

# **Framework for Establishing an Internal Threshold of Toxicological Concern (TTC)**

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The threshold of toxicological concern (TTC) is an important risk assessment tool that establishes acceptable low-level exposure values to be applied to chemicals with limited toxicological data. The concept relies on knowledge of the range of toxicological hazard/potency for structurally relevant classes of chemicals for which good toxicity data exist. The non-cancer TTC databases consist of distributions of oral no-observed-effect levels (NOELs) identified from toxicity studies. The TTC threshold limits were established by identifying a low-percentile NOEL value (i.e. 5<sup>th</sup> percentile) from the database and applying an appropriate uncertainty factor. Given the fact that the data comprising the TTC are from external oral exposures, the corresponding threshold limits are representative of external exposures. There are multiple situations in risk assessment where it is more appropriate to address internal exposure rather than external exposure. The current presentation will provide a proof-of-concept framework for establishing an internal TTC based on estimated steady state blood concentration. The approach utilizes pharmacokinetic modeling to convert the external exposures from the existing TTC database to an internal blood concentration. The presentation will also discuss the challenges associated with this work as well as the criteria need for success.