

Safety Assessment and Regulatory Aspects of Consumer Goods

Betina J. Lew, PhD, DABT, ERT

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!!!





And many more!!!!

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

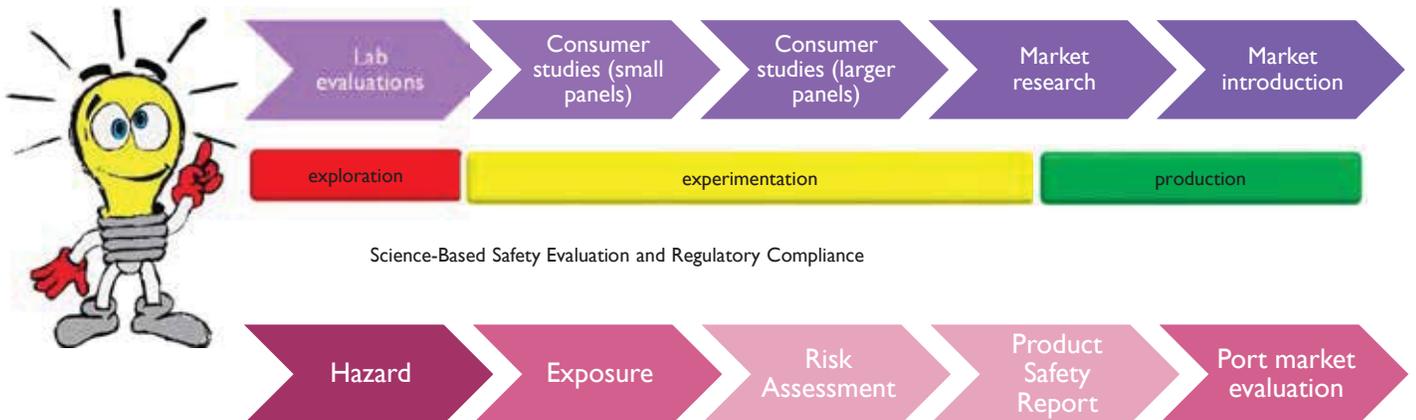
What Toxicologists Do in Consumer Goods Companies? (Depends a Lot on the Company!)

- 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?



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

	USA	Canada	EU	Japan
Antiperspirant	OTC	Cosmetics	Cosmetics	Quasi drug
Hair dyes	Cosmetics	Cosmetics	Cosmetics	Quasi drug
Lipsticks	Cosmetics	Cosmetics	Cosmetics	Cosmetics
Sunscreens	OTC	Drug (Monographed) or Natural Product	Cosmetics (Compliant with Regulations)	Cosmetics (Compliant with Regulations)
Toothpaste	Fluoride (Monographed)	Cat IV Monographed NHP		

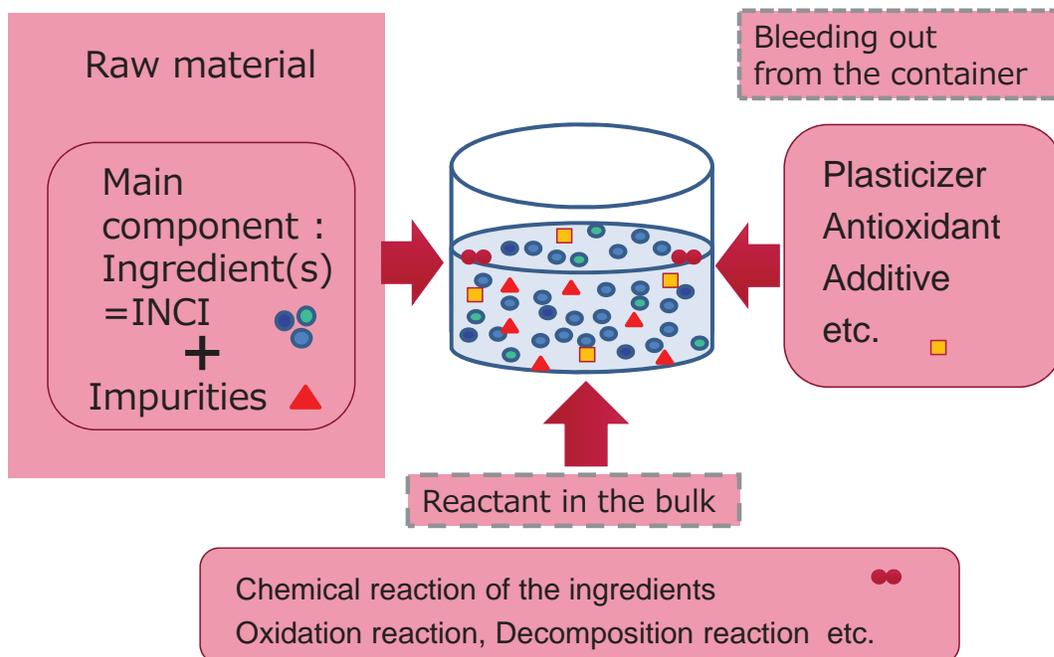
US Regulation: Drug or Cosmetic? (FD&C Act):

