EUROPEAN COMMISSION
HEALTH & CONSUMER PROTECTION DIRECTORATE-GENERAL

Directorate D - Public Health and Risk Assessment
Unit D5 – Risk Assessment

Brussels, 11 July 2011

Joint meeting of the European Commission Scientific Committees and the European Food Safety Authority (EFSA) Working Groups on the Threshold of Toxicological Concern (TTC), Brussels, 8 June 2011

Introduction

Both the European Commission Scientific Committees (SCCS, SCHER, SCENIHR) and the EFSA Scientific Committee have been elaborating opinions on the TTC concept and its potential applicability to non-food (the Commission Scientific Committees) and to food application. The meeting was held in order to review the draft opinions of the two WGs in order to identify and address potentially diverging views in line with the legal obligation of both bodies (EC Scientific Committees and EFSA) to address and eventually resolve diverging opinions.

The meeting was convened in the Health and Consumers Directorate General premises on 8 June 2011. Participating in the meeting were:
from the EFSA WG,
from the Commission Scientific Committees WG, D. Maurici and D. Liem from the EFSA Scientific Committee Unit, K. Kilian and T. Daskaleros from the Health and Consumers DG Risk Assessment Unit, and M. Marini from the Relations with Agencies and Advisory Groups Unit of the Health and Consumers DG.

Introduction (European Commission)

T. Daskaleros welcomed the participants. A tour de table followed for introductions.

Background (Commission)

T. Daskaleros explained the background for convening the meeting between European Commission and EFSA SC experts explaining that both bodies have been working on TTC-opinions which although have a different scope of work (consumer products, food), they are underpinned by the same science. He went on to mention that the Commission SC work started earlier, and was almost finished when EFSA started its in-depth review of the two databases that underpin the TTC approach, which included work conducted both by the EFSA Working Group and by a contractor, the results of which may be also pertinent to the Commission SC WG.

In terms of expectations from the meeting, Mr. Daskaleros explained that the aim of the meeting was for EFSA to provide information on the database analysis to the

Commission to review evidence and to examine whether divergences in opinion remain after considering the final set of data and whether those can be addressed either by agreeing to modify the relevant texts of the opinion or by explaining the basis for the divergence.

Mr. Daskaleros also informed the group that had resigned from being Chair and Rapporteur of the Commission Scientific Committee WG. replaced him as Chair and a rapporteur would be nominated in the near future.

Declarations of Interest

None

Presentation on EFSA draft opinion

provided an overview of the EFSA draft opinion, highlighting the work of the EFSA Working Group and the contractor on the databases underpinning the TTC concept and indicating the points of potential divergence between the EFSA and the Commission SC draft opinions on TTC. The presentation served as the basis for the discussion which followed.

Discussion

The key points of the discussion are summarised below.

Analysis of databases:

Representation of relevant chemicals in databases

- Based on contractor's analysis, EFSA considers both data bases sufficiently cover the "world of chemicals" and food ingredients in particular.
- For cosmetics there is currently no analysis available on whether structures are sufficiently represented, especially for hair dyes, UV-filters, complex structures with combinations of functional groups. Comparison based on molecular descriptors should be done for cosmetic ingredients as has been done for the substances in the two databases underpinning the TTC approach.
- Many structures used as flavourings are also present in cosmetics.
- Concerns were expressed that databases of industrial chemicals may not adequately represent the world of "consumer-relevant" chemicals: however, the Munro database is not specific for industrial chemicals, as it also includes pharmaceuticals, food use chemicals, environmental, agricultural and consumer chemicals. EFSA is confident that the TTC Values derived from the Munro database would be representative for food use chemicals – it is the adequacy of the representation of typical structures that is important, not the presence of chemicals with a specific use. In order to build up confidence also for cosmetic ingredients it was proposed to perform a systematic analysis comparing TTC values and experimental NOAELs.
- Carcinogenicity database: Including carcinogens which are irrelevant for humans might dilute the derived threshold value hence a proposal was made to examine

the consequences of including only carcinogens recognised to have human relevance (EU, IARC, IRIS) –

- EFSA considers the TTC value for genotoxic carcinogens sufficiently conservative;, the most potent carcinogens are excluded from the TTC approach, and introducing a selection bias for other potent carcinogens would be contrary to probabilistic approach of TTC, use of the TTC approach implies that the risk for a certain (low) percentage of substances may be underestimated.

