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The Accidental Toxicologist
A Career in the Science of Poisons

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What is Toxicology?

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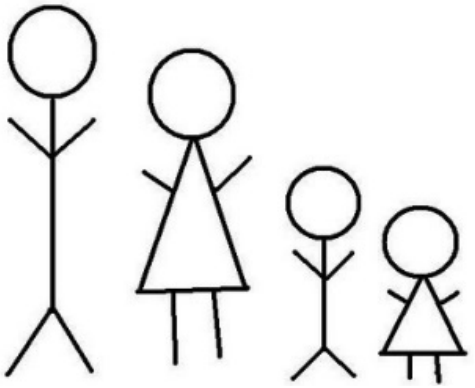
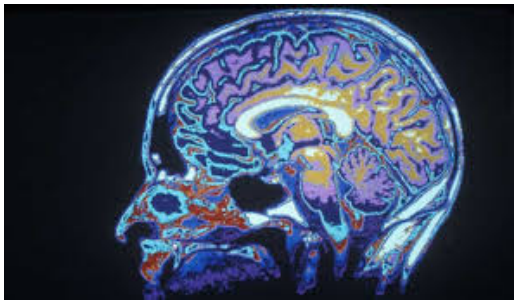
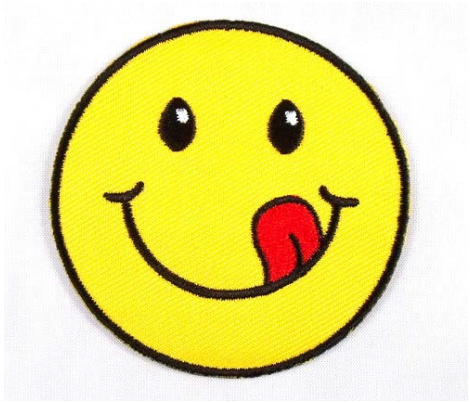
Study of the adverse *effects* of *chemicals* on living *organisms*

