

# Pesticide Residues in Food

Food Toxicology

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## 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  $\neq$  or = Risk

## Pesticide Data Program

### 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, Pyrethrins, Rotenone.

## Pesticides, 2

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

## Pesticides, 3

- Organophosphorus insecticides.
  - Azinphos-methyl, Dichlorvos, Chlorpyrifos, Fenthion, Diazinon,

- Malathion, Parathion.
- Pyrethroid insecticides.
  - Fenvalerate, Permethrin, Resmethrin.

## Pesticides, 4

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

## Pesticides, 5

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

## Pesticides, 6

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

## 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, FFDC.
- 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”

### 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

- Hazard Identification.
  - Toxicity testing, adverse effects.
- Dose-Response Assessment.
  - Quantitative toxicity.
- Exposure Assessment.
  - Food, water, home, workplace.
- 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.

## Dose - Response 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.

### 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.
- 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).

## 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

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

## 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.

## 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