Luxembourg, 12 March 2019

Scientific Committee on Consumer Safety (SCCS)
Meeting of the Working Group on Methodologies

27 February 2019, Brussels

Scientific Workshop on Alternative Methods to Animal Testing in Human Health Risk Assessment of Cosmetic Ingredients

MINUTES

1. Welcome and presentation of the Programme

Giulio Gallo, deputy head of Unit SANTE C2 hosting the Secretariat of the Scientific Committees in Luxembourg, opened the scientific workshop.

The Chair of the SCCS Working Group on methodologies, *Vera Rogiers*, welcomed the 70 participants including representatives from SCHEER/SCCS, cosmetic associations, industries, universities, national authorities, EU Agencies and Commission services.
This was a closed scientific workshop on SCCS invitation only. All speakers presented their work for the purpose of the meeting discussion only, without permission for distribution or publication.

The goal was to discuss a way forward for the SCCS cosmetic ingredients' risk assessment without animal data in the safety file. Some conclusions were drafted for SCCS reflection and internal use (no mandatory commitment).

2. Presentations made

- *Matt Dent, Unilever, United Kingdom: Application of the ICCR principles to Next Generation Risk Assessment ('Ab Initio' case studies)*

'Next Generation Risk Assessment' (NGRA) is defined as an exposure-led, hypothesis driven risk assessment approach that integrates *in silico* (including Quantitative Structure–Activity Relationship (Q)SARs and other computational modelling approaches), *in chemico* and *in vitro* approaches to deliver human relevant safety decisions without the use of animal data.

- *Heli Hollnagel, DOW Europe, Switzerland: TTC approach as a risk assessment tool for cosmetic impurities. Proposal of higher threshold values*

TTC is a concept allowing, under specific conditions, to conclude without the need to run new animal studies whether a certain low level chronic human exposure is of negligible health concern or whether further work is necessary. Different approaches were shown.

- *Corie Ellison, Procter & Gamble, Unites States of America: Internal TTC: Where are we today? What is possible for the near future?*

The TTC is an important risk assessment concept, which has evolved over the last 50 years, and establishes acceptable low-level exposure values to be applied to chemicals with limited toxicological data. This concept is based on external oral toxicity data, usually, the No-Observed-Adverse-Effect-Level (NOAEL), and as such, the corresponding threshold limits represent external exposures. Therefore, as part of the Cosmetics Europe Long Range Science Strategy (LRSS) research program, a project was initiated that is working towards the development of internal TTCs (iTTC) that can be used for the human safety assessment.

- *Emilio Benfenati, EFSA expert, Mario Negri University, Italy: Read across combined with QSAR in risk assessment. How far are we?*

The presentation addressed the perspectives in the area of non-testing methods to be integrated within a single weight-of-evidence approach. The advantages and still open issues connected with a toolbox to combine evidence by using multiple *in silico* models, read across, hazard and exposure, screening and prioritisation, were put forward . It was discussed what is necessary to make further progress.

- *Mark Cronin, Univ. of Liverpool, United Kingdom: From data to knowledge: approaches for organising, integrating data and interpreting multiple data streams in risk assessment*

There are multiple types of data that can be used to assist in the development and acceptance of risk assessment without the necessity for further testing. In addition, knowledge of mechanisms of action and / or Adverse Outcome Pathway (AOP) can be used to support the information and develop knowledge about the chemical to allow a safety decision to be made. An example was elaborated to show the flow of possibilities.

- *Andrew Worth, Joint Research Centre (European Commission, Ispra): Building confidence in new approach data: towards a confidence framework for ab initio risk assessment*

This presentation took as a starting point the principles for Next Generation Risk Assessment (NGRA) proposed by the International Cooperation on Cosmetics Regulation (ICCR). It was considered how uncertainty assessment could be applied to this ab initio approach. It was concluded that the validation of New Approach Methodologies (NAMs) can be regarded as an input to the overall uncertainty assessment, but that the challenge is to reconcile a variety of validation/uncertainty frameworks which have so far been developed by different (technology) communities, such as in vitro toxicology, QSAR modelling, read-across and Physiologically-Based Kinetics (PBPK) modelling. Ongoing activities and challenges related to the uncertainty assessment of NAMs were also presented.

