This is the Final Statement of Reasons for specific regulatory levels for one chemical, naphthalene, listed as known to the State to cause cancer under the Safe Drinking Water and Toxic Enforcement Act of 1986 (hereinafter “the Act” or Proposition 65; Health and Safety Code section 25249.5 et seq.). On July 2, 2004, the Office of Environmental Health Hazard Assessment (OEHHA) issued a Notice of Proposed Rulemaking to adopt regulatory levels for ten chemicals listed pursuant to the Act as known to the State to cause cancer or reproductive toxicity (Title 22, California Code of Regulations, §12000). The Notice set forth proposed regulatory levels for two chemicals listed as known to cause cancer (1,2-dichloropropane and naphthalene) for adoption in Title 22, Cal. Code of Regs., §12705(b), and for eight chemicals listed as known to cause reproductive toxicity (1,2-dibromo-3-chloropropane, disodium cyanodithioimidocarbonate, ethyl dipropylthiocarbamate, ethylene glycol monomethyl ether, ethylene glycol monomethyl ether acetate, methyl bromide as a structural fumigant, sodium dimethyldithiocarbamate and thiophanate-methyl) for adoption in §12805. The Initial Statement of Reasons set forth the grounds for the proposed regulations.

Pursuant to the Notice of Proposed Rulemaking, a public comment period was held between July 2 and August 23, 2004, and a public hearing was held on August 23, 2004. In response to the public comments received, the technical support document for the proposed regulatory level for naphthalene was updated. A public comment period on the updated technical support document was held between June 21 and July 6, 2005. Documents and information relied upon by OEHHA in adopting the proposed regulatory level for naphthalene were added to the rulemaking file. A public comment period on the added documents and information was held between July 1 and July 18, 2005.

On July 2, 2004, OEHHA provided the technical support documents forming the basis for the proposed regulatory levels for chemicals listed as known to the State to cause cancer to the members of the Carcinogen Identification Committee for their review and comment as allowed by Title 22, Cal. Code of Regs., §12302(e). No comments were received from any committee members.

This regulation hereby adopts a regulatory level for naphthalene, one chemical included in the Notice of Proposed Rulemaking. Regulatory levels for eight other chemicals included in the Notice of Proposed Rulemaking were adopted and effective on January 22, 2005 (1,2-dichloropropane, 1,2-dibromo-3-chloropropane, disodium cyanodithioimidocarbonate, ethyl dipropylthiocarbamate, ethylene glycol monomethyl ether, ethylene glycol monomethyl ether acetate, methyl bromide as a structural fumigant and thiophanate-methyl). A regulatory level for sodium dimethyldithiocarbamate, also
included in the Notice of Proposed Rulemaking, will be covered by a separate Final Statement of Reasons.

UPDATE OF INITIAL STATEMENT OF REASONS

UPDATE OF TECHNICAL INFORMATION IN THE INITIAL STATEMENT OF REASONS

All data, studies, reports, or other documents relied on for this regulation were identified in the Initial Statement of Reasons of July 2, 2004, except as noted immediately below.

The technical support document “No Significant Risk Level (NSRL) for the Proposition 65 Carcinogen Naphthalene,” included with this notice as Attachment 1, has been modified based upon comments received. One sentence stating that the National Toxicology Program (NTP) has listed naphthalene as “reasonably anticipated to be a human carcinogen” was added on page two. An editorial change was made on page two to abbreviate “National Toxicology Program” to NTP. One sentence was added on page five to explain the choice of the default linear model for cancer potency derivation. Four sentences were added on page seven to explain why the NSRL is considered applicable to multiple routes of exposure. The date of the document was updated to June 2005. Three references were added in support of the above described changes to the technical supporting document (Buckpitt A, Boland B, Isbell M, Morin D, Shultz M, Baldwin R, Chan K, Karlsson A, Lin C, Taff A, West J, Fanucchi M, Van Winkle L and Plopper C, 2002. Naphthalene-induced respiratory tract toxicity: metabolic mechanisms of toxicity. Drug Metab Rev 34:791-820; NTP, 2004. Report on Carcinogens, Eleventh Edition. Carcinogen Profiles. U.S. Department of Health and Human Services, Public Health Service. National Institute of Environmental Health Sciences, Research Triangle Park, NC; OEHHA, 2004). These changes do not alter the NSRL value proposed for naphthalene. All changes are noted in underline/strikeout in Attachment 1.

SUMMARY AND RESPONSE TO COMMENTS RECEIVED DURING THE INITIAL NOTICE PERIOD OF JULY 2, 2004 THROUGH AUGUST 23, 2004

Two sets of comments were received regarding the proposed NSRL for naphthalene, the first from Gary K. Whitmyre, risksciences, LLC, on behalf of the BASF Corporation, and the second, from the ad hoc Naphthalene Coalition.

