OCCUPATIONAL HEALTH HAZARD RISK ASSESSMENT PROJECT FOR CALIFORNIA:

Identification of Chemicals of Concern, Possible Risk Assessment Methods, and Examples of Health Protective Occupational Air Concentrations

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Note to Reader

The chemicals of concern reviewed in this report were chosen based on the December 2006 version of the Proposition 65 list. During 2007, two additional chemicals potentially relevant to the workplace have been listed under Proposition 65 and several risk assessments have been completed by the Office of Environmental Health Hazard Assessment (OEHHA) or are in draft form. These updates are not included in this report.

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Executive Summary

The Office of Environmental Health Hazard Assessment (OEHHA) prepared this document as part of the Occupational Health Hazard Risk Assessment Project, under a contract with the Hazard Evaluation System and Information Service (HESIS) of the California Department of Public Health (CDPH) (formerly the California Department of Health Services). The overall goal of the project was to identify chemicals that may pose risks of chronic disease and health damage to workers and to quantify the health risks from exposure to selected workplace chemicals identified as causing cancer, reproductive and/or developmental toxicity. This information is intended to assist HESIS in more effectively recommending protective occupational standards as part of its legislative mandate.

The specific aims of the project were to:

- Identify chemicals relevant to an occupational setting (hereafter referred to as "workplace chemicals") that are listed as causing cancer, reproductive and/or developmental toxicity under Proposition 65 (Health and Safety Code Section 25249.5 et seq.), officially known as the Safe Drinking Water and Toxic Enforcement Act of 1986.

- Identify workplace chemicals that may pose a risk to workers because of a lack of an occupational exposure limit or because the occupational exposure limit is based on a less protective endpoint (e.g., irritation instead of cancer).

- Calculate air concentrations associated with specified levels of cancer risk for selected workplace chemicals listed as causing cancer under Proposition 65.

- Calculate air concentrations relevant to an occupational exposure scenario and protective for reproductive and/or developmental toxicity for selected workplace chemicals listed as causing reproductive and/or developmental toxicity under Proposition 65.

- Describe the methodologies used to calculate air concentrations for selected workplace chemicals.

- Discuss scientific issues related to occupational quantitative dose-response assessments.

- Make recommendations to HESIS on providing consistent protection for California workers and community residents from health risks associated with exposure to carcinogens, reproductive toxicants and developmental toxicants.

The major results of the project are highlighted below.

- The Proposition 65 list (Title 22, California Code of Regulations, Section 12000), dated December 2006, was screened for “workplace chemicals” by identifying industrial
chemicals with evidence of current use, and excluding certain classes of compounds (e.g.,
drugs, pesticides, banned chemicals).

- Forty-four workplace chemicals that are listed as known to the state to cause cancer under
  Proposition 65 do not have a permissible exposure limit (PEL) established in California.

- Sixty-two workplace chemicals listed as known to cause cancer under Proposition 65
  have PELs but are not regulated specifically as occupational carcinogens in California.
  Screening level assessments of the cancer risk were carried out assuming worker
  exposure via inhalation at the current PEL for 38 of these carcinogens. Seven of the 38
  chemicals had cancer risks at the PEL of less than 1 in 1,000, a level often considered
  significant in occupational settings. Cancer risks of more than 100 in 1,000 were
  estimated for six of the 38 chemicals assuming exposure at the PEL. For the remaining
  chemicals, cancer risks at the PEL were between 1 and 100 in 1,000. To further evaluate
  potential cancer concerns for workers, more detailed risk assessments are recommended
  which would include examination of available data on actual worker exposure.

- Five workplace chemicals listed as known to cause reproductive and/or developmental
  toxicity do not have a PEL established in California.

- Fourteen workplace chemicals listed as known to cause reproductive and/or
devontational toxicity have a PEL in California that does not explicitly account for those
effects. The extent to which these PELs are protective for reproductive and/or
developmental health risks is unclear and should be assessed further.

- About 60% of the workplace chemicals identified as of concern in this report are used as
chemical or dye intermediates. Intermediates are typically used in closed systems with
relatively limited potential for worker exposure. However, exposure can still occur with
closed systems (e.g., from fugitive emissions and during repair and maintenance), and
about half of these intermediates have other industrial uses that may pose a higher
exposure concern.

- About 20% of the workplace chemicals of concern are used as solvents, which generally
  pose higher concern for worker exposure.

- About 40% of the workplace chemicals of concern have been identified as being skin
  absorbable and could pose cancer, reproductive and/or developmental risks via the
dermal route in addition to the inhalation route of exposure.

- About 60% of the workplace chemicals of concern are high production volume chemicals
(>1 million pounds produced in and/or imported into the U.S., based on data from 2002).

The report also provides a number of specific recommendations to HESIS for the derivation of
health protective occupational air concentrations using a risk-based approach.


Introduction

Although risk assessment is well established as the basis for developing environmental standards, this methodology has not been consistently applied in the derivation of occupational standards such as permissible exposure limits (PELs). Because of the lack of a consistent scientific basis for PELs, the chronic health risks associated with worker exposure at the PEL vary between chemicals. Further, in many cases an important health effect like cancer or reproductive toxicity may not be considered in the derivation of the PEL. In California, the state maintains a list of chemicals known to cause cancer or reproductive and/or developmental toxicity under the Safe Drinking Water and Toxic Enforcement Act (Proposition 65). OEHHA has conducted quantitative risk assessments on numerous chemicals, developing cancer potency values for carcinogens and various types of health assessment levels for reproductive and developmental toxicants, and other chronic health toxicants. The process that has been used under the California Occupational Safety and Health (Cal/OSHA) Program for establishing PELs has not typically considered the hazard identification information from Proposition 65 or formally incorporated quantitative risk assessments available on chemicals of interest in the workplace. A recent effort has been launched under Cal/OSHA to more formally account for health effects in establishing PELs, and to evaluate worker health considerations separately from technical and economic considerations.

To begin to address the gaps between environmental and occupational regulation of chronic toxicants, the following approach was taken:

- Chemicals listed as known to the state of California to cause cancer or reproductive harm (i.e., reproductive and/or developmental toxicity) under Proposition 65 were screened for relevance to the workplace ("workplace chemicals").

- Workplace chemicals listed under Proposition 65 that do not have Cal/OSHA PELs were identified.

- Workplace chemicals listed as known to cause cancer under Proposition 65 that have Cal/OSHA PELs but are not specifically regulated as occupational carcinogens were identified.

- Workplace chemicals listed as known to cause reproductive and/or developmental toxicity under Proposition 65 that have Cal/OSHA PELs that are not specifically based on those health endpoints were identified.

- Risk assessments conducted by the Office of Environmental Health Hazard Assessment (OEHHA) or the U.S. Environmental Protection Agency (U.S. EPA) were obtained for selected workplace chemicals.
• For selected carcinogens and reproductive and/or developmental toxicants with existing risk assessments, occupational air concentrations protective for those endpoints were derived.

• For selected workplace chemicals listed as causing cancer and that have a unit risk level and established PEL, the cancer risks assuming worker exposure at the PEL were calculated.

• For two workplace chemicals that are listed as causing developmental toxicity and have an existing risk assessment and established PEL, occupational air concentrations were calculated based on the existing risk assessments and compared to the PEL.

• For selected workplace chemicals identified as causing other chronic damage (such as neurological damage or respiratory toxicity), occupational air concentrations were derived based on existing risk assessments and compared to the PEL.

The specific methods used to carry out the above approach and the results of the calculations are described in detail in the main report below. Scientific and policy issues involved in using existing risk assessments to derive occupational air concentrations are highlighted and discussed. Recommendations to HESIS for further work are provided.
Screening of Proposition 65 List for Workplace Chemicals

The Proposition 65 list (http://www.oehha.ca.gov/prop65/prop65_list/files/P65single120806.pdf) was screened for workplace chemicals using the methods described below. Identification of relevant occupational exposure levels is also discussed.

1. Various sources available on the Internet were searched for information relevant to the identity, production volume and potential for exposure for the chemicals of interest. Some of the primary sources of this information were:

   Toxic Substances Control Act (TSCA) 2002 Inventory Update Rule (IUR), non-confidential production volume information (available at: http://www.epa.gov/opptintr/iur/tools/data/2002-vol.htm)

   National Toxicology Program (NTP) 11th Annual Report on Carcinogens (ROC) (available at: http://ntp-server.niehs.nih.gov/index.cfm?objectid=32BA9724-F1F6-975E-7FCE50709CB4C932)


   Internet search engines (e.g., Google; available at http://www.google.com/)

2. Based on the data obtained in step 1:

   The identity of each chemical on the Proposition 65 list was categorized qualitatively (e.g., "pesticide", "drug", "chemical intermediate", "byproduct").

   Chemicals likely to be in current use were identified.

3. Chemicals that were considered less relevant to occupational exposure concerns or are regulated primarily under programs other than Cal/OSHA were identified and removed from further consideration. The following general categories were removed:

   Pesticides (including all categories such as insecticides, herbicides etc.)¹

   Drugs

   Certain consumer products (e.g., tobacco, alcohol)

¹ Certain chemicals that have been used as pesticides also have current industrial uses relevant to the workplace; these were retained for consideration in this report.
Chemicals with no indication of current production or use in the U.S. (based on TSCA 2002 data and other relevant data)

Banned chemicals (e.g., DDT, PCBs)

Chemicals with voluntary ban (e.g., PBBs)

Chemicals recognized as significant health hazards that have largely been replaced by other chemicals (e.g., 2-bromopropane replaced by 1-bromopropane)

Chemicals used only as research/laboratory chemicals

Individual polycyclic aromatic hydrocarbons (PAHs) formed as byproducts, or used as laboratory/research chemicals only

Most chemicals formed only as unintentional byproducts (e.g., TCDD)

Mixed categories of substances (e.g., soots, tars, and mineral oils) and certain mixtures without real world exposure (e.g., carbon black extracts; gasoline engine exhaust [condensates and extracts]; wholly vaporized unleaded gasoline)

4. Some workplace chemicals were chosen for further analysis; for example, to illustrate the development of an occupational air concentration. To select workplace chemicals for further analysis, additional screening on the type of production process and the specific use of the chemical was done:

Solvents: Given the nature and use of solvents, these were considered high priority for further analysis.

Chemical intermediates & dyes: These chemicals are generally produced and/or used in a closed process, making worker exposure less of a concern and further analysis a lower priority.

5. Occupational exposure levels established under Cal/OSHA or by other governmental and private agencies for workplace chemicals listed under Proposition 65 were obtained using a variety of sources, discussed below:

Cal/OSHA PELs were obtained from [http://www.dir.ca.gov/Title8/5155table_ac1.html](http://www.dir.ca.gov/Title8/5155table_ac1.html). The basis for the PEL was obtained from the vertical standard\(^2\) for the chemical

---

\(^2\) Cal/OSHA describes vertical standards as follows: “Most safety and health standards are horizontal or ‘general,’ which means they apply to any employer in any industry, e.g., fire protection, working surfaces and first aid. Other standards apply only to a particular industry and are called vertical or ‘specific,’ e.g., construction, petroleum or logging and sawmills.” (see [http://www.dir.ca.gov/doshpol/ppc-2attacha.htm](http://www.dir.ca.gov/doshpol/ppc-2attacha.htm)) Certain hazardous substances,
HESIS values were obtained from HESIS Hazard Alerts.

Federal Occupational Safety and Health Administration (OSHA) PELs were obtained from http://www.osha.gov/SLTC/pel/.

National Institute for Occupational Safety and Health (NIOSH) recommended exposure limits (RELs) were obtained from the Pocket Guide to Chemical Hazards, available on the NIOSH website (http://www.cdc.gov/niosh/npg/) or from NIOSH (1992).

Threshold limit values (TLVs) derived by the American Conference of Governmental Industrial Hygienists (ACGIH) and the basis for the values were obtained from ACGIH (2006). ACGIH (2007) was consulted for recent updates of the TLVs.

International exposure limits and American Industrial Hygiene Association (AIHA) workplace environmental exposure limits (WEELs) were obtained from ACGIH (2006).
Cancer Risk Assessment Methods for an Occupational Setting

For the current document, cancer risk was calculated for inhalation exposures in the occupational setting using a measure of carcinogenic potency called the unit risk level. The unit risk level is defined as the excess cancer risk associated with lifetime inhalation exposure to a unit air concentration (e.g., 1 μg/m³) of a given chemical. At low air concentrations, cancer risk is approximated by the product of the unit risk level and the lifetime average exposure concentration of the chemical of interest.

To estimate cancer risks assuming worker exposure at current PELs and to derive occupational air concentrations for carcinogens using existing risk assessments, the following approach was taken:

1. Unit risk levels from existing cancer risk assessments conducted by OEHHA or by the U.S. EPA were obtained from:

   Technical Support Document for Describing Available Cancer Potency Factors, Appendix J (OEHHA, 2005). This document reports OEHHA unit risk values, which in some cases were adopted from U.S. EPA. (http://www.oehha.ca.gov/air/hot_spots/pdf/May2005Hotspots.pdf)

   Cancer risk assessments conducted by OEHHA pursuant to Proposition 65 or as part of the development of a Public Health Goal. In these cases, the cancer potencies in (mg/kg-day)⁻¹ were multiplied by the human breathing rate divided by body weight (20 m³/70 kg) to derive unit risk values in (mg/m³)⁻¹.


2. A workplace exposure scenario for cancer risk assessment was developed:

   Following HESIS, workers were assumed to be exposed at the PEL for 8 hours per day, 5 days per week, 50 weeks per year for 40 years. This is a health conservative, default exposure scenario for assessing cancer risks in the workplace. No adjustment was made for the potentially increased breathing rate of workers, however, which would be an even more conservative approach, increasing risks by a factor of 1.5 (i.e., 50% higher risk).

3. Cancer risks associated with worker exposure at the existing Cal/OSHA PELs were calculated for selected chemicals that are currently regulated.

Excess lifetime cancer risk can be estimated as the product between the lifetime average air concentration and the unit risk level. This linear approximation holds at low average air concentrations. Based on the assumption that a worker is exposed to the PEL over an entire working lifetime, the excess cancer risk would be:
Excess lifetime cancer risk = \( \frac{8}{24} \times \frac{5}{7} \times \frac{50}{52} \times \frac{40}{70} \times \text{URL} \) (1)

where

\[ \text{PEL} = \text{permissible exposure limit in mg/m}^3 \]

\[ \text{URL} = \text{unit risk level in (mg/m}^3\text{)}^{-1} \]

In some cases the PEL was high enough that the linear approximation was no longer accurate. In these cases it was necessary to estimate risk associated with the lifetime average air concentration using the following equation:

\[
\text{Excess lifetime cancer risk} = 1 - e^{-(\text{URL} \times C_{\text{avg}})}
\] (2)

where \(\text{URL}\) is the unit risk level in (mg/m\(^3\))\(^{-1}\) and \(C_{\text{avg}}\) in (mg/m\(^3\)) is the PEL weighted by the factors shown in Equation (1).

4. Occupational air concentrations were calculated for selected carcinogens.

Occupational air concentrations were calculated assuming a worker exposure scenario and target cancer risk levels of 1 in 1,000, 1 in 10,000 and 1 in 100,000. The general equation is as follows:

\[
C_{\text{occ}} = \frac{\text{Cancer risk}}{\text{URL}} \times \frac{24 \text{ hours}}{8 \text{ hours}} \times \frac{7 \text{ days}}{5 \text{ days}} \times \frac{52 \text{ weeks}}{50 \text{ weeks}} \times \frac{70 \text{ years}}{40 \text{ years}}
\] (3)

where

\[ \text{C}_{\text{occ}} = \text{occupational air concentration in mg/m}^3 \]

\[ \text{Cancer risk} = \text{target cancer risk level (e.g., 1 in 1,000 [1 x 10}^{-3}\text{])} \]

\[ \text{URL} = \text{unit risk level in (mg/m}^3\text{)}^{-1} \]
Noncancer Risk Assessment Methods for an Occupational Setting

OEHHA (2000a) has published noncancer risk assessment methodology for deriving inhalation reference exposure levels, which is consistent with the approach published by U.S. EPA (1994). OEHHA is currently updating the guidance document to incorporate new advances in noncancer risk assessment. OSHA (1993) has applied similar methodologies for carrying out risk assessments of noncarcinogens for the occupational setting. For the current project, existing noncancer chronic health risk assessments carried out by OEHHA or U.S. EPA were used to derive occupational air concentrations by adjusting only those aspects of the assessments that relate specifically to occupational exposure issues. Other scientific decisions made in the existing risk assessments that do not relate specifically to occupational exposure were not reconsidered, and scientific literature published more recently than the existing assessments was not reviewed.

In the current document, only chronic exposures to noncarcinogens were considered. Short-term and even single exposures to hazardous substances are also of concern in the workplace. OEHHA and others have published guidelines on developing acute reference exposure levels (see, for example, OEHHA [1999a], and the National Research Council [NRC, 2001]).

To derive occupational concentrations for noncarcinogens using existing noncancer chronic health risk assessments the following general steps were followed:

- Available noncancer chronic health risk assessments conducted by OEHHA, U.S. EPA or other agencies for the chemical of interest that are applicable to inhalation exposures were identified.

- The assessments were reviewed for the following general considerations:
  
  - When was the assessment conducted?
  - What studies were selected for analysis?
  - Was a no observed adverse effect level (NOAEL) or lowest observed adverse effect level (LOAEL) identified?
  - Was a benchmark dose (BMD) or benchmark concentration (BMC) derived?
  - Did the study of interest examine chronic or subchronic exposures?
  - Were uncertainty/safety factors applied and if so what was the basis for these factors?
  - What are the target health endpoints that the health assessment value protects for?

- The assessment(s) most appropriate for the occupational setting were selected using scientific judgment. Some of the general considerations in the selection included the following:

  - Assessments that were recent and reviewed known relevant studies were preferred. The date of the assessment was not always an indication of how
inclusive it was, so the comprehensiveness of an assessment was reviewed on a case by case basis.

- An assessment based on a well-conducted human (typically worker) study was generally preferred over an assessment based on animal data for particular health endpoints, but this was assessed on a case by case basis.
- An assessment based on a NOAEL or a BMD/BMC analysis was generally preferred over one based on a LOAEL, but this was assessed on a case by case basis.
- An assessment based on a chronic study was generally preferred over one that used subchronic data.
- An assessment that analyzed and justified each uncertainty factor was generally preferred over an assessment that applied a generic factor, but this was assessed on a case by case basis. The assessment using a generic factor may be more current or protective of a more severe health endpoint, for example, and the generic factor could be adjusted following appropriate guidelines.
- The assessment protective of the most sensitive chronic health endpoints was generally preferred.

- Uncertainty factors were adjusted/removed based on relevance to an occupational setting:
  - An intraspecies uncertainty factor applied specifically to protect children may not be appropriate to an occupational setting, for example. Adjustment of the intraspecies factor was assessed on a case by case basis.

- The noncancer chronic health assessment value was adjusted to reflect an appropriate occupational exposure scenario.

Specific methods are detailed below.

1. Identification of available noncancer chronic health risk assessments

OEHHA conducts chronic health risk assessments for noncarcinogens under different programs. The most relevant assessments are those for inhalation exposures to chronic toxicants. OEHHA derives chronic reference exposure levels (cRELs), which are protective of the public exposed to the hazardous substance over a lifetime (OEHHA, 2000a). OEHHA also derives maximum allowable dose levels (MADLs) for reproductive and developmental toxicants, which in some cases are applicable to inhalation exposures. U.S. EPA derives reference concentrations (RfCs), which are air concentrations without appreciable risk of adverse effects on the general population exposed continuously via inhalation. The National Toxicology Program (NTP) Center for the Evaluation of Risks to Human Reproduction (CERHR) also conducts thorough evaluations of the data on reproductive and developmental toxicants, including identification of NOAELs, which could be used to develop health assessment values.
2. Selection of appropriate noncancer chronic health risk assessments

The underlying basis for an existing noncancer chronic health assessment value was examined and described. Assessments that used the most comprehensive database, chronic studies, and studies in workers generally were more relevant for the occupational setting. Assessments based on LOAELs would generally require a larger uncertainty factor and were less desirable as the basis for an occupational concentration. Assessments that identified a NOAEL or conducted a dose-response analysis to generate a BMC were considered more reliable.

3. Evaluation and adjustment of uncertainty factors

OEHHA (2000a) provides guidance on the application of appropriate uncertainty factors. Selection of appropriate uncertainty factors depends on particular aspects of the study and whether or not a NOAEL is used as the basis for the assessment, for example. The individual uncertainty factors typically range from 1 (if the factor is not needed) to 10.

Considerations used to select uncertainty factors and the applicability of these factors to an occupational scenario are summarized in Table 1 below. The LOAEL uncertainty factor, the subchronic uncertainty factor, and the interspecies uncertainty factor are all applicable in an occupational setting. The intraspecies uncertainty factor would typically be the factor considered for adjustment under an occupational scenario. The purpose of this factor is to account for differences in sensitivity among the exposed human population. Issues to be considered in adjusting uncertainty factors for assessments of worker populations are discussed in more detail following Table 1.

Table 1. Description of uncertainty factors and relevance to occupational scenario

<table>
<thead>
<tr>
<th>Type of uncertainty factor</th>
<th>Definition and range</th>
<th>Relevance to occupational scenario</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOAEL uncertainty factor</td>
<td>This factor extrapolates from a LOAEL to a NOAEL. The value is set at 1 if a NOAEL or BMCL (the lower bound on the benchmark concentration) is available. Values less than 10 may be selected if the effect is considered mild.</td>
<td>If a LOAEL is used as the underlying basis for a health assessment value, this uncertainty factor would be required under any scenario and should not be adjusted.</td>
</tr>
<tr>
<td>Subchronic uncertainty factor</td>
<td>This factor extrapolates from a subchronic to a chronic exposure for human or animal studies. If a study duration is greater than 12% of the natural lifespan of the species, this factor is set to 1 (OEHHA, 2000a). If the study lasts between 8-12% of the natural lifespan, the factor is set at 3. For studies that are less than 8% of the natural lifespan, this factor is set at 10.</td>
<td>If a subchronic animal or human study is used as the underlying basis for a chronic health assessment value, this uncertainty factor would be required under any scenario and should not be adjusted.</td>
</tr>
<tr>
<td>Type of uncertainty factor</td>
<td>Definition and range</td>
<td>Relevance to occupational scenario</td>
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<tr>
<td>----------------------------</td>
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<tr>
<td>Interspecies uncertainty factor</td>
<td>This factor extrapolates from animals to humans. Values from 1 to 10 have been applied, with factors of 1, 3 or 10 conventionally used. If the study is based on humans, this factor is set to 1. In cases where the U.S. EPA procedure for deriving human equivalent concentrations (HECs) for risk assessments based on animal data has been applied, a factor of 3 has typically been used. The HEC procedure is assumed to account for a portion of the interspecies differences.</td>
<td>The same considerations for extrapolating between animals and humans would apply in an occupational scenario, so whatever decisions were made regarding this factor would still apply and the factor should not be adjusted.</td>
</tr>
<tr>
<td>Intraspecies uncertainty factor</td>
<td>The intraspecies factor is applied to address interindividual variability and to protect sensitive subpopulations. A 10-fold uncertainty factor has typically been used to account for known human variability.</td>
<td>This factor was assessed on a case by case basis. Values of 1, $10^{0.5}$ and 10 were applied in deriving occupational concentrations.</td>
</tr>
</tbody>
</table>

More recent risk assessments by OEHHA, U.S. EPA and others have used measured data and toxicokinetic models to adjust for kinetic differences between humans and experimental animals, and between different individuals and lifestages in the general human population. Where such explicit models are available, the uncertainty factors for inter- or intraspecies differences are correspondingly reduced. In considering the applicability to the occupational setting of health assessment levels (e.g., cREL, RfC) that have been derived using toxicokinetic models, it would be important to apply values and ranges of the model parameters appropriate for a worker population, rather than for the general population which may include children.

As noted in Table 1, the default factor of 10 for intraspecies differences (also referred to as interindividual variability) has generally in the past been considered to protect sensitive subpopulations, including children and the elderly, that may not be present in an occupational setting (OEHHA, 2000a). However, there could be situations where the sensitive population of concern, such as pregnant women, is part of the worker population. In evaluating risks associated with occupational exposure to glycol ethers, OSHA (1993) noted that the “healthy worker effect” is not applicable to the developing fetus. There is no reason to assume that fetuses of female workers would be a homogeneous population, nor an intrinsically healthier population. OSHA further stated that “a fetus has two parents who contribute to its genetic identity, and there is no reason to assume that the father of a fetus of a working mother is also a ‘healthy worker’.” Thus in selecting an appropriate intraspecies uncertainty factor for the occupational setting, the specific type of toxicity must be considered along with other factors on a case by case basis.

U.S. EPA (2003a) used a factor of 3 to account for interindividual variability in workers when deriving an acceptable exposure limit for occupational exposures to 1-bromopropane (n-propyl bromide), discussing this choice as follows:
Although workers employed in the types of industrial sectors that are part of this SNAP [Significant New Alternatives Policy] review likely represent a generally healthy population, preexisting reproductive conditions as well as general variability in fertility would not impact a worker’s overt health or employment status, and would be largely unobserved. It is estimated that 6% of adult males are infertile (Purves, 1992), and that 40%–90% of these cases are due to deficient sperm production of unidentifiable origin (Griffin, 1994). Given this information, EPA concludes that a significant portion of the male population has pre-existing reproductive deficits. EPA’s risk guidelines for deriving community based reference concentrations recommend a factor of 10 in accounting for intraspecies variability. EPA believes that in the case of nPB [n-propyl bromide], a lower uncertainty factor [UF] is appropriate to account for variability within the worker population. This UF is intended to protect for potential “unobserved” reproductive medical conditions (e.g., decreased sperm motility, aberrant sperm formation) that are known to exist among otherwise healthy males of working age. Because we are concerned about exposures in the workplace, not exposures to the full population, and because exposures would not be continuous, such as would be expected when developing an RfC, we employed an UF of three as an upper bound instead of the full uncertainty factor of 10 for intrahuman variability.”

Although U.S. EPA noted that male workers would be subject to pre-existing reproductive deficits that would not lead to removal from the workforce, a reduced value of 3 was still chosen for the intraspecies uncertainty factor. U.S. EPA justified this by noting that exposures would only be in the workplace, rather than to the full population, and that worker exposures would not be continuous. While the assumption that the worker population is more homogeneous than the general population is relevant to the question of interindividual variability, the issue of exposure continuity raised by U.S. EPA is not typically considered in setting this factor.

The Netherlands applies a default factor of 3 for intraspecies differences in deriving the "margin of safety" for occupational exposures, based on the assumption variability among workers would be less than in the general public (Health Council of the Netherlands, 2000). In discussing the choice of 3 as the default intraspecies factor for workers in the Netherlands, de Raat et al. (1997) stated that,

> “An arbitrary factor of 3 can be applied in case protection of the occupational population is aimed at, and a factor of 10 can be applied in case the assessment is dealing with risks for the general population (for additional discussion see Calabrese (1985) and Hattis et al. (1987)). The offspring of the worker must be regarded as a member of the general population. This means that a higher factor must be employed for the intraspecies variation in case embryotoxic or teratogenic effects are starting points of extrapolation.”

The two references cited by de Raat et al. discuss interindividual human variability in general, but neither provides evidence for a lower variability in workers (Calabrese, 1985; Hattis et al., 1987).
The Interdepartmental Group on Health Risks from Chemicals (IGHRC, 2003) discussed the use of uncertainty factors in human health risk assessment conducted in the United Kingdom (UK). The UK has not specified default uncertainty factors for occupational risk assessment. IGHRC also summarized the approaches taken by other countries, discussing the approach of the Netherlands as follows:

“Another point to note is that a default factor of three is used to allow for variability in the worker population, compared to the traditional default of 10. The justification for this lower default is that the worker population does not include very young, elderly or infirm people and thus it is assumed that the intraspecies differences are smaller in the worker population than in the general public (Hakkert et al., 1996). However, no data or analyses are presented to support either this assumption or the value of three that is adopted.”

Vermeire et al. (1999) discussed uncertainty factors proposed by a number of agencies and authors. The choice of 3 as the default intraspecies factor for workers by the Netherlands was noted but not explained further. Vermeire et al. found that Kalberlah and Schneider (1998; as cited by Vermeire et al. 1999), in a report prepared for the Federal Environmental Agency of Germany, proposed using a factor of 25 to account for both interspecies and intraspecies differences for the general population and a reduced combined intra- and interspecies factor of 5 for workers. Vermeire et al. stated that “As the authors admit, it can be noted that this proposal is based on an overall impression based on several substance-specific examples. The combined factor for workers accounting for both inter- and intraspecies variation is not adequately explained.” Vermeire et al. also reported that the European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC, 1995; as cited by Vermeire et al. 1999) proposed an intraspecies factor of 3 for the general population and 2 for workers, but the ECETOC justification for these choices was not discussed in the paper.

ECETOC (2003) has published updated guidance on assessment factors for human health risk assessment, which is also referenced as the source of default factors for deriving occupational exposure limits (ECETOC, 2006). ECETOC (2003) concluded that default intraspecies assessment factors of 5 for the general population and 3 for the worker population were adequate. To justify these choices, ECETOC (2003) described analyses of intraspecies differences published by Renwick and Lazarus (1998; as cited by ECETOC, 2003) and Hattis et al. (1999; as cited by ECETOC, 2003). ECETOC reports that Renwick and Lazarus estimated an upper 95th percentile of intraspecies variability in a human population of 4.3, while Hattis et al. reported a value of 3.8 for this parameter. The 90th percentile values were 3.7 and 3.2, respectively (ECETOC, 2003). Thus, ECETOC concluded that a value of 5 (i.e., more conservative than the 95th percentile) for the general population and a value of 3 (i.e., close to the 90th percentile) for the “more homogeneous” worker population were justified. As in the other publications discussed above, ECETOC did not present evidence to support the conclusion that pharmacokinetic and pharmacodynamic parameters are necessarily less variable for workers.

Thus, although a reduced interindividual variability for workers may be reasonable, there is no clear scientific basis for making that a default assumption. For the analyses conducted in the
current document, the intraspecies uncertainty factor was examined on a case by case basis, with factors of 1, $10^{0.5}$ (or approximately 3), and 10 being applied depending on the situation.

4. Adjustment for occupational exposure

Noncancer health risk assessments for chronic toxicants typically are protective for general population exposures that are assumed to occur 24 hours per day, 7 days per week. Under an occupational scenario, only exposures that occur during the time period at work are of concern. Because occupational exposures occur for a shorter time period, the air concentration that would be protective for worker exposures could potentially be higher than that for community environmental exposures, depending on the type of chronic toxicant.

For chronic toxicants where average exposure over the exposure period is appropriate to consider in deriving a protective level, two occupational scenarios were considered:

Exposure scenario one: The first scenario assumed workers are exposed at the PEL for 8 hours per day, 5 days per week.

Exposure scenario two: The second scenario accounted for workers being exposed at the PEL during an 8 hour work day, while accounting for the likely increased breathing rate of workers. Workers were assumed to breathe 10 m$^3$ out of a daily breathing rate of 20 m$^3$/day, and be exposed at the PEL for 5 days per week. This is a more health conservative approach than scenario one and has been applied by OEHHA, U.S. EPA and others.

Following the approach taken by HESIS in developing recommended PELs, calculations for chronic toxicants were carried out using the less conservative exposure scenario one, with some examples given using exposure scenario two.

For developmental toxicants, averaging of exposures is not always considered appropriate because a short-term exposure, or even a single exposure, that exceeds a safe level and occurs during a critical phase of development could produce the adverse effect (U.S. EPA, 1991). For the current document, occupational concentrations were derived for developmental toxicants both with and without adjustment for the shorter duration of worker exposure to illustrate the impact of exposure averaging. The issue of how to average exposures for particular types of toxicants is an area of ongoing research and will need to be explored further in determining occupational risk assessment methodology.

5. Calculation of occupational air concentration for a noncarcinogen

Occupational air concentrations were calculated for volatile compounds in the current document; methods for particulates are not discussed. The occupational air concentration was calculated as follows for risk assessments based on studies in animals:

$$C_{occ} = \frac{\text{NOAEL}_{HEC} \text{ or LOAEL}_{HEC} \text{ or BMCL}_{HEC} \times \frac{24}{8} \times \frac{7}{5}}{UF_{adj}}$$

(4)
where

\[ C_{occ} = \text{occupational air concentration in mg/m}^3 \]

\[ \text{NOAEL}_{HEC} = \text{no observed adverse effect level as a human equivalent air concentration in mg/m}^3 \]

\[ \text{LOAEL}_{HEC} = \text{lowest observed adverse effect level as a human equivalent air concentration in mg/m}^3 \]

\[ \text{BMCL}_{HEC} = \text{the lower 95\% confidence limit of the concentration producing a 5\% incidence of the critical effect as a human equivalent air concentration in mg/m}^3 \]

\[ \text{UF}_{adj} = \text{the total uncertainty factor after adjustment based on occupational considerations} \]

The NOAEL\textsubscript{HEC}, LOAEL\textsubscript{HEC} or BMCL\textsubscript{HEC} were taken from existing risk assessments on the chemical of interest. These values incorporate factors to account for continuous exposure, which is the relevant scenario for protection of the general public. The factors “24/8” and “7/5” adjust the continuous exposure scenario to an occupational scenario. If the more conservative exposure scenario \textit{(i.e.,)} scenario two) was applied, the factor “24/8” in Equation (4) was replaced by “20/10” (which accounts for the increased breathing rate during a workday).

For developmental toxicants, adjusting for a shorter duration of worker exposure \textit{(i.e.,}} increasing the exposure limit) is not generally recommended. A pregnant woman may be exposed to a chemical at work, but may also be exposed outside work to the same chemical or a different chemical acting by the same mechanism. Assigning all allowable exposure to the workday provides no margin of exposure for this serious health effect, which can be induced by a very short-term or even single exposure during a critical window of development. Calculations for developmental toxicants were shown with exposure averaging (Equation [4]) and without (removing the factors “24/8 and “7/5” from Equation [4]) for demonstration purposes.

OEHHA and U.S. EPA have in some cases applied an adjustment to the NOAEL, LOAEL or BMCL derived from animal studies for chemicals that may behave differently when inhaled by humans versus animals. This adjustment is not needed if human studies are available. For gases, the adjustment is related to the regional gas dose ratio (RGDR). If the gas has respiratory effects only, the RGDR is calculated as the ratio of the relative (animals/humans) minute volume to the relative (animals/humans) surface area for the lung region of concern. If the gas has systemic effects, the RGDR is the ratio of the animal blood:air partition coefficient to the human blood:air partition coefficient. Typically there are insufficient data to determine the RGDR for systemically acting gases and the default ratio is set to one. If the RGDR is set to one, the NOAEL, LOAEL or BMCL from the animal studies are used in Equation (4) without further adjustment. In the current document, the gases of interest with animal studies were all systemically acting and the RGDR was set to one in all cases.
In cases where the risk assessment identified a NOAEL, LOAEL or BMCL from an adequate study in workers, the value was taken directly and used as shown in Equation (5):

$$C_{occ} = \frac{NOAEL_{occ} \text{ or LOAEL}_{occ} \text{ or BMCL}_{occ}}{UF_{adj}}$$  \hspace{1cm} (5)

Values for individual uncertainty factors typically range from 1-10, with 3 being applied in some cases as an approximation for the square root of 10 (3.16). Total uncertainty factors are rounded off to reflect this approximation (i.e., a total factor of 3 \(\times\) 3 is considered equivalent to \(10^{0.5} \times 10^{0.5}\), or 10).

To convert an occupational air concentration in mg/m\(^3\) to ppm, the appropriate conversion factor was obtained from the NIOSH Pocket Guide (http://www.cdc.gov/niosh/npg/) or estimated using the following equation:

$$1 \text{ ppm} = (0.0409 \times \text{MW}) \text{mg/m}^3$$  \hspace{1cm} (6)

where

$$\text{MW} = \text{molecular weight of the chemical of interest}$$

6. Comparison to current PEL

The occupational air concentration was compared to the current PEL, if available, by calculating the ratio between the two values.

7. Other considerations

The approach outlined above accounts only for inhalation exposures to workers. For some chemicals, dermal absorption may be significant in an occupational setting, adding substantially to a worker’s internal dose (Bos et al., 1998). This important issue should be considered in establishing occupational risk assessment guidelines. In the current document, the potential increase in cancer risk associated with dermal absorption is discussed for the example of 4,4’-methyleneedianiline.
Results of Screening for Workplace Chemicals

Workplace chemicals listed as known to cause cancer under Proposition 65 that do not have Cal/OSHA PELs

Table 2 shows the workplace chemicals listed as known to cause cancer under Proposition 65 that do not have Cal/OSHA PELs. The ACGIH TLVs and NIOSH RELs are provided where available. If other organizations or jurisdictions (e.g., AIHA or other countries) have established an occupational level, this is noted by a check mark (“✓”) (based on data from ACGIH, 2006). The potential for skin absorption is indicated, based on skin notations3 determined by ACGIH or by other organizations/jurisdictions. Table A-1 (Appendix A) summarizes additional data on these chemicals, including production/import volume data and information on use/identity.

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3 In the California Code of Regulations (Title 8, § 5155), the skin notation is described as follows: “The substances designated by ‘S’ in the skin notation column of Table AC-1 [Permissible Exposure Limits for Chemical Contaminants] may be absorbed into the bloodstream through the skin, the mucous membranes and/or the eye, and contribute to the overall exposure. Appropriate protective clothing shall be provided for and used by employees as necessary to prevent skin absorption.” ACGIH (2006) describes the “Skin” notation as follows: “The designation ‘Skin’ in the ‘Notations’ column refers to the potential significant contribution to the overall exposure by the cutaneous route, including mucous membranes and the eyes, either by contact with vapors or, of probable greater significance, by direct skin contact with the substance. Where repeated dermal application studies have shown significant absorption or systemic effects following exposure, a Skin notation would be considered. The Skin notation also alerts the industrial hygienist that overexposure may occur following dermal contact, even when exposures are at or below the TLV.”
Table 2. Workplace chemicals listed as known to cause cancer under Proposition 65 that do not have Cal/OSHA PELs

<table>
<thead>
<tr>
<th>Chemical/Agent</th>
<th>Year Listed</th>
<th>ACGIH</th>
<th>NIOSH</th>
<th>Occupational Levels Available in Other Jurisdictionsa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetamide</td>
<td>1987</td>
<td>0.1 ppm (Ceiling) Skin</td>
<td>Eye, skin, URTb irritation; A2</td>
<td>✓</td>
</tr>
<tr>
<td>p-Aminoazobenzene</td>
<td>1990</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Benzofuran</td>
<td>1990</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Benzotrichloride</td>
<td>1987</td>
<td>0.1 ppm (Ceiling) Skin</td>
<td>Eye, skin, URTb irritation; A2</td>
<td>--</td>
</tr>
<tr>
<td>2,2-Bis(bromomethyl)-1,3-propanediol</td>
<td>1996</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Ceramic fibers (airborne particles of respirable size)</td>
<td>1990</td>
<td>0.2 f/cc Pulmonary fibrosis; pulmonary function; A2</td>
<td>0.5 f/cc Lung cancer, mesothelioma, and other adverse respiratory health effects; Ca</td>
<td>✓</td>
</tr>
<tr>
<td>Chlorinated paraffins (average chain length, C12; approximately 60 percent chlorine by weight)</td>
<td>1989</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>3-Chloro-2-methylpropene</td>
<td>1989</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>C.I. Direct Blue 15</td>
<td>1997</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>C.I. Direct Blue 218</td>
<td>1997</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>p-Cresidine</td>
<td>1988</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Cupferron</td>
<td>1988</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>D&amp;C Orange No. 17</td>
<td>1990</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>D&amp;C Red No. 9</td>
<td>1990</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>D&amp;C Red No. 19</td>
<td>1990</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>4,4’-Diaminodiphenyl ether (4,4’-Oxydianiline)</td>
<td>1988</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>2,4-Diaminotoluene; Diaminotoluene (mixed) (See footnote e)</td>
<td>1988; 1990</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
</tbody>
</table>

Occupational Risk Project 20 December 2007 OEHHA
<table>
<thead>
<tr>
<th>Chemical/Agent</th>
<th>Year Listed</th>
<th>ACGIH TLV</th>
<th>ACGIH TLV Basis; Carcinogen Classification</th>
<th>NIOSH REL</th>
<th>NIOSH REL Basis; Notes</th>
<th>Occupational Levels Available in Other Jurisdictions¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>20 Dichloroacetic acid</td>
<td>1996</td>
<td>0.5 ppm; Skin</td>
<td>URT and eye irritation; testicular damage; A³</td>
<td>--</td>
<td>--</td>
<td>✓; Skin</td>
</tr>
<tr>
<td>21 Diesel engine exhaust</td>
<td>1990</td>
<td>--</td>
<td>--</td>
<td>Lowest feasible concentration</td>
<td>Potential for cancer; tumors of the lung in animals; Ca</td>
<td>✓</td>
</tr>
<tr>
<td>22 Diethyl sulfate</td>
<td>1988</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>✓; Skin</td>
</tr>
<tr>
<td>23 Diglycidyl resorcinol ether (DGRE)</td>
<td>1989</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>✓</td>
</tr>
<tr>
<td>24 Dihydrosafrole</td>
<td>1988</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td></td>
</tr>
<tr>
<td>25 3,3¹-Dimethoxybenzidine dihydrochloride</td>
<td>1990</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td></td>
</tr>
<tr>
<td>26 Ethylene thiourea</td>
<td>1988</td>
<td>--</td>
<td>--</td>
<td>Lowest feasible concentration</td>
<td>Potential for cancer and teratogenesis; liver, thyroid &amp; lymphatic system tumors in animals; Ca</td>
<td>✓</td>
</tr>
<tr>
<td>27 Furan</td>
<td>1993</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>✓; Skin</td>
</tr>
<tr>
<td>28 Isoprene</td>
<td>1996</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>✓</td>
</tr>
<tr>
<td>29 Methyl carbamate</td>
<td>1998</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td></td>
</tr>
<tr>
<td>30 Methylene glycol</td>
<td>2001</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td></td>
</tr>
<tr>
<td>31 N-Methylolacrylamide</td>
<td>1990</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td></td>
</tr>
<tr>
<td>32 Nitrilotriacetic acid</td>
<td>1988</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td></td>
</tr>
<tr>
<td>33 p-Nitrosodiphenylamine</td>
<td>1988</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td></td>
</tr>
<tr>
<td>34 N-Nitrosodiphenylamine</td>
<td>1988</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td></td>
</tr>
<tr>
<td>35 o-Phenylenediamine and its salts</td>
<td>1998</td>
<td>0.1 mg/m³</td>
<td>Anemia; A³</td>
<td>--</td>
<td>--</td>
<td>✓; Skin</td>
</tr>
<tr>
<td>36 1,3-Propane sultone</td>
<td>1988</td>
<td>Levels as low as possible</td>
<td>Cancer; A³</td>
<td>Lowest feasible concentration</td>
<td>Skin tumors, leukemia, gliomas in rats and mice; Ca</td>
<td>✓³; Skin</td>
</tr>
<tr>
<td>37 Propylene glycol mono-t-butyl ether</td>
<td>2004</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td></td>
</tr>
<tr>
<td>Chemical/Agent</td>
<td>Year Listed</td>
<td>ACGIH</td>
<td>NIOSH</td>
<td>Occupational Levels Available in Other Jurisdictions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>--------------------------------------------</td>
<td>-------------</td>
<td>-------</td>
<td>-------</td>
<td>-----------------------------------------------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quinoline and its strong acid salts</td>
<td>1997</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Styrene oxide</td>
<td>1988</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tetrafluoroethylene</td>
<td>1997</td>
<td>2 ppm</td>
<td>Kidney and liver damage; liver and kidney cancer;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>A3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thiourea</td>
<td>1988</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trimethyl phosphate</td>
<td>1996</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tris(2-chloroethyl) phosphate</td>
<td>1992</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vinyl fluoride</td>
<td>1997</td>
<td>1 ppm</td>
<td>Liver cancer; liver damage; A2</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- If an occupational level has been set by another jurisdiction, as reported by ACGIH (2006), it is noted with a “✓”. If a jurisdiction has established a skin notation, as described above, it is noted as “Skin.”
- URT = upper respiratory tract
- A2 is the ACGIH classification for “suspected human carcinogen,” used primarily when there is limited evidence of carcinogenicity in humans and sufficient evidence of carcinogenicity in experimental animals with relevance to humans (ACGIH, 2006).
- Ca is the NIOSH designation for “potential occupational carcinogen.”
- 2,4-Diaminotoluene and diaminotoluene (mixed isomers) are listed individually under Proposition 65, but are treated as one entry here.
- A3 is the ACGIH classification for “confirmed animal carcinogen with unknown relevance to humans,” which is typically used for agents that are carcinogenic in experimental animals “at a relatively high dose, by route(s) of administration, at site(s), of histologic types(s), or by mechanism(s) that may not be relevant to worker exposure” (ACGIH, 2006).
- The German MAK (maximum workplace concentration) Commission identified skin absorption and sensitization as important for diglycidyl resorcinol ether (DGRE) but did not set a specific occupational level, which is in accordance with the policy for carcinogens (DFG, 2006).
- Lowest feasible level.
About 70% of the 44 substances shown in Table 2 have been listed as known to the state of California to cause cancer under Proposition 65 for 15 or more years. Nineteen of the 44 substances, or about 40%, have an occupational health assessment level established by one or more agencies or jurisdictions.

