

SCIENTIFIC COMMITTEE ON CONSUMER PRODUCTS (SCCP) – SCIENTIFIC COMMITTEE ON HEALTH AND ENVIRONMENTAL RISKS (SCHER) – SCIENTIFIC COMMITTEE ON EMERGING AND NEWLY IDENTIFIED HEALTH RISKS (SCENIHR)

Request for a scientific opinion: Use of the Threshold of Toxicological Concern (TTC) approach for the health risk assessment of chemicals

The concept of TTC has its roots in the concept that 'safe levels of exposure' can be identified for individual chemicals with known toxicological profiles. TTC is an approach that aims to establish 'safe exposure levels' for chemicals for which toxicological data are not available based on chemical structure and toxicity data of structurally related chemicals.

Starting with the generic approach ('exposure threshold') used by the US FDA in the 80s, the TTC concept has evolved over the years to take into account extensive analysis of available data on mainly the oral toxicity data of substances, intake/exposures to the substances, and on the basis of a structure based decision tree to find applications mainly in the food area.

The TTC approach has been used to evaluate flavouring substances (JECFA, EFSA), food contact materials (US FDA), genotoxic impurities in pharmaceuticals (EMA) and for the risk assessment of chemicals (WHO IPCS). Recent publications have suggested that the TTC approach can also find uses in other categories of chemicals and more specifically on chemicals (or trace contaminants) in consumer products, food additives, pesticides and cosmetics.

Specifically for cosmetics, COLIPA, the European cosmetics industry association sponsored work by a group of experts to examine the potential use of the TTC concept in the safety evaluation of cosmetic ingredients. In its report, the group concluded that *'overall the TTC approach provides a useful additional tool for the safety evaluation of cosmetic ingredients and impurities of known chemical structure in the absence of chemical-specific toxicology data'*. However, the group went on to conclude that *'the TTC approach relates to systemic effects, and use of the proposed procedure would not provide an assessment of any local effects at the site of application'*. In addition the expert group identified the need for the careful *'...consideration of whether route-dependent differences in first-pass metabolism could affect the applicability of TTC values derived from oral data to the topical route. Analysis has shown that the oral TTC values are valid for topical exposures and that the relationship between the external topical dose and the internal dose can be taken into account by conservative default adjustment factors'*.

Terms of Reference

The SCCP/SCHER/SCENIHR are requested to critically review the COLIPA Expert Group report on the use of the Threshold of Toxicological Concern (TTC) concept in the safety

¹ International Fragrance Association

evaluation of cosmetic products and the publicly available scientific literature on the concept of TTC and answer the following questions:

1. Do the SCCP/SCHER/SCENIHR consider the TTC approach appropriate for the human health risk assessment of chemical substances?
2. In elaborating their opinion(s), and if the available information allows it, the SCCP/SCHER/SCENIHR are asked to address the following:
 - a. The possible application of the TTC approach to chemical substances in various product types from which an exposure of consumers is likely to occur in normal use situations, including cosmetic products, consumer products, and others.
 - b. The distinction between intentionally added ingredients and substances present in a particular product as inadvertent contaminants
 - c. The quality and type of data that will need to be available before the TTC concept can be applied in the risk assessment of chemicals.
 - d. Identification of classes of chemicals, exposure situations, toxicity end points for which the TTC concept may be appropriate and those for which it may not be
 - e. Additional research needed to strengthen the Threshold of Toxicological Concern approach and its usefulness for the human health risk assessment of chemical substances