Exposure → Dose → Effects





The *dose* makes the poison…



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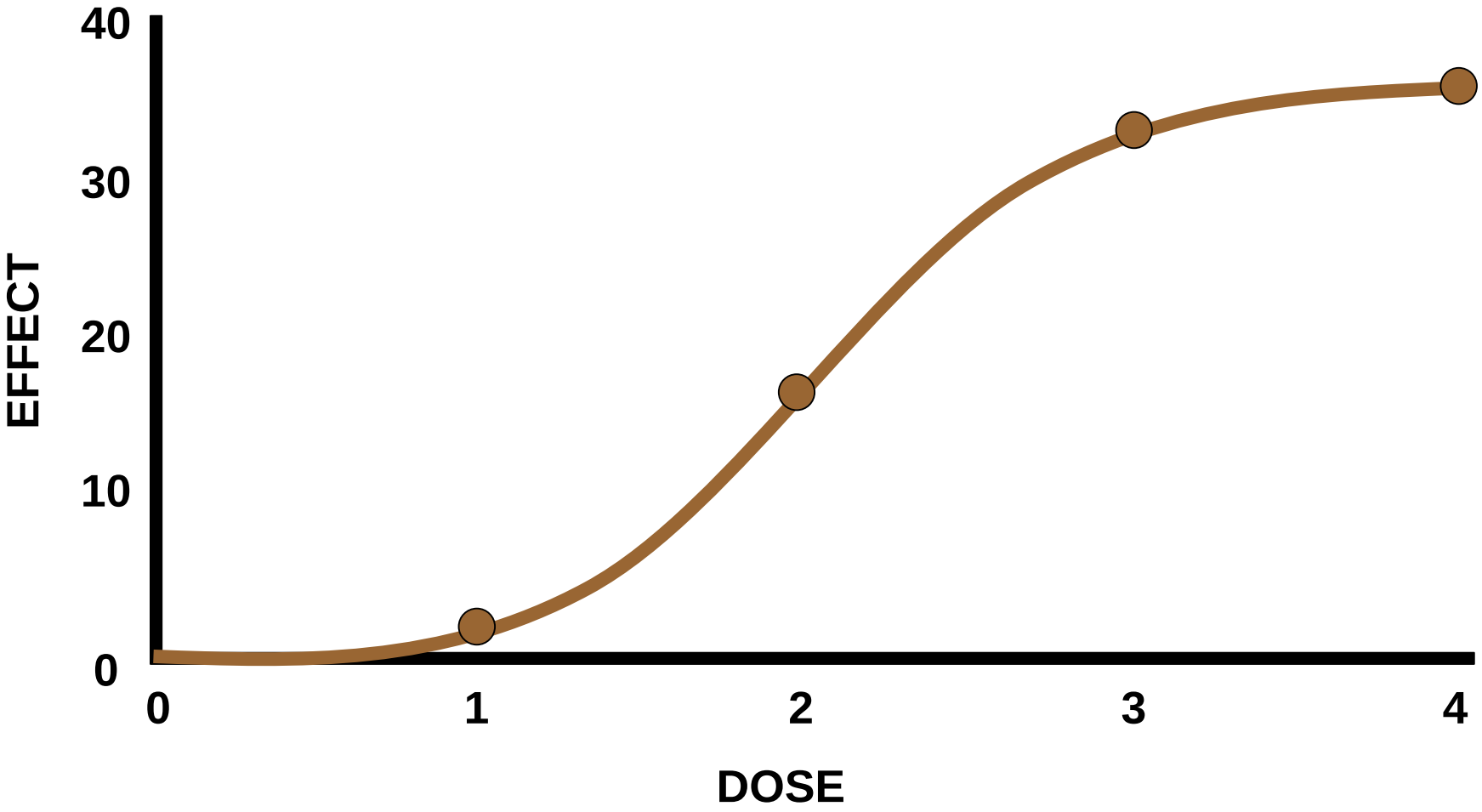
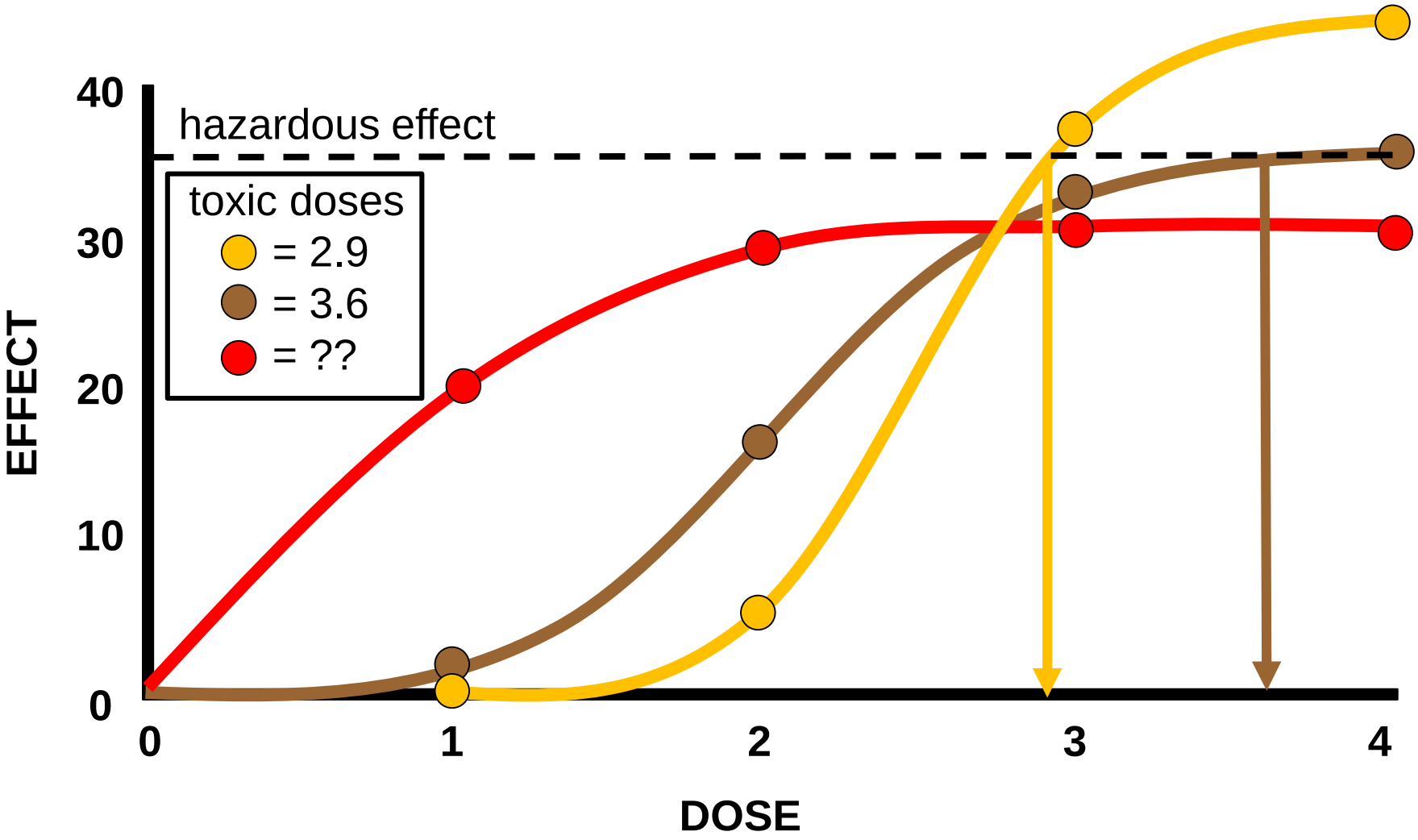
… but *what* dose?