Half of the agents in Table 2 are chemical or dye intermediates (see Table A-1). Some of these agents (e.g., furan, diaminotoluene, chlorendic acid, 3,3’-dimethoxybenzidine dihydrochloride, and trimethyl phosphate) are used in closed systems or controlled situations during the manufacturing process, which minimizes the potential for worker exposure. Occupational exposure may occur from fugitive emissions, during repair and maintenance operations, or if the chemicals are also used for non-manufacturing purposes. The use of chlorendic acid as an extreme pressure lubricant is an example of an alternative use that could pose an exposure concern.

ACGIH has developed TLVs for seven of these substances: benzotrichloride, ceramic fibers, dichloroacetic acid, o-phenylenediamine, 1,3-propane sultone, tetrafluoroethylene and vinyl fluoride. Benzotrichloride, ceramic fibers, and vinyl fluoride are classified by ACGIH as suspected human carcinogens (A2). Dichloroacetic acid, o-phenylenediamine, 1,3-propane sultone and tetrafluoroethylene are considered confirmed animal carcinogens with unknown relevance to humans (A3). The TLVs for 1,3-propane sultone, tetrafluoroethylene and vinyl fluoride are based on protecting against cancer. None of the TLVs were developed using quantitative risk assessment, in which estimated cancer risks associated with the levels are calculated and reported. Thus, it is unclear what level of protection the TLV provides, even if ACGIH indicated that it is based on cancer.

NIOSH identifies five of the substances, ceramic fibers, diaminotoluene, diesel engine exhaust, ethylene thiourea, and 1,3-propane sultone, as occupational carcinogens (Ca). The REL for ceramic fibers is based on protecting against cancer, and was derived using quantitative risk assessment. NIOSH has not carried out quantitative risk assessments for the other NIOSH-identified occupational carcinogens listed in Table 2. NIOSH RELs for occupational carcinogens have generally been set at the level NIOSH defines as the “lowest feasible concentration.” Under a policy adopted in 1995, NIOSH asserted that RELs will be developed based on a quantitative analysis of animal or human data, with consideration of the technological feasibility of controlling workplace exposures to the REL.

HESIS (2002) recommended a PEL of 0.02 mg/m³ for diesel engine exhaust to protect against cancer in its Health Hazard Advisory. The HESIS PEL was based on the OEHHA diesel exhaust unit risk value.

Based on skin notations determined by ACGIH or other agencies/jurisdictions (ACGIH, 2006), skin absorption is a potentially significant exposure route in addition to inhalation for 12 of the 20 carcinogens in Table 2 that were evaluated by these agencies. For the remaining 24 chemicals listed in Table 2, information on the potential for skin absorption was not identified.
Workplace chemicals listed as known to cause reproductive and/or developmental toxicity under Proposition 65 that do not have Cal/OSHA PELs

Table 3 shows the workplace chemicals listed as known to cause reproductive and/or developmental toxicity under Proposition 65 that do not have Cal/OSHA PELs. The ACGIH TLVs and NIOSH RELs, with “Skin” notations if applicable, are provided where available. If other organizations or jurisdictions (e.g., AIHA or other countries) have established an occupational level for the chemical and/or have identified a potential for skin absorption, this is noted as well (based on data from ACGIH, 2006). Additional data on these chemicals, including production volume data and information on the use/identity, are provided in Appendix A, Table A-1.
<table>
<thead>
<tr>
<th>Chemical/Agent</th>
<th>Year Listed</th>
<th>ACGIH TLV</th>
<th>ACGIH TLV Basis; Notes</th>
<th>NIOSH REL</th>
<th>NIOSH REL Basis; Notes</th>
<th>Occupational Levels in Other Jurisdictions(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-Bromopropane</td>
<td>2004</td>
<td>10 ppm</td>
<td>Liver damage; embryo/fetal damage; neurotoxicity</td>
<td>--</td>
<td>--</td>
<td>✓; Skin(^b)</td>
</tr>
<tr>
<td>Butyl benzyl phthalate</td>
<td>2005</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>✓</td>
</tr>
<tr>
<td>Di-(n)-hexyl phthalate</td>
<td>2005</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>✓(^c)</td>
</tr>
<tr>
<td>Ethylene thiourea</td>
<td>1993</td>
<td>--</td>
<td>Lowest feasible concentration</td>
<td>Potential for cancer and teratogenesis; liver, thyroid &amp; lymphatic system tumors in animals; Ca</td>
<td>--</td>
<td></td>
</tr>
<tr>
<td>N-Methylpyrrolidone</td>
<td>2001</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>✓; Skin</td>
</tr>
</tbody>
</table>

\(^a\) If an occupational level has been set by another jurisdiction, as reported by ACGIH (2006), it is noted with a “✓”. If a jurisdiction has established a skin notation, it is noted as “Skin.”

\(^b\) Skin notation is from HESIS (2003) Hazard Alert.

\(^c\) ACGIH (2006) does not specifically list di-\(n\)-hexyl phthalate, but certain jurisdictions (e.g., Sweden) have established levels for phthalates as a class of compounds.
Five chemicals that were listed as reproductive and/or developmental toxicants under Proposition 65 as of December 2006 and identified here as being of potential importance in the workplace do not have Cal/OSHA PELs. With the exception of ethylene thiourea, the workplace chemicals listed in Table 3 are relatively recent additions to the Proposition 65 list. Table 3 does not include drugs and pesticides, because those classes of chemicals were removed as part of the initial screening of the list. Some drugs and pesticides are reproductive and developmental toxicants of industrial significance, however. HESIS has issued Hazard Alerts for cycloheximide (HESIS, 1987) and ribavirin (HESIS, 1990), two drugs of concern for occupational exposure.

ACGIH has developed a TLV for 1-bromopropane to protect against liver damage, embryo and fetal damage, and neurotoxicity. Canada has a regulatory limit of 10 ppm for 1-bromopropane, and Finland’s limit is 30 ppm. HESIS (2003) issued a Hazard Alert on 1-bromopropane and recommended a PEL of 1-3 ppm and a skin notation to protect against reproductive and developmental toxicity. The proposed PEL is still under consideration by Cal/OSHA.

Regulatory levels of 3-5 mg/m³ have been adopted for butyl benzyl phthalate by other countries. In Sweden, a level of 3 mg/m³ is applied to all phthalates for which no chemical-specific limit has been defined; this level would apply to di-n-hexyl phthalate, for example.

NIOSH identified ethylene thiourea as an occupational carcinogen with the potential to induce teratogenesis and recommended that exposures be kept to the lowest feasible concentration.

HESIS recently developed a Health Hazard Advisory on N-methylpyrrolidone to warn of its developmental and reproductive toxicity (HESIS, 2006). AIHA adopted a WEEL of 10 ppm and a skin notation for N-methylpyrrolidone. Fourteen other countries have adopted values for N-methylpyrrolidone ranging from 1 to 100 ppm. Most of the countries also have adopted skin notations for N-methylpyrrolidone (ACGIH, 2006).

Both 1-bromopropane and N-methylpyrrolidone are used as solvents, increasing concern for worker exposure. The phthalates are used as plasticizers, with butyl benzyl phthalate also used as a chemical intermediate. Ethylene thiourea is used in rubber curing and as a chemical intermediate (see Table A-1 for information on use and exposure).
Workplace chemicals listed as known to cause cancer under Proposition 65 that have Cal/OSHA PELs but are not regulated as occupational carcinogens

Table 4 shows the workplace chemicals listed as carcinogens under Proposition 65 have Cal/OSHA PELs, but are not regulated as occupational carcinogens. The Table summarizes the following information for each chemical:

- Cal/OSHA PEL
- Basis for the Cal/OSHA PEL (if available on-line)
- ACGIH TLV
- Basis for the ACGIH TLV
- Current OSHA PEL
- PEL developed by OSHA (1989) as part of a PEL update project
- Basis for the OSHA (1989) PEL
- NIOSH REL

The basis for the Cal/OSHA PEL was obtained from the Cal/OSHA Standards Board website (http://www.dir.ca.gov/oshsb/archives.html); this information was not available for all agents. The ACGIH TLVs and the basis for the TLVs were taken from the ACGIH database summary table (ACGIH, 2006); updated TLVs were obtained from ACGIH (2007). If no basis was given in the ACGIH summary table, the TLV basis was obtained from the documentation for the individual chemicals (ACGIH, 2006). The PELs developed by OSHA in 1989 and the basis for those PELs were obtained from the January 19, 1989 Final Rule on Air Contaminants Project (OSHA, 1989; also see http://www.cdc.gov/niosh/pel88/pelstart.html). This Final Rule was remanded by the U.S. Circuit Court of Appeals and these 1989 PELs are not currently in force. The current OSHA PELs, which generally are the PELs that were in force prior to the 1989 update project, were obtained from the OSHA website (http://www.osha.gov/SLTC/pel/index.html). The NIOSH RELs were obtained from the NIOSH Pocket Guide to Chemical Hazards (http://www.cdc.gov/niosh/npg/) or from NIOSH (1992).
Table 4. Workplace chemicals listed as known to cause cancer under Proposition 65 that have Cal/OSHA PELs but are not regulated as occupational carcinogens

<table>
<thead>
<tr>
<th>Chemical/Agent</th>
<th>Year Listed</th>
<th>Cal/OSHA PEL</th>
<th>Cal/OSHA PEL Basis/Notes</th>
<th>ACGIH TLV</th>
<th>ACGIH TLV Basis; Carcinogen Classification</th>
<th>OSHA PEL Current</th>
<th>OSHA (1989) PEL</th>
<th>OSHA (1989) PEL Basis</th>
<th>NIOSH REL/Health Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Acetaldehyde</td>
<td>1988</td>
<td>25 ppm (Ceiling)</td>
<td>Control mucous membrane irritation. See footnote b</td>
<td>25 ppm (Ceiling)</td>
<td>Eye &amp; URT irritation; A3</td>
<td>200 ppm</td>
<td>100 ppm</td>
<td>Conjunctivitis; sensory irritation</td>
<td>Ca Potential for cancer, eye, skin and respiratory irritation, nasal tumors in animals, mutagenesis in vitro</td>
</tr>
<tr>
<td>2 Acrylamide</td>
<td>1990</td>
<td>0.03 mg/m³ Skin</td>
<td>--</td>
<td>0.03 mg/m³ Skin</td>
<td>CNS impairment A3</td>
<td>0.3 mg/m³ Skin</td>
<td>0.03 mg/m³ Skin</td>
<td>Cancer; QRA</td>
<td>0.03 mg/m³ Skin</td>
</tr>
<tr>
<td>3 Aniline</td>
<td>1990</td>
<td>2 ppm Skin</td>
<td>--</td>
<td>2 ppm Skin</td>
<td>Methemoglobinemia A3</td>
<td>5 ppm Skin</td>
<td>2 ppm Skin</td>
<td>Methemoglobinemia</td>
<td>Ca Potential for cancer, spleen tumors in animals</td>
</tr>
<tr>
<td>4 o-Anisidine</td>
<td>1987</td>
<td>0.5 mg/m³ Skin</td>
<td>--</td>
<td>0.5 mg/m³ Skin</td>
<td>Methemoglobinemia; A3</td>
<td>0.5 mg/m³ Skin</td>
<td>--</td>
<td>--</td>
<td>0.5 mg/m³ Skin</td>
</tr>
<tr>
<td>5 Antimony oxide</td>
<td>1990</td>
<td>0.5 mg/m³</td>
<td>--</td>
<td>0.5 mg/m³ (antimony &amp; compounds) See footnote d</td>
<td>Skin &amp; URT irritation; not classified (antimony &amp; compounds)</td>
<td>0.5 mg/m³</td>
<td>--</td>
<td>--</td>
<td>0.5 mg/m³</td>
</tr>
<tr>
<td>6 Benzyl chloride</td>
<td>1990</td>
<td>1 ppm</td>
<td>--</td>
<td>1 ppm</td>
<td>Eye, skin &amp; URT irritation; A3</td>
<td>1 ppm</td>
<td>--</td>
<td>--</td>
<td>1 ppm (Ceiling)</td>
</tr>
<tr>
<td>Chemical/Agent</td>
<td>Year Listed</td>
<td>Cal/OSHA PEL</td>
<td>Cal/OSHA PEL Basis/Notes</td>
<td>ACGIH TLV</td>
<td>ACGIH TLV Basis; Carcinogen Classification</td>
<td>OSHA PEL Current</td>
<td>OSHA (1989) PEL</td>
<td>OSHA (1989) PEL Basis</td>
<td>NIOSH REL/Health Effects</td>
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<td>-------------------------</td>
</tr>
<tr>
<td>7 Beryllium &amp; beryllium compounds</td>
<td>1987</td>
<td>0.0002 mg/m³</td>
<td>--</td>
<td>0.002 mg/m³</td>
<td>Sensitization &amp; beryllium disease</td>
<td>0.002 mg/m³</td>
<td>Cancer (lung); berylliosis; A1</td>
<td>Sensitization; chronic beryllium disease (berylliosis); A1 (proposed)</td>
<td>0.002 mg/m³</td>
</tr>
<tr>
<td>8 Bis(2-chloroethyl) ether (Dichloroethyl ether)</td>
<td>1988</td>
<td>5 ppm Skin</td>
<td>--</td>
<td>5 ppm Skin</td>
<td>URT &amp; eye irritation; nausea; A4</td>
<td>15 ppm</td>
<td>5 ppm Skin</td>
<td>Eye and nasal irritation, lung injury, nausea</td>
<td>--</td>
</tr>
<tr>
<td>9 Bromoethane (Ethyl bromide)</td>
<td>2000</td>
<td>5 ppm Skin</td>
<td>--</td>
<td>5 ppm Skin</td>
<td>Liver damage; CNS impairment A3</td>
<td>200 ppm</td>
<td>200 ppm</td>
<td>Narcosis, kidney and liver damage, and respiratory irritation</td>
<td>--</td>
</tr>
<tr>
<td>10 Carbon black (airborne, unbound particles of respirable size)</td>
<td>2003</td>
<td>3.5 mg/m³</td>
<td>See footnote b</td>
<td>3.5 mg/m³</td>
<td>--</td>
<td>3.5 mg/m³</td>
<td>--</td>
<td>2 ppm</td>
<td>Cancer; QRA</td>
</tr>
<tr>
<td>11 Carbon tetrachloride</td>
<td>1987</td>
<td>2 ppm Skin</td>
<td>--</td>
<td>5 ppm Skin</td>
<td>Liver damage; A2</td>
<td>10 ppm</td>
<td>2 ppm</td>
<td>--</td>
<td>5 ppm Skin</td>
</tr>
<tr>
<td>12 Catechol</td>
<td>2003</td>
<td>5 ppm Skin</td>
<td>--</td>
<td>5 ppm Skin</td>
<td>Eye irritation; dermatitis; URT irritation; A3</td>
<td>--</td>
<td>5 ppm Skin</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>13 Chloroethane (Ethyl chloride)</td>
<td>1990</td>
<td>100 ppm Skin</td>
<td>Tumor formation in several animal species</td>
<td>100 ppm Skin</td>
<td>Liver damage; A3</td>
<td>1,000 ppm</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Chemical/Agent</td>
<td>Year Listed</td>
<td>Cal/OSHA PEL</td>
<td>Cal/OSHA PEL Basis/Notes</td>
<td>ACGIH TLV</td>
<td>ACGIH TLV Basis; Carcinogen Classification</td>
<td>OSHA PEL Current</td>
<td>OSHA (1989) PEL</td>
<td>OSHA (1989) PEL Basis</td>
<td>NIOSH REL/Health Effects</td>
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<td>--------------------------</td>
</tr>
<tr>
<td>14 Chloroform</td>
<td>1987</td>
<td>2 ppm</td>
<td></td>
<td>10 ppm</td>
<td>Liver damage; embryo/fetal damage; CNS impairment; A3</td>
<td>50 ppm (Ceiling)</td>
<td>2 ppm</td>
<td>Cancer; QRA</td>
<td>2 ppm (STEL) Cancer; QRA</td>
</tr>
<tr>
<td>15 1-Chloro-4-nitrobenzene (p-Nitrochlorobenzene)</td>
<td>1999</td>
<td>0.64 mg/m³ Skin</td>
<td>--</td>
<td>0.64 mg/m³ Skin</td>
<td>Methemoglobinemia; A3</td>
<td>1 mg/m³ Skin</td>
<td>1 mg/m³ Skin</td>
<td>Methemoglobinemia and spleen, liver, and kidney damage</td>
<td>Ca Skin Potential for cancer, vascular and liver tumors in animals</td>
</tr>
<tr>
<td>16 Chloroprene</td>
<td>2000</td>
<td>10 ppm Skin</td>
<td>--</td>
<td>10 ppm Skin</td>
<td>URT &amp; eye irritation; not classified</td>
<td>25 ppm Skin</td>
<td>10 ppm Skin</td>
<td>Reproductive &amp; systemic effects</td>
<td>1 ppm (Ceiling) Ca Lung and skin cancer, reproductive effects</td>
</tr>
<tr>
<td>17 Cobalt and certain cobalt compounds (see footnote c)</td>
<td>1992, 2000, 2005</td>
<td>0.02 mg/m³</td>
<td>Control myocardial effects. See footnote b</td>
<td>0.02 mg/m³</td>
<td>Asthma; pulmonary function; myocardial effects; A3</td>
<td>0.1 mg/m³</td>
<td>0.05 mg/m³</td>
<td>Respiratory disease &amp; pulmonary sensitization</td>
<td>0.05 mg/m³ Dermatitis, potential for pulmonary fibrosis</td>
</tr>
<tr>
<td>18 p-Dichlorobenzene</td>
<td>1989</td>
<td>10 ppm</td>
<td></td>
<td>10 ppm</td>
<td>Eye irritation; kidney damage; A3</td>
<td>75 ppm</td>
<td>75 ppm</td>
<td>Eye damage; vertigo, neuropathic effects</td>
<td>Ca Potential for cancer, eye and URT irritation, liver toxicity, kidney and liver cancer in animals</td>
</tr>
<tr>
<td>19 1,4-Dichloro-2-butene</td>
<td>1990</td>
<td>0.005 ppm Skin</td>
<td>Hematological changes and effects on the epithelium in rats.</td>
<td>0.005 ppm Skin</td>
<td>URT &amp; eye irritation; A2</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>20 1,1-Dichloroethane</td>
<td>1990</td>
<td>100 ppm</td>
<td>--</td>
<td>100 ppm</td>
<td>URT &amp; eye irritation; liver &amp; kidney damage A4</td>
<td>100 ppm</td>
<td>100 ppm</td>
<td>Hepatotoxicity</td>
<td>100 ppm Narcotic effects, possible liver, kidney, lung damage</td>
</tr>
<tr>
<td>21 1,2-Dichloropropane (Propylene dichloride)</td>
<td>1990</td>
<td>75 ppm</td>
<td>--</td>
<td>10 ppm</td>
<td>URT irritation; body weight effects; A4</td>
<td>75 ppm</td>
<td>--</td>
<td>--</td>
<td>Ca Potential for cancer, narcosis, eye irritation, mammary gland and liver tumors in animals</td>
</tr>
<tr>
<td>Chemical/Agent</td>
<td>Year Listed</td>
<td>Cal/OSHA PEL</td>
<td>Cal/OSHA PEL Basis/Notes</td>
<td>ACGIH TLV</td>
<td>ACGIH TLV Basis; Carcinogen Classification</td>
<td>OSHA PEL Current</td>
<td>OSHA (1989) PEL</td>
<td>OSHA (1989) PEL Basis</td>
<td>NIOSH REL/ Health Effects</td>
</tr>
<tr>
<td>---</td>
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<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Di(2-ethylhexyl)phthalate</td>
<td>1988</td>
<td>5 mg/m³</td>
<td>--</td>
<td>5 mg/m³</td>
<td>LRT irritation; A3</td>
<td>5 mg/m³</td>
<td>5 mg/m³</td>
<td>--</td>
<td>Neuropathic; hepatic; other systemic toxicity</td>
</tr>
<tr>
<td>1,1-Dimethylhydrazine</td>
<td>1989</td>
<td>0.01 ppm Skin</td>
<td>Slight increase in nasal tumors in rats exposed at 0.05 ppm. See footnote b.</td>
<td>0.01 ppm Skin</td>
<td>URT irritation; nasal cancer; A3</td>
<td>0.5 ppm Skin</td>
<td>--</td>
<td>--</td>
<td>0.06 mg/m³ Ca Potential for cancer, blood, liver, skin effects, multisite animal tumors</td>
</tr>
<tr>
<td>Dimethyl sulfate</td>
<td>1988</td>
<td>0.1 ppm Skin</td>
<td>--</td>
<td>0.1 ppm Skin</td>
<td>Eye &amp; skin irritation; A3</td>
<td>1 ppm Skin</td>
<td>0.1 ppm Skin</td>
<td>--</td>
<td>Cancer</td>
</tr>
<tr>
<td>2,4-Dinitrotoluene; 2,6-Dinitrotoluene; Dinitrotoluene mixture, 2,4-/2,6- (See footnote f)</td>
<td>1988; 1995; 1996</td>
<td>0.15 mg/m³ Skin</td>
<td>--</td>
<td>0.2 mg/m³ Skin</td>
<td>Cardiac impairment; reproductive effects; A3</td>
<td>1.5 mg/m³ Skin</td>
<td>--</td>
<td>--</td>
<td>1.5 mg/m³ Skin Ca Potential for cancer, reproductive, multisite animal tumors</td>
</tr>
<tr>
<td>1,4-Dioxane</td>
<td>1988</td>
<td>25 ppm Skin</td>
<td>--</td>
<td>20 ppm Skin</td>
<td>Liver damage; A3</td>
<td>100 ppm Skin</td>
<td>25 ppm Skin</td>
<td>Kidney, liver damage; cancer</td>
<td>1 ppm (Ceiling) Ca Potential for cancer, liver and kidney effects, multisite animal tumors</td>
</tr>
<tr>
<td>Epichlorohydrin</td>
<td>1987</td>
<td>0.05 ppm Skin</td>
<td>Lowered to control reproductive and respiratory effects and the possibility of carcinogenic effects</td>
<td>0.5 ppm Skin</td>
<td>URT irritation; male reproductive; A3</td>
<td>5 ppm Skin</td>
<td>2 ppm Skin</td>
<td>Dermal, respiratory, liver, and kidney effects</td>
<td>Ca Respiratory cancer, mutagenesis, repro, kidney, liver and respiratory effects</td>
</tr>
<tr>
<td>Ethyl acrylate</td>
<td>1989</td>
<td>5 ppm Skin</td>
<td>--</td>
<td>5 ppm</td>
<td>URT &amp; GI irritation; CNS impairment; eye irritation; skin sensitization; A4</td>
<td>25 ppm Skin</td>
<td>5 ppm Skin</td>
<td>Severe eye, nose, skin irritation</td>
<td>Ca Potential for cancer, forestomach tumors in animals</td>
</tr>
<tr>
<td>Chemical/Agent</td>
<td>Year Listed</td>
<td>Cal/OSHA PEL</td>
<td>Cal/OSHA PEL Basis/Notes</td>
<td>ACGIH TLV</td>
<td>ACGIH TLV Basis; Carcinogen Classification</td>
<td>OSHA PEL Current</td>
<td>OSHA (1989) PEL</td>
<td>OSHA (1989) PEL Basis</td>
<td>NIOSH REL/Health Effects</td>
</tr>
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<td>---------------------------</td>
</tr>
<tr>
<td>Ethylbenzene</td>
<td>2004</td>
<td>100 ppm</td>
<td>--</td>
<td>100 ppm</td>
<td>URT irritation; CNS impairment; eye irritation; A3</td>
<td>100 ppm</td>
<td>100 ppm</td>
<td>Skin, mucous membrane, eye irritation</td>
<td>100 ppm; Eye, skin and URT irritation</td>
</tr>
<tr>
<td>Ethylene dichloride (1,2-Dichloroethane)</td>
<td>1987</td>
<td>1 ppm</td>
<td>--</td>
<td>10 ppm</td>
<td>Liver damage; nausea; A4</td>
<td>50 ppm</td>
<td>1 ppm</td>
<td>Liver damage; GI toxicity; cancer</td>
<td>1 ppm; Ca; Potential for cancer, nervous system, respiratory, cardiovascular, and liver effects</td>
</tr>
<tr>
<td>Glasswool fibers (airborne particles of respirable size)</td>
<td>1990</td>
<td>1.0 f/cc</td>
<td>See footnote b</td>
<td>1.0 f/cc</td>
<td>Skin and mucous membrane irritation; A3</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Hexachlorobenzene</td>
<td>1987</td>
<td>0.002 mg/m³ Skin</td>
<td>Hephatic and neurological effects. Hepatic tumors in animals noted. See footnotes b &amp; g</td>
<td>0.002 mg/m³ Skin</td>
<td>Porphyrin effects; skin damage; CNS impairment A3</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Hexachloroethane</td>
<td>1990</td>
<td>1 ppm Skin</td>
<td>--</td>
<td>1 ppm Skin</td>
<td>Liver &amp; kidney damage; A3</td>
<td>1 ppm</td>
<td>1 ppm Skin</td>
<td>Serious injury potential to several organ systems. See footnote b.</td>
<td>1 ppm Ca; Potential for cancer, liver tumors in animals</td>
</tr>
<tr>
<td>Hydrazine</td>
<td>1988</td>
<td>0.01 ppm Skin</td>
<td>Slight increases in nasal tumors in rats. See footnote b.</td>
<td>0.01 ppm Skin</td>
<td>URT cancer; A3</td>
<td>1 ppm Skin</td>
<td>0.1 ppm Skin</td>
<td>Cancer; liver disease; hematopoietic effects</td>
<td>0.03 ppm Ca; Potential for cancer, blood, liver and skin effects, multisite animal tumors</td>
</tr>
<tr>
<td>Indium phosphide</td>
<td>2001</td>
<td>0.1 mg/m³</td>
<td>--</td>
<td>0.1 mg/m³</td>
<td>Pulmonary edema; pneumonitis; dental erosion; malaise; not classified</td>
<td>--</td>
<td>0.1 mg/m³</td>
<td>Chronic lung function impairment</td>
<td>0.1 mg/m³; Highly toxic effects, eye and respiratory irritation</td>
</tr>
<tr>
<td>Chemical/Agent</td>
<td>Year Listed</td>
<td>Cal/OSHA PEL</td>
<td>Cal/OSHA PEL Basis/Notes</td>
<td>ACGIH TLV</td>
<td>ACGIH TLV Basis; Carcinogen Classification</td>
<td>OSHA PEL Current</td>
<td>OSHA (1989) PEL</td>
<td>OSHA (1989) PEL Basis</td>
<td>NIOSH REL/Health Effects</td>
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<td>------------------------</td>
</tr>
<tr>
<td>36 Lead and lead compounds</td>
<td>1992</td>
<td>0.05 mg/m³</td>
<td>0.05 mg/m³</td>
<td>Numerous health effects including reproductive toxicity; not an occupational carcinogen</td>
<td>2 ppm Skin</td>
<td>Eye, skin &amp; URT irritation; A3</td>
<td>0.05 mg/m³</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>37 2-Methylaziridine (Propyleneimine)</td>
<td>1988</td>
<td>2 ppm Skin</td>
<td>--</td>
<td>0.01 ppm Skin</td>
<td>URT irritation; lung cancer; eye irritation; liver damage; A3</td>
<td>2 ppm Skin</td>
<td>--</td>
<td>--</td>
<td>2 ppm, Skin Ca Potential for cancer, brain and mammary tumors in animals</td>
</tr>
<tr>
<td>38 Methylhydrazine and its salts</td>
<td>1992</td>
<td>0.01 ppm Skin</td>
<td>--</td>
<td>0.01 ppm Skin</td>
<td>Eye damage; CNS impairment; not classified</td>
<td>0.2 ppm (Ceiling) Skin</td>
<td>--</td>
<td>--</td>
<td>0.04 ppm (Ceiling) Ca Potential for cancer, blood, liver and skin effects, multisite animal tumors</td>
</tr>
<tr>
<td>39 Methyl iodide</td>
<td>1988</td>
<td>2 ppm Skin</td>
<td>--</td>
<td>2 ppm Skin</td>
<td>Eye damage; CNS impairment; not classified</td>
<td>5 ppm Skin</td>
<td>2 ppm Skin</td>
<td>--</td>
<td>2 ppm Skin Ca Potential for cancer, multisite animal tumors</td>
</tr>
<tr>
<td>40 Naphthalene</td>
<td>2002</td>
<td>10 ppm</td>
<td>--</td>
<td>10 ppm Skin</td>
<td>Hematologic effects; URT &amp; eye irritation; eye damage; A4</td>
<td>10 ppm</td>
<td>10 ppm</td>
<td>--</td>
<td>10 ppm Hemolysis and eye irritation that causes cataracts</td>
</tr>
<tr>
<td>41 Nickel (metallic)</td>
<td>1989</td>
<td>1 mg/m³</td>
<td>--</td>
<td>1.5 mg/m³</td>
<td>Dermatitis; pneumoconiosis; A5</td>
<td>1 mg/m³</td>
<td>--</td>
<td>--</td>
<td>0.015 mg/m³ Ca Lung and nasal cancer, skin effects</td>
</tr>
<tr>
<td>42 Nickel carbonyl</td>
<td>1987</td>
<td>0.001 ppm</td>
<td>--</td>
<td>0.05 ppm</td>
<td>Lung &amp; nasal cancer not classified See footnote j</td>
<td>0.001 ppm</td>
<td>0.001 ppm</td>
<td>Lung and nasal cancer</td>
<td>0.001 ppm Ca Lung and nasal cancer</td>
</tr>
<tr>
<td>Chemical/Agent</td>
<td>Year Listed</td>
<td>Cal/OSHA PEL</td>
<td>Cal/OSHA PEL Basis/Notes</td>
<td>ACGIH TLV</td>
<td>ACGIH TLV Basis; Carcinogen Classification</td>
<td>OSHA PEL Current</td>
<td>OSHA (1989) PEL</td>
<td>OSHA (1989) PEL Basis</td>
<td>NIOSH REL/Health Effects</td>
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</tr>
<tr>
<td>43 Nickel compounds</td>
<td>2004&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.1 mg/m³ (soluble)</td>
<td>1 mg/m³ (insoluble)</td>
<td>0.1 mg/m³ (soluble)</td>
<td>Soluble: lung damage; nasal cancer; A4 Insoluble: lung cancer; A1</td>
<td>1 mg/m³ (soluble)</td>
<td>0.1 mg/m³ (soluble)</td>
<td>Lung irritation, pathological changes that may presage cancer</td>
<td>0.015 mg/m³ (all compounds except nickel carbonyl) Ca Lung and nasal cancer, skin effects</td>
</tr>
<tr>
<td>44 Nitrobenzene</td>
<td>1997</td>
<td>1 ppm Skin</td>
<td>--</td>
<td>1 ppm Skin</td>
<td>Methemoglobinemia; A3</td>
<td>1 ppm Skin</td>
<td>--</td>
<td>--</td>
<td>1 ppm Skin Anoxia resulting from methemoglobin formation, anemia</td>
</tr>
<tr>
<td>45 Nitromethane</td>
<td>1997</td>
<td>2 ppm</td>
<td>Renal toxicity in rats</td>
<td>20 ppm</td>
<td>Thyroid effects; URT irritation; lung damage; A3</td>
<td>100 ppm</td>
<td>--</td>
<td>--</td>
<td>Ca Potential for cancer, liver tumors in rats</td>
</tr>
<tr>
<td>46 2-Nitropropane</td>
<td>1988</td>
<td>10 ppm</td>
<td>--</td>
<td>10 ppm</td>
<td>Liver damage; liver cancer; A3</td>
<td>10 ppm</td>
<td>25 ppm</td>
<td>Cancer</td>
<td>2 ppm Skin Anoxia resulting from methemoglobin formation</td>
</tr>
<tr>
<td>47 o-Nitrotoluene</td>
<td>1998</td>
<td>2 ppm Skin</td>
<td>--</td>
<td>2 ppm Skin</td>
<td>Methemoglobinemia; not classified</td>
<td>5 ppm Skin</td>
<td>2 ppm Skin</td>
<td>Methemoglobinemia</td>
<td>2 ppm Skin Anoxia resulting from methemoglobin formation</td>
</tr>
<tr>
<td>48 Phenyl glycidyl ether</td>
<td>1990</td>
<td>0.1 ppm Skin</td>
<td>Lowered based on toxicity in rats at 5 ppm. Skin notation based on human and animal sensitization. See footnote b.</td>
<td>0.1 ppm Skin; SEN</td>
<td>Testicular damage; A3</td>
<td>10 ppm</td>
<td>1 ppm</td>
<td>Skin sensitization; skin, respiratory tract irritation; testicular damage; liver necrosis</td>
<td>1 ppm (Ceiling) Ca Skin and mucous membrane effects, potential for sensitization, possible hematopoietic and reproductive effects, nasal cancer and precancerous lesions in rats</td>
</tr>
<tr>
<td>49 Phenylhydrazine and its salts</td>
<td>1992</td>
<td>5 ppm Skin</td>
<td>--</td>
<td>0.1 ppm Skin</td>
<td>Anemia; URT &amp; skin irritation; A3</td>
<td>5 ppm Skin</td>
<td>5 ppm Skin</td>
<td>Acute blood-related toxicity; possibly cancer</td>
<td>0.14 ppm (Ceiling) Skin Ca Potential for cancer, blood, liver and skin effects, multisite animal tumors</td>
</tr>
<tr>
<td>Chemical/Agent</td>
<td>Year Listed</td>
<td>Cal/OSHA PEL</td>
<td>Cal/OSHA PEL Basis/Notes</td>
<td>ACGIH TLV</td>
<td>ACGIH TLV Basis; Carcinogen Classification</td>
<td>OSHA PEL Current</td>
<td>OSHA (1989) PEL</td>
<td>OSHA (1989) PEL Basis</td>
<td>NIOSH REL/Health Effects</td>
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</tr>
<tr>
<td>Propylene oxide</td>
<td>1988</td>
<td>2 ppm</td>
<td>Respiratory effects. Carcinogenic effects also noted. See footnote l.</td>
<td>2 ppm SEN</td>
<td>Eye &amp; URT irritation; A3</td>
<td>100 ppm</td>
<td>20 ppm</td>
<td>Primary irritation; CNS depression</td>
<td>Lowest feasible Ca Potential for cancer, nasal tumors in animals</td>
</tr>
<tr>
<td>Pyridine</td>
<td>2002</td>
<td>5 ppm</td>
<td>--</td>
<td>1 ppm</td>
<td>Skin irritation; liver &amp; kidney damage; A3</td>
<td>5 ppm</td>
<td>--</td>
<td>--</td>
<td>5 ppm Mild eye, mucous membrane irritation, narcosis, kidney and liver damage in animals</td>
</tr>
<tr>
<td>Silica, crystalline (airborne particles of respirable size)</td>
<td>1988</td>
<td>0.1 mg/m³ (Quartz, silica[fused] &amp; tripoli) 0.05 mg/m³ (Cristobalite &amp; tridymite)</td>
<td>--</td>
<td>0.025 mg/m³ (α-Quartz and cristobalite)</td>
<td>Pulmonary fibrosis; lung cancer; A2</td>
<td>10 mg/m³ divided by (%SiO₂ + 2) Use ½ the value calculated for respirable quartz for cristobalite &amp; tridymite</td>
<td>0.1 mg/m³ (Quartz) 0.05 mg/m³ (Cristobalite and tridymite)</td>
<td>Silicosis</td>
<td>0.05 mg/m³ Ca Silicosis</td>
</tr>
<tr>
<td>Strong inorganic acid mists containing sulfuric acid</td>
<td>2003</td>
<td>1 mg/m³ (sulfuric acid)</td>
<td>--</td>
<td>0.2 mg/m³ (sulfuric acid)</td>
<td>Pulmonary function; A2 (for sulfuric acid in strong inorganic acid mists)</td>
<td>1 mg/m³ (sulfuric acid)</td>
<td>--</td>
<td>--</td>
<td>1 mg/m³ (sulfuric acid) Pulmonary irritation</td>
</tr>
<tr>
<td>1,1,2,2-Tetrachloroethane (Perchloroethylene)</td>
<td>1990</td>
<td>1 ppm Skin</td>
<td>--</td>
<td>1 ppm Skin</td>
<td>Liver damage; A3</td>
<td>5 ppm Skin</td>
<td>1 ppm Skin</td>
<td>Fatty infiltration of liver; serious liver damage</td>
<td>1 ppm Skin Ca Potential for cancer, liver, gastrointestinal, and nervous system effects, liver tumors in animals</td>
</tr>
<tr>
<td>Tetrachloroethylene</td>
<td>1988</td>
<td>25 ppm</td>
<td>See footnote b</td>
<td>25 ppm</td>
<td>CNS impairment; A3</td>
<td>100 ppm</td>
<td>25 ppm</td>
<td>Cancer; QRA</td>
<td>Ca Potential for cancer, liver tumors in animals</td>
</tr>
<tr>
<td>Chemical/Agent</td>
<td>Year Listed</td>
<td>Cal/OSHA PEL</td>
<td>Cal/OSHA PEL Basis/Notes</td>
<td>ACGIH TLV</td>
<td>ACGIH TLV Basis; Carcinogen Classification</td>
<td>OSHA PEL Current</td>
<td>OSHA (1989) PEL</td>
<td>OSHA (1989) PEL</td>
<td>NIOSH REL/Health Effects</td>
</tr>
<tr>
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<td>--------------------------------</td>
</tr>
<tr>
<td>Toluene diisocyanate</td>
<td>1989</td>
<td>0.005 ppm</td>
<td>--</td>
<td>0.005 ppm SEN</td>
<td>Respiratory sensitization; asthma; eye irritation; A4</td>
<td>0.02 (Ceiling)</td>
<td>0.005 ppm</td>
<td>Pulmonary sensitization</td>
<td>Ca Potential for cancer, multisite animal tumors</td>
</tr>
<tr>
<td>o-Toluidine</td>
<td>1988</td>
<td>2 ppm Skin</td>
<td>--</td>
<td>2 ppm Skin</td>
<td>Methemoglobinemia; A3</td>
<td>5 ppm Skin</td>
<td>5 ppm Skin</td>
<td>Cancer; QRA</td>
<td>Ca Skin Potential for cancer, multisite animal tumors</td>
</tr>
<tr>
<td>Trichloroethylene</td>
<td>1988</td>
<td>25 ppm</td>
<td>See footnote b</td>
<td>10 ppm</td>
<td>CNS impairment; cognitive decrements; renal toxicity; A2</td>
<td>100 ppm</td>
<td>50 ppm</td>
<td>CNS effects</td>
<td>25 ppm Ca Potential for cancer, CNS effects, liver tumors in animals</td>
</tr>
<tr>
<td>1,2,3-Trichloropropane</td>
<td>1992</td>
<td>10 ppm</td>
<td>--</td>
<td>10 ppm Skin</td>
<td>Liver &amp; kidney damage; eye &amp; URT irritation; A3</td>
<td>50 ppm</td>
<td>10 ppm</td>
<td>Liver and kidney damage</td>
<td>10 ppm Skin Ca Eye and mucous membrane irritation, potential for cancer, liver and kidney effects, narcosis in animals</td>
</tr>
<tr>
<td>Vanadium pentoxide (orthorhombic crystalline form)</td>
<td>2005</td>
<td>0.05 mg/m³</td>
<td>--</td>
<td>0.05 mg/m³</td>
<td>Irritation, lung; CNS effects; liver damage; kidney damage; A3</td>
<td>Dust: 0.5 mg/m³ (Ceiling) Fume: 0.1 mg/m³ (Ceiling)</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>4-Vinylcyclohexene</td>
<td>1996</td>
<td>0.1 ppm Skin</td>
<td>See footnote b</td>
<td>0.1 ppm</td>
<td>Female &amp; male reproductive damage; A3</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Vinyl trichloride (1,1,2-Trichloroethane)</td>
<td>1990</td>
<td>10 ppm Skin</td>
<td>--</td>
<td>10 ppm Skin</td>
<td>CNS impairment; liver damage; A3</td>
<td>10 ppm Skin</td>
<td>--</td>
<td>--</td>
<td>10 ppm Skin Ca Potential for cancer, CNS effects, liver tumors in animals</td>
</tr>
</tbody>
</table>
OSHA (1989) developed and adopted PELs as part of an update project. The OSHA Final Rule was remanded and the 1989 PELs are not currently in force.

b. The Cal/OSHA Airborne Contaminants Advisory Committee convened in 1997 prepared a “Carcinogen Position Statement” that applied to certain substances they reviewed (indicated in Table 4 using footnote b): “This substance has been identified by the International Agency for Research on Cancer as a carcinogen (Group 2B or higher). The exposure limits recommended have been primarily set on the basis of other types of toxic results, damage or interference with organ systems, irritation, respiratory problems, etc. Quantitative risk assessments can be used to estimate risks of cancer at various exposure levels in order to set a Permissible Exposure Limit. No such risk assessments have been conducted by this committee. Currently, neither the Division of Occupational Safety and Health nor the Occupational Safety and Health Standards Board have standard methods for performing these assessments or a useful criterion against which limits might be set. Cal/OSHA should reconsider the Permissible Exposure Limit proposed here if such a carcinogen guideline policy is adopted and appropriate resources can be allocated for an occupational risk assessment for this substance.” (see http://www.dir.ca.gov/oshsb/aircontaminant2.html)

c. QRA indicates that OSHA conducted a quantitative risk assessment and determined cancer risks associated with the proposed PEL as part of the 1989 PEL update project.

d. Antimony trioxide production is classified by ACGIH as an A2 carcinogen. ACGIH recommends that worker exposures during antimony trioxide production be kept to “levels as low as possible” based on potential for lung cancer and pneumoconiosis.

e. Cobalt metal powder (1992), cobalt [II] oxide (1992), cobalt sulfate (2005), and cobalt sulfate heptahydrate (2000) are listed as known to cause cancer under Proposition 65 (date of listing shown in parentheses).

f. 2,4-Dinitrotoluene, 2,6-dinitrotoluene and dinitrotoluene mixture, 2,4-2,6- are listed individually as known to cause cancer under Proposition 65, but are treated as one entry here. A Cal/OSHA PEL is established for 2,4-dinitrotoluene; the ACGIH TLV, OSHA PEL and NIOSH REL are for dinitrotoluene (mixed isomers). Evidence of current use was identified for 2,4-dinitrotoluene and mixed isomers.

g. The Cal/OSHA PEL was lowered to protect employees from hepatic and neurological effects, with the ACGIH TLV documentation cited as supporting this change (see http://www.dir.ca.gov/oshsb/airbornecontaminants2005ISOR.pdf). It was also noted that “several studies have demonstrated excesses of hepatic tumors in different species,” but cancer was not specifically cited as a reason for the PEL revision.

h. OSHA (1989) stated that the PEL of 1 ppm was adopted from the ACGIH TLV established in 1968, which was based on animal studies showing the potential for serious injury to several organ systems. OSHA discussed a proposal by ACGIH to raise the TLV from 1 ppm to 10 ppm, and concluded that increasing the PEL to 10 ppm would “increase the significant risk of cancer potentially associated with exposure to this substance.” However, OSHA did not conduct a risk assessment for hexachloroethane, and did not determine the extent to which the current PEL was protective for cancer.

i. Lead and lead compounds as a group were listed as known to cause cancer in 1992; various lead compounds were listed individually as carcinogens in 1988 and 1989.

j. Although the ACGIH (2007) summary table indicates that the TLV basis for nickel carbonyl was lung and nasal cancer, there was no carcinogen classification reported. The documentation for nickel carbonyl (ACGIH, 2006) was therefore consulted to resolve this discrepancy. According to the documentation, the TLV basis actually was “to minimize the potential for pulmonary damage reported in rats and acutely exposed workers, teratogenicity and embryotoxicity reported in Syrian hamsters, and possible central nervous system (CNS) effects reported among workers and various experimental animals acutely exposed to high concentrations. The documentation goes on to say that “this value should also be sufficiently low to minimize any potential carcinogenic effects,” but that “sufficient data were not available to recommend Skin, SEN or carcinogenicity notations…”

k. Nickel compounds as a group were listed as known to cause cancer in 2004; various inorganic nickel compounds were listed individually in 1987 and 1989.

l. Two statements were made regarding the basis for the Cal/OSHA propylene oxide PEL; one which mentioned nasal cancer, and the second which highlighted only respiratory effects. ACGIH was specifically cited in the setting of the Cal/OSHA PEL. Since the ACGIH TLV protects for respiratory effects only, this was the presumed primary basis for the PEL. The quote from the Initial Statement of Reasons (http://www.dir.ca.gov/oshsb/airbornecontaminants2005ISOR.pdf) is as follows: “The proposed limit is necessary to control harmful upper respiratory effects, and the possibility of nasal cancer that has been observed in several species of laboratory animals. This proposed limit for propylene oxide was adopted by the ACGIH in 2001. The ACGIH limit was set based on non-cancer effects observed in laboratory animals. The Advisory Committee considered these effects and relied on a 1994 risk assessment by the United States Environmental Protection Agency (USEPA). This assessment estimated a carcinogenic risk of 1/10,000 at 0.93 mg/m^3 for 24 hour-7 day exposure. The Committee estimated that this was equivalent to a 1/1,000 risk for an occupational exposure at 0.7 ppm propylene oxide. At the March 30, 2004, advisory meeting, additional scientific and feasibility data was provided that supported the ACGIH TLV level of 2 ppm instead of the Committee’s recommended level. The proposed change is necessary to prevent harmful respiratory effects noted above and is supported by the ACGIH document for propylene oxide.”
### Table 4 Abbreviations

ACGIH carcinogen classifications (ACGIH, 2006):

- **A1**: “Confirmed human carcinogen” based on the weight of evidence from epidemiologic studies.
- **A2**: “Suspected human carcinogen” used primarily when there is limited evidence of carcinogenicity in humans and sufficient evidence of carcinogenicity in experimental animals with relevance to humans.
- **A3**: “Confirmed animal carcinogen with unknown relevance to humans,” which is typically used for agents that are carcinogenic in experimental animals “at a relatively high dose, by route(s) of administration, at site(s), of histologic types(s), or by mechanism(s) that may not be relevant to worker exposure.”
- **A4**: “Not classifiable as a human carcinogen” which is typically used for agents which “cause concern that they could be carcinogenic for humans but which cannot be assessed conclusively because of a lack of data. *In vitro* or animal studies do not provide indications of carcinogenicity which are sufficient to classify the agent into one of the other categories.”
- **A5**: “Not suspected as a human carcinogen” based on properly conducted epidemiologic studies in humans, or based on evidence suggesting a lack of carcinogenicity in experimental animals that is supported by mechanistic data.

