Decision tree for the safety assessment of botanical cosmetic ingredients

Personal Care Products Council
CIR Science and Support Committee
Using the Decision Tree

• Provided as a guidance tool for finished product manufacturers
  – Not a ‘set in stone’ pathway
  – Flexibility around the various points

• Ingredients need to be evaluated on a case by case basis
  – Even within a group

• Common Sense
  – Cucumber needs less intense review than Ivy Leaf

• Extracts are generally used in low concentrations
Highlighted Notes

- Botanicals are often complex mixtures.
- Their composition is subject to considerable variability
  - Species variation
  - Geographical origin
- May contain high concentrations of potentially toxic constituents - α-solanine
- Botanical materials produced by different methods may differ to some extent and should be fully characterized to assure that there is adequate equivalence.
Decision tree for the safety assessment of botanical cosmetic ingredient

1a. Is the ingredient a traditional food or medicine?

2. Is cosmetic exposure similar to traditional use?

3. Assess local tolerance

4. Is there sufficient safety data to cover the cosmetic use?

5. Is the ingredient well characterized?

6. Are the components similar to traditional food ingredients?

7. Proceed to safety assessment
Decision tree for the safety assessment of botanical cosmetic ingredient

1a. Is the ingredient a traditional food or medicine?
   - Y

2. Is cosmetic exposure similar to traditional use?
   - Y
   - N → 1b. Is the ingredient a part of a traditional food or medicine?
     - Y
     - N
     - ≥ 5. Is the ingredient well characterized?
       - Y → 4. Is there sufficient safety data to cover the cosmetic use?
         - Y → 3. Assess local tolerance
         - N → 7. Proceed to safety assessment
       - N
     - ≥ 6. Are the components similar to traditional food ingredients?
       - Y
       - N → 7. Proceed to safety assessment
   - N
1- The ingredient is a traditional food or herbal drug

- Food may be sourced from cultivated or wild sources and may be from various plant parts such as seeds, berries, leaves, etc.
- The traditional use of a food should be comprehensively substantiated (composition, exposure, quality & history of safe use).
- Novel food and novel food ingredients that have been submitted to a comprehensive assessment and registered as such could be included in this section.
- ‘Traditional’ herbal drugs from botanical sources should have been registered as such according to well defined regulation. The data supporting both their quality and safety should be available.
- The botanical intended to be used as a cosmetic ingredient should be similar to its traditional counterpart used as food and/or herbal drug in terms of composition, specifications and quality and safety.

(Chamomile Flower Tea)
2- Is cosmetic exposure similar to traditional use

• The intended systemic exposure of the botanical ingredient under assessment should be similar to that of its traditional counterpart used as food and / or herbal drug.

(Chamomile aqueous extract)
3- Assess local tolerance

- A large majority of food and herbal drugs could be demonstrated to be safe by ingestion. However, they may contain unknown substances with a potential to produce contact irritation, phototoxicity or photoallergy, skin sensitization or type IV allergy.
- Provided the availability of reliable data the local tolerance of botanicals intended to be used as cosmetic ingredient should be carefully assessed in terms of:
  - Irritation – skin and eye
  - Type IV sensitization
  - Phototoxicity, Photoallergy
1a. Is the ingredient a traditional food or medicine?

2. Is cosmetic exposure similar to traditional use?

3. Assess local tolerance

4. Is there sufficient safety data to cover the cosmetic use?

5. Is the ingredient well characterized?

6. Are the components similar to traditional food ingredients?

7. Proceed to safety assessment

Decision tree for the safety assessment of botanical cosmetic ingredient
4- Is there sufficient safety data to cover cosmetic use

- If the intended systemic exposure of the botanical ingredient under evaluation is superior to that of its traditional counterpart used as a food and/or herbal drug, its systemic safety should be substantiated.
- The safety should be supported by reliable data including in vivo, in vitro, in silico, or human data.
- If the systemic safety of the botanical is demonstrated at the intended exposure then proceed to the local tolerance assessment.

