Characterizing the Risks of Acrylamide in Food

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Overview

◆ The Challenge of Risk Characterization

◆ Examining Current Risk Characterizations of Acrylamide in Food

◆ Key Issues for Risk Characterization
Risk Characterization

- Summarizes scientific knowledge about the a risk
- Important information for decision-makers
- Key part of risk communication
What Should be In a Risk Characterization?

• "The description of the nature and often the magnitude of human risk, including attendant uncertainty."
  

• Integration of hazard identification, hazard characterization and exposure assessment into an estimation of the adverse effects likely to occur in a given population, including attendant uncertainties

  *Joint FAO/WHO Expert Consultation on Application of risk analysis to food standards issues*
Key Points

Risk Characterization should:
- Address the potential adverse effects
- Be quantitative
- Characterize uncertainty

“Well-balanced risk characterizations present risk conclusions and information regarding the strengths and limitations of the assessment for other risk assessors, EPA decision-makers, and the public”

Risk Characterization of Acrylamide in Food

- Petition to Establish Interim Acceptable Levels for Acrylamide In Major Food Sources Submitted by the CENTER FOR SCIENCE IN THE PUBLIC INTEREST US Department of HHS/US FDA - June 4, 2003
- Risk Assessment of Acrylamide Intake from Foods with Special Emphasis on Cancer Risk Report from the Scientific Committee of the Norwegian Food Control Authority - 6 June 2002
- Risk Assessment of Acrylamide Intake from Cereal-Based Baby Foods Report from the Scientific Committee of the Norwegian Food Control Authority - 13 December 2002
- Assessment of Cancer Risk due to Acrylamide Intake from Coffee Consumption Report from the Scientific Committee of the Norwegian Food Control Authority - 13 December 2002
- EUROPEAN COMMISSION - HEALTH & CONSUMER PROTECTION DIRECTORATE-GENERAL Scientific Committee on Food - Opinion of the Scientific Committee on Food on new findings regarding the presence of acrylamide in food - SCF/CS/CNTM/CONT/4 Final 3 July 2002

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Characterizing Hazards

- All assessments discuss cancer, genotoxic potential, and neurotoxicity
- Some mention reproductive/developmental toxicity
- Most discuss both toxicologic and epidemiologic evidence
Quantifying Risks - Exposure

- Dybing & Sanner - Norwegians - food and coffee
  - Male - mean 0.49 µg/kg/day (97.5 - 1.62 µg/kg/day)
  - Female - mean 0.46 µg/kg/day (97.5 - 1.45 µg/kg/day)

- CSPI - American diet - CSFII with “modifying factors”
  - 0.53 µg/kg/day
  - No discussion of distribution

- Konings, E.J.M., et al. - Dutch diet
  - Mean intake 0.48 µg/kg/day
  - 99th percentile 1.0 µg/kg/day
Quantifying Risks - NonCancer

- Dybing & Sanner
  - NOAEL of 0.5 mg/kg/day - rat peripheric neuropathy
  - NOAEL of 5 and 2 mg/kg/day - rat repro/developmental

- CSPI
  - Use FDA ADI of 12 µg/day (0.17 µg/kg/day) - rat neurotoxicity

  - NOAEL of 0.5 mg/kg/day - rat peripheric neuropathy
Characterizing NonCancer Risk

- Dybing & Sanner
  - Margin of safety for average male - ~1000
  - Highest intake (97.5th 13 yr old boy) - 175

- CSPI
  - “Using our exposure estimate of 34 micrograms per day, it appears that the average American is consuming three times as much acrylamide as that [FDA] safe level”

  - Margin of exposure of 333 for high exposure group
  - “the risk of neurotoxicity even at a lifelong intake of 4 µg/kg/day is negligible”

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Quantifying Risks - Cancer

- Dybing & Sanner
  - Carcinogenic potency of $1 \times 10^{-3}$ per $\mu$g/kg/day

- CSPI
  - Use EPA potency of $4.5 \times 10^{-3}$ per $\mu$g/kg/day

  - Use potency of $0.7 \times 10^{-3}$ per $\mu$g/kg/day
  - Based on WHO estimate of $10^{-5}$ risk for 1$\mu$g/day
  - Also use $1 \times 10^{-3}$ per $\mu$g/kg/day
Characterizing Cancer Risks - Lifetime Individual Risk

- Dybing & Sanner
  - Lifetime male cancer risk (mean) \(0.6 \times 10^{-3}\)

- CSPI
  - Lifetime cancer risk \(2.4 \times 10^{-3}\)

  - Lifetime mean cancer risk (WHO potency) \(0.3 \times 10^{-3}\)
  - Lifetime cancer risk mean (NCFA potency) \(0.5 \times 10^{-3}\)
Characterizing Uncertainty

- No one does formal quantitative uncertainty analysis

- Konings *et al.* present cancer risk estimates from alternative potency values

- Studies that quantitatively characterize variability in exposure present range of risk estimates to reflect different intake in specific groups
Characterizing Uncertainty

- Dybing & Sanner
  - Excellent qualitative discussion of uncertainties in toxicology, exposure, and risk assessment
  - Emphasize conservative nature of their calculations

- CSPI
  - Discuss uncertainty in exposure and potency, suggest possible increased sensitivity of fetus
  - Emphasize uncertainty in exposure, especially high consumers

  - Some discussion of uncertainties in toxicology, exposure, risk assessment and bioavailability
  - “risk estimations have to be handled with great care”
What Do We Learn?

- Very small differences in mean exposure estimates, even high percentiles less than 2 fold differences

- Substantial differences in estimates of noncancer “safe” levels leads to interpretations from “negligible” to significant fraction of population over ADI

- 8-fold range of cancer risk estimates (all well above conventional benchmarks) driven by different cancer potency values
Critical Issues for Risk Characterization

» Exposure
  ▶ Refine estimates of population intake
  ▶ Are there modifying factors like bioavailability?

» Toxicology
  ▶ Appropriate studies/endpoints for noncancer assessment
  ▶ Relevance of animal data including mechanism, doses, tumor types
  ▶ Species similarities and differences in pharmacokinetics and pharmacodynamics
Critical Issues for Risk Characterization

- Risk assessment
  - Adequacy of margins-of-exposure
  - Appropriate dose-response relationship for cancer
    - Additive/linear?
    - Multiplicative?
    - Other?
  - Can we develop a “best estimate” of risk?
  - What about tradeoffs?

- Integration with emerging epidemiology

- Others?
Thank You!