- **Ca**: NIOSH designation for “potential occupational carcinogen.”
- **CNS**: Central nervous system
- **GI**: Gastrointestinal
- **LRT**: Lower respiratory tract
- **PAH**: Polycyclic aromatic hydrocarbon
- **PNS**: Peripheral nervous system
- **URT**: Upper respiratory tract
- **QRA**: Quantitative risk assessment
- **STEL**: Short-term exposure limit
Discussion of Table 4

Certain substances are regulated in California as occupational carcinogens and specific standards (developed by OSHA and adopted under Cal/OSHA) to protect workers potentially exposed to the substances are applied. (See Division of Occupational Safety and Health [DOSH, 2005] and Title 8, California Code of Regulations, Article 110). The 62 agents shown in Table 4 are listed as known to the state to cause cancer under Proposition 65, but are not regulated as occupational carcinogens under Cal/OSHA. In developing the Cal/OSHA PELs for these 62 agents,\(^4\) carcinogenic effects of a chemical were acknowledged in some cases, but a formal assessment of cancer risk was not conducted for any of these agents. Table 4 was developed to help determine which of these 62 agents have Cal/OSHA PELs that did not consider cancer as a health endpoint and therefore may be of higher priority for HESIS to re-evaluate.

Table 4 provides the Cal/OSHA PEL and information on the basis for the PEL, if that information was available online (sources provided in introduction to Table 4 above and in the screening methods). It also summarizes available information on ACGIH TLVs, OSHA PELs (both current and those developed during the 1989 update project) and NIOSH RELs for the 62 agents. The ACGIH documentation on TLVs is particularly helpful in determining the probable basis for many of the Cal/OSHA PELs, because the ACGIH TLVs have typically been the starting point for the development of the PELs (Cohen et al., 2006). ACGIH TLVs have also been the primary starting point for the development of the current OSHA PELs and the OSHA (1989) PELs. Because Cal/OSHA PELs have been updated more frequently than OSHA PELs, the exposure limits in California tend in general to be lower (i.e., more health conservative) than those at the federal level. NIOSH RELs have not generally been used as the basis for PELs developed by Cal/OSHA or OSHA; these values are listed in Table 4 for comparison purposes.

The following analysis of the information in Table 4 is a qualitative exercise. Table 6 below summarizes quantitative estimates of cancer risks associated with selected Cal/OSHA PELs listed in Table 4.

Cal/OSHA PELs with basis available online

The specific basis for the current Cal/OSHA PEL was available from the Occupational Safety and Health Standards Board website for 15 of the 62 chemicals/agents listed in Table 4. Cancer

\(^4\) The following substances are listed by DOSH (2005) as having carcinogen standards: 2-acetilaminofluorene, acrylonitrile, 4-aminodiphenyl, arsenic (inorganic), asbestos, benzene, benzidine and its salts, bis-chloromethyl ether, 1,3-butadiene, cadmium, coke oven emissions, 1,2-dibromo-3-chloropropane (DBCP), 3,3'-dichlorobenzidine and its salts, 4-dimethylaminoazobenzene, ethylene dibromide, ethylene oxide, ethyleneimine, formaldehyde, methyl chloromethyl ether (chloromethyl methyl ether), 4,4'-methylenedis bis (2-chloroaniline), methylene chloride (dichloromethane), methylenedianiline, alpha-naphthylamine, beta-naphthylamine, 4-nitrobenzene, N-nitrosodimethylamine, beta-propiolactone, vinyl chloride. OSHA recently completed a quantitative risk assessment for hexavalent chromium based on its carcinogenic effects, so hexavalent chromium compounds will also be regulated as occupational carcinogens in California.

\(^5\) For these 62 agents, Table 4 summarizes 64 Cal/OSHA PELs. Crystalline silica has two PELs; one for the quartz form and one for the cristobalite and tridymite forms. There are also two PELs for nickel compounds, one for the soluble and one for the insoluble forms.
was noted as the PEL basis, or as part of the PEL basis, for five agents: chloroethane, 1,1-dimethylhydrazine, epichlorohydrin, hydrazine and methylhydrazine. Noncancer effects were specified as the Cal/OSHA PEL basis for ten agents: acetaldehyde, beryllium and beryllium compounds, cobalt and cobalt compounds, p-dichlorobenzene, 1,4-dichloro-2-butene, hexachlorobenzene, lead (basis identified from vertical standard), nitromethane, phenyl glycidyl ether and propylene oxide. For hexachlorobenzene, the basis given was hepatic and neurological effects, but the occurrence of hepatic tumors in animals was also mentioned in the discussion of the PEL. For propylene oxide, the PEL basis was harmful respiratory effects, but carcinogenic effects were also described.

Agents identified as carcinogens by a Cal/OSHA Advisory Committee

A Cal/OSHA Advisory Committee acknowledged that 12 of the agents listed in Table 4 had been identified by the International Agency for Research on Cancer (IARC) as carcinogens, but stated that the PELs for these agents were based primarily on other toxicity endpoints: acetaldehyde, carbon tetrachloride, cobalt (elemental and inorganic compounds, as Co), p-dichlorobenzene, 1,1-dimethylhydrazine, glasswool fibers, hexachlorobenzene, hydrazine, phenyl glycidyl ether, tetrachloroethylene, trichloroethylene, and 4-vinylcyclohexene (see Table 4, footnote b). The Committee did not perform quantitative cancer risk assessments to derive PELs for these agents, citing a lack of risk assessment guidance and resource limitations as the reasons (see http://www.dir.ca.gov/oshsb/aircontaminant2.html).

Discussion of Cal/OSHA PELs that are identical to current ACGIH TLVs

About 70% of the Cal/OSHA PELs listed in Table 4 are the same as the current ACGIH TLVs. ACGIH has assigned carcinogen classifications for 56 of the 62 agents listed in Table 4, with the majority of those (39) having A3 classifications (confirmed animal carcinogens with unknown relevance to humans) currently. However, ACGIH (2006; 2007) mentioned cancer in the basis for only nine of the current TLVs listed in Table 4.

Although the Cal/OSHA PELs in Table 4 are in most cases identical to the TLVs, this does not mean that the basis for the Cal/OSHA PEL is necessarily the same as the TLV. For example, the Cal/OSHA PEL for acrylamide is 0.03 mg/m³, which is the same as the TLV. The TLV basis is central nervous system (CNS) impairment. However, the value of 0.03 mg/m³ was also derived for acrylamide by OSHA (1989) using a quantitative cancer risk assessment. Thus, the Cal/OSHA PEL may have been derived from the OSHA (1989) PEL which did explicitly account for the carcinogenic effects of acrylamide. Similarly, the Cal/OSHA PEL for tetrachloroethylene is the same as the ACGIH TLV, which is based on CNS effects. However, the Cal/OSHA PEL is also the same as the OSHA (1989) PEL, which was selected based on a quantitative cancer risk assessment with pharmacokinetic adjustments. A summary of the

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6 ACGIH has proposed A3 classifications for two additional agents (toluene diisocyanate, currently A4 [not classifiable as a human carcinogen]; and vanadium pentoxide; currently A4). Five agents currently have A2 classifications (suspected human carcinogen). Two agents (nickel, [insoluble compounds]; beryllium) are classified as A1 (confirmed human carcinogen). Ten agents (including nickel [soluble compounds]) are currently classified as A4. One agent (nickel metal) is classified as A5 (not suspected as a human carcinogen).
possible health basis for the Cal/OSHA PELs from Cal/OSHA documentation (where available) or by inference through comparison to the ACGIH TLVs and OSHA (1989) PELs is provided in a later table (Table 19).

**Discussion of Cal/OSHA PELs that are different from current ACGIH TLVs**

Sixteen agents in Table 4 have Cal/OSHA PELs that differ from the ACGIH TLVs. The Cal/OSHA PELs are higher than the ACGIH TLVs for eight agents (1,2-dichloropropane, 1,4-dioxane, nickel compounds [insoluble], phenylhydrazine, pyridine, silica, sulfuric acid and trichloroethylene). ACGIH has updated the TLVs for all eight of these agents, mostly within the last ten years (ACGIH, 2006). Prior to the updates, the ACGIH TLVs were identical to the current Cal/OSHA PELs for seven of these eight agents (see ACGIH [2006] for the TLV history for the other seven agents), with trichloroethylene being the exception. For these seven agents, it is therefore likely a review of the updated TLVs has not yet been completed under Cal/OSHA, and that the current Cal/OSHA PELs for these seven agents are based on earlier TLVs. ACGIH cited lung cancer as the basis for two of the updated TLVs (insoluble nickel compounds and silica) for which Cal/OSHA has not yet completed a review.

The origin of the Cal/OSHA PEL for trichloroethylene is not clear. Trichloroethylene was one of the agents that was acknowledged as being a carcinogen by the Cal/OSHA Advisory Committee but was not quantitatively assessed by the Committee. At the time of making that statement, the Advisory Committee was only considering lowering the short-term exposure limit for trichloroethylene, however, so no information on the specific basis for the 8-hour PEL was given. The Cal/OSHA PEL of 25 ppm is identical to the NIOSH REL, which is based on potential for cancer, central nervous system effects and liver tumors in animals (NIOSH, 1992).

Eight substances have Cal/OSHA PELs that are lower than the current ACGIH TLVs: beryllium and beryllium compounds, carbon tetrachloride, chloroform, epichlorohydrin, ethylene dichloride, nickel carbonyl, nickel (metallic), and nitromethane. These eight substances are discussed below.

Beryllium and beryllium compounds: The current Cal/OSHA PEL of 0.0002 mg/m³ is ten times lower than the current ACGIH TLV (0.002 mg/m³). ACGIH documentation was referenced in the selection of the Cal/OSHA PEL, which is based on sensitization and chronic beryllium disease ([http://www.dir.ca.gov/oshsb/airbornecontaminants2005ISOR.pdf](http://www.dir.ca.gov/oshsb/airbornecontaminants2005ISOR.pdf)). The Cal/OSHA PEL of 0.0002 mg/m³ was derived from an earlier proposal for an updated TLV by ACGIH (see history of TLVs in the documentation for beryllium, in ACGIH [2006]). However, ACGIH had already proposed a lower TLV (0.00002 mg/m³) than the value of 0.0002 mg/m³ being considered for the Cal/OSHA PEL. Because the information was received too late in the process to be reviewed, it was noted that the updated TLV would be considered at a later date. Currently, ACGIH (2007) is proposing an even lower TLV for beryllium and compounds of 0.00005 mg/m³, based on sensitization and chronic beryllium disease.

Carbon tetrachloride: The Cal/OSHA PEL of 2 ppm is the same as the OSHA (1989) PEL, derived as part of the PEL update project. OSHA conducted a quantitative cancer risk
assessment for carbon tetrachloride, deriving a PEL of 2 ppm, which was estimated to be associated with 3.7 (maximum likelihood estimate [MLE]) to 5.2 (upper confidence bound [UCB]) excess cases of cancer per 1,000 workers. Carbon tetrachloride is one of the agents that was acknowledged as being a carcinogen by the Cal/OSHA Advisory Committee but that was not quantitatively assessed by the Committee. At the time of making that statement, however, the Advisory Committee was only considering the short-term exposure limit (STEL) for carbon tetrachloride. It appears that the carbon tetrachloride Cal/OSHA PEL for an 8-hour exposure may be based on a quantitative cancer risk assessment conducted by OSHA.

Chloroform: The Cal/OSHA PEL of 2 ppm is the same as the OSHA (1989) PEL, derived as part of the PEL update project. OSHA (1989) conducted a quantitative cancer risk assessment for chloroform, estimating that the PEL of 2 ppm would be associated with 0.27 (MLE) to 1.80 (UCB) excess cases of cancer per 1,000 workers. It appears that Cal/OSHA may have adopted the OSHA (1989) PEL for chloroform.

Epichlorohydrin: Epichlorohydrin was reviewed by a Cal/OSHA Advisory Committee. The Committee recommended that the epichlorohydrin PEL be lowered to 0.05 ppm to provide protection for reproductive and respiratory effects, and the possibility of carcinogenic effects (http://www.dir.ca.gov/oshsb/airbornecontaminants20051SOR.pdf). The Committee noted that their recommendation differed from the ACGIH TLV, stating that the TLV did not provide an adequate margin of safety for reproductive effects.

Ethylene dichloride: The Cal/OSHA PEL of 1 ppm is the same as the OSHA (1989) PEL, derived as part of the PEL update project. OSHA (1989) concluded that the PEL of 1 ppm was necessary to “protect workers against the significant risks of liver damage, gastrointestinal toxicity, and cancer.” A quantitative assessment of cancer risk was not conducted by OSHA for ethylene dichloride, however.

Nickel carbonyl: The Cal/OSHA PEL is 0.001 ppm for nickel carbonyl, while the current ACGIH TLV is 0.05 ppm. The Cal/OSHA PEL is the same as the OSHA (1989) PEL, and the NIOSH REL, both of which are based on lung and nasal cancer. The PEL of 0.001 ppm also matches the previous ACGIH TLV, which was in effect for nickel carbonyl from 1954-1976.

Nickel (metallic): The current Cal/OSHA PEL for nickel (metallic) is 1 mg/m³, while the current ACGIH TLV is 1.5 mg/m³. The current OSHA PEL is also 1 mg/m³; metallic nickel was not addressed as part of the 1989 update project. The ACGIH (2006) documentation for nickel shows that the TLV for metallic nickel was 1 mg/m³, the same as the current Cal/OSHA PEL, through 1997. In 1998, ACGIH raised the PEL for elemental and metal nickel to 1.5 mg/m³, to protect for dermatitis and pneumoconiosis. ACGIH also established a carcinogen classification for metallic nickel of A5, not suspected as a human carcinogen. Thus, it appears that the Cal/OSHA PEL for metallic nickel was derived from the earlier ACGIH TLV. Nickel and nickel compounds have been discussed in recent Cal/OSHA meetings and the PELs for these substances will likely be updated.
Nitromethane: The Cal/OSHA PEL for nitromethane is 2 ppm, while the current ACGIH TLV is 20 ppm. The current OSHA PEL is 100 ppm; nitromethane was not addressed as part of the 1989 update project. Consulting the Initial Statement of Reasons (http://www.dir.ca.gov/oshsb/aircontaminant2.html) for the nitromethane PEL indicates that ACGIH was cited as the source for the 2 ppm PEL: “The PEL for nitromethane is proposed to be lowered from 100 ppm to 2 ppm (5 mg/m³) on the basis of observed renal toxicity in rats at 300 ppm. This limit was adopted by the ACGIH in 1996, and is consistent with the recommendation of the Committee. The proposed limit is supported by the ACGIH document for nitromethane.” Based on the ACGIH documentation for nitromethane, however, there is no indication that ACGIH ever adopted a PEL of 2 ppm. The TLV for nitromethane was 100 ppm from 1947 to 1993 and 20 ppm from 1994 to present. The current TLV of 20 ppm is based on thyroid effects, upper respiratory tract irritation, and lung damage. It is unclear how a PEL of 2 ppm was selected for nitromethane.

Thus, of the eight Cal/OSHA PELs that are lower than the current ACGIH TLVS, four of them appear to have been based on work by ACGIH (although for nitromethane the ACGIH source material cited could not be identified), three may have been based on the OSHA (1989) PEL, and one (epichlorohydrin) was derived based on original work by the Cal/OSHA Advisory Committee.

**Summary of Cal/OSHA PELs in Table 4**

Approximately 90% of the Cal/OSHA PELs in Table 4 likely can be traced to ACGIH. This result is consistent with the process used to update Cal/OSHA PELs, as noted above.

Based on the qualitative analysis described here, cancer may have been considered in deriving as many as 19 of the Cal/OSHA PELs listed in Table 4. For the remaining 45 PELs in Table 4, either cancer does not appear to have been considered as an endpoint, or information is not available. Determining whether or not cancer is the likely basis for the Cal/OSHA PELs does not resolve the issue of how protective the Cal/OSHA PELs actually are, however. The levels of protection provided by Cal/OSHA PELs for selected workplace chemicals from Table 4, as determined by a quantitative estimation of cancer risk, are provided in Table 6.

**Comments on exposure information for Table 4 workplace chemicals**

The basis for the Cal/OSHA PEL is an important consideration in identifying priorities for further work, but the potential for exposure is also a key factor. Table A-2 (Appendix A) provides available information on the chemical identity, use, production/import volume and other exposure information for the substances listed in Table 4. More than two thirds of the agents listed in Table 4 are used as chemical intermediates, which are likely contained in closed systems with limited worker exposure and may therefore be of lower priority. However, over half of these chemical intermediates also have other industrial uses for which worker exposure may be substantial. About one quarter of the 62 Proposition 65 listed carcinogens in Table 4 are used as solvents, which pose more of a concern for worker exposure. About half of the
carcinogens in Table 4 have a skin designation, indicating that the dermal route of exposure may be significant. This increases concern for worker exposure to these compounds.
Workplace chemicals listed as known to cause reproductive and/or developmental toxicity under Proposition 65 that are regulated under Cal/OSHA on a different or unclear basis

Table 5 summarizes the workplace chemicals listed as causing reproductive and/or developmental toxicity under Proposition 65 that are regulated under Cal/OSHA on a different or unclear basis. Table 5 includes the identity of the chemical, the Cal/OSHA PEL and basis, where available, the ACGIH TLV and basis, the OSHA PEL, the NIOSH REL and the REL basis (or other relevant NIOSH documentation on the substance).
Table 5. Workplace chemicals listed as known to cause reproductive and/or developmental toxicity under Proposition 65 that are regulated under Cal/OSHA on a different or unclear basis

<table>
<thead>
<tr>
<th>Chemical/Agent</th>
<th>Year Listed/Toxicity</th>
<th>Cal/OSHA PEL</th>
<th>PEL Basis</th>
<th>ACGIH TLV</th>
<th>TLV Basis</th>
<th>OSHA PEL Current</th>
<th>OSHA (1989) PEL</th>
<th>OSHA (1989) PEL Basis</th>
<th>NIOSH REL/Health Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Arsenic (inorganic oxides)</td>
<td>1997 d</td>
<td>0.01 mg/m³</td>
<td>Cancer</td>
<td>0.01 mg/m³</td>
<td>Lung cancer</td>
<td>0.01 mg/m³</td>
<td>--</td>
<td>--</td>
<td>0.002 mg/m³ Lung &amp; lymphatic cancer, dermatitis</td>
</tr>
<tr>
<td>2 Benzene</td>
<td>1997 d, m</td>
<td>1 ppm Skin</td>
<td>Cancer</td>
<td>0.5 ppm Skin</td>
<td>Leukemia</td>
<td>1 ppm</td>
<td>--</td>
<td>--</td>
<td>0.1 ppm Cancer (leukemia)</td>
</tr>
<tr>
<td>3 1,3-Butadiene</td>
<td>2004 d, f, m</td>
<td>1 ppm</td>
<td>Cancer</td>
<td>2 ppm</td>
<td>Cancer</td>
<td>1 ppm</td>
<td>--</td>
<td>--</td>
<td>Ca Hematopoietic cancer, teratogenicity &amp; reproductive effects</td>
</tr>
<tr>
<td>4 Cadmium</td>
<td>1997 d, m</td>
<td>0.005 mg/m³</td>
<td>Cancer; lung and kidney disease</td>
<td>0.01 mg/m³</td>
<td>0.002 mg/m³ (respirable)</td>
<td>Kidney damage</td>
<td>0.005 mg/m³</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>5 Carbon disulfide</td>
<td>1989 d, f, m</td>
<td>4 ppm Skin</td>
<td>--</td>
<td>1 ppm Skin</td>
<td>PNS impairment</td>
<td>20 ppm</td>
<td>4 ppm</td>
<td>Cardiovascular disease, reproductive effects; neurological effects</td>
<td>1 ppm Skin Cardiovascular CNS, &amp; reproductive effects</td>
</tr>
<tr>
<td>6 Carbon monoxide</td>
<td>1989 d</td>
<td>25 ppm</td>
<td>--</td>
<td>25 ppm</td>
<td>Carboxy-hemoglobinemia</td>
<td>50 ppm</td>
<td>35 ppm</td>
<td>Carboxyhemoglobinemia (protect workers with cardiovascular/pulmonary impairment)</td>
<td>35 ppm Cardiovascular effects</td>
</tr>
<tr>
<td>7 Di-n-butyl phthalate (DBP)</td>
<td>2005 d, f, m</td>
<td>5 mg/m³</td>
<td>--</td>
<td>5 mg/m³</td>
<td>Testicular damage, eye &amp; URT irritation</td>
<td>5 mg/m³</td>
<td>--</td>
<td>--</td>
<td>5 mg/m³ Eye &amp; respiratory irritant</td>
</tr>
<tr>
<td>Chemical/Agent</td>
<td>Year Listed/Toxicitya</td>
<td>Cal/OSHA PEL</td>
<td>PEL Basis</td>
<td>ACGIH TLV</td>
<td>TLV Basis</td>
<td>OSHA PEL Current</td>
<td>OSHA (1989) PEL</td>
<td>OSHA (1989) PEL Basis</td>
<td>NIOSH REL/Health Effects</td>
</tr>
<tr>
<td>----------------</td>
<td>-----------------------</td>
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<td>-----------</td>
<td>-----------</td>
<td>-----------</td>
<td>------------------</td>
<td>----------------</td>
<td>------------------------</td>
<td>--------------------------</td>
</tr>
<tr>
<td>8 Di(2-ethylhexyl) phthalate (DEHP)</td>
<td>2003 d, m</td>
<td>5 mg/m³</td>
<td>--</td>
<td>5 mg/m³</td>
<td>LRT irritation</td>
<td>5 mg/m³</td>
<td>5 mg/m³</td>
<td>--</td>
<td>Neuropathic; hepatic; other systemic toxicity</td>
</tr>
<tr>
<td>9 Dinitrobenzene (m-, o-, p-) (See footnote b)</td>
<td>1990 m</td>
<td>0.15 ppm Skin</td>
<td>--</td>
<td>0.15 ppm Skin</td>
<td>Methemoglobinemia; eye damage</td>
<td>0.15 ppm Skin</td>
<td>--</td>
<td>--</td>
<td>Skin Anoxia, liver damage</td>
</tr>
<tr>
<td>10 2,4-Dinitrotoluene; 2,6-Dinitrotoluene; Dinitrotoluene (technical grade) (See footnote c)</td>
<td>1999; m 1999; m 1999; f,m</td>
<td>0.15 mg/m³ Skin</td>
<td>--</td>
<td>0.2 mg/m³ Skin</td>
<td>Cardiac impairment; reproductive effects</td>
<td>1.5 mg/m³ Skin</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>11 Hexachlorobenzene</td>
<td>1989 d</td>
<td>0.002 mg/m³ Skin</td>
<td>Hepatic and neurological effects; hepatic tumors in animals noted.</td>
<td>0.002 mg/m³ Skin</td>
<td>Porphyrin effects; skin damage; CNS impairment</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>Ca Anoxia, liver damage</td>
</tr>
<tr>
<td>12 Methyl chloride</td>
<td>2000 d</td>
<td>105 mg/m³ (See footnote d)</td>
<td>--</td>
<td>50 ppm Skin</td>
<td>CNS impairment; liver and kidney; testicular damage; teratogenic effects</td>
<td>100 ppm</td>
<td>50 ppm</td>
<td>Neurotoxicity</td>
<td>Ca Potential for cancer; possible teratogenic effects; tumors of the kidney, forestomach and lung in animals</td>
</tr>
<tr>
<td>13 Nickel carbonyl</td>
<td>1996 d</td>
<td>0.001 ppm</td>
<td>--</td>
<td>0.05 ppm</td>
<td>Lung &amp; nasal cancer</td>
<td>0.001 ppm</td>
<td>0.001 ppm</td>
<td>Lung and nasal cancer</td>
<td>0.001 ppm Ca Lung and nasal cancer</td>
</tr>
<tr>
<td>14 Toluene</td>
<td>1991 d</td>
<td>50 ppm Skin</td>
<td>--</td>
<td>20 ppm Skin (See footnote e)</td>
<td>Visual impairment; female reproductive system damage; pregnancy loss</td>
<td>200 ppm</td>
<td>100 ppm</td>
<td>Hepatotoxicity, behavioral and nervous system effects</td>
<td>100 ppm CNS depression</td>
</tr>
</tbody>
</table>

a. Type of reproductive toxicity for which the chemical is listed under Proposition 65: d = developmental, m = male reproductive, f = female reproductive.
b. The isomers of dinitrobenzene were listed individually in 1990, all for male reproductive toxicity, but are treated as one entry here. Evidence of current use was found for one of the three isomers (o-dinitrobenzene).

c. 2,4-Dinitrotoluene, 2,6-dinitrotoluene and dinitrotoluene, technical grade are listed individually under Proposition 65, but are treated as one entry here. A Cal/OSHA PEL has been established for 2,4-dinitrotoluene, while the ACGIH TLV, OSHA PEL and NIOSH REL are for dinitrotoluene (mixed isomers). Evidence of current use was identified for 2,4-dinitrotoluene and mixed isomers.

d. The Cal/OSHA PEL for methyl chloride is listed as 105 mg/m³ and 5 ppm, which is a typographical error (Bob Barish, pers. comm., 2007). The PEL in terms of ppm should be 50.

e. ACGIH (2007) just adopted the revised TLV of 20 ppm for toluene. The Cal/OSHA PEL of 50 ppm is the same as the previous ACGIH TLV, which was based on URT and eye irritation, and CNS impairment.
Discussion of Table 5

Information regarding the basis of the Cal/OSHA PELs was available for five of the 14 agents in Table 5: arsenic, benzene, 1,3-butadiene, cadmium, and hexachlorobenzene. The basis of the PEL was cancer for four of these five substances and hepatic and neurological effects for one (hexachlorobenzene). None of these five PELs specifically address reproductive or developmental toxicity.

Arsenic, benzene, 1,3-butadiene and cadmium are regulated under Cal/OSHA to protect against cancer. These chemicals have comprehensive standards which include specific requirements for training, health hazard warnings, medical surveillance, etc., in addition to PELs. While the low exposure limits for these chemicals may also protect for reproductive and/or developmental toxicity, the chemicals are not identified as reproductive or developmental toxicants, and the standards do not specifically address these health endpoints.

The Cal/OSHA PEL for hexachlorobenzene is intended to address hepatic and neurological effects; the observation of hepatic tumors in animals was also mentioned in the discussion of the PEL basis (http://www.dir.ca.gov/oshsb/airbornecontaminants2005ISOR.pdf). The Cal/OSHA Advisory Committee noted that hexachlorobenzene has been identified as a carcinogen by IARC, but that no cancer risk assessment was conducted. The PEL is the same as the TLV for hexachlorobenzene. The ACGIH documentation for the TLV was cited in describing the basis for the hexachlorobenzene PEL. The TLV is intended to "minimize the potential for increased formation and excretion of porphyrins (porphyrogenicity) leading to dermal lesions and ulcerations, neurotoxicity, and possible liver cancer reported only in animals" (from ACGIH documentation, provided in ACGIH [2006]). The ACGIH documentation for hexachlorobenzene (HCB) also states that, "A large database existed on reproductive/developmental toxicity of HCB, including a four-generation study with no indication for reproductive toxicity or teratogenicity." In contrast, the Scientific Advisory Panel under Proposition 65 listed hexachlorobenzene as known to the state to cause reproductive toxicity, based on developmental effects, in 1989. A risk assessment for the developmental effects of hexachlorobenzene is not available, so it is not clear whether the PEL would be protective for that effect.

For the other nine agents listed in Table 5 the basis for the Cal/OSHA PEL was not available, but can be inferred by comparison to the TLV and/or the OSHA (1989) PEL. Based on this comparison, five of these nine agents have PELs that may have been intended to protect for reproductive and/or developmental toxicity: carbon disulfide, carbon monoxide, di-n-butyl phthalate, 2,4-dinitrotoluene and methyl chloride. These five agents are discussed in more detail below.

The Cal/OSHA PEL for carbon disulfide is the same as the OSHA (1989) PEL. Thus, the Cal/OSHA PEL is probably intended to protect for the same health endpoints, which include adverse reproductive effects such as fetotoxicity and teratogenicity.

The Cal/OSHA PEL for carbon monoxide, which is the same as the TLV, may be intended to protect against developmental toxicity. While the TLV was specifically
intended to address carboxyhemoglobinemia, the ACGIH documentation further notes that, “The recommended TLV should also provide a margin of safety for individuals particularly susceptible to the adverse effects of carbon monoxide exposure, including pregnant workers (i.e., the fetus) and those with chronic heart and respiratory diseases.”

The Cal/OSHA PEL for di-\textit{n}-butyl phthalate (5 mg/m$^3$), which is the same as the TLV, may be intended to address reproductive toxicity. The TLV is based on ocular and respiratory tract irritation, and reproductive effects, including testicular damage. ACGIH (2006) stated that the reproductive system appears to be the primary target for di-\textit{n}-butyl phthalate, but concluded that the data were insufficient to establish a no-effect level. The extent to which the PEL protects against the male and female reproductive toxicity and developmental toxicity of di-\textit{n}-butyl phthalate identified under Proposition 65 is unclear.

The Cal/OSHA PEL for 2,4-dinitrotoluene is 0.15 mg/m$^3$, which is nearly the same as the TLV of 0.2 mg/m$^3$ for mixed isomers of dinitrotoluene. The TLV is based on cardiac impairment and reproductive effects.

The Cal/OSHA PEL for methyl chloride is listed as 5 ppm and also as 105 mg/m$^3$, which corresponds to 50 ppm. The entry of “5 ppm” was identified as a typographical error, confirmed by Barish (pers. comm., 2007). The actual Cal/OSHA PEL should be 50 ppm. Both ACGIH and OSHA (1989) have exposure limits for methyl chloride of 50 ppm. It is probable that the Cal/OSHA PEL for methyl chloride is derived from the ACGIH TLV of 50 ppm, which is based on CNS impairment, liver and kidney damage, testicular damage and teratogenic effects.

The PELs and TLVs for di(2-ethylhexyl)phthalate (DEHP) and dinitrobenzene are the same, so the PEL basis for those chemicals is most likely the same as the TLV basis. These TLVs did not include reproductive and/or development toxicity as part of the basis, as detailed below.

The Cal/OSHA PEL for DEHP is the same as the TLV, so the PEL may be intended to protect for lower respiratory tract irritation. Although the reproductive and developmental toxicity of DEHP was discussed in the documentation for the TLV, ACGIH concluded that “In summary, there are no data that implicate DEHP as a reproductive or developmental toxin by either dermal contact or inhalation routes of exposure; data for animals showing that such changes have occurred are identified only with massive oral or parenteral doses.” However, DEHP is listed as known to cause both male reproductive toxicity and developmental toxicity under Proposition 65. Additionally, although the reproductive and developmental risks of DEHP by the inhalation and dermal routes have not yet been assessed, exposure to DEHP via the inhalation route is known to produce an internal dose. The Cal/OSHA PEL for DEHP is also identical to the OSHA (1989) PEL, which was based on protecting for neuropathic, hepatic and other systemic toxicity. Regarding the potential reproductive and developmental toxicity of DEHP, OSHA (1989) stated only that intraperitoneal doses of DEHP produced “slight effects on embryonic and fetal development” in animals. As
noted, this is not an accurate characterization of the evidence for the reproductive and developmental toxicity of DEHP.

The Cal/OSHA PEL for dinitrobenzene, which is the same as the TLV, may be intended to address methemoglobinemia and eye damage. Based on the ACGIH documentation, there is no indication that male reproductive toxicity, the endpoint of concern under Proposition 65, was considered in establishing the TLVs.

ACGIH (2007) just adopted a new TLV for toluene of 20 ppm, based on visual impairment, female reproductive damage, and pregnancy loss. The current Cal/OSHA PEL is identical to the previous TLV of 50 ppm, which was based on upper respiratory tract and eye irritation and central nervous system impairment.

The Cal/OSHA PEL of 0.001 ppm for nickel carbonyl is the same as the OSHA (1989) PEL, and the NIOSH REL, both of which are based on lung and nasal cancer. The PEL of 0.001 ppm also matches the previous ACGIH TLV, which was in effect for nickel carbonyl from 1954-1976. Since the Cal/OSHA PEL for nickel carbonyl is likely based on protecting for cancer, it may be sufficiently low to also protect for the compound’s developmental effects, but this should be evaluated quantitatively.

In summary, reproductive and/or developmental toxicity was likely at least part of the basis for setting the Cal/OSHA PELs for five of the 14 agents listed in Table 5: carbon disulfide, carbon monoxide, di-n-butyl phthalate, 2,4-dinitrotoluene and methyl chloride. These PELs may not address all possible reproductive endpoints (male, female and developmental), however. For example, di-n-butyl phthalate is listed as a developmental, male reproductive and female reproductive toxicant under Proposition 65, while ACGIH (2006) cites only “testicular damage and URT irritation” as the basis for the TLV, the likely source of the Cal/OSHA PEL.

A quantitative assessment of the potential for reproductive and/or developmental toxicity associated with worker exposure at the PEL has not been carried out, so the level of protection provided by the current Cal/OSHA PEL is not clear for any of the agents listed in Table 5. For the agents with PELs that are based at least in part on reproductive and/or developmental effects, these exposure limits may not be sufficiently protective because the levels were set qualitatively. However, it is also true that even if reproductive harm was not considered in setting a PEL, the limit may still be sufficiently protective, depending on the relative sensitivity of the health endpoint that was the basis for the PEL compared to reproductive and/or developmental toxicity. For example, chemicals that are regulated as occupational carcinogens may have standards that would protect workers from reproductive harm. Additional work is recommended to quantitatively evaluate the adequacy of the current PELs for workplace chemicals listed as known to cause reproductive and/or developmental toxicity under Proposition 65.

