Nutrition Product Safety Program

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Importance of a Safety Program

- Ensure safe products
  - Manufacturer is responsible for the safety of their product
- Enhance consumer confidence
- Support the company and brand reputation
- Safety is important
  - Safety program, dedicated safety scientist, resources

Safety Program Responsibilities

Involved early and throughout the products' lifetime

- Pre-market: Safety Assessment of Raw Materials and Finished Goods
- Product Development: Support Development and Clinical and Consumer Product Tests
- Post-market: Monitor and Respond to Adverse Events and Safety Questions

Preliminary Safety Review

- Early in process
- Top-line assessment of safety
- Resource for new product directions
- Identify possible risks and solutions early in development

Sources of Safety Information

- Supplier
  - Ingredient characteristics
  - Non-published studies
- Publicly available literature
  - Web-based search
  - Pubmed, scientific organizations, government
- ABG-Nutrilite
  - Quality Assurance/Analytical Services
  - Product Development

Process to Evaluate Safety

Review and summarize the various sources of relevant information; may include:

- Clinical studies
- Animal toxicity tests
- Non-toxicity animal tests
- In vitro studies
- Pharmacology, metabolism studies
- Bioassays
- History of Use

Process to Evaluate Safety

Conduct risk assessment by evaluating:

- Toxicity endpoints. The most relevant are human clinical study outcomes, followed by chronic/subchronic animal studies, then other animal or in vitro studies. Best sources are peer reviewed, published scientific articles.

- If toxicity endpoints are not available, look for statements such as “no adverse events” reported; or studies evaluating effect of known chemical constituents.

Process to Evaluate Safety

Evaluate additional considerations such as:

- Long history of use
- Are there any specific market considerations (ie upper limits for vitamins/minerals)

Process to Evaluate Safety

Same Standard of Safety
is Applied Globally

Process to Evaluate Safety

Regulatory Compliance

PRELIMINARY GO
Information sufficient and shows safe use

INSUFFICIENT DATA
to determine safety (additional data needed- identify gaps and how to get additional information)

CONCERN
Preliminary information reveals possibly unsafe for proposed use

Safety Assessment Report-Ingredient

If the ingredient will be used in product, then Safety Assessment Report (SAR) is written for the individual ingredient

- Scientific name, part, processing, extract ratio
- Literature review of animal, human, in vitro studies
- Risk assessment: acceptable daily intake, interactions, contraindications, identify any risks associated with intake

Guidelines for SARs

- There are several authoritative bodies with guidance documents on how to conduct a safety assessment on botanical or food ingredients
  - US IOM; US NTP
  - Health Canada
  - Australia TGA
  - WHO
  - ILSI
- SARs follow internationally recognized guidance documents

Guidelines for SARs

- Highlighted method of Safety Assessments
  - Determination of No Adverse Effect Level
  - Use of Safety Factors
  - Estimate of Acceptable Daily Intake (or Upper Limit of Safety)
  - Consideration of all available studies
  - Ingredient evaluated on a case-by-case basis

Toxicology Studies

- Genetic
- Acute
- Short-term or sub-chronic
- Chronic
- Specialized studies
  - Reproductive tox, developmental tox, neurotox

Human Studies

- Clinical studies
- Epidemiology studies
- Case reports
- Useful if documented dose-response, side effects, highest observed safe dose, duration of intake

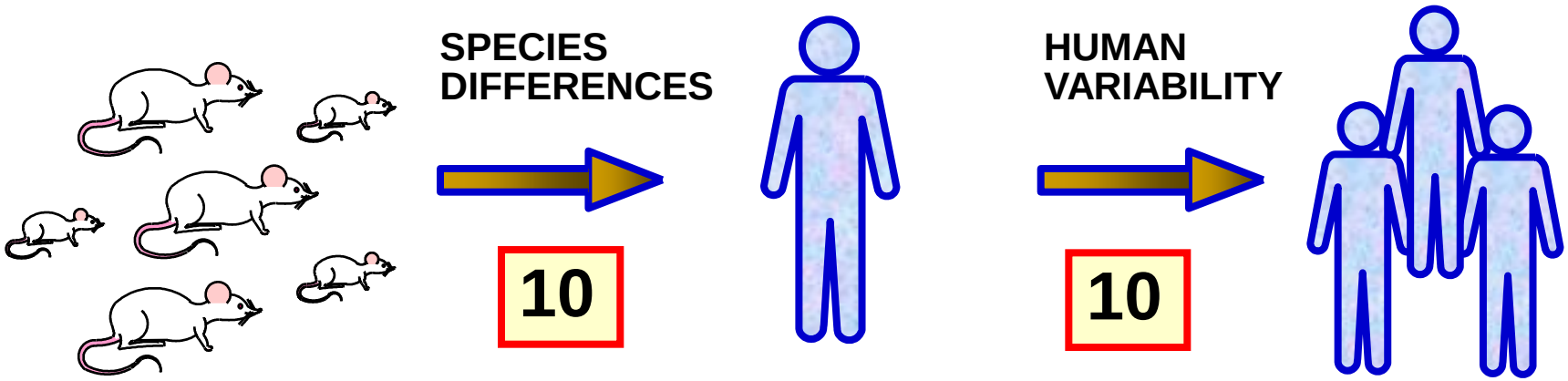
NOAEL

- NOAEL is the No Observable Adverse Effect Level. It is the greatest dose of an agent that causes no detectable adverse alteration of morphology, function, growth, development or lifespan of the target.
- NOAEL is commonly obtained from animal toxicology studies
- For human studies, highest observed safe dose can generally substitute

Using NOAEL

- The NOAEL from animal studies is used to determine the allowable daily intake for humans
- A safety factor or margin of safety is used to find a safe dose for humans

Use of Safety Factors



Safety factors are used to extrapolate from <u>animals to an average human</u> and <u>from average humans to potentially sensitive sub-populations</u>

10 X **10** = **100**

A standard safety factor of 100 is generally applied; Safety factor is also the margin of safety (MOS)

Acceptable Daily Intake

ADI is an estimate of the amount of a [food additive] that can be ingested daily over a lifetime without appreciable health risk (JCFA/WHO)

$$\text{ADI} = \frac{\text{NOAEL}}{\text{SAFETY FACTOR (100)}}$$

Other Potential Toxicants

May be called upon to review other issues:

- Naturally occurring (mycotoxins)
- Produced during processing
- Present due to known uses (pesticides, solvent residues)
- Present unintentionally (metals)

Product Safety Assessment Report

- Overview of the finished good or product
- Safety summaries of all active ingredients
- List of interactions, contraindications
- Possible side effects
- Cautionary statement
- Previous marketing experience
- Clinical or consumer preference study results

How SARs are used

- Inquiries or inspections, requests for more information, complaints, addressing adverse events
- Registrations
- Support introduction of ingredient new to specific markets
- Company SARs are recognized in all (80+) markets

Support Clinical and Consumer Preference Testing

- Safety provides input to:
  - Informed consent
  - Study protocol
  - Study group
  - Advise on potential side effects
  - Follow up evaluation

Monitor and Respond to Adverse Events and Safety Questions

- Review Adverse Event databases
- Requirement for post-market surveillance
- Monitor and review AE reports and trends
- Use AE reports to advise on product design or reformulation
- Respond to safety related questions
- Monitor literature for new studies
- Evaluate new, often controversial, studies

Company-wide support of safety of products

Product safety is a shared responsibility among all departments

- Product Development
- Quality Assurance
- Technical Regulatory Affairs
- Analytical Services
- Project Management
- Marketing
- Legal
- Customer Service

Thank You !

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