

RISK21

Tiered Evaluation Strategy Sub-Team Integrated Evaluation Strategy



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RISK21 WORKSHOP

OMNI SHOREHAM

WASHINGTON, DC

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IES Risk Sub-Team Roster

2

Global, multi-sector representation
n=31 scientists, 23 affiliations

- **Academia (n=7; 5 institutions)**

- Imperial College London
- Johns Hopkins School of Public Health
- Michigan State University
- Utrecht University
- UCLA

- **Consultants**

- CXR Biosciences
- Parker Doe Partnership

- **Non-Profit**

- Humane Society of the United States

- **Government (n=12; 6 agencies)**

- BfR, Germany
- European Commission / JRC
- Health Canada
- NIEHS
- US Environmental Protection Agency
- US Food and Drug Administration

- **Industry (n=9; 9 companies)**

- BASF
- Bayer CropScience
- Dow AgroSciences
- Dow Chemical
- DuPont
- ExxonMobil
- Monsanto
- Procter & Gamble
- Syngenta

Overarching Goals of our Professional Activities



- **Health protection.**
- **Predict adverse effects of a chemical or product.**
- **Predict the circumstances in which adverse effects may occur.**
- **Identify when those situations could arise and provide recommendations so that they don't.**

What is our current approach?



- A battery of animal studies that have developed and expanded over many years to identify effects.
- Established methods are used to extrapolate the animal data in order to predict consequences for humans if they are exposed.
- Use established methods that predict potential human exposure or contact with the chemical(s) of concern.
- This is the essence of Risk Assessment

What are we trying to achieve?



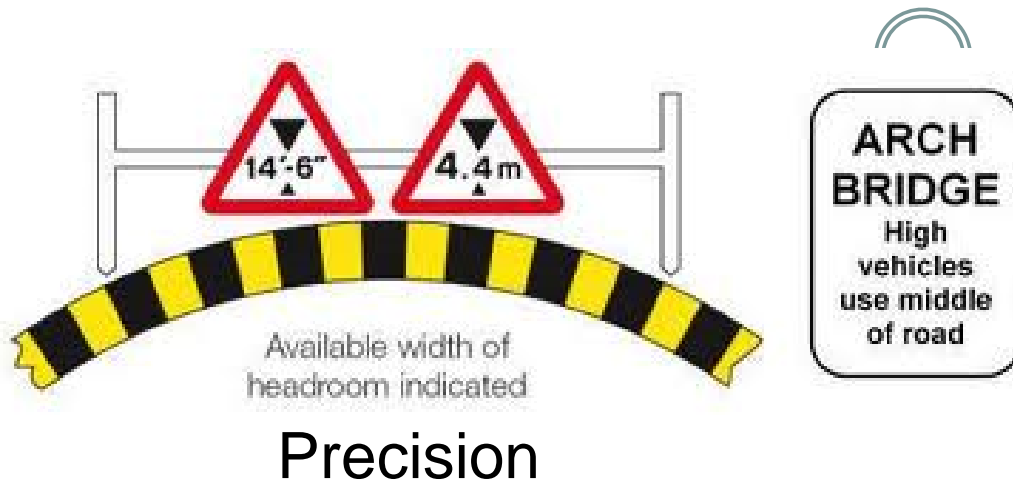
- **VISION:**

- An integrated evaluation **framework** that flexibly **incorporates new technologies** and approaches for chemical products and contaminants that better **informs** health risks and utilizes resources more **efficiently** than the current paradigm.

- **MISSION:**

- Establish a framework that provides **flexible, rapid, efficient, transparent and cost-effective** approaches for creating and interpreting data relevant for **scientifically-sound decision making** that protects human health.

Precision or Accuracy



Accuracy



We need to know that the bus will go under the bridge.

Not that it is 3.897m high.

