University of Idaho

Special Topic: Pesticide Residues in Food

Principles of Environmental Toxicology
Instructor: Gregory Möller, Ph.D.
University of Idaho

Learning Objectives

- Develop an introductory understanding of pesticide use and monitoring in the human food chain.
- Know the major classes of pesticides.
- Understand the legal basis for monitoring.
- Comprehend the risk vs. benefits analysis basis of
  - FIFRA, FQPA

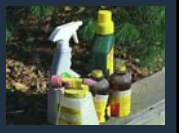
Pesticides

- Economic and public health poisons.
  - Control of insects, weeds, rodents and other pest animals.
  - Bacterial, fungal and viral infection in agriculture, homes and public health applications.
- Natural chemicals, synthetic chemicals, biological agents.
- Residue ≠ or = Risk

Pesticide Data Program

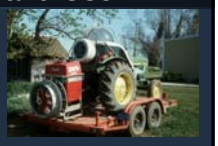
- USDA: Annual survey of target commodities for target chemicals and multi-residue screening (12,446 samples).
- Year 2004 overall results.
  - Detectable residue.
    - 70% of fruit & veg samples.
    - >50% of drinking water samples.
  - Residue exceeding tolerance.
    - 0.2% of samples.
  - Residue without tolerance.
    - 5.2% of samples.
  - http://www.ams.usda.gov/science/pdp/Summary2003.pdf

Scope of US Commercial Activity



- About 865 Active Ingredients (1996).
  - 350 in food chain.
  - ~20,000 products, 9000 tolerances.
  - 1.25 billion pounds (AI) pesticides.
  - Herbicides are >50% of volume, >50% sales; most top 10 use.
- Retail sales.
  - >$10 B (Ag, Non-Ag).
  - >$8 B (Agricultural).

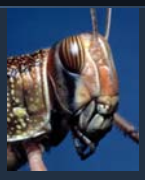
Trends in Regulation and Use



- Lower use rate.
- Low-volume application.
- Risk mitigation requirements.
- Integrated Pest Management (IPM).
- Conditional registration (monitoring).
- Safer chemicals.
- Biopesticide use.
- Increased exposure concerns.
  - Patterns, routes and levels.
  - Applicator training.

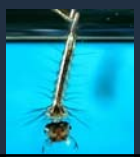
Major Classes of Pesticides

- Insecticides.
- Herbicides.
- Fungicides.
- Rodenticides.
- Bactericides.
- Biopesticides.
- Special application.



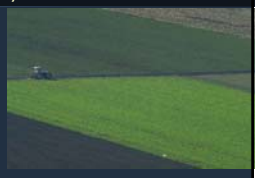
Special Application Chemicals

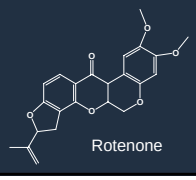
- Acaracides, Algicides, Avicides, Bactericides, Piscicides, Virucides, Molluscicides.
- Insect attractants, Insect repellants, Bird repellents, Mammal repellents.
- Plant growth activators.
- Synergists.



Pesticides, 1

- Antibiotic insecticides.
  - Abamectin, Spinosad.
- Arsenical insecticides.
  - Lead arsenate.
- Botanical insecticides.
  - Nicotine, Pyrithrins, Rotenone.

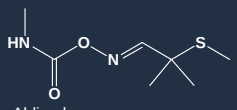




Rotenone

Pesticides, 2

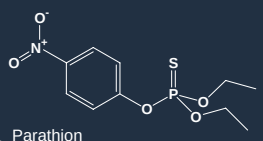
- Bacterium
  - *Bacillus thuringiensis* (Bt)
- Carbamate insecticides.
  - Aldicarb, Carbaryl, Carbofuran, Oxamyl.
- Organochlorine insecticides.
  - Aldrin, Dieldrin, DDT, Endrin, Methoxychlor, Pentachlorophenol.



Aldicarb

Pesticides, 3

- Organophosphorus insecticides.
  - Azinphos-methyl, Dichlorvos, Chlorpyriphos, Fenthion, Diazinon,
  - Malathion, Parathion.
- Pyrethroid insecticides.
  - Fenvalerate, Permerthrin, Resmethrin.



Parathion

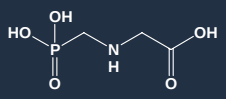
Pesticides, 4

- Botanical rodenticides.
  - Strychnine.
- Coumarin rodenticides.
  - Brodifacoum, Bromodialone, Warfarin.
- Inorganic rodenticides.
  - Zinc Phosphide.
- Unclassified rodenticides.
  - Ergocalciferol, Sodium Fluoroacetate.

Strychnine

Pesticides, 5

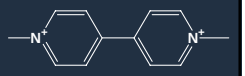
- Amide herbicides.
  - Metolachlor.
- Dinitrophenol herbicides.
  - Dinoseb.
- Imidazolinone herbicides.
  - Imazethapyr.
- Organophosphorus herbicides.
  - Glyphosate.