Table A-3 (Appendix A) provides use, exposure and production/import volume information for the chemicals listed in Table 5. More than half of these chemicals are used as chemical intermediates, for which worker exposure is less likely, but most of them (~75%) have other uses as well. Three of the chemicals are used as solvents, which are of greater concern for exposure.
Six of the 14 chemicals have skin notations, indicating the potential for exposure via the dermal route.
Results for Cancer Risk Estimation at PEL: Chemicals Not Regulated as Occupational Carcinogens

Table 6 shows the estimated cancer risks for workplace chemicals listed as known to cause cancer under Proposition 65 that are not regulated in California as occupational carcinogens. The calculations assume occupational exposure at the current Cal/OSHA PEL and are based on OEHHA or U.S. EPA unit risk values. The “estimated excess cancer cases per 1,000 workers” is determined by multiplying the excess lifetime cancer risk by 1,000. Table 6 also lists the cancer risks as estimated by OSHA during the 1989 update process using quantitative risk assessment for proposed PELs that match the current Cal/OSHA PELs.
### Table 6. Estimated cancer risk associated with the Cal/OSHA PEL for workplace chemicals listed as causing cancer under Proposition 65 that are not regulated as occupational carcinogens

<table>
<thead>
<tr>
<th>Chemical</th>
<th>Cal/OSHA PEL (mg/m³)</th>
<th>OEHHA Unit Risk Value(s) (mg/m³)</th>
<th>U.S. EPA Unit Risk Value (mg/m³)</th>
<th>Estimated Excess Lifetime Cancer Risk&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Estimated Excess Cancer Cases Per 1,000 Workers&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Estimated Excess Cancer Cases Per 1,000 Workers (OSHA, 1989)&lt;sup&gt;c&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Acetaldehyde</td>
<td>45</td>
<td>2.7 x 10⁻³</td>
<td>2.2 x 10⁻³</td>
<td>1.3-1.6 x 10⁻²</td>
<td>13-16</td>
<td>1 (MLE&lt;sup&gt;d&lt;/sup&gt;); 5 (UCB&lt;sup&gt;e&lt;/sup&gt;)</td>
</tr>
<tr>
<td>2 Acrylamide</td>
<td>0.03; Skin</td>
<td>1.3</td>
<td>1.3</td>
<td>5.1 x 10⁻²</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>3 Aniline</td>
<td>7.6; Skin</td>
<td>1.6 x 10⁻²</td>
<td>--</td>
<td>1.6 x 10⁻²</td>
<td>2</td>
<td>--</td>
</tr>
<tr>
<td>4 o-Anisidine</td>
<td>0.5; Skin</td>
<td>4.0 x 10⁻²</td>
<td>--</td>
<td>2.6 x 10⁻²</td>
<td>3</td>
<td>--</td>
</tr>
<tr>
<td>5 Benzyl chloride</td>
<td>5</td>
<td>4.9 x 10⁻²</td>
<td>--</td>
<td>3.2 x 10⁻²</td>
<td>32</td>
<td>--</td>
</tr>
<tr>
<td>6 Beryllium</td>
<td>0.0002</td>
<td>2.4</td>
<td>2.4</td>
<td>6.3 x 10⁻⁵</td>
<td>0.06</td>
<td>--</td>
</tr>
<tr>
<td>7 Bis (2-chloroethyl) ether (Dichloroethyl ether)</td>
<td>30; Skin</td>
<td>7.1 x 10⁻¹</td>
<td>3.3 x 10⁻¹</td>
<td>7.3-9.4 x 10⁻¹</td>
<td>730-940</td>
<td>--</td>
</tr>
<tr>
<td>8 Carbon tetrachloride</td>
<td>12.6; Skin</td>
<td>4.2 x 10⁻²</td>
<td>1.5 x 10⁻²</td>
<td>2.5-6.9 x 10⁻²</td>
<td>25-69</td>
<td>3.7 (MLE); 5.2 (UCB)</td>
</tr>
<tr>
<td>9 Chloroethane (Ethyl chloride)</td>
<td>264; Skin</td>
<td>1.3 x 10⁻⁵</td>
<td>--</td>
<td>4.5 x 10⁻²</td>
<td>45</td>
<td>--</td>
</tr>
<tr>
<td>10 Chloroform</td>
<td>9.78</td>
<td>5.3 x 10⁻⁵</td>
<td>2.3 x 10⁻⁵</td>
<td>6.8-29 x 10⁻⁵</td>
<td>7-29</td>
<td>0.27 (MLE); 1.80 (UCB)</td>
</tr>
<tr>
<td>11 p-Dichlorobenzene</td>
<td>60</td>
<td>1.1 x 10⁻⁴</td>
<td>--</td>
<td>8.6 x 10⁻²</td>
<td>86</td>
<td>--</td>
</tr>
<tr>
<td>12 1,1-Dichloroethane</td>
<td>400</td>
<td>1.6 x 10⁻⁴</td>
<td>--</td>
<td>8.4 x 10⁻²</td>
<td>84</td>
<td>--</td>
</tr>
<tr>
<td>13 1,2-Dichloropropane (Propylene dichloride)</td>
<td>350</td>
<td>2.1 x 10⁻⁵; 1.0 x 10⁻²</td>
<td>See footnote g</td>
<td>--</td>
<td>3.7-6.2 x 10⁻¹</td>
<td>370-620</td>
</tr>
<tr>
<td>14 Di(2-ethylhexyl)phthalate (Di-sec-octylphthalate)</td>
<td>5</td>
<td>6.3 x 10⁻⁵; See footnote h</td>
<td>--</td>
<td>4.1 x 10⁻¹</td>
<td>0.4</td>
<td>--</td>
</tr>
<tr>
<td>15 2,4-Dinitrotoluene</td>
<td>0.15; Skin</td>
<td>8.9 x 10⁻²</td>
<td>--</td>
<td>1.7 x 10⁻¹</td>
<td>2</td>
<td>--</td>
</tr>
<tr>
<td>16 1,4-Dioxane</td>
<td>0.9; Skin</td>
<td>7.7 x 10⁻⁴</td>
<td>--</td>
<td>9.1 x 10⁻⁴</td>
<td>91</td>
<td>--</td>
</tr>
<tr>
<td>17 Epichlorohydrin</td>
<td>0.19; Skin</td>
<td>2.3 x 10⁻⁴</td>
<td>1.2 x 10⁻⁴</td>
<td>0.30-5.7 x 10⁻⁴</td>
<td>0.03-0.6</td>
<td>--</td>
</tr>
<tr>
<td>18 Ethylene dichloride</td>
<td>4</td>
<td>2.1 x 10⁻⁶; 2.6 x 10⁻⁷</td>
<td>--</td>
<td>1.1-1.4 x 10⁻⁶</td>
<td>11-14</td>
<td>--</td>
</tr>
<tr>
<td>19 Hexachlorobenzene</td>
<td>0.002; Skin</td>
<td>5.1 x 10⁻⁵</td>
<td>4.6 x 10⁻⁵</td>
<td>1.2-1.3 x 10⁻⁵</td>
<td>0.1</td>
<td>--</td>
</tr>
<tr>
<td>20 Hexachloroethane</td>
<td>10; Skin</td>
<td>1.1 x 10⁻⁵</td>
<td>4.0 x 10⁻⁵</td>
<td>0.52-1.4 x 10⁻⁵</td>
<td>5-14</td>
<td>--</td>
</tr>
<tr>
<td>21 Hydrazine</td>
<td>0.013; Skin</td>
<td>4.9</td>
<td>4.9</td>
<td>8.3 x 10⁻⁵</td>
<td>8</td>
<td>--</td>
</tr>
<tr>
<td>22 Lead and lead compounds</td>
<td>0.05</td>
<td>1.2 x 10⁻⁵</td>
<td>--</td>
<td>7.8 x 10⁻⁵</td>
<td>0.08</td>
<td>--</td>
</tr>
<tr>
<td>23 Methyleneimine (Propyleneimine)</td>
<td>5; Skin</td>
<td>7.1</td>
<td>--</td>
<td>9.9 x 10⁻⁴</td>
<td>990</td>
<td>--</td>
</tr>
<tr>
<td>24 Methyldiaziridine</td>
<td>0.019; Skin</td>
<td>2.2</td>
<td>--</td>
<td>5.5 x 10⁻⁴</td>
<td>6</td>
<td>--</td>
</tr>
<tr>
<td>25 Naphthalene</td>
<td>50</td>
<td>3.4 x 10⁻⁵</td>
<td>--</td>
<td>2.2 x 10⁻⁵</td>
<td>220</td>
<td>--</td>
</tr>
<tr>
<td>Chemical</td>
<td>Cal/OSHA PEL (mg/m³)</td>
<td>OEHHA Unit Risk Value(s) (mg/m³)⁻¹</td>
<td>U.S. EPA Unit Risk Value (mg/m³)⁻¹</td>
<td>Estimated Excess Lifetime Cancer Riskᵃ</td>
<td>Estimated Excess Cancer Cases Per 1,000 Workersᵇ</td>
<td>Estimated Excess Cancer Cases Per 1,000 Workers (OSHA, 1989)c</td>
</tr>
<tr>
<td>----------------------------------------------</td>
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<td>-----------------------------------</td>
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<td>----------------------------------------</td>
<td>-----------------------------------------------</td>
<td>-------------------------------------------------</td>
</tr>
<tr>
<td>26 Nickel (metallic)</td>
<td>1</td>
<td>2.6 x 10⁻¹</td>
<td>--</td>
<td>3.4 x 10⁻⁴</td>
<td>34</td>
<td>--</td>
</tr>
<tr>
<td>27 Nickel carbonyl</td>
<td>0.007</td>
<td>2.6 x 10⁻¹</td>
<td>--</td>
<td>2.4 x 10⁻⁴</td>
<td>0.2</td>
<td>--</td>
</tr>
<tr>
<td>28 Nickel compounds (insoluble)</td>
<td>1</td>
<td>2.6 x 10⁻¹</td>
<td>--</td>
<td>3.4 x 10⁻²</td>
<td>34</td>
<td>--</td>
</tr>
<tr>
<td>29 Nickel compounds (soluble)</td>
<td>0.1</td>
<td>2.6 x 10⁻¹</td>
<td>--</td>
<td>3.4 x 10⁻³</td>
<td>3</td>
<td>--</td>
</tr>
<tr>
<td>30 Phenyl glycidyl ether</td>
<td>0.6; Skin</td>
<td>4.0 x 10⁻²</td>
<td>--</td>
<td>3.1 x 10⁻³</td>
<td>3</td>
<td>--</td>
</tr>
<tr>
<td>31 Phenylhydrazine</td>
<td>20; Skin</td>
<td>1.9 x 10⁻¹</td>
<td>--</td>
<td>5.0 x 10⁻¹</td>
<td>500</td>
<td>--</td>
</tr>
<tr>
<td>32 Propylene oxide</td>
<td>4.75</td>
<td>3.7 x 10⁻²</td>
<td>3.7 x 10⁻³</td>
<td>2.3 x 10⁻²</td>
<td>2</td>
<td>--</td>
</tr>
<tr>
<td>33 1,1,2,2-Tetrachloroethane</td>
<td>7; Skin</td>
<td>5.8 x 10⁻²</td>
<td>5.8 x 10⁻²</td>
<td>5.3 x 10⁻²</td>
<td>53</td>
<td>--</td>
</tr>
<tr>
<td>34 Tetrachloroethylene (Perchloroethylene)</td>
<td>170</td>
<td>5.9 x 10⁻²</td>
<td>--</td>
<td>1.3 x 10⁻¹</td>
<td>130</td>
<td>680 mg/m³:</td>
</tr>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td>45 (best estimate);</td>
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<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>650 (UCB)</td>
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<td>340 mg/m³:</td>
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<td></td>
<td></td>
<td>27 (best estimate);</td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>420 (UCB)</td>
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<td></td>
<td>68 mg/m³:</td>
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<td></td>
<td></td>
<td></td>
<td>6.4 (best estimate);</td>
</tr>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>110 (UCB)</td>
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<td></td>
<td></td>
<td></td>
<td>See footnote j</td>
</tr>
<tr>
<td>35 Toluene diisocyanate</td>
<td>0.04</td>
<td>1.1 x 10⁻²</td>
<td>--</td>
<td>5.8 x 10⁻⁵</td>
<td>0.06</td>
<td>--</td>
</tr>
<tr>
<td>36 α-Toluidine</td>
<td>9; Skin</td>
<td>5.1 x 10⁻²</td>
<td>--</td>
<td>6.0 x 10⁻⁴</td>
<td>60</td>
<td>0.055 (MLE);</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.64 (UCB)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>See footnote j</td>
</tr>
<tr>
<td>37 Trichloroethylene</td>
<td>135</td>
<td>2.0 x 10⁻¹</td>
<td>Withdrawn</td>
<td>3.8 x 10⁻²</td>
<td>35</td>
<td>--</td>
</tr>
<tr>
<td>38 Vinyl trichloride (1,1,2-trichloroethane)</td>
<td>45; Skin</td>
<td>1.6 x 10⁻²</td>
<td>1.6 x 10⁻²</td>
<td>9.4 x 10⁻²</td>
<td>94</td>
<td>--</td>
</tr>
</tbody>
</table>

a. Calculated based on both the OEHHA and U.S. EPA unit risk values; results reported as a range where applicable. Calculation assumes exposure 8 hours per day, 5 days per week, 50 weeks per year, 40 years (Equation [1]). Equation (2) was applied in cases where the simple linear approximation does not hold. These values do not account for the increased breathing rate expected for workers.

b. Based on results for estimated excess lifetime cancer risk; range of values reflects ranges in OEHHA and/or U.S. EPA unit risk values.

c. OSHA (1989) published a Final Rule on Air Contaminants with the findings of the PEL update project, including the results of quantitative risk assessments (QRAs) that were conducted for certain substances. This rule was remanded and is not in force. The cancer risk estimates reported in Table 6 are for PELs derived by OSHA (1989) that are numerically the same as the current Cal/OSHA PELs.

d. Double dash indicates that a quantitative risk assessment was not conducted by OSHA for this substance.
e. MLE = maximum likelihood estimate
f. UCB = upper confidence bound
g. OEHHA has published two cancer potency values, one under Proposition 65 (OEHHA, 2004) and one under the Public Health Goal program (OEHHA, 1999b). The two values differ primarily due to a difference in the interspecies extrapolation factor. Under Proposition 65, the factor \( (b_{wh}/b_{wa})^{1/3} \) is used (as mandated by regulation); under the PHG program \( (b_{wh}/b_{wa})^{1/4} \) is used.
h. OEHHA (2005) published a unit risk value of \( 2.4 \times 10^{-3} \) for DEHP, based on a cancer potency value that was derived in 1988 by the California Department of Health Services. An updated cancer potency value was derived by OEHHA (2002), and the unit risk value shown in Table 6 is based on the updated potency.
i. OSHA (1989) lowered the PEL for tetrachloroethylene to 25 ppm (170 mg/m\(^3\)), citing a pharmacokinetic analysis of cancer risks conducted by Hattis (as described by OSHA, 1989). OSHA (1989) reported the estimated excess cancer cases per 1,000 workers derived by Hattis for 100 ppm (680 mg/m\(^3\)), 50 ppm (340 mg/m\(^3\)) and 10 ppm (68 mg/m\(^3\)) perchloroethylene. “Best estimate” was the term used by Hattis to describe the results.
j. OSHA (1989) considered lowering the PEL to 2 ppm, and reported cancer risk estimates associated with that value, as well as the value of 5 ppm that was ultimately retained by OSHA as the PEL. The estimates listed in Table 6 correspond to the proposed PEL of 2 ppm, which is the same as the current Cal/OSHA PEL.
Discussion of Table 6

Table 6 shows the estimated excess cancer cases per 1,000 workers assumed to be exposed over a working lifetime at the Cal/OSHA PEL to 38 Proposition 65 carcinogens, for which OEHHA and/or U.S. EPA unit risk values were available. These substances are regulated under Cal/OSHA, but not as occupational carcinogens.

Based on the calculation using OEHHA or U.S. EPA unit risk values, the estimated excess cancer cases per 1,000 workers exposed at the Cal/OSHA PEL is less than one for seven of the 38 chemicals in Table 6 (beryllium, di(2-ethylhexyl)phthalate, epichlorohydrin, hexachlorobenzene, lead and lead compounds, nickel carbonyl and toluene diisocyanate). One excess cancer case per 1,000 workers is interpreted by OSHA as being a significant risk for occupational carcinogens based on the 1980 Supreme Court Benzene Decision (hereafter referred to as the “Benzene Decision”).

Cancer was considered in setting the Cal/OSHA PEL for two of these seven chemicals, epichlorohydrin and nickel carbonyl (see Table 4).

The upper range of estimated excess cancer cases at the Cal/OSHA PEL based on OEHHA or U.S. EPA unit risk values is between 1 and 10 per 1,000 workers for nine of the chemicals in Table 6, and between 10 and 100 per 1,000 workers for 16. Greater than 100 excess cancers per 1,000 workers are estimated to occur at the PEL for the remaining six chemicals (bis (2-chloroethyl) ether, 1,2-dichloropropane, methylaziridine, naphthalene, phenylhydrazine and tetrachloroethylene). For one of these chemicals with the highest estimated cancer risks, phenylhydrazine, the Cal/OSHA PEL may be intended to account in part for cancer. In proposing a phenylhydrazine PEL of 5 ppm, which is the same as the Cal/OSHA PEL, OSHA (1989) indicated that the limit was intended to account for the possibility of carcinogenic effects. However, this phenylhydrazine PEL is associated with an estimated 500 cancer cases per 1,000 workers. This example illustrates the pitfalls of setting PELs based on a qualitative evaluation of cancer data, instead of a quantitative risk assessment.

\[ \text{OSHA, in a number of publications (see OSHA, 1996, for example) has described the “Benzene Decision” as follows: “In the 1980 ‘Benzene Decision,’ the Supreme Court, in its discussion of the level of risk that Congress authorized OSHA to regulate, indicated its view of the boundaries of acceptable and unacceptable risk. The Court stated: ‘It is the Agency’s responsibility to determine in the first instance what it considers to be a ‘significant’ risk. Some risks are plainly acceptable and others are plainly unacceptable. If for example, the odds are one in a billion that a person will die from cancer by taking a drink of chlorinated water, the risk clearly could not be considered significant. On the other hand, if the odds are one in a thousand that regular inhalation of gasoline vapors that are 2 percent benzene will be fatal, a reasonable person might well consider the risk significant and take the appropriate steps to decrease or eliminate it. (I.U.D. v. A.P.I., 448 U.S. 607, 655).’ So a risk of } (1/1,000)(10^{-3}) \text{ is clearly significant. It represents the uppermost end of the million-fold range suggested by the Court, somewhere below which the boundary of acceptable versus unacceptable risk must fall. The Court further stated that ‘while the Agency must support its findings that a certain level of risk exists with substantial evidence, we recognize that its determination that a particular level of risk is significant will be based largely on policy considerations.’ With regard to the methods used to determine the risk level present (as opposed to the policy choice of whether that level is ‘significant’ or not), the Court added that assessment under the OSH Act is ‘not a mathematical straitjacket,’ and that ‘OSHA is not required to support its findings with anything approaching scientific certainty.’ The Court ruled that ‘a reviewing court [is] to give OSHA some leeway where its findings must be made on the frontiers of scientific knowledge [and that]...the Agency is free to use conservative assumptions in interpreting the data with respect to carcinogens, risking error on the side of overprotection rather than underprotection’ (448 U.S. at 655, 656).”} \]
Five of the six chemicals with estimated cancer risks of more than 1 in 10 are produced or imported at levels greater than 1 million pounds per year. Tetrachloroethylene has been used as a dry cleaning solvent, but this use is being phased out in California; it is also used as a chemical intermediate and vapor degreaser. The other five chemicals with the highest estimated cancer risks are primarily used as chemical intermediates (bis (2-chloroethyl) ether, 1,2-dichloropropane, methyldiaziridine, naphthalene and phenylhydrazine). Chemical intermediates are typically contained in closed systems, suggesting that worker exposures to these substances may be well controlled. Worker exposure could still occur as a result of fugitive emissions and during repair and maintenance operations. Additional uses of the chemicals for purposes other than as intermediates could increase the potential for exposure. The use of bis (2-chloroethyl) ether as a solvent, naphthalene in scintillation counting fluid and phenylhydrazine as a reagent in chemical analyses are examples.

OSHA conducted quantitative cancer risk assessments for four of the substances listed in Table 6 as part of the 1989 PEL update project: acrylamide, carbon tetrachloride, chloroform, and o-toluidine.\(^8\) Comparing OSHA’s estimates of the upper bound excess cancer cases associated with exposure at the PEL to those based on OEHHA and/or U.S. EPA unit risk values shows that OSHA (1989) generally took a less conservative approach (Table 7). In one case, the upper bound estimates are the same (acrylamide).

### Table 7. Comparison of OEHHA, U.S. EPA and OSHA cancer risk estimates from Table 6

<table>
<thead>
<tr>
<th>Substance</th>
<th>Estimated cancer cases per 1,000 workers exposed at PEL (range based on OEHHA and U.S. EPA unit risk values)</th>
<th>Estimated cancer cases per 1,000 workers exposed at PEL (OSHA upper bound estimates)</th>
<th>Ratio of OEHHA and U.S. EPA estimates to OSHA upper bound estimates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acrylamide</td>
<td>5</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Carbon tetrachloride</td>
<td>25-69</td>
<td>5.2</td>
<td>4.8-13</td>
</tr>
<tr>
<td>Chloroform</td>
<td>7-29</td>
<td>1.8</td>
<td>3.8-16</td>
</tr>
<tr>
<td>o-Toluidine</td>
<td>60</td>
<td>0.64</td>
<td>94</td>
</tr>
</tbody>
</table>

Some of the likely sources of the differences in the OEHHA and U.S. EPA compared to OSHA upper bound estimates are choice of study used as the basis for the cancer risk assessment and different methods and/or assumptions applied in the assessment, such as different interspecies extrapolation methods and the use of pharmacokinetic adjustments. Additional discussion of potential sources for these differences is provided following Table 9.

---

\(^8\) OSHA (1989) also cited a quantitative cancer risk assessment conducted by Hattis for tetrachloroethylene (as described in OSHA, 1989), and used that assessment to select a PEL, which fell within the range of values assessed by Hattis. See Table 6 and footnote i. The estimated cancer cases at the final PEL chosen by OSHA (1989) were not determined.
Skin notations on half of the 38 chemicals indicate that the estimated cancer risks for workers exposed at the PEL would likely be higher for these chemicals than what is reported in Table 6 if dermal exposure were taken into account.
Results for Cancer Risk Estimation at PEL: Chemicals Regulated as Occupational Carcinogens

Table 8 shows the estimated cancer risks for workplace chemicals listed as known to cause cancer under Proposition 65 that are regulated in California as occupational carcinogens. The calculations assume occupational exposure at the current Cal/OSHA PEL and are based on OEHHA or U.S. EPA unit risk values. The “estimated excess cancer cases per 1,000 workers” is estimated by multiplying the excess lifetime cancer risk by 1,000. Table 8 also lists the cancer risks as estimated by OSHA using quantitative risk assessment as part of deriving certain OSHA PELs. For the chemicals in Table 8 that have OSHA quantitative risk assessments, the Cal/OSHA PELs are the same as the OSHA PELs.
Table 8. Estimated cancer risks associated with the Cal/OSHA PELs for Proposition 65 carcinogens that are regulated as occupational carcinogens

<table>
<thead>
<tr>
<th>Chemical</th>
<th>Chemical [Cal/OSHA PEL[a]] (mg/m^3 or as noted)</th>
<th>OEHHA Unit Risk Value [mg/m^3] [^{1}] or as noted</th>
<th>U.S. EPA Unit Risk Value [mg/m^3] [^{1}] or as noted</th>
<th>Estimated Excess Lifetime Cancer Riskb (range based on OEHHA and U.S. EPA unit risk values)</th>
<th>Estimated Excess Cancer Cases Per 1,000 Workers</th>
<th>OSHA Estimates of Excess Cancer Cases Per 1,000 Workers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acrylonitrile</td>
<td>4.5; Skin</td>
<td>2.9 x 10^-3</td>
<td>6.8 x 10^-2</td>
<td>0.4-1.7 x 10^-1</td>
<td>40-170</td>
<td>--</td>
</tr>
<tr>
<td>Arsenic</td>
<td>0.01</td>
<td>3.3</td>
<td>4.3</td>
<td>4.3-5.6 x 10^-3</td>
<td>4-6</td>
<td>--</td>
</tr>
<tr>
<td>Asbestos</td>
<td>0.1 f/cc</td>
<td>1.9 (f/cc)[^{1}]</td>
<td>0.23 (f/cc)[^{1}]</td>
<td>0.3-2.5 x 10^-3</td>
<td>3-25</td>
<td>3.4[^{a}]</td>
</tr>
<tr>
<td>Benzene</td>
<td>3.19; Skin</td>
<td>2.9 x 10^-2</td>
<td>2.2 – 7.8 x 10^-3</td>
<td>0.092-1.2 x 10^-2</td>
<td>0.9-12</td>
<td>10 (MLE); 22 (UCB)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>See footnote d</td>
</tr>
<tr>
<td>1,3-Butadiene</td>
<td>2.2</td>
<td>1.7 x 10^-1</td>
<td>3.0 x 10^-2</td>
<td>0.86-4.9 x 10^-2</td>
<td>9-49</td>
<td>1.3-8.1 (MLE); 2.3-12.2 (UCB)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>See footnote e</td>
</tr>
<tr>
<td>Cadmium</td>
<td>0.005</td>
<td>4.2</td>
<td>1.8</td>
<td>1.2-2.7 x 10^-1</td>
<td>1-3</td>
<td>3-15 (MLEs, human and animal data) 5.1 (UCB, human data)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>See footnote f</td>
</tr>
<tr>
<td>Chromium VI</td>
<td>0.005</td>
<td>1.5 x 10^-2</td>
<td>12</td>
<td>0.78-9.8 x 10^-2</td>
<td>8-98</td>
<td>10 – 45 (MLE); 15-75 (UCB)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>See footnote g</td>
</tr>
<tr>
<td>Dichloromethane (Methylene chloride)</td>
<td>87</td>
<td>1.0 x 10^-3</td>
<td>4.7 x 10^-1</td>
<td>0.53-1.1 x 10^-2</td>
<td>5-11</td>
<td>3.6[^{b}]</td>
</tr>
<tr>
<td>Ethylene dibromide</td>
<td>1; Skin</td>
<td>7.1 x 10^-2</td>
<td>6.0 x 10^-1</td>
<td>0.93-7.8 x 10^-2</td>
<td>9-78</td>
<td>--</td>
</tr>
<tr>
<td>Ethyleneimine</td>
<td>1; Skin</td>
<td>1.9 x 10^-1</td>
<td>--</td>
<td>9.2 x 10^-1</td>
<td>920</td>
<td>--</td>
</tr>
<tr>
<td>Ethylene oxide</td>
<td>2</td>
<td>8.8 x 10^-2</td>
<td>--</td>
<td>2.3 x 10^-2</td>
<td>23</td>
<td>1.2-2.3 (MLE); 2.1-3.1 (UCB)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>See footnote i</td>
</tr>
<tr>
<td>Formaldehyde</td>
<td>0.9</td>
<td>6.0 x 10^-3</td>
<td>1.3 x 10^-2</td>
<td>0.71-1.5 x 10^-3</td>
<td>0.7-2</td>
<td>0.0056 (MLE); 2.64 (UCB)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>See footnote j</td>
</tr>
<tr>
<td>4,4’- Methyleneedianiline</td>
<td>0.08; Skin</td>
<td>4.6 x 10^-1</td>
<td>--</td>
<td>4.8 x 10^-3</td>
<td>5</td>
<td>0.8 (MLE); 0.9 (UCB)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>See footnote k</td>
</tr>
<tr>
<td>Vinyl chloride</td>
<td>3; Skin</td>
<td>7.8 x 10^-4</td>
<td>4.4 x 10^-3</td>
<td>0.17-3.1 x 10^-3</td>
<td>2-31</td>
<td>--</td>
</tr>
</tbody>
</table>

a. For the substances in Table 8 with OSHA QRAs, the OSHA PEL is the same as the Cal/OSHA PEL.
b. Assumes exposure 8 hours per day, 5 days per week, 50 weeks per year, 40 years; does not account for increased breathing rate expected for workers.
c. From OSHA (1994) based on an OSHA (1983) assessment of the risk of asbestos-related cancer mortality from lung cancer, mesothelioma and gastrointestinal cancer. The lung cancer potency was derived as the midpoint of the best estimates from 11 epidemiological studies. The ratio of the mesothelioma to lung cancer potencies was determined from four studies with data on both types of cancers, and used to derive the best estimate for mesothelioma cancer potency from the best estimate of lung cancer potency. Risk from gastrointestinal cancer was estimated to be one tenth that from lung cancer. OSHA (1983) noted that there would be at least a three-fold uncertainty around the best estimate for lung cancer potency.
c. From OSHA (1996) risk assessment for 1,3-butadiene, based on estimates from animal cancer data. OSHA noted that the range of MLEs (1.3 – 8.1) is consistent with a preliminary estimate of 8 per 1,000 from an epidemiological study.

f. OSHA (1992a) concluded that the best estimates of excess risk at the PEL were 15 per 1,000 from animal data, 3 per 1,000 from human data using an OSHA relative risk model, and 3.9 to 9 per 1,000 from human data using NIOSH models. OSHA (1992a) also reported an upper bound estimate from human data of 5.1 per 1,000 based on the OSHA relative risk model. This value is noted for comparison to the OEHHA and U.S. EPA estimates which were based on assessments of human data using relative risk models.

g. From OSHA (2006) based on an assessment of excess lung cancer cases using the preferred cohorts of Gibb and Luippold (as cited by OSHA, 2006).

h. OSHA (1997) stated that it “has chosen for its final risk estimate to couple one measure of central tendency (the MLE of the dose-response parameters) with a somewhat ‘conservative’ measure (the 95th percentile of the distribution of human GST [glutathione S-transferase] metabolites (internal dose)), describing the estimate shown in Table 8 as the “MLE of cancer risk using the upper 95th percentile of the human internal dose distribution.”

i. In lowering the PEL to 1 ppm, OSHA (1984) noted that “the excess cancer risk from EtO exposure at 1 ppm over a working lifetime are [sic] significant” and that “OSHA has determined that significant risk is not eliminated by lowering the TWA to 1 ppm.”

j. OSHA (1992b) cites OSHA (1987) as the source for the cancer risk estimates, which were derived by Clement Associates using animal and human data.

k. OSHA (1992c) notes that the estimates would be 10 times higher if an interspecies extrapolation factor based on surface area were applied. The MLE risk estimate includes exposure from skin absorption.
Discussion of Table 8

Table 8 shows estimated excess cancer cases per 1,000 workers calculated based on OEHHA and U.S. EPA unit risk values for 14 Proposition 65 carcinogens that are regulated as occupational carcinogens under Cal/OSHA and OSHA. The calculation assumes that the workers are exposed at the Cal/OSHA PEL over their working lifetime. Table 8 also summarizes results of quantitative risk assessments carried out by OSHA to determine the significance of cancer risks at current PELs, consistent with the Benzene Decision (see footnote 6 on page 55), as part of the process for developing substance-specific standards. OSHA estimates of excess cancer cases at the PEL were identified for nine of the substances in Table 8. The current Cal/OSHA and OSHA PELs are the same for these nine substances. The PELs for these nine substances were initially developed by OSHA and subsequently adopted under Cal/OSHA.

Three of the 14 chemicals in Table 8 have ranges of estimated cancer risks that include 1 in 1,000 (formaldehyde: 0.7 to 2; benzene: 0.9 to 12; cadmium: 1 to 3), based on OEHHA and U.S. EPA unit risk values. Two of the nine chemicals that OSHA assessed have estimated MLE cancer risks, which is the measure that OSHA uses to evaluate significance of risk, that are below 1 in 1,000 (formaldehyde: 0.0056; 4,4’-methylenedianiline: 0.8). The remainder of the estimates based on OEHHA, U.S. EPA or OSHA QRAs are higher than the 1 excess cancer case per 1,000 workers, the cancer risk level that OSHA targets as “significant” based on the Benzene Decision. The final PELs for these occupational carcinogens incorporate both risk assessment and risk management issues, such as technical and economic feasibility, however. Thus, the estimated cancer risks associated with worker exposure at the PELs are expected to vary from this preferred target. When the cancer risks associated with the PEL exceed this target, OSHA has noted that a significant risk to workers remains (see for example, OSHA, 1984).

Estimated cancer risks associated with exposure at the PELs for acrylonitrile and ethyleneimine range to particularly high values (170 and 920 per 1,000, respectively) when calculated using OEHHA or U.S. EPA unit risk values (OSHA risk estimates were not located for these chemicals). Acrylonitrile is used primarily as a monomer in the production of acrylic fibers so the potential for worker exposure may be limited. Ethyleneimine is used in the manufacture of other chemicals and as an intermediate and monomer for pharmaceuticals and other products. Worker exposure to this chemical is likely to be limited.

In Table 9 below, the estimates of excess cancer cases produced using the OEHHA and U.S. EPA unit risk values are compared to the upper bound estimates (or highest available) reported by OSHA in its final risk assessments for the chemicals in Table 8. OEHHA and U.S. EPA tend to follow the same general cancer risk guidelines, although the studies used in the assessments or the specific modeling approach chosen may differ between the agencies. OSHA has taken varying approaches that tend to be less health conservative than OEHHA or U.S. EPA. In spite of these differences among the agencies, most of the upper bound estimates are remarkably similar.
Table 9. Comparison of OEHHA, U.S. EPA and OSHA cancer risk estimates from Table 8

<table>
<thead>
<tr>
<th>Substance</th>
<th>Estimated cancer cases per 1,000 workers exposed at current PEL (range based on OEHHA and U.S. EPA unit risk values)</th>
<th>Estimated cancer cases per 1,000 workers exposed at current PEL (OSHA upper bound or highest reported estimate)</th>
<th>Ratio of OEHHA/U.S. EPA estimates to OSHA estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asbestos</td>
<td>3-25</td>
<td>3.4</td>
<td>0.9-7.5</td>
</tr>
<tr>
<td>Benzene</td>
<td>0.9-12</td>
<td>22</td>
<td>0.04-0.55</td>
</tr>
<tr>
<td>1,3-Butadiene</td>
<td>9.49</td>
<td>12.2</td>
<td>1.1-6.0</td>
</tr>
<tr>
<td>Cadmium</td>
<td>1-3</td>
<td>5.1</td>
<td>0.2-0.6</td>
</tr>
<tr>
<td>Chromium VI</td>
<td>8.98</td>
<td>75</td>
<td>0.1-1.3</td>
</tr>
<tr>
<td>Dichloromethane</td>
<td>5-11</td>
<td>3.6</td>
<td>1.4-3.0</td>
</tr>
<tr>
<td>Ethylene oxide</td>
<td>23</td>
<td>3.1</td>
<td>7.4</td>
</tr>
<tr>
<td>Formaldehyde</td>
<td>0.7-2</td>
<td>2.64</td>
<td>0.3-0.8</td>
</tr>
<tr>
<td>4,4’-Methylenedianiline</td>
<td>5</td>
<td>0.9</td>
<td>5.6</td>
</tr>
</tbody>
</table>

The cancer risk assessment approaches taken by OEHHA and U.S. EPA compared to OSHA differ in a number of respects. Depending on when the reviews were conducted, the risk assessments may be based on different epidemiological or animal studies. Different modeling approaches may have been selected by the agencies in analyzing human or animal data. PBPK dose adjustments may have been applied in some assessments but not others. If animal data are the basis for the cancer potency, the interspecies extrapolation factors are likely to differ. OSHA has generally assumed that doses to animals are equivalent to doses in humans (i.e., equivalence of dose on a body weight basis), making the interspecies extrapolation factor equal to 1. OEHHA and U.S. EPA instead assume equivalence on a surface area basis, resulting in interspecies extrapolation factors of either \((\frac{b_{\text{human}}}{b_{\text{animal}}})^{1/3}\) or \((\frac{b_{\text{human}}}{b_{\text{animal}}})^{1/4}\). The OEHHA and U.S. EPA approaches to interspecies extrapolation can lead to potencies that are approximately 3 to 14 times higher than the OSHA approach, depending on the animal species studied, the animal body weight chosen, and the exponent selected for the interspecies factor. OSHA has generally relied on maximum likelihood estimates of cancer risk in making final decisions on the PEL, although in many cases upper bound cancer risk estimates are also reported in the assessments (see Table 8). OEHHA and U.S. EPA typically derive an upper bound estimate of cancer potency. The upper 95% confidence bound is a more stable measure of cancer potency compared to the maximum likelihood estimate (Crump, 1996). With regard to worker exposure, OSHA has assumed a 45 year working lifetime, while in this document a 40 year working lifetime was assumed.

OSHA’s (1992c) 4,4’-methylenedianiline (MDA) risk assessment included an analysis of the risk associated with dermal contact since the chemical is easily absorbed through the skin. OSHA estimated that workers exposed to an airborne level of 0.1 mg/m³ would receive approximately 73% of their total dose via dermal exposure. The cancer risk calculations were thus based on a total dose (inhalation plus dermal) that was more than three-fold higher than the dose from inhalation exposure alone. OSHA noted that it went beyond the traditional regulatory methodology in making estimates of risk from dermal deposition of MDA. Additional
compounds in Table 8 that may pose cancer risks via the dermal route include acrylonitrile, benzene, ethylene dibromide, ethyleneimine, and vinyl chloride, which have skin designations.
Results for Estimation of Occupational Air Concentrations for Selected Carcinogens

Table 10 below summarizes estimated occupational air concentrations ($C_{occ}$) associated with various risk levels for selected workplace chemicals listed as known to cause cancer under Proposition 65. The calculations were done using the OEHHA unit risk levels listed in Table 6 above and equation 3. The Cal/OSHA PEL is listed for reference purposes, along with the known or inferred basis for the PEL (see Table 4 for more details).

Table 10. Estimated occupational concentrations associated with various cancer risk levels for selected workplace chemicals.

<table>
<thead>
<tr>
<th>Chemical</th>
<th>$C_{occ}$ at specified cancer risk level$^a$ (ppm)</th>
<th>Cal/OSHA PEL (ppm)</th>
<th>Cal/OSHA PEL known or inferred basis$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 in 1,000</td>
<td>1 in 10,000</td>
<td>1 in 100,000</td>
</tr>
<tr>
<td>Chloroethane</td>
<td>2</td>
<td>0.2</td>
<td>0.02</td>
</tr>
<tr>
<td>1,4-Dioxane</td>
<td>0.3</td>
<td>0.03</td>
<td>0.003</td>
</tr>
<tr>
<td>Epichlorohydrin</td>
<td>0.09</td>
<td>0.009</td>
<td>0.0009</td>
</tr>
<tr>
<td>Ethylene dichloride</td>
<td>0.09</td>
<td>0.009</td>
<td>0.0009</td>
</tr>
<tr>
<td>1,1,2,2-Tetrachloroethane</td>
<td>0.02</td>
<td>0.002</td>
<td>0.0002</td>
</tr>
<tr>
<td>Toluene diisocyanate</td>
<td>0.1</td>
<td>0.01</td>
<td>0.001</td>
</tr>
<tr>
<td>Trichloroethylene</td>
<td>0.7</td>
<td>0.07</td>
<td>0.007</td>
</tr>
</tbody>
</table>

a. Rounded to one significant figure. Assumes exposure 8 hours per day, 5 days per week, 50 weeks per year, 40 years; does not account for increased breathing rate expected for workers.

b. The basis for the Cal/OSHA PEL was determined either from Cal/OSHA documentation, or inferred by comparison to ACGIH TLVs, OSHA (1989) PELs, or NIOSH RELs. See Table 4 for more details.

As Table 10 shows, even if cancer was considered qualitatively as part of the basis, the PEL may be considerably higher than the health-based occupational concentration associated with a 1 in 1,000 risk level, often cited as a significant risk in occupational settings. For example, the chloroethane PEL was lowered based on tumorigenicity concerns, but the PEL is 50 times higher than the level associated with a 1 in 1,000 risk level. Conversely, if a noncancer endpoint with a low threshold was considered (e.g., sensitization), the PEL may be in the range of levels associated with cancer risks considered acceptable in an occupational setting. For example, the PEL for toluene diisocyanate (TDI) was chosen to address respiratory sensitization; this PEL is well below the level associated with a 1 in 1,000 cancer risk.
The example calculations summarized in Table 10 demonstrate the importance of quantitatively assessing the cancer risks and presenting a range of health-based occupational concentrations with associated risk levels to decision makers. This would allow risk managers to make an informed choice for the PEL, and be aware of the potential for increased cancer risks when they consider higher PELs to address technical feasibility or economic concerns.
Derivation of Occupational Air Concentrations for Two Developmental Toxicants: Example Calculations

Occupational concentrations were derived for two chemicals listed under Proposition 65 as developmental toxicants: N-methylpyrrolidone, which does not have a Cal/OSHA PEL, and toluene, which has a PEL that is likely based on respiratory and eye irritation and CNS effects. Possible approaches for applying existing risk assessments to the occupational setting are illustrated and the results discussed.

Developmental Toxicant Example 1: N-Methylpyrrolidone

Summary of existing values

<table>
<thead>
<tr>
<th></th>
<th>Inh.</th>
<th>Basis: Developmental toxicity</th>
<th>Dermal</th>
<th>Basis: Developmental toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>OEHHA MADL</td>
<td>3.2 mg/d</td>
<td></td>
<td>17 mg/d</td>
<td></td>
</tr>
<tr>
<td>U.S. EPA RfC</td>
<td>Not available</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cal/OSHA PEL</td>
<td>Not regulated</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACGIH TLV</td>
<td>Not available</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conversion factor</td>
<td>1 ppm = 4.05 mg/m³</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

OEHHA (2003) estimated maximum allowable dose levels (MADLs) for N-methylpyrrolidone (NMP) for inhalation and dermal exposures. Calculation of the MADL involves identifying the NOAEL for reproductive and/or developmental toxicity and dividing by 1,000, which is a requirement of Proposition 65. The NOAEL identified as the basis for the inhalation MADL can be used to derive an occupational air concentration.

Derivation of a cREL based on OEHHA inhalation MADL

OEHHA (2003) identified a NOAEL of 50 ppm based on a two-generation inhalation study in rats. The dams were exposed 6 hours per day. Following OEHHA (2000a), a cREL can be derived based on this NOAEL as summarized below:

<table>
<thead>
<tr>
<th>Key study</th>
<th>Solomon et al. (1995; also Staples et al. 1990; as cited by OEHHA, 2003)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study population</td>
<td>Rats</td>
</tr>
<tr>
<td>Exposure method</td>
<td>Discontinuous inhalation</td>
</tr>
<tr>
<td>Critical effects</td>
<td>Decreased fetal weight and decreased pup weight</td>
</tr>
<tr>
<td>LOAEL</td>
<td>116 ppm</td>
</tr>
</tbody>
</table>
NOAEL: 50 ppm  
Exposure continuity: 6 hours/day, 7 days/week  
Exposure duration: From age 34 days until weaning in females (interrupted from Day 20 of gestation to Day 4 postpartum) and from age 34 days until the end of mating period for males  
Average experimental exposure: 12.5 ppm for NOAEL group (50 ppm x 6/24)  
Human equivalent concentration: 12.5 ppm (gas with systemic effects, based on RGDR [regional gas dose ratio] = 1)  
LOAEL uncertainty factor: 1  
Subchronic uncertainty factor: 1  
Interspecies uncertainty factor: 3 (as discussed in the methods, an interspecies factor of 3 has typically been applied when a human equivalent concentration has been used as the exposure metric for assessments based on animal studies)  
Intraspecies uncertainty factor: 10  
Cumulative uncertainty factor: 30  
Inhalation reference exposure level: 0.4 ppm or 1.6 mg/m$^3$  

With a human equivalent concentration of 12.5 ppm based on the Solomon et al. study and a total uncertainty factor of 30, a cREL of 0.40 ppm or 1.6 mg/m$^3$ is estimated. The cREL is protective for the general population exposed continuously. The adjustment of the cREL to account for an occupational exposure is described below.

Adjustment of uncertainty factors for occupational setting

A default intraspecies factor of 10 to protect for sensitive subpopulations was applied for the cREL derivation described above. For developmental toxicants, pregnant women are the target population of concern and would potentially be present in the workplace. Thus, an intraspecies factor of 10 may be appropriate in this case. For the current example, an intraspecies factor of either 3 or 10 is applied. The total uncertainty factor applied for an occupational scenario is 10 or 30.

Calculation of occupational concentration

As discussed in the methods section, adjusting exposure to account for an occupational scenario may not be appropriate for developmental toxicants. For the current example, three methods for exposure averaging were applied to derive occupational concentrations:

Method 1: Animal NOAEL adjusted for continuous exposure, adjustment for shorter worker exposure duration applied.

Method 2: Animal NOAEL adjusted for continuous exposure, no adjustment for worker exposure duration.
Method 3: Animal NOAEL **not** adjusted for continuous exposure, **no** adjustment for worker exposure duration.

Based on these three exposure averaging methods and applying a UF of either 30 or 10, the occupational concentrations are:

Method 1:

\[
C_{oc} = \frac{12.5 \text{ ppm}}{30} \times \frac{24 \text{ hr/d}}{8 \text{ hr/d}} \times \frac{7 \text{ d/wk}}{5 \text{ d/wk}} = 2 \text{ ppm}
\]

\[
C_{oc} = \frac{12.5 \text{ ppm}}{10} \times \frac{24 \text{ hr/d}}{8 \text{ hr/d}} \times \frac{7 \text{ d/wk}}{5 \text{ d/wk}} = 5 \text{ ppm}
\]

Method 2:

\[
C_{oc} = \frac{12.5 \text{ ppm}}{30} = 0.4 \text{ ppm}
\]

\[
C_{oc} = \frac{12.5 \text{ ppm}}{10} = 1 \text{ ppm}
\]

Method 3:

\[
C_{oc} = \frac{50 \text{ ppm}}{30} = 2 \text{ ppm}
\]

\[
C_{oc} = \frac{50 \text{ ppm}}{10} = 5 \text{ ppm}
\]

Methods 1 and 3 produced the same results (rounded to one significant figure). This is expected, because the exposure conditions in the animal study (6 hours per day, 7 days per week) produce an adjustment factor (0.25) that is nearly identical to the adjustment factor (0.23) based on occupational exposure (8 hours per day, 5 days per week). Thus, these adjustment factors cancel out in Method 1, producing the same results as not applying exposure averaging at all (Method 3). Method 2, under which the animal results are adjusted for continuous exposure but the shorter duration of worker exposure is not considered, produces more conservative results.

Occupational concentrations for NMP using the methods described above range from 0.4 to 5 ppm, and are summarized in Table 11. Occupational exposure limits available for NMP internationally are summarized in Table 12.
Table 11. Summary of occupational concentrations for N-methylpyrrolidone derived based on an existing OEHHA risk assessment

<table>
<thead>
<tr>
<th>$C_{occ}$ (ppm)</th>
<th>Total UF</th>
<th>Exposure Averaging Approach</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.4</td>
<td>30</td>
<td>Animal NOAEL adjusted for continuous exposure, with no adjustment for occupational exposure</td>
</tr>
<tr>
<td>1</td>
<td>10</td>
<td>Animal NOAEL adjusted for continuous exposure, with no adjustment for occupational exposure</td>
</tr>
<tr>
<td>2</td>
<td>30</td>
<td>Animal NOAEL <strong>not</strong> adjusted for continuous exposure, with adjustment for occupational exposure</td>
</tr>
<tr>
<td>5</td>
<td>10</td>
<td>Animal NOAEL <strong>not</strong> adjusted for continuous exposure, with adjustment for occupational exposure</td>
</tr>
</tbody>
</table>

Table 12. Occupational exposure limits set for N-methylpyrrolidone by other countries (ACGIH, 2006)

<table>
<thead>
<tr>
<th>Country</th>
<th>Occupational Exposure Value TWA$^a$ (ppm)</th>
<th>Comments/Notations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australia</td>
<td>25</td>
<td>Skin</td>
</tr>
<tr>
<td>Canada – Ontario</td>
<td>100</td>
<td>--</td>
</tr>
<tr>
<td>Finland</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>Germany</td>
<td>20</td>
<td>Skin; values are for exposure to the vapor</td>
</tr>
<tr>
<td>Ireland</td>
<td>25</td>
<td>Skin</td>
</tr>
<tr>
<td>Japan</td>
<td>1</td>
<td>Skin</td>
</tr>
<tr>
<td>Netherlands</td>
<td>20</td>
<td>--</td>
</tr>
<tr>
<td>New Zealand</td>
<td>25</td>
<td>Skin</td>
</tr>
<tr>
<td>Norway</td>
<td>5</td>
<td>Skin</td>
</tr>
<tr>
<td>Poland</td>
<td>30</td>
<td>Skin</td>
</tr>
<tr>
<td>South Africa</td>
<td>100</td>
<td>--</td>
</tr>
<tr>
<td>Spain</td>
<td>25</td>
<td>Skin</td>
</tr>
<tr>
<td>Country</td>
<td>Occupational Exposure Value TWA&lt;sup&gt;a&lt;/sup&gt; (ppm)</td>
<td>Comments/Notations</td>
</tr>
<tr>
<td>------------------</td>
<td>--------------------------------------------------</td>
<td>--------------------</td>
</tr>
<tr>
<td>Sweden</td>
<td>50</td>
<td>--</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>25</td>
<td>Skin</td>
</tr>
</tbody>
</table>

<sup>a</sup> As reported by ACGIH (2006). TWA = time-weighted average.

The most health conservative exposure limits are those derived by Japan (1 ppm) and Norway (5 ppm), which are comparable to the occupational concentrations derived based on the OEHHA inhalation MADL assessment. AIHA has also developed a WEEL of 10 ppm for NMP (ACGIH, 2006).