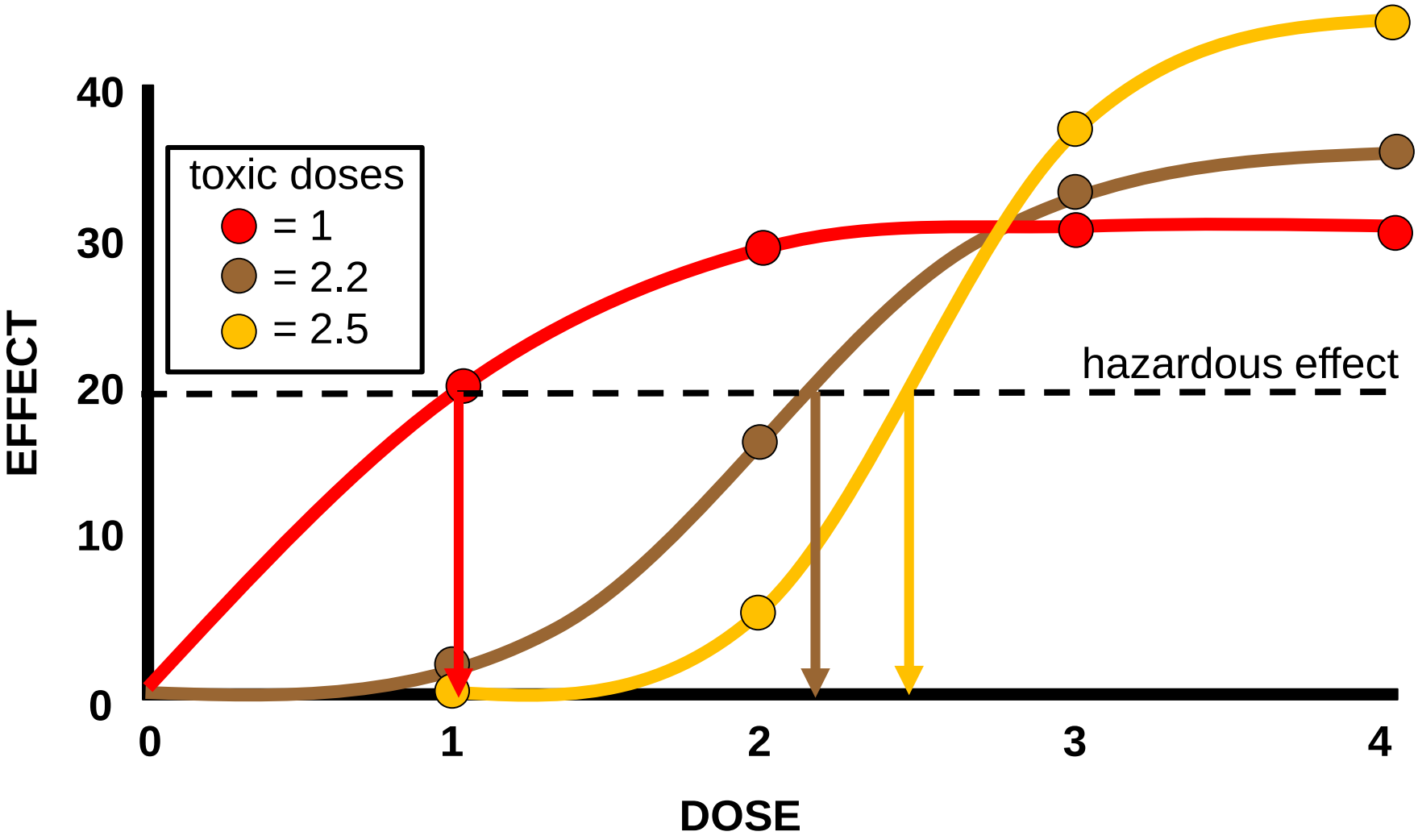
Dose Response Analysis



Determining Hazard



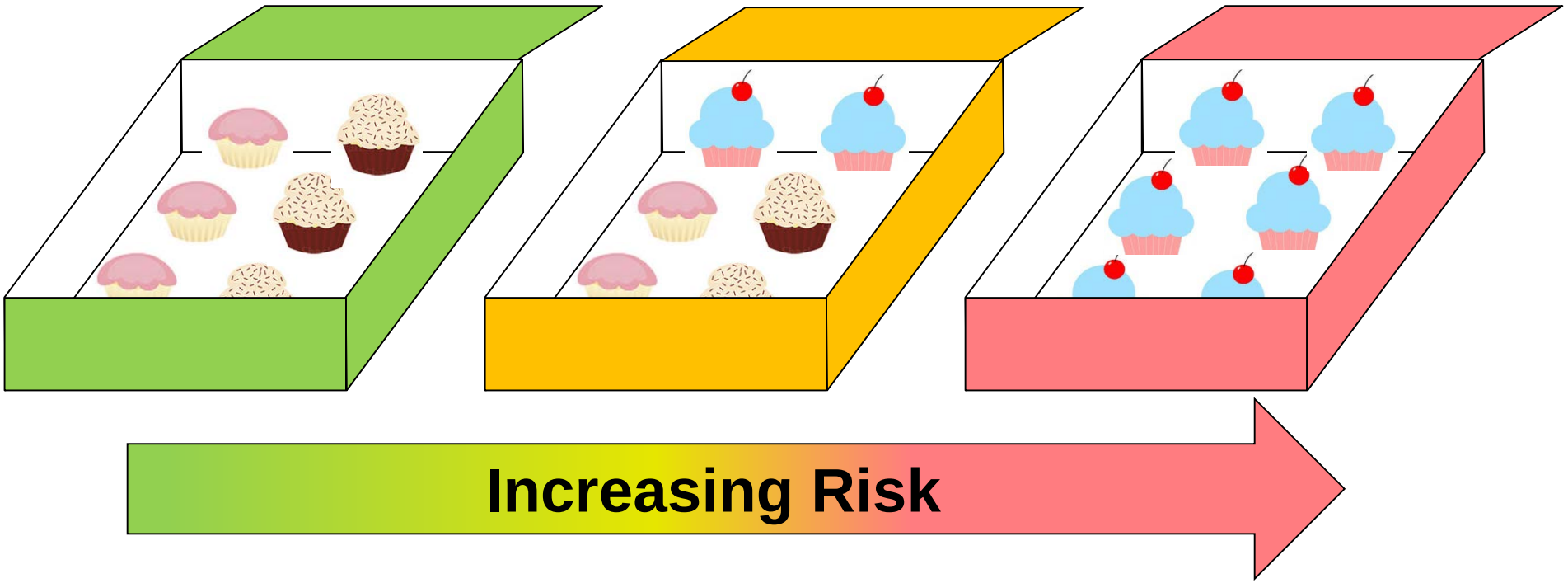
Determining Hazard



Determining Risk

Risk = probability of effect from *hazard* under given *exposure*

Risk = f (Hazard x Exposure)