Glyphosate

Pesticides, 6

- Phenoxyacetic herbicides.
  - 2,4 D.
- Quaternary ammonium herbicides.
  - Diquat, Paraquat.
- Thiocarbamate herbicides.
  - Molinate.
- Triazine herbicides
  - Atrazine.
- Sulfonylurea herbicides.
  - Metsulfuron.



Paraquat

Legal Basis for Monitoring

- 1906 The Jungle (U. Sinclair).
- 1906 Federal Meat Inspection Act; 1906 Pure Foods and Drug Act.
  - 1938 Federal Food, Drug and Cosmetic Act, FFDCA.
- 1910 Federal Insecticide Act, then
- 1947 Federal Insecticide, Fungicide and Rodenticide Act.
- Modern amendments.

Delaney Clause

- 1958 Delaney Clause (FFDCA)
  - Zero-risk cancer standard for residues in processed foods.

Legal Basis for Monitoring, 2

- Federal jurisdiction.
  - EPA, FDA (HHS), FSIS (USDA), AMS (USDA)
- Authority.
  - FIFRA, FFDCA, FMIA, PPIA, EPIA
- EPA – Registration, RA, tolerance, environmental quality.
- FDA – Tolerance enforcement.
- FDA, FSIS, AMS
  - Food monitoring.
- State primacy for FIFRA.
- 1996 Food Quality Protection Act.

Legal Basis for Monitoring, 3

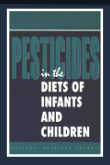
- SDWA - Safe Drinking Water Act.
  - Maximum contaminant levels.
- CWA - Clean Water Act.
  - NPDES discharge permits.
- RCRA - Resource Conservation and Recovery Act.
  - Listed wastes.
- CERCLA (Superfund)
  - Hazardous substances.

Why FQPA?

- Years in the making: adopts most scientific recommendations
- Delaney Paradox
  - Different regulations for processed and raw foods
  - No detectable level of carcinogens allowed in processed foods
  - Court decisions requiring enforcement of Delaney, 1993/95

Motivation for Change

- NAS "Kids" Study: Pesticides in the Diets of Infants and Children, 1993.
- Minor crop pressure, streamlining.
- 1996 Election year opportunism.
  - Origins in Commerce Committee: Consumers.
  - Unanimous passage, House/Senate.



NAS Kid's Study Results

- The exposure of children to pesticides is substantially different from that of adults.
- The government needs to do more to address the unique risks posed to children.

Consumed by “Kids"

Non-nursing infant subgroup

Commodity	g /kg/day
milk	10.9
apples	6.3
oranges	2.7
peaches	2.1
soybeans*	1.6
pears	1.6
carrots	1.5

*component as soybean oil

NAS

Children: Not Just Little Adults

- About 300 Active Ingredients (AI) registered for top 20 commodities eaten by infants and children.

Some FQPA Changes

- Kids as the dose model.
- Additive toxicity.
- Aggregate exposure.
- Endocrine disruption.
- “Reasonable certainty of no harm” health standard.
- Right-to-know.

FIFRA

- Federal Insecticide, Fungicide, and Rodenticide Act.
- FIFRA is a Licensing Authority...labels are the license.
- FIFRA is one of the few risk vs. benefits statutes.

FIFRA

- FIFRA gives EPA strong authority to require any data necessary to evaluate risk to human health and the environment.
  - Registration is national in scope and authority.
  - Registrant-generated data used to evaluate risk.

Human Health

NAS Risk Assessment Process

1. Hazard Identification.
   - Toxicity testing, adverse effects.
2. Dose-Response Assessment.
   - Quantitative toxicity.
3. Exposure Assessment.
   - Food, water, home, workplace.
4. Risk Characterization.
   - Risk = Toxicity x Exposure.

Agrichemical Registration

- As many as 70 specific tests may be required (> $10M cost).
  - Health effects and toxicology.
  - Environmental fate.
  - Ecological effects.
  - Residue chemistry.
- Commercial development.
  - 10 yr cycle, $50M.

TTR: Total Toxic Residue

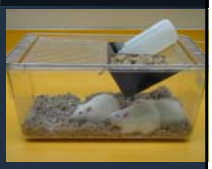
- Agrichemical residue plant/animal metabolism.
- Typically with radiolabeled parent compound (AI).
- Track and identify metabolic products.
  - Attempt to identify >80-90% TTR.
- Separate toxicology trials for major metabolites sometimes warranted.
- Effects of food processing and use of product as animal feed.

Human Health

- Prior to Food Use Registration.
- Ecological.
  - Acute and chronic.
  - Aquatic and terrestrial.
- Human Health.
  - Acute and chronic.
  - Populations and sub-populations.
  - Special protection for children.

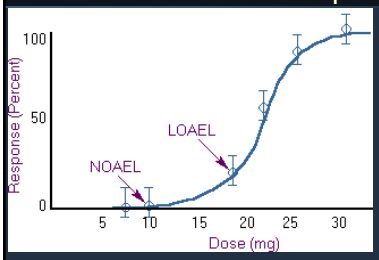
Risk = Toxicity x Exposure

- Dosage - Response Experiment.
- No observed effect level (NOEL).
  - Threshold Effect: mg/kg/day
- NOEL / 100 for uncertainty is the Reference Dose, RfD.
- Possible safety factors.
  - 10x to 100x.
  - Sub-population sensitivity.



