Occupational Health Hazard Risk Assessment Project for California

Sara Hoover, Chief
Safer Alternatives Assessment & Biomonitoring Section
Office of Environmental Health Hazard Assessment

CIHC Annual Meeting, San Diego, December 10, 2008

Introduction

- Project conceived by Dr. Julia Quint, former Chief of HESIS in CDPH

- Overall goals
  - Identify chemicals of concern to workers
  - Develop and apply risk assessment methods for the workplace
  - Provide examples of protective exposure limits

Background

- OEHHA
  - Lead state agency for identifying and evaluating chemical hazards

- Proposition 65
  - Safe Drinking Water and Toxic Enforcement Act of 1986
  - State is required to maintain a list of chemicals identified as causing
    - Cancer
    - Male and female reproductive toxicity
    - Developmental toxicity

Primary Elements of Project

- Screen Proposition 65 list for workplace **chemicals of concern**
- Describe and apply **cancer and noncancer risk assessment** methods for workplace
- Provide input to HESIS on **priorities for further evaluation**

Screening for "Workplace Chemicals" on Proposition 65 List

- Determine type/use of chemical (e.g., solvent)
- Remove certain substances (e.g., drugs, banned chemicals)
- Identify evidence for current use
  - Primarily U.S. production/import volume as a surrogate
  - No California inventory available

Prop 65 Workplace Chemicals of Concern

- 122 workplace chemicals either unregulated or under-regulated
  - No PELs: 44 carcinogens, 5 reproductive/developmental toxicants
  - Have PELs but are not regulated explicitly for appropriate endpoint: 62 carcinogens, 14 reproductive/developmental toxicants
- Characteristics
  - High production volume: ~60%
  - Chemical/dye intermediates: ~60%
  - Solvents: ~20%
  - Other use types: Plasticizers, stabilizers, flame retardants, dyes, catalysts, alloys, batteries, fuel-related, various industrial applications

The Four Steps of Risk Assessment

- Hazard identification
  - Determine the types of health effects a chemical could cause - cancer or noncancer
- Toxicity or dose-response assessment
  - Determine the relationship between levels of exposure to a chemical and the probability of health effects
- Exposure assessment
  - Estimate how much of a chemical a person is exposed to under particular circumstances
- Risk characterization
  - Combine the dose-response and exposure assessments to
    - Estimate the level of risk
    - Determine acceptable level of exposure

Risk Management

- Risk assessors provide scientific input to risk managers
  - Health protective levels of exposure
  - Options for reducing risk
- Risk managers separately consider other factors
  - Economic considerations
  - Technical feasibility
  - Stakeholder concerns

Cancer Risk Assessment Basics

- Some risk at any dose of a carcinogen
- Lifetime exposure for an adult male
  - For workers, need to adjust for shorter exposure
- Sensitive subpopulations and early lifestages not typically considered

Cancer Example 1: Hexachlorobenzene

- Listed under Proposition 65 as known to cause cancer (1987) and developmental toxicity (1989)
- Cal/OSHA PEL: 0.002 mg/m^3 (or 2 $\mu g/m^3$)
  - Based on hepatic and neurological effects; hepatic tumors in animals noted
  - Cal/OSHA Advisory Committee acknowledged HCB to be a carcinogen
  - PEL based on other effects due to lack of policy and resources to conduct risk assessment

Understanding the Unit Risk Value

- Definition:

  The excess cancer risk associated with a continuous lifetime inhalation exposure to a unit air concentration (e.g., 1 $\mu g/m^3$) of a given chemical

- The hexachlorobenzene unit risk value of 0.00051 $(\mu g/m^3)^{-1}$ can be understood most simply as follows:

  If 10,000 people inhaled 1 $\mu g/m^3$ of HCB every day for life, approximately 5 excess cases of cancer would be expected in that population