A challenge for regulatory toxicologists

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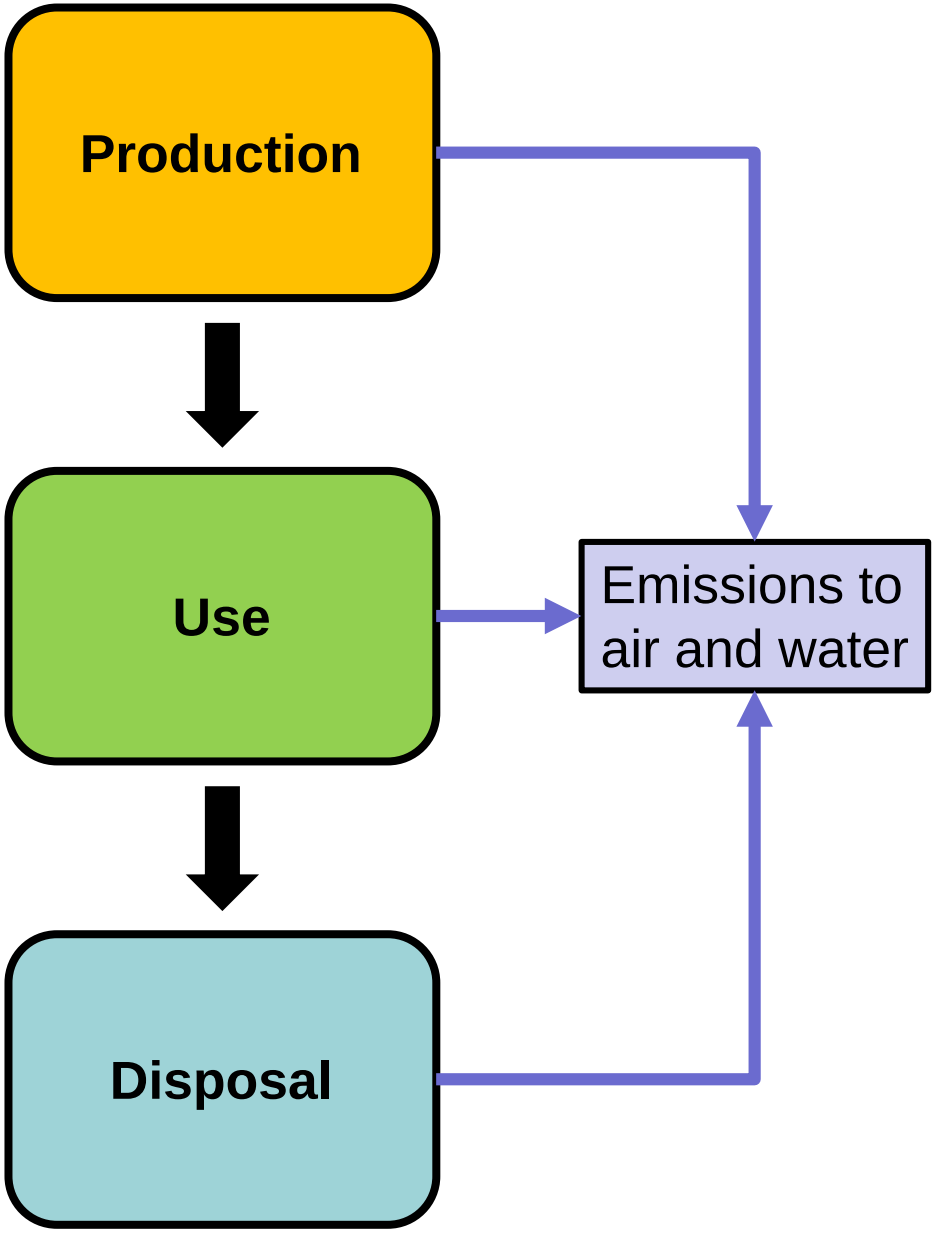
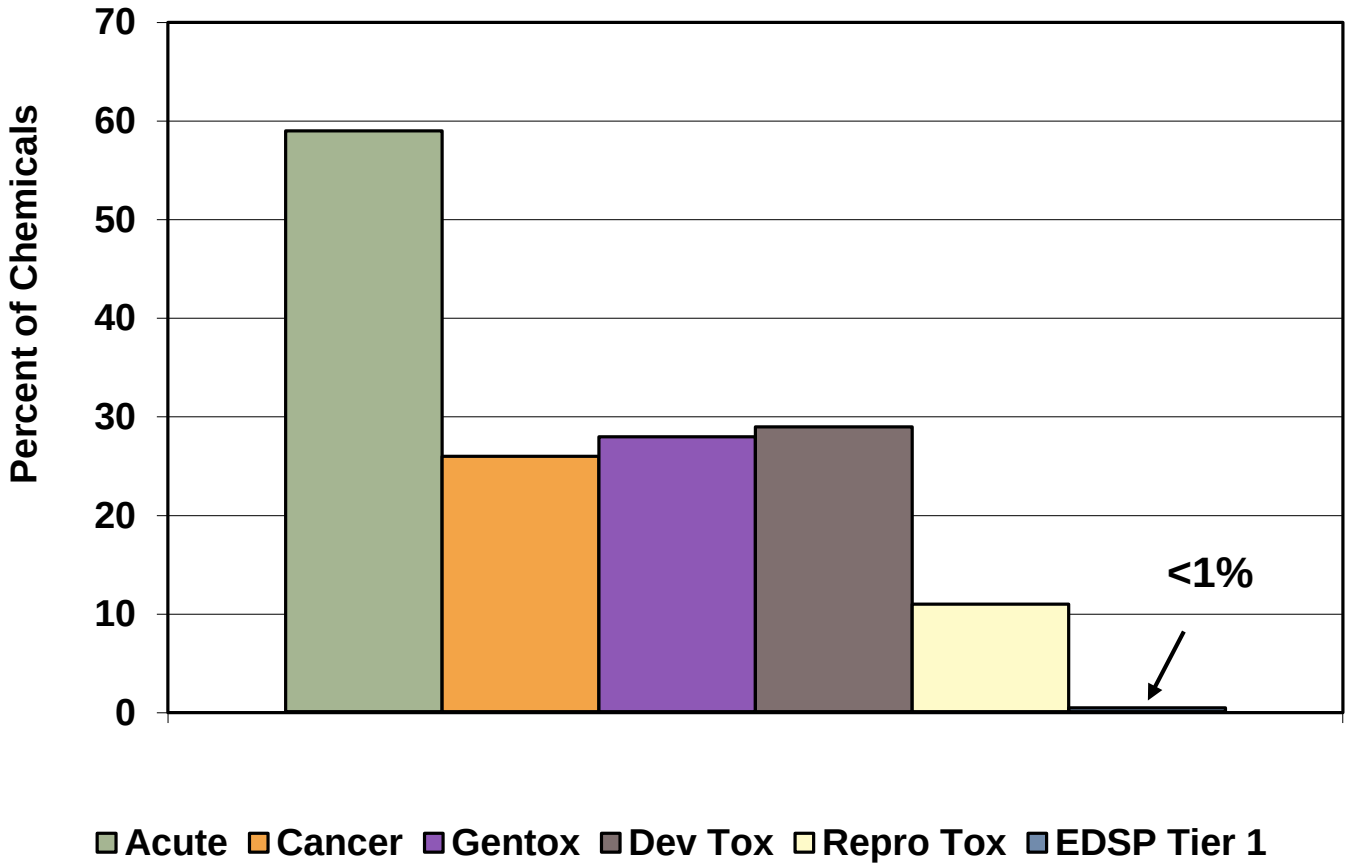
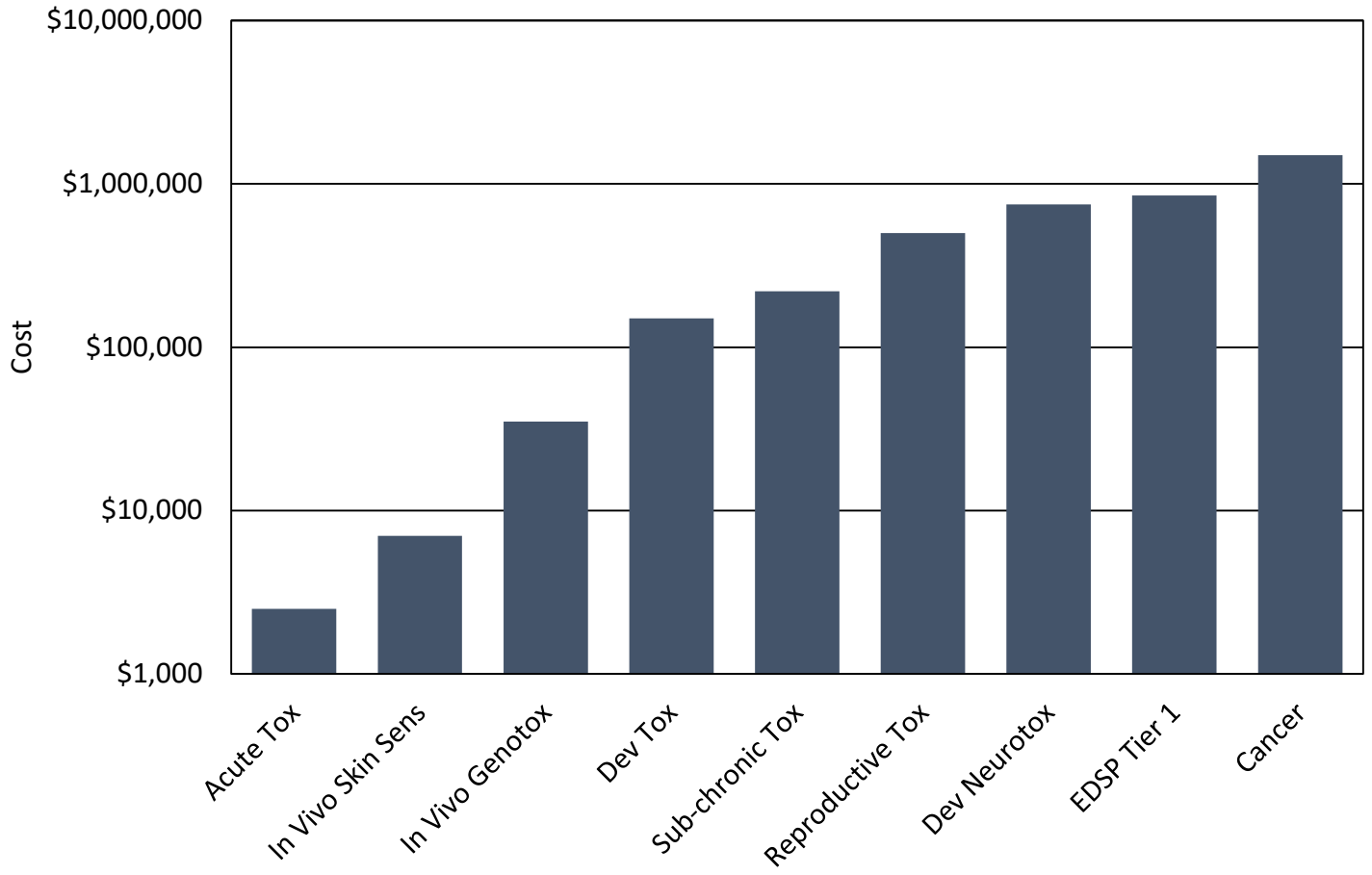