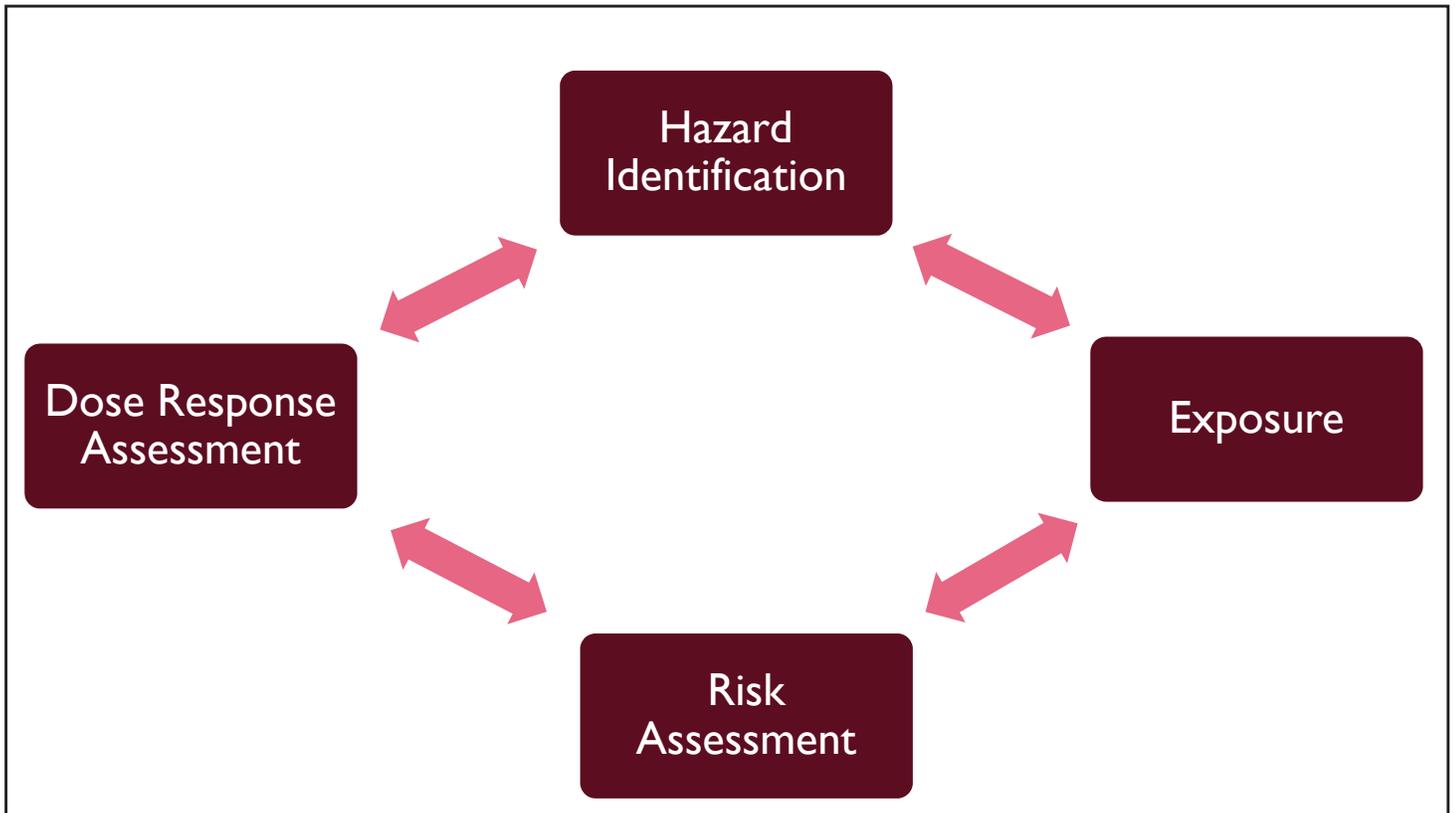
- Cosmetics: "for cleansing, beautifying, promoting attractiveness, or altering the appearance"
- Drug: "articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease" and "articles (other than food) intended to affect the structure or any function of the body of man 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?





