

toxSummary: An R Shiny App for Visualization and Summarization of Repeat-dose Toxicology Study Results Throughout a Drug Development Program

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PROBLEM STATEMENT

Prior to initiation of a clinical trial, repeat-dose toxicology studies are conducted in multiple species to support the safety of the proposed clinical dosing regimen. The primary metric used to extrapolate the safety of clinical dosage from repeat-dose toxicology study results is the safety margin. Another important consideration in drug safety evaluation is the nature and severity of the toxicities observed at doses above the NOAEL. As toxicity studies of various durations are typically conducted in multiple species and potentially via multiple routes of administration, it can be challenging to effectively integrate all of this information.

APPLICATION FEATURES

- ❑ toxSummary shiny app allow users to interactively visualize safety margins and the severity of user-defined significant toxicities across studies throughout a drug development program in a single figure.
- ❑ toxSummary app can also present this information in tabular form that can be exported in various formats, e.g., CSV, Excel or Word files.
- ❑ These functionalities are designed to facilitate holistic evaluation of the drug safety by integrating the results of multiple toxicology studies in the context of a clinical dosing regimen.

TECHNICAL FEATURES

- ❑ Shiny is an R package that allow to create interactive web application using R programming language.
- ❑ App can be connected to SQLite database to automate data entry of dose and pharmacokinetics parameter.
- ❑ App was wrapped in R package so easily can be installed and use.
- ❑ Added option to easily host in Posit Connect (Posit paid hosting service) server for production level use.

FUTURE DIRECTIONS

- ❑ Submit to CRAN so it can easily be used by industry.
- ❑ This is an open-source project that has been shared with industry stakeholders via the PHUSE consortium.
- ❑ A PHUSE project has been proposed to develop practical methods to store and share toxicology study summary information in a machine-readable format for use by applications such as the one presented here.

