Overview of US EPA Risk Assessment and Risk Management Approach to the Utilization of Higher Tier Studies

Kevin Costello, Edward Odenkirchen and Garland Waleko

USEPA Office of Pesticide Programs

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Standard Ecological Risk Assessments

- The Agency calls in a standard set of environmental fate and ecotoxicity data for every pesticide
- The fate data are used to characterize and predict exposure values
- Estimated exposure is compared to toxicity endpoints from ecotox data
  - Exposure above a level of concern (LOC) indicates a potential concern warranting further analysis
  - Endpoints of concern are survival, growth and reproduction
- Non-guideline data (including open literature) are considered either quantitatively or in risk characterization

Goals of Tiered Risk Assessments

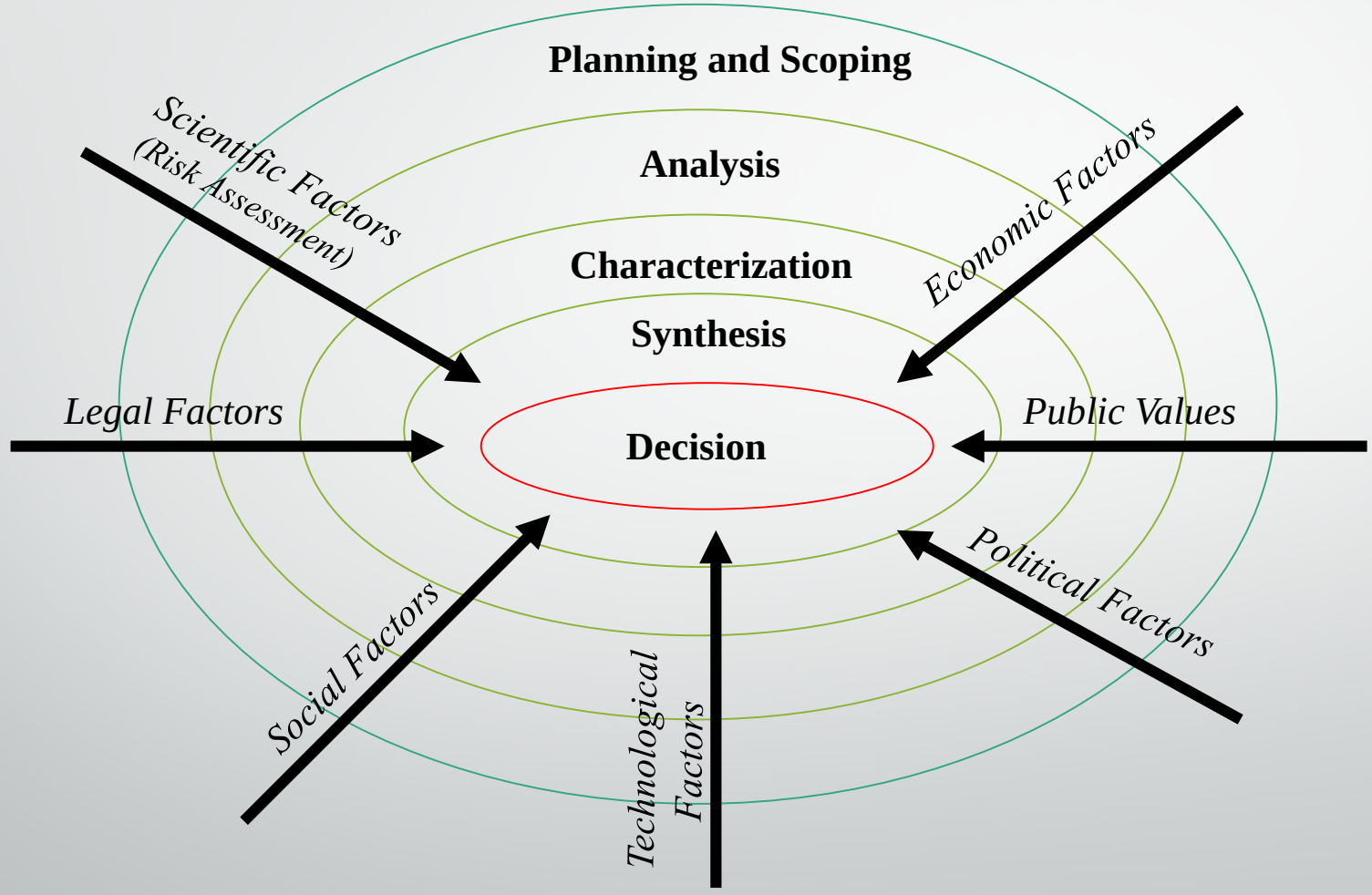
Implement a refined assessment process that

- Addresses a broad spectrum of effects
- Reflects more realistic use scenarios and field conditions
- Incorporates probabilistic tools and methods
- Is designed to rely on existing data requirements for registration at lower tiers
- Focuses additional data requirements in upper tiers for reducing uncertainty

Risk Assessments in the Risk Management Process

- Risk assessments are one factor considered when making a risk management decision
- Public comments factor into the decision, and receive responses
- Additional refinements or higher tier studies can be considered or called in if they are necessary for making the decision.

Risk Management Decision Framework



Role of the Risk Manager

- Responsible for leading OPP's registration or reevaluation process
- Risk managers must:
  - Consider the results of the risk assessments
  - Have an understanding of the benefits of a pesticide, as well as alternative pesticides that are already registered
  - Develop measures needed to mitigate identified risks
  - Negotiate modifications to the product or labeling that must be made to mitigate risk

Role of Benefits Assessments

- Ecological & Worker: FIFRA requires consideration of both risks & benefits
  - Established methodologies for estimating costs for growers and for evaluating alternatives
  - If either the risks or benefits are low, decision may not need much additional analysis.
- Dietary: FFDCA does not allow for risk/benefit balancing.
  - However, Agency looks for best solutions that would have the least impact on growers

When does the Agency Use Higher Tier Studies?