Quality of database

- Databases dependent on high quality studies;
- NOAEL setting is sometimes different in different areas (e.g. OP, neurotoxicity);
- Analysis of databases should be standardised, quality checked;
- Munro used regulatory studies which should be of generally good quality. Repeated dose toxicity studies take account of metabolism – do molecular descriptors support such considerations?

Cramer classification

- Modernisation of Toxtree needed? Cramer classes stem from 1978 and are also basis for TOXTREE. Toxicological knowledge gained afterwards and new structures should be implemented. Analysis by EFSA shows ca 5% misclassification of substances with high hazard in class I, which is considered acceptable by EFSA, SANCO SCs more sceptical.
- Substances misclassified in class I should be analysed to obtain information for update of Toxtree.
- EFSA considers basis for derivation of TTC value for Cramer Class II is not adequate, but that for class I and III is. SANCO SCs consider Cramer classes not well defined hence their inclination to propose Cramer III as default and modernisation of data base/classification system. Both groups agreed that if there are good arguments for classification in class I, then the TTC value for class I could be used.

Specific areas of potential divergence in the opinions and proposed actions to resolve

- For most points views are not substantially different, but the current wording of the opinions might give that impression
- How to deal with endocrine active substances, is the chapter 4.3.4 in the EFSA sufficient, is there a need to address this topic in the non-food opinion also.

Representation of relevant chemicals in database/Coverage of complex structures

- No principle disagreement
- Remaining doubts on the part of the Commission SCs as to whether there is sufficient representation of complex structures relevant for cosmetics (hair dyes, UV-filters)

- EFSA considers analysis done relevant for all chemicals, not specifically for food, but feels they cannot comment on cosmetic ingredients
- analysis of coverage should be done for cosmetics

Action: SANCO SC opinion Summary should be rephrased to more accurately emphasize specific concerns for cosmetics (and possibly other consumer chemicals) to avoid giving the impression that there is general concern on databases as it reads now.

EFSA sees no need to change wording, are confident that database represents food chemicals and give sufficiently conservative TTC values.

Carcinogenicity database:

- EFSA considers carcinogenicity database sufficiently conservative, SANCO SCs raise concern on inclusion of carcinogens irrelevant for humans with lower potency. However, the TTC value is endorsed by both groups but further work is recommended to strengthen its scientific basis.

Action: EFSA will acknowledge in its opinion the Commission SC concerns.

Topic should be-visited when more information on US work is obtained

Cramer classes

- agreement on non-acceptance of class II
- EFSA accepts class I and III
- Commission SC recommend class III as default, require justification for class I

Modernisation of databases:

- Not much disagreement, EFSA work supports the currently available database, but expansion and modernisation would be welcomed by both bodies to get more confidence, but it is not anticipated that TTC values would significantly change

Action: Apparent discrepancy comes from the wording of conclusions with EFSA stating confidence, SANCO focussing on doubts, wordings of both opinions should be reviewed accordingly.

Exposure

- No disagreement – no further action

<u>Conclusion and next steps:</u>

The main conclusions from the discussion were that there is broad and general agreement between the two groups, and that differences identified in the two opinions are more due to presentation (editing) and emphasis on certain points rather than on substance. Both groups have agreed to re-examine and redraft the relevant sections of the opinions to minimize the potential for misinterpretations and to reconvene in the Fall (following the EFSA public consultation of the TTC opinion) to ensure that this agreement is fully

reflected in the two opinions before the documents are adopted by the respective Committees.