

Consideration of the Proposed Work Plan for Acrylamide in Food

Technical Discussion: Part I of Work Plan -- NSRL for Acrylamide

Staff Presentation

**Meeting of the OEHHA Science Advisory Board's
Carcinogen Identification Committee (CIC)**

Sacramento, California

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Office of Environmental Health Hazard Assessment



Basis of the NSRL

- **NSRL (0.2 $\mu\text{g}/\text{day}$) adopted in 1990**
 - Utilized cancer potency from U.S. EPA (1989)
 - Combined tumor incidences of multiple-responding sites among female rats given acrylamide in drinking water for two years (Johnson *et al.* 1986)
- **Current U.S. FDA (1998) assessment is also based on multiple tumor responses seen in the Johnson *et al.* (1986) study**



Animal Cancer Studies Published Before 1990

- **Long-term drinking water studies in male and female F344 rats (Johnson *et al.*, 1986)**
 - **Females: tumors of the mammary gland, CNS, thyroid, oral cavity, uterus and clitoral gland**
 - **Males: tumors of the thyroid and testis**
- **Several limited-term studies in mice by multiple routes of exposure (Bull *et al.*, 1984a,b; Robinson *et al.* 1986)**
 - **Lung tumors (oral, i.p.)**
 - **Initiation of skin tumors (oral, i.p., dermal)**



New Animal Cancer Studies

- **Two-year drinking water studies in male and female F344 rats (Friedman *et al.*, 1995)**
 - Reported increased tumor formation at multiple sites in both sexes
 - U.S. FDA (1998) rejected this study for hazard identification and quantitative risk assessment.



Human Cancer Studies Since the NSRL Adopted in 1990

- **Retrospective cohort study of acrylamide-exposed workers**
 - Marsh *et al.* (1999)
 - Comments by Granath *et al.* (2001) and Schulz *et al.* (2001)
- **Case-control diet studies**
 - Mucci *et al.* (2003)
 - Pelucchi *et al.* (2003)



Recent Genotoxicity Studies

- **Induction of mutations and chromosomal damage in mammalian cells**
- **Mechanism unclear**
 - Protein-mediated responses vs. DNA adducts
 - Direct action of acrylamide vs. glycidamide metabolite
- **Two sets of dose-response studies**
 - Linear formation of micronuclei in blood lymphocytes over wide range of doses



Recent Studies of Metabolism and Pharmacokinetics

- **Metabolism**
 - Epoxide formation (P450 2E1 dependent)
 - Cysteine binding
- **Wide distribution throughout the body**
 - Long half-life
- **Proportion of acrylamide metabolized to glycidamide is greater in rats than in humans**



Recent Studies on the Bioavailability of Acrylamide from Foods

- **Study of rats fed fried rat chow (Tareke *et al.*, 2000)**
 - Increased acrylamide-Hb adducts in rats fed fried chow
 - Hb adduct levels suggested complete uptake from food to blood
- **Study of human volunteers ingesting home fries (Sorgel *et al.*, 2002)**
 - Increased acrylamide levels in urine and breastmilk

