



Science Highlight from the ACC LRI | February 3, 2021

Internal Threshold of Toxicological Concern (iTTC)



New Publication

[*Internal Threshold of Toxicological Concern \(iTTC\): Where we are today and what is possible in the near future?*](#)

- With increasing interest in non-animal alternatives and new approach methodologies (NAMs), many researchers in academia, government, and the private sector have increased focus on the potential to use the Threshold of Toxicological Concern (TTC) in tiered risk-based applications for commodity and consumer chemicals.
- The TTC is an important risk assessment tool that establishes acceptable low-level exposure values for risk-based prioritization and safety evaluations for chemicals with limited toxicological data.
 - ✓ Read the LRI [TTC Q & A document](#) and view the LRI [TTC web video](#) to learn more about the derivation and application of TTCs.
- One of the next steps in the evolution of the TTC is to develop the [iTTC](#) – a safe exposure level that is representative of internal exposures.
 - ✓ The derivation of iTTC values requires conversion of chemical-specific external NOAELs (in mg/kg/day) in the TTC database to estimated internal plasma concentrations.
 - ✓ This conversion, using [PBPK modeling](#), will permit iTTC values to be used in advanced risk-based safety evaluations based on results from *in vitro* test systems.
- [Cosmetics Europe](#), the [Research Institute for Fragrance Materials \(RIFM\)](#), and the [ACC LRI](#) are collaborating to support the scientific studies needed to generate the data and conduct pharmacokinetic modeling to establish iTTC values.
 - ✓ The new publication [*Internal Threshold of Toxicological Concern \(iTTC\): Where we are today and what is possible in the near future?*](#) (Ellison et al., 2020) describes details of this research and discusses the next steps in the iTTC project.

This Science Highlight was prepared by Richard A. Becker Ph.D. DABT of the ACC LRI. The views expressed are his alone. Reference to commercial products, services, or links does not imply ACC endorsement.

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