Hazard vs Risk

PFNDAI Webinar

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October 31, 2023

Definitions

- Hazard – a source of potential harm

- Risk - the likelihood of harm from a hazard

Risk Assessment of Food Additives

1. **Hazard Identification**
2. **Dose Response Assessment**
3. **Exposure Assessment**
4. **Risk Assessment**

Risk = Hazard x Exposure

Hazard Identification

Questions	Toxicology studies
Will a consumer get sick shortly after exposure?	Short-term toxicity studies
Is it safe for pregnant/nursing consumers?	Developmental/Reproductive toxicity studies
Does the additive have a potential to cause cancer?	Genetic toxicity studies Carcinogenicity studies
Will small amounts over time lead to sickness?	Longer-term toxicity studies

Guideline Toxicity Studies for Hazard Identification

- **Validated methodologies**
- **Fit-for-purpose study designs**
- **Designed to measure adversity**
- **Comprehensive battery from *in vitro* to multi-species *in vivo***
- **Defined principles for utility in risk assessment**

Dose Response Assessment

"All things are poison, and nothing is without poison; only the dose makes a thing not a poison."

Paracelsus

The Dose Makes the Poison

Dose Response Assessment

No Observed Adverse Effect Level (NOAEL): based on results of all animal studies including chronic, cancer, and developmental/ reproductive studies

Acceptable Daily Intake (ADI): the amount of additive that is considered safe to consume each day over the course of a person's lifetime

ADI is protective for all population group

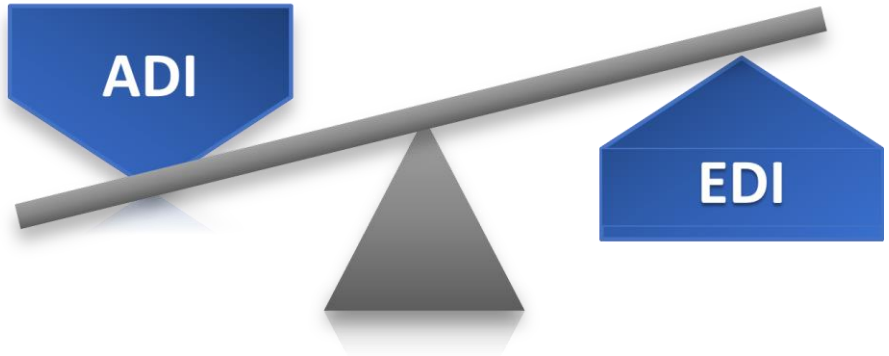
ADI is established based on application of uncertainty factors (UF) to the NOAEL (both in mg/kg bw/day)

ADI = NOAEL : UF

Typically, UF = 100 (10 x 10)

Exposure & Risk Assessment

Estimated Daily Intake (EDI): provides estimates of daily human intake based on consumption rates of various foods/beverages likely to contain the additive.



CASE STUDY: ASPARTAME

IARC vs JECFA

Summer 2023

- Methyl ester of the aspartic acid & phenylalanine dipeptide
- Breaks down in small intestine into its constituent amino acids & methanol
- 200 times sweeter than table sugar => low calories
- ADI* = 40 mg/kg bw/day => 2.4 g/day for a 60 kg adult
- Can of diet soda (350 ml) contains ~180 mg; ~13 cans of diet soda to consume daily to surpass the ADI

* People with difficulty metabolizing phenylalanine because of a rare genetic disorder phenylketonuria (PKU) should avoid or restrict aspartame

Divergent principles led to conflicting opinions

Focus on HAZARD & limited evidence

International Agency Research on Cancer

World Health Organization

Possibly carcinogenic to humans (Group 2B) based on limited evidence for cancer in humans and in experimental animals

> "..but chance, bias or confounding could not be ruled out as an explanation for the positive findings".

Focus on RISK & totality of evidence

JECFA

JOINT FAO/WHO EXPERT COMMITTEE ON FOOD ADDITIVES

- No convincing evidence from experimental animal or human data that aspartame causes cancer
- No reason to change the ADI

Safety studies with aspartame

- Over 100 animal studies designed to identify possible toxic effects on the reproductive and nervous systems, carcinogenicity, metabolism, & other.
- Not genotoxic (not damaging to DNA)
- 12 carcinogenicity studies of aspartame: all apart for 3 by Soffritti et al.* (2005; 2007; 2010) showed negative results

  *there were serious limitations in the design, execution, reporting and interpretation of these studies (EFSA, FDA, JECFA)
- Human epidemiological studies: examined the association between aspartame and cancer in cohort studies & found positive association in some of them

  Reverse causality, chance, bias and confounding by socioeconomic or lifestyle factors, or consumption of other dietary components, could not be completely ruled out

29 national regulators reaffirmed safety of aspartame after the IARC/JECFA report

- US FDA
- European Food Safety Authority
- Food Safety and Standards Authority of India
- China National Food Safety Risk Assessment Center
- United Kingdom Food Standards Agency
- Health Canada
- Food Standards Australia New Zealand
- South Korea Ministry of Food and Drug Safety
- Japan Food Safety Commission
- Brazil Health Regulatory Agency (Anvisa)..

FDA Response to Reviews of Aspartame

- The FDA is aware of the International Agency for Research on Cancer (IARC) and Joint FAO/WHO Expert Committee on Food Additives (JECFA) conclusions about aspartame issued July 14, 2023. Aspartame being labeled by IARC as "possibly carcinogenic to humans" does not mean that aspartame is actually linked to cancer.
- The FDA disagrees with IARC's conclusion that these studies support classifying aspartame as a possible carcinogen to humans. FDA scientists reviewed the scientific information included in IARC's review in 2021 when it was first made available and identified significant shortcomings in the studies on which IARC relied. We note that JECFA did not raise safety concerns for aspartame under the current levels of use and did not change the Acceptable Daily Intake (ADI).
- Aspartame and Other Sweeteners in Food | FDA

Conclusions

- HAZARD ≠ RISK
- Regulatory/policy decisions should be based on science-based risk assessments, not only hazard identification
- Avoid situations where divergent opinions create consumer confusion

Any Questions