Comment:  Gary K. Whitmyre comments that potential carcinogenicity in humans is supported for the inhalation route by the NTP’s 1992 and 2000 inhalation studies of naphthalene. He concurs with OEHHA’s selection of the NTP 2000 studies as the basis for deriving a cancer potency for naphthalene. He further asserts that “the 2-year NTP studies in mice (NTP, 1992) and rats (NTP, 2000) confirm that the respiratory system is the only site of carcinogenesis in laboratory animals exposed by chronic inhalation of naphthalene.”

The commenter states that potential carcinogenicity in humans is not supported for non-inhalation routes. Dr. Whitmyre notes that the International Agency for Research on Cancer (IARC, 2002. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Volume 82, pp. 367-435. Some Traditional Herbal Medicines, Some Mycotoxins, Naphthalene and Styrene. IARC, Lyon, France) has stated that the cancer studies of naphthalene in animals by routes of exposure other than inhalation were too limited for an evaluation of carcinogenicity. The commenter asserts that all tumors observed in the NTP studies were “localized tumors at the site of chronic irritation by introduction of the chemical to the respiratory tract,” and that “the observed tumors as well as the non-neoplastic changes would not be expected to occur if naphthalene were introduced by different exposure routes, such as resulting from dermal or oral administration.” The commenter goes on to cite the draft U.S. Environmental Protection Agency’s (U.S. EPA) Proposed Guidelines for Carcinogen Risk Assessment from 1996 regarding the inference of carcinogenicity by one route of exposure when the cancer data are available for a different route of exposure. Dr. Whitmyre states that the U.S. EPA guidelines specify that (1) full use should be made of all biological and mechanistic data; and (2) if a chemical can be shown to be carcinogenic by one route of exposure it should no longer be automatically assumed that the chemical is carcinogenic by other routes of exposure. He further quotes the U.S. EPA 1996 Guidelines as stating “Route-to-route extrapolation has both qualitative and quantitative aspects. For the qualitative aspect, the assessor weighs the degree to which positive results through one route of exposure in human or animal studies support a judgment that similar results would have been observed in appropriate studies using [another] route of exposure…In general, confidence in making such a judgment is strengthened when the tumor effects are observed at a site distant from the portal of entry and when the absorption through the route of exposure of interest is similar to absorption via the tested routes.” (Note: Subsequent to the submission of comments by Dr. Whitmyre, a final version of the U.S. EPA cancer guidelines has been published [U.S. EPA, 2005. Guidelines for Carcinogen Risk
Similarly, the *ad hoc* Naphthalene Coalition states in their comments that the proposed No Significant Risk Level (NSRL) should apply to the inhalation route of exposure only. The Coalition asserts that the weight of the scientific evidence indicates that nasal tumors are the direct result of exposure at the “portal of entry” and not systemic exposure. The Coalition states that exposure to naphthalene by the oral route would not be expected to cause nasal tumors, and that naphthalene has never been shown to cause tumors when it is given orally.

Response: Naphthalene is listed as known to the State to cause cancer (Title 22, Cal. Code of Regs., §12000). This listing applies to all routes of exposure. IARC (2002) concluded that there is “sufficient evidence in experimental animals for the carcinogenicity of naphthalene” and that naphthalene is “possibly carcinogenic to humans (Group 2B)”, without specifying a particular route of exposure. NTP (NTP, 2004. *Report on Carcinogens, Eleventh Edition. Carcinogen Profiles.* U.S. Department of Health and Human Services, Public Health Service. National Institute of Environmental Health Sciences, Research Triangle Park, NC.2004) listed naphthalene as “reasonably anticipated to be a human carcinogen” based on sufficient evidence from studies in experimental animals. There are no adequate bioassay data available to directly assess the carcinogenicity of naphthalene by routes of exposure other than inhalation. With regard to carcinogenesis studies by non-inhalation routes, IARC (2002) states that, “The studies by oral administration in rats, intraperitoneal administration in mice and subcutaneous administration in rats were too limited for an evaluation of the carcinogenicity of naphthalene.” Without such bioassay data or other compelling scientific evidence, there is no basis to conclude that naphthalene is not carcinogenic by other routes of exposure.

There are data available which indicate that naphthalene poses a carcinogenic risk to humans by any route of exposure, and that the carcinogenic effects are not likely to be confined to the portal of entry. Naphthalene is absorbed via the inhalation, oral, dermal and intraperitoneal routes of exposure (NTP, 2000; IARC, 2002). Following absorption, metabolism of naphthalene occurs at multiple sites in the body, including the liver and lung (NTP, 2000). Metabolites of naphthalene include 2-naphthol, naphthalene-1,4-diol (1,4-dihydroxynaphthalene), 1,2-naphthoquinone, and 1,4-naphthoquinone (IARC, 2002), which have been shown to induce