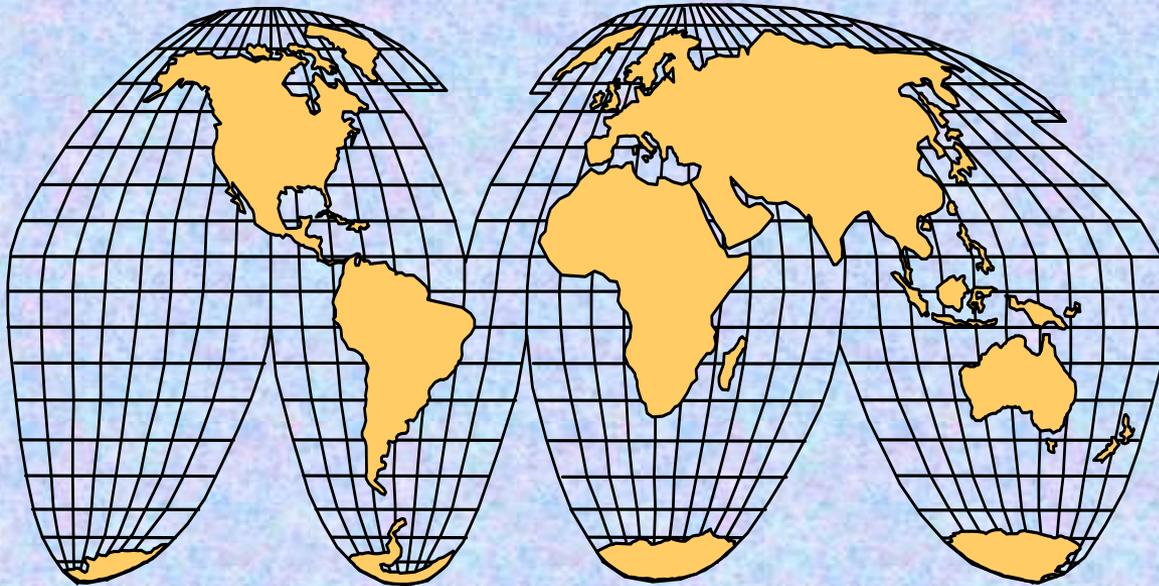


NANOTECHNOLOGY & COSMETIC SAFETY



A WORLD OF SAFE PRODUCTS
Bob Hamilton - Amway

HOW DO YOU DEFINE SAFETY?

