Safety Assessment and Regulatory Aspects of Consumer Goods

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SOT Annual Meeting, Sunday, March 11, 2018

The Main Goals of this Presentation Are:

• Overview of the different types of companies related to consumer goods

• Clarify to the audience the different roles in which the toxicologist may be involved

• Overview of safety assessment of consumer goods:
  • Cosmetics
  • Biocides
  • Medical devices

• Regulatory aspects of safety assessment
When I finish college/grad school I want to be a toxicologist in private industry

Consumer Goods!!!
What All These Products Have in Common?

- They are all used by millions of consumers every day
  - Adults, children, infants, and pets may be exposed
- They are broadly available on shelves
  - (over-the-counter (OTC), cleaners, bactericidal, cosmetics, personal care, vitamins and minerals, etc.)
- They must be safe when used under normal use instructions
- They are chemical-based (most likely)
- They have fragrances
- They have botanicals

What are the Differences Between Them?

- They may be used by the consumer in the house
- They may be used on the consumer
- Some need pre market registration:
  - Depending on country
  - Depending on claims
  - Depending on use instructions
They are Fun to Work With!

- Touch lives of billions of consumers every day!

- Different challenges

- Different route of exposure

- Different regulatory bodies

- Global opportunities

What Toxicologists Do in Consumer Goods Companies? (Depends a Lot on the Company!)

- Product Safety
  - Claim Support
  - Clinical support
  - Postmarket surveillance

- Regulatory management public relations (consumer relations)

- Legal team support
How We Do Product Safety?

- Product classification
  - Is it a cosmetic/OTC/drug/quasi drug/medical devices?
  - Is it a cleaner or a biocide/pesticide?
- Does it have active ingredients/monographed?
- In which geographies is it being launched?
- Claims substantiation?

When and How We Assess Safety?

Science-Based Safety Evaluation and Regulatory Compliance
Product Classification (Example: Cosmetics)

- Classification may vary with geography
- May vary with claims
- Pre-market registration will vary with
  - Geography
  - Claims
  - Composition

Cosmetics

- EU: "any substance or preparation intended to be placed in contact with the various external parts of the human body (epidermis, hair system, nails, lips and external genital organs) or with the teeth and the mucous membranes of the oral cavity with a view exclusively or mainly to cleaning them, perfuming them, changing their appearance and/or correcting body odours and/or protecting them or keeping them in good condition."
- Canada: "any substance or mixture of substances, manufactured, sold or represented for use in cleansing, improving or altering the complexion, skin, hair, or teeth and includes deodorants and perfumes."
- US: "articles intended to be rubbed, poured, sprinkled, or sprayed on, introduced into, or otherwise applied to the human body...for cleansing, beautifying, promoting attractiveness, or altering the appearance"
Examples

<table>
<thead>
<tr>
<th></th>
<th>USA</th>
<th>Canada</th>
<th>EU</th>
<th>Japan</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antiperspirant</td>
<td>OTC</td>
<td>Cosmetics</td>
<td>Cosmetics</td>
<td>Quasi drug</td>
</tr>
<tr>
<td>Hair dyes</td>
<td>Cosmetics</td>
<td>Cosmetics</td>
<td>Cosmetics</td>
<td>Quasi drug</td>
</tr>
<tr>
<td>Lipsticks</td>
<td>Cosmetics</td>
<td>Cosmetics</td>
<td>Cosmetics</td>
<td>Cosmetics</td>
</tr>
<tr>
<td>Sunscreens</td>
<td>OTC</td>
<td>Drug (Monographed) or Natural Product</td>
<td>Cosmetics (Compliant with Regulations)</td>
<td>Cosmetics (Compliant with Regulations)</td>
</tr>
<tr>
<td>Toothpaste</td>
<td>Fluoride (Monographed)</td>
<td>Cat IV Monographed NHP</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

US Regulation: Drug or Cosmetic? (FD&C Act):

- **Cosmetics:** "for cleansing, beautifying, promoting attractiveness, or altering the appearance"
- **Drug:** "articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease" and "articles (other than food) intended to affect the structure or any function of the body of man or other animals"
- **Mixed:**
  - shampoo (cosmetic); antidandruff (drug); toothpastes (with fluoride: =drug), deodorants that are also antiperspirants, and moisturizers and makeup marketed with sun-protection claims.
- **Claims:**
  - Restore hair growth, reduce cellulite, treat varicose veins, increase or decrease the production of melanin (pigment) in the skin, or regenerate cells
  - Essential oils: fragrance=cosmetics, sleep aid, quit smoking, reducing pain=drug
Safety of Cosmetics

• What are the important factors in safety?
  • Safety of the product itself (microbial contamination)
  • Safety of the consumer that will be exposed to the product
  • Safety of the package
  • Safety of the environment ** (we will focus on consumer safety → people and their pets)

What Do We Have to Assess in the Finished Product?