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	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	eChemPortal
Hazardous Substances Data Bank	HSDB
INCHEM	IPCS-INCHEM
ACToR	ACToR
TOXNET	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	Health Canada
Human and Environmental Risk Assessment	HERA
NIH PubChem	PubChem
US FDA cosmetics ingredients	Cosmetics Ingredients FDA
European Chemicals Agency	ECHA
Household Products Database	household prod
Google	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)

Name	CAS	[] high
MIPA-Laureth Sulfate	118742-72-8	42.48
Laureth-3	68439-50-9	42.48
Laureth-7 Citrate	565429-75-6	15
Tocopherol	1406-66-2	0.03
Hydrogenated Palm Glycerides Citrate	91052-16-3	0.01

[]=Concentration

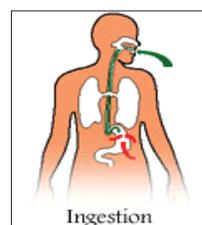
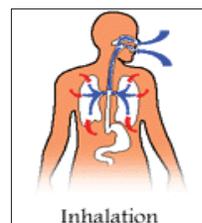
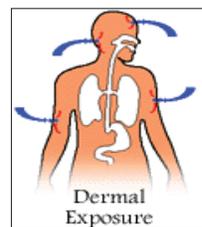
Raw Material Impurities

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

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



Society of Toxicology - 2008

Exposure

Time of Exposure

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

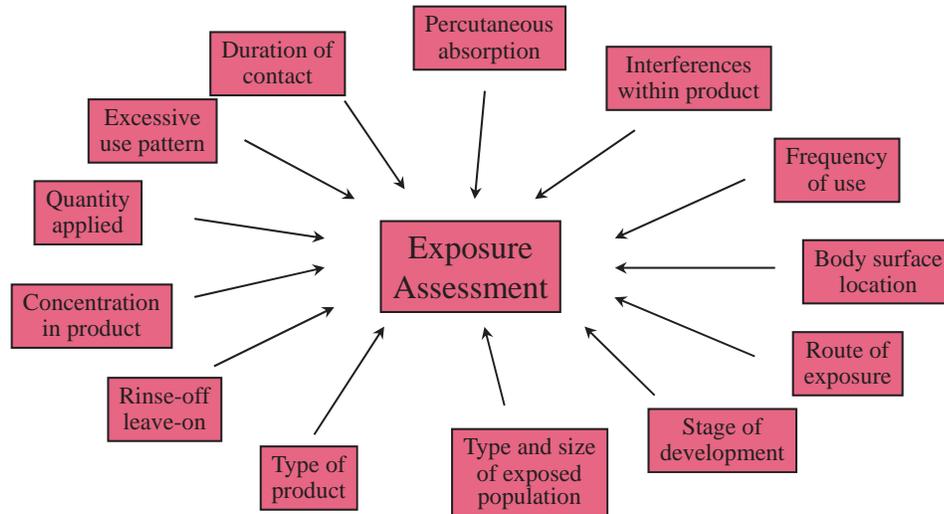
Duration and frequency contribute to **dose**. Both may alter toxic effects.

- **Acute** Exposure=usually entails a single exposure
- **Chronic** Exposures=multiple exposures over time (frequency)



Society of Toxicology - 2008

Exposure-Based Risk Assessment of Consumer Goods → Key Considerations



Considerations in Exposure

Surface Area	CM ²
Product Remaining on Skin	%
Absorption of Material	%
% of Lifetime Exposure Duration	%
Application of Product	G/Use
Conversion Factor	MG/G
Frequency Developmental	Uses/Day
Type I Allergy Ratio	
Body Weight	KG
Dilution	%
Frequency of Use	Uses/Day

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

Name	CAS	[] high	[] product	exposure (mg/day)	exposure mg/kg/day
MIPA-Laureth Sulfate	118742-72-8	42.48	14.868	25.2756	0.42126
Laureth-3	68439-50-9	42.48	14.868	25.2756	0.42126
Laureth-7 Citrate	565429-75-6	15	5.25	8.925	0.14875
Tocopherol	1406-66-2	0.03	0.0105	0.01785	0.0002975
Hydrogenated Palm Glycerides Citrate	91052-16-3	0.01	0.0035	0.00595	9.91667E-05

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)
- http://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccs_o_190.pdf
- 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?

