Visualization of Group Related Differences in Histopatholgy Data

Project Scope

Histopathology data comprise a major component of toxicology studies and are typically presented in data tables (tabular format) in study reports. Can these data be graphically displayed in a visual format which provides a means for rapidly identifying and communicating treatment group differences, patterns in response, and/or changes in phenotypic expression ? Can cross-domain analyses (including organ weights, clinical pathology and histopathology data) be graphically displayed for analyses ? Can data from multiple studies be aggregated or graphically displayed for analysis ? How does incorporation of the SEND (Standard for Exchange of Nonclinical Data) standard enable this technology?

To canvas opinion from toxicologists, pathologists, bioinformatics specialists and software designers on current methods of data visualization and how those might be improved or expanded to improve data analyses compared to currently used tabular (incidence) formats. To communicate points of discussion, ideas, case examples, etc. with key stake holders (the pharmaceutical industry, software developers/vendors, CROs, US FDA) via the Advance Hub, poster presentations and publications.

Vision

To explore the use of various software applications for visually displaying histopathology data in novel ways to aid with data analysis and communication of findings, and to promote the use of the SEND standard for enabling this technology

Prior Project Plans

The project completed its third year of activity (2017 to 2018). Project plans included the following.
1) Evaluate the use of the "sunburst" graphical display (termed HistoGraphic) and application for visualizing histopathology data from the IMI eTOX database
3) Explore use of the "sunburst" (HistoGraphic) application for simultaneously displaying microscopic findings and relevant biomarkers. As an example, initial efforts can focus on liver lesions and serum ALT, AST, ALKP and/or bilirubin changes
3) Collaborate with the Nonclinical Scripts working group for development and evaluation of novel software applications, such as HistoGraphic, for data visualization. The first two projects listed above are a component of this activity
4) Create mock SEND datasets of histopathology data for incorporation into various software applications to evaluate multi-study data displays

Summary of Projects

After 3 years of activity, the project has reached a natural conclusion with development of HistoGraphic for graphically displaying histopathology data from multiple toxicology studies which were obtained from the European Union's IMI eTOX database. Deliverables from the project team included 3 posters presented at FDA PHUSE CSS meetings and one publication. It is the project team's intent to place HistoGraphic on a publicly assessed site for downloading. Following completion of this project, a new project has been endorsed by PHUSE for initiation in 2018: Data Visualization as an Enabler for Nonclinical Safety Signal Detection. This project will include a collaborative relationship with the EU's IMI eTRANSAFE initiative (Enhancing Translational Safety Assessment through Integrative Knowledge Management) eTRANSAFE.

Milestones

Tasks

Upcoming milestones for 2018 FDA PHUSE Computational Sciences Symposium, 4-6 March 2018 in Silver Spring, Maryland, USA:

- Prepare and submit abstract for poster presentation. Completed 5 Jan 2018.
- Prepare and submit draft poster and copyright grant form. Due 2 Feb 2018.
- Submit final poster. Due 16 Feb 2018. Completed Feb 2018

Deliverables for 2015

March 2015 - March 2016 (completed)

1) Identify a panel of Toxicologists and Pathologists (2 weeks)
2) Supply of intended usage and a selection of 'use-cases' (6 weeks)
http://etransafe.eu/ 3) Gap analysis results (12 weeks)
4) Recommended visualisations (26 weeks)
5) Approach to fill gaps in SEND standard (52 weeks)
6) Communicate project results at 2016 FDA PHUSE Computational Sciences Symposium (52 weeks)

April 2016 - March 2017 (completed)

1) Prepare first draft of manuscript (July 2016) - completed
2) Prepare final draft of manuscript (October 2016) - completed
3) Submit to Regulatory Toxicology and Pharmacology (November 2016) - completed October 2016
4) Discuss cross-domain and cross-study graphical displays, including examples (by December 2016) - completed
5) Submit abstract for poster presentation for 2017 FDA PHUSE CSS (January 2017) - completed
6) Submit poster for 2017 FDA PHUSE CSS (February 2017) - completed
7) Poster presentation at 2017 FDA PHUSE CSS (March 2017) - completed

April 2017 - March 2018 (completed)

1) Obtain eTOX datasets and incorporate into HistoGraphic display tool (completed November 2017)
2) Submit abstract for poster presentation for 2018 FDA PHUSE CSS (completed January 2018)
3) Submit poster for 2018 FDA PHUSE CSS (completed February 2018)
4) Poster presentation at 2018 FDA PHUSE CSS - (completed March 2018)

Data Visualisation Examples

- Published References
  - - Nigsch F. et al, Expert Opin Drug Metab Toxicol. 2011 Dec;7(12):1497-511. Computational methods for early predictive safety assessment from biological and chemical data. (PMID: 22050465) - See chapter 2.4 + figures 3 and 4 for histopath findings heatmap and individual data. digest.
  - -Ondov BD et al. Interactive metagenomic visualization in a web browser. BMC Bioinformatics 2011, 12:385. Available as open source at http://www.biomedcentral.com/1471-2105/12/385
- AstraZeneca data visualization - screen shots
- Definiens Image Minor - screen shots
- Novartis Translational Safety Platform - example
- INDS SEND Explorer - Demo of pre-version
- INDS SEND Explorer - Demo 2
- INDS SEND Explorer - Screen shots for PHUSE CSS 2016 poster
- PointCross ToxVision - Demo
- PointCross ToxVision - heatmap of LB (clinical laboratory data)

- Survey results to histopathology visualization project questionnaire
- Summary of responses to histopathology visualizaton questionnaire
- Survey results from European Society of Toxicologic Pathology 2015 annual meeting
- Poster presented at 2016 FDA PHUSE Computational Science Symposium

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Deliverables for 2016

Publication in Regulatory Toxicology and Pharmacology

- Graphical display of histopathology data from toxicology studies for drug discovery and development: an industry survey

Poster presented at 2017 FDA PHUSE Computational Sciences Symposium

- Graphical display of histopathology data from multiple toxicology studies

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Deliverables for 2017

- Poster presented at Japan Toxicology Conference, Tokyo, July 2017
- Krona license information
- Summary of project deliverables 2015 - 2018
- Poster presented at 2018 FDA PHUSE CSS, March 2018