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Linkages Between Human and Environmental Exposure Assessment

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Outline

- Similarities / Differences in Approaches
- Pesticide Risk Assessment – background for examples
- Opportunities to Integrate/Harmonise
- Best practices across the disciplines
- Research and Monitoring

Approaches –
The Basics are the same:

- Human and environmental assessments share the same goal - to estimate the routes, magnitude and duration of exposure to compare with toxicity data to estimate risk.
- The disciplines are linked because:
  - Humans and other organisms share the same environment and have common biological origins
  - The laws of physics, chemistry and biology apply!
- **In both disciplines, risks are largely driven by exposure**

Approaches – Fundamental concepts are the same:

- Same exposure routes
  - Ingestion (Food & Water)
  - Dermal
  - Inhalation (Air (terrestrial) or Water (Aquatic Organisms))
- Same kinetic considerations
  - Uptake, depuration, dissipation, transformation, etc
- Same chemical property considerations
  - Solubility, Kow, pH, etc
- Similar biochemical pathways (metabolism, mode of action, dose response, etc. are conserved to some extent across taxonomic groups)

Some Differences

Human	Environmental
Focus on protecting individuals	Focus on protecting populations or ecosystems
Effect endpoints of interest usually sub-lethal	Effect endpoints of interest usually lethality
Consider range of routes and durations of exposure routes	Tend to focus on single media (e.g. food), even where the potential for other routes is clear (e.g. dermal exposure of birds to pesticides)

Some Differences *cont*

Human

- Exposure influenced by activities (diet, occupation, age, etc)
- Geographic factors (weather, soil, etc.) indirectly influence exposures (e.g. residues)
- Several species used to address potential effects on one species

Environmental

- Exposure influenced by ecology
- Geographic factors (weather, soil, etc.) directly and indirectly influence exposures (e.g. run-off into aquatic systems)
- A few species used to address potential effects on multiple species

The basic frameworks are the same, <u>but</u>:

- Ecological assessments are more diverse
  - It is more straightforward to identify protections goals for humans than at a habitat or ecosystem level.
  - The wide range of protection goals means environmental assessment frameworks are generally less standardised or focussed than those for assessing human health.

- In some areas, approaches for environmental assessments are less developed
  - e.g., While both fields are developing approaches that better consider aggregate effects across exposure routes, and cumulative effects of mixtures, this area is currently more advanced for human assessments.

Pesticide Risk Assessment - Background

- Relatively data rich - most countries mandate extensive pre-market assessments

- Diverse range of products and uses, with wide variety of chemistries
  - Herbicides, Fungicides, Insecticides, Biocides
  - Agricultural, Forestry, Domestic and Industrial uses

- Diverse exposure scenarios
  - Potential human exposure:
    - diet and drinking water,
    - during application and post-application activities
    - in residential settings
  - Potential environmental exposure in multiple media via a range of routes

Pesticide Risk Assessment - Background

- International regulatory agencies have achieved a very high level of cooperation
  - Harmonised data requirements and assessment approaches
  - International evaluations (OECD and NAFTA) are now the norm

- Rich databases have allowed the development of sophisticated models, e.g., for aggregate and cumulative health assessments

Yet - human and environmental assessments are still largely "two solitudes"

- **How can we learn and leverage from each other?**

Opportunities to integrate / harmonise:

Harmonise terminology (which can drive approaches)

- e.g. Expressing risk:
  - “Margin of Exposure” for occupational assessments
  - “Percent of ADI or ARD” for dietary assessments
  - “Risk or Hazard Quotients” for environmental receptors

Opportunities to integrate / harmonise:

Integrate data and models across disciplines, e.g:

- Pesticide field worker assessments are based on generic “Transfer Coefficients” for dislodgeable foliar residues
  - Could same concept be applied for birds and small mammals?

- Pesticide residue kinetic models and data requirements differ for food, foliar and environmental residues
  - Principles are the same; Can we harmonise?
    - e.g. Could “crosswalk” of North American and European ecoregions for environmental dissipation studies also apply for foliar residue studies?

- Can we make more use of existing data?
    - e.g., Could we use mammalian dermal absorption studies to improve assessments for birds and small mammals?

