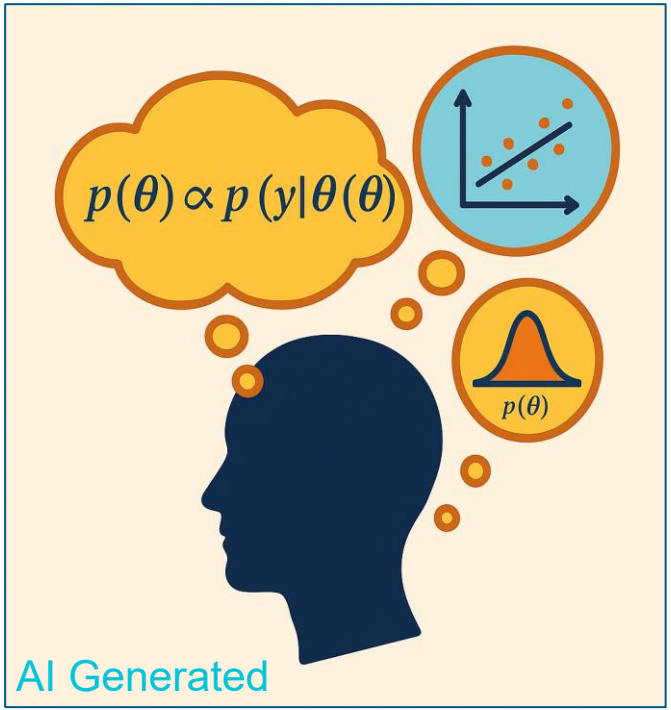
Implementing Innovative Safety Evaluation Methods:

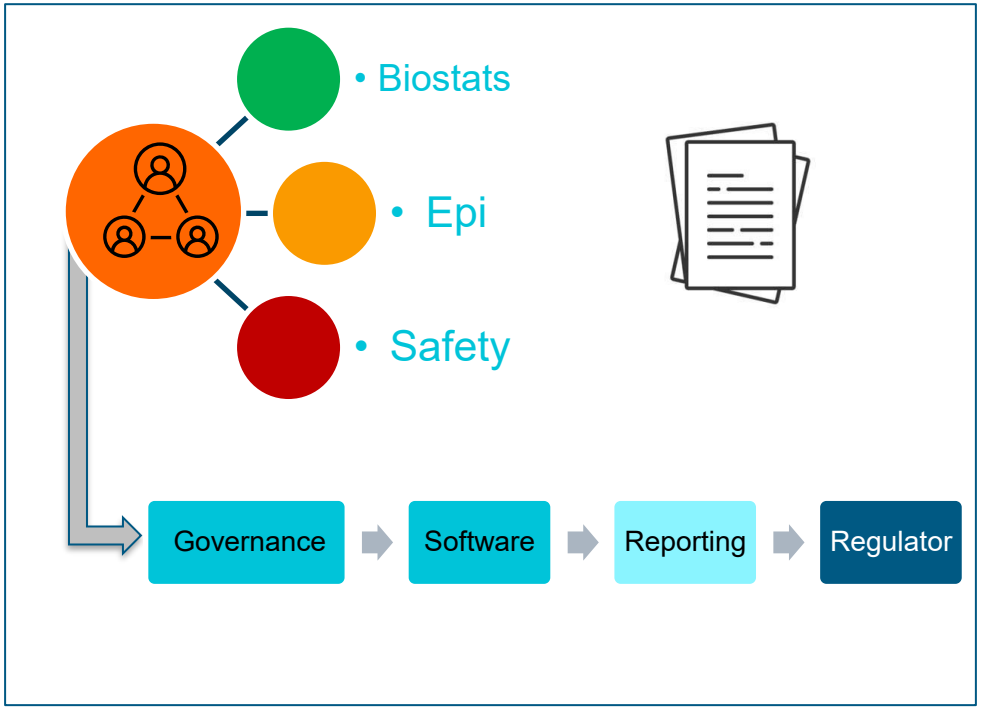
Overcoming challenges and sharing successes

Naomi Givens, PSI Conference 2025

In collaboration with Dooti Roy & the Safety Implementation Working Group

Exciting New Methodology for Safety Data – now what?





"We are a community dedicated to leading and promoting the use of statistics within the healthcare industry for the benefit of patients."

