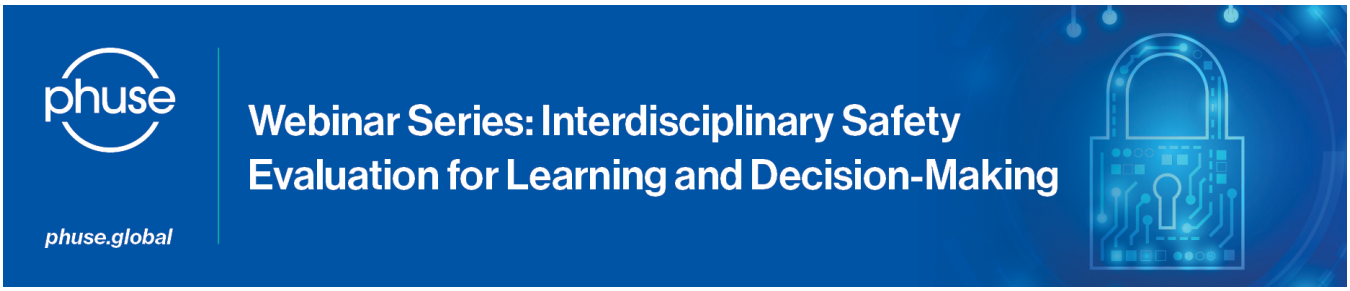
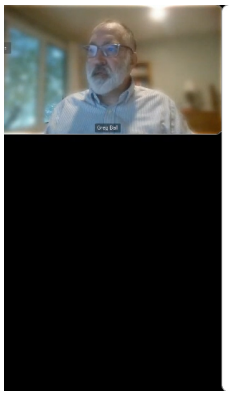
Safety Analytics Webinar Series: Overall Safety Assessment – Interactive Safety Graphics for Regulatory Decision-Making



Catch up Here!

This Webinar took place 4 October. Catch up by viewing the recording or reading the slides.



Webinar Series: Interdisciplinary Safety Evaluation for Learning and Decisionmaking

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To meet the spirit of the IND safety reporting final rule, sponsors have developed processes and procedures to evaluate, assess and act on accumulating safety information during development on an ongoing basis.

Co-promoted by ASA Biopharm, DIA Communities, and PHUSE

Webinar Series: Interdisciplinary Safety Evaluation for Learning and Decisionmaking

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Webinar 4: Overall Safety Assessment – Interactive Safety Graphics for Regulatory Decision-Making

Summary:

This webinar examined the use of graphical approaches to evaluate clinical trial safety data, with an emphasis on new developments in interactive graphical approaches. Mat Soukup (FDA) discussed past efforts to move from tabular summaries and line listings of safety data to graphic representations – efforts made possible through a collaboration of academia, industry, and regulatory parties and hosted on CTSpedia. Steve Mallett (Veramed) summarised some of the unique challenges in safety data analysis, highlighting how standards and tools for visualising safety data have evolved in recent years, and discussed future trends with a focus on collaboration across industry, regulators and academia. Jeremy Wildfire (Gilead) presented on his experience developing the safetyGraphics R package, a collaboration involving members from over 15 organisations, including pharmaceutical companies, academia and the FDA. Finally, the panel discussed next steps for making open-source tools a standard part of the clinical trial workflow.

The audience also asked the following questions during the webinar:

Questions	Answers
Can you suggest any references or books for R Shiny?	It depends on what you're looking for, but pretty much anything by Hadley Wickham is good. Several are linked from his home page: https://hadley.nz/. His new Shiny book is definitely worth checking out also: https://mastering-shiny.org/.
Is it possible to create interactive graphics in SAS?	Some limited interactivity is likely to be possible using base SAS; more is available in JMP. (Link to Zak's 2019 PHUSE webinar on interactive graphs in submissions, in case not already provided in Jeremy's talk: https://www.youtube.com/watch?v=u26-A2NTj2k.)
Do you have any R class recommendations for a clinician who does safety monitoring?	There are lots of online resources for learning R (e.g. https://www.datacamp.com/). DIA has also sponsored workshops specifically for clinicians interested in safety graphics, so keep an eye on their upcoming conferences.
What kind of software do you recommend for developing an interactive safety analytic tool?	We'd generally recommend starting with R Shiny. The FDA Statistical Software Clarifying Statement states that the FDA does not require use of any specific software for statistical analysis: https://www.fda.gov/media/161196/download.
Do I have to be aware of any (privacy) measures if I use a publicly available tool (eDISH plot) for a specific clinical trial data?	This FAQ covers the basics of this topic. For more details, contact your organisation's IT department.
Where can I find previous webinar recordings?	All previous recordings and slides are linked here.
The examples are of single studies. Can you comment on the challenges of visualising pooled study data, e.g. a volcano plot?	Visualisation of pooled safety data should consider appropriate statistical methods to account for differences between studies, e.g. meta-analysis methods. Otherwise, naively pooled data can show paradoxical results, i.e. pooled data shows a trend in the opposite direction to the individual studies (see Simpson's paradox). For example, the statistical analysis used to produce the volcano plot should include the study as a covariate in the model.
Are there any papers or resources to learn more about the upset plot and volcano plot, etc.?	More information on the upset plot can be found here and here. The interactive volcano plot shown in the presentation (based on a hierarchical Bayesian model) was produced using JMP software. Unfortunately, this isn't open-source software to my knowledge.
where can one get the dataset? I would like to try and produce some volcano graphs using SAS.	The dataset for the specific volcano plot in the presentation isn't available. But you should be able to produce a basic volcano plot in SAS by conducting a number of different statistical analyses (e.g. differences in AE incidence between treatment groups by the MedDRA body system) and producing a scatter plot with the magnitude of the treatment effect (e.g. treatment difference) on the horizontal axis and the strength of the evidence (e.g. log of the p-value) on the vertical axis.
Please also add the link that Jeremy had for the available data from Lilly in the summary. Thanks again!	https://github.com/SafetyGraphics/safetyData

Presenter	Bio

Jeremy Wildfire, *Gilead*

Jeremy Wildfire is a data scientist at Gilead and is focused on creating modern tools that improve the analysis pipeline for clinical trials. Jeremy has served as the technical lead for the Interactive Safety Graphics (ISG) sub-team of the ASA Biopharm-DIA Safety Working Group since 2018. The working group is an interdisciplinary effort that seeks to provide a clinical safety workflow for monitoring during clinical development in an open-source model. The ISG team created a workflow to monitor hepatoxicity using the safetyGraphics R package and a well-documented based on the safety clinician's monitoring practice. The working group has recently expanded its focus to include additional safety domains such as adverse events, QT and nephrotoxicity.

Steve Mallett, *Veramed*

Steve Mallett has over 25 years' experience working in the pharmaceutical industry as a statistical programmer and statistician. He has supported many medicine development projects, from early phase through to medical affairs. Steve recently joined Veramed as a senior manager and is also an active member of the PSI special interest group for data visualisation.

Mat Soukup, *FDA/CDER*

Mat Soukup received his PhD in Biostatistics from the University of Virginia in 2004 and joined the FDA/CDER as a statistical reviewer shortly thereafter. In 2010, he joined the Division of Biometrics VII as Team Lead and now serves as Deputy Division Director. In these roles, Mat has contributed and promoted appropriate statistical methodologies for the quantitative assessment of safety across a broad spectrum of topics such as meta-analysis, causal inference, signal detection, statistical graphics, and design of safety outcome trials.

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