Technical Challenges of Complying with the New Requirements of Proposition 65

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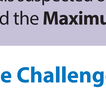
BACKGROUND

- California's Proposition 65 (Prop 65) regulation was recently updated to include new Clear and Reasonable Warning labeling rules, which take effect August 30, 2018.

Old Label

WARNING: This product may contain a chemical known to the State of California to cause cancer, or birth defects or other reproductive harm.

New Label



WARNING: This product can expose you to chemicals including **[name of one or more chemicals]**, which is **[are]** known to the State of California to cause cancer and birth defects or other reproductive harm. For more information go to www.P65Warnings.ca.gov.

- New warning label is required when product use would result in exposures to Prop 65-listed chemical(s) above the Safe Harbor Level(s) (SHLs; **see box below**).
- Violations of these new rules may be subject to a $2,500 fine.
- Potential lawsuits for failing to comply with the new labeling rules are initiated with a 60-day notice.
- When a manufacturer/retailer learns its product contains a Prop 65-listed chemical, it may:
  - Add the proper warning label to the product,
  - Reformulate the product,
  - Stop selling the product, or
  - Demonstrate the product's compliance with the SHL.
- Approximately 591 of the over 800 Prop 65-listed chemicals do not have SHLs.

What Is a Safe Harbor Level?

The California Office of Environmental Health Hazard Assessment (CalOEHHA) sets acceptable exposure levels of Prop 65-listed chemicals (*i.e.*, levels that do not pose a significant risk of cancer or adverse reproductive/developmental effects). These values are referred to as **Safe Harbor Levels**.

- For suspected carcinogens, the SHL is called the **No Significant Risk Level (NSRL)**.
- For chemicals suspected of causing reproductive or developmental effects, the SHL is called the **Maximum Allowable Dose Level (MADL)**.

Compliance Challenges

- SHLs apply to both workers and consumers.
- Exposure must be quantified for all exposure routes.
- Manufacturers need full and accurate knowledge of product composition and impurities.
- Many Prop 65-listed chemicals lack SHLs.

CHALLENGE 1: APPROPRIATELY EVALUATING EXPOSURE

Identify Relevant Consumer Exposure Routes

- Exposures can occur *via* oral, dermal, or inhalation pathways; all should be considered, even if exposure will be unintentional.
- The mere presence of a chemical ≠ exposure. Determine whether chemical is bioaccessible to consumers under the appropriate exposure pathways.
- Design an appropriate testing program to support exposure scenario-specific risk assessment **(see Challenge 2)**.
- Consider whether the chemical's SHL is relevant for the product's exposure route(s). Extrapolating between exposure routes may be necessary **(see Challenge 3)**.

Determine Exposure Factors

- Develop exposure factors – *e.g.*, How often/for how long does the consumer come into contact with the product?
- Should also reflect any sub-populations of interest (*i.e.*, intended user).
  - Use specific information on body weight, breathing rate, skin surface area, *etc.*
- No guidance regarding usage patterns for many products (*e.g.*, how many times an average person uses a paperclip in a day). Can develop exposure factors using:
  - Scientific literature or regulatory models (*e.g.*, Dutch National Institute for Public Health and the Environment [RIVM] ConsExpo, United States Environmental Protection Agency Consumer Exposure Model [US EPA CEM]).
  - Product directions or instructions (*e.g.*, exposure duration, method of contact).
  - **"Bound" Exposures:** Estimate a reasonable maximum number of times a person might use a product in a day.
  - **Video Logging:** Expensive and time-consuming, but can provide real-world, supportable evidence.

CASE EXAMPLE: INHALATION AND DERMAL EXPOSURE TO HOME MAINTENANCE PRODUCT

- Prop 65 chemicals were identified in a home flooring maintenance product.
- Both dermal and inhalation exposures were of concern, due to volatile organic compounds (VOCs) in product.
- Workers and consumers could be exposed to product.

Approach:

- Used manufacturing specifications to determine "worst-case" exposure concentrations.
- Assessed dermal exposure using standard US EPA risk assessment guidance.
- For inhalation exposure, assessed worker exposures using air dispersion modeling, with actual data on manufacturing facility room size/ventilation/*etc.*, and consumer exposures using conservative assumptions for the equivalent factors reflecting home use of the product.
- Product testing was determined to be unnecessary based on exposure analysis results.