Opportunities to integrate / harmonise:

Use data-rich fields to inform data-poor fields:

- e.g. Pharmaceutical data have been used to validate/refine inter- and intra- species uncertainty factors
  - Could pesticide data for mammals, birds and fish be similarly used to derive uncertainty (extrapolation) factors for assessments of less well characterised chemicals ?

Best Practice: Focus Where the Risk Is

- **Challenge:**
  - Scope and complexity of assessments is increasing, while resources for both regulated and regulatory communities are decreasing

- **Best Practices**:
  - Up front problem formulation to focus effort on risk drivers
  - Appropriate complexity of models – avoid unnecessarily complex or resource intensive approaches

    – **Can we develop shared tiered across the disciplines approaches that minimise evaluation and data generation efforts?**

Best Practice: Effort Commensurate with Risk

- **Challenge:**
  - Extrapolation of surrogate data results in the need to address both its inherent variability and uncertainty in how well it simulates “reality”.
  - Adequate ccharacterization of variability/uncertainty, and the biases they introduce, is critical in regulatory assessments that must be transparent and consistent.
  - However, resources are limited – need to balance assessment effort with level of risk

- **Best Practices**
  - **Can we develop common guidance across the disciplines for data needs, model choice and construct, and interpretation?**

Model Choice \ Complexity

Probabilistic:

- Often viewed as the “gold standard”
- Can characterize variability and uncertainty:
- Can address exposure/risk across a range of conditions
- Can address spatial and temporal co-occurrence of exposures
- Facilitates identification of risk drivers
- Can be more refined or realistic

- However:
  - Data intensive
  - Labor intensive
  - Only as good as underlying data and assumptions
  - Interpretation can be complex

Model Choice \ Complexity

Deterministic:

- Simpler
- Less labor intensive
- Require less supporting data
- Can be more transparent and “easier” to interpret
- Can serve a valuable role in tiered approaches by identifying where to best focus additional effort

- However:
  - Can sometimes result in conservative assessments
  - Only qualitative characterization of variability/uncertainty

Example: Pesticide Assessment Models

Range of Complexity:

Human Health

- Toxicology – deterministic
- Exposure
  - Dietary - probabilistic
  - Occupational, Residential, Aggregate - generally deterministic but piloting probabilistic
  - Cumulative – probabilistic

Environment

- Toxicology – deterministic or Species Sensitivity Distributions
- Piloting probabilistic methods for aquatic effects
- Piloting methods for characterisation of avian acute effects

Research and Monitoring

Challenge:

- R & M data are needed to assess and strengthen model performance and to provide feedback on risk management decision
- Insufficient capacity to address all needs

Best Practices:

- Harmonise data requirements across disciplines and prioritise by potential contribution to:
  - Confidence in approaches and tools
  - Effective and practical risk mitigation
  - International harmonization / collaboration / work sharing
  - Capacity for quick response to emerging issues
- **Most exposure data are process-driven or “generic” rather than chemical specific:**
  - **Can we better use “Task Force” approaches for efficient data generation and analysis?**

Pesticide research – some "successes"

- Comparative toxicity to fish and amphibians
  - used to test assumption of equivalent toxicity
- Deposition in forest canopies
  - used to refine spray deposition to forest canopies, floor, streams, etc.
- Buffer Zone Calculator
  - used to refine no-spray buffer zones for specific site conditions and application practices
- Human biomonitoring studies
  - used to validate models and assess effectiveness of risk reduction measures
- Environmental residues (food, air, soil and water)
  - used in risk assessments, to validate models and to assess risk reduction measures

Some current pesticide R & M priorities that will inform both disciplines

- Effectiveness of exposure mitigation strategies (e.g., vegetative filter strips, drift reduction technologies).
- Characterisation of watersheds to refine water modeling predictions.
- Pesticide use information.
- Exposure activity data (dietary, occupational, residential, environmental)

  - **Note - all are “generic” data!**

The Future: Integrated Testing Strategies?

Traditional approach

- Standardised batteries of toxicology, fate and exposure data

21st Century Integrated Testing

- Integrate *in vitro* data, model predictions (QSAR, PBPK), etc., to develop hypothesis on likely exposures and toxicological potential)
- Prioritise additional (*in vivo*) testing
- Problem Formulation and Assessment

- Potential to
  - Reduce animal testing
  - Improve efficiency (review times/costs for regulators and testing costs for industry)

    – **Can common approaches be developed for human health and the environment?**