GUIDING PRINCIPLES for DATA REQUIREMENTS

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Office of Pesticide Programs
U.S. Environmental Protection Agency
Washington DC, 20460

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The Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) authorizes EPA to register pesticides and require supporting studies as stipulated under 40 Code of Federal Regulations (CFR) Part 158 to meet statutory safety standards. Part 158 also establishes data requirements for pesticide tolerances under section 408 of the Federal Food, Drug, and Cosmetic Act (FFDCA). The studies in Part 158 provide the scientific basis for characterizing the potential risks associated with pesticide exposure. There is flexibility, however, in implementing Part 158. Additional data can be required (§158.75), alternative approaches can be accepted, and studies can be waived (§158.45).

These guiding principles for data requirements will enable OPP staff to focus on the information most relevant to the assessment. The goal is to ensure there is sufficient information to reliably support registration decisions that are protective of public health and the environment while avoiding the generation and evaluation of data that does not materially influence the scientific certainty of a regulatory decision. It is important to only require data that adequately inform regulatory decision making and thereby avoid unnecessary use of time and resources, data generation costs, and animal testing. Delayed regulatory decisions affect the delivery of health and environmental protections and access to benefits such as pest management tools and safer products.

OPP has a long history of practicing flexibility in implementing Part 158 data requirements. The guiding principles re-emphasize this practice in the context of new and emerging tools which may be used to support risk assessment and risk management decisions. Databases of relevant information have grown, and our understanding of hazards and risks associated with pesticide exposures has advanced over time. Furthermore, research initiatives (*e.g.,* EPA's Chemical Safety for Sustainability Research Program) will develop new predictive technologies that will enhance our ability to evaluate chemicals and their effects of concern for a given exposure scenario. These science developments will advance OPP's strategic direction of using "Integrated Approaches to Testing and Assessment", which like these guiding principles, promotes a hypothesis based, systematic, integrative use of exposure and hazard information. Full use of existing knowledge and the integration of different types of information to focus assessments appropriately are concepts consistent with the 2007 and 2009 National Research Council reports, Toxicity Testing in the 21st Century: A Vision and a Strategy and Science and Decisions: Advancing Risk Assessment.

The following principles are intended to help guide the identification of data needs, promote and optimize full use of existing knowledge, provide consistency in the data request process across all scientific disciplines and all OPP divisions, and focus on the data needed to allow for a scientifically sound and credible characterization of a specific pesticide's risk profile for the exposure scenarios of interest.

These principles apply both to review of registration applications for new chemicals or uses and re-evaluation of existing pesticide uses through registration review.

I. Principles for Problem Formulation/Risk Management[1]

a. There needs to be sufficient data available to make a risk management decision for each pesticide exposure scenario of interest.

i. The level of certainty/uncertainty, relative to the available data, should be acceptable for the risk management decision(s) being made. If risks are low based on low expected toxicity or low estimated exposures (relative to the available toxicity data), additional confirmatory data may not be needed to make a risk conclusion. Therefore, it is important to characterize the nature and source of uncertainties and their impact on the risk assessment conclusions. A plausible range of potential risks and the characterization of confidence/uncertainty around that range should be presented (*e.g.,* EPA's Risk Characterization Handbook). This characterization is particularly important if the cost of mitigating is high or the risks are high if exposures are not reduced.

ii. Additional data should be required only if expected to improve the utility of the risk assessment for decision-making (*i.e.*, make a difference in risk conclusions, including those for Federally-listed species, and risk mitigation decisions) (*e.g.,* see guidance on EPA Focus Meetings and an example in the assessment for cryolite (p. 2)).

b. Before requesting data, risk management options (*e.g.*, lower application rates, reduced number of applications, engineering controls, requirement for buffer zones, etc.) should be considered (being mindful of the practicality and cost of the management options). Potentially, exposure could be sufficiently reduced such that new data to refine the risk assessment would not be necessary.

II. Principles for Risk Assessment

a. The decision to request data for a pesticidal substance should start with the 40 CFR §158.45 data requirements relevant to each scientific discipline for the various types of pesticides (*i.e*., conventional, microbial, antimicrobial, and biochemical active ingredients). In some cases, not all of the 'required' or 'conditionally required' data may be triggered or needed. In other cases, additional data beyond the established requirements may be important to the risk management decision.

b. "Starting from scratch" should be avoided if possible; instead, there should be a reliance on what is already known about the pesticidal substance and the uses(s) being assessed. The decision to request data should be built on previous risk assessments when available.