Cancer Risk Associated with Current Cal/OSHA PEL for Hexachlorobenzene

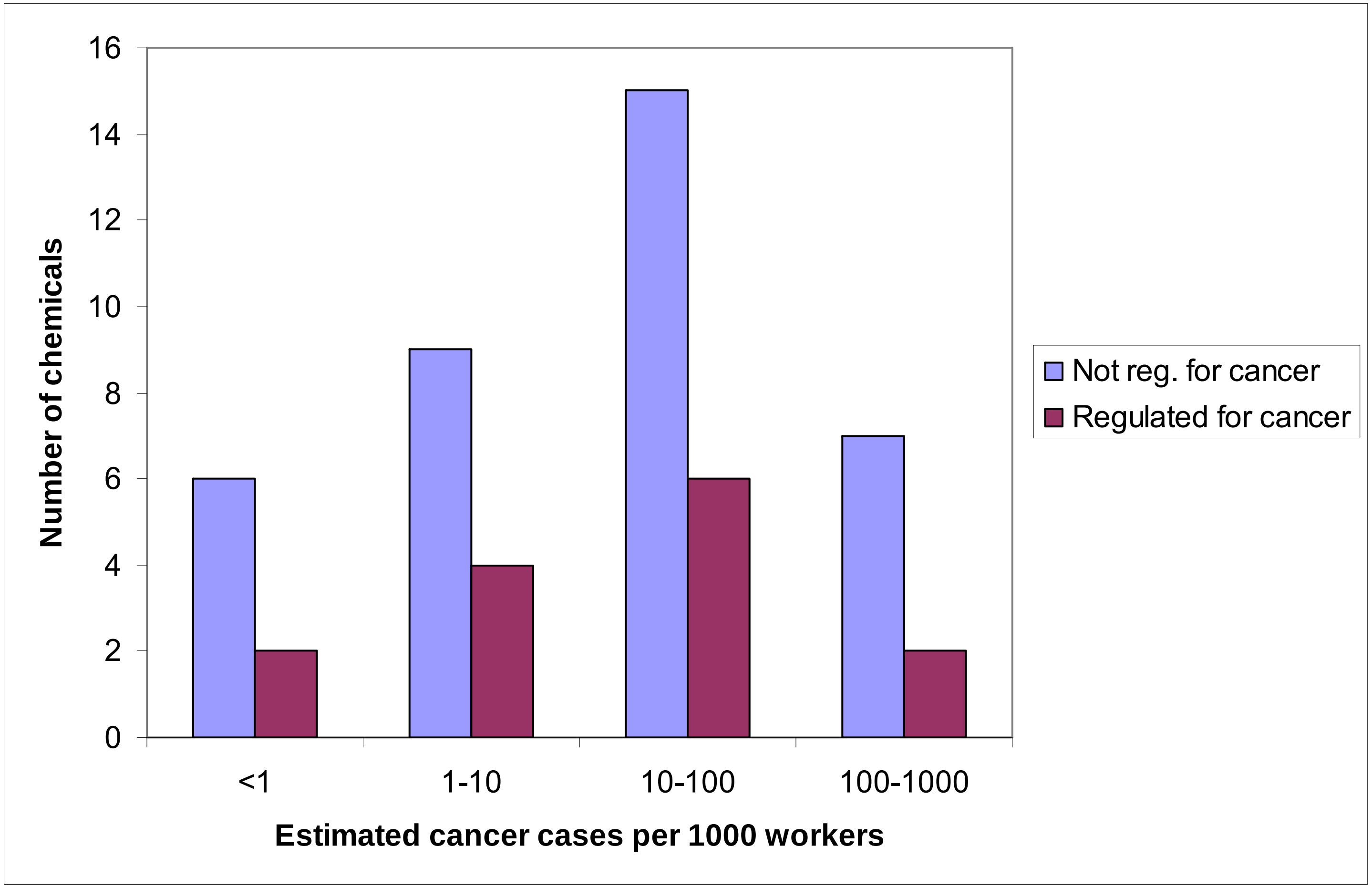
- Cancer risk at current Cal/OSHA PEL:

$$\text{Risk} = \boxed{0.00051\,(\mu g/m^3)^{-1}} \times \boxed{2\,\mu g/m^3} \times \boxed{\frac{10}{20} \times \frac{5}{7} \times \frac{50}{52} \times \frac{40}{70}} = 2 \times 10^{-4}$$

Unit Risk — PEL — Worker Exposure Factors

- Also can be expressed as "2 in 10,000"
- Compared to "acceptable" cancer risk levels (determined by risk managers):
  - 1 in 100,000 under Proposition 65
  - 1 in 1,000 commonly applied for workplace