(chamomile oil)
1b- Is the ingredient a part of a traditional food or medicine?

- If yes proceed to Step 2
- If no for the following reasons proceed to Step 5 – Characterization.
  - Plant or plant parts that are not used as food
  - Botanical drugs not registered or without documented safety
  - All other botanical materials including plant parts, processed plant parts, extracts, tinctures, etc. must undergo a rigorous evaluation for safety.
    (non-aqueous chamomile extract)
Decision for the safety assessment of botanical cosmetic ingredient

1a. Is the ingredient a traditional food or medicine?
   - Y
   - N

2. Is cosmetic exposure similar to traditional use?
   - Y
   - N

1b. Is the ingredient a part of a traditional food or medicine?
   - Y
   - N

5. Is the ingredient well characterized?
   - Y
   - N

6. Are the components similar to traditional food ingredients?
   - Y
   - N

4. Is there sufficient safety data to cover the cosmetic use?
   - Y
   - N

3. Assess local tolerance

7. Proceed to safety assessment

Characterize Ingredient
5- Is the ingredient well characterized?

- Appropriate characterization of a plant derived ingredient is crucial both from a botanical and chemical point of view.
- Characterization is the most important component of an accurate and reliable safety risk assessment.
- Characterization includes:
  - Plant-derived Ingredient Identification
  - Chemical Characterization
  - Specifications
1a. Is the ingredient a traditional food or medicine?

Y

2. Is cosmetic exposure similar to traditional use?

N

1b. Is the ingredient a part of a traditional food or medicine?

N

5. Is the ingredient well characterized?

Y

6. Are the components similar to traditional food ingredients?

Y

4. Is there sufficient safety data to cover the cosmetic use?

Y

3. Assess local tolerance

N

7. Proceed to safety assessment

N

Characterize Ingredient

N

Y
**Decision tree for the safety assessment of botanical cosmetic ingredient**

1a. Is the ingredient a traditional food or medicine?  
- **Y**
- **N** 

2. Is cosmetic exposure similar to traditional use?  
- **Y**
- **N**

1b. Is the ingredient a part of a traditional food or medicine?  
- **Y**
- **N** 

5. Is the ingredient well characterized?  
- **Y**
- **N**

6. Are the components similar to traditional food ingredients?  
- **Y**
- **N**

4. Is there sufficient safety data to cover the cosmetic use?  
- **Y**
- **N**

3. Assess local tolerance  
- **Y**
- **N**

7. Proceed to safety assessment
5- *Plant-derived Ingredient Identification*

- **Scientific name (plant family, genus, species, common names)**
  - Part(s) of the plant used
  - Geographic origin (continent, country, region)
  - Cultivar
  - The primary processes (drying, fermentation,…)

- **Extraction method**
5- Chemical Characterization

• Content of macronutrients & micronutrients:
  • Proteins
  • Fats, lipids & fatty acids?
  • Carbohydrates (simple & complex)
  • Vitamins
  • Minerals

• Analytical data on chemical
  • Salicylic acid in willow bark
  • Caffeine in tea

• Analytical data regarding the level of naturally occurring known toxicants
  • Pyrrolizidine alkaloids in comfrey
  • Heavy metals
  • Cyanogenic glycosides from almond
5- Chemical Characterization

• A chromatographic ‘fingerprint’ of specific marker chemicals is encouraged to:
  – define the variability of botanicals
  – detect adulteration and therefore confirm authenticity

• A detailed chemical composition and concentration data are needed for a Threshold of Toxicological Concern (TTC) approach
7- Proceed to safety assessment

- Safety Assessment may include the following (alone or in combination)
  - TTC (Threshold of Toxicological Concern)
  - Read Across/Chemical Grouping
    - Joint FAO/WHO Expert Committee on Food Additives (JECFA)
  - *In Silico*
    - SAR (Structure Activity Relationship)
    - Metabolic Profiling
  - *In Vivo* and/or *In Vitro* Assays