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 ≠ 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, Pyrithrins, 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, Chlorpyrphos, Fenthion, Diazinon,
• Malathion, Parathion.
• Pyrethroid insecticides.
  – Fenvalerate, Permerthrin, 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).
  – 1938 Federal Food, Drug and Cosmetic Act, FFDCA.
• 1910 Federal Insecticide Act, then
• Modern amendments.

Delaney Clause
• 1958 Delaney Clause (FFDCA)

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.
  – 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
• Minor crop pressure, streamlining.
• 1996 Election year opportunism.
  – Origins in Commerce Committee: Consumers.
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 = Toxicty 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