CHALLENGE 2: DESIGNING A PRODUCT SAMPLING AND TESTING PROGRAM

Select a Test Laboratory and Proper Analytical Methods

- Choose a lab with existing Prop 65 testing experience and well-developed analytical methods. Specialized or customized sampling techniques may be required and should be discussed up front.
- Using appropriate analytical methods is critical to collecting appropriate chemical data.
  - Standard total content methods are often selected due to ease/cost, but may overestimate exposure. Also consider whether total or speciated metals analyses are toxicologically relevant (*e.g.*, total chromium *vs.* hexavalent chromium).
  - Select test methods applicable to the exposure pathways evaluated (off-gassing for inhalation, wipe testing for dermal exposure, *etc.*).
- Detection limits must be sensitive enough to meet Prop 65 limits and exposure levels.
- Consider whether the product ingredients/raw materials may contain other Prop 65-listed chemicals.
- Ensure data meet accuracy and precision criteria and are of sufficient quality.

Product Sampling

- Each product, batch, and formulation at issue must be tested to ensure representativeness and capture variability.
- Multiple colors or sizes of product may need to be tested, depending on the exposure scenarios evaluated.
- Product sampling approaches must consider, and extrapolate to, consumer exposure and exposure duration.

CASE EXAMPLE: TESTING PROGRAM DESIGN FOR OUTDOOR CONSTRUCTION PRODUCT

- Manufacturer interested in proactively addressing internal regulatory compliance for vinyl chloride, a Prop 65-listed chemical.
- Supplier information and product ingredients revealed that products potentially contained numerous other Prop 65-listed chemicals (VOCs, metals, Polycyclic aromatic hydrocarbons, *etc.*).
- Multiple relevant consumer exposure routes, based on the product's intended use.

Approach:

- Designed a complex, tiered sampling and testing program to assess exposure to a broad range of Prop 65-listed chemicals.
  - **Tier 1 Testing:** "Standard" test methods for total content analysis.
  - **Tier 2 Testing:** "Specialized" sampling and analysis of any chemicals detected in Tier 1.
    - Customized off-gassing sampling and analysis of VOCs to assess inhalation exposure.
    - Specialized dermal and gastric biofluid extraction to assess dermal exposure and ingestion exposure, respectively.
- Tier 2 results were used to assess consumer risks from exposure to the Prop 65-listed chemicals of interest.

CHALLENGE 3: EVALUATING CHEMICALS WITHOUT SHLS

Develop Toxicity Criteria

- Research relevant toxicity studies and appropriate endpoints.
  - Reconcile conflicting data, sex differences, and differences in quality of studies.
  - Preferable to use data from relevant exposure route(s).
- Use Prop 65-specific methods (*e.g.*, for NSRL, derive unit risk level using a multistage model).
- Qualitatively understand chemicals' mode of action and adverse effects' relevance to humans.

Extrapolating Across Species and Exposure Routes

- Adjustment factors are needed for extrapolating from animal to human exposures.
- Qualitatively assess whether product exposure is relevant to chemicals' Prop 65 listing (*e.g.*, if chemical causes lung cancer *via* inhalation, will it also cause lung cancer *via* ingestion).
- If extrapolation across exposure routes is needed, understanding relative bioavailability is critical.
  - Use appropriate time-averaging period (differ for reproductive *vs.* carcinogenic effects); and
  - Understand the local metabolism of the compound.

CASE EXAMPLE: N–N–DIMETHYL–P–TOLUIDINE (DMPT) IN OFFICE EQUIPMENT

- Basis for DMPT's Prop 65 listing was a study from the National Toxicology Program (oral exposure caused "cancers of the liver and nose in male and female rats, cancer of the liver in male and female mice, and cancers of the lung and forestomach in female mice" [NTP, 2012]).
- DMPT has no SHL, so needed to develop an NSRL. Exposures to DMPT in office equipment only involved inhalation exposure.
- Additional considerations:
  - Cancer hazard based on animal data and the oral exposure route only; no human information, and only inhalation exposure was relevant for product use.
  - Study showed multiple, sex-specific cancers with unclear relevance to inhalation exposure.
  - Lack of information on the bioavailability, distribution, and metabolism of DMPT *via* any exposure route.

Approach:

- Assumed inhalation exposure would result in similar toxic effects as ingestion exposure (lungs were a target *via* oral exposure), and assumed equivalent systemic dose *via* both pathways.
- Selected liver tumors as the basis for the NSRL based on consistency in response between sex and species and because this was the most sensitive endpoint (*i.e.*, resulted in the most conservative NSRL).
- Extrapolated doses from animals to humans using appropriate adjustment factors.