- Raw material
  - Main component : Ingredient(s) =INCI + Impurities △

- Reactant in the bulk

- Chemical reaction of the ingredients
  - Oxidation reaction, Decomposition reaction etc.

- Bleeding out from the container
  - Plasticizer
  - Antioxidant
  - Additive etc.
Chemical Hazard Identification

- All Literature available
  - Public
  - Trade associations
- Internal databases
- Supplier Information
- Regulatory perspective:
  - No animal work can be done for products to be launched in Europe and other geographies
- Alternative methods
Examples of Literature Search Strategy

- Personal Care Products Council, PCPC
- Agency for Toxic Substances and Disease Registry, ATSDR
- California Prop 65, prop65
- National Industrial Chemicals Notification and Assessment Scheme (Australia), NICNAS
- Scientific Committee on Consumer Safety (SCCS), SCCS
- US Environmental Protection Agency, EPA SRS
- National Toxicology Program, NTP (Database Search)
- eChemPortal
- Hazardous Substances Data Bank, HSDB
- INCH EM, INCHEM
- ACToR
- TOXNET
- Chemical Carcinogenesis Research Information System, CCRIS
- Genetic Toxicology Data Bank, GENETOX
- Carcinogenic Potency Database, CPDB
- European Food Safety Authority (EFSA), EFSA
- Cosmos Database, Cosmos
- European Commission Database, cosing
- Fragrance and Flavor Database, RIFM/FEMA
- Health Canada
- Human and Environmental Risk Assessment, HERA
- NIH PubChem
- US FDA cosmetics ingredients
- European Chemicals Agency, ECHA
- Household Products Database
- Google

Prepare a Hazard Summary–Endpoints

- **Local effects**
  - Skin irritation
  - Eye irritation
  - Skin sensitization
  - Photo-toxicity

- **Systemic effects**
  - Genotoxicity (mutagenicity, clastogenicity)
  - Carcinogenicity
  - Internal organ toxicity
  - Developmental toxicity
  - Reproductive toxicity
  - Type I allergy (if needed)
Raw Material Assessment

- Composed of intentionally added chemicals and impurities
- Generally new raw material → completely new material, new supplier, replacement

Raw Material Name: Welcome to SOT
Use (up to 35% in a cleansing oil)

<table>
<thead>
<tr>
<th>Name</th>
<th>CAS</th>
<th>[] high</th>
</tr>
</thead>
<tbody>
<tr>
<td>MIPA-Laureth Sulfate</td>
<td>118742-72-8</td>
<td>42.48</td>
</tr>
<tr>
<td>Laureth-3</td>
<td>68439-50-9</td>
<td>42.48</td>
</tr>
<tr>
<td>Laureth-7 Citrate</td>
<td>565429-75-6</td>
<td>15</td>
</tr>
<tr>
<td>Tocopherol</td>
<td>1406-66-2</td>
<td>0.03</td>
</tr>
<tr>
<td>Hydrogenated Palm Glycerides Citrate</td>
<td>91052-16-3</td>
<td>0.01</td>
</tr>
</tbody>
</table>

[ ]=Concentration

Raw Material Impurities

<table>
<thead>
<tr>
<th>Name</th>
<th>CAS</th>
<th>amount</th>
<th>units</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethylene Oxide</td>
<td>75-21-8</td>
<td>0.0001</td>
<td>% IMPURITY</td>
</tr>
<tr>
<td>1, 4 Dioxane</td>
<td>123-91-1</td>
<td>0.001</td>
<td>% IMPURITY</td>
</tr>
<tr>
<td>Nickel</td>
<td>7740-02-0</td>
<td>0.0002</td>
<td>% IMPURITY</td>
</tr>
<tr>
<td>Lead</td>
<td>7439-92-1</td>
<td>0.001</td>
<td>% IMPURITY</td>
</tr>
<tr>
<td>Cadmium</td>
<td>7440-43-9</td>
<td>0.0002</td>
<td>% IMPURITY</td>
</tr>
<tr>
<td>Mercury</td>
<td>7439-97-6</td>
<td>0.0001</td>
<td>% IMPURITY</td>
</tr>
<tr>
<td>Arsenic</td>
<td>7440-38-2</td>
<td>0.0001</td>
<td>% IMPURITY</td>
</tr>
<tr>
<td>Nitrosamines</td>
<td></td>
<td>0.000005</td>
<td>% IMPURITY</td>
</tr>
</tbody>
</table>
Exposure