The estimates of occupational air concentrations presented above do not explicitly account for dermal absorption, which is of concern for NMP. AIHA has a skin notation for NMP, as do most of the other jurisdictions that have established occupational levels for this chemical (ACGIH, 2006). Thus, the estimated occupational concentrations may not be sufficiently protective. OEHHA’s MADL for dermal exposure is more than five times higher than that for inhalation exposure, however, so dermal absorption of NMP may not contribute significantly to the overall risk of developmental harm.

An additional concern for NMP is that it is a developmental toxicant, meaning that it could pose a risk from short-term exposure. The occupational concentrations for NMP were derived here using various methods to account for exposure conditions in the animal study and in the occupational setting, as described above. The issue of exposure averaging must be addressed in setting occupational limits for developmental toxicants. A short-term exposure limit and/or ceiling limit should also be set for developmental toxicants.
Developmental Toxicant Example 2: Toluene

Summary of existing values

- **OEHHA MADL**: 13 mg/d (inhalation)  
  Basis: Developmental toxicity

- **OEHHA cREL**: 0.08 ppm (0.3 mg/m³)  
  Hazard index target: Nervous system; respiratory system; development

- **U.S. EPA RfC**: 1.3 ppm (5 mg/m³)  
  Critical effect: Neurological effects in occupationally-exposed workers

- **Cal/OSHA PEL**: 50 ppm (188 mg/m³)  
  Basis: Not available. Because the Cal/OSHA PEL is the same as the current ACGIH TLV-TWA, the basis is assumed to be equivalent.

- **ACGIH TLV**: 20 ppm (75 mg/m³)  
  ACGIH (2007) provides the basis for this newly revised TLV as visual impairment, female reproductive damage, and pregnancy loss.

Conversion factor: 1 ppm = 3.77 mg/m³

Selection of risk assessment

The OEHHA MADL was derived to protect for developmental toxicity based on data summarized in Donald *et al.* (1991). The OEHHA (2000b) cREL analysis used studies on neurological effects to derive a cREL that is also protective for respiratory system effects and developmental toxicity. The U.S. EPA (2005a) RfC was based on occupational studies of neurological effects, with U.S. EPA commenting that "Animal studies have demonstrated reproductive and developmental effects of toluene at exposure levels higher than those used for the determination of the point of departure." The more recent OEHHA (2000b) and U.S. EPA (2005a) assessments which are described as accounting for neurological effects in addition to developmental effects may be preferred. However, for comparison purposes and to ensure that the assessments are protective for developmental effects, the NOAEL underlying the OEHHA MADL was also used to generate occupational concentrations.
**Occupational concentration for toluene based on OEHHA cREL**

Summary of OEHHA cREL derivation (adapted from OEHHA, 2000b)

<table>
<thead>
<tr>
<th>Study</th>
<th>Hillefors-Berglund et al. (1995); supported by Orbaek and Nise (1989), Foo et al. (1990) (as cited by OEHHA, 2000b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study population</td>
<td>Male Sprague-Dawley rats</td>
</tr>
<tr>
<td>Exposure method</td>
<td>Inhalation</td>
</tr>
<tr>
<td>Critical effects</td>
<td>Decreased brain (subcortical limbic area) weight, altered dopamine receptor (caudate-putamen) binding</td>
</tr>
<tr>
<td>LOAEL</td>
<td>80 ppm</td>
</tr>
<tr>
<td>NOAEL</td>
<td>40 ppm</td>
</tr>
<tr>
<td>Exposure continuity</td>
<td>6 hours/day, 5 days/week</td>
</tr>
<tr>
<td>Exposure duration</td>
<td>4 weeks, followed by 29-40 days recovery</td>
</tr>
<tr>
<td>Average experimental exposure</td>
<td>7 ppm (40 × 6/24 hours × 5/7 days)</td>
</tr>
<tr>
<td>Human equivalent concentration</td>
<td>7 ppm (gas with systemic effects, based on RGDR = 1.0)</td>
</tr>
<tr>
<td>Subchronic uncertainty factor</td>
<td>10</td>
</tr>
<tr>
<td>Interspecies uncertainty factor</td>
<td>1 (see below)</td>
</tr>
<tr>
<td>Intraspecies uncertainty factor</td>
<td>10</td>
</tr>
<tr>
<td>Cumulative uncertainty factor</td>
<td>100</td>
</tr>
<tr>
<td>Inhalation reference exposure level</td>
<td>0.07 ppm (70 ppb; 0.3 mg/m³; 300 μg/m³)</td>
</tr>
</tbody>
</table>

Supportive human study

<table>
<thead>
<tr>
<th>Study population</th>
<th>Foo et al., 1990 (as cited by OEHHA, 2000b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study</td>
<td>30 female workers in an electronic assembly plant</td>
</tr>
<tr>
<td>Exposure method</td>
<td>Occupational inhalation</td>
</tr>
<tr>
<td>Critical effects</td>
<td>Neurobehavioral deficits in 6 out of 8 tests</td>
</tr>
<tr>
<td>LOAEL</td>
<td>88 ppm</td>
</tr>
<tr>
<td>NOAEL</td>
<td>Not observed</td>
</tr>
<tr>
<td>Exposure continuity</td>
<td>10 m³/day occupational inhalation rate, 5 days/week</td>
</tr>
<tr>
<td>Exposure duration</td>
<td>5.7 + 3.2 years (exposed group); 2.5 + 2.7 years (controls)</td>
</tr>
<tr>
<td>LOAEL uncertainty factor</td>
<td>10</td>
</tr>
<tr>
<td>Subchronic uncertainty factor</td>
<td>3</td>
</tr>
<tr>
<td>Interspecies uncertainty factor</td>
<td>1</td>
</tr>
<tr>
<td>Intraspecies uncertainty factor</td>
<td>10</td>
</tr>
<tr>
<td>Cumulative uncertainty factor</td>
<td>300</td>
</tr>
<tr>
<td>Inhalation reference exposure level</td>
<td>0.1 ppm (100 ppb; 0.4 mg/m³; 400 μg/m³)</td>
</tr>
</tbody>
</table>
OEHHA used a study in rats to derive the cREL because the study had well characterized exposures and more sensitive measures of neurological effects compared to the human studies. OEHHA also showed that the cREL based on the animal study was comparable to cRELs derived based on human studies. No interspecies uncertainty factor was applied because "the uncertainty in the interspecies extrapolation is reduced by the availability of human epidemiological data with generally consistent effect levels, after appropriate duration corrections." The subchronic uncertainty factor of 10 was included because the animal study was only 4 weeks long (or only 3.8% of the animals' lifespan) (OEHHA, 2000a). The default intraspecies factor of 10 was also applied.

**Adjustment of uncertainty factors in OEHHA assessment for occupational setting**

The LOAEL uncertainty factor and the subchronic uncertainty factor still apply and should not be adjusted. OEHHA applied a default intraspecies factor of 10 in deriving RELs based either on animal or human data. The cREL is based on data from only a portion of the target population, *i.e.*, female workers, so an intraspecies factor is still considered appropriate for deriving an occupational concentration for toluene. For illustration purposes, intraspecies factors of 10 and 3 were used to derive occupational concentrations below.

**Calculation of occupational concentration based on OEHHA cREL**

Occupational concentrations were derived assuming total uncertainty factors of either 100 or 30 and adjusting for workplace exposure:

\[
C_{occ} = \frac{7 \text{ ppm}}{100} \times \frac{24 \text{ hr/d}}{8 \text{ hr/d}} \times \frac{7 \text{ d/wk}}{5 \text{ d/wk}} = 0.3 \text{ ppm}
\]

\[
C_{occ} = \frac{7 \text{ ppm}}{30} \times \frac{24 \text{ hr/d}}{8 \text{ hr/d}} \times \frac{7 \text{ d/wk}}{5 \text{ d/wk}} = 1 \text{ ppm}
\]

**Occupational concentration for toluene based on U.S. EPA RfC**

An uncertainty factor of 10 for intraspecies variability was applied based on the following discussion: "A total uncertainty factor of 10 was applied to the adjusted average NOAEL (*i.e.*, 10 for consideration of intraspecies variation). A 10-fold uncertainty factor for intraspecies
differences ($\text{UF}_{\text{H}}$) was used to account for potentially susceptible human subpopulations and lifestages. This 10-fold uncertainty factor includes consideration of the Pelekis et al. (2001) model employing pharmacokinetic information to derive a chemical-specific intraspecies UF for toluene that accounts for childhood exposure only. Their analysis suggests an informed quantitation of adult-to-child variability reported to be in the 3-fold range. The Pelekis model is based on the pharmacokinetic differences between adults and children. However, differences in human susceptibility may also be due to lifestage (e.g., advanced age) differences among the adult population, genetic polymorphisms, decreased renal clearance in disease states, and unknown pharmacodynamic variations in response to toluene exposure. Since the variability defined in the Pelekis model may not account for these additional differences in pharmacokinetics and pharmacodynamics, a full factor of 10 is used."

A subchronic uncertainty factor of 1 was used, although not all studies were chronic: "An uncertainty factor to account for extrapolating from less than chronic results ($\text{UF}_{\text{S}}$) was not necessary. Most of the studies used in the analysis were of chronic duration."

The RfC based on this analysis was 5 mg/m$^3$.

**Adjustment of uncertainty factors in U.S. EPA assessment for occupational setting**

The intraspecies factor of 10 applied by U.S. EPA (2005a) was designed to address the susceptibility of children (a factor in the 3-fold range) and differences in the adult population, including advanced age, genetic polymorphisms, decreased renal clearance in disease states, and other pharmacodynamic variations. The RfC is based on data from ten studies of the relevant target population, *i.e.*, workers, so an intraspecies factor may not be appropriate for deriving an occupational concentration for toluene. Occupational concentrations using intraspecies factors of 3 and 1 are derived below.

**Calculation of occupational concentration based on U.S. EPA RfC**

Because the NOAEL is derived from occupational studies, an adjustment for occupational exposure is not required. Using total uncertainty factors of 3 and 1, the occupational concentrations for toluene are estimated as follows:

$$C_{\text{occ}} = \frac{34 \text{ ppm}}{3} = 11 \text{ ppm}$$

$C_{\text{occ}} = \text{NOAEL} = 34 \text{ ppm}$

*Occupational concentration derived based on NOAEL underlying OEHHA MADL*

OEHHA derived an inhalation MADL of 13 mg/d for toluene, which is protective for developmental effects and accounts for an assumed 50% absorption via inhalation. Donald et al. (1991) summarized the data reviewed to identify a NOAEL of 500 ppm for fetotoxicity from an inhalation study in rats which is the basis for the MADL. The rats were exposed 6 hours/day,
giving an adjusted NOAEL of 125 ppm. Under Proposition 65, a mandatory factor of 1,000 is applied to the NOAEL to derive a MADL, with additional factors used to convert the air concentration to a daily intake in µg/day. Donald et al. (1991) note that if the U.S. EPA guidelines were followed instead, an uncertainty factor of 100 (10 for interspecies and 10 for intraspecies variability) would be applied. In an occupational setting, a value of 10 for the interspecies uncertainty factor would be appropriate. With regard to the intraspecies factor, pregnant women are the target population of concern for developmental toxicants and would potentially be present in the workplace. Thus, an intraspecies factor of 10 may still be appropriate in this case. For the current example, an intraspecies factor of either 3 or 10 is applied. The calculation of \( C_{occ} \) using a total uncertainty factor of 30 or 100 is shown below.

\[
C_{occ} = \frac{125 \text{ ppm}}{30} \times \frac{24}{8} \times \frac{7}{5} = 18 \text{ ppm}
\]

\[
C_{occ} = \frac{125 \text{ ppm}}{100} \times \frac{24}{8} \times \frac{7}{5} = 5 \text{ ppm}
\]

\[
C_{occ} = \frac{125 \text{ ppm}}{100} = 1 \text{ ppm}
\]

**Summary of occupational concentrations derived for toluene**

Occupational concentrations for toluene ranging from 0.3 to 34 ppm were derived, depending on the assessment used as the basis for the derivation, the uncertainty factors applied, and whether or not an adjustment was made for occupational exposure (Table 13). Even the least conservative approach produces an occupational concentration lower than the current PEL of 50 ppm. However, the least conservative value of 34 ppm does not appear to provide sufficient protection for the developmental effects of toluene, based on the range of concentrations (1 to 18 ppm) derived using the OEHHA MADL analysis. ACGIH recently lowered the TLV for toluene to 20 ppm, based on visual impairment, female reproductive system damage, and pregnancy loss. The toluene PEL should be reviewed and adjusted to ensure that it is protective for the neurological, developmental and reproductive effects of toluene.

The estimates of occupational air concentrations presented in Table 13 do not account for potential dermal absorption, which is of concern for toluene. Cal/OSHA and ACGIH both have
skin notations for toluene, as do some other jurisdictions (ACGIH, 2006). Thus, the occupational concentrations derived above may not be sufficiently protective for toluene.

Table 13. Summary of occupational concentrations for toluene derived based on existing OEHHA cREL, U.S. EPA RfC, and OEHHA MADL assessments

<table>
<thead>
<tr>
<th>$C_{oc}$ (ppm)</th>
<th>Basis</th>
<th>Total Uncertainty Factor</th>
<th>Ratio of Cal/OSHA PEL (50 ppm) to $C_{oc}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.3</td>
<td>LOAEL, neurological effects in rats, OEHHA cREL analysis</td>
<td>100</td>
<td>170</td>
</tr>
<tr>
<td>1</td>
<td>LOAEL, neurological effects in rats, OEHHA cREL analysis</td>
<td>30</td>
<td>50</td>
</tr>
<tr>
<td>11</td>
<td>NOAEL, neurological effects in occupational studies, U.S. EPA RfC analysis</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>34</td>
<td>NOAEL, developmental effects in rats, OEHHA MADL analysis; with adjustment for occupational exposure</td>
<td>1</td>
<td>1.5</td>
</tr>
<tr>
<td>18</td>
<td>NOAEL, developmental effects in rats, OEHHA MADL analysis; with adjustment for occupational exposure</td>
<td>30</td>
<td>3</td>
</tr>
<tr>
<td>4</td>
<td>NOAEL, developmental effects in rats, OEHHA MADL analysis; with no adjustment for occupational exposure</td>
<td>30</td>
<td>12.5</td>
</tr>
<tr>
<td>5</td>
<td>NOAEL, developmental effects in rats, OEHHA MADL analysis; with adjustment for occupational exposure</td>
<td>100</td>
<td>10</td>
</tr>
<tr>
<td>1</td>
<td>NOAEL, developmental effects in rats, OEHHA MADL analysis; with no adjustment for occupational exposure</td>
<td>100</td>
<td>50</td>
</tr>
</tbody>
</table>
Derivation of Occupational Air Concentrations for Selected Chronic Toxicants: Example Calculations

Four chronic toxicants were selected to illustrate possible methods for deriving occupational concentrations from existing risk assessments: n-hexane, phthalic anhydride, styrene and xylenes.

**Chronic Toxicant Example 1: n-Hexane**

**Summary of existing values**

- **OEHHA cREL:** 2 ppm (7 mg/m³)  
  Hazard index target: Nervous system
- **U.S. EPA RfC:** 0.2 ppm (0.7 mg/m³)  
  Critical effect: Peripheral neuropathy
- **Cal/OSHA PEL:** 50 ppm (180 mg/m³)  
  PEL basis: Not available. Because the Cal/OSHA PEL is the same as the ACGIH TLV, the basis is assumed to be equivalent.
- **ACGIH TLV:** 50 ppm (180 mg/m³)  
  TLV basis: CNS impairment, peripheral neuropathy, and eye irritation
- **Conversion factor:** 1 ppm = 3.53 mg/m³

**Selection of risk assessment**

Although the OEHHA (2000c) assessment for n-hexane was conducted prior to the U.S. EPA (2005b) assessment, the Huang et al. (1989; as cited by U.S. EPA, 2005b) study used by U.S. EPA as the basis for the RfC was also reviewed by OEHHA. U.S. EPA (2005b) did not review the Miyagaki (1967; as cited by OEHHA, 2000c) study, selected by OEHHA as the basis for the cREL. The Miyagaki study was a chronic study in mice while the Huang et al. study was a subchronic study in rats. Miyagaki studied commercial grade hexane, while Huang et al. studied 99% pure hexane. The Huang et al. study provided sufficient data for a dose-response assessment, which U.S. EPA carried out. For comparison purposes, both the OEHHA cREL and the U.S. EPA RfC assessments were used to derive occupational air concentrations.
**Summary of cREL derivations (adapted from OEHHA, 2000c):**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value/Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Key study</td>
<td>Miyagaki (1967), as cited by OEHHA (2000c)</td>
</tr>
<tr>
<td>Study population</td>
<td>Male mice</td>
</tr>
<tr>
<td>Exposure method</td>
<td>Discontinuous inhalation</td>
</tr>
<tr>
<td>Critical effects</td>
<td>Peripheral neuropathy (electromyographic alterations; dose related abnormal posture and muscle atrophy)</td>
</tr>
<tr>
<td>LOAEL</td>
<td>250 ppm</td>
</tr>
<tr>
<td>NOAEL</td>
<td>100 ppm</td>
</tr>
<tr>
<td>Exposure continuity</td>
<td>24 hours/day, 6 days/week</td>
</tr>
<tr>
<td>Exposure duration</td>
<td>1 year</td>
</tr>
<tr>
<td>Average experimental exposure</td>
<td>57.9 ppm for NOAEL group (100 ppm x 0.675 x 6/7) (adjustment of 0.675 accounts for concentration of n-hexane in commercial grade hexane)</td>
</tr>
<tr>
<td>Human equivalent concentration</td>
<td>57.9 ppm (gas with systemic effects, based on RGDR = 1)</td>
</tr>
<tr>
<td>LOAEL uncertainty factor</td>
<td>1</td>
</tr>
<tr>
<td>Subchronic uncertainty factor</td>
<td>1</td>
</tr>
<tr>
<td>Interspecies uncertainty factor</td>
<td>3</td>
</tr>
<tr>
<td>Intraspecies uncertainty factor</td>
<td>10</td>
</tr>
<tr>
<td>Cumulative uncertainty factor</td>
<td>30</td>
</tr>
<tr>
<td>Inhalation reference exposure level</td>
<td>2 ppm (2000 ppb; 7 mg/m$^3$; 7000 $\mu$g/m$^3$)</td>
</tr>
</tbody>
</table>

OEHHA selected the Miyagaki (1967) study in male mice instead of studies of workers (Sanagi *et al*., 1980; Chang *et al*., 1993; as cited by OEHHA, 2000c), because the worker exposure was confounded by exposures to other chemicals, and would result in RELs that were lower than the one selected by OEHHA. The REL based on the Sanagi *et al*., study was calculated to be 700 $\mu$g/m$^3$ (from a LOAEL of 21 ppm, using a time-weighted average exposure) and based on Chang *et al*. (1993) was 1,000 $\mu$g/m$^3$ (from a LOAEL of 83 ppm, using a time-weighted average exposure).
Summary of U.S. EPA (2005b) RfC assessment adapted from IRIS

<table>
<thead>
<tr>
<th>Critical Effect</th>
<th>Experimental Doses*</th>
<th>UF</th>
<th>RfC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral neuropathy (decreased MCV at 12 weeks)</td>
<td>BMCL: 550 mg/m³</td>
<td>300</td>
<td>7E-1 mg/m³</td>
</tr>
<tr>
<td></td>
<td>BMCL : 430 mg/m³</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rat subchronic inhalation study</td>
<td>BMCL\textsubscript{ADJ}: 215 mg/m³</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Huang \textit{et al}., 1989</td>
<td>BMCL\textsubscript{HEC}: 215 mg/m³</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Conversion Factors and Assumptions (from U.S. EPA, 2005b) -- MW = 86.18. Assuming 25°C and 760 mm Hg, 1 ppm = 86.18/24.45 = 3.52 mg/m³. Duration adjustment of exposure concentrations was employed (12 hours/day, 7 days/week): BMCL\textsubscript{ADJ} = 430 mg/m³ × 12h/24h = 215 mg/m³. The BMCL\textsubscript{HEC} was calculated for an extrarespiratory effect of a category 3 gas. The blood:gas (air) partition coefficient (H\textsubscript{b/g}) value for n-hexane in humans (H) is 0.8 (Perbellini \textit{et al}., 1985) whereas a value of 2.29 has been reported in rats (A) (Gargas \textit{et al}., 1989). According to the RfC methodology (U.S. EPA, 1994), where the ratio of animal to human blood:air partition coefficients \[([H_{b/g}]_A /[H_{b/g}]_H)\] is greater than one, a value of one is used for the ratio by default. Thus, BMCL\textsubscript{HEC} = 215 × \[[H_{b/g}]_A /[H_{b/g}]_H\] = 215 mg/m³.

U.S. EPA applied a total uncertainty factor of 300, which was made up of 10 for intraspecies variation, 3 for interspecies differences, 3 to extrapolate from a less than lifetime study to a chronic exposure, and 3 to account for database deficiencies.

The 3-fold factor for interspecies differences was applied to address residual toxicokinetic and toxicodynamic uncertainties in extrapolating from animals to humans. The 3-fold factor for extrapolating from subchronic to chronic was reduced from 10 based on an analysis of the "time required for a newly synthesized neurofilament protein to be transported from the neuronal cell body to the axon terminal in the longest axons of the central nervous system and the peripheral nervous system of an adult rat," which was determined by U.S. EPA to be 16 weeks. Since the study was 32 weeks long, U.S. EPA did not apply a full factor of 10 for the extrapolation.

U.S. EPA also applied a factor of 3 to account for database uncertainties, because of the "lack of multigeneration reproductive and developmental studies following exposure to pure n-hexane and the uncertainty associated with low-dose developmental effects of exposure to n-hexane." The interspecies factor of 10 was based on U.S. EPA's analysis of potential differences in sensitivity between adults and children to the neurotoxic effects of n-hexane and potential differences in metabolism of n-hexane within the human population in general as well as between adults and children.

\textbf{Adjustment of uncertainty factors}

\textbf{OEHHA assessment}

The LOAEL uncertainty factor, the subchronic uncertainty factor and the interspecies uncertainty factor relate to characteristics of the animal bioassay and of n-hexane, and therefore still apply in an occupational setting. The only uncertainty factor considered for adjustment is the intraspecies
factor. OEHHA commented on the intraspecies uncertainty factor in deriving the cREL for n-hexane as follows: "...human studies (especially that of Chang et al., 1993) have shown that some individuals develop peripheral neuropathy within months, whereas others remain symptom-free despite years of employment at the same occupation at the same workplace." Thus, the intraspecies uncertainty factor is clearly applicable to the occupational setting. An additional concern regarding the sensitivity of workers to n-hexane is that they are likely to be co-exposed to other chemicals, which could potentiate the effects of n-hexane. The possible potentiation of n-hexane's neurological effects by other chemicals was discussed by OEHHA (2000c) in noting that the RELs based on worker exposure are 7 to 10-fold lower than the cREL based on data in mice. Based on the above considerations, an intraspecies uncertainty factor of 10 would still be recommended for workers. For illustration purposes, intraspecies factors of 10 and 3 are used to generate occupational concentrations below.

**U.S. EPA assessment**

The uncertainty factors for interspecies extrapolation (3) and from subchronic to chronic (3) were not adjusted. Based on OEHHA (2000a) guidance, the uncertainty factor of 3 for database deficiencies was dropped. Based on U.S. EPA’s discussion of potential interindividual differences in metabolism, an intraspecies uncertainty factor of 3 was selected. This factor was reduced from 10 because a portion of the factor accounted for differences between adults and children. A total uncertainty factor of 30 (rounded from 27) was applied to the BMCL\(_{\text{HEC}}\) of 215 mg/m\(^3\).

**Calculation of occupational concentrations**

Chronic exposure to n-hexane can result in neurotoxicity. There are two approaches for adjusting exposure to account for an occupational setting. OEHHA and U.S. EPA both assume that workers breathe more heavily during the workday, inhaling 10 m\(^3\) during the 8-hour workday out of 20 m\(^3\) per 24 hours. Another approach, applied by HESIS, has been to account for 8 hours per day at work out of 24 hours total. Both approaches are applied for illustration purposes.

The equations for the occupational concentration are shown below:

**Approach 1:**

\[
C_{\text{occ}} = \frac{\text{NOAEL}_{\text{HEC}} \text{ or BMCL}_{\text{HEC}}}{\text{UF}_{\text{adj}}} \times \frac{24}{8} \times \frac{7}{5}
\]

**Approach 2:**

\[
C_{\text{occ}} = \frac{\text{NOAEL}_{\text{HEC}} \text{ or BMCL}_{\text{HEC}}}{\text{UF}_{\text{adj}}} \times \frac{20}{10} \times \frac{7}{5}
\]
The NOAEL and BMCL are expressed as human equivalent air concentrations in mg/m³.

The results using the different options for the total uncertainty factor, the two approaches for adjusting for occupational exposure, and using either the OEHHA cREL or the U.S. EPA RfC are summarized in Tables 14 and 15 below.

### Table 14. Occupational concentrations for n-hexane based on OEHHA cREL assessment

<table>
<thead>
<tr>
<th>NOAEL HEC (mg/m³)</th>
<th>Exposure Factor</th>
<th>UFₐdj</th>
<th>Cₐocc (mg/m³)</th>
<th>Cₐocc (ppm)</th>
<th>Ratio of Cal/OSHA PEL (50 ppm) to Cₐocc</th>
</tr>
</thead>
<tbody>
<tr>
<td>204</td>
<td>( \frac{24}{8} \times \frac{7}{5} )</td>
<td>30</td>
<td>28.6</td>
<td>8</td>
<td>6</td>
</tr>
<tr>
<td>204</td>
<td>( \frac{24}{8} \times \frac{7}{5} )</td>
<td>(10^b)</td>
<td>85.7</td>
<td>24</td>
<td>2</td>
</tr>
<tr>
<td>204</td>
<td>( \frac{20}{10} \times \frac{7}{5} )</td>
<td>10</td>
<td>19.0</td>
<td>5</td>
<td>9</td>
</tr>
<tr>
<td>204</td>
<td>( \frac{20}{10} \times \frac{7}{5} )</td>
<td>10</td>
<td>57.1</td>
<td>16</td>
<td>3</td>
</tr>
</tbody>
</table>

*a. NOAEL HEC of 57.9 ppm was converted to mg/m³ using the conversion factor 3.53 mg/m³/ppm.
b. The total uncertainty factor of 3 x 3 was rounded to 10 as discussed in the methods section.

### Table 15. Occupational concentrations for n-hexane based on U.S. EPA RfC assessment

<table>
<thead>
<tr>
<th>BMCL HEC (mg/m³)</th>
<th>Exposure Factor</th>
<th>UFₐdj</th>
<th>Cₐocc (mg/m³)</th>
<th>Cₐocc (ppm)</th>
<th>Ratio of Cal/OSHA PEL (50 ppm) to Cₐocc</th>
</tr>
</thead>
<tbody>
<tr>
<td>215</td>
<td>( \frac{24}{8} \times \frac{7}{5} )</td>
<td>30</td>
<td>30.1</td>
<td>9</td>
<td>6</td>
</tr>
<tr>
<td>215</td>
<td>( \frac{20}{10} \times \frac{7}{5} )</td>
<td>30</td>
<td>20.1</td>
<td>6</td>
<td>8</td>
</tr>
</tbody>
</table>

The occupational air concentrations based on the OEHHA assessment range from approximately 5 to 24 ppm, depending on the total uncertainty factor and the exposure scenario. The results based on the U.S. EPA assessment are within the same range. Even if the least conservative approach is applied, generating an occupational air concentration of 24 ppm, this is less than half the current PEL of 50 ppm. Review of the n-hexane PEL is recommended.
The estimates of occupational air concentrations presented above do not account for potential dermal absorption, which is of concern for n-hexane. Cal/OSHA and ACGIH have skin notations for n-hexane, as do some other jurisdictions (ACGIH, 2006).
**Chronic Toxicant Example 2: Phthalic anhydride**

*Summary of existing values*

OEHHA cREL: 0.003 ppm (0.02 mg/m³)  
Hazard index target: Respiratory system

U.S. EPA RfC (not available)

Cal/OSHA PEL: 1 ppm (6 mg/m³)  
PEL basis: Not available. Because the Cal/OSHA PEL is the same as the ACGIH TLV, the basis is assumed to be equivalent.

ACGIH TLV: 1 ppm (6 mg/m³)  
TLV basis: Upper respiratory tract, eye and skin irritation (ACGIH, 2006). Also identified as a sensitizer.

Conversion factor: 1 ppm = 6.06 mg/m³

*Selection of risk assessment*

U.S. EPA (1988) conducted an assessment of the oral route of exposure for phthalic anhydride, but has not evaluated inhalation exposures. The OEHHA (2000d) assessment was selected as most appropriate.

*Summary of cREL derivation (adapted from OEHHA, 2000d):*

<table>
<thead>
<tr>
<th>Study</th>
<th>Nielsen et al. (1988; 1991, as cited by OEHHA, 2000d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study population</td>
<td>23 occupationally exposed workers</td>
</tr>
<tr>
<td>Exposure method</td>
<td>Discontinuous occupational inhalation exposures</td>
</tr>
<tr>
<td>Critical effects</td>
<td>Increased incidence of conjunctivitis, rhinitis, asthma, and chronic bronchitis</td>
</tr>
<tr>
<td>LOAEL</td>
<td>6.5 mg/m³ (mean of 6.1 and 6.8)</td>
</tr>
<tr>
<td>NOAEL</td>
<td>Not observed</td>
</tr>
<tr>
<td>Exposure continuity</td>
<td>8 hours/day, 5 days/week</td>
</tr>
<tr>
<td>Exposure duration</td>
<td>Mean of 13.3 years</td>
</tr>
<tr>
<td>Average experimental exposure</td>
<td>2.3 mg/m³ for LOAEL group (6.5 mg/m³ × 10/20 × 5/7)</td>
</tr>
<tr>
<td>LOAEL uncertainty factor</td>
<td>10</td>
</tr>
<tr>
<td>Subchronic uncertainty factor</td>
<td>1</td>
</tr>
<tr>
<td>Interspecies uncertainty factor</td>
<td>1</td>
</tr>
<tr>
<td>Intraspecies uncertainty factor</td>
<td>10</td>
</tr>
<tr>
<td>Cumulative uncertainty factor</td>
<td>100</td>
</tr>
<tr>
<td>Inhalation reference exposure level</td>
<td>0.02 mg/m³ (20 μg/m³)</td>
</tr>
</tbody>
</table>

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**OEHHA**
OEHHA (2000d) discussed the strengths and weaknesses of the cREL and the selection of the Nielsen \textit{et al.} study: "The strengths of the inhalation REL for phthalic anhydride include the use of human exposure data from workers exposed over a period of years. Major areas of uncertainty are (1) the uncertainty in estimating exposure, (2) the potential variability in exposure concentration, (3) potential low exposures of the group considered as controls, (4) potential confounding by exposures to other chemicals, (5) the limited nature of the study, (6) the lack of reproductive and developmental toxicity studies, and (6) the lack of observation of a NOAEL in the key study. Another area of uncertainty is the apparent 10-fold greater sensitivity to bronchoconstriction from PA [phthalic anhydride] exposure in guinea pigs (a model for human asthmatics) in comparison to occupationally exposed workers. The study in rats by Protsenko (1970) identified a LOAEL of 0.2 mg/m$^3$ and a NOAEL of 0.02 mg/m$^3$ for decreased sperm motility. However, this result from 1970 has not been verified or further explored in more recent toxicological or epidemiological studies. The small sample size of 6/group further weakens confidence in this result. Therefore, the study in workers by Nielsen \textit{et al.} (1988, 1991) was chosen as the basis for the REL for PA."

\textit{Adjustment of uncertainty factors}

The cREL is based on a LOAEL identified in workers. The only uncertainty factor (UF) considered for adjustment is the intraspecies factor. OEHHA (2000d) applied the default factor of 10 in this assessment. For illustration purposes, intraspecies factors of 10, 3 and 1 were used to derive occupational concentrations for phthalic anhydride below.

\textit{Calculation of occupational concentration}

The exposure data from the Nielsen \textit{et al.} study was summarized by OEHHA as follows: "Time-weighted average air concentrations for workers from the loading of PA was 6.1 (range: 1.8-14.9) and 6.8 mg PA/m$^3$ (range: 1.5-17.4) in plants A and B, respectively. Similar exposure levels in both plants led to pooling of data. The exposure duration of the "heavy" group was estimated at approximately 30 minutes two times a day, corresponding to the time of loading, and resulted in a full-day time weighted exposure estimate of 0.4 mg PA/m$^3$." Based on these data, OEHHA estimated an average air concentration of 6.5 mg/m$^3$ (the average of 6.1 and 6.8 mg/m$^3$ from the two plants) for the exposed workers. OEHHA applied a default approach for adjusting discontinuous occupational exposures to continuous exposures (relevant for community residents) and derived an "average experimental exposure" (shown as LOAEL$_{adj}$ in the equation below) of 2.3 mg/m$^3$:

$$\text{LOAEL}_{adj} = 6.5 \text{ mg/m}^3 \times \frac{10 \text{ m}^3/\text{d}}{20 \text{ m}^3/\text{d}} \times \frac{5 \text{ d}}{7 \text{ d}} = 2.3 \text{ mg/m}^3$$

This approach assumes that workers were exposed to phthalic anhydride at a level of 6.5 mg/m$^3$ for the entire 8-hour workday, with a breathing rate of 10 m$^3$ during the workday out of a total of 20 m$^3$/day and a workweek of 5 days. The default adjustment for continuous exposure that OEHHA applied in the assessment of community residents is not required for an occupational risk assessment. For the occupational assessment, the LOAEL of 6.5 mg/m$^3$ could be taken.
directly, or the time-weighted average exposure concentration of 0.4 mg/m³ over the workday reported by Nielsen et al. could be used. For illustration purposes, both measures of the LOAEL for workers are used to derive occupational concentrations. Table 16 summarizes the possible values for the occupational concentration, depending on which total UF (which varies with the selection of the interspecies factor) and which LOAEL are selected.

Table 16. Occupational concentrations for phthalic anhydride based on an existing OEHHA risk assessment

<table>
<thead>
<tr>
<th>LOAEL (mg/m³)</th>
<th>UF&lt;sub&gt;adj&lt;/sub&gt;</th>
<th>C&lt;sub&gt;occ&lt;/sub&gt; (mg/m³)</th>
<th>C&lt;sub&gt;occ&lt;/sub&gt; (ppm)</th>
<th>Ratio of Cal/OSHA PEL (1 ppm) to C&lt;sub&gt;occ&lt;/sub&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.5</td>
<td>10</td>
<td>0.65</td>
<td>0.1</td>
<td>10</td>
</tr>
<tr>
<td>6.5</td>
<td>30</td>
<td>0.22</td>
<td>0.04</td>
<td>25</td>
</tr>
<tr>
<td>6.5</td>
<td>100</td>
<td>0.065</td>
<td>0.01</td>
<td>100</td>
</tr>
<tr>
<td>0.4</td>
<td>10</td>
<td>0.04</td>
<td>0.007</td>
<td>140</td>
</tr>
<tr>
<td>0.4</td>
<td>30</td>
<td>0.013</td>
<td>0.002</td>
<td>500</td>
</tr>
<tr>
<td>0.4</td>
<td>100</td>
<td>0.004</td>
<td>0.0007</td>
<td>1400</td>
</tr>
</tbody>
</table>

a. Since this study was in workers, the LOAEL can be taken directly from the study, and no adjustment for an occupational exposure scenario is necessary.

The calculated occupational concentrations range from a low of 0.0007 ppm to a high of 0.1 ppm. Even the least conservative value of 0.1 ppm is a factor of 10 lower than the current Cal/OSHA PEL of 1 ppm.

ACGIH (2006) indicates in the phthalic anhydride documentation (updated in 2001) that the TLV of 1 ppm is "intended to reduce the potential for dermal, ocular, and respiratory tract irritation as evidenced in experimental animal studies and workers exposed at approximately 2 to 5 ppm." However, ACGIH did not review the studies by Nielsen et al. in setting the TLV. The TLV, and therefore the current PEL, is actually set close to the LOAEL in workers for respiratory toxicity of 6.5 mg/m³ (expressed as the average air concentration during direct exposure to phthalic anhydride) or more than 10 times higher than the LOAEL of 0.4 mg/m³ (expressed as the time-weighted average of the air concentration during the work day). Further, OEHHA (2000d) discussed data that may support an even lower air concentration for protection of male reproductive toxicity. The phthalic anhydride PEL should be reviewed.
Chronic Toxicant Example 3: Styrene

Summary of existing values

<table>
<thead>
<tr>
<th>Source</th>
<th>Value</th>
<th>Unit</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>OEHHA cREL</td>
<td>0.2 ppm (0.9 mg/m³)</td>
<td></td>
<td>Hazard index target: Nervous system</td>
</tr>
<tr>
<td>U.S. EPA RfC</td>
<td>0.23 ppm (1 mg/m³)</td>
<td></td>
<td>Critical effect: CNS effects</td>
</tr>
<tr>
<td>Cal/OSHA PEL</td>
<td>50 ppm (215 mg/m³)</td>
<td></td>
<td>PEL basis: Not available.</td>
</tr>
<tr>
<td>ACGIH TLV</td>
<td>20 ppm (85 mg/m³)</td>
<td></td>
<td>TLV basis: CNS impairment, URT irritation, peripheral neuropathy</td>
</tr>
</tbody>
</table>

Conversion factor: 1 ppm = 4.26 mg/m³

Selection of assessment

The assessments by OEHHA (2000e) and U.S. EPA (1993) are nearly identical, producing a health assessment value of 0.2 ppm based on neurological effects using the same study (Mutti et al., 1984). OEHHA used a benchmark concentration approach, while U.S. EPA applied uncertainty factors to an estimated NOAEL. The OEHHA assessment is chosen for further analysis.

Summary of cREL derivation (adapted from OEHHA, 2000e):

<table>
<thead>
<tr>
<th>Study</th>
<th>Mutti et al. (1984) (as cited by OEHHA, 2000e)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study population</td>
<td>Human (occupational)</td>
</tr>
<tr>
<td>Exposure method</td>
<td>Inhalation</td>
</tr>
<tr>
<td>Critical effect</td>
<td>Central nervous system</td>
</tr>
<tr>
<td>LOAEL</td>
<td>15 ppm</td>
</tr>
<tr>
<td>NOAEL</td>
<td>Not established</td>
</tr>
<tr>
<td>BMC05</td>
<td>1.7 ppm</td>
</tr>
<tr>
<td>Exposure continuity</td>
<td>8 hr/d (10 m³ per 20 m³ day), 5 d/wk</td>
</tr>
<tr>
<td>Exposure duration</td>
<td>8.6 years (average years at work)</td>
</tr>
<tr>
<td>Average occupational exposure</td>
<td>0.61 ppm (1.7 x 10/20 x 5/7)</td>
</tr>
<tr>
<td>Human equivalent concentration</td>
<td>0.61 ppm</td>
</tr>
<tr>
<td>LOAEL uncertainty factor</td>
<td>Not needed in the BMC approach</td>
</tr>
<tr>
<td>Subchronic uncertainty factor</td>
<td>1 (average exposure 12.3% of lifetime)</td>
</tr>
<tr>
<td>Interspecies uncertainty factor</td>
<td>1</td>
</tr>
<tr>
<td>Intraspecies uncertainty factor</td>
<td>3</td>
</tr>
<tr>
<td>Cumulative uncertainty factor</td>
<td>3</td>
</tr>
<tr>
<td>Inhalation reference exposure level</td>
<td>0.2 ppm (200 ppb; 0.9 mg/m³; 900 μg/m³)</td>
</tr>
</tbody>
</table>
The cREL derivation was based on a well-conducted occupational study, which OEHHA used to conduct a dose-response analysis. The BMC$_{05}$ of 1.7 ppm is the lower 95% confidence limit on the concentration that would produce a 5% incidence. OEHHA also estimated the MLE for a 5% response, which was 4 ppm. This cREL assessment is ideal for application to the occupational setting.

**Adjustment of uncertainty factors**

The only uncertainty factor applied in this case was the intraspecies factor of 3. OEHHA applied this factor to the BMC$_{05}$ derived based on a population of healthy human subjects in order to ensure that the cREL will be protective for the "vast majority of individuals." Because the BMC$_{05}$ was derived based on a well-conducted study of workers, the target population of interest, the intraspecies factor of 3 may not be needed. Calculations of the occupational concentration were carried out using intraspecies factors of 1 and 3.

**Calculation of occupational concentration**

The BMC$_{05}$ of 1.7 ppm was estimated using a well-conducted occupational study, and can therefore be taken directly with no adjustment for occupational exposure. The BMC$_{05}$ was divided by a total uncertainty factor of 1 or 3 to derive occupational concentrations, as shown in Table 17:

**Table 17. Occupational concentrations for styrene based on an existing OEHHA risk assessment**

<table>
<thead>
<tr>
<th>BMC$_{05}$ (ppm)</th>
<th>Total UF</th>
<th>$C_{occ}$ (ppm)</th>
<th>Ratio of Cal/OSHA PEL (50 ppm) to $C_{occ}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.7</td>
<td>3</td>
<td>0.6</td>
<td>80</td>
</tr>
<tr>
<td>1.7</td>
<td>1</td>
<td>2</td>
<td>25</td>
</tr>
</tbody>
</table>

Even using the least conservative approach, the occupational concentration estimated to protect for the neurological effects of styrene is 2 ppm, which a factor of 25 lower than the current Cal/OSHA PEL of 50 ppm. Further, the PEL of 50 ppm is set more than 3 times higher than the LOAEL of 15 ppm observed in workers in the Mutti *et al.* study. Review of the styrene PEL is recommended.

The estimates of occupational air concentrations presented above do not account for potential dermal absorption, which is of concern for styrene. Cal/OSHA has a skin notation for styrene, as do some other jurisdictions (ACGIH, 2006).
Chronic Toxicant Example 4: Xylenes (m-, o-, p-)

Summary of existing values

<table>
<thead>
<tr>
<th>Source</th>
<th>cREL (ppm)</th>
<th>Hazard index target:</th>
<th>Critical effect:</th>
</tr>
</thead>
<tbody>
<tr>
<td>OEHHA</td>
<td>0.2 ppm (7 mg/m$^3$)</td>
<td>Nervous system; respiratory system</td>
<td></td>
</tr>
<tr>
<td>U.S. EPA</td>
<td>0.02 ppm (0.1 mg/m$^3$)</td>
<td></td>
<td>Impaired motor coordination</td>
</tr>
<tr>
<td>Cal/OSHA PEL</td>
<td>100 ppm (435 mg/m$^3$)</td>
<td>PEL basis: Not available. Because the Cal/OSHA PEL is the same as the ACGIH TLV, the basis is assumed to be equivalent.</td>
<td></td>
</tr>
<tr>
<td>ACGIH TLV</td>
<td>100 ppm (435 mg/m$^3$)</td>
<td>TLV basis: Upper respiratory tract and eye irritation; CNS impairment</td>
<td></td>
</tr>
</tbody>
</table>

Conversion factor: 1 ppm = 4.34 mg/m$^3$

Selection of assessment

The OEHHA (2000f) cREL was based on a study in workers, while the U.S. EPA (2003b) RfC was based on a subchronic inhalation study in rats. The OEHHA assessment is considered more relevant to the occupational setting and was selected for further analysis.