Summary of Estimated Cancer Cases



Interpreting High Cancer Risk Estimates

- Real world exposures may be less than assumed
- Insufficient cancer studies in humans
  - Difficult to study: long latency period, workplace exposures difficult to characterize
  - Systematic follow up often not performed
  - Insufficient work history data collected by cancer registries
- Rely on animal data
  - Human dose at PEL comparable to animal dose when high cancer risks predicted

Comparison of Worker and Animal Doses

Chemical	Estimated Excess Cancer Cases per 1000 Workers	Worker Dose Based on PEL[1] (mg/kg-day)	Lowest Animal Dose[2] Producing Tumors (mg/kg-day)	Ratio of Animal Dose to Worker Dose	Animal Dose Adjusted to Human	Ratio of Adjusted Dose to Worker Dose
Bis(2-chloroethyl) ether	940	2	40 ⇨ 88% tumor	20	3	1.5
Methylaziridine	990	0.3	3 ⇨ 81% tumor	10	0.5	1.5
Naphthalene	220	3	6 ⇨ 14% tumor	2	1	0.33
Phenylhydrazine	500	1	13⇨ 53% tumor	13	1	1

1. Assumes worker breathes 10 m^3 during the workday, and works 5 d/wk, 50 wk/yr, 40 yr out of a 70 yr lifespan.
2. Lowest non-zero dose in bioassay(s) underlying cancer potency. Control rates: 10%, 0%, 0%, 13%, respectively.

Noncancer Risk Assessment Basics

- No significant adverse health effect expected below specific threshold
  - "No observed adverse effect level"
- Apply "uncertainty factors" (UFs)
  - Address various issues, including effects on sensitive subpopulations
  - Re-evaluate UFs for workers
- General population continuously exposed for life
  - Adjust for shorter worker exposure

Noncancer Example: Benzene

- Noncancer effects
  - Developmental and male reproductive toxicity
  - Blood and nervous system toxicity
- Cal/OSHA PEL
  - Regulated as an occupational carcinogen
  - PEL does not explicitly account for developmental/reproductive toxicity
- OEHHA noncancer assessments
  - Inhalation exposure level – various health effects
  - Safe harbor level - developmental toxicity

Example: Adjusting Noncancer Inhalation Exposure Level for Benzene

- Study population: 303 refinery workers (Tsai *et al*., 1983)
- Critical effect: Blood effects
- NOAEL: 0.53 ppm ← start with worker NOAEL
- LOAEL factor: 1
- Subchronic factor: 1
- Interspecies factor: 1
- Intraspecies factor: 1, 3 or 10 ← possible worker values
- Cumulative uncertainty factor: 1, 3 or 10
- Example health-based occupational air concentrations: 0.05, 0.2, or 0.5 ppm

➢ For this worker study, no adjustment for exposure needed

Summary of Example Health-Based Occupational Air Concentrations (C_{occ}) for Benzene

Basis for Example C_{occ}	**Example C_{occ} (ppm)**
Hematological effects in refinery workers	0.5 0.2 0.05
Hematological effects in neonates	0.04 0.01
1 in 1,000 cancer risk	0.05

Current Cal/OSHA PEL: *1 ppm (includes feasibility)*

Current ACGIH TLV: *0.5 ppm*

Priorities for Further Evaluation

- Chemicals used in California with potential for worker exposure
  - Real world exposure data needed
- Level of toxicity
  - For example, estimated excess cancer risk at PEL
- Existence of safer alternatives

Some Considerations for Occupational Risk Assessment

- "Acceptable" cancer risk levels for workers
- Choice of intraspecies uncertainty factor for noncancer assessment
  - Variations in worker populations
- Procedures for evaluating worker exposure
  - Exposure adjustments – averaging, breathing rate
  - Accounting for dermal exposure
  - Toxicokinetic modeling

For More Information

- Full report:
  http://www.cdph.ca.gov/programs/hesis/Documents/riskreport.pdf
- OEHHA web site:
  www.oehha.ca.gov
- Proposition 65:
  http://www.oehha.ca.gov/prop65.html