The Evolving Nature of Information Needs: A View from the Health Risk Assessment Trenches

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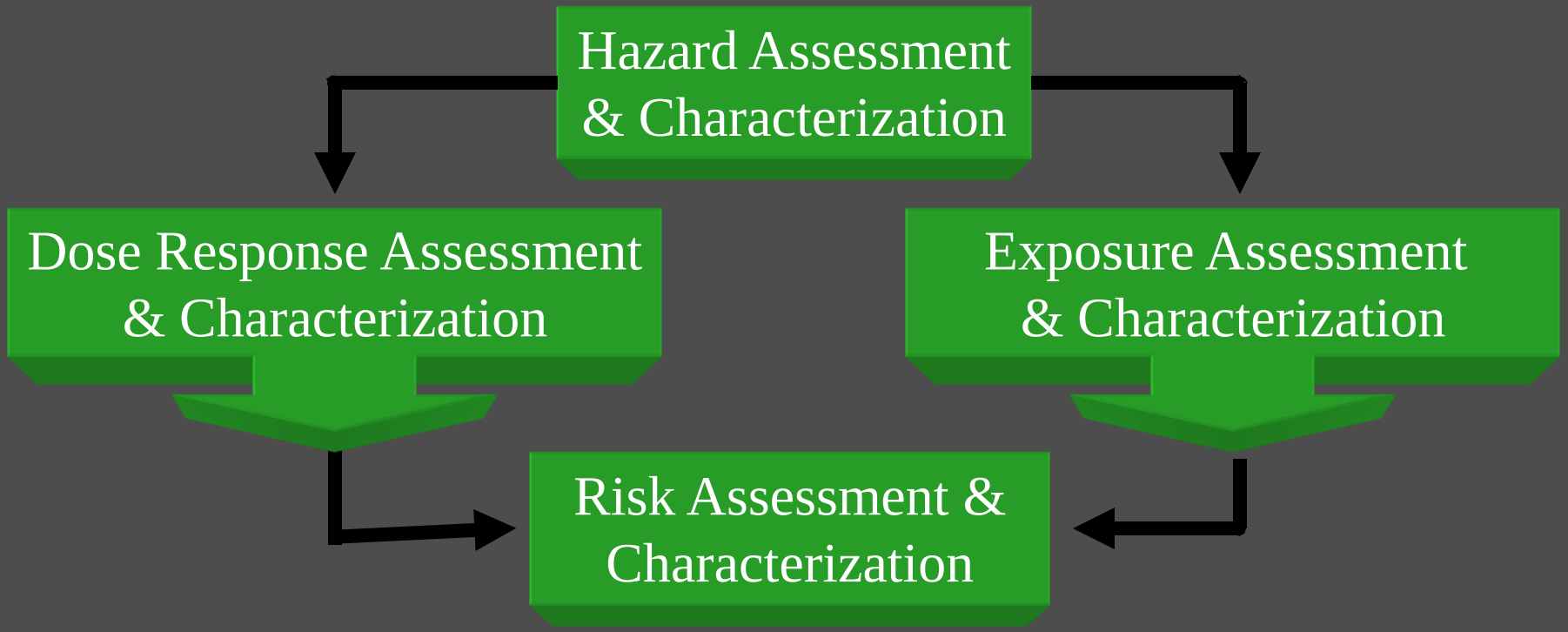
Objectives of Talk

