

Toxicology Data Basis for Risk Analysis

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Risk Analysis

- ◆ Sources of concern
- ◆ Sources of information
- ◆ Sources of uncertainty
- ◆ Data → Policy
- ◆ Relative risks



Sources of Concern



1. Whole food
2. Food components
3. Food contaminants
4. Food additives
5. Interactions
6. Nutrition – related considerations



Sources of Concern

1. Whole food

- ♦ very hard to test in animals
- ♦ nutritional value based on composition
- ♦ wholesome



2. Food Components

- ♦ toxins – alkaloids; harsh conditions
- ♦ pharmacological activity – dietary supplements
- ♦ constituents – fat, protein, carbohydrates, etc.
- ♦ allergens



3. Food Contaminants

- ♦ toxins – mycotoxins
- ♦ toxicants
 - ♦ avoidable – from processing, handling
 - ♦ unavoidable – heavy metals
- ♦ pesticides
- ♦ allergens – from processing



4. Food Additives

- ♦ preservatives
- ♦ flavoring agents
- ♦ colors
- ♦ consistency modifiers
- ♦ leachates from food wraps, containers



5. Interactions

- ♦ none
- ♦ additive
- ♦ inhibitory
- ♦ supra-additive or potentiation
- ♦ dietary supplements and drugs



6. Nutrition-related Considerations

- ♦ nutrient or micronutrient deficiency
- ♦ caloric intake
- ♦ interactions
- ♦ anti-nutritive effects - genetically modified foods



Sources of Information



1. Human data
2. Animal data
3. In vitro, short term screens
4. SAR or predictive model data
5. mechanistic knowledge

Sources of Uncertainty

- ◆ human to human (10x)
- ◆ animal to human (10x)
- ◆ subchronic to chronic (10x)
- ◆ route to route
- ◆ high to low dose
- ◆ quality of database

Safe Level of Intake

Cancer endpoints

- assume no threshold
- upper bound estimate of relative risk from cancer slope

Non-cancer endpoints

- assume threshold
- NOAEL/uncertainty factor

Experience Translated to Policy

- ◆ Constituents Policy
 - carcinogenic contaminant in a noncare additive
 - reasonable certainty of no harm
- ◆ Threshold of Regulation
 - untested migrant, <0.5 ppb in total diet
 - reasonable certainty of no harm
- ◆ DES Proviso to the Delaney Clause
 - no residue of a carcinogen in edible tissues

Relative Risks

Deaths: Food Related

Cancer, $<1 \times 10^{-6}$ from lifetime exposure

Mad Cow disease, 125 world-wide

Food poisoning, 5,000 deaths/yr

Obesity-related, $>330,000$ /yr

Relative Risks

Deaths: Food related

Cancer, $<1 \times 10^{-6}$

Mad Cow disease, 120 world-wide

food poisoning, 5,000 deaths/yr

Obesity-related, $>330,000$ /yr

Non-food related

SARS, >750 deaths world-wide

Influenza, 30-40,000/yr

Breast cancer, 40,000/yr

Medical errors, 100,000/yr

Cardiovascular disease, 400,000/yr



Summary

Risk Analysis – Food Safety

- ◆ Complex
- ◆ Controversial
- ◆ Involves uncertainty
- ◆ Certain life-style choice create high risk