


# Overview of Human Health Risk Assessment Process

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# Mission of Health Effects Division

- Assess the risks of pesticide use to humans and domestic animals
  - We have both the Subdivision F Guidelines and the 40CFR Toxicology Data Requirements to get the data we need for risk assessment



# Data Needs

- HED needs both exposure data and toxicity data to assess the risks
  - The basis for the toxicity data requirements and the dietary exposure data are from the old FDA days
  - Non-dietary exposure data come later
  - FQPA has brought about the need for other data



# Exposure Data

- Exposure data is for both dietary (including water) and non-dietary sources (including applicators, mixer-loaders, residential and reentry into treated fields)
  - Jeff Evans will discuss non-dietary sources
  - Rick Loranger will discuss dietary exposure



# Toxicity Data

- Toxicity data requirements are meant to provide data and endpoints that can be used to:
  - Assess the hazards of pesticides over various routes (oral, dermal and inhalation) durations of time (short, intermediate and long term)
  - Assess hazards during critical periods of life stages



# Durations of Exposure

- These durations of times for any route of exposure are as follows:
  - Acute
    - Single day
    - May use toxicity endpoints of concern from acute neurotoxicity, developmental toxicity, developmental neurotoxicity studies
  - Short term
    - 1-30 days
    - May use toxicity endpoints of concerns from the studies mentioned above plus subchronic studies in mice, rats and/or dogs
  - Intermediate
    - 1-180 days
    - All the above plus subchronic and multi-generation reproduction studies
  - Chronic or long term
    - Greater than 180 days
    - May use toxicity endpoints of concern from chronic toxicity/cancer (rat), cancer (mouse), chronic (dog), multi-generation reproduction (rat) studies



# Critical Testing Period

- Examples of the critical period testing would be as follows:
  - Developmental toxicity
    - During critical periods of gestation examines growth and development of fetuses
  - Reproduction
    - Through reproductive cycle of 2 generations examines reproductive changes in parents and toxicity to offspring
  - Developmental neurotoxicity
    - Prenatal and postnatal, examines functional and morphological hazard in the offspring



# Proposed Changes to Part 158

- The proposed 2005 draft of Part 158 is similar in format & design to the 1984 version
  - Food/Non-food
  - Required/Conditionally required
  - Many footnotes
- Options for toxicity data requirements for non-food uses
  - The key is exposure
    - Magnitude, duration and frequency



# Character of Changes

- There are no sweeping changes but some evolution of data requirements
- But what has changed?
  - Better explanation of why we need the data
  - Explanation of why the data requirements have changed
    - Re-registration process (1988 FIFRA Amendments)
    - The 1983 National Academy Science report
    - The proposed changes in 1994
    - The 1996 FQPA Mandate with emphasis on children's health risk



# Toxicology Data Requirements: Acute Testing

Guide-line	Current requirement	Guide-line	Proposed requirement	Change
81-1	Acute oral toxicity - rat	870.1100	Acute oral toxicity - rat	<b>Modified test substance</b>
81-2	Acute dermal toxicity	870.1200	Acute dermal toxicity	<b>Modified test substance</b>
81-3	Acute inhalation toxicity - rat	870.1300	Acute inhalation toxicity - rat	No changes
81-4	Primary eye irritation - rabbit	870.2400	Primary eye irritation - rabbit	<b>Added testing using the TGAI to support end-use products</b>
81-5	Primary dermal irritation	870.2500	Primary dermal irritation	<b>Added testing using the TGAI to support end-use products</b>



# Toxicology Data Requirements: Acute Testing

Guide-line	Current requirement	Guide-line	Proposed requirement	Change
81-6	Dermal sensitization	870.2600	Dermal sensitization	<b>Added testing using the TGAI to support end-use products</b>
81-7	Acute delayed neurotoxicity - hen	870.6100	Delayed neurotoxicity (acute) - hen	No changes
--	None	870.6200	Acute neurotoxicity - rat	<b>New requirement</b>



# Toxicology Data Requirements: Subchronic Testing

Guide-line	Current requirement	Guide-line	Proposed requirement	Change
82-1	90-day Feeding - rodent	870.3100	90-day Feeding - rodent	Requirement modified to <b>include 2 rodent species</b>
82-1	90-day Feeding – non-rodent	870.3150	90-day Feeding – non-rodent	No changes
82-2	21-day Dermal	870.3200	21-day Dermal	<b>Changed from CR to R for all food uses.</b> Not required for nonfood uses.
82-3	90-day Dermal	870.3250	90-day Dermal	<b>Changed from CR to R for all nonfood uses.</b>
82-4	90-day Inhalation - rat	870.3465	90-day Inhalation - rat	No changes



# Toxicology Data Requirements: Subchronic Testing

Guide-line	Current requirement	Guide-line	Proposed requirement	Change
82-5	90-day Neurotoxicity - mammal	870.6200	90-day Neurotoxicity - rat	<b>Changed from CR to R</b>
82-5	90-day Neurotoxicity - hen	870.6100	28-day Neurotoxicity - hen	<b>New -conditional requirement.</b> Replaces 90-day neurotoxicity hen study



# Toxicology Data Requirements: Chronic Testing

<b>Guide-line</b>	<b>Current requirement</b>	<b>Guide-line</b>	<b>Proposed requirement</b>	<b>Change</b>
83-1	Chronic feeding – rodent and non-rodent	870.4100	Chronic feeding – rodent and non-rodent	No changes
83-2	Oncogenicity – rat and mouse, preferred	870.6100	Carcinogenicity – rat and mouse, preferred	Changed name. Proposed requirement to perform range-finding studies



# Toxicology Data Requirements: Developmental Toxicity & Reproduction

Guide-line	Current requirement	Guide-line	Proposed requirement	Change
83-3	Teratogenicity – 2 species	870.3700	Prenatal developmental toxicity – rat and rabbit, preferred	Changed name. <b>Testing required on a second species</b> for food and nonfood uses
83-4	Reproduction – 2 generation	870.3800	Reproduction	<b>Changed from CR to R for nonfood</b> uses based on potential exposure.
	None	870.6300	Developmental neurotoxicity	<b>New – conditional requirement</b> science-based approach to testing.



# Toxicology Data Requirements: Mutagenicity Testing

Guide-line	Current requirement	Guide-line	Proposed requirement	Change
84-2	Gene mutation	870.5100	Bacterial reverse mutation assay	Replaces current mutagenicity battery
84-2	Structural chromosome aberration	870.5300 870.5375	<i>In vitro</i> mammalian cell assay	Replaces current mutagenicity battery
84-4	Other genotoxic effects	870.5385 870.5395	<i>In vivo</i> cytogenetics	Replaces current mutagenicity battery
			Other mutagenicity studies	No changes



# Toxicology Data Requirements: Special Testing

Guide-line	Current requirement	Guide-line	Proposed requirement	Change
85-1	General metabolism	870.7485	General metabolism	No changes
85-2	Dermal penetration	870.7600	Dermal penetration	No changes
85-1	Domestic animal safety	870.7200	Companion animal safety	No changes
	None	870.6500	Scheduled controlled operant behavior	Replaces current neurotoxicity battery.
	None	870.6850	Peripheral nerve function	Replaces current neurotoxicity battery



# Toxicology Data Requirements: Special Testing

Guide-line	Current requirement	Guide-line	Proposed requirement	Change
	None	870.6855	Neurophysiology: Sensory evoked potentials	Replaces current neurotoxicity battery
	None	870.7800	Immunotoxicity	<b>New requirement.</b> Required for food uses and nonfood uses.