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Analyses & Displays for Hepatotoxicity

Description

This project produces two white papers providing recommendations for analyses and displays to assess hepatotoxicity in Phase II to IV clinical trials and integrated submissions.

Stage 1 focuses on a standardised set of analyses and outputs to evaluate whether there is reasonable medical evidence to rule out potential drug-induced liver injury (DILI). Stage 2 addresses situations where DILI cannot be excluded, outlining additional analyses needed to further characterise the safety signal and assess causality.

The project aims to improve consistency, transparency and efficiency in hepatotoxicity evaluation across the industry. As a value add, the team will also develop an open-source Hepatotox tool to support the generation of recommended analyses and outputs for both stages. This will enable practical implementation of the guidance and support more robust and reproducible safety assessments.

Q4 2026

Proposed
End Date

Stage 2 white
paper & updated
Hepatotox tool

Deliverable

Completed the review
and compilation of the
recent assessments of
SBAs where there was a
liver safety concern and
a working draft of the
Stage 2 white paper

Key Achievements
This Quarter:

Stage 2 white paper and
updated Hepatotox tool

Deliverables &
Targets Planned for
the Next Quarter:

Melvin Munsaka
& Terry Walsh

Leads



Project Status: Green
Accepting New Members

- Ongoing review of the draft Stage 2 white paper and R code program updates for the Hepatotox tool

Project Status

Best Practices for Informing Benefit-Risk and Communicating Safety Information

Description

Recent advances in analysing and reporting clinical trial safety data have not yet led to clearer communication of safety profiles in prescribing information. Adverse drug reactions are often presented as simple percentages without sufficient context on timing, exposure, severity, reversibility, background risk, or clinical relevance, limiting informed benefit-risk decision-making.

A landscape review explores drug safety communication, benefit-risk judgement under uncertainty, and decision-making safeguards used in other high-consequence fields. Findings suggest that many communication challenges stem from upstream decision-making issues, including poorly framed questions, hidden assumptions, value judgements, and insufficient challenge. These cannot be addressed through improved presentation alone.

The project aims to enhance how safety information supports benefit-risk decisions by identifying ways to communicate safety findings more clearly, meaningfully, and transparently. It evaluates how safety data are summarised and contextualised to better reflect the underlying evidence and clinical relevance. The project also considers structured benefit-risk frameworks, estimands, and aggregated safety assessments across studies. Deliverables focus on practical communication principles, illustrative examples, and consensus recommendations that stakeholders can apply directly.

Q3 2028

Proposed
End Date

- Conference presentation
- White paper
- Webinar

Deliverable

Project approved

Key Achievements
This Quarter:

Project kick off

Deliverables &
Targets Planned for
the Next Quarter:

Katarina Hedman

Leads



Project Status: Green
Accepting New Members

- Project approved by PHUSE Leadership
- Calling for Volenteers

Project Status

Estimands in Safety Analytics

Description

This project develops a user-friendly, centralised education portal on safety estimands, designed to support practical application across the industry. It will consolidate and reference existing guidance and insights from external groups, presenting them in a clear, complementary and accessible format.

A key objective is to deliver a structured education series that increases confidence among safety scientists in defining and applying appropriate safety estimands. The project also aims to expand their routine use in practice and broaden the range of estimators applied in safety analytics.

By combining curated content, practical examples and targeted training materials, the portal will serve as a comprehensive, one-stop resource. It will support consistent understanding, improve communication of estimands, and promote more robust and standardised approaches to safety analysis across organisations.

Q4 2026

**Proposed
End Date**

**Series of training
modules
& webinars**

Deliverable

- Training modules for the five sub-topics of this project have been completed (slide decks plus detailed speaker notes for each).
- Introductory video to the entire project content has also been completed.
- Dissemination of the work at conferences and company-internal venues has begun.

**Key Achievements
This Quarter:**

- Proofreading and final lock-down of slides and speaker notes.
- Posting on the Safety Analytics Education Library.
- Development and execution of further plans for dissemination (conferences, webinars, etc.).