- *Susana Proença, University Utrecht, The Netherlands: In vitro biokinetics QVIVE and Physiologically-based kinetic modelling*

In vitro models have emerged in last years as alternatives to animal experimentation in risk assessment. These models increase the knowledge on toxicity mechanisms but the effective concentrations obtained cannot be directly extrapolated to *in vivo* situation. Most often the *in vitro* models used are representative of organs that will only be exposed to the tested chemical once it is absorbed and enters the blood stream. Hence, all physiological processes that change the tested chemical concentration in the target organ should be accounted for, through PBPK. Parameters of importance that could introduce mistakes were discussed.

- *Carsten Goebel, Coty, Germany: How to perform risk assessment of a new cosmetic ingredient using new approach methodologies?*

An example of a hair dye was presented. to show that risk assessment, also covering systemic toxicity, can be done without animal testing. For aromatic amine hair dyes of the p-phenylenediamine (PPD)-type, there are robust and consistent *in vivo, ex vivo* and *in vitro* data indicating that these molecules are metabolically transformed by N-acetyltranferase 1 in the skin (first pass effect) and systemically in the liver by N-acetyltranferase 2.
Besides local toxicity, which can today be evaluated using different NAMs, it was shown how to deal with systemic toxicity for this particular case.

- *Gladys Ouedraogo, l'Oréal, France: Case study EU ToxRisk: Parabens*

Case studies play a key role in exploring the value of NAMs in safety assessment. The paraben case study in the field of repeated dose systemic toxicity is part of the EU-Tox

Risk project. The results obtained were used to show the value of the tiered NGRA strategy as put forward by the ICCR.

4. Next steps

The SCCS will discuss all new information during their next WG meetings on Methodologies. Experts may be invited on AD-HOC basis in the future to further discuss some points of interest e.g. for example the TTC values newly proposed by the industry need some more explanation. In that context a list of some impurities, present in recent SCCS dossiers, was prepared for which industry could see whether these would be safe using the new TTC values. Cosmetics Europe replied positively and wishes to continue the dialogue.

As a follow up, the SCCS expressed the idea to write, together with the presenters, a perspective scientific paper to propose a way forward based on different valid and validated NAMs that could be used in the NGRA of new cosmetic compounds for which no experimental animal data exists.

5. Next meeting(s)

26 March 2019

6. List of participants

SCCS Members

1. Dr Ulrike BERNAUER
2. Dr Laurent BODIN
3. Prof. Qasim CHAUDHRY (Chair SCCS)
4. Prof. Pieter-Jan COENRAADS (Vice-chair SCCS)
5. Dr Janine EZENDAM
6. Dr Eric GAFFET
7. Prof. Corrado L. GALLI
8. Dr Berit GRANUM
9. Prof. Eirini PANTERI
10. Prof. Vera ROGIERS (Vice-chair SCCS and chair of the WG)
11. Dr Christophe ROUSSELLE
12. Dr Maciej STEPNIK
13. Prof. Tamara VANHAECKE

SCCS External Experts

14. Dr Aglaia KOUTSODIMOU
15. Dr Alain SIMONNARD
16. Dr Natalie VON GÖTZ

SCHEER members

17. Dr Wim DE JONG
18. Dr Raquel DUARTE-DAVIDSON

19. Dr Rodica Mariana ION
20. Dr Renate KRÄTKE (Vice-chair SCHEER)
21. Dr Ana PROYKOVA
22. Dr Theodoros SAMARAS
23. Dr Theo VERMEIRE (Chair SCHEER)

A**pologies**

24. Prof. Maria DUSINSKA

SCCS Secretariat (DG SANTE C2)

1. Giulio GALLO
2. Natacha GRENIER
3. Diana HEROLD

DG GROW D4

4. Olga TKATCHENKO
5. George MANIKAS