**Route** of Exposure

- The route (site) of exposure is an important determinant of the ultimate dose—different routes may result in different rates of absorption.
  - Dermal (skin)
  - Inhalation (lung)
  - Oral ingestion (Gastrointestinal)
  - Injection
- The route of exposure may be important if there are tissue-specific toxic responses.
- Toxic effects may be local or systemic

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Society of Toxicology - 2008

Exposure

**Time** of Exposure

- How long an organism is exposed to a chemical is important

**Duration** and **frequency** contribute to dose. Both may alter toxic effects.

- **Acute** Exposure=usually entails a single exposure
- **Chronic** Exposures=multiple exposures over time (frequency)
### Exposure-Based Risk Assessment of Consumer Goods

**Key Considerations**

- **Type and size of exposed population**
- **Stage of development**
- **Route of exposure**
- **Body surface location**
- **Frequency of use**
- **Interferences within product**
- **Percutaneous absorption**
- **Excessive use pattern**
- **Quantity applied**
- **Concentration in product**
- **Rinse-off leave-on**
- **Type of product**
- **Type and size of exposed population**
- **Duration of contact**

### Considerations in Exposure

<table>
<thead>
<tr>
<th>Consideration</th>
<th>Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surface Area</td>
<td>CM²</td>
</tr>
<tr>
<td>Product Remaining on Skin</td>
<td>%</td>
</tr>
<tr>
<td>Absorption of Material</td>
<td>%</td>
</tr>
<tr>
<td>% of Lifetime Exposure Duration</td>
<td>%</td>
</tr>
<tr>
<td>Application of Product</td>
<td>G/Use</td>
</tr>
<tr>
<td>Conversion Factor</td>
<td>MG/G</td>
</tr>
<tr>
<td>Frequency Developmental</td>
<td>Uses/Day</td>
</tr>
<tr>
<td>Type I Allergy Ratio</td>
<td></td>
</tr>
<tr>
<td>Body Weight</td>
<td>KG</td>
</tr>
<tr>
<td>Dilution</td>
<td>%</td>
</tr>
<tr>
<td>Frequency of Use</td>
<td>Uses/Day</td>
</tr>
</tbody>
</table>

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*Betina J. Lew*
Raw Material Name: North Carolina Loves Your Skin
Use (up to 35% in a cleansing oil) → exposure assessment

<table>
<thead>
<tr>
<th>Name</th>
<th>CAS</th>
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<th>[] product</th>
<th>exposure (mg/day)</th>
<th>exposure mg/kg/day</th>
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<tr>
<td>MIPA-Laureth Sulfate</td>
<td>118742-72-8</td>
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<td>25.2756</td>
<td>0.42126</td>
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<td>42.48</td>
<td>14.868</td>
<td>25.2756</td>
<td>0.42126</td>
</tr>
<tr>
<td>Laureth-7 Citrate</td>
<td>565429-75-6</td>
<td>15</td>
<td>5.25</td>
<td>8.925</td>
<td>0.14875</td>
</tr>
<tr>
<td>Tocopherol</td>
<td>1406-66-2</td>
<td>0.03</td>
<td>0.0105</td>
<td>0.01785</td>
<td>0.0002975</td>
</tr>
<tr>
<td>Hydrogenated Palm Glycerides Citrate</td>
<td>91052-16-3</td>
<td>0.01</td>
<td>0.0035</td>
<td>0.00595</td>
<td>9.91667E-05</td>
</tr>
</tbody>
</table>

Cleansing oil 35% 1.7g

Safety Assessment Guidelines

• THE Scientific Committee on Consumer Safety (SCCS) → notes of guidance for the testing of cosmetic ingredients and their safety evaluation (main source for cosmetic Habits and Practices)


• US EPA exposure handbook

Adobe Acrobat Document
Safety Assessment of Finished Product

- Ingredients (Hazard assessment → hopefully already done!)
- Type of product
- Exposure
  - Amount used
  - Frequency of use
  - Target population
  - Routes of exposure
- Micro
- All studies available
- Use instructions
- Claims
- Post-market surveillance

Summary

- Consumer goods=many different product categories
- Different regulations require different studies/assessment
- Claims may affect classification
- Work closely with clinical and regulatory
Questions?