Too many chemicals, not enough data



Modified from Judson, et al *EHP* (2010)

Economic cost of current test methods



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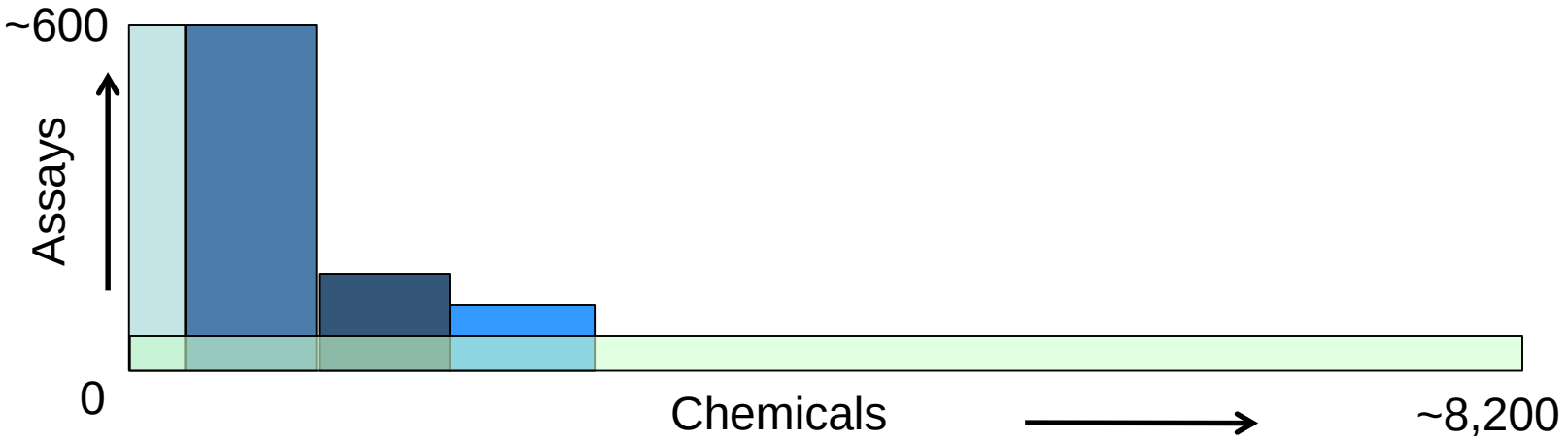
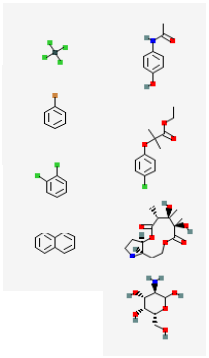
High-Throughput Screening for Toxicity Testing

Collaborative and Complementary Approaches to Chemical Screening

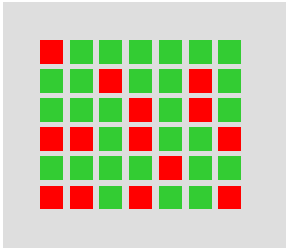
	Chemicals	Assays	Endpoints
ToxCast Phase I	293	~600	~1100
ToxCast Phase II	767	~600	~1100
ToxCast Phase IIIa	1001	~100	~100
E1K (endocrine)	880	~50	~120
Tox21	8,193	~25	~50