Safety Implementation Working Group

Within existing Benefit Risk SIG

Promoting Statistical Insight

janssen | PHARMACEUTICAL COMPANIES OF Johnson & Johnson

MERCK

ucb

CSL Seqirus

Cytel

SANOFI

GSK

POLARIS DATA LABS

Boehringer Ingelheim

WILDFELL SOFTWARE LLC

ASAP PROCESS CONSULTING

Pfizer

Brainstorming Kick-Off Meeting(s)

Promoting Statistical Insight

People and Culture

Industry Guidance & Regulatory requirements

Background Rates & Decision Rules

Tools and Packages

Cross Association Collaboration

Table 7. Deaths, Safety Population, Pooled Analyses[1]

Deaths	Drug Name Dosage X N = XXX n (%)	Drug Name Dosage Y N = XXX n (%)	Active Control N = XXX n (%)	Placebo N = XXX n (%)	Risk Difference (%) (95% CI)[2]
Total deaths	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**X (Y, Z)**
Cause of death 1	n (%)	n (%)	n (%)	n (%)	X (Y, Z)
Cause of death 2	n (%)	n (%)	n (%)	n (%)	X (Y, Z)
Treatment-emergent deaths[3]	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**X (Y, Z)**
Cause of death 1	n (%)	n (%)	n (%)	n (%)	X (Y, Z)
Cause of death 2	n (%)	n (%)	n (%)	n (%)	X (Y, Z)
Nontreatment-emergent deaths[4]	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**X (Y, Z)**
Cause of death 1	n (%)	n (%)	n (%)	n (%)	X (Y, Z)
Cause of death 2	n (%)	n (%)	n (%)	n (%)	X (Y, Z)
Cause of death 3	n (%)	n (%)	n (%)	n (%)	X (Y, Z)

Source: [include Applicant source, datasets and/or software tools used].
[1] Duration = [e.g., X week double-blind treatment period or median and a range indicating pooled trial durations].
[2] Difference is shown between [treatment arms] (e.g., difference is shown between Drug Name dosage X vs. placebo).
[3] Treatment-emergent AE defined as [definition], MedDRA version X.
[4] Defined as [(e.g., deaths beyond the protocol-defined treatment-emergent adverse event period in the same trial or deaths from other trials with drug)].
Abbreviations: AE, adverse event; MedDRA, Medical Dictionary for Regulatory Activities; N, number of patients in treatment arm; n, number of patients with adverse event

Templates & code for ISS

Consolidation of Brainstorming

2025 Focus

Successful adoption - considerations beyond the science

- How to get new methodology and process improvements adopted in companies
- Best practice for 'getting to yes', including senior stakeholder management, engaging developers and end-users
- Successful adoption pathways

Aggregate safety process - how to operationalise?

- Share experiences of and develop guidance for the implementation of aggregate safety review and reporting to FDA

Consolidation of Brainstorming

Beyond 2025

Operationalising ISS reporting	• Share experiences of ISS reporting, develop an ISS template
Background rate generation - benefits and pitfalls	• Partner with Epidemiology colleagues to educate on contextualisation of data to get to a suitable background rate • Promote the use of the statistician skillset to generate operating characteristics and sensitivity analyses
Use of tools/ visualisations - for us and our colleagues	• Share tools companies have developed and encourage release of them as open-source packages • Share experience of 'interactive' tool being used in a submission
Safety estimands	• Efficacy estimands are well established and should also be applied to key safety endpoints but is it happening? • Share knowledge/experiences
Safety speak	• Can we speak a common language across disciplines, Safety, Epi and Biostats? How can we influence/advocate

Turning Safety Inventions → Innovations

- **Motivated by observation** that although a multitude of novel methodologies are being published in safety, broad scale adoption remains low and tenacious.
- **Goal is to create a comprehensive guide** by the end of 2025 which acts as a North Star for inventors and ultimately contributes to more successful innovations
- **Deep dive into the life-cycle of selected novel safety inventions**, focusing on product development, value proposition, reception, barriers to uptake and learnings
- **Bring community awareness across regions** (EU/US) and drive communal uptake of safety focused inventions. Right science at the right time.
- **Workstream:** Dooti Roy (Lead), Arnab Sarkar, Brian Waterhouse, Benjamin Knoeferl, Michael Colopy

Operationalising the FDA Final Rule: compliance on anticipated events in clinical trials

2025 Goal

- Review case studies on aggregate safety reporting process implementation
- Develop process maps and guidance on roles/responsibilities and outsourcing
- Share best practice and tools

Current Status & Next Steps

- Initial proposal drafted & key contributors identified
- Key topics and deliverables outlined
- Begin case study collection and analysis
- Draft initial process map and roles and responsiblities chart

Workstream: Matthias Trampisch (Lead), Marianna Grinberg, Barbara Hendrickson, Greg Ball

Working Group Members

Co-Leads: **Naomi Givens and Dooti Roy**

Workstream Leads: Dooti Roy (Invention to Innovation)

Matthias Trampisch (Operationalising the FDA Final Rule)

Working Group Members:

Greg Ball	Glen Colopy
Mike Colopy	Mac Gordon
Marianna Grinberg	Jackie Hee
Barbara Hendrickson	Leah Isakov
Benjamin Knoeferl	Rosanne Lane
Florence Le Maulf	Serene Jiang
Kevin Roberts	Arnab Sarkar
Brian Waterhouse	

Summary

- We have formed group of statisticians and safety scientists with a broad range of experience to share best practice and develop guidance for the implementation of novel methodologies in safety assessment and evaluation.
- We have a goal to improve the conversion rate of inventions to innovations, ultimately benefiting patients.
- If you have enthusiasm for the subject and some time that you can dedicate to the working group **don't hesitate to get in touch!**