**A clear definition gives
a clear target**

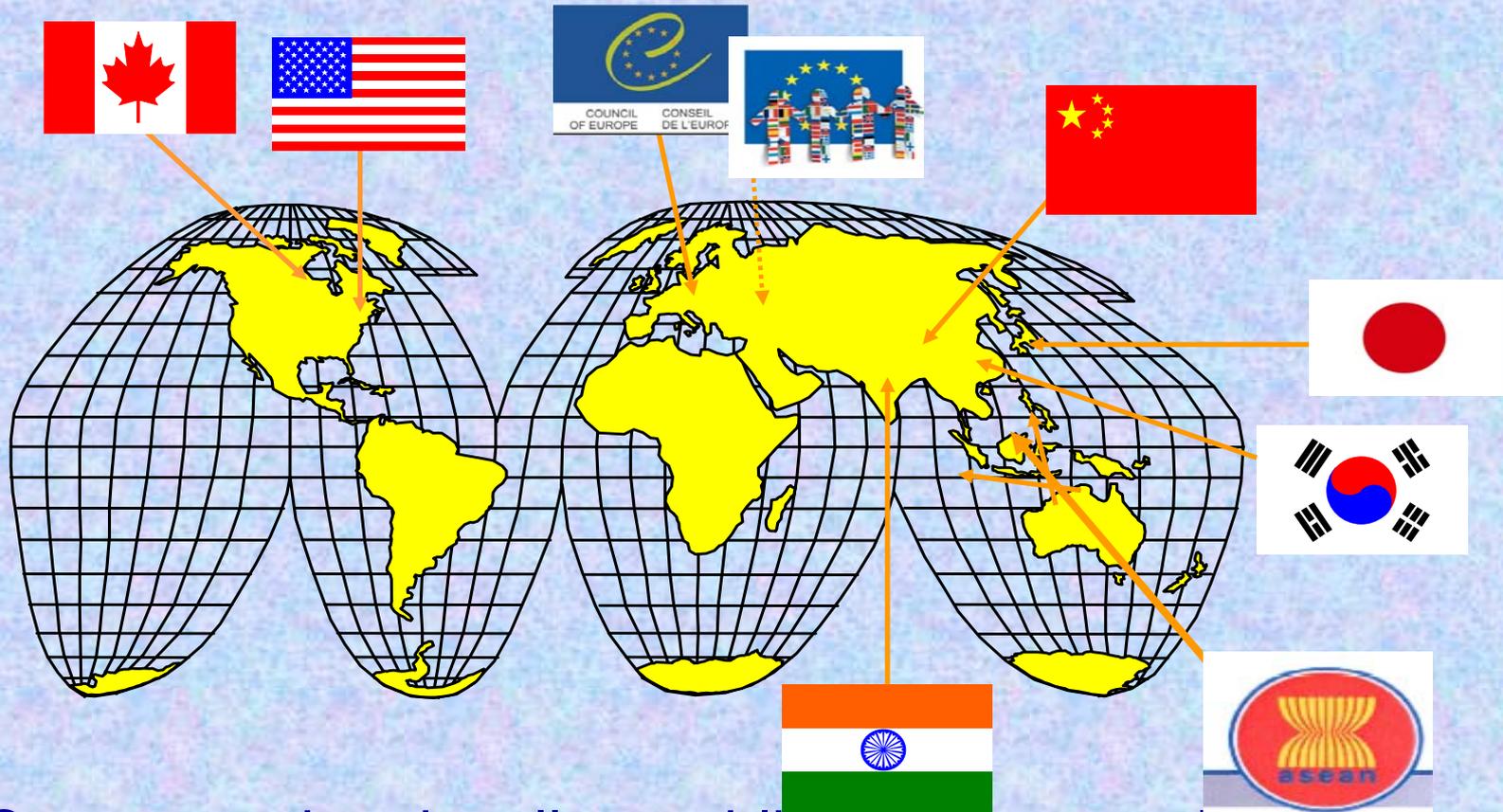




Safe as used = acceptable risk

- Potential hazards
 - Immediate/visible (skin/eye reactions)
 - Long term/hidden (systemic reactions)
 - Ingredients/ formula combination/ interaction
- Exposure
 - route, duration, frequency, amount
- Special populations?
- What risk is acceptable?

Compliance Requirements



Country and regionally established laws regulate cosmetic manufacturing, importation, marketing.
Those laws specifically address product safety.



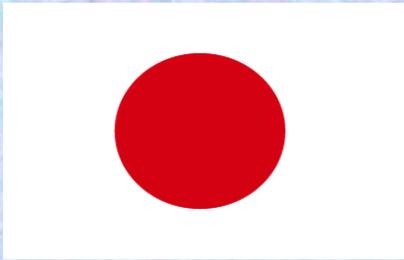
US Compliance

FOOD DRUG AND COSMETIC ACT. Sec. 361.

Adulterated cosmetics: A cosmetic shall be deemed to be adulterated--If it bears or contains any poisonous or ***deleterious substance which may render it injurious to users*** under the conditions of use prescribed in the labeling thereof, or ***under such conditions of use as are customary or usual ...***

FDA cannot require pre-market safety testing of cosmetic products. If, however, the safety has not been substantiated, that product label must read

"WARNING: The safety of this product has not been determined."



Japan Compliance

PHARMACEUTICAL AFFAIRS LAW OF JAPAN (1960; 2005).

Controls and regulates drugs, quasi-drugs, cosmetics and medical devices to assure quality, efficacy, and **safety**.

