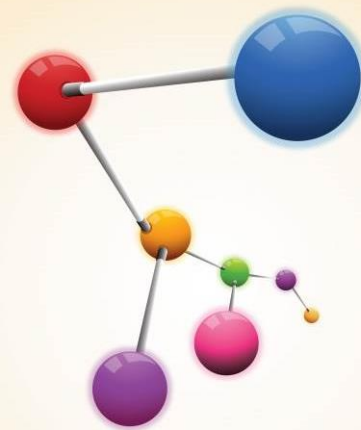


Threshold of Toxicological Concern Task Force

ABOUT THE TASK FORCE

The Threshold of Toxicological Concern (TTC) concept is a pragmatic but conservative science-based tool to help regulators and industry assess potential health risk from substances when specific toxicological data are not yet available. The use of the TTC principle enables to: 1) apply a practical risk assessment tool that is needed to address low level exposures as more and more sensitive analytical techniques become available; 2) Prioritise toxicological testing based on estimated human exposures; 3) Reduce the use of laboratory animals; and 4) Make better use of financial and human resources in both industry and public sector.



WHAT'S NEW?

The task force contributed to European Union funded project COSMOS.

PUBLICATION on the 'Origin of the TTC values for compounds that are genotoxic and/or carcinogenic and an approach for their re-evaluation' in *Critical Reviews in Toxicology* (Boobis *et al.*, 2017). The review has already been viewed over 720 times in the first 4 months.

PUBLICATION on 'Thresholds of Toxicological Concern for Cosmetics-Related Substances: New Database, Thresholds, and Enrichment of Chemical Space' *Food and Chemical Toxicology* (in press)

ACTIVITIES

Uncertainty in Risk Assessment: A Comparison of TTC versus Chemical-Specific Approaches – *New*

This activity plans to provide a differentiated review and comparison of quantitative and qualitative uncertainties associated with different steps of 1) data generation in toxicological studies and No Observed Adverse Effect Level / Benchmark Dose, Lower

Confidence Limit derivation; 2) assumptions made in risk assessment based on specific data; 3) derivation of thresholds from large groups of substances, i.e. TTC; and 4) derivation of thresholds from small groups of substances.

Carcinogen Dose-Response Database for Threshold of Toxicological Concern – Funded by CEFIC-LRI

This activity is funded by the European Chemical Industry Council Long-range Research Initiative (CEFIC-LRI). Building on the evaluation of the Cancer Potency Database (CPDB) by the ILSI Europe CPDB Expert Group, the project

aims to generate a fully-curated, quality-controlled and publically-available database on genotoxic and non-genotoxic carcinogens. The novel database will form the basis of analysis of TTC distributions for cancer thresholds.

Threshold of Toxicological Concern Task Force

MEMBER COMPANIES

- BASF SE
- Dow Europe
- DSM
- Givaudan International
- Pierre Fabre Dermo-Cosmétique
- Procter & Gamble
- Südzucker Group
- Syngenta
- The Coca-Cola Company
- WALA Heilmittel

ACTIVITIES (CTD)

Is the 0.15 µg/day Tier of the Threshold of Toxicological Concern (TTC) still appropriate? – **Completed**

The TTC-based exposure limit of 0.15 µg/day is based on an evaluation of the Cancer Potency Database (CPDB) that includes information from carcinogenicity studies of over 700 chemicals. The expert group examines whether the TTC exposure limit of 0.15 µg/day for DNA-reactive

substances is still appropriate when account is taken of the mode of action (e.g. mutagenic or not) and knowledge on human relevance. The project describes a science-based and pragmatic approach to strengthening the scientific underpinnings of the cancer-based TTC tier.

RECENT PUBLICATIONS

C. Yang, S.M. Barlow, K.L. Muldoon Jacobs, V. Vitcheva, A.R. Boobis, S.P. Felter, K.B. Arvidson, D. Keller, M.T.D. Cronin, S. Enoch, A. Worth and H.M. Hollnagel. **Thresholds of Toxicological Concern for Cosmetics-Related Substances: New Database, Thresholds, and Enrichment of Chemical Space.** *Food and Chemical Toxicology* 2017 (in press).

A. Boobis, P. Brown, M.T.D. Cronin, J. Edwards, C.L. Galli, J. Goodman, A. Jacobs, D. Kirkland, M. Luijten, C. Marsaux, M. Martin, C. Yang and H.M. Hollnagel. **Origin of the TTC values for compounds that are genotoxic and/or carcinogenic and an approach for their re-evaluation.** *Critical Reviews in Toxicology* 2017.

F.M. Williams, H. Rothe, G. Barrett, A. Chiodini, J. Whyte, M.T.D. Cronin, N.A. Monteiro-Riviere, J. Plautz, C. Roper, J. Westerhout, C. Yang and R.H. Guy. **Assessing the safety of cosmetic chemicals: Consideration of a flux decision tree to predict dermally delivered systemic dose for comparison with oral TTC (Threshold of Toxicological Concern).** *Regulatory Toxicology and Pharmacology* 2016;76:174-186

I. Dewhurst and A.G. Renwick. **Evaluation of the Threshold of Toxicological Concern (TTC) – Challenges and Approaches.** *Regulatory Toxicology and Pharmacology* 2013;(1):168-177.

All publications commissioned by this task force are available on our website: www.ils.eu.

For more information on ILSI Europe's activities, don't forget to follow us on Twitter @ILSI_Europe and connect with us on LinkedIn.

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