 EPA

Dose - Response



- No observed adverse effect level.
- Lowest observed adverse effect level.

 NLM

Reference Dose

- Derived from animal studies - best available data
- No observable adverse effect level (NOAEL)
- Uncertainty factors added to account for differences in species (10x) and differences among individuals (10x) = 100x

Reference Dose, RfD

- An aggregate daily exposure to a pesticide residue at or below the RfD is considered generally acceptable by EPA.
  - Expressed as 100% or less of the RfD.
- Additional mechanisms of risk assessment if carcinogenic.
  - Non-threshold effects.

 EPA

Reference Dose - Cancer

- The dose that will not increase cancer incidence more than 1/1,000,000 over background
- Animal studies done at high doses and extrapolated to low doses
- Small populations extrapolated to large populations

Tolerance

- Tolerance is established by review of field efficacy data, crop residue data, daily/lifetime dietary exposure and RfD.
  - Maximum legal pesticide residue level.
  - Absence of tolerance: adulterated.
- Required for "Emergency Exemptions"

Maximum Residue Levels (MRL)

- International tolerances
- Established by World Health Organization, Food and Agriculture Organization (WHO-FAO)
- 50% equivalent to US
- US 20% more stringent, 30% less

TMRC

- Theoretical Maximum Residue Contribution. EPA
- Dietary exposures.
  - Aggregate exposures: foods, water, non-occupational exposure.
- Estimate of residues consumed daily if each food item contained pesticide residues equal to the tolerance.
  - Worst case estimate if no data.
    - Food contains residues at tolerance levels.
    - 100% of the crop is treated.
    - No removal by cooking.

Risk Cup

- Each new crop use of a chemical adds to the dose total.
- Cannot exceed 100% of RfD.
- 70 yr exposure.

Safety Standard

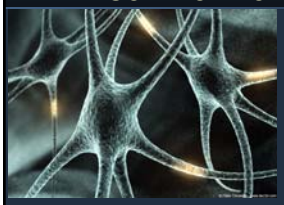
- The statute establishes a strong health-based safety standard for pesticide residues in foods:
  - A single, safe, "reasonable certainty of no harm" standard for both raw & processed foods (all foods must be safe).

 EPA

FQPA Tolerances

- Tolerance re-evaluation.
- New law required review of ALL tolerances.
- 1996 Schedule:
  - 33% within 3 years
  - 66% within 6 years
  - 100% within 10 years
- Priority for review given to pesticides that had greatest risk to public health
  - OP's, OC's, developmental tox.

Common Toxicity Mechanism



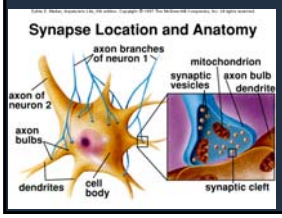
- Additive toxicity (2+2=4)
  - Neurotoxicity from organophosphorous and carbamate insecticides
- Risk cup (RfD) implication

Cholinesterase Inhibition

Cholinesterase Inhibition

- Acetylcholine is the chemical mediator responsible for physiological transmission of nerve impulses across the synapse.
- Acetylcholinesterase is the enzyme that modulates ACh.

Cholinesterase Inhibition Animation

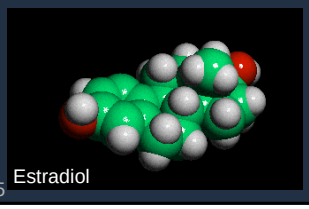


Aggregate Exposure

- Aggregate exposure to pesticides used in calculation of risks.
- Drinking water, yard/household chemicals, non-occupational exposure.
  - About 25% of all water used in the U.S. is from groundwater.
  - Approximately 50% of population use gw as their main supply of drinking water.
    - e.g. Atrazine concerns

Endocrine Disrupters

- Chemicals which interfere with endocrine system function.
- Consists of glands and the hormones they produce.
  - Pituitary, thyroid, and adrenal glands, the female ovaries and male testes.


Estradiol

Endocrine Disrupters, 2

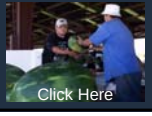
- Hormones are biochemicals.
  - Produced by endocrine glands.
  - Travel through the bloodstream and cause responses in other parts of the body.
- Hormones of primary concern.
  - Estrogen, androgen and thyroid hormones.

Consumer Right-to-Know

- FQPA required a number of new actions to take place.
- "Pesticides and Food" brochure.
- Publication of data summaries in the Federal Register (new).

Pesticide Food Poisoning

At 4 a.m., July 4, 1985, three adults who ate a solid green watermelon purchased in Oakland, California, had rapid onset of nausea, vomiting, diarrhea, profuse sweating, excessive tearing, muscle fasciculations, and bradycardia. Aldicarb, a carbamate insecticide and potent AChE inhibitor not registered for watermelons, was found in the samples. In the next month, 762 probable or possible cases were reported. The most severe signs and symptoms included seizures, loss of consciousness, cardiac arrhythmia, hypotension, dehydration, and anaphylaxis.


Click Here