Computational Toxicology Approaches

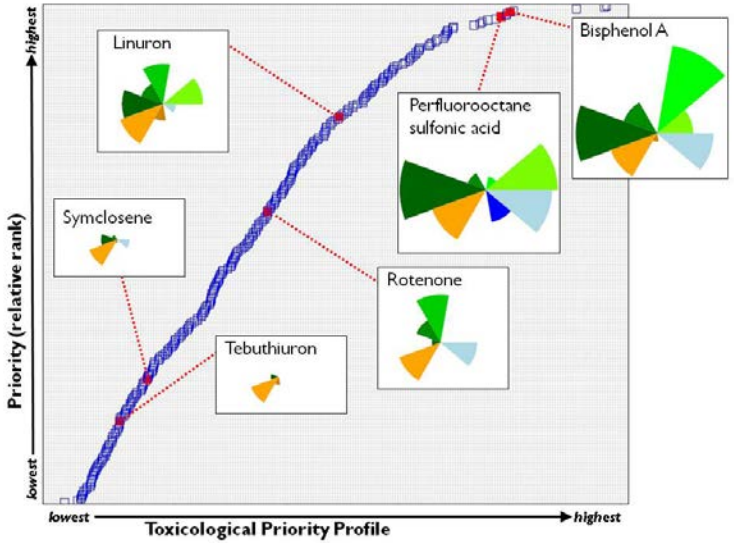


Thousands of chemicals



High throughput biology and chemistry

Bioinformatics/ machine Learning



Predictive toxicology

Benefits

- Less expensive
- More chemicals faster
- Fewer animals

High Throughput Exposure Predictions

= hazardous dose

= exposure estimate

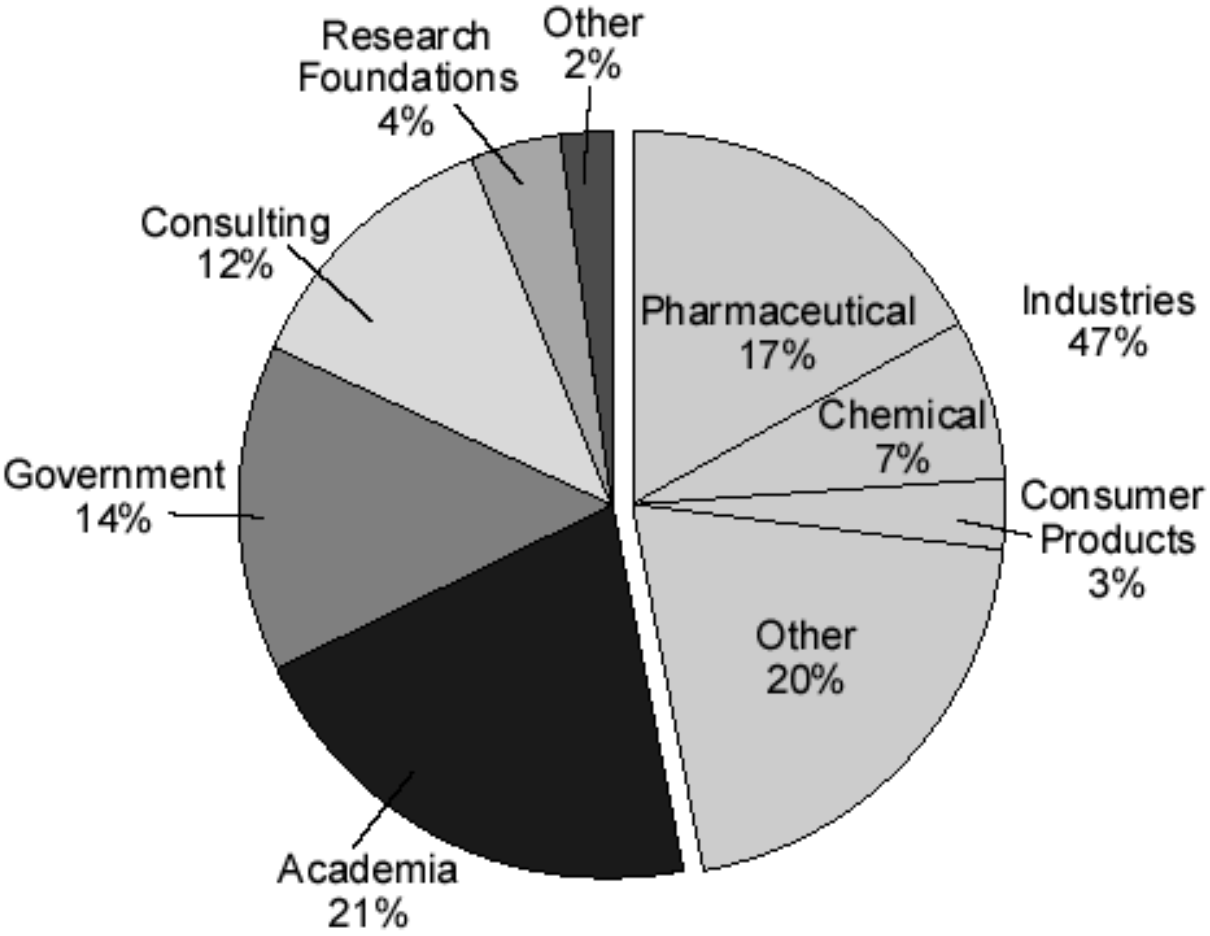
Wetmore *et al*. (2012)