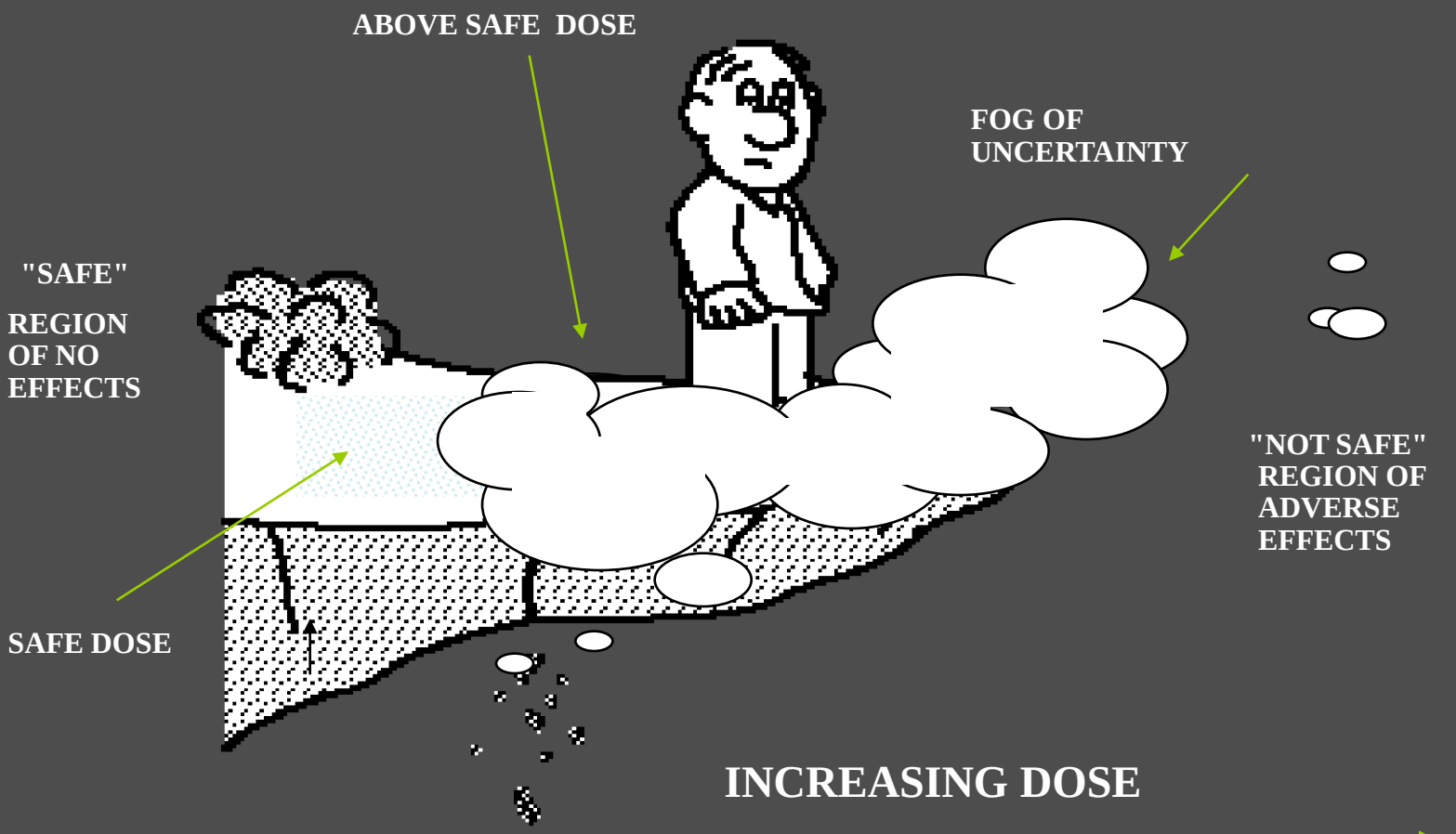
- The paradigm used to make decisions in health risk assessment
  - What are the information needs?
- Key drivers resulting in evolving nature of information needs
  - Why are the needs changing?
- Areas for future risk data growth
  - What new information will be needed?

Risk Assessment Paradigm

NAS 4-Step Paradigm



The Risk Value Process



This process incorporates the fundamental concepts of toxicology – that for non-cancer effects, there is an exposure threshold below which exposure is safe and the onset of toxicity is a function of the exposure concentration.

Risk Value Derivation for Dose-Response Assessment

$$\text{Risk Value} = \frac{\text{Measure of Dose-Response}}{\text{Factors to Address Uncertainty in Extrapolation}}$$

Nearly all groups - whether evaluating food, product, environmental, or occupational risk - use this basic concept for non-cancer dose-response assessments. However, the specific terminology differs among these groups.

Risk Characterization

$$\text{Hazard Quotient} = \frac{\text{Exposure Estimate}}{\text{Safe Dose Estimate}}$$

Nearly all groups - whether evaluating food, product, environmental, or occupational risk - use this basic concept for non-cancer dose-response assessments. However, the specific terminology differs among these groups.