- When the standard risk assessment, in the context of other factors, is not enough to answer the questions at hand
- When potential risks and benefits both appear to be great
- When the expenditure of resources is warranted by the decision to be made

Tier II Honey Bee Toxicity Studies (semi-field)

- Standard risk assessment could not address questions about the role of pesticides in honey bee declines
  - Available studies addressed acute toxicity to adult bees, but not to larva or colonies
  - Protection of bees an important public value, and economically important
- Appropriately vulnerable exposure scenario was used and agreed upon by the Agency/international community (e.g., bees exposed in tunnels or long-term feeding of colonies).
- Risk assessment/protection goals clearly defined (assessment endpoint = colony strength/survival measurement endpoint = overwintering success, sustained impacts on colony strength/fitness)
- Study outcomes related directly to risk assessment process (e.g., used to interpret residues in pollen/nectar)
- Single population (not entire community)

PBPK Modeling in Risk Assessment

- State-of-the-art science developed in conjunction with registrants
- PBPK modelling is a scientifically sound and robust approach to estimating the internal dose of a chemical at a target site and as a means to evaluate and describe the uncertainty in risk assessments.
- PBPK models consist of a series of mathematical representations of biological tissues and physiological processes in the body

PBPK Modeling in Risk Assessment

- Model applications in risk assessments:
  - interspecies extrapolation, intraspecies extrapolation, route-to-route extrapolation, estimation of response from varying exposure conditions, and high-to-low dose extrapolation
- Very resource intensive, has required multiple rounds of peer review

How the Agency Uses Voluntarily Submitted Studies

- The best-case scenario involves collaboration on the design of a study meant to answer a specific question
- Many high-quality studies are submitted without this kind of planning
  - For the pyrethroids, there are dozens of such studies
  - The utility of these studies for the risk management decision is determined after they are completed and submitted

Types of Voluntarily Submitted Studies

- Some studies might refine quantitative risk assessment
  - Studies can refine model inputs for risk assessment
  - Studies can be used to develop new models, but this is costly
  - Studies which expand risk assessment from the lab to the field
- Some studies provide lines of evidence for the risk management decision
  - Studies can inform potential mitigation
  - Studies can present potential risk using less conservative scenarios

Studies which refine inputs to models

- Calculation of partitioning coefficients for free dissolved pyrethroids instead of those for whole water (including suspended sediments)
  - Resulting modeled acute concentrations were up to 10 times lower
  - EPA's risk assessment evaluated the effect on risk quotients
  - Predicted risks to aquatic invertebrates remain
- Studies measuring removal of pyrethroids during wastewater treatment
  - Bench scale water treatment removal study (designed in collaboration with OPP)
  - Wastewater monitoring performed before and after treatment

Studies which inform potential mitigation

- Source evaluation of residential uses in surface water runoff – The Pyrethroid Working Group Pathway Identification Study in which residential sprays were simulated by application to walls, lawns and driveways set up to receive a known amount of "rainfall."
- Runoff of material applied to impermeable surfaces was much greater than that applied to grass or walls near grass
- Results of this and other runoff studies were described in the risk assessment, but not applied quantitatively
- The Pathway Identification Study informed mitigation that reduced the area on a structure that could be treated with pyrethroids

Studies which provide lines of evidence from the field

- Mesocosm studies can show population or community effects from exposure to pesticides
- May show that certain affected populations might be adversely effected temporarily, only to recover later.
- Some species might not recover, but be replaced by other similar species

Mesocosms, continued

- Historically, mesocosm data conducted under FIFRA have been difficult to interpret
  - Confounding factors contributing to uncertainty in results
  - Study designs not appropriately focused (trying to assess too many endpoints/attributes with finite resources, such that none are done with the level of rigor needed
  - Regulatory assessment endpoint not clearly defined (what level of impact and duration of recovery is "acceptable"?)
- Mesocosm may not align with risk assessment goals
  - E.g: Many mesocosm studies evaluate short term, single pulse exposure; difficult to extrapolate to national-level risk assessment goals

Use of mesocosms for atrazine

- Data from many mesocosms were used quantitatively to develop a water concentration LOC for atrazine reregistration decision
  - Endpoint of concern based on primary productivity
  - Several years of analysis in preparation for the 2003 RED
  - Revised twice in response to 2007 and 2009 Science Advisory Panels
- Original tool relied on 35 atrazine mesocosms
- After 2009, 46 mesocosms from a set of 86 were employed
- Very resource intensive, very data intensive
- The need for the information in the decision-making process must merit the resource expenditure

Conventional Registration Review Status

- The resources OPP can spend on individual registration review cases is tied to those needed for the program as a whole
- OPP has currently completed:
  - 386 draft risk assessments (~47% remaining)
  - 311 proposed interim decisions (~57% remaining)
  - 273 final or interim decisions (~62% remaining)
- Each risk assessment and proposed decision requires peer review, and opens a public comment period
- If mitigation is needed, time is required for negotiations

Conclusions

- "Higher tier" studies work best when designed with the Agency to answer specific questions tied to risk management goals
- Resource constraints limit the number of voluntarily submitted studies OPP can fully review
- However, the Agency does use "higher tier" studies in many risk assessments
- Some studies directly apply to our quantitative risk assessments, and some provide lines of evidence for risk management decisions
- The level of effort must conform to the complexity of a decision