Summary of cREL derivation (adapted from OEHHA, 2000f):

<table>
<thead>
<tr>
<th>Study</th>
<th>Uchida et al. (1993) (as cited by OEHHA, 2000f)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study population</td>
<td>175 xylene-exposed factory workers and control population of 241 factory workers</td>
</tr>
<tr>
<td>Exposure method</td>
<td>Inhalation</td>
</tr>
<tr>
<td>Critical effects</td>
<td>Dose related increase in the prevalence of eye irritation, sore throat, floating sensation, and poor appetite.</td>
</tr>
<tr>
<td>LOAEL</td>
<td>14.2 ppm (geometric mean)</td>
</tr>
<tr>
<td>NOAEL</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Exposure continuity</td>
<td>8 hr/d (10 m$^3$/day inhalation rate), 5 d/wk</td>
</tr>
<tr>
<td>Exposure duration</td>
<td>Occupational exposure for 7 years (average)</td>
</tr>
<tr>
<td>Average occupational exposure</td>
<td>5.1 ppm for LOAEL group (14.2 x 10/20 x 5/7)</td>
</tr>
<tr>
<td>Human equivalent concentration</td>
<td>5.1 ppm for LOAEL group</td>
</tr>
<tr>
<td>LOAEL uncertainty factor</td>
<td>3</td>
</tr>
<tr>
<td>Subchronic uncertainty factor</td>
<td>1</td>
</tr>
<tr>
<td>Interspecies uncertainty factor</td>
<td>1</td>
</tr>
<tr>
<td>Intraspecies uncertainty factor</td>
<td>10</td>
</tr>
<tr>
<td>Cumulative uncertainty factor</td>
<td>30</td>
</tr>
<tr>
<td>Inhalation reference exposure level</td>
<td>0.2 ppm (200 ppb; 0.7 mg/m$^3$; 700 μg/m$^3$) for mixed xylenes or for total of individual isomers</td>
</tr>
</tbody>
</table>
OEHHA discussed the strengths and weaknesses of the cREL: "The strengths of the inhalation
REL for xylene include the use of human exposure data from 175 workers exposed over a period
of years. Major areas of uncertainty are the uncertainty in estimating exposure, the potential
variability in exposure concentration, and the lack of observation of a NOAEL in the key study."

Adjustment of uncertainty factors

OEHHA (2000f) discussed the choice of a LOAEL uncertainty factor of 3 instead of 10 as
follows: "A UF of 3, rather than 10, was applied for the LOAEL to NOAEL extrapolation due to
the generally mild adverse effects observed and the principally low incidence (<50%) of the
effects.” OEHHA selected a subchronic uncertainty factor of 1, although the mean exposure
duration for the workers was 7 years (less than 12.3% of lifetime), explaining this decision as
follows: "A factor of 1 was used for subchronic uncertainty. Although the average occupational
exposure was only 7 years, there were 176 xylene-exposed workers of average age 29.7 ± 9.0
years (arithmetic mean ± SD) for whom, according to the report, there had been essentially no
change in workplace in their working life. Thus, many workers would likely have been exposed
for more than 8.4 years, the cut-off point for chronic human exposure."

The only uncertainty factor considered for adjustment is the intraspecies factor. OEHHA applied
a default intraspecies factor of 10. For the example of xylenes, an intraspecies factor of 1, 3 or
10 was used to derive occupational concentrations below. With the LOAEL uncertainty factor of
3, the total uncertainty factors used were 3, 10 or 30.

Calculation of occupational concentration

The LOAEL was based on an occupational study, so no adjustment for occupational exposure
was required. A total UF of 3, 10 or 30 was applied to derive occupational concentrations
summarized in Table 18.

Table 18. Occupational concentrations for xylenes based on an existing OEHHA risk
assessment

<table>
<thead>
<tr>
<th>LOAEL (ppm)</th>
<th>$U_{\text{adj}}$</th>
<th>$C_{\text{occ}}$ (ppm)</th>
<th>Ratio of Cal/OSHA PEL (100 ppm) to $C_{\text{occ}}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>14.2</td>
<td>3</td>
<td>5</td>
<td>20</td>
</tr>
<tr>
<td>14.2</td>
<td>10</td>
<td>1</td>
<td>100</td>
</tr>
<tr>
<td>14.2</td>
<td>30</td>
<td>0.5</td>
<td>200</td>
</tr>
</tbody>
</table>

Even using the least conservative approach, the occupational concentration estimated to protect
for the neurological and respiratory effects of xylenes is approximately 5 ppm, which is a factor
of 20 lower than the current Cal/OSHA PEL of 100 ppm. Further, the LOAEL for neurological
and respiratory effects in workers of 14.2 ppm is a factor of 7 lower than the current PEL, even
without the application of any uncertainty factor.
The ACGIH documentation for the TLV for xylenes (dated 2001; included in ACGIH, 2006) did not review the Uchida (1993) study, which was the basis for the cREL. In selecting a TLV of 100 ppm (equivalent to the current PEL), ACGIH cites studies from human volunteers rather than chronic occupational studies: "Controlled studies in volunteers\(^{(107)}\) inhaling 64 to 150 ppm or up to 300 to 400 ppm\(^{(108, 109)}\) have failed to show any evidence for neurologic impairment. There was no concentration-response relationship between eyes closed:eyes open ratio for volunteers exposed at 64 to 400 ppm xylene\(^{(93)}\). Human volunteers exposed at 200 ppm xylene for 3 to 5 minutes complained of ocular and upper respiratory tract irritation\(^{(1)}\). A concentration of 100 ppm for 8 hours was considered a satisfactory air concentration\(^{(86)}\). The final reference cited to justify the 100 ppm TLV was from 1943 (86; Nelson et al.). The TLV of 100 ppm has not changed since 1967. Review of the current PEL for xylenes is recommended.

The above values do not account for potential dermal absorption, which has been noted as a concern for xylenes by some jurisdictions (ACGIH, 2006).
Summary of Key Results

Workplace chemicals listed as known to the state to cause cancer under Proposition 65 that may pose risks to workers

A key goal of the project was to identify chemicals listed under Proposition 65 that may pose concerns to workers because no PEL has been established or the existing PEL is based on an endpoint other than cancer. Table 19 summarizes 106 workplace chemicals that are not regulated specifically as occupational carcinogens under Cal/OSHA. Of these, 62 of the chemicals have Cal/OSHA PELs (noted by a “✓”). The basis for the Cal/OSHA PEL is provided if it was available from online sources described above. If the basis for the PEL was not available, Table 19 lists possible sources for the PEL, with the inferred basis, as determined from these other sources (e.g., ACGIH [2006], OSHA [1989]), also provided. If a unit risk value was identified from any source, that is indicated by a “✓.” The range of cancer risks as determined based on calculations using OEHHA or U.S. EPA unit risk values is also listed (see Table 6 for more details). If a unit risk value was available from some source but a calculation of the estimated cancer cases at the PEL was not done for that chemical, for example because the unit risk is a draft or provisional value, that is indicated by a double dash (“--”).

The shading in the table indicates either that no information exists, or that the information is not relevant. For example, if a chemical has no available PEL or unit risk value, the entire row is shaded. If a chemical has a Cal/OSHA PEL and the basis for the PEL was available based on Cal/OSHA documentation, then the cells for other possible sources for the PELs are shaded, as those are not relevant for this case. In this way, the table can be quickly scanned to assess the highest priorities for PEL reevaluation and where information is lacking.

Some key findings regarding workplace chemicals known to cause cancer under Proposition 65 include:

- One hundred and six workplace chemicals listed as known to cause cancer under Proposition 65 are of potential concern for workers because they are not specifically regulated as occupational carcinogens. The designation of a workplace chemical as a carcinogenic substance triggers strict protective standards to protect workers who handle those substances. These 106 substances listed by the state as causing cancer under Proposition 65 are not currently regulated as carcinogenic substances in the workplace.

- Sixty-two of the 106 chemicals in Table 19 have Cal/OSHA PELs, but are not specifically regulated as occupational carcinogens. Of these 62 chemicals, cancer was cited as the basis for the PEL or was noted as a health endpoint of concern for seven, and may have been considered for an additional 12. The notation of cancer in the PEL basis does not trigger the stringent standards required for occupational carcinogens noted above.
For six of the seven chemicals having a PEL basis that relied on or mentioned cancer, but that are not regulated as occupational carcinogens, quantitative risk estimates are available (Table 6). The risk estimates, based on OEHHA or U.S. EPA unit risk values, range over three orders of magnitude, from 0.03 to 45 per 1,000. The cancer risk associated with the PEL was estimated to be below 1 in 1,000 for two of these six chemicals, epichlorohydrin and hexachlorobenzene.

Cancer risk estimates are available for ten of the additional 12 chemicals with Cal/OSHA PELs that may have been intended to address carcinogenic effects, although these chemicals are not currently regulated as occupational carcinogens. The risk estimates, based on OEHHA or U.S. EPA unit risk values, range over three orders of magnitude, from 0.2 to 500 per 1,000. The cancer risk associated with the PEL was below 1 in 1,000 for one of these ten chemicals, nickel carbonyl.

Cancer risk estimates are available for 22 Cal/OSHA PELs that are based on effects other than cancer or have an unknown basis and ranged over four orders of magnitude, from 0.06 to 990. The cancer risk at the PEL was below 1 in 1,000 for four of these chemicals.

Unit risk values are available from at least one source for 79 of the 106 chemicals in Table 19, making development of health-based occupational concentrations associated with specific risk levels relatively straightforward for those chemicals (examples of deriving health-based concentrations are provided in the current document; see Table 10).

Dermal exposure is of potential concern for approximately 40% of the chemicals in Table 19 (not all of the chemicals in Table 19 were evaluated for skin absorption).

Of the 106 chemicals in Table 19, more than 60% are used as chemical or dye intermediates which are likely to be used in closed systems, minimizing worker exposure. However, as discussed above, worker exposure can still occur with closed systems and about half of the chemical intermediates have alternative uses that may pose more of an exposure concern.

About 20% of the 106 chemicals in Table 19 are used as solvents, which are likely to be of concern for worker exposure.

More than half of the substances in Table 19 are high production volume chemicals (>1 million pounds produced and/or imported annually) (see Tables A-1 and A-2).

The Proposition 65 list was screened using a crude surrogate for exposure, i.e., production and/or import volume in 2002, to identify workplace chemicals. If
better data become available on the industrial chemicals in use in California, the Proposition 65 list should be re-screened.

- Table 19 does not include drugs or pesticides, some of which may pose occupational health concerns.
Table 19. Summary of workplace chemicals listed as known to cause cancer under Proposition 65 that are not regulated as occupational carcinogens: Cal/OSHA PEL basis and unit risk value availability

<table>
<thead>
<tr>
<th>Chemical</th>
<th>Cal/OSHA PEL in regulation</th>
<th>Basis for Cal/OSHA PEL</th>
<th>Possible sources for Cal/OSHA PEL</th>
<th>Unit risk value available</th>
<th>Estimated cancer cases per 1,000 workers exposed at the current PEL (range from Table 6)&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Acetamide</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 Acetaldehyde</td>
<td>✓</td>
<td>Mucous membrane irritation</td>
<td></td>
<td>✓</td>
<td>13-16</td>
</tr>
<tr>
<td>3 p-Aminoaazobenzene</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 Aniline</td>
<td>✓</td>
<td>Methemoglobinemia</td>
<td>Methemoglobinemia</td>
<td>✓</td>
<td>2</td>
</tr>
<tr>
<td>5 o-Anisidine</td>
<td>✓</td>
<td>Methemoglobinemia</td>
<td></td>
<td>✓</td>
<td>3</td>
</tr>
<tr>
<td>7 Antimony oxide</td>
<td>✓</td>
<td>Skin &amp; URT irritation</td>
<td></td>
<td>b</td>
<td>--</td>
</tr>
<tr>
<td>8 Benzofuran</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9 Benzotrichloride</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10 Benzyl chloride</td>
<td>✓</td>
<td>Eye, skin &amp; URT irritation</td>
<td></td>
<td>✓</td>
<td>32</td>
</tr>
<tr>
<td>11 Beryllium &amp; beryllium</td>
<td>✓</td>
<td>Sensitization and beryllium disease</td>
<td></td>
<td></td>
<td>0.06</td>
</tr>
<tr>
<td>compounds</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15 Carbon black (airborne,</td>
<td>✓</td>
<td>Liver damage, CNS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>unbound particles of</td>
<td></td>
<td>impairment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>respirable size)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16 Carbon tetrachloride</td>
<td>✓</td>
<td>Eye &amp; URT irritation; dermatitis</td>
<td></td>
<td>✓</td>
<td>25-69</td>
</tr>
<tr>
<td>17 Catechol</td>
<td>✓</td>
<td>Eye &amp; URT irritation; dermatitis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18 Ceramic fibers (airborne</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>particles of respirable size)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>19 Chlorendic acid</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chemical</td>
<td>Cal/OSHA PEL in regulation</td>
<td>Basis for Cal/OSHA PEL</td>
<td>Possible sources for Cal/OSHA PEL</td>
<td>Unit risk value available</td>
<td>Estimated cancer cases per 1,000 workers exposed at the current PEL (range from Table 6)</td>
</tr>
<tr>
<td>----------</td>
<td>---------------------------</td>
<td>------------------------</td>
<td>---------------------------------</td>
<td>--------------------------</td>
<td>----------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>20 Chlorinated paraffins (average chain length, C12; approximately 60% chlorine by weight)</td>
<td>✓</td>
<td>Tumor formation in several animal species</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>21 p-Chloroaniline</td>
<td>✓</td>
<td>Cancers; QRA</td>
<td>✓</td>
<td>45</td>
<td></td>
</tr>
<tr>
<td>22 Chloroethane</td>
<td>✓</td>
<td>Tumor formation in several animal species</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>23 Chloroform</td>
<td>✓</td>
<td>Cancer; QRA</td>
<td>✓</td>
<td>7-29</td>
<td></td>
</tr>
<tr>
<td>24 1-Chloro-2-methylpropene</td>
<td>✓</td>
<td>Tumor formation in several animal species</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>25 1-Chloro-4-nitrobenzene</td>
<td>✓</td>
<td>Methemoglobinemia</td>
<td>Methemoglobinemia, spleen, liver and kidney damage</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>26 Chloroprene</td>
<td>✓</td>
<td>URT &amp; eye irritation</td>
<td>Reproductive and systemic effects</td>
<td>f</td>
<td></td>
</tr>
<tr>
<td>27 C.I. Direct Blue 15</td>
<td>✓</td>
<td>Control myocardial effects</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>28 C.I. Direct Blue 218</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>29 Cobalt and certain cobalt compounds</td>
<td>✓</td>
<td>Control myocardial effects</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30 p-Cresidine</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>31 Cupferron</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>32 D&amp;C Orange No. 17</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>33 D&amp;C Red No. 9</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>34 D&amp;C Red No. 19</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>35 4,4’-Diaminodiphenyl ether</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>36 2,4-Diaminotoluene; diaminotoluene (mixed)</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>37 Dichloroacetic acid</td>
<td>✓</td>
<td>Control renal toxicity &amp; eye irritation</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>38 p-Dichlorobenzene</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Possible sources for Cal/OSHA PEL:
- ACGIH (2006)
- OSHA (1989)
<table>
<thead>
<tr>
<th>Chemical</th>
<th>Cal/OSHA PEL in regulation</th>
<th>Basis for Cal/OSHA PEL</th>
<th>Possible sources for Cal/OSHA PEL</th>
<th>Unit risk value available</th>
<th>Estimated cancer cases per 1,000 workers exposed at the current PEL (range from Table 6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>39 1,4-Dichloro-2-butene</td>
<td>✓</td>
<td>Hematological changes and effects on the epithelium in rats</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>40 1,1-Dichloroethane</td>
<td>✓</td>
<td>URT &amp; eye irritation; liver &amp; kidney damage</td>
<td></td>
<td>✓</td>
<td>84</td>
</tr>
<tr>
<td>41 1,2-Dichloropropane</td>
<td>✓</td>
<td>Likely based on earlier TLV; health effect basis not known</td>
<td></td>
<td>✓</td>
<td>370-620</td>
</tr>
<tr>
<td>42 Diesel engine exhaust</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>43 Di(2-ethylhexyl)phthalate</td>
<td>✓</td>
<td>LRT irritation</td>
<td>Neuropathic, hepatic and other systemic toxicity</td>
<td>✓</td>
<td>0.4</td>
</tr>
<tr>
<td>44 Diethyl sulfate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>45 Diglycidyl resorcinol ether</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>46 Dihyrosafrole</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>47 3,3'-Dimethoxybenzidine dihydrochloride</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>48 1,1-Dimethylhydrazine</td>
<td>✓</td>
<td>Slight increase in nasal tumors in rats</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>49 Dimethyl sulfate</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>50 2,4-Dinitrotoluene; 2,6-dinitrotoluene; dinitrotoluene mixture, 2,4,2,6- (See footnote g)</td>
<td>✓</td>
<td>Cardiac impairment; reproductive effects</td>
<td></td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>51 1,4-Dioxane</td>
<td>✓</td>
<td>Likely based on earlier TLV; health effect basis not known</td>
<td>Kidney, liver damage, cancer</td>
<td>✓</td>
<td>91</td>
</tr>
<tr>
<td>Chemical</td>
<td>Cal/OSHA PEL in regulation</td>
<td>Basis for Cal/OSHA PEL</td>
<td>Possible sources for Cal/OSHA PEL</td>
<td>Unit risk value available</td>
<td>Estimated cancer cases per 1,000 workers exposed at the current PEL (range from Table 6)</td>
</tr>
<tr>
<td>---------------------------</td>
<td>-----------------------------</td>
<td>--------------------------------------------------------------------------------------</td>
<td>----------------------------------</td>
<td>---------------------------</td>
<td>----------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Epichlorohydrin</td>
<td>✓</td>
<td>Control reproductive and respiratory effects and the possibility of carcinogenic effects</td>
<td></td>
<td></td>
<td>0.03-0.6</td>
</tr>
<tr>
<td>Ethyl acrylate</td>
<td>✓</td>
<td>URT &amp; GI tract irritation; CNS impairment; eye irritation; skin sensitization</td>
<td>Severe eye, nose, skin irritation</td>
<td>f</td>
<td>--</td>
</tr>
<tr>
<td>Ethylbenzene</td>
<td>✓</td>
<td>URT irritation; CNS impairment; eye irritation</td>
<td>Eye irritation</td>
<td>d</td>
<td>--</td>
</tr>
<tr>
<td>Ethylene dichloride</td>
<td>✓</td>
<td>Liver damage; nausea</td>
<td>Liver damage; GI toxicity; cancer</td>
<td></td>
<td>11-14</td>
</tr>
<tr>
<td>Ethylene thiourea</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Furan</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glasswool fibers (airborne particles of respirable size)</td>
<td>✓</td>
<td>Skin and mucous membrane irritation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hexachlorobenzene</td>
<td>✓</td>
<td>Hepatic and neurological effects; hepatic tumors in animals also noted</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hexachloroethane</td>
<td>✓</td>
<td>Liver &amp; kidney damage</td>
<td>Serious injury potential to several organ systems</td>
<td>✓</td>
<td>5-14</td>
</tr>
<tr>
<td>Hydrazine</td>
<td>✓</td>
<td>Slight increases in nasal tumors in rats</td>
<td></td>
<td></td>
<td>8</td>
</tr>
<tr>
<td>Indium phosphide</td>
<td>✓</td>
<td>Pulmonary edema; pneumonitis; dental erosion; malaise</td>
<td>Chronic lung function impairment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isoprene</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chemical</td>
<td>Cal/OSHA PEL in regulation</td>
<td>Basis for Cal/OSHA PEL</td>
<td>Possible sources for Cal/OSHA PEL</td>
<td>Unit risk value available</td>
<td>Estimated cancer cases per 1,000 workers exposed at the current PEL (range from Table 6)*</td>
</tr>
<tr>
<td>----------</td>
<td>--------------------------</td>
<td>-----------------------</td>
<td>-------------------------------</td>
<td>--------------------------</td>
<td>-----------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>64 Lead and lead compounds</td>
<td>✓</td>
<td>Numerous health effects including reproductive toxicity; not regulated as occupational carcinogen</td>
<td></td>
<td>✓</td>
<td>0.08</td>
</tr>
<tr>
<td>65 2-Methylaziridine (propyleneimine)</td>
<td>✓</td>
<td></td>
<td>Eye, skin &amp; URT irritation</td>
<td>✓</td>
<td>0.08</td>
</tr>
<tr>
<td>66 Methyl carbamate</td>
<td>✓</td>
<td></td>
<td></td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>67 Methyleneugenol</td>
<td>✓</td>
<td></td>
<td></td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>68 Methylhydrazine and its salts</td>
<td>✓</td>
<td>Increase in nasal adenomatous polyps in rats</td>
<td></td>
<td>✓</td>
<td>990</td>
</tr>
<tr>
<td>69 Methyl iodide</td>
<td>✓</td>
<td></td>
<td>Eye damage, CNS impairment</td>
<td></td>
<td>6</td>
</tr>
<tr>
<td>70 N-Methyloacrylamide</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>71 Naphthalene</td>
<td>✓</td>
<td>Hematologic effects, URT &amp; eye irritation, eye damage</td>
<td>Eye irritation and serious ocular effects</td>
<td>✓</td>
<td>220</td>
</tr>
<tr>
<td>72 Nickel (metallic)</td>
<td>✓</td>
<td>Likely based on an earlier TLV; health basis not known</td>
<td>Lung irritation, precancerous changes</td>
<td>✓</td>
<td>34</td>
</tr>
<tr>
<td>73 Nickel carbonyl</td>
<td>✓</td>
<td></td>
<td>Lung and nasal cancer</td>
<td>✓</td>
<td>0.2</td>
</tr>
<tr>
<td>74 Nickel compounds</td>
<td>✓</td>
<td>Renal toxicity in rats</td>
<td></td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>soluble</td>
<td></td>
<td></td>
<td>Lung &amp; nasal cancer</td>
<td></td>
<td></td>
</tr>
<tr>
<td>insoluble</td>
<td></td>
<td></td>
<td>Likely based on earlier TLV; health basis not known</td>
<td></td>
<td></td>
</tr>
<tr>
<td>75 Nitrilotriacetic acid</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>76 Nitrobenzene</td>
<td>✓</td>
<td></td>
<td>Methemoglobinemia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>77 Nitromethane</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
<td>d</td>
</tr>
<tr>
<td>78 2-Nitropropane</td>
<td>✓</td>
<td></td>
<td>Liver damage, liver cancer</td>
<td>Cancer</td>
<td>f</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Chemical</th>
<th>Cal/OSHA PEL in regulation</th>
<th>Basis for Cal/OSHA PEL</th>
<th>Possible sources for Cal/OSHA PEL</th>
<th>Unit risk value available</th>
<th>Estimated cancer cases per 1,000 workers exposed at the current PEL (range from Table 6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>o-Nitrotoluene</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>p-Nitrosodiphenylamine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N-Nitrosodiphenylamine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>o-Phenylenediamine and its salts</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phenyl glycidyl ether</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>Phenylhydrazine and its salts</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
<td>Reduce health risks associated with acute blood-related toxicity and possibly cancer</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>✓</td>
<td>500</td>
</tr>
<tr>
<td>1,3-Propane sultone</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Propylene glycol mono-&lt;br&gt;butyl ether</td>
<td></td>
<td></td>
<td></td>
<td>d</td>
<td></td>
</tr>
<tr>
<td>Propylene oxide</td>
<td>✓</td>
<td></td>
<td>Respiratory effects; carcinogenic effects also noted</td>
<td>✓</td>
<td>2</td>
</tr>
<tr>
<td>Pyridine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quinoline and its strong acid salts</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Silica, crystalline particles of respirable size</td>
<td></td>
<td></td>
<td></td>
<td>e</td>
<td></td>
</tr>
<tr>
<td>Quartz</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cristobalite &amp; tridymite</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Strong inorganic acid mists containing sulfuric acid</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1,1,2,2-&lt;br&gt;Tetrachloroethane</td>
<td></td>
<td></td>
<td>Liver damage</td>
<td>✓</td>
<td>53</td>
</tr>
<tr>
<td>Chemical</td>
<td>Cal/OSHA PEL in regulation</td>
<td>Basis for Cal/OSHA PEL</td>
<td>Possible sources for Cal/OSHA PEL</td>
<td>Unit risk value available</td>
<td>Estimated cancer cases per 1,000 workers exposed at the current PEL (range from Table 6)</td>
</tr>
<tr>
<td>------------------------------------------------------------------------</td>
<td>---------------------------</td>
<td>------------------------</td>
<td>---------------------------------</td>
<td>--------------------------</td>
<td>----------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Tetrachloroethylene (perchloroethylene)</td>
<td>✓</td>
<td>CNS impairment</td>
<td>Cancer QRA</td>
<td>✓</td>
<td>130</td>
</tr>
<tr>
<td>Tetrafluoroethylene</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thiourea</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Toluene diisocyanate</td>
<td>✓</td>
<td>Respiratory sensitization; asthma; eye irritation</td>
<td>Pulmonary sensitization</td>
<td>✓</td>
<td>0.06</td>
</tr>
<tr>
<td>o-Toluidine</td>
<td>✓</td>
<td>Methemoglobinemia</td>
<td></td>
<td>✓</td>
<td>60</td>
</tr>
<tr>
<td>Trichloroethylene</td>
<td>✓</td>
<td>See footnote h</td>
<td></td>
<td>✓</td>
<td>35</td>
</tr>
<tr>
<td>1,2,3-Trichloropropene</td>
<td>✓</td>
<td>Liver &amp; kidney damage; eye &amp; URT irritation</td>
<td>Liver and kidney damage</td>
<td>d</td>
<td>--</td>
</tr>
<tr>
<td>Trimethyl phosphate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tris(2-chloroethyl)phosphate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vanadium pentoxide (orthorhombic crystalline form)</td>
<td>✓</td>
<td></td>
<td>Irritation, lung</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4-Vinylcyclohexene</td>
<td>✓</td>
<td></td>
<td>Female &amp; male reproductive damage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vinyl fluoride</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vinyl trichloride (1,1,2-trichloroethane)</td>
<td>✓</td>
<td></td>
<td>CNS impairment, liver damage</td>
<td>✓</td>
<td>94</td>
</tr>
</tbody>
</table>

a. Range includes cancer risk estimates based on OEHHA and U.S. EPA unit risk values (see Table 6).
b. A unit risk factor was derived for antimony oxide by the National Research Council (NRC, 2000).
d. Draft OEHHA cancer potency and/or unit risk value available.
e. Quantitative cancer risk assessment available in the published literature.
g. The Cal/OSHA PEL (0.15 mg/m³), unit risk value and cancer risk estimate are for 2,4-dinitrotoluene. The TLV (0.2 mg/m³) is for dinitrotoluene (mixed isomers).
h. Not available; Cal/OSHA PEL is the same as NIOSH REL, which is based on CNS effects and potential for cancer.
Another goal of the project was to identify chemicals listed as known to the state to cause reproductive and/or developmental toxicity that may pose risks to workers due to lack of regulation, or regulation that is not based explicitly on these endpoints. Table 20 lists 19 chemicals identified as causing male reproductive toxicity, female reproductive toxicity and/or developmental toxicity that either have no Cal/OSHA PEL, or have Cal/OSHA PELs based on other endpoints. Of these, 14 of the chemicals have Cal/OSHA PELs (noted by a “✓”). The basis for the Cal/OSHA PEL is provided if it was available from online sources described above. If the basis for the PEL was not available, Table 20 lists possible sources for the PEL, with the probable basis, as determined from these other sources (i.e., ACGIH [2006], OSHA [1989] or current OSHA sources), also provided. The shading in Table 20 indicates that no information exists, or that the information is not relevant, as described for Table 19 above.

As discussed under Table 5, the Cal/OSHA PELs for five of the chemicals listed in Table 20 may be intended to protect for reproductive and/or developmental effects: carbon disulfide, carbon monoxide, di-n-butyl phthalate, 2,4-dinitrotoluene, and methyl chloride. However, the level of protection afforded by the Cal/OSHA PELs for the reproductive risks of these chemicals is not known and should be evaluated. In addition, the specific effect potentially addressed by the PEL does not necessarily account for all the relevant reproductive effects. For example, di-n-butyl phthalate is listed as a developmental, male reproductive and female reproductive toxicant under Proposition 65, while ACGIH (2006) cites only “testicular damage and URT irritation” as the basis for the TLV, the likely source of the Cal/OSHA PEL.

Four of the chemicals listed in Table 20 are regulated as occupational carcinogens (arsenic, benzene, 1,3-butadiene and cadmium). Thus, the current standards for these chemicals may be sufficient to address reproductive and/or developmental toxicity. However, this should be confirmed, and the issue of notifying workers of the potential for reproductive harm should also be addressed.

In addition to the occupational carcinogens noted above, the remaining five chemicals in Table 20 that currently have Cal/OSHA PELs do not appear to be regulated on the basis of the reproductive or developmental effects of the chemicals: DEHP, dinitrobenzene, hexachlorobenzene, nickel carbonyl and toluene. Since the PEL for nickel carbonyl is likely based on cancer, this limit may be sufficiently low to address reproductive harm but this should be evaluated.

As discussed following Table 5, a qualitative analysis of the basis for the PELs is not sufficient to determine how protective these exposure limits are. All of the current Cal/OSHA PELs for workplace chemicals listed as known to cause reproductive and/or developmental toxicity under Proposition 65 should be evaluated quantitatively.

Table 20 does not include workplace chemicals that are known to have Cal/OSHA PELs that were confirmed to be at least in part based on reproductive and/or developmental toxicity. The
PELs may not address all types of reproductive endpoints relevant to these chemicals, however. For example, ethylene dibromide is regulated under Cal/OSHA for cancer and male sterility, so it was not identified as a potentially underregulated chemical in this report. However, ethylene dibromide is listed as known to the state to cause developmental and female reproductive toxicity, in addition to male reproductive toxicity. This highlights the critical importance for the health basis for the Cal/OSHA PEL to be listed along with its numerical value, in order to improve hazard communication to workers and more easily identify chemicals which may need re-evaluation as new toxicity information becomes available.

In contrast to chemicals listed as known to cause cancer (Table 19), health assessment values are not as readily available for reproductive or developmental toxicants. Of the 19 chemicals listed in Table 20, six have at least one health assessment value that specifically addresses reproductive and/or developmental toxicity. An additional two chemicals have health assessment values based on other endpoints. If these values were set based on an alternative endpoint that was determined to be more sensitive than reproductive and/or developmental toxicity, these assessments could still be useful for evaluating whether the PEL is sufficiently protective. The absence of health assessment values for the remaining chemicals in Table 20 underlines the importance of conducting risk assessments on chemicals known to the state to cause reproductive and/or developmental toxicity.

Of the 19 chemicals in Table 20, more than half are used as chemical or dye intermediates, which may be of less exposure concern as they are typically contained in closed systems. However, exposure to these chemicals can still occur as a result of fugitive emissions or during repair and maintenance of the system. In addition, 75% of these chemical intermediates have other reported industrial uses. Six of the chemicals in Table 20 have been used as solvents, making worker exposure of greater concern. Eight of the 19 chemicals in Table 20 have been identified as being skin absorbable. Fifteen of the 19 chemicals in Table 20 are high production volume chemicals (>1 million pounds produced and/or imported annually).
Table 20. Summary of chemicals listed as known to the state to cause reproductive and/or developmental toxicity that are not specifically regulated in the California workplace on that basis

<table>
<thead>
<tr>
<th>Chemical</th>
<th>Cal/OSHA PEL in regulation</th>
<th>Basis for Cal/OSHA PEL, if available</th>
<th>Possible sources for Cal/OSHA PEL</th>
<th>Health assessment inhalation level available</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>ACGIH (2006)</td>
<td>OSHA (1989) or current OSHA assessments</td>
</tr>
<tr>
<td>1</td>
<td>Arsenic (inorganic oxides)</td>
<td>✓</td>
<td>Cancer</td>
<td>Cancer</td>
</tr>
<tr>
<td>2</td>
<td>Benzene</td>
<td>✓</td>
<td>Cancer</td>
<td>Cancer, QRA</td>
</tr>
<tr>
<td>3</td>
<td>1-Bromopropane</td>
<td></td>
<td></td>
<td>See footnote b</td>
</tr>
<tr>
<td>4</td>
<td>1,3-Butadiene</td>
<td>✓</td>
<td>Cancer</td>
<td>Cancer, QRA</td>
</tr>
<tr>
<td>5</td>
<td>Butyl benzyl phthalate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Cadmium</td>
<td>✓</td>
<td>Cancer, lung and kidney disease</td>
<td>Cancer, QRA</td>
</tr>
<tr>
<td>7</td>
<td>Carbon disulfide</td>
<td>✓</td>
<td></td>
<td>Cardiovascular disease; reproductive effects; neurological effects</td>
</tr>
<tr>
<td>8</td>
<td>Carbon monoxide</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Di-n-butyl phthalate</td>
<td>✓</td>
<td>Testicular damage, URT irritation</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Di(2-ethylhexyl) phthalate (DEHP)</td>
<td>✓</td>
<td>LRT irritation</td>
<td>Neuropathic; hepatic; other systemic toxicity</td>
</tr>
<tr>
<td>11</td>
<td>Di-n-hexyl phthalate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chemical</td>
<td>Cal/OSHA PEL in regulation</td>
<td>Basis for Cal/OSHA PEL, if available</td>
<td>Possible sources for Cal/OSHA PEL</td>
<td>Health assessment inhalation level available</td>
</tr>
<tr>
<td>--------------------------------------</td>
<td>-----------------------------</td>
<td>--------------------------------------</td>
<td>----------------------------------</td>
<td>---------------------------------------------</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>OSHA (1989) or current OSHA assessments</td>
<td>OEHHA MADL (a)</td>
</tr>
<tr>
<td>12 Dinitrobenzene ((m-, o-, p-))</td>
<td>✓</td>
<td></td>
<td></td>
<td>✓(^{c})</td>
</tr>
<tr>
<td>13 2,4-Dinitrotoluene; 2,6-Dinitrotoluene; Dinitrotoluene (technical grade)</td>
<td>✓(^{c})</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14 Ethylene thiourea</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15 Hexachlorobenzene</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16 Methyl chloride(^{e})</td>
<td>✓</td>
<td></td>
<td>CNS impairment; liver and kidney damage; testicular damage; teratogenic effects</td>
<td>Neurotoxicity</td>
</tr>
<tr>
<td>17 N-Methylpyrrolidone</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18 Nickel carbonyl</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>19 Toluene</td>
<td>✓</td>
<td></td>
<td>Likely based on earlier TLV: URT &amp; eye irritation; CNS impairment(^{f})</td>
<td>✓(^{c})</td>
</tr>
</tbody>
</table>

a. The OEHHA MADL is developed for reproductive and/or developmental effects. Only MADLs available for inhalation exposures or with the exposure route not specified are noted in Table 20.

b. Preliminary/draft OEHHA assessment available.

c. A MADL is available for \(m\)-dinitrobenzene.

d. The Cal/OSHA PEL (0.15 mg/m\(^3\)) is for 2,4-dinitrotoluene, while the TLV (0.2 mg/m\(^3\)) is for dinitrotoluene (mixed isomers).

e. The Cal/OSHA PEL of 5 ppm for methyl chloride is a typographical error; the actual PEL should be 50 ppm (Barish, pers. comm., 2007). Both ACGIH (2006) and OSHA (1989) set a level of 50 ppm for methyl chloride.

f. ACGIH (2007) just adopted a revised TLV of 20 ppm for toluene based on visual impairment, female reproductive system damage and pregnancy loss. The Cal/OSHA PEL of 50 ppm is the same as the previous ACGIH TLV, which was based on URT and eye irritation, and CNS impairment, as shown above.
Summary of Key Results (continued)

Quantitative dose-response assessments for workplace chemicals listed as known to the state to cause cancer under Proposition 65

A further goal of the project was for OEHHA to carry out quantitative dose-response assessments for selected Proposition 65 chemicals and determine health-based occupational air concentrations associated with specified risk levels. The results for the quantitative assessments are presented in Tables 6 and 8 for workplace chemicals listed as known to cause cancer that had available OEHHA unit risk values. Occupational concentrations associated with specific risk levels are summarized in Table 10 for selected workplace carcinogens. Some of the key findings from the quantitative assessments of carcinogens are highlighted below.

- Table 6 lists cancer risks estimated for worker exposure at the PEL for 38 workplace chemicals that are not regulated specifically as occupational carcinogens.
  - For seven of these chemicals, cancer risk at the PEL was less than one in 1,000 based on assessments using OEHHA or U.S. EPA unit risk values.
  - For 25 of these chemicals, cancer risk at the PEL was between one and 100 in 1,000.
  - For six of these chemicals, cancer risk exceeded 100 in 1,000.

- Table 8 lists cancer risks estimated for worker exposure at the PEL for 14 workplace chemicals that are regulated as occupational carcinogens.
  - Three of the 14 chemicals in Table 8 have ranges of estimated cancer risks that include 1 in 1,000, based on assessments using OEHHA or U.S. EPA unit risk values.
  - Two of the seven chemicals that OSHA assessed have estimated MLE cancer risks, which is the measure that OSHA uses to evaluate significance of risk, that are below 1 in 1,000.
  - The remainder of the cancer risk estimates based on OEHHA, U.S. EPA or OSHA QRAs are higher than the 1 in 1,000, the cancer risk level that OSHA targets as “significant” based on the Benzene Decision. Some risk is expected to remain at the PEL, because of the consideration of technical and economic feasibility.

- Table 10 shows examples of health-based occupational concentrations for a range of cancer risk levels for chemicals that are not currently regulated as occupational carcinogens. The health-based occupational air concentration associated with a cancer risk of 1 in 1,000 is at least an order of magnitude lower than the current PEL for five of the seven example compounds.
Quantitative dose-response assessments for workplace chemicals listed as known to the state to cause reproductive and/or developmental toxicity under Proposition 65 or known to induce chronic toxic effects

The current document provides examples of how occupational concentrations for developmental toxicants and toxicants posing chronic health risks might be derived based on existing risk assessments. Some of the key findings and important issues that will need to be addressed are highlighted below.

- Existing risk assessments for reproductive and/or developmental toxicants or chronic toxicants carried out for the general population can be applied to the occupational setting, by adjusting the uncertainty factors applied and accounting for a worker exposure scenario.

- In contrast to carcinogens, the availability of risk assessments that explicitly address reproductive and/or developmental toxicity is much more limited. The extent of reproductive and/or developmental risk at the current PEL is unclear and should be assessed further for these toxicants.

- In all of the example calculations, the health-based occupational concentrations generated using existing noncancer risk assessments were less than the existing PELs, even using the least conservative approaches.

- When selecting appropriate risk assessments to set an occupational exposure limit, the risk assessment based on the most sensitive endpoint should be selected. In that way, all relevant endpoints are addressed. For example, if a chemical induces respiratory sensitization at a level lower than male reproductive toxicity, an occupational exposure limit based on sensitization should be sufficiently protective for the reproductive effects as well.

- Using existing risk assessments would help the state leverage scarce resources. If significant new information is available that would substantially alter the findings of a risk assessment, however, it may not be appropriate to rely on an older risk assessment. This would have to be determined on a case by case basis, and would be of particular concern if new data were to show that existing risk assessments are not sufficiently protective. At a minimum, however, PELs should be adjusted to be at least as protective as existing risk assessments.

- In the current document, calculations to derive an 8-hour exposure limit for developmental toxicants were carried out either by adjusting for the shorter duration of worker exposure or by not making that adjustment. Adjusting for exposure duration increases the health-based occupational concentration by a factor of four (“24/8 x 7/5”) or three (“20/10 x 7/5”), if an increased breathing rate of the worker is considered. The approach to setting occupational limits for developmental toxicants must address the issue of exposure averaging.
In cases where short-term exposures or even single exposures have the potential to cause the health endpoint of concern, such as developmental toxicants, short-term exposure limits should also be set.
Recommendations to HESIS

The current document demonstrates the feasibility of using existing OEHHA cancer and noncancer risk assessments to update occupational standards in California. To further assist HESIS with developing protective standards, some additional recommendations are offered:

- Set priorities for recommending protective occupational exposure limits for substances identified in Tables 19 and 20 by considering the following factors, where data are available:
  - Current basis for Cal/OSHA PEL.
  - Use of the chemical in California.
  - Potential for worker exposure to the chemical, including number of workers potentially exposed to the chemical and actual level of exposure.
  - Extent of toxicity: for example, estimated excess cancer risk or comparisons of the current PEL to health-based occupational concentrations for reproductive and/or developmental toxicity or other chronic health endpoints.
  - Existence of safer alternatives.
  - Industrial hygiene air monitoring and/or biological monitoring exposure data.

- Use the guidance information in this report as a starting point for selecting appropriate method(s) to derive protective occupational concentrations for carcinogens, reproductive toxicants and noncancer chronic toxicants from existing OEHHA quantitative risk assessments. Apply and extend the guidance provided here to address the following issues:
  - “Acceptable” cancer risk levels in an occupational setting.
  - Choice of unit risk value.
  - Selection of noncancer health assessment value protective of the most sensitive endpoint.
  - Methods for assessing occupational exposure to a carcinogen.
  - Appropriate intraspecies uncertainty factors for an occupational setting, with consideration of the particular worker population and the type of toxicant.
• Procedures to average exposure and establish short-term exposure limits for developmental toxicants and other toxicants for which single or peak exposures may pose a particular concern.

• Procedures to account for dermal exposures.

• Adjustment for the occupational setting of cancer and noncancer risk assessments that develop and apply specific toxicokinetic models.

• As the science on cancer and noncancer risk assessment moves forward and new OEHHA guidance becomes available, methods to adjust existing risk assessments for the occupational setting should be correspondingly updated.

• Continue to monitor OEHHA’s Proposition 65 List and new and revised cancer and noncancer risk assessments to identify industrial chemicals that may be of concern for California workers (the results in this report are based on the December 2006 Proposition 65 list).

• Identify Proposition 65 drugs and pesticides relevant to the workplace in California that do not have existing Cal/OSHA PELs or for which the existing PELs do not protect against cancer or reproductive and/or developmental toxicity.

Concluding Remarks

By using lists and risk assessments already developed by OEHHA, priorities for developing protective occupational standards can be efficiently identified by HESIS, and scarce state resources can be leveraged to the maximum benefit. Drawing on OEHHA’s analyses will also provide a stronger scientific basis for developing protective occupational standards.
Glossary

BMC: Benchmark concentration.

BMCL_HEC: The lower 95% confidence limit of the concentration producing a 5% incidence of the critical effect (OEHHA, 2000a), expressed as a human equivalent concentration.

BMD: Benchmark dose.

Cancer potency factor: The excess cancer risk associated with lifetime exposure to a unit dose (e.g., 1 mg/kg-day) of a given chemical.

Chronic reference exposure level (cREL): The concentration at or below which no adverse health effects are anticipated in the general population assuming continuous inhalation exposure.

CNS: Central nervous system.

HEC: Human equivalent concentration.

Lowest observed adverse effect level (LOAEL): The lowest exposure level with a biologically or statistically significant increase in the frequency or severity of adverse effects among an exposed population relative to a control group.

LRT: Lower respiratory tract.

Maximum allowable dose level (MADL): Daily intake level at which the chemical would have no observable adverse reproductive effect assuming exposure at 1,000 times that level.

MLE: Maximum likelihood estimate.

No observed adverse effect level (NOAEL): An exposure level with no biologically or statistically significant increase in the frequency or severity of adverse effects among an exposed population relative to a control group.

No significant risk level (NSRL): The daily intake level associated with an excess lifetime cancer risk of 1 in 100,000.

Permissible exposure limit (PEL): A legal limit specifying the concentration of a chemical in air that a worker can be exposed to, averaged over an 8-hour work day.

PNS: Peripheral nervous system.

QRA: Quantitative risk assessment.
REL: Reference exposure level.

Reference concentration (RfC): The concentration that is likely to be without an appreciable risk of deleterious effects to the human population (including sensitive subgroups) assuming continuous inhalation exposure.

RGDR: Regional gas dose ratio.

STEL: Short term exposure limit.

Threshold limit value (TLV): As defined by ACGIH (2006), “Threshold limit values (TLVs®) refer to airborne concentrations of chemical substances and represent conditions under which it is believed that nearly all workers may be repeatedly exposed, day after day, over a working lifetime, without adverse health effects. TLVs® are developed to protect workers who are normal, healthy adults.”

