Hazard Identification

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Toxicology Definition

The study of poisons
and
the adverse effects of chemical and
physical agents on living organisms.

Paracelsus- The Father of Toxicology

- "All things are poison and nothing is without poison, only the dose permits something not to be poisonous."
  - Substances often considered toxic can be beneficial in small doses, and conversely an ordinarily benign substance like water can be deadly if over-consumed

Introduction to Hazard Identification

- Hazard Identification is the process of determining whether exposure to a chemical can cause an increase in the incidence of specific adverse health effects (e.g., cancer, birth defects).

- The process examines the available scientific data for a given chemical (or group of chemicals) and develops a weight of evidence to characterize the link between the negative effects and the chemical agent.

Hazard Identification, cont'd

- Collection of Data
  - Various Sources
  - Toxicological and Epidemiological Studies

- Information should answer these questions
  - Does exposure to the substance produce any adverse effects?
  - If yes, what are the circumstances of the exposure?

- Hazard ≠ Risk
  - Findings in animal studies does not mean same results will happen in humans
  - Saccharin

Factors that Influence Toxic Effects

Form and innate chemical activity	Pharmacokinetics
Dosage, especially dose-time relationship	• Absorption • Distribution • Metabolism • Excretion
Route of Exposure	
Age	
Sex	

Highlights of Our Safety Standards

- Toxicology evaluations should be based on high quality safety studies
- Fair evaluation of the entire record
- Benefits of ingredient not weighed in safety decision
- Assessments designed to support safe use of ingredients in all segments of the population (e.g. pregnant women, children, etc)
- Safe standards are the same for natural and synthetic ingredients

Endpoints of Toxicological Concern

- Acute Toxicity
- Mutagenicity
- Repeated Dose Toxicity
- Carcinogenicity
- Reproductive Toxicity
- Developmental Toxicity

Which studies tell you about the additive's:

Safety in pregnant women?

Safety for use long-term?

Safety for use short-term?

Consumer Safety is First and Foremost

- We ask ourselves several questions during the safety evaluation:

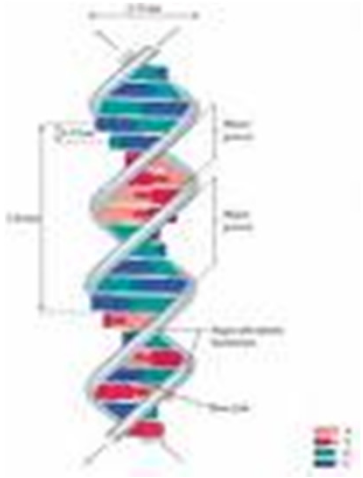
Potential Issue	Toxicology Studies
Will a consumer get sick shortly exposure to the additive?	Short-term toxicity studies
What if a consumer is pregnant/nursing?	Reproductive toxicity studies
Will any of the ingredients have a potential to cause cancer?	Cancer studies; genetic toxicity studies
Will small amounts over time lead to sickness?	Longer-term toxicity studies

Acute Toxicity

- Application of a single or short period of time (generally less than 1 day)
- Typically addresses expected outcome from accidental exposure to a chemical
- Tests rarely used for food ingredients.
- The acute toxicity of a substance is defined by its LD_{50} / lethal dose that will kill 50% of a group of exposed animals; usually rodents
- Timing for results: One Month

Mutagenicity Testing

- Determines if an ingredient has the potential to affect DNA
- DNA damage contributes to various disorders such as cancer
- DNA damage may have an increased incidence of genetic disease in future generations
- In-vitro (human or bacterial cells) and in-vivo assays (rats or mice) used
- Examples: Ionizing radiation; food dye, butter yellow
- Timing for results: 5 months



Repeated Dose Toxicity

- Designed to assess effects of repeated exposures to a test material
- A 90-day study duration is most common; typically rats
- Test article administered via the route of intended human exposure (e.g. oral, inhalation)
- Evaluates systemic toxicity to various organs throughout the body (e.g. lungs, kidney, liver, brain etc.)
- If toxic symptoms are expressed, they are referred to as symptoms of “subchronic toxicity”
- Establishes No-Observed-Effect Level (NOEL)
- Timing: 9 months

Developmental Toxicity

- Evaluates adverse effects of a chemical on growth and development
- Evaluations typically performed in rabbits or rats
- Test material usually given during critical periods of organogenesis (days 6-15 rats; days 6-18 rabbits)
- Example: Vitamin A
- Timing for results: 9 months

Reproductive Toxicity

- Evaluates the adverse effects of chemicals on male and female fertility
- Typically conducted in rats
- Test material administered prior to mating, during mating, gestation and lactation
- Assessments made on the number of pregnancies, litter size, and number of stillbirths
- Timing for results: 14 months

Infertility?

The McCoughey Septuplets

Carcinogenicity

- Looks for effects that take time to develop (e.g. cancer)
- Typically conducted in rats or mice
- Test article administered via the route of intended human exposure
- Involves continuous feeding of the test substance to rodents for 20-24 months.
- Number and type of tumors determined
- Timing for results: 3 years

Organ Specific Toxic Effects

- Blood/Cardiovascular Toxicity (effects on blood cells, bone marrow or heart)
- Immunotoxicity (e.g. leukemia, allergy, immune deficiency)
- Kidney toxicity (high blood flow; can concentrate toxicants)
- Liver Toxicity (high blood flow; site of metabolism)
- Neurotoxicity (damage to brain and spinal cord)

Bridging the Results

- Was any evidence of toxicity observed?
- If yes, what do we know about the doses that produced the toxic effects?
  - Dose-Response Assessment is the process of quantitatively evaluating the toxicity of a chemical agent as a function of the dose administered.
  - The relationship between the dose of the chemical administered and the incidence of adverse health effects forms the basis for the quantitative dose-response relationship.
  - From these relationships, toxicity values (e.g., acceptable daily intake values) are derived that can be used to estimate the potential for adverse effects in an exposed population
- Remember, a finding of toxicity does not automatically mean the same will occur in humans
- The manner in which we characterize the hazard will be discussed in the next module