

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."

Risk Assessment in the Federal Government: Managing the Process. National Academy of Sciences, 1983

- ⌘ 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”

US EPA Risk Characterization Policy and Guidance (1995)

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
- ⌘ Konings, E.J.M, et al. (2003) Acrylamide exposure from foods of the Dutch population and an assessment of the consequent risks. *Food and Chemical Toxicology* 41:1569–1579
- ⌘ Dybing, E, and Sanner, T. (2003) Risk Assessment of Acrylamide in Foods. *Toxicological Sciences* 75:7-15
- ⌘ 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

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 $\mu\text{g}/\text{kg}/\text{day}$ (97.5 - 1.62 $\mu\text{g}/\text{kg}/\text{day}$)
 - ☑ Female - mean 0.46 $\mu\text{g}/\text{kg}/\text{day}$ (97.5 - 1.45 $\mu\text{g}/\text{kg}/\text{day}$)

- ⌘ CSPI - American diet - CSFII with “modifying factors”
 - ☑ 0.53 $\mu\text{g}/\text{kg}/\text{day}$
 - ☑ No discussion of distribution

- ⌘ Konings, E.J.M., *et al.* - Dutch diet
 - ☑ Mean intake 0.48 $\mu\text{g}/\text{kg}/\text{day}$
 - ☑ 99th percentile 1.0 $\mu\text{g}/\text{kg}/\text{day}$

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

⌘ Konings, E.J.M., *et al.*

- ☑ 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”

⌘ Konings, E.J.M., *et al.*

- ☒ Margin of exposure of 333 for high exposure group
- ☒ “the risk of neurotoxicity even at a lifelong intake of 4 $\mu\text{g}/\text{kg}/\text{day}$ is negligible”

Quantifying Risks - Cancer

⌘ Dybing & Sanner

- ☑ Carcinogenic potency of 1×10^{-3} per $\mu\text{g}/\text{kg}/\text{day}$

⌘ CSPI

- ☑ Use EPA potency of 4.5×10^{-3} per $\mu\text{g}/\text{kg}/\text{day}$

⌘ Konings, E.J.M., *et al.*

- ☑ Use potency of 0.7×10^{-3} per $\mu\text{g}/\text{kg}/\text{day}$

- ☑ Based on WHO estimate of 10^{-5} risk for $1 \mu\text{g}/\text{day}$

- ☑ Also use 1×10^{-3} per $\mu\text{g}/\text{kg}/\text{day}$

Characterizing Cancer Risks - Lifetime Individual Risk

⌘ Dybing & Sanner

⊞ Lifetime male cancer risk (mean) 0.6×10^{-3}

⌘ CSPI

⊞ Lifetime cancer risk 2.4×10^{-3}

⌘ Konings, E.J.M., *et al.*

⊞ Lifetime mean cancer risk (WHO potency) 0.3×10^{-3}

⊞ Lifetime cancer risk mean (NCFA potency) 0.5×10^{-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

⌘ Konings, E.J.M., *et al.*

- ☑ 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!