UCB: Upper confidence bound.

UF: Uncertainty factor.

Unit risk value: The excess cancer risk associated with a lifetime inhalation exposure to a unit air concentration (e.g., 1 μg/m³) of a given chemical.

URT: Upper respiratory tract.

WEEL: Workplace environmental exposure limit.
References

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Office of Environmental Health Hazard Assessment (OEHHA, 2003). *Proposition 65 Maximum Allowable Dose Level (MADL) for Reproductive Toxicity for N-Methylpyrrolidone for Dermal and Inhalation Exposures.* Reproductive and Cancer Hazard Assessment Section, OEHHA.


### Appendix A: Workplace Chemicals Listed Under Proposition 65

<table>
<thead>
<tr>
<th>Table</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A-1</td>
<td>Workplace chemicals listed as known to the state to cause cancer or reproductive and/or developmental toxicity under Proposition 65 that do not have Cal/OSHA PELs</td>
</tr>
<tr>
<td>A-2</td>
<td>Workplace chemicals listed as known to the state to cause cancer under Proposition 65 that are regulated occupationally based on various endpoints in California</td>
</tr>
<tr>
<td>A-3</td>
<td>Workplace chemicals listed as known to the state to cause reproductive and/or developmental toxicity under Proposition 65 that are regulated occupationally based on various endpoints in California</td>
</tr>
<tr>
<td>Chemical</td>
<td>Type of Toxicity</td>
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<tr>
<td>------------------------------</td>
<td>------------------</td>
</tr>
<tr>
<td>Acetamide</td>
<td>cancer</td>
</tr>
<tr>
<td>p-Aminoazobenzene</td>
<td>cancer</td>
</tr>
<tr>
<td>Benzofuran</td>
<td>cancer</td>
</tr>
<tr>
<td>Benzotrichloride</td>
<td>cancer</td>
</tr>
<tr>
<td>2,2-Bis(bromomethyl)-1,3-propanediol</td>
<td>cancer</td>
</tr>
<tr>
<td>1-Bromopropane</td>
<td>developmental, female, male</td>
</tr>
</tbody>
</table>

Table A-1. Workplace chemicals listed as known to the state to cause cancer or reproductive and/or developmental toxicity under Proposition 65 that do not have Cal/OSHA PELs
<table>
<thead>
<tr>
<th>Chemical</th>
<th>Type of Toxicity</th>
<th>CAS No.</th>
<th>Year Listed</th>
<th>Identity</th>
<th>Production/ Import Volume Range in pounds (TSCA, 2002)</th>
<th>Additional Comments on Occupational Exposure/Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Butyl benzyl phthalate (BBP)</td>
<td>developmental</td>
<td>85687</td>
<td>2005</td>
<td>Plasticizer; chemical intermediate</td>
<td>&gt;50M-100M</td>
<td>&quot;Occupational exposure may occur during its production and in its use as a plasticizer in polyvinyl chloride products such as vinyl floor tiles.&quot; (Text in quotes from IARC, 1999)</td>
</tr>
<tr>
<td>Ceramic fibers (airborne particles of respirable size)</td>
<td>cancer</td>
<td>---</td>
<td>1990</td>
<td>Insulation; replacement for asbestos</td>
<td>NA – see comments</td>
<td>Worldwide production in the 1980s was ~150-175 million lbs, with half produced in the US (NTP, 2005). REL established by NIOSH in 2006.</td>
</tr>
<tr>
<td>Chlorendic acid</td>
<td>cancer</td>
<td>115286</td>
<td>1989</td>
<td>Flame retardant, chemical intermediate; hardening agent; extreme pressure lubricant.</td>
<td>&gt;500K-1M</td>
<td>&quot;The primary route of potential human exposure to chlorendic acid is dermal contact, while some small exposure may possibly occur through inhalation. It is manufactured in an essentially closed system which would seem to minimize, although not eliminate, potential occupational exposure during the manufacturing process (NTP 1987). When used as a reactive flame-retardant or hardening agent, chlorendic acid bonds covalently to the polymer, resulting in less potential for human exposure. In its uses as an extreme pressure lubricant and a chemical intermediate, there is the possibility of human exposure to chlorendic acid.&quot; (Text in quotes from NTP, 2005)</td>
</tr>
<tr>
<td>Chemical</td>
<td>Type of Toxicity</td>
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<td>Year Listed</td>
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</tr>
<tr>
<td>Chlorinated paraffins (Average chain length, C12; approximately 60 percent chlorine by weight)</td>
<td>cancer</td>
<td>108171262</td>
<td>1989</td>
<td>Primarily used as industrial cutting fluids; used in flame retardants and plasticizers</td>
<td>&gt;50M-100M (listed as paraffin waxes and hydrocarbon waxes, chloro)</td>
<td>Worldwide production 300,000 metric tons per year. Major producer in US is Dover Chemical Corporation. The primary routes of potential human exposure include ingestion, both directly and through contamination of foodstuffs (Campbell and McConnell 1980) and dermal contact with products containing chlorinated paraffins (HSDB 2000). Various chlorinated paraffins exhibit little or no potential to irritate the skin of humans, and no incidents of human intoxication have been reported in workers involved in the handling or manufacturing of chlorinated paraffins (NTP 1986). Occupational exposure is likely in production plants or in industries using chlorinated paraffins (WHO 1996).” (Text in quotes from NTP, 2005)</td>
</tr>
<tr>
<td>p-Chloroaniline</td>
<td>cancer</td>
<td>106478</td>
<td>1994</td>
<td>Chemical intermediate/dye intermediate</td>
<td>10K-500K</td>
<td></td>
</tr>
<tr>
<td>3-Chloro-2-methylpropene</td>
<td>cancer</td>
<td>563473</td>
<td>1989</td>
<td>Chemical intermediate</td>
<td>&gt;10M-50M</td>
<td>&quot;As there is only one known U.S. manufacturer, and 90% to 95% of the 3-chloro-2-methylpropene produced is used by this firm to produce carbofuran, the majority of occupational exposure to the chemical is site-limited. The workers are required to wear gloves, which reduces the likelihood of dermal exposure. The average air concentration in the manufacturing plant is 17 ppb (0.013 mg/kg per day worker exposure); chemical operators’ breathing zone samples showed an average concentration of 48 ppb.&quot; (Text in quotes from NTP, 2005) (Note – 2002 TSCA data shows two firms)</td>
</tr>
</tbody>
</table>

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OEHHA
<table>
<thead>
<tr>
<th>Chemical</th>
<th>Type of Toxicity</th>
<th>CAS No.</th>
<th>Year Listed</th>
<th>Identity</th>
<th>Production/Import Volume Range in pounds (TSCA, 2002)</th>
<th>Additional Comments on Occupational Exposure/Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>C.I. Direct Blue 15</td>
<td>cancer</td>
<td>2429745</td>
<td>1997</td>
<td>Dye</td>
<td>&gt;500K-1M</td>
<td>&quot;Industrial exposure to dyes may occur through inhalation of dust or mist, through accidental ingestion, or from direct contact of the dye with skin.&quot; (NTP TR 397, 1992)</td>
</tr>
<tr>
<td>C.I. Direct Blue 218</td>
<td>cancer</td>
<td>28407376</td>
<td>1997</td>
<td>Dye for cellulose, acetate, nylon, silk, wool, tissue, papers, and textile goods with a urea-formaldehyde finish</td>
<td>10K-500K</td>
<td>&quot;Industrial exposure to dyes may occur through inhalation of dust or mist, through accidental ingestion, or from direct contact of the dye with skin.&quot; (NTP TR 430, 1994)</td>
</tr>
<tr>
<td>p-Cresidine</td>
<td>cancer</td>
<td>120718</td>
<td>1988</td>
<td>Chemical intermediate</td>
<td>10K-500K</td>
<td>&quot;p-Cresidine has been produced commercially since 1926. Its use as a dye intermediate could result in occupational exposure...&quot; (IARC, 1982a). &quot;The primary routes of potential human exposure to p-cresidine are inhalation and dermal contact. Potential occupational exposure is believed to be limited to workers in dye-production facilities.&quot; (Text in quotes from NTP, 2005)</td>
</tr>
<tr>
<td>D&amp;C Orange No. 17</td>
<td>cancer</td>
<td>3468631</td>
<td>1990</td>
<td>Dye</td>
<td>10K-500K</td>
<td>&quot;The risk of possible exposure seems to be greatest for those engaged in analytical or research studies involving use of the chemical. Workers may be potentially exposed to the compound during manufacturing processes.&quot; (Text in quotes from NTP, 2005)</td>
</tr>
<tr>
<td>D&amp;C Red No. 9</td>
<td>cancer</td>
<td>5160021</td>
<td>1990</td>
<td>Dye</td>
<td>&gt;1M-10M</td>
<td>Used in printing inks, coated paper, crayons, paints, polystyrene and rubber, baking enamels. High production volume chemical.</td>
</tr>
<tr>
<td>Chemical</td>
<td>Type of Toxicity</td>
<td>CAS No.</td>
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</tr>
<tr>
<td>D&amp;C Red No. 19</td>
<td>cancer</td>
<td>81889</td>
<td>1990</td>
<td>Dye (paper, wool, silk, plastics); used in dye lasers; biological stain</td>
<td>10K-500K</td>
<td>Listed as an &quot;inert ingredient&quot; in pesticides (<a href="http://npic.orst.edu/factsheets/inerts.pdf">http://npic.orst.edu/factsheets/inerts.pdf</a>). &quot;Rhodamine B is a red colored dye that is used in cosmetic products. We report a case of 17 patients who were exposed to aerosolized Rhodamine B inside a maintenance shop.&quot; (Text in quotes from Dire and Wilkinson, 1987)</td>
</tr>
<tr>
<td>4,4'-Diaminodiphenyl ether (4,4'-Oxydianiline)</td>
<td>cancer</td>
<td>101804</td>
<td>1988</td>
<td>Chemical intermediate for resin</td>
<td>&gt;1M-10M</td>
<td>&quot;Occupational exposure to 4,4'-diaminodiphenyl ether probably occurs during its manufacture and its conversion to polyimide-type resins&quot; (Text in quotes from IARC, 1982b). &quot;Exposure may occur through inhalation of dust or through eye and skin contact&quot; (Text in quotes from NTP, 2005, citing HSDB)</td>
</tr>
</tbody>
</table>
| 2,4-Diaminotoluene                            | cancer           | 95807   | 1988        | Chemical intermediate for TDI primarily. Also used to produce dyes and polyurethane foams.                | 10K-500K                                             | "The primary routes of potential human exposure to 2,4-diaminotoluene are dermal contact and inhalation."
<pre><code>                                                                                                                                                                                                                                                             |
</code></pre>
<p>| Diaminotoluene (mixed)                        | cancer           | 25376458 | 1990        | Chemical intermediate                                  | &gt;500M-1B                                              |                                                                                                                                                                                                                                                                                                         |
| Dichloroacetic acid                           | cancer           | 79436   | 1996        | Chemical intermediate                                  | 10K-500K                                             | Ontario Ministry of Labour recently adopted an occupational exposure limit of 0.5 ppm and a skin notation for dichloroacetic acid (<a href="http://www.e-laws.gov.on.ca/DBLaws/Reps/English/900833_e.htm">see http://www.e-laws.gov.on.ca/DBLaws/Reps/English/900833_e.htm</a>)                                                                                                      |
| Diesel engine exhaust                        | cancer           | ---     | 1990        | Byproduct of diesel fuel use                           | --                                                   | Mechanics; toll booth workers; roadside inspection workers (HESIS, 2002).                                                                                                                                                                                                                               |
| Di-n-hexyl phthalate (DnHP)                   | female, male     | 84753   | 2005        | Plasticizer                                            | &gt;1M-10M                                              |                                                                                                                                                                                                                                                                                                         |
| Diethyl sulfate                              | cancer           | 64675   | 1988        | Ethylating agent, alkylation agent, chemical intermediate | &gt;1M-10M                                              | Most exposures are probably associated with its use as a chemical intermediate. It has been documented that workers involved in the production of ethanol by the strong acid process were frequently exposed to diethyl sulfate (NTP, 2005).                                                                                           |</p>
<table>
<thead>
<tr>
<th>Chemical</th>
<th>Type of Toxicity</th>
<th>CAS No.</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Diglycidyl resorcinol ether (DGRE)</td>
<td>cancer</td>
<td>101906</td>
<td>1989</td>
<td>Epoxy resin; curing agent; reactive diluent in production of other epoxy resins; coating for metals and pavement</td>
<td>10K-500K</td>
<td>&quot;Much occupational exposure to glycidyl ethers results from the use of proprietary or trade name products which do not disclose the presence of toxic agents in their formulations. This complicates efforts to take appropriate precautionary measures for the prevention of occupational disease. For example, unrecognized hazardous situations can occur where protective coatings containing epoxy resins are sprayed, thereby facilitating the inhalation of even non-volatile materials, and where there is skin contact with epoxy resins containing glycidyl ethers...NIOSH has previously estimated that approximately 1,000,000 workers are exposed to epoxy resins.&quot; (Text in quotes from NIOSH (1978))</td>
</tr>
<tr>
<td>Dihydrosafrole</td>
<td>cancer</td>
<td>94586</td>
<td>1988</td>
<td>Chemical intermediate; formerly used as a fragrance and flavoring agent</td>
<td>10K-500K</td>
<td>&quot;1,2-(Methylenedioxy)-4-propylbenzene may be released during its manufacture and use as an intermediate in the production of piperonyl butoxide, a synergist for pyrethroid insecticides&quot; (Text in quotes taken from HSDB, 2002)</td>
</tr>
<tr>
<td>3,3'-Dimethoxybenzidine dihydrochloride</td>
<td>cancer</td>
<td>20325400</td>
<td>1990</td>
<td>Dye intermediate</td>
<td>10K-500K</td>
<td>&quot;The primary routes of potential human exposure to 3,3'-dimethoxybenzidine are inhalation and dermal contact. Exposure to 3,3'-dimethoxybenzidine can occur during its use as a chemical intermediate in the production of azo dyes, o-dianisidine diisocyanate formulations, textile processing, and packaging processes...Workers potentially exposed to the chemical include dye makers and o-dianisidine diisocyanate production workers. However, present dye production processes for 3,3'-dimethoxybenzidine and its dye derivatives generally are closed systems with minimal risk to workers.&quot; (Text in quotes from NTP, 2005)</td>
</tr>
<tr>
<td>Chemical</td>
<td>Type of Toxicity</td>
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</tr>
<tr>
<td>Ethylene thiourea</td>
<td>cancer; developmental</td>
<td>96457</td>
<td>1988; 1993</td>
<td>Rubber curing; chemical intermediate</td>
<td>10K-500K</td>
<td>&quot;Occupational exposure by dermal and inhalation routes may occur in the rubber and plastics industry and where ethylenebisdithiocarbamate fungicides are used.&quot; (Text in quotes from U.S. EPA, 2000)</td>
</tr>
<tr>
<td>Furan</td>
<td>cancer</td>
<td>110009</td>
<td>1993</td>
<td>Chemical intermediate; found in fuel exhaust/atmospheric transformation product</td>
<td>&gt;10M-50M</td>
<td>&quot;Since the industrial processes in which furan is used are conducted in closed systems and its volatility requires that furan be handled in closed containers, occupational exposure is limited (NTP 1993). However, furan may be released in the effluent from oil refining, coal mining, and coal gasification&quot; (Text in quotes from NTP, 2005)</td>
</tr>
<tr>
<td>Isoprene</td>
<td>cancer</td>
<td>78795</td>
<td>1996</td>
<td>Production of synthetic rubber; plastics</td>
<td>&gt;100M-500M</td>
<td>&quot;Recent surveys of air levels of isoprene in US monomer and polymer manufacturing facilities have demonstrated TWA concentrations &lt;1 ppm in 90% of collected samples, and 98% were &lt;10 ppm.&quot; (Text in quotes from Leber, 2001)  &quot;Isoprene is formed endogenously in humans and is generally the major hydrocarbon (up to 70% in human breath) (Gelmont et al. 1981).&quot;  &quot;Isoprene is emitted from plants and trees and is widely present in the environment at low concentrations (Taalman 1996).&quot;  &quot;The primary source of isoprene in indoor air is environmental tobacco smoke.&quot; (Text in previous three quotes from NTP, 2005)</td>
</tr>
<tr>
<td>Chemical</td>
<td>Type of Toxicity</td>
<td>CAS No.</td>
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</tr>
<tr>
<td>Methyl carbamate</td>
<td>cancer</td>
<td>598550</td>
<td>1998</td>
<td>Chemical intermediate</td>
<td>&gt;1M-10M</td>
<td>&quot;Occupational exposure to methyl carbamate may occur through inhalation and dermal contact with this compound at workplaces where methyl carbamate is produced or used.&quot; (HSDB, 2003) &quot;No information on human exposure to methyl carbamate was available, but such exposure might be significant in view of the compound's wide use. The primary routes of human exposure are inhalation and dermal contact.&quot; (NTP TR 328, 1987)</td>
</tr>
<tr>
<td>Methyleugenol</td>
<td>cancer</td>
<td>93152</td>
<td>2001</td>
<td>Flavoring agent; anesthetic; insect attractant</td>
<td>10K-500K</td>
<td>&quot;Occupational exposure to methyleugenol occurs through dermal contact, inhalation, and ingestion&quot; (Text in quotes from NTP, 2005).</td>
</tr>
<tr>
<td>N-Methylolacrylamide</td>
<td>cancer</td>
<td>924425</td>
<td>1990</td>
<td>Cross-linking agent for production of polymers; binder for paper products</td>
<td>&gt;10M-50M</td>
<td>&quot;EPA is hereby withdrawing a proposed rule that would have prohibited the manufacture, importation, distribution, and use of acrylamide and N-methylolacrylamide (NMA) grouts. In 1991, EPA proposed the rule in order to protect grouters from neurotoxic and carcinogenic risks arising from significant dermal and inhalation exposure to the acrylamide and NMA in these grouts. EPA found that grouters were exposed when using these grouts, even while wearing the best practical personal protective equipment (PPE) available at the time the rule was proposed. EPA has found that there is now affordable PPE that provides adequate protection from exposure to the acrylamide and NMA in these grouts. EPA has determined that as long as appropriate PPE is used during grouting operations, it is no longer necessary to prohibit the use of these grouts to protect the health of grouters.&quot; (Text in quotes from U.S. EPA, 2002)</td>
</tr>
</tbody>
</table>

Readily absorbed through skin (MSDS).
<table>
<thead>
<tr>
<th>Chemical</th>
<th>Type of Toxicity</th>
<th>CAS No.</th>
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</tr>
</thead>
<tbody>
<tr>
<td>N-Methylpyrrolidone</td>
<td>developmental</td>
<td>872504</td>
<td>2001</td>
<td>Solvent</td>
<td>&gt;100M-500M</td>
<td>Degreasing; paint thinners; paints &amp; adhesives; printing press cleaners; methylene chloride substitute to prevent air pollution.</td>
</tr>
<tr>
<td>Nitrilotriacetic acid</td>
<td>cancer</td>
<td>139139</td>
<td>1988</td>
<td>Chelating agent used in laundry detergent, eluting agent</td>
<td>10K-500K</td>
<td>&quot;The primary routes of potential human exposure to nitrilotriacetic acid are inhalation, ingestion, and dermal contact. Potential occupational exposure occurs through inhalation and dermal contact during the manufacture of the compound or its salts, during water treatment, and during other production procedures in which the compound is used.&quot; (Text in quotes taken from NTP, 2005)</td>
</tr>
<tr>
<td>p-Nitrosodiphenylamine</td>
<td>cancer</td>
<td>156105</td>
<td>1988</td>
<td>Chemical/dye intermediate; rubber vulcanization accelerator</td>
<td>10K-500K</td>
<td>&quot;para-Nitrosodiphenylamine has been produced commercially since at least 1970. Its use as a chemical intermediate could result in occupational exposure.&quot; (Text in quotes from IARC, 1982a)</td>
</tr>
<tr>
<td>N-Nitrosodiphenylamine</td>
<td>cancer</td>
<td>86306</td>
<td>1988</td>
<td>Used in rubber manufacturing</td>
<td>10K-500K</td>
<td>One company is listed as producing this chemical in 2002.</td>
</tr>
<tr>
<td>o-Phenylenediamine and its salts</td>
<td>cancer</td>
<td>95545</td>
<td>1998</td>
<td>Chemical and dye intermediate; synthesis of fungicides, corrosion inhibitors, pigments and pharmaceuticals; removal of elemental sulfur in mining and aldehyde color formers in polymeric products.</td>
<td>Parent compound: &gt;1M-10M</td>
<td>Sensitizer/asthmagen</td>
</tr>
<tr>
<td>1,3-Propane sultone</td>
<td>cancer</td>
<td>1120714</td>
<td>1988</td>
<td>Chemical intermediate</td>
<td>10K-500K</td>
<td>&quot;Workers involved in the formulation of compounds made from 1,3-propane sultone or the production of its end products are at the greatest risk of potential exposure.&quot; (Text in quotes from NTP, 2005)</td>
</tr>
<tr>
<td>Chemical</td>
<td>Type of Toxicity</td>
<td>CAS No.</td>
<td>Year Listed</td>
<td>Identity</td>
<td>Production/Import Volume Range in pounds (TSCA, 2002)</td>
<td>Additional Comments on Occupational Exposure/Use</td>
</tr>
<tr>
<td>--------------------------------</td>
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<td>--------------------------------------------------------------------------</td>
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<td>---------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Propylene glycol mono- tert- butyl ether</td>
<td>cancer</td>
<td>57018527</td>
<td>2004</td>
<td>Solvent in all purpose cleaners, inks, adhesives, nail polish lacquers.</td>
<td>&gt;1M-10M</td>
<td>&quot;Due to the high production volume and widespread use, there is a high potential for occupational and consumer exposure as a result of contact with propylene glycol mono- tert-butyl ether-containing products mainly via inhalation and dermal absorption. Occupational exposures during the manufacturing process are thought to be low since the manufacturing process is largely enclosed (Boatman, 2001).&quot; (Text in quotes from NTP TR 515, 2004)</td>
</tr>
<tr>
<td>Quinoline and its strong acid salts</td>
<td>cancer</td>
<td>---</td>
<td>1997</td>
<td>Primarily as chemical intermediate. Also as catalyst, corrosion inhibitor, preservative, solvent for resins and terpenes, in metallurgy.</td>
<td>10K-500K</td>
<td></td>
</tr>
<tr>
<td>Styrene oxide</td>
<td>cancer</td>
<td>96093</td>
<td>1988</td>
<td>Chemical intermediate; reactive diluent in epoxy resins</td>
<td>10K-500K</td>
<td>&quot;Occupational exposure to styrene oxide occurs most often to workers in the fabricated rubber products, paints, and allied products industry...In personal exposure samples taken at a U.S. boat manufacturing company, the average concentration of styrene oxide in air was 0.14 mg/m³ (28.5 ppb) for 19 workers who also were heavily exposed to styrene, at a mean concentration of 64 mg/m³.&quot; (Text in quotes from NTP, 2005)</td>
</tr>
<tr>
<td>Tetrafluoroethylene</td>
<td>cancer</td>
<td>116143</td>
<td>1997</td>
<td>Production of fluoropolymers (e.g., Teflon)</td>
<td>&gt;50M-100M</td>
<td>&quot;The primary route of exposure to TFE is inhalation...Potential occupational exposure to TFE may occur with workers involved in the production of polymers and copolymers of products containing the chemical.&quot; (Text in quotes from NTP, 2005)</td>
</tr>
<tr>
<td>Chemical</td>
<td>Type of Toxicity</td>
<td>CAS No.</td>
<td>Year Listed</td>
<td>Identity</td>
<td>Production/Import Volume Range in pounds (TSCA, 2002)</td>
<td>Additional Comments on Occupational Exposure/Use</td>
</tr>
<tr>
<td>----------</td>
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<td>-------------</td>
<td>----------</td>
<td>-----------------------------------------------------</td>
<td>--------------------------------------------------</td>
</tr>
<tr>
<td>Thiourea</td>
<td>cancer</td>
<td>62566</td>
<td>1988</td>
<td>Used in photography, drying cleaning, hair formulations; chemical intermediate; reagent</td>
<td>&gt;500K-1M</td>
<td>&quot;The primary routes of potential human exposure to thiourea are inhalation and dermal contact. The greatest risk of potential exposure exists for workers involved in the production or use of thiourea. Potential occupational exposure also occurs during the formulation of products made from the compound.&quot; (Text in quotes from NTP, 2005)</td>
</tr>
<tr>
<td>Trimethyl phosphate</td>
<td>cancer</td>
<td>512561</td>
<td>1996</td>
<td>Methylating agent, color inhibitor, solvent, gasoline additive.</td>
<td>10-500K</td>
<td>&quot;As trimethyl phosphate is produced in a closed system, exposure during synthesis may be excluded. Since this chemical is used as a polymerization catalyst, the possibility of workplace exposure through dermal route is possible when the product is filled into barrels. Dermal uptake at work place is considered to be the main exposure route while inhalation plays a minor role. Although there is no actual exposure data, using the physical-chemical properties and the EUSES model, exposure levels were calculated to be 0.5 - 3.0 mg/m³ for inhalation and 0 - 0.1 mg/cm²/day for the dermal route. However workers wear personal protective equipment (e.g. chemical cartridge respirator with an organic vapour cartridge) during the filling process. Therefore, the exposure at work place is considered to be very low at the present situation.&quot; (Text in quotes from OECD, 1996)</td>
</tr>
<tr>
<td>Tris(2-chloroethyl) phosphate</td>
<td>cancer</td>
<td>115968</td>
<td>1992</td>
<td>Flame retardant</td>
<td>&gt;1M-10M</td>
<td></td>
</tr>
</tbody>
</table>

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**Occupational Risk Project**

A-12

**December 2007**

**OEHHA**
<table>
<thead>
<tr>
<th>Chemical</th>
<th>Type of Toxicity</th>
<th>CAS No.</th>
<th>Year Listed</th>
<th>Identity</th>
<th>Production/Import Volume Range in pounds (TSCA, 2002)</th>
<th>Additional Comments on Occupational Exposure/Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vinyl fluoride</td>
<td>cancer</td>
<td>75025</td>
<td>1997</td>
<td>Chemical intermediate in production of polyvinyl fluoride and other fluoropolymers</td>
<td>&gt;1M-10M</td>
<td>&quot;Occupational exposure to vinyl fluoride occurs primarily by inhalation (HSDB 2001). Skin and eye contact can occur among workers handling liquid vinyl fluoride. Handling liquid vinyl fluoride also would cause frostbite (IPCS 1993). Occupational exposure to vinyl fluoride was studied in a manufacturing and polymerization facility in the United States. In eight personal air samples taken at the manufacturing facility, concentrations of vinyl fluoride generally were less than 2 ppm (3.76 mg/m³). In one personal sample, however, the concentration of vinyl fluoride was 21 ppm (39.5 mg/m³). Vinyl fluoride concentrations in seven personal samples taken in the polymerization facility ranged from 1 to 4 ppm (1.88 to 7.52 mg/m³). In four general working areas, the vinyl fluoride concentrations ranged from 1 to 5 ppm (1.88 to 9.4 mg/m³) (IARC 1995).&quot; (Text in quotes from NTP, 2005)</td>
</tr>
</tbody>
</table>
Table A-2. Workplace chemicals listed as known to the state to cause cancer under Proposition 65 that are regulated occupationally (based on various endpoints) in California

<table>
<thead>
<tr>
<th>Chemical</th>
<th>CAS No.</th>
<th>Year Listed</th>
<th>Identity</th>
<th>Production/Import Volume Range in Pounds (TSCA, 2002; unless otherwise noted)</th>
<th>Cal/OSHA PEL (mg/m³)</th>
<th>Cal/OSHA PEL (ppm)</th>
<th>Cal/OSHA PEL Notations/Vertical Standard</th>
<th>Cal/OSHA PEL Basis</th>
<th>TLV-TWA (mg/m³)</th>
<th>TLV-TWA (ppm)</th>
<th>TLV Comments/Notations</th>
<th>TLV Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetaldehyde</td>
<td>75070</td>
<td>1988</td>
<td>Chemical intermediate</td>
<td>&gt;100M-500M</td>
<td>45</td>
<td>25</td>
<td>Ceiling</td>
<td>The acetaldehyde PEL is set to control mucous membrane irritation. See footnote a.</td>
<td>45</td>
<td>25</td>
<td>STEL ceiling limit; A3</td>
<td>Eye &amp; URT irritation</td>
</tr>
<tr>
<td>Acrylamide</td>
<td>79061</td>
<td>1990</td>
<td>Coagulant; other industrial uses; formed in certain foods during cooking</td>
<td>&gt;100M-500M</td>
<td>0.03</td>
<td>--</td>
<td>S</td>
<td>--</td>
<td>0.03</td>
<td>--</td>
<td>Skin; A3</td>
<td>CNS impairment</td>
</tr>
<tr>
<td>Acrylonitrile</td>
<td>107131</td>
<td>1987</td>
<td>Co-monomer in production of acrylic and modacrylic fibers</td>
<td>&gt;1B</td>
<td>4.5</td>
<td>2</td>
<td>S</td>
<td>5213</td>
<td>Cancer hazard</td>
<td>4</td>
<td>2</td>
<td>Skin; A3</td>
</tr>
<tr>
<td>Aniline</td>
<td>62533</td>
<td>1990</td>
<td>Chemical intermediate</td>
<td>&gt;1B</td>
<td>7.6</td>
<td>2</td>
<td>S</td>
<td>--</td>
<td>7.6</td>
<td>2</td>
<td>Skin; A3; BEI</td>
<td>Methemoglobinemia</td>
</tr>
<tr>
<td>o-Anisidine</td>
<td>90040</td>
<td>1987</td>
<td>Dye intermediate</td>
<td>10K-500K</td>
<td>0.5</td>
<td>0.1</td>
<td>S</td>
<td>--</td>
<td>0.5</td>
<td>--</td>
<td>Skin; A3; BEI</td>
<td>Methemoglobinemia</td>
</tr>
<tr>
<td>Antimony oxide (Antimony trioxide)</td>
<td>1309644</td>
<td>1990</td>
<td>Flame retardant</td>
<td>&gt;1M-10M</td>
<td>0.5</td>
<td>--</td>
<td>Antimony and compounds</td>
<td>--</td>
<td>0.5 (antimony and compounds)</td>
<td>--</td>
<td>Skin &amp; URT irritation (antimony and compounds)</td>
<td>Lung cancer, pneumoconiosis (antimony trioxide production)</td>
</tr>
<tr>
<td>Chemical</td>
<td>CAS No.</td>
<td>Year Listed</td>
<td>Identity</td>
<td>Production/ Import Volume Range in Pounds (TSCA, 2002; unless otherwise noted)</td>
<td>Cal/OSHA PEL (mg/m³)</td>
<td>Cal/OSHA PEL (ppm)</td>
<td>Cal/OSHA PEL Notations/ Vertical Standard</td>
<td>Cal/OSHA PEL Basis¹</td>
<td>TLV-TWA (mg/m³)</td>
<td>TLV-TWA (ppm)</td>
<td>TLV Comments/ Notations</td>
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<td></td>
</tr>
<tr>
<td>Arsenic (inorganic arsenic compounds)</td>
<td>--</td>
<td>1987</td>
<td>Alloy component; electrical device component; semiconductor device component</td>
<td>USGS (2007) estimated ~2M arsenic and 18M arsenic compounds imported in 2006.</td>
<td>0.01</td>
<td>--</td>
<td>5214 Cancer hazard</td>
<td>0.01</td>
<td>--</td>
<td>0.5</td>
<td>A1; BEI Lung cancer</td>
<td></td>
</tr>
<tr>
<td>Benzene</td>
<td>71432</td>
<td>1987</td>
<td>Chemical intermediate; found in fuels; solvent</td>
<td>&gt;1B</td>
<td>3.2</td>
<td>1.0</td>
<td>S 5218 Cancer hazard</td>
<td>2</td>
<td>0.01</td>
<td>0.5</td>
<td>Skin; A1; BEI Leukemia</td>
<td></td>
</tr>
<tr>
<td>Benzyl chloride</td>
<td>100447</td>
<td>1990</td>
<td>Chemical and dye intermediate; photographic developer</td>
<td>&gt;50M-100M</td>
<td>5</td>
<td>1</td>
<td>-- Sensitization and beryllium disease</td>
<td>0.002</td>
<td>29</td>
<td>5</td>
<td>A3 Eye, skin &amp; URT irritation</td>
<td></td>
</tr>
<tr>
<td>Beryllium and beryllium compounds</td>
<td>---</td>
<td>1987</td>
<td>Alloys; space optics; rocket fuel; aircraft parts</td>
<td>USGS (2007) estimated ~220K produced, ~150K imported in 2006.</td>
<td>0.0002</td>
<td>--</td>
<td>-- Sensitization and beryllium disease</td>
<td>0.002 (current)</td>
<td>29</td>
<td>5</td>
<td>A1 Skin; SEN; A1 Cancer (lung), berylliosis</td>
<td></td>
</tr>
<tr>
<td>Di(2-chloroethyl)ether</td>
<td>111444</td>
<td>1988</td>
<td>Solvent; chemical intermediate</td>
<td>&gt;1M-10M</td>
<td>30</td>
<td>5</td>
<td>S -- Sensitization and beryllium disease</td>
<td>0.00005 (proposed)</td>
<td>29</td>
<td>5</td>
<td>A4 Skin; A4 URT &amp; eye irritation; nausea</td>
<td></td>
</tr>
<tr>
<td>Bromoethane</td>
<td>74964</td>
<td>2000</td>
<td>Chemical intermediate</td>
<td>&gt;500K-1M</td>
<td>22</td>
<td>5</td>
<td>-- Sensitization and beryllium disease</td>
<td>22</td>
<td>5</td>
<td>5</td>
<td>Skin; A3 Liver damage; CNS impairment</td>
<td></td>
</tr>
<tr>
<td>Chemical</td>
<td>CAS No.</td>
<td>Year Listed</td>
<td>Identity Description</td>
<td>Production/ Import Volume Range in Pounds (TSCA, 2002; unless otherwise noted)</td>
<td>Cal/OSHA PEL (mg/m³)</td>
<td>Cal/OSHA PEL (ppm)</td>
<td>Cal/OSHA PEL Notations/ Vertical Standard</td>
<td>Cal/OSHA PEL Basis¹</td>
<td>TLV-TWA (mg/m³)</td>
<td>TLV-TWA (ppm)</td>
<td>TLV Comments/ Notations</td>
<td>TLV Basis</td>
</tr>
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<td>-----------------------------------------------</td>
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<td>---------------</td>
</tr>
<tr>
<td>1,3-Butadiene</td>
<td>106990</td>
<td>1988</td>
<td>Chemical intermediate</td>
<td>&gt;1B</td>
<td>2.2</td>
<td>1</td>
<td>5201</td>
<td>Carcinogen</td>
<td>4.4</td>
<td>2</td>
<td>A2; BEI</td>
<td>Cancer</td>
</tr>
<tr>
<td>Cadmium and cadmium compounds</td>
<td>---</td>
<td>1987</td>
<td>Electroplating; batteries; chemical intermediate</td>
<td>USGS (2007) estimated 2M produced, 300K imported in 2006</td>
<td>0.005</td>
<td>--</td>
<td>5207</td>
<td>Cancer hazard; lung and kidney disease</td>
<td>0.01</td>
<td>0.002</td>
<td>(respirable)</td>
<td>A2; BEI</td>
</tr>
<tr>
<td>Carbon black (airborne, unbound particles of respirable size)</td>
<td>1333864</td>
<td>2003</td>
<td>Used in many industrial applications - e.g., rubber products, pigment</td>
<td>&gt;500K-1M</td>
<td>3.5</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>3.5</td>
<td>--</td>
<td>A4; BEI</td>
<td>Minimize complaints of excessive dirtiness</td>
</tr>
<tr>
<td>Carbon tetrachloride</td>
<td>56235</td>
<td>1987</td>
<td>Industrial applications</td>
<td>&gt;100M-500M</td>
<td>12.6</td>
<td>2</td>
<td>S</td>
<td>See footnote a.</td>
<td>31</td>
<td>5</td>
<td>Skin; A3</td>
<td>Liver damage</td>
</tr>
<tr>
<td>Chloroethane (Ethyl chloride)</td>
<td>75003</td>
<td>1990</td>
<td>Chemical intermediate/solvent</td>
<td>&gt;50M-100M</td>
<td>264</td>
<td>100</td>
<td>S</td>
<td>The PEL is based on tumor formation in several laboratory animal species.</td>
<td>264</td>
<td>100</td>
<td>Skin; A3</td>
<td>Liver damage; embryo/fetal damage; CNS impairment</td>
</tr>
<tr>
<td>Chloroform</td>
<td>67663</td>
<td>1987</td>
<td>Chemical intermediate</td>
<td>&gt;500M-1B</td>
<td>9.78</td>
<td>2</td>
<td>--</td>
<td>--</td>
<td>49</td>
<td>10</td>
<td>A3; BEI</td>
<td>Lung cancer</td>
</tr>
<tr>
<td>Chloromethyl methyl ether (technical grade)</td>
<td>107302</td>
<td>1987</td>
<td>Chemical intermediate/solvent</td>
<td>&gt;10M-50M</td>
<td>--</td>
<td>--</td>
<td>5209</td>
<td>Cancer suspect agent</td>
<td>Levels as low as possible</td>
<td>Levels as low as possible</td>
<td>A2; BEI</td>
<td>Methemoglobinemia</td>
</tr>
<tr>
<td>1-Chloro-4-nitrobenzene</td>
<td>100005</td>
<td>1999</td>
<td>Chemical intermediate</td>
<td>&gt;10M-50M</td>
<td>0.64</td>
<td>0.1</td>
<td>S</td>
<td>--</td>
<td>0.64</td>
<td>0.10</td>
<td>Skin; A3; BEIₘ</td>
<td>URT &amp; eye irritation</td>
</tr>
</tbody>
</table>

¹ Cal/OSHA PEL Basis: The PEL is based on tumor formation in several laboratory animal species.
<table>
<thead>
<tr>
<th>Chemical</th>
<th>CAS No.</th>
<th>Year Listed</th>
<th>Identity</th>
<th>Production/Import Volume Range in Pounds (TSCA, 2002; unless otherwise noted)</th>
<th>Cal/OSHA PEL (mg/m³)</th>
<th>Cal/OSHA PEL (ppm)</th>
<th>Cal/OSHA PEL Notations/Vertical Standard</th>
<th>Cal/OSHA PEL Basis*</th>
<th>TLV-TWA (mg/m³)</th>
<th>TLV-TWA (ppm)</th>
<th>TLV Comments/Notations</th>
<th>TLV Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chromium (hexavalent compounds)</td>
<td></td>
<td>--</td>
<td>Corrosion inhibitor; metal finishing and chrome plating; stainless steel manufacture; manufacture of pigments and wood preservatives</td>
<td>&gt;50M-100M (chromium [VI] oxide); USGS (2007) estimated ~300K produced, ~800K imported for chromium in 2006</td>
<td>0.005</td>
<td>--</td>
<td>--</td>
<td>PEL is adopted from OSHA, which derived the value in 2006 based on a quantitative cancer risk assessment. Chromium VI was earlier identified by a Cal/OSHA Advisory Committee as a carcinogen (see footnote a).</td>
<td>0.05 water soluble</td>
<td>0.01 water insoluble</td>
<td>--</td>
<td>A1; BEI</td>
</tr>
<tr>
<td>Cobalt and certain cobalt compounds (see footnote b)</td>
<td></td>
<td>--</td>
<td>Alloys; chemical intermediate; catalyst; pigment; enamel coatings; batteries; electroplating</td>
<td>USGS (2007) estimated for cobalt: ~5M produced, ~26M imported in 2006</td>
<td>0.02</td>
<td>--</td>
<td>--</td>
<td>PEL for intended to control myocardial effects. See footnote a.</td>
<td>0.02 --</td>
<td>--</td>
<td>A3; BEI</td>
<td>Asthma; pulmonary function; myocardial effects</td>
</tr>
<tr>
<td>p-Dichlorobenzene</td>
<td>106467</td>
<td>1989</td>
<td>Chemical intermediate; deodorant; pesticide</td>
<td>&gt;50M-100M</td>
<td>60</td>
<td>10</td>
<td>--</td>
<td></td>
<td>60</td>
<td>10</td>
<td>A3</td>
<td>Eye irritation; kidney damage</td>
</tr>
<tr>
<td>3,3'-Dichlorobenzidine</td>
<td>91941</td>
<td>1987</td>
<td>Dye intermediate</td>
<td>10K-500K</td>
<td>--</td>
<td>--</td>
<td>S 5209</td>
<td>Cancer suspect agent Levels as low as possible</td>
<td>Levels as low as possible</td>
<td>A3</td>
<td>Bladder cancer; eye irritation</td>
<td></td>
</tr>
<tr>
<td>3,3'-Dichlorobenzidine dihydrochloride</td>
<td>612839</td>
<td>1998</td>
<td>Dye intermediate</td>
<td>&gt;10M-50M</td>
<td>--</td>
<td>--</td>
<td>S 5209</td>
<td>Cancer suspect agent Levels as low as possible (for parent compound)</td>
<td>Levels as low as possible (for parent compound)</td>
<td>A3 (for parent compound)</td>
<td>Bladder cancer; eye irritation (for parent compound)</td>
<td></td>
</tr>
<tr>
<td>Chemical</td>
<td>CAS No.</td>
<td>Year Listed</td>
<td>Identity</td>
<td>Production/Import Volume Range in Pounds (TSCA, 2002; unless otherwise noted)</td>
<td>Cal/OSHA PEL (mg/m³)</td>
<td>Cal/OSHA PEL (ppm)</td>
<td>Cal/OSHA PEL Notations/Vertical Standard</td>
<td>Cal/OSHA PEL Basis¹</td>
<td>TLV-TWA (mg/m³)</td>
<td>TLV-TWA (ppm)</td>
<td>Comments/Notations</td>
<td></td>
</tr>
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<td>----------------------------------</td>
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<td>1,4-Dichloro-2-butene</td>
<td>764410</td>
<td>1990</td>
<td>Chemical intermediate</td>
<td>&gt;50M-100M</td>
<td>0.025</td>
<td>0.005</td>
<td>S</td>
<td>--</td>
<td>0.026</td>
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<td>Skin; A2</td>
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<td>URT &amp; eye irritation</td>
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<td>1,1-Dichloroethane</td>
<td>75343</td>
<td>1990</td>
<td>Solvent</td>
<td>10K-500K</td>
<td>400</td>
<td>100</td>
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<td>405</td>
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<td>URT &amp; eye irritation; liver &amp; kidney damage</td>
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<td>Dichloromethane (Methylene chloride)</td>
<td>75092</td>
<td>1988</td>
<td>Chemical intermediate; solvent</td>
<td>&gt;100M-500M</td>
<td>87</td>
<td>25</td>
<td>5202</td>
<td>Carcinogen</td>
<td>174</td>
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<td>A3; BEI</td>
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<td>1,2-Dichloropropene</td>
<td>78875</td>
<td>1990</td>
<td>Chemical intermediate; fumigant</td>
<td>&gt;100M-500M</td>
<td>350</td>
<td>75</td>
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<td>46</td>
<td>10</td>
<td>URT irritation; body weight effects</td>
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<td>Di(2-ethylhexyl)phthalate</td>
<td>117817</td>
<td>1988</td>
<td>Plasticizer</td>
<td>&gt;100M-500M</td>
<td>5</td>
<td>--</td>
<td>--</td>
<td>5</td>
<td>--</td>
<td>--</td>
<td>A3</td>
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<td>LRT irritation</td>
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<td>1,1-Dimethylhydrazine (UDMH)</td>
<td>57147</td>
<td>1989</td>
<td>Rocket fuel; chemical intermediate</td>
<td>10K-500K</td>
<td>0.025</td>
<td>0.01</td>
<td>S</td>
<td>--</td>
<td>0.025</td>
<td>0.01</td>
<td>Skin; A3</td>
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<td>URT irritation; nasal cancer</td>
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<td>Dimethyl sulfate</td>
<td>77781</td>
<td>1988</td>
<td>Solvent; methylating and sulfating agent</td>
<td>&gt;10M-50M</td>
<td>0.5</td>
<td>0.1</td>
<td>S</td>
<td>--</td>
<td>0.5</td>
<td>0.1</td>
<td>Skin; A3</td>
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<td></td>
<td></td>
<td></td>
<td>Eye &amp; skin irritation</td>
<td></td>
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<tr>
<td>2,4-Dinitrotoluene; 2,6-Dinitrotoluene; Dinitrotoluene mixture, 2,4-/2,6-;</td>
<td>121142; 606202; 25321146</td>
<td>1988; 1995; 1996;</td>
<td>Chemical intermediate - manufacture of polyurethanes; production of explosives; dye intermediate; plasticizer</td>
<td>2,4-DNT: 10K-500K; 2,6-DNT: &gt;100M-500M in 1994; no subsequent reports Mixed isomers: &gt;1B</td>
<td>0.15 (2,4-DNT)</td>
<td>--</td>
<td>S</td>
<td>--</td>
<td>0.2 (mixed isomers)</td>
<td>--</td>
<td>Mixed isomers; Skin; A3; BEIm</td>
<td>Cardiac impairment; reproductive effects</td>
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</table>

¹ Cal/OSHA PEL Basis: PEL is based on hematological changes and effects on the epithelium observed in rats. 1,4-dichloro-2-butene has been shown to be mutagenic.