Approval to manufacture or import “shall be based on an examination of the name, ingredients and quantities, directions, dosage, indications and effects, properties, side effects, etc. of the drug, quasi-drug, **cosmetic**, or medical device.” using an application process

Application process Article 18, 3 (3): The data which must be attached to the applications for approval to manufacture or import cosmetics:

- data concerning the origin of the cosmetic, the background of its discovery, and the conditions of use in foreign countries
- data concerning physicochemical properties
- data concerning **safety**



EU Compliance

Council Directive 76/768/EEC is designed to protect consumer health from possible deleterious effects **due to the presence of specific substances** or preparations which harm humans because of their intrinsic unsafe properties.

Council Directive 93/35/EEC, Article 2 amendment

“A cosmetic product put on the market within the Community must not cause damage to human health when applied under **normal or reasonably foreseeable conditions of use**, taking into account, in particular, the product’s presentation, its labeling, any instructions for its use and disposal as well as any other indication or information provided by the manufacturer or his authorized agent or by any other person responsible for placing the product on the Community market”.

Enforcement



- No pre-market formula approval
- Safety Data required; Format variation
- In market surveillance, inspect for cause
- Positive lists (Negative lists) of ingredients
- Guidance Advice:
 - Informal – CIR
 - Formal – SCCP
- Facility & Import inspection



NOTE:

- Country specific testing – non-standard protocols; local laboratory
- Animal testing limitations



SINGLE GLOBAL SAFETY STANDARD

- **Local Tissue Effects--Good Tolerance**
- **Systemic Toxicity**
- **Documentation as required**

Expected Safety Data

EU Council Scientific Committee for Consumer Product issues cosmetic safety scientific opinions for ingredients and safety evaluation procedures. Including:

Tolerance to Product

- Skin Irritation
- Skin Allergy
- Eye Irritation
- Photoirritation and photoallergy

Systemic Effects of Raw Materials

- Organ system effects
- Reproductive effects
- Genotoxicity and cancer

Risk assessment procedures

Default exposure assumptions



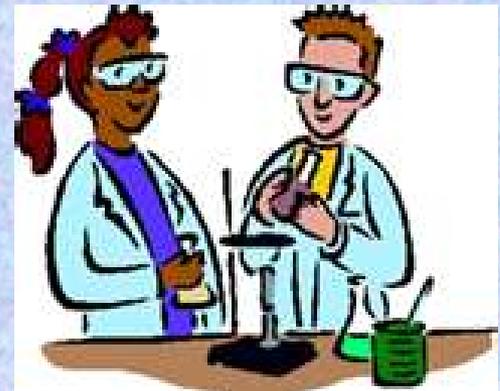
FORMULA SAFETY TESTS

- **(H)RIPT for skin allergy**
- **Patch tests for irritation**
- **Exaggerated use with expert assessment**
- ***In vitro* eye irritation studies**
- **Special studies exposure.**
- **General tolerance in-use.**
 - Consumer studies
 - Marketing history
 - Published information

SYSTEM EFFECTS CALCULATION TOXICOLOGY STUDIES

Calculated Margin of Safety:

- No Adverse (animal) Effect Level = NO(A)EL.
- Estimate ingredient exposure via product (Default guidance values)
- Calculated margin of safety = lowest NO(A)EL divided by systemic exposure for each raw material
- MOS for each RM must be ≥ 100 for organ system effects (CMR excluded)
- Data Sources:
 - Published literature
 - Supplier data



ADVERSE EVENT SURVEILLANCE

- Poison Control – First Response
- In House Data Collection & Screening
 - Evaluate by exposure
 - By ingredient
 - By population
- Qualified Safety Assessment
 - Incorporate AE in safety summary

Safety Considerations for Novel Ingredients & Forms

- Available research prioritized by proximity to product application.
- Additional weight given to “quality of study” and evidence of human experience.
- High “precautionary” concern for consumer safety.
- Use of risk paradigms in assessment & management of consumer use and product manufacture.

Safety Considerations for Nanotechnology

- Consistency with particulate ingredient experience.
- Confidence in risk management safety history.
- Health value of sunscreen applications.
- Data currently indicate acceptable margins of safety vs. benefit.

Additional Considerations for Nanotechnology

- Manufacturing Controls
 - EH&S Oversight & Protection
 - OSHA
- Environmental impact
 - Manufacturing
 - Consumer Use
 - Disposal