**Deliverables &
Targets Planned for
the Next Quarter:**

**Andreas Sashegyi
& Michael Colopy**

Leads



Project Status: Green

- On track

Project Status

Interactive Analyses and Displays for Laboratory Data

Description

This project focuses on the development of interactive analyses and displays for laboratory data in Phase II to III clinical trials and integrated submissions. Interactive outputs provide a more flexible and user-friendly approach to reviewing laboratory data, enabling users to explore results without significantly increasing submission volume.

The initiative will define key features and best practices for interactive tools, ensuring they are fit for regulatory review and aligned with user needs. It also recognises that multiple groups are independently developing interactive solutions, creating an opportunity to align efforts and promote consistency.

In addition to defining desired functionality, the project will include educational materials to support interpretation and effective use of these analyses and displays. The resulting deliverable will provide guidance that supports improved data review, enhances usability, and advances the adoption of interactive approaches across the industry.

Q4 2027

Proposed
End Date

Specification
document

Deliverable

Christopher
Smith

Lead

Finalised interactive
displays blog post for
publication

Key Achievements
This Quarter:

Publish blog post on
interactive tools

Deliverables &
Targets Planned for
the Next Quarter:



Project Status: Green

- Specific WG meetings to be scheduled ad hoc, as current project activities are being completed with the Safety Education group.

Project Status

Process for Aggregate Assessment of Clinical Trial AE Data (PrOACTS)

Description

This project addresses the need for clear, practical processes for aggregate assessment of adverse event (AE) data during early clinical development, as encouraged by the FDA’s 2021 draft update to the Final Rule, which provides limited methodological guidance.

The initiative will define approaches for AE assessment across development stages, recognising differences between early-phase studies and Phase III. It will establish consistent practices for grouping related preferred terms and align processes across analysis plans, SDTM/ADaM specifications, and output displays.

The project will identify key challenges in detecting safety signals, evaluate appropriate analytical methods, and clarify important concepts such as ‘significance’ in a clinical (non-statistical) context. It will also address limitations such as small sample sizes and uncertain background rates.

Additionally, industry practices will be assessed through targeted surveys. The outputs will support more consistent, transparent and effective safety evaluations for both internal stakeholders and regulators.

Q4 2027

Proposed
End Date

White paper

Deliverable

This quarter, we have seen a wealth of activity regarding finalising the white paper ToC, having deep team engagement and authoring the white paper in draft format. The dedication to the white paper has been impressive and has ensured we have started a product that will be a welcomed and professional addition to the PHUSE library. Eventually, we’ll be looking for peer-reviewed manuscripts to accompany the white paper.

Key Achievements
This Quarter:

The next quarter will include further development of the draft sections of the white paper, linking the sections and beginning to craft what the final draft version will include.

Deliverables &
Targets Planned for
the Next Quarter:

Mac Gordon &
Peg Fletcher

Leads



Project Status: Green

- We are in the beginning to mid stages of developing the white paper, with main sections in draft development mode.

Project Status

Safety Analytics Education

Description

This project focuses on the development and delivery of education for clinical trial safety analyses, with an emphasis on Phase II to III studies. It addresses a recognised gap in formal training, where the scientific expertise required for planning, interpreting and communicating safety analyses is often limited across roles such as medical, statistics and medical writing.

The initiative aims to improve the quality, consistency and understanding of safety analyses, enabling more efficient alignment on analysis plans and interpretation of results. As the field continues to evolve, ongoing education is essential to support best practices and informed decision-making.

Building on existing efforts - such as PHUSE CSS workshops, collaborations with external organisations, a dedicated Safety Analytics Education website, and a webinar series - the project will establish a coordinated platform for future educational activities. This will enhance capability across stakeholders and strengthen PHUSE's leadership in the safety analytics domain.

Ongoing

Proposed End Date

- Enhance the Safety Analytics Education website
- Webinar series

Deliverable

Confirmed dates and held kick-off meetings for two webinars:

- DMC overview (5 November)
- Statistician/clinician discussion (10 December)

Key Achievements This Quarter:

- Working with presenters to confirm two other webinars: FDA safety guidances and FDA/sponsor views of safety analyses for a drug application
- Drafted blog post on interactive tools in conjunction with the interactive labs group and sent to PHUSE leadership for review; working with authors to finalise content

Deliverables & Targets Planned for the Next Quarter:

Christopher Smith & William Palo

Leads



Project Status: Green
Accepting New Members

- No concerns at the moment. Everything moving forward.

Project Status