Drivers for Change

- Science Drivers
  - Improved understanding of molecular toxicology
  - Improved computing resources –
    - Incorporation of biomathematics
    - Information sharing capacity increased
- Regulatory Drivers
  - Output Needs to Increase
    - Collaboration and Harmonization initiatives
  - Methods need to improve
    - Focus on MOA Frameworks
    - Alternative to animal testing
    - Systems biology focus

Create the future - Collaborate

- International Programme on Chemical Safety (IPCS): Harmonization Project
- Methods Harmonization
  - *Harmonization is not standardization*
  - Understanding the methods and practices used by various organizations
  - Developing confidence in and acceptance of assessments using different approaches
  - Willingness to work toward a convergence of methodologies as long-term goal

Alliance for Risk Assessment (*ARA*) (www.allianceforrisk.org)

Stakeholder Process

States, Fed. Agencies, Public Interests, Industry

Initiation of Risk Issue

Document Draft

Peer Reviews

Release to Public

Risk Information Exchange (RiskIE)

ARA Process

Steering Committee

Non-profit Collaborators

Risk Document Development

Training and Certification

Risk Communication

Risk Research And Tools

Peer Review & Consult

RiskIE

Risk Information Exchange

www.allianceforrisk.org/RiskIE.htm

- An interactive Database to Communicate In-Progress Risk & Toxicity Assessments
- Includes over 7000 projects being conducted by more than 27 organizations representing 13 countries
- Available at the Alliance for Risk Assessment (*ARA*) website

