Toxicology Data
Basis for Risk Analysis

Bernard A. Schwetz, D.V.M, Ph.D.
Acting Director, Office for Human Research Protections
Department of Health and Human Services
CSL/JIFSAN Joint Symposium

June 11, 2003
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, <1x10^-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