Introduction and Aims

The Threat of Toxicological Concern (TC) approach is being considered as one of the alternatives for the safety assessment of cosmetics ingredients. In 2012, European Scientific Committees (SCs) published the opinion that the TTC approach in itself is scientifically acceptable for human health risk assessment of systemic toxic effects caused by chemicals present at very low levels [1]. Both SCCS/SCHER/SCENIHR and EFSA reports [2] noted the activities of COSMOS partners in the efforts related to develop a new non-cancer TTC dataset enriched with cosmetics ingredients and to address the oral-to-dermal extrapolation. This poster illustrates the construction process of the TTC dataset including data sources, toxicity data curation process, and the NOAEL/LOAEL decisions through quality control sessions.

Methods

STEP 1: Establish a COSMOS Oral Toxicity Database

1-A. oRepeatDose ToxDB

- A subset of COSMOS DB
- Oral repeat-dose toxicity data were compiled either from the existing sources or harvested according to the following inclusion criteria. (See Figure 1)

1-B. Substance inclusion criteria

- Cosmetics ingredients and chemicals used in cosmetics products
- Chemicals in Cosmetics Inventory (EU CosIng and US PCPC)
- > 60% of US FDA PAFA substances are found in Cosmetics Inventory.

1-C. Study inclusion criteria

<table>
<thead>
<tr>
<th>Study Parameters</th>
<th>Exceptions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study type:</td>
<td>Chronic, Carcinogenicity, Subacute, Subchronic, Reproductive developmental, Neurotoxicity, Immunotoxicity</td>
</tr>
<tr>
<td>Duration:</td>
<td>Treatment time ≥ 28 days</td>
</tr>
<tr>
<td>Species:</td>
<td>Rat/mouse/dog/monkey</td>
</tr>
<tr>
<td>Route:</td>
<td>Oral – dietary, drinking water, gavage</td>
</tr>
<tr>
<td>Dose:</td>
<td>No single dose studies; reasonable dose separation (LD, LD, HD)</td>
</tr>
<tr>
<td>Effects:</td>
<td>- Effects description at dose level</td>
</tr>
<tr>
<td></td>
<td>- Non-neoplastic</td>
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<td></td>
<td>- Systemic effects</td>
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</tbody>
</table>

1-D. Data record reliability criteria

- Categories: EPA ToxRefDB [3], FDA PAFA [4]
- Example: FDA Redbook [5] vs. Core minimum
- Meet the guideline and acceptable studies
  - Meet OPPTS or OCSP guidelines
  - Meet the current standard of FDA Redbook
  - # animal/1000/sex/sex, 3 dose levels, all full scale tests including Inhalation required.

- Not meet the guideline, but meet the database minimum standard
  - Not meet the guidelines, but acceptable literature publications
  - Not meet the current FDA Redbook, but meet the core minimum standard
  - # animal/1000/sex/sex for chronic, min 2 dose levels, clinical signs, food/water consumption, ophthalmology, clinical chemistry not required, hematology with RBC and WBC only, 7 minimum organs for histopath.

- Not meet the minimum/ core standard
  - Deficient studies (data not used)
  - Unsuitable studies (data not used)

1-E. Reference traceability criteria – citations must be traceable.

1-F. Curation Method

- Existing data from FDA PAFA/CERS and ToxDB were automatically imported. Some data from NTP, ECHA substance registration database, and SCCS opinions were manually entered.
- New studies as well as corrections were added to the database by (re)harvesting data. (~ 30% of the PAFA data in the TTC dataset has been revisited.)
- Data entry tool – ToxDB modified for COSMOS use
- Data harvesting – Harvesting organised with a full-time COSMOS toxicologist
- Data record quality control (QC) – scheduled reviews and discussions within COSMOS

References

3. ToxRefDB (USEPA National Center for Computational Toxicology). http://actor.epa.gov/action/ACTRef_ToxRefDB_Help_04f4b2d12010.pdf

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