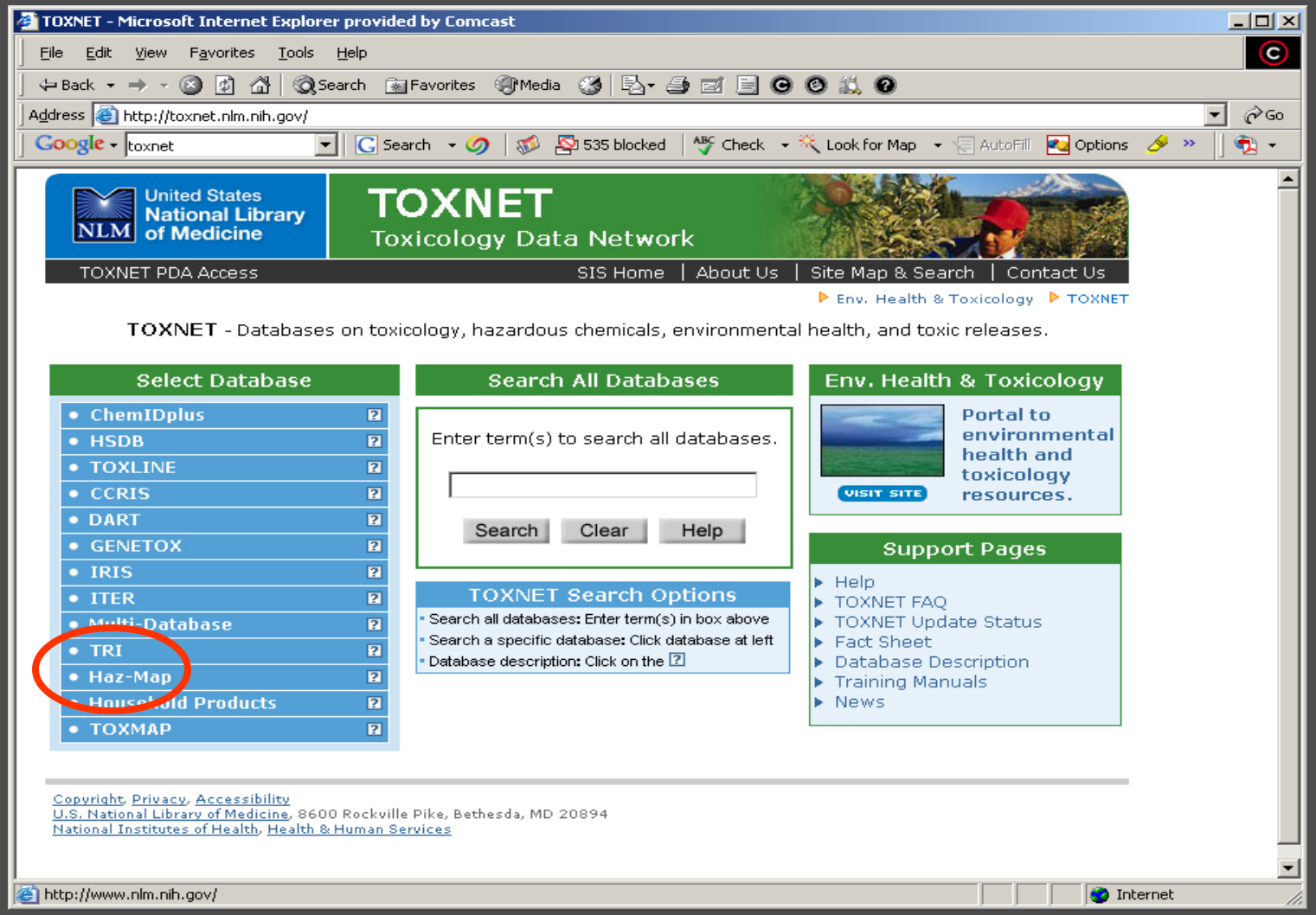
ITER

International Toxicity Estimates for Risk

www.tera.org/ITER
http://toxnet.nlm.nih.gov

- Provides chronic human health risk values and cancer classifications from organizations around the world for over 650 chemicals
- Includes a synopsis that explains the underlying basis and rationale for each risk value and differences in risk values
- A link to each organization's website or source document
- A forum through which independent parties can share their peer reviewed risk values

NLM's TOXNET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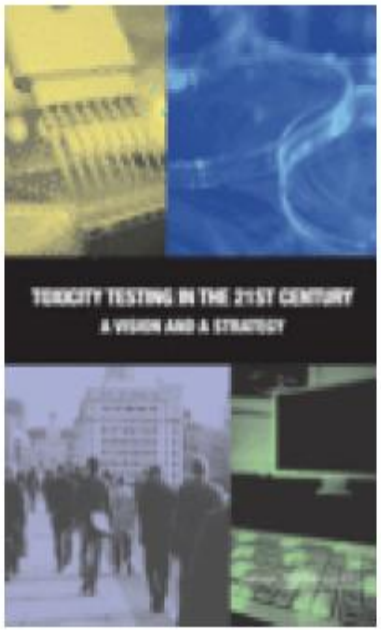
Trends in Dose Response Assessment

- Mode of action rather than endpoint-based assessment – harmonize cancer and non-cancer
- Earlier assimilation of empirical dose-response data – use biomarkers
- Development of frameworks to have risk assessors thinking in the context of data to replace default assumptions based on MOA



Toxicity Testing in the 21st Century: A Vision and a Strategy

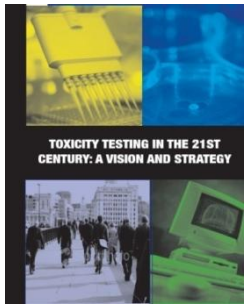
Committee on Toxicity Testing and Assessment of Environmental Agents, National Research Council

ISBN: 0-309-10993-0, 216 pages, 6 x 9, (2007)

This PDF is available from the National Academies Press at:

http://www.nap.edu/catalog/11970.html

A New Paradigm: Activation of Toxicity Pathways



Exposure

Tissue Dose

Biologic Interaction

Perturbation

Higher yet

Biologic Inputs

Normal Biologic Function

Early Cellular Changes

Adaptive Stress Responses

Cell Injury

Morbidity and Mortality

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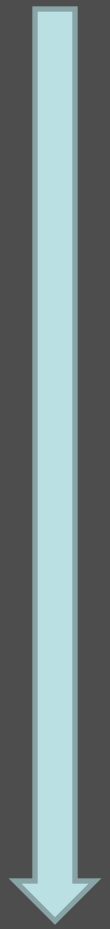
Effect of MOA Emphasis

- Piles of new raw data – requiring libraries for data shared in a common format
  - E.g., NIEHS TOXCAST efforts
- Tools for managing data inputs and outputs (predictions) from QSAR and other modeling
- Increase need for “tool boxes” and decision support systems that integrate results across models – e.g., ECHA QSAR and Exposure modeling suites

Evolving Data Needs



- Individual Study Data
  - PubMed/Toxline
- Compilations for a single substance – multiple studies
  - IRIS
- Comparisons of content among integrated compilations
  - ITER
- Application resources
  - CHEMM

The 2010 "Tricorder"

- One-stop shopping
  - Rich source of toxicology data, and
  - Rich source of methodology information, and
  - User algorithms (or at least exports to user tools)
- Tools to identify the most relevant content
    - Need access to everything, but want most relevant first: relevance sorting, quality filters, value of information tools, decision logics
- Compatibility with mobile technology
    - Do we have an App for that?

Questions