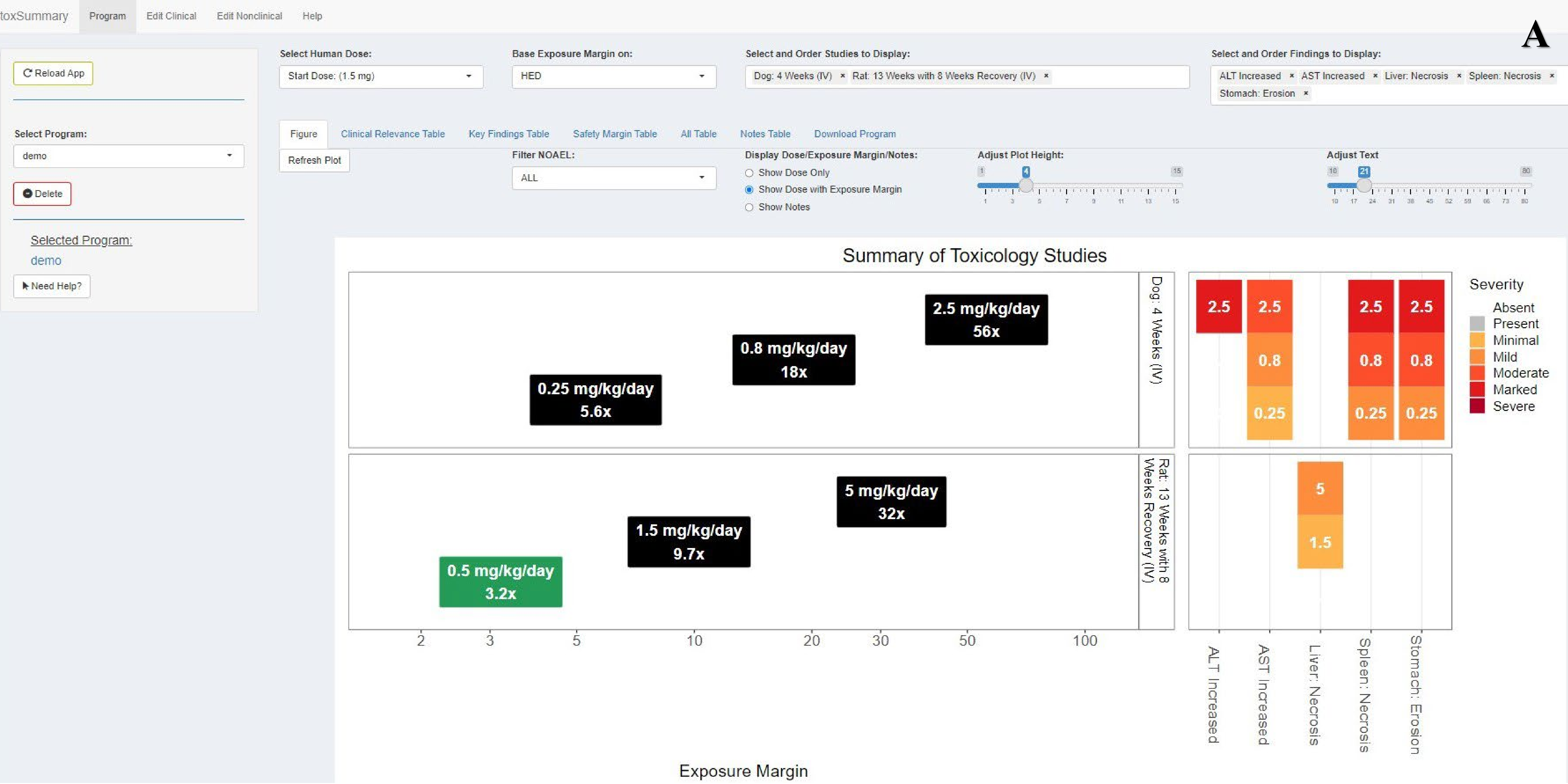


Fig: A is screenshot of main page of toxSummary web app

Findings	Reversibility	Study	Dose (mg/kg/day)	Clinical Exposure Margin
ALT Increased	Reversible	Dog: 39 Weeks with 8 Weeks Recovery (SC)	0.25	5.56
			0.8	17.78
		Dog: 4 Weeks (IV)	2.5	55.56
			0.8	5.16
	Not Assessed	Rat: 13 Weeks (SC)	2.5	16.13
			8	51.61
			0.08	1.78
AST Increased	Reversible	Dog: 13 Weeks with 8 Weeks Recovery (IV)	0.4	8.89
			1	22.22
		Dog: 39 Weeks with 8 Weeks Recovery (SC)	0.25	5.56
			0.8	17.78
			0.25	5.56
		Dog: 4 Weeks (IV)	0.8	17.78
			2.5	55.56

Fig: B shows screenshot of Clinical Relevance Table

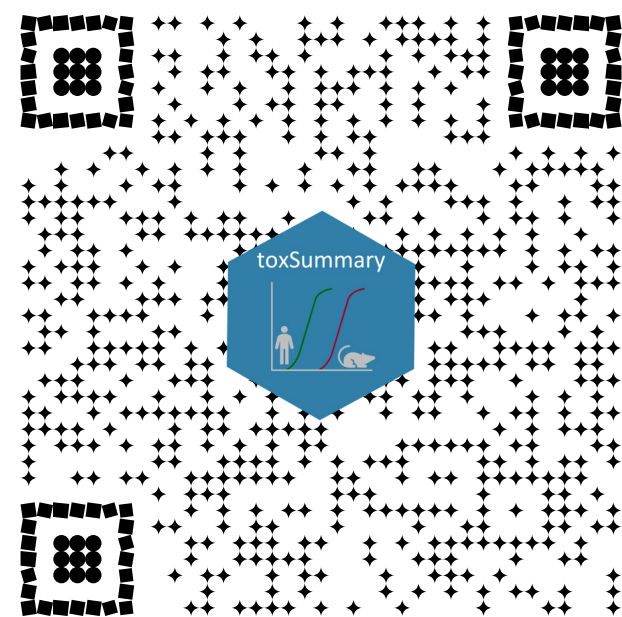
LINKS

A publicly accessible version of the application:

<https://phuse-org.shinyapps.io/toxSummary/>

The source code to the public application:

<https://github.com/phuse-org/toxSummary>



ACKNOWLEDGEMENTS

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DISCLAIMER

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