See footnote a.

Mixed isomers; Skin; A3; BEIm
<table>
<thead>
<tr>
<th>Chemical</th>
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<th>Cal/OSHA PEL (ppm)</th>
<th>Cal/OSHA PEL Notations/Vertical Standard</th>
<th>Cal/OSHA PEL Basis¹</th>
<th>TLV-TWA (mg/m³)</th>
<th>TLV-TWA (ppm)</th>
<th>TLV Comments/Notations</th>
<th>TLV Basis</th>
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<tbody>
<tr>
<td>1,4-Dioxane</td>
<td>123911</td>
<td>1988</td>
<td>Solvent; stabilizer</td>
<td>&gt;1M-10M</td>
<td>90</td>
<td>25</td>
<td>S</td>
<td>--</td>
<td>72</td>
<td>20</td>
<td>Skin; A3</td>
<td>Liver damage</td>
</tr>
<tr>
<td>Epichlorohydrin</td>
<td>106898</td>
<td>1987</td>
<td>Solvent; stabilizer; chemical intermediate</td>
<td>&gt;500M-1B</td>
<td>0.19</td>
<td>0.05</td>
<td>S</td>
<td>--</td>
<td>1.9</td>
<td>0.5</td>
<td>Skin; A3</td>
<td>Lowered to control reproductive and respiratory effects and the possibility of carcinogenic effects.</td>
</tr>
<tr>
<td>Ethyl acrylate</td>
<td>140885</td>
<td>1989</td>
<td>Monomer used to produce polymers and copolymers</td>
<td>&gt;100M-500M</td>
<td>20</td>
<td>5</td>
<td>S</td>
<td>--</td>
<td>20</td>
<td>5</td>
<td>A4</td>
<td>URT irritation; male reproductive</td>
</tr>
<tr>
<td>Ethylbenzene</td>
<td>100414</td>
<td>2004</td>
<td>Solvent; chemical intermediate; fuel component</td>
<td>&gt;1B</td>
<td>435</td>
<td>100</td>
<td>--</td>
<td>--</td>
<td>434</td>
<td>100</td>
<td>A3; BEI</td>
<td>URT irritation; CNS impairment; eye irritation</td>
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<tr>
<td>Ethylene dibromide (1,2-Dichloroethane)</td>
<td>106934</td>
<td>1987</td>
<td>Chemical intermediate; solvent; pesticide</td>
<td>&gt;1M-10M</td>
<td>1</td>
<td>0.13</td>
<td>S</td>
<td>5219</td>
<td>41</td>
<td>10</td>
<td>A4</td>
<td>Liver damage; nausea</td>
</tr>
<tr>
<td>Ethyleneimine</td>
<td>151564</td>
<td>1988</td>
<td>Chemical intermediate; fumigant</td>
<td>&gt;1B</td>
<td>2</td>
<td>1</td>
<td>S</td>
<td>5209</td>
<td>0.9</td>
<td>0.5</td>
<td>Skin; A3</td>
<td>Cancer: eye, URT &amp; skin irritation</td>
</tr>
<tr>
<td>Ethylene oxide (gas)</td>
<td>75218</td>
<td>1987</td>
<td>Chemical intermediate; byproduct of combustion</td>
<td>&gt;1B</td>
<td>--</td>
<td>0.75</td>
<td>--</td>
<td>5217</td>
<td>0.4</td>
<td>0.3</td>
<td>Ceiling; SEN; A2</td>
<td>Cancer: CNS impairment</td>
</tr>
<tr>
<td>Glasswool fibers (airborne particles of respirable size)</td>
<td>---</td>
<td>1990</td>
<td>Respirable fiberglass</td>
<td>--</td>
<td>--</td>
<td>1 f/cc</td>
<td>--</td>
<td>See footnote a.</td>
<td>1 f/cc</td>
<td>--</td>
<td>A3</td>
<td>Skin and mucous membrane irritation</td>
</tr>
</tbody>
</table>

¹ Cal/OSHA PEL Basis:
- A2: Acute toxicity
- A3: Acute toxicity and irritation
- A4: Acute toxicity, irritation, and upper respiratory tract (URT) irritation

Note: CEILING: SEN (see footnote a.)
<table>
<thead>
<tr>
<th>Chemical</th>
<th>CAS No.</th>
<th>Year Listed</th>
<th>Identity</th>
<th>Production/Import Volume Range in Pounds (TSCA, 2002; unless otherwise noted)</th>
<th>Cal/OSHA PEL (mg/m³)</th>
<th>Cal/OSHA PEL (ppm)</th>
<th>Cal/OSHA PEL Notations/Vertical Standard</th>
<th>Cal/OSHA PEL Basis¹</th>
<th>TLV-TWA (mg/m³)</th>
<th>TLV-TWA (ppm)</th>
<th>TLV Comments/Notations</th>
<th>TLV Basis</th>
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<tbody>
<tr>
<td>Hexachlorobenzene</td>
<td>118741</td>
<td>1987</td>
<td>Chemical intermediate; fungicide</td>
<td>10K-500K</td>
<td>0.002</td>
<td>--</td>
<td>S</td>
<td>The PEL was lowered based on hepatic and neurological effects. See footnote a.</td>
<td>0.002</td>
<td>--</td>
<td>A3</td>
<td>Liver; metabolic disorders</td>
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<tr>
<td>Hexachloroethane</td>
<td>67721</td>
<td>1990</td>
<td>Various industrial applications (smoke generation, chlorine generation for aluminum foundries and emissions testing)</td>
<td>10K-500K</td>
<td>10</td>
<td>1</td>
<td>S</td>
<td>--</td>
<td>10</td>
<td>1</td>
<td>Skin; A3</td>
<td>Liver &amp; kidney damage</td>
</tr>
<tr>
<td>Hydrazine</td>
<td>302012</td>
<td>1988</td>
<td>Chemical intermediate; rocket propellant; other industrial applications</td>
<td>&gt;1M-10M</td>
<td>0.013</td>
<td>0.01</td>
<td>S</td>
<td>PEL was lowered to 0.01 ppm based on observations of slight increases in nasal tumors in rats at 0.05 ppm. See footnote a.</td>
<td>0.013</td>
<td>0.01</td>
<td>A3</td>
<td>URT cancer</td>
</tr>
<tr>
<td>Indium phosphide</td>
<td>22398807</td>
<td>2001</td>
<td>Semiconductor</td>
<td>USGS (2007) estimated ~300K imports of indium in 2006</td>
<td>0.1</td>
<td>--</td>
<td>Indium compounds</td>
<td>--</td>
<td>0.1</td>
<td>--</td>
<td>Pulmonary edema; pneumonitis; dental erosion; malaise</td>
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<tr>
<td>Chemical</td>
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<td>Year Listed</td>
<td>Identity</td>
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<td>Cal/OSHA PEL Notations/Vertical Standard</td>
<td>Cal/OSHA PEL Basis¹</td>
<td>TLV-TWA (mg/m³)</td>
<td>TLV-TWA (ppm)</td>
<td>TLV Comments/Notations</td>
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<tr>
<td>Lead and lead compounds</td>
<td>--</td>
<td>1992</td>
<td>Used in the manufacture of various products, such as batteries, ammunition, solder, pipes, cable covering; in crystal, ceramic glazes</td>
<td>Lead oxide 1M-10M; lead chloride 10K-500K; USGS (2007) estimated ~4M of lead produced in 2006</td>
<td>0.05</td>
<td>--</td>
<td>5198</td>
<td>Numerous health effects including reproductive toxicity; not regulated as an occupational carcinogen</td>
<td>0.05</td>
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<td>A3; BEI</td>
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<td>2-Methylaziridine (Propyleneimine)</td>
<td>75558</td>
<td>1988</td>
<td>Chemical intermediate</td>
<td>10K-500K</td>
<td>5</td>
<td>2</td>
<td>S</td>
<td>--</td>
<td>5</td>
<td>2</td>
<td>Skin; A3</td>
<td>Eye, skin &amp; URT irritation</td>
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<td>4,4'-Methylene bis(2-chloroaniline)</td>
<td>101144</td>
<td>1987</td>
<td>Curing agent</td>
<td>&gt;1M-10M</td>
<td>0.01</td>
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<td>S</td>
<td>5215</td>
<td>0.1</td>
<td>0.01</td>
<td>Skin; A2; BEI</td>
<td>Bladder cancer; methemoglobinemia</td>
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<td>4,4'-Methyleneedianiline</td>
<td>101779</td>
<td>1988</td>
<td>Chemical intermediate (primarily used to produce disocyanate and polyisocyanates)</td>
<td>&gt;1M-10M</td>
<td>0.08</td>
<td>0.01</td>
<td>5200</td>
<td>Carcinogen and liver toxin</td>
<td>0.8</td>
<td>0.1</td>
<td>Skin; A3</td>
<td>Liver damage</td>
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<td>Methylhydrazine and its salts</td>
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<td>1992</td>
<td>Rocket fuel; chemical intermediate; solvent</td>
<td>Methylhydrazine: 10K-500K</td>
<td>0.019</td>
<td>0.01</td>
<td>S</td>
<td>--</td>
<td>0.02</td>
<td>0.01</td>
<td>Skin; A3</td>
<td>URT irritation; lung cancer; eye irritation; liver damage</td>
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<tr>
<td>Methyl iodide</td>
<td>74884</td>
<td>1988</td>
<td>Methylating agent; used in microscopy; etching agent; in fire extinguishers</td>
<td>10K-500K</td>
<td>10</td>
<td>2</td>
<td>S</td>
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<td>12</td>
<td>2</td>
<td>Skin</td>
<td>Eye damage; CNS impairment</td>
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<td>Cal/OSHA PEL (mg/m³)</td>
<td>Cal/OSHA PEL (ppm)</td>
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<td>TLV-TWA (mg/m³)</td>
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<td>Naphthalene</td>
<td>91203</td>
<td>2002</td>
<td>Chemical intermediate; deodorant; in fuel exhaust; moth repellant</td>
<td>&gt;100M-500M</td>
<td>50</td>
<td>10</td>
<td>--</td>
<td>--</td>
<td>52</td>
<td>10</td>
<td>Skin; A4</td>
<td>Hematologic effects; URT &amp; eye irritation; eye damage</td>
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<td>1-Naphthylamine</td>
<td>134327</td>
<td>1989</td>
<td>Chemical intermediate; dye intermediate</td>
<td>10K-500K</td>
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<td>--</td>
<td>52009</td>
<td>Cancer suspect agent</td>
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<td>Nickel (metallic)</td>
<td>7440020</td>
<td>1989</td>
<td>Alloys; silver; stainless steel; electroplating; batteries; electrodes; ceramics; chemical intermediate</td>
<td>USGS (2007) estimated ~400M nickel imported in 2006</td>
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<td>--</td>
<td>1.5</td>
<td>--</td>
<td>A5</td>
<td>Dermatitis; pneumoconiosis</td>
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<td>Nickel carbonyl</td>
<td>13463393</td>
<td>1987</td>
<td>Chemical intermediate; catalyst</td>
<td>See nickel</td>
<td>0.007</td>
<td>0.001</td>
<td>--</td>
<td>--</td>
<td>0.12</td>
<td>0.05</td>
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<td>Lung &amp; nasal cancer</td>
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<td>Nickel compounds</td>
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<td>2004</td>
<td>Chemical intermediate; batteries; ceramics; fuel cell electrodes; catalysts</td>
<td>See nickel 0.1 (soluble) 1 (insoluble)</td>
<td>0.1 (soluble)</td>
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<td>--</td>
<td>--</td>
<td>0.1</td>
<td>--</td>
<td>A4</td>
<td>Soluble: Lung damage; nasal cancer</td>
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<td>Nitrobenzene</td>
<td>98953</td>
<td>1997</td>
<td>Chemical intermediate - mostly aniline</td>
<td>&gt;1B</td>
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<td>S</td>
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<td>5</td>
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<td>Skin; A3; BEI</td>
<td>Methemoglobinemia</td>
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<td>Nitromethane</td>
<td>75525</td>
<td>1997</td>
<td>Solvent; rocket propellant; racing fuel additive</td>
<td>&gt;10M-50M</td>
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<td>2</td>
<td>--</td>
<td>The PEL was lowered from 100 to 2 ppm based on renal toxicity in rats at 300 ppm.</td>
<td>50</td>
<td>20</td>
<td>A3</td>
<td>Thyroid effects; URT irritation; lung damage</td>
</tr>
</tbody>
</table>

¹ Notation: A1 = acute health effects; A2 = chronic health effects; A3 = respiratory effects; A4 = skin effects; A5 = other health effects.
<table>
<thead>
<tr>
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<th>TLV-TWA (mg/m³)</th>
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<th>TLV Basis</th>
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<tr>
<td>2-Nitropropane</td>
<td>79469</td>
<td>1988</td>
<td>Chemical intermediate; racing fuel additive; rocket propellant; solvent</td>
<td>&gt;10M-50M</td>
<td>35</td>
<td>10</td>
<td>--</td>
<td>--</td>
<td>36</td>
<td>10</td>
<td>A3</td>
<td>Liver damage; liver cancer</td>
</tr>
<tr>
<td>o-Nitrotoluene</td>
<td>88722</td>
<td>1998</td>
<td>Chemical intermediate</td>
<td>&gt;10M-50M</td>
<td>11</td>
<td>2</td>
<td>All isomers; S</td>
<td>--</td>
<td>11</td>
<td>2</td>
<td>--</td>
<td>All isomers; Skin; BEI₃</td>
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<tr>
<td>Phenyl glycidyl ether</td>
<td>122601</td>
<td>1990</td>
<td>Chemical intermediate; stabilizer; plasticizer; monomer for photoreactive polymers; in epoxy resins</td>
<td>10K-500K</td>
<td>0.6</td>
<td>0.1</td>
<td>S</td>
<td>--</td>
<td>0.6</td>
<td>0.1</td>
<td>Skin; SEN; A3</td>
<td>Testicular damage</td>
</tr>
<tr>
<td>Phenylhydrazine and its salts</td>
<td>---</td>
<td>1992</td>
<td>Chemical intermediate</td>
<td>&gt;1M-10M</td>
<td>20</td>
<td>5</td>
<td>S</td>
<td>--</td>
<td>0.4</td>
<td>0.1</td>
<td>Skin; A3</td>
<td>Anemia; URT &amp; skin irritation</td>
</tr>
<tr>
<td>Propylene oxide</td>
<td>75569</td>
<td>1988</td>
<td>Chemical intermediate; pesticide</td>
<td>&gt;1B</td>
<td>4.75</td>
<td>2</td>
<td>--</td>
<td>Based on respiratory effects; carcinogenic effects noted. See footnote d.</td>
<td>5</td>
<td>2</td>
<td>SEN; A3</td>
<td>Eye &amp; URT irritation</td>
</tr>
<tr>
<td>Pyridine</td>
<td>110861</td>
<td>2002</td>
<td>Chemical intermediate</td>
<td>&gt;10M-50M</td>
<td>15</td>
<td>5</td>
<td>--</td>
<td>--</td>
<td>3</td>
<td>1</td>
<td>A3</td>
<td>Skin irritation; liver &amp; kidney damage</td>
</tr>
<tr>
<td>Silica, crystalline (airborne particles of respirable size)</td>
<td>---</td>
<td>1988</td>
<td>Glass-making; metallurgical applications: abrasives; fillers; ceramics; filtration; petroleum industry</td>
<td>&gt;500K-1M</td>
<td>Cristobalite &amp; tridymite, respirable dust: 0.05</td>
<td>Quartz, silica (fused) &amp; tripoli, respirable dust: 0.1</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>α-Quartz and Cristobalite: 0.025 (respirable fraction)</td>
<td>A2</td>
<td>Pulmonary fibrosis; lung cancer</td>
</tr>
</tbody>
</table>

**Notes:**

- **PEL** denotes Permissible Exposure Limit.
- **TLV-TWA** denotes Threshold Limit Value—Time Weighted Average.
- **TLV** denotes Tolerable Limit Value.
- **Comments/Notations** include additional information or notations related to the chemical's health effects.
- **TLV Basis** specifies the basis for the threshold limit value.

**Footnotes:**

- a: See footnote a.
- b: See footnote b.
- c: See footnote c.
- d: See footnote d.
<table>
<thead>
<tr>
<th>Chemical</th>
<th>CAS No.</th>
<th>Year Listed</th>
<th>Identity</th>
<th>Production/ Import Volume Range in Pounds (TSCA, 2002; unless otherwise noted)</th>
<th>Cal/OSHA PEL (mg/m³)</th>
<th>Cal/OSHA PEL (ppm)</th>
<th>Cal/OSHA PEL Notations/ Vertical Standard</th>
<th>Cal/OSHA PEL Basis</th>
<th>TLV-TWA (mg/m³)</th>
<th>TLV-TWA (ppm)</th>
<th>TLV Comments/ Notations</th>
<th>TLV Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strong inorganic acid mists containing sulfuric acid</td>
<td>--</td>
<td>2003</td>
<td>Generated during manufacture/use of sulfuric acid, sulfur trioxide or oleum. Sulfuric acid used primarily as a chemical intermediate in the manufacture of fertilizer, as a reagent to make explosives, other acids, and glue; in the purification of petroleum products; and in lead-acid batteries</td>
<td>Sulfuric acid: &gt;1B</td>
<td>1</td>
<td>--</td>
<td>PEL is for sulfuric acid</td>
<td>--</td>
<td>0.2</td>
<td>--</td>
<td>--</td>
<td>Pulmonary function</td>
</tr>
<tr>
<td>1,1,2,2-Tetrachloroethane (Perchloroethylene)</td>
<td>79345</td>
<td>1990</td>
<td>Chemical intermediate/solvent</td>
<td>&gt;1M-10M</td>
<td>7</td>
<td>1</td>
<td>S</td>
<td>--</td>
<td>7</td>
<td>1</td>
<td>Skin; A3</td>
<td>Liver damage</td>
</tr>
<tr>
<td>Tetrachloroethylene (Perchloroethylene)</td>
<td>127184</td>
<td>1988</td>
<td>Dry cleaning fluid; chemical intermediate; vapor degreaser</td>
<td>&gt;100M-500M</td>
<td>170</td>
<td>25</td>
<td>--</td>
<td>See footnote a.</td>
<td>170</td>
<td>25</td>
<td>A3; BEI</td>
<td>CNS impairment</td>
</tr>
<tr>
<td>Toluene diisocyanate</td>
<td>26471625</td>
<td>1989</td>
<td>Chemical intermediate</td>
<td>&gt;1B</td>
<td>0.04</td>
<td>0.005</td>
<td>--</td>
<td>--</td>
<td>0.04</td>
<td>0.005</td>
<td>SEN; A4 (inhalable fraction and vapor) (proposed)</td>
<td>Respiratory sensitization; asthma; eye irritation</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>SEN; A3</td>
<td>Asthma (proposed)</td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>Chemical</th>
<th>CAS No.</th>
<th>Year Listed</th>
<th>Identity</th>
<th>Production/Import Volume Range in Pounds (TSCA, 2002; unless otherwise noted)</th>
<th>Cal/OSHA PEL (mg/m³)</th>
<th>Cal/OSHA PEL (ppm)</th>
<th>Cal/OSHA PEL Notations/Vertical Standard</th>
<th>Cal/OSHA PEL Basis¹</th>
<th>TLV-TWA (mg/m³)</th>
<th>TLV-TWA (ppm)</th>
<th>TLV Comments/Notations</th>
<th>TLV Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td>o-Toluidine</td>
<td>95534</td>
<td>1988</td>
<td>Dye intermediate</td>
<td>&gt;10M-50M</td>
<td>9</td>
<td>2</td>
<td>S</td>
<td>--</td>
<td>9</td>
<td>2</td>
<td></td>
<td>Skin; A3; BEIₘ</td>
</tr>
<tr>
<td>Trichloroethylene</td>
<td>79016</td>
<td>1988</td>
<td>Solvent; chemical intermediate</td>
<td>&gt;100M-500M</td>
<td>135</td>
<td>25</td>
<td>--</td>
<td>See footnote a.</td>
<td>269</td>
<td>10</td>
<td></td>
<td>CNS impairment; cognitive decrements; renal toxicity</td>
</tr>
<tr>
<td>1,2,3-Trichloropropane</td>
<td>96184</td>
<td>1992</td>
<td>Chemical intermediate; solvent; paint and varnish remover; cleaning and degreasing agent</td>
<td>&gt;1M-10M</td>
<td>60</td>
<td>10</td>
<td>--</td>
<td>--</td>
<td>60</td>
<td>10</td>
<td></td>
<td>Liver &amp; kidney damage; eye &amp; URT irritation</td>
</tr>
<tr>
<td>Vanadium pentoxide (orthorhombic crystalline form)</td>
<td>1314621</td>
<td>2005</td>
<td>Chemical intermediate; catalyst</td>
<td>USGS (2007) estimated approximately 5M imports of vanadium pentoxide in 2006</td>
<td>0.05 (respirable dust and fume)</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>0.05 (respirable)</td>
<td>0.02 (inhalable) (proposed)</td>
<td>--</td>
<td>A4; BEIₘ</td>
</tr>
<tr>
<td>Vinyl chloride</td>
<td>75014</td>
<td>1987</td>
<td>Chemical intermediate; monomer for production of polyvinyl chloride</td>
<td>&gt;1B</td>
<td>--</td>
<td>1</td>
<td>S 5210</td>
<td>Cancer suspect agent</td>
<td>3</td>
<td>1</td>
<td></td>
<td>Liver cancer; liver damage</td>
</tr>
<tr>
<td>Chemical</td>
<td>CAS No.</td>
<td>Year Listed</td>
<td>Identity</td>
<td>Production/ Import Volume Range in Pounds (TSCA, 2002; unless otherwise noted)</td>
<td>Cal(OSHA) PEL (mg/m³)</td>
<td>Cal(OSHA) PEL (ppm)</td>
<td>Cal(OSHA) PEL Notations/ Vertical Standard</td>
<td>Cal(OSHA) PEL Basis</td>
<td>TLV-TWA (mg/m³)</td>
<td>TLV-TWA (ppm)</td>
<td>TLV Comments/ Notations</td>
<td>TLV Basis</td>
</tr>
<tr>
<td>----------</td>
<td>---------</td>
<td>-------------</td>
<td>---------</td>
<td>--------------------------------------------------------------------------------</td>
<td>------------------------</td>
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<td>----------------------</td>
<td>----------------</td>
<td>----------------</td>
<td>-----------------------------</td>
<td>-------------</td>
</tr>
<tr>
<td>4-Vinylcyclohexene</td>
<td>100403</td>
<td>1996</td>
<td>Precursor for vinylcyclohexene dioxide</td>
<td>&gt;1M-10M</td>
<td>0.4</td>
<td>0.1</td>
<td>S</td>
<td>PELs for 4-vinyl cyclohexene and vinyl cyclohexene dioxide were changed by adding a skin designation to 4-vinyl cyclohexene and reducing the PEL for vinyl cyclohexene dioxide to 0.1 ppm based on a dermal LD50 value of 20 ml/kg in rabbits and the carcinogenic potential of these compounds. See footnote a.</td>
<td>0.4</td>
<td>0.1</td>
<td>A3</td>
<td>Female &amp; male reproductive damage</td>
</tr>
<tr>
<td>Vinyl trichloride (1,1,2-Trichloroethane)</td>
<td>79005</td>
<td>1990</td>
<td>Chemical intermediate; solvent</td>
<td>&gt;100M-500M</td>
<td>45</td>
<td>10</td>
<td>S</td>
<td>--</td>
<td>55</td>
<td>10</td>
<td>Skin; A3</td>
<td>CNS impairment; liver damage</td>
</tr>
</tbody>
</table>

a. For the subset of chemicals listed below, the Cal/OSHA Advisory Committee charged with reviewing PELs explicitly acknowledged the failure to address the carcinogenicity of the compounds and/or the failure to conduct a quantitative risk assessment by stating “This substance has been identified by the International Agency for Research on Cancer as a carcinogen (Group 2B or higher). The exposure limits recommended have been primarily set on the basis of other types of toxic results, damage or interference with organ systems, irritation, respiratory problems, etc. Quantitative risk assessments can be used to estimate risks of cancer at various exposure levels in order to set a Permissible Exposure Limit. No such risk assessments have been conducted by this committee” (http://www.dir.ca.gov/oshsb/aircontaminant2.html). This position statement applied to: acetaldehyde, carbon tetrachloride, cobalt (elemental and inorganic compounds as Co), Cr VI compounds, p-dichlorobenzene, 1,1–dimethylhydrazine, glass (fibrous), heptachlor, hexachlorobenzene, hydrazine, perchloroethylene, phenyl glycidyl ether, trichloroethylene, vinyl acetate, 4-vinyl cyclohexene, and vinyl cyclohexene dioxide.

b. Cobalt metal powder (1992), cobalt [II] oxide (1992), cobalt sulfate (2005), and cobalt sulfate heptahydrate (2000) are listed as known to cause cancer under Proposition 65, with dates of listing shown in parentheses.

c. Nickel compounds as a group were listed in 2004. Various inorganic nickel compounds had been listed individually in 1987 and 1989.

d. This proposed limit for propylene oxide was adopted by ACGIH in 2001. The ACGIH limit was set based on non-cancer effects observed in laboratory animals. The Cal/OSHA Advisory Committee considered these effects and decided to rely on a 1994 risk assessment by the U.S. EPA. The U.S. EPA assessment estimated a carcinogenic risk of 1/10,000 at 0.03 mg/m³ for a 24 hr/d, 7 d/wk exposure. The Committee estimated that this was equivalent to a 1/1,000 risk for an occupational exposure at 0.7 ppm propylene oxide. The Initial Statement of Reasons for the propylene oxide PEL noted that during the March 30, 2004, advisory meeting, additional scientific and feasibility data was provided that supported the ACGIH TLV level of 2 ppm instead of the Committee’s recommended level.
The proposed change in the Cal/OSHA PEL was considered necessary to prevent harmful respiratory effects and was supported by the ACGIH document for propylene oxide.

**Abbreviations for Table A-2**

- BEI: Biological exposure index
- BEIM: Biological exposure index for methemoglobin inducers
- CNS: Central nervous system
- GI: Gastrointestinal
- LRT: Lower respiratory tract
- PNS: Peripheral nervous system
- S: Skin notation
- SEN: Potential for sensitization
- URT: Upper respiratory tract

**Production volume (pounds):**

- B: billion
- K: thousand
- M: million

**ACGIH carcinogen classifications (ACGIH, 2006):**

A1: “Confirmed human carcinogen” based on the weight of evidence from epidemiologic studies.

A2: “Suspected human carcinogen” used primarily when there is limited evidence of carcinogenicity in humans and sufficient evidence of carcinogenicity in experimental animals with relevance to humans.

A3: “Confirmed animal carcinogen with unknown relevance to humans,” which is typically used for agents that are carcinogenic in experimental animals “at a relatively high dose, by route(s) of administration, at site(s), of histologic types(s), or by mechanism(s) that may not be relevant to worker exposure.”

A4: “Not classifiable as a human carcinogen” which is typically used for agents which “cause concern that they could be carcinogenic for humans but which cannot be assessed conclusively because of a lack of data. *In vitro* or animal studies do not provide indications of carcinogenicity which are sufficient to classify the agent into one of the other categories.”

A5: “Not suspected as a human carcinogen” based on properly conducted epidemiologic studies in humans, or based on evidence suggesting a lack of carcinogenicity in experimental animals that is supported by mechanistic data.
### Table A-3. Workplace chemicals listed as known to the state to cause reproductive and/or developmental toxicity under Proposition 65 that are regulated occupationally based on various endpoints in California

<table>
<thead>
<tr>
<th>Chemical Identity</th>
<th>Chemical Type</th>
<th>CAS No.</th>
<th>Date Listed</th>
<th>Production Volume Range in Pounds (TSCA, 2002)</th>
<th>Cal/OSHA PEL (mg/m³)</th>
<th>Cal/OSHA PEL (ppm)</th>
<th>Cal/OSHA PEL Notations/ Vertical Standard</th>
<th>PEL Basis</th>
<th>TLV-TWA (mg/m³)</th>
<th>TLV-TWA (ppm)</th>
<th>TLV Notations</th>
<th>TLV Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arsenic (inorganic oxides)</td>
<td>d*</td>
<td>---</td>
<td>1997</td>
<td>Chemical intermediate; pigment; ceramic enamel; preservative; drug; pesticide</td>
<td>&gt;1M-10M (arsenic trioxide)</td>
<td>0.01</td>
<td>--</td>
<td>5214</td>
<td>Cancer hazard</td>
<td>0.01</td>
<td>--</td>
<td>A1; BEI</td>
</tr>
<tr>
<td>Benzene</td>
<td>d, m</td>
<td>71432</td>
<td>1997</td>
<td>Chemical intermediate; found in gasoline and other fuels; solvent</td>
<td>&gt;1B</td>
<td>3.2</td>
<td>1.0</td>
<td>S 5218</td>
<td>Cancer hazard</td>
<td>2</td>
<td>0.5</td>
<td>Skin; A1; BEI</td>
</tr>
<tr>
<td>1,3-Butadiene</td>
<td>d, f, m</td>
<td>106990</td>
<td>2004</td>
<td>Chemical intermediate</td>
<td>&gt;1B</td>
<td>2.2</td>
<td>1</td>
<td>5201</td>
<td>Carcinogen</td>
<td>4.4</td>
<td>2</td>
<td>A2</td>
</tr>
<tr>
<td>Cadmium</td>
<td>d, m</td>
<td>---</td>
<td>1997</td>
<td>Chemical intermediate; batteries; chemical intermediate</td>
<td>USGS (2007) estimated ~2M produced, ~300K imported in 2006</td>
<td>0.005</td>
<td>--</td>
<td>5207</td>
<td>Cancer hazard; lung and kidney disease</td>
<td>0.01</td>
<td>0.002 (respirable)</td>
<td>--</td>
</tr>
<tr>
<td>Carbon disulfide</td>
<td>d, f, m</td>
<td>75150</td>
<td>1989</td>
<td>Industrial applications</td>
<td>&gt;10M-50M</td>
<td>12</td>
<td>4</td>
<td>S</td>
<td>NA</td>
<td>3</td>
<td>1</td>
<td>Skin; A4</td>
</tr>
<tr>
<td>Carbon monoxide</td>
<td>d</td>
<td>630080</td>
<td>1989</td>
<td>Byproduct</td>
<td>---</td>
<td>29</td>
<td>25</td>
<td>NA</td>
<td>29</td>
<td>25</td>
<td>BEI</td>
<td>Carboxyhemoglobinemia</td>
</tr>
<tr>
<td>Di-n-butyl phthalate (DBP)</td>
<td>d, f, m</td>
<td>84742</td>
<td>2005</td>
<td>Solvent; plasticizer</td>
<td>&gt;10M-50M</td>
<td>5</td>
<td>--</td>
<td>--</td>
<td>NA</td>
<td>5</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Di(2-ethylhexyl)phthalate</td>
<td>d, m</td>
<td>117817</td>
<td>2003</td>
<td>Plasticizer</td>
<td>&gt;100M-500M</td>
<td>5</td>
<td>--</td>
<td>--</td>
<td>NA</td>
<td>5</td>
<td>--</td>
<td>A3</td>
</tr>
<tr>
<td><em>m</em>-Dinitrobenzene</td>
<td>m</td>
<td>99650</td>
<td>1990</td>
<td>Chemical intermediate</td>
<td>&gt;10-50M in 1986; no subsequent reports</td>
<td>1</td>
<td>0.15</td>
<td>S</td>
<td>NA</td>
<td>1</td>
<td>0.15</td>
<td>Skin; BEI</td>
</tr>
<tr>
<td>Chemical Identity</td>
<td>CAS No</td>
<td>Date Listed</td>
<td>Type</td>
<td>Identity</td>
<td>Production Volume Range in Pounds (TSCA, 2002)</td>
<td>Cal/OSHA PEL (mg/m³)</td>
<td>Cal/OSHA PEL (ppm)</td>
<td>Cal/OSHA PEL Notations/Vertical Standard</td>
<td>PEL Basis</td>
<td>TLV-TWA (mg/m³)</td>
<td>TLV-TWA (ppm)</td>
<td>TLV Basis</td>
</tr>
<tr>
<td>-------------------</td>
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<td>----------------</td>
<td>----------------</td>
<td>------------</td>
</tr>
<tr>
<td>o-Dinitrobenzene</td>
<td>m</td>
<td>528290</td>
<td>1990</td>
<td>Chemical intermediate</td>
<td>Chemical intermediate</td>
<td>&gt;1M-10M</td>
<td>1</td>
<td>0.15</td>
<td>S</td>
<td>NA</td>
<td>1</td>
<td>0.15</td>
</tr>
<tr>
<td>p-Dinitrobenzene</td>
<td>m</td>
<td>100254</td>
<td>1990</td>
<td>Chemical intermediate</td>
<td>Chemical intermediate</td>
<td>&gt;500K-1M in 1986; no subsequent reports</td>
<td>1</td>
<td>0.15</td>
<td>S</td>
<td>NA</td>
<td>1</td>
<td>0.15</td>
</tr>
<tr>
<td>2,4-Dinitrotoluene; 2,6-Dinitrotoluene; Dinitrotoluene (technical grade)</td>
<td>m; m; f, m</td>
<td>121142</td>
<td>1999; 1999; 1999</td>
<td>Chemical intermediate in manufacture of polyurethanes; production of explosives; dye intermediate; plasticizer</td>
<td>Chemical intermediate in manufacture of polyurethanes; production of explosives; dye intermediate; plasticizer</td>
<td>&gt;500M-1B</td>
<td>0.19</td>
<td>0.05</td>
<td>S</td>
<td>NA</td>
<td>0.2 (mixed isomers)</td>
<td>Skin; A₃; BEIₘₐ</td>
</tr>
<tr>
<td>Epichlorohydrin</td>
<td>m</td>
<td>106898</td>
<td>1996</td>
<td>Solvent; stabilizer; chemical intermediate</td>
<td>Chemical intermediate in manufacture of polyurethanes; production of explosives; dye intermediate; plasticizer</td>
<td>&gt;500M-1B</td>
<td>1</td>
<td>0.13</td>
<td>S</td>
<td>5219</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Ethylene dibromide</td>
<td>d, m</td>
<td>106934</td>
<td>1998</td>
<td>Chemical intermediate; solvent; pesticide</td>
<td>Chemical intermediate; solvent; pesticide</td>
<td>&gt;1M-10M</td>
<td>18</td>
<td>5</td>
<td>S</td>
<td>Cancer hazard; male sterility</td>
<td>18</td>
<td>5</td>
</tr>
<tr>
<td>Ethylene glycol monoethyl ether</td>
<td>d, m</td>
<td>110805</td>
<td>1989</td>
<td>Solvent</td>
<td>Solvent</td>
<td>&gt;50M-100M</td>
<td>27</td>
<td>5</td>
<td>S</td>
<td>Not available online; known</td>
<td>27</td>
<td>5</td>
</tr>
<tr>
<td>Ethylene glycol monoethyl ether</td>
<td>d, m</td>
<td>111159</td>
<td>1993</td>
<td>Solvent</td>
<td>Solvent</td>
<td>&gt;50M-100M</td>
<td>27</td>
<td>5</td>
<td>S</td>
<td>Not available online; known</td>
<td>27</td>
<td>5</td>
</tr>
<tr>
<td>Chemical</td>
<td>Type</td>
<td>CAS No.</td>
<td>Date Listed</td>
<td>Identity</td>
<td>Production Volume Range (TSCA, 2002)</td>
<td>Cal/OSHA PEL (mg/m³)</td>
<td>Cal/OSHA PEL (ppm)</td>
<td>Cal/OSHA PEL Notations/Vertical Standard</td>
<td>PEL Basis</td>
<td>TLV-TWA (mg/m³)</td>
<td>TLV-TWA (ppm)</td>
<td>TLV Notations</td>
</tr>
<tr>
<td>--------------------------------------------</td>
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<td>acetate</td>
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<tr>
<td>Ethylene glycol monomethyl ether acetate</td>
<td>d, m</td>
<td>109864</td>
<td>1989</td>
<td>Solvent</td>
<td>&gt;10M-50M</td>
<td>16</td>
<td>5</td>
<td>S</td>
<td>Not available online; known by HESIS to be lowered based on reproductive toxicity&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.1</td>
<td>Skin</td>
<td>Hematologic &amp; reproductive effects (adopted 2006)</td>
</tr>
<tr>
<td>Ethylene glycol monomethyl ether acetate</td>
<td>d, m</td>
<td>110496</td>
<td>1993</td>
<td>Solvent</td>
<td>&gt;500K-1M in 1990; no subsequent reports</td>
<td>24</td>
<td>5</td>
<td>--</td>
<td>Not available online; known by HESIS to be lowered based on reproductive toxicity&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.1</td>
<td>Skin</td>
<td>Hematologic &amp; reproductive effects (adopted 2006)</td>
</tr>
<tr>
<td>Ethylene oxide</td>
<td>f</td>
<td>75218</td>
<td>1987</td>
<td>Chemical intermediate; fungicide</td>
<td>&gt;1B</td>
<td>2</td>
<td>1</td>
<td>5220</td>
<td>Cancer and reproductive hazard</td>
<td>2</td>
<td>1</td>
<td>A2</td>
</tr>
<tr>
<td>Hexachlorobenzene</td>
<td>d</td>
<td>118741</td>
<td>1989</td>
<td>Chemical intermediate; fungicide</td>
<td>10K-500K</td>
<td>0.002</td>
<td>--</td>
<td>S</td>
<td>The PEL was lowered based on hepatic and neurological effects. See footnote a to Table A-2.</td>
<td>0.002</td>
<td></td>
<td>Porphyrin effects; skin damage; CNS impairment</td>
</tr>
<tr>
<td>Lead</td>
<td>d, f, m</td>
<td></td>
<td>1987</td>
<td>Used in the manufacture of various products, such as batteries, ammunition, solder, pipes, cable covering; in crystal, ceramic glazes</td>
<td>USGS (2007) estimated ~4M of lead produced in 2006</td>
<td>0.05</td>
<td>--</td>
<td>5198</td>
<td>Numerous health effects including reproductive toxicity</td>
<td>0.05</td>
<td>--</td>
<td>CNS; blood; kidney; reproductive</td>
</tr>
<tr>
<td>Chemical</td>
<td>Type</td>
<td>CAS No.</td>
<td>Date Listed</td>
<td>Identity</td>
<td>Production Volume Range in Pounds (TSCA, 2002)</td>
<td>Cal/OSHA PEL (mg/m³)</td>
<td>Cal/OSHA PEL (ppm)</td>
<td>Cal/OSHA PEL Notations/ Vertical Standard</td>
<td>PEL Basis</td>
<td>TLV-TWA (mg/m³)</td>
<td>TLV-TWA (ppm)</td>
<td>TLV Notations</td>
</tr>
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</tr>
<tr>
<td>Mercury and mercury compounds</td>
<td>d</td>
<td>d</td>
<td>1990</td>
<td>Thermometers; barometers; switches; fluorescent lamps; batteries; pigments; catalysts; explosives; fungicides; research.</td>
<td>Elemental mercury: 10K-500K in 1990; no subsequent reports. Phenylmercuric acetate &gt;1M-10M</td>
<td>0.01 (alkyl)</td>
<td>0.01 (aryl)</td>
<td>0.025 (metallic and inorganic compounds)</td>
<td>S</td>
<td>0.01</td>
<td>0.1</td>
<td>Skin</td>
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<td></td>
<td>S PEL for mercury and inorganic compounds was lowered to 0.025 mg/m³ to control reproductive risks and to be consistent with the World Health Organization’s recommendation (described in the ACGIH document for mercury) to control biological levels below 50µg/g of creatinine.</td>
<td>0.025</td>
<td>0.01</td>
<td>0.1</td>
<td>Skin; A4; BEI</td>
</tr>
<tr>
<td>Methyl chloride</td>
<td>d</td>
<td>74873</td>
<td>2000</td>
<td>Chemical intermediate; extractant; diluent; solvent; blowing agent; fumigant</td>
<td>&gt;1B</td>
<td>105</td>
<td>5</td>
<td>--</td>
<td>--</td>
<td>104</td>
<td>50</td>
<td>Skin</td>
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<td>--</td>
<td>Alkyl: CNS &amp; PNS impairment; kidney damage</td>
</tr>
<tr>
<td>Nickel carbonyl</td>
<td>d</td>
<td>13463393</td>
<td>1996</td>
<td>Chemical intermediate; catalyst</td>
<td>USGS (2007) estimated ~400M nickel imported in 2006</td>
<td>0.007</td>
<td>0.001</td>
<td>--</td>
<td>--</td>
<td>0.3</td>
<td>0.05</td>
<td>Skin</td>
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<td>--</td>
<td>--</td>
<td>Nickel; kidney damage; testicular damage; teratogenic effects</td>
</tr>
<tr>
<td>Chemical</td>
<td>Type</td>
<td>CAS No.</td>
<td>Date Listed</td>
<td>Identity</td>
<td>Production Volume Range in Pounds (TSCA, 2002)</td>
<td>Cal/OSHA PEL (mg/m$^3$)</td>
<td>Cal/OSHA PEL (ppm)</td>
<td>Cal/OSHA PEL Notations/ Vertical Standard</td>
<td>PEL Basis</td>
<td>TLV-TWA (mg/m$^3$)</td>
<td>TLV-TWA (ppm)</td>
<td>PEL Basis</td>
</tr>
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</tr>
<tr>
<td>Toluene</td>
<td>d</td>
<td>108883</td>
<td>1991</td>
<td>Chemical intermediate; solvent</td>
<td>&gt;1B</td>
<td>188</td>
<td>50</td>
<td>S</td>
<td>--</td>
<td>189 (current)</td>
<td>50 (proposed)</td>
<td>Skin; A4; BEI</td>
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</tbody>
</table>

a. Type of reproductive toxicity for which chemical is listed under Proposition 65: d = developmental, m = male reproductive, f = female reproductive.
b. Documentation for the lowering of the glycol ether PELs based on reproductive toxicity is not available on line. A HESIS Fact Sheet is available (HESIS, 1989).

See abbreviations following Table A-2.
Appendix References


Toxic Substances Control Act (TSCA, 2002). Inventory Update Rule (IUR), non-confidential production volume information (available at: [http://www.epa.gov/opptintr/iur/tools/data/2002-vol.htm](http://www.epa.gov/opptintr/iur/tools/data/2002-vol.htm)).
