate (Large Pharma), Limited (Biotech), Lack of standard
Cross-Trial / Program-Level Safety Aggregation	Understand evolving program safety profile	IB updates, late-phase programs	Common (Manual), Limited (Automated)
Simple Trend Visualizations (rates over time, forest plots)	Support interpretation of tables	Internal reviews, slides	Common
Bayesian / Statistical Signal Detection (e.g., blinded monitoring)	Earlier detection of unexpected risks	Select programs, expert teams	Occasional / Pilot
Predictive Safety Modeling (ML, simulations)	Forecast risk for new doses/indications	Exploratory decision support	Rare / Experimental

Why does so many safety inventions struggle with adoption and scalability?

Not due to regulatory objections

- There have been ongoing shift in regulatory expectations

- *21 CFR 312.32 & 2025 FDA Final Guidance* on Safety Reporting emphasize aggregate safety data analysis during trials (beyond individual case reports) to detect clinically significant increases in serious adverse events, with formal Safety Surveillance Plans

- Recently FDA launched “Real time clinical trial” initiative also aimed at improving safety monitoring among other objectives.

- Regulators have been open to consider quantitative safety analyses (in conjunction with clinical judgement and holistic evidence review) for decision making (FDA Draft Guidance on Bayesian Methods 2026)

Not due to lack of inventions

Original Articles

Bayesian Hierarchical Modeling for Detecting Safety Signals in Clinical Trials

H. Amy Xia, Haijun Ma & Bradley P. Carlin

Pages 1006

Cite this

Full Artic

Abstra

Main Paper

Bayesian methods for design and analysis of safety

Karen L. Price,
James D. Stam

First published

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MAIN PAPER

Bayesian detection of potential risk using in safety data

Saurabh Mukhopadhyay, Brian Waterhouse, Alan Hartford

First published: 30 August 2018 | https://doi.org/10.1002/pst.1898 |

Read the full text ›

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Cardinal

A Harmonized Catalog of Pharmaceutical Tables, Listings, and Graphs

teal.modules.bsafe 0.1.0 Reference Changelog Versions

B-SAFE Shiny Module

Check no status | Docs passing | Test Coverage 82.99% | repo status Active

Installation

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Why:

To formulate a strategic path with specific actions to take and to avoid for effective and efficient conversion of Safety Inventions to Innovations

What:

We deep dived into three independent Safety Innovations to understand how they were developed, what worked in favor of adoption and what were some of the learnings

How:

We met regularly over the course of ~6 months to first introduce the innovation to the group and then collected detailed information on key aspects and summarized findings and recommendations

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Team: SAFE Innovators

- Dooti Roy, Boehringer Ingelheim (Sub-team Lead)
- Benjamin Knoeferl, Boehringer Ingelheim
- Brian Waterhouse, Merck
- Arnab Sarkar (ex-Sanofi)
- Christian Conrad, (Sanofi)
- William Koetse (AbbVie)
- Greg Ball (Independent Consultant)

Focus

Use Case	Company	Innovation	Purpose	Statistical Framework
BDRIBS	AbbVie	Blinded Bayesian signal detection; interactive R/Shiny tool	Detect risk without unblinding trials	Bayesian relative risk (Poisson → Binomial, posterior on risk ratio)
B-Safe	Boehringer Ingelheim	Bayesian historical borrowing; open-source R/Shiny app	Improve estimation precision especially for rare events	Robust MAP priors, binomial & Poisson likelihoods (incidence proportion and exposure adjusted AE rates)
3S	Sanofi	Aggregated safety surveillance framework; evidence synthesis	Program-level safety risk assessment	Bayesian hierarchical MAC model combining blinded/unblinded + historical data

Aspects of Consideration

Novel Approach

Description of the innovative method

Value Proposition

Benefits and advantages

Scope – when is it most helpful

Development Process

Stakeholders mapping

Timeline and milestones

Collaboration efforts

Target user buy-in

Sponsorship and funding

Infrastructure requirements

Upskilling needs

Product launch and storytelling

Prioritized Rollout plan

Support and Maintenance

Champion(s)

Opensource availability

Reception

Feedback from early adopters and ambassadors

Success stories and impact assessment

Barriers to Adoption

Challenges faced during implementation

Lessons learned and best practices

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Success Model for Adoption of Quantitative Safety Innovations

Barriers to scalability and adoption

User understanding

Unclear end-user need and value proposition

Weak connection to day-to-day workflows

Limited onboarding creates mistrust of advanced methods

Scaling challenges

Pilot success does not translate into routine practice

Infrastructure and standards are insufficient

No dependable maintenance or support model

Ownership gaps

Adoption depends too heavily on one champion

Broader cross-functional ownership is missing

Governance for long-term adoption is unclear

Breaking Silos

PHUSE Safety Analytics WG, PSI Safety Methodology Implementation WG and ASA BIOP Safety WG are collaborating!

Goal:

Co-creation of standard tools and methods together with Safety Clinicians, Knowledge share, and create systematic impact

Two Initiatives:

- Interactive Safety Visualization for ongoing safety monitoring (contact: Dooti Roy)
- Aggregate Safety Analyses and Reporting (contact: Matthias Trampisch)

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Final Thoughts

- In current safety analyses and reporting practice, advanced quantitative approaches are not fully leveraged.
- Despite availability of multiple scientific methods and tools which could enhance safety monitoring, signal detection and safety reporting, broad adoption of these safety inventions remain low.
- Adoption succeeded where innovation combined rigorous methods with usability, stakeholder buy-in, workflow integration, and organizational support.
- Key barriers to successful at scale adoption are lack of user understanding, scaling challenges and ownership gaps.
- There are ongoing initiatives which aim to bring users closer to the inventors to co-create solutions across the industry and regulatory landscape.

References

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Thank *you* for listening!

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