Risk = f (Hazard x Exposure)

Accomplishments

- Characterizing the biological activity of ~2000 chemicals in over 700 biochemical and cell-based assays.
- Additional assays being developed to fill data gaps in the high-throughput screens.
- Exposure estimates for over 7,000 chemicals based on production volume and chemical use
- Database of chemical-product categories that maps over 45,000 chemicals to ~8,000 product uses or functions
- Steady-state IVIVE models for hundreds of chemicals based on high-throughput in vitro assays
- Virtual tissue models are being constructed based on data collected from both high-throughput and “fit-for-purpose” assays and used to inform shape of the dose-response curve.

Careers in Toxicology



www.toxicology.org

Preparing to be a Toxicologist

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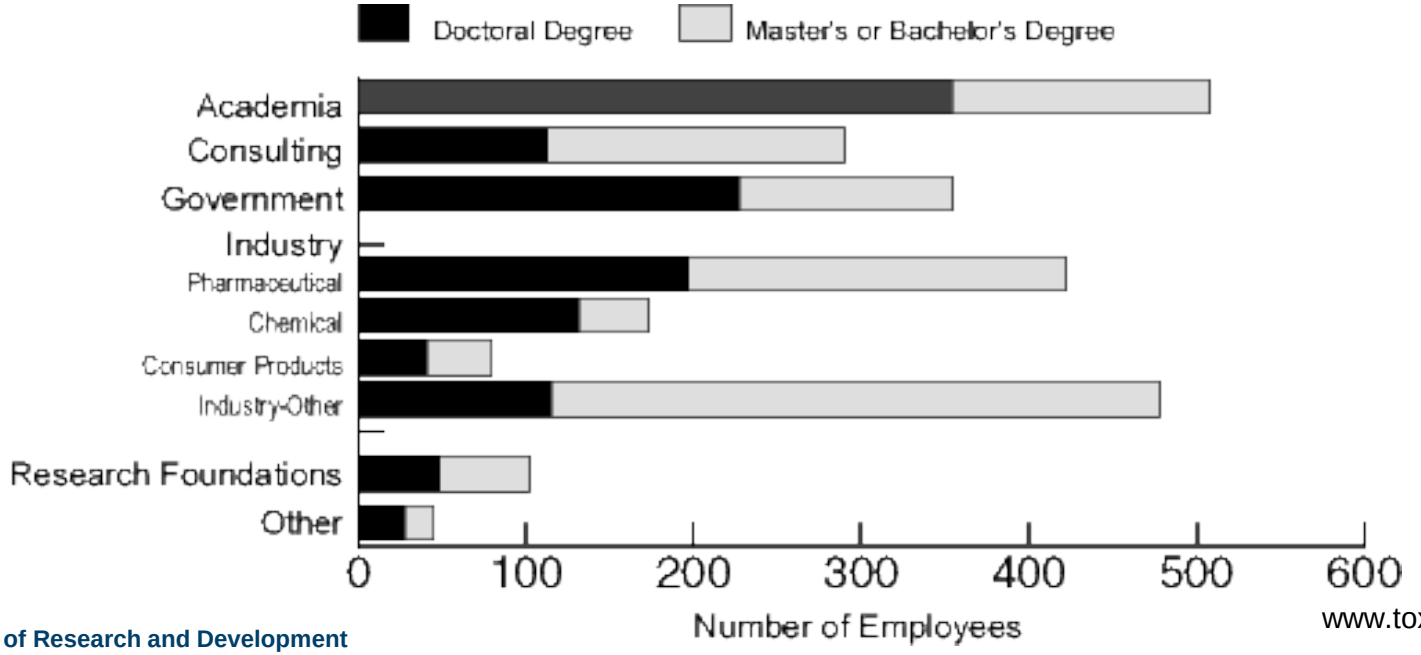
Career Skills

- Strong communication and writing
- Computer knowledge
- Good laboratory practice
- Project management
- Statistics experience

Education

- Computer science
- Math
- Biology
- Chemistry
- Toxicology
- Biochemistry
- Physics
- Statistics
- Pharmacology
- ***RESEARCH***



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Your career as a Toxicologist

Challenges for future Toxicologists

- Mixtures = Real world exposures
- Episodic exposures
- Biological plausibility and statistical significance
- Mechanisms of action
- Differential susceptibility
- Human relevance of non-animal models

Summary and Additional Resources

What do toxicologists do?

- Determine the potential harmful effects of chemicals and the dose that will cause these effects.

Where do toxicologists work?

- Industry, academia, and government

How much more school?

- Post-baccalaureate degrees

Resources

- Society of Toxicology: www.toxicology.org
- US EPA National Center for Computational Toxicology (www.usepa.gov/ncct)
- Risk Bites “A New Way to Evaluate Chemical Safety – TOX21” (YouTube)
- Me! (cowden.john@epa.gov)

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Questions?