[1] The design of a risk assessment and the information and technical analyses relevant to risk management are identified in the problem formulation stage. See EPA's Guidelines for Ecological Risk Assessment for a conceptual model of problem formulation phase of ecological risk assessments)

c. The scientific rationale for requesting data in the context of the risk assessment and risk management decision should be clear, transparent and consistent both within and across OPP Divisions.

i. It is important to maintain clear distinctions among facts (data), assumptions ("best professional judgment", specific to an assessment, made in the absence of specific data), and science policy decisions (principles that guide scientific decisions *e.g.*, EPA's Risk Characterization Handbook which emphasizes transparency, clarity, consistency, and reasonableness in risk characterization (see Section 1.3) USEPA, 2000).In particular, transparency provides explicitness in distinguishing between data and assumptions as well as articulating the logic and rationale around conclusions.

ii. Because of the uncertainties associated with risk assessment, a qualitative, semi-quantitative, and/or quantitative consideration of the strengths and weaknesses of the available hazard and exposure data that impact the risk conclusions (built on information from previous risk assessment(s), if possible) should be presented.

d. The decision to request or not request data should be based on a weight-of-evidence (WoE) approach and should be related back to the "Problem Formulation" (*e.g.*, USEPA, 2011 presents a weight of evidence analysis that will be used by EPA to evaluate results from the EPA Endocrine Tier 1 Screening program to identify candidate chemicals for Tier 2 testing). Things to consider in the WoE approach are:

i. Nature of exposure and hazard (using multiple lines of evidence from *in vivo studies*, incident data, quantitative structure–activity relationship models, *in vitro assays*, information on related compounds, *etc.*).

ii. Mode of pesticide action and mode of toxicity action.

iii. Other information beyond required studies (*e.g.*, open literature, government reports, international assessments) (*e.g.*, USEPA Guidance for Identifying, Selecting and Evaluating Open Literature Studies promotes the consideration of multiple sources of information when conducting risk assessments for pesticides, not just studies conducted specifically to support pesticide registration, and provides guidance to make transparent to the public how OPP identifies, selects, and ensures that the data used in pesticide risk assessments is of sufficient scientific quality).

iv. Bridging data across pesticidal substances and/or taxa (*e.g.,* formation of chemical categories and read across methods using *in vivo* or *in vitro* data, (Q)SARs, *etc*.). Recent examples of this approach include a bridging analysis of pyrethroids in ecological risk assessment and the evaluation of data from neurodevelopmental studies on pyrethroids and consideration of

comparative sensitivity. QSAR guidance provides assistance on evaluating predicted activities and properties of untested chemicals based on their structural similarity to chemicals with known activities and properties (NAFTA TWG, 2012).

v. How the expected/predicted exposure values relate to the expected/ predicted/empirical hazard values in the context of the uncertainty characterization (*e.g.*, if exposure estimates are well above the hazard values, then additional data may not be needed or vice versa) (*e.g.*, Section 5. Risk Characterization of USEPA, 1998).

e. Resources should be focused appropriately regarding the need to refine a risk assessment using integrated, hypothesis-based tiered approaches based on what is known about the toxicity potential and the pesticide uses/exposure.

III. Summary

These guiding principles are intended to encourage creative thinking and innovation, and guide OPP scientists as to the factors that should be considered in determining what data are needed to adequately assess risks to pesticides. The rationale for data determinations (to require, waive, or rely on data from similar pesticides) should be transparently documented. Although a chosen path may implicate data compensation issues, which would need to be considered and addressed, this should not factor into the decision, scientific considerations should be foremost in determinations of the need for data. However, care should be taken to identify potential data compensation issues for the risk manager.

OPP staff is encouraged to seek advice from the appropriate review committees as necessary. For example, to facilitate and ensure consistency regarding data decisions, OPP recently established a new committee, the Hazard Science Policy Committee, as a central forum and advisory body for discussing critical issues identified in pesticide human health risk assessment. Similarly, the De Minimis Review Committee was also recently established jointly under OPP's Science Policy Council and OPP's Risk Manager's Forum to ensure scientific robustness and consistency around cases that suggest that additional data and a quantitative assessment are not needed to evaluate ecological or human health risks, thus allowing the focus of resources on higher risk scenarios.

Although this document was prepared for OPP staff, these principles are generally viewed as guidance for data waiver requests by registrants (whose responsibility is to show that their pesticidal substance(s) meets the FIFRA and FFDCA protection standards).

References

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