Adverse Effect

Risk Assessment



- Risk Assessment is essentially comparing
 - a Biological Response Profile
 - with
 - an Exposure and Use Profile
- How could we categorise Biological Response?
- How could we categorise Exposure and Use?
- How could we link the two?

Factors or Inherent Properties for Consideration

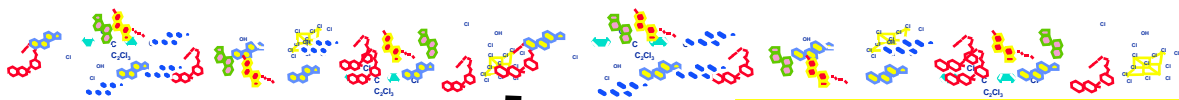


- **Chemical Properties**
 - Determines biological response
 - Dictates use and exposure
- **Biological Response**
 - Nature of effects and adverse effect(s)
 - Minimum dose and duration to cause effect(s)
- **Use and Exposure**
 - Dose and Duration

Tiered Testing

Most tiered testing discussions have been focused on developing approaches that are geared toward limiting or eliminating whole animal testing.

Specifically decreasing or eliminating use of mammalian experiments using primates, canines, rodents, and related species.



Existing Knowledge,
exposure, use,
toxicity data, SAR,
metabolism
prediction, degradate
analysis, QSAR

In Vitro Profiling:
Molecular
interactions, Cellular
Responses
QBAR

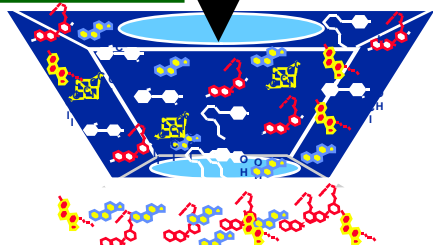
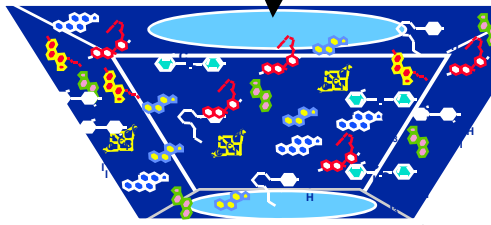
**Efficient
Focused *In Vivo*
Testing**

Evaluation for Relevant Effects

Screening
and
Prioritization

Research:
Learn &
Refine

Risk Characterization, Evaluation, and Decision

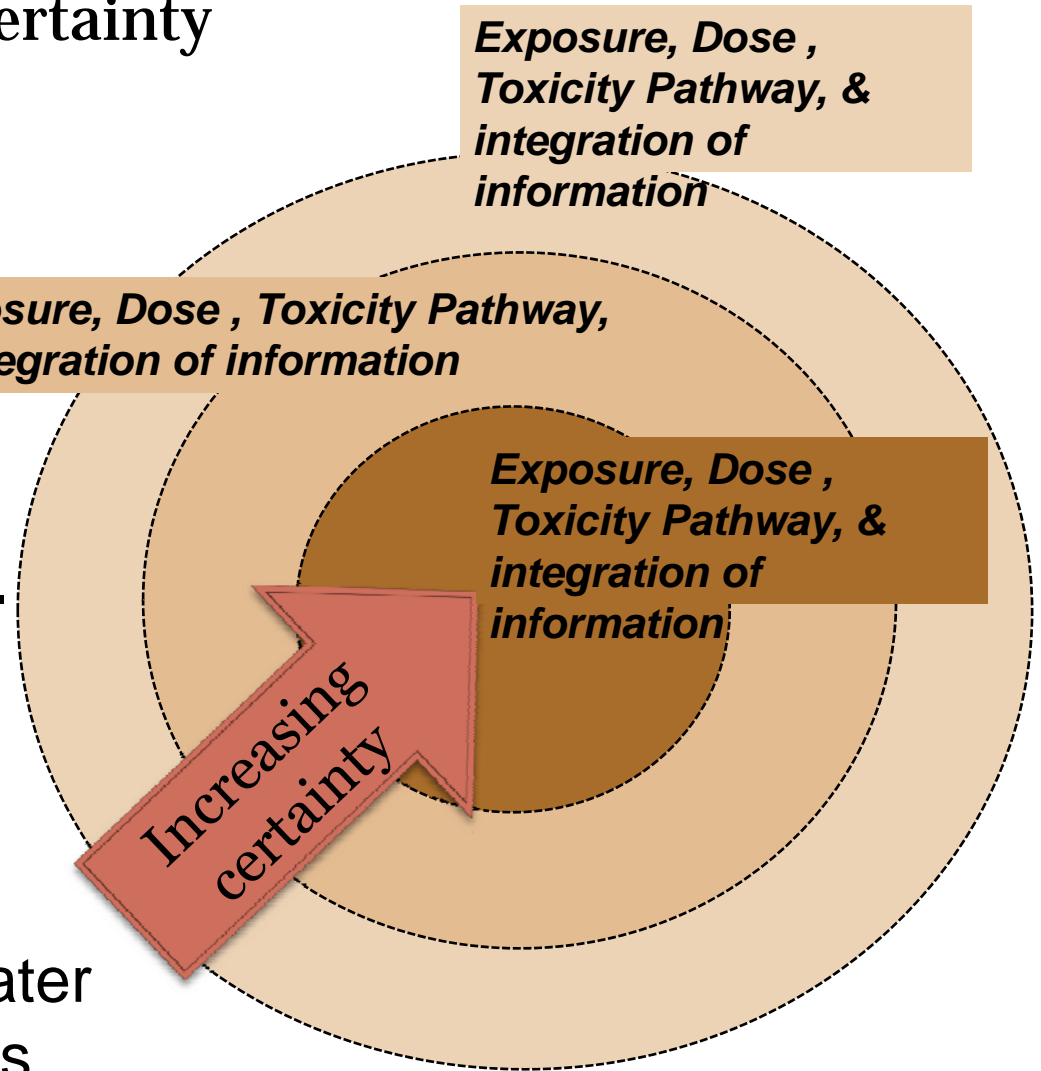


We typically equate more certainty with more animal testing.

This is the current model; the future will be different.

Less reliance on animal testing; more knowledge-based instead.

Could mean more detailed *in vitro* assays, enhanced exposure assessment, greater specificity of *in silico* models.



Greater certainty necessitates increased understanding, quantitative data, and greater integration at each level.

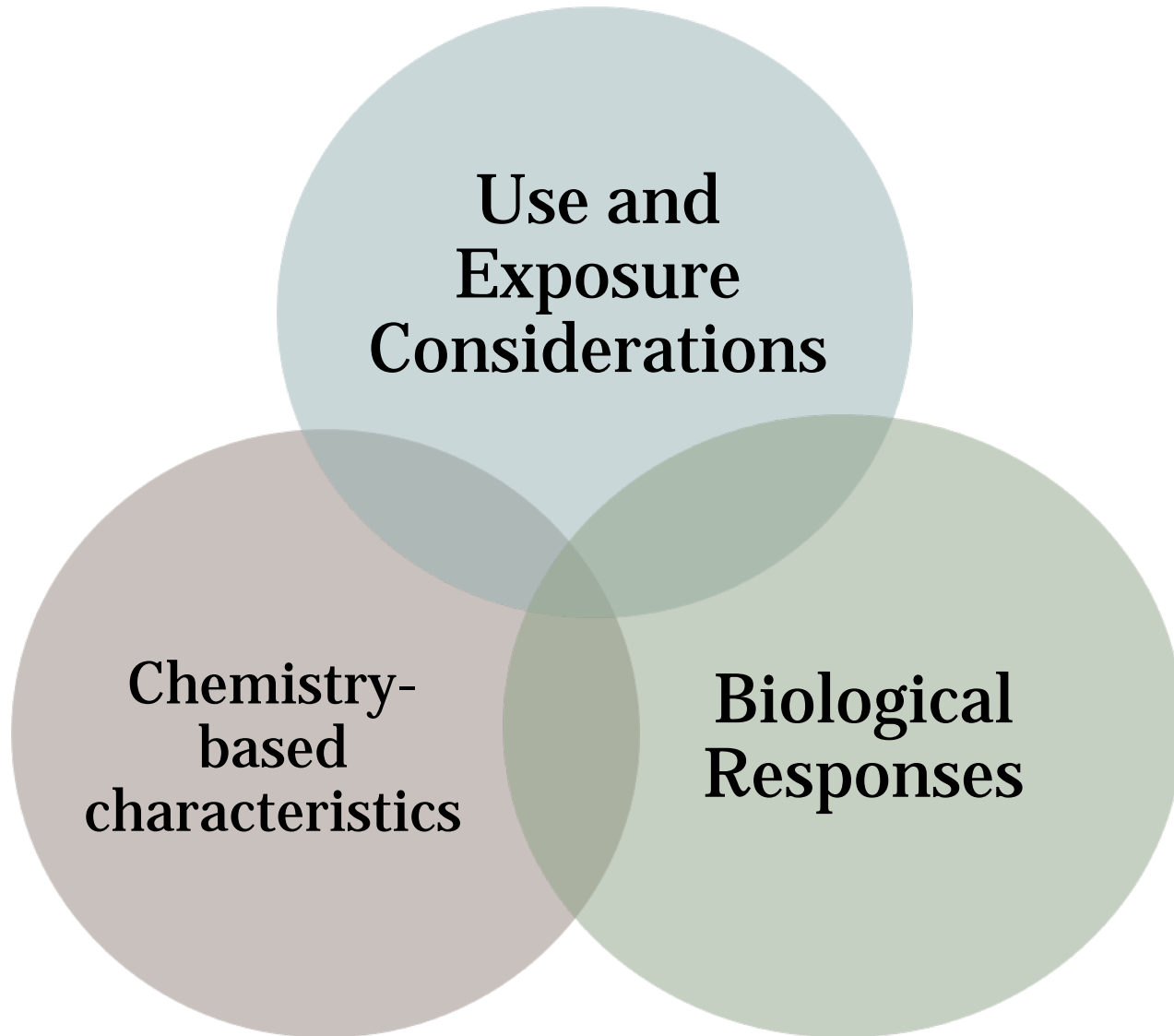
How are we going to accomplish this?

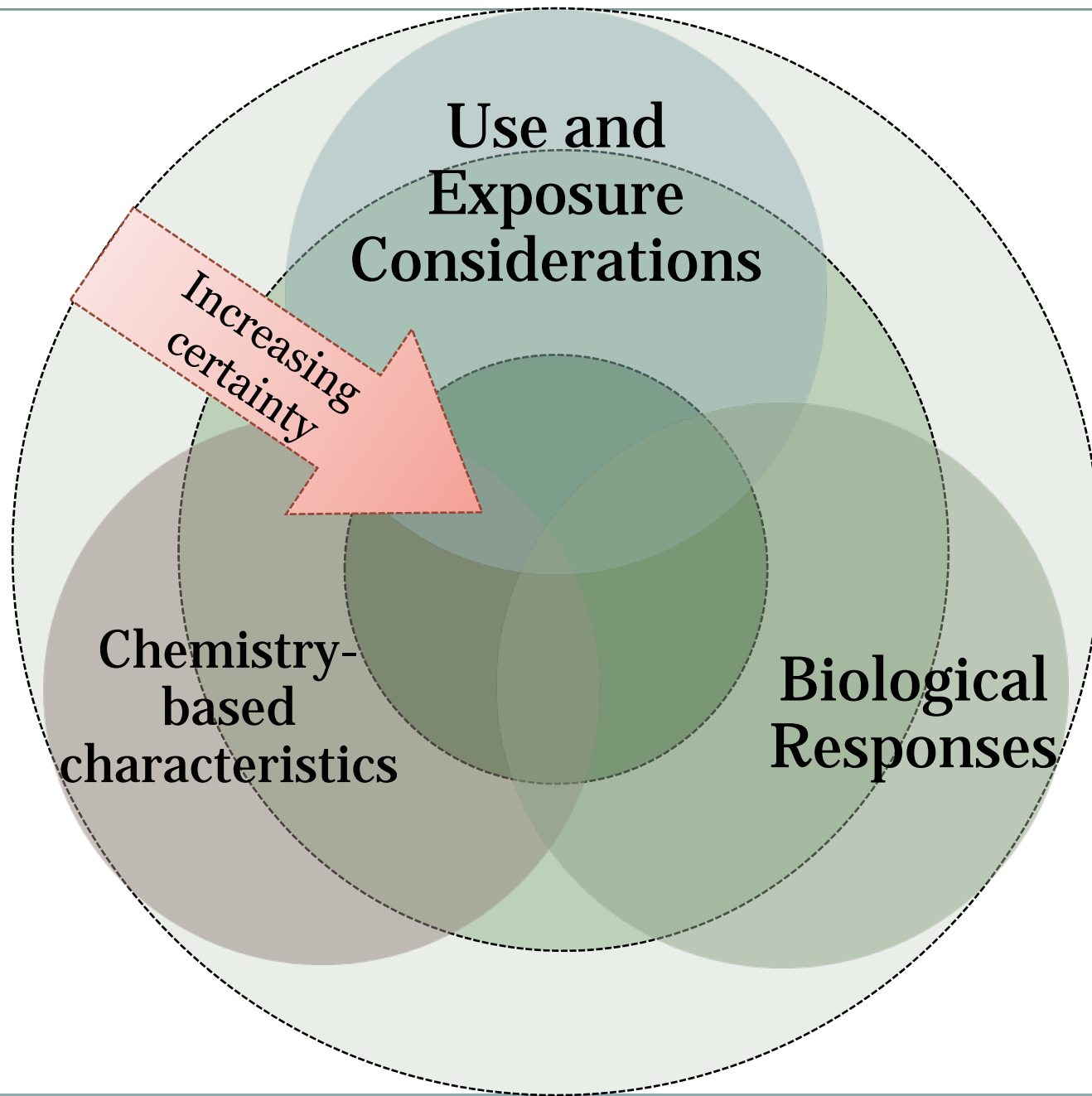


- **STRATEGY:**

- Develop and define categories of information (e.g., use & exposure, chemistry characteristics, biological responses)
- Establish an inquiry-based framework to achieve a fixed level of confidence with different data requirements (rather than our current system of fixed data with varying confidence)
- Evolve current databases into publicly available integrated knowledgebases – work with case examples
 - ✦ Funding of relational evaluation systems that allow read across for a wide range of inherent properties (structures, biological effects, use patterns) will be critical for success.
- Evaluate new technologies as they are developed and understand how they might contribute to risk characterization.

Factors or Inherent Properties





**Use and
Exposure
Considerations**

*Increasing
certainty*

**Chemistry-
based
characteristics**

**Biological
Responses**

Goal



- An **integrated evaluation strategy** that provides the necessary scientific **knowledge** to make a regulatory determination of the **potential for an adverse impact**, from the use of a chemical, on public health with **speed, efficiency and accuracy.**

The Future Risk and Safety Determination

- Safety and risk management decision-based testing.
- Inherent properties (chemistry, biology, use, and exposure) directs assessment strategy.
- Inherent properties categorized into accessible knowledgebases.
- Testing only as necessary
- Testing in animals is rare

“To innovate is not to reform”

Edmund Burke (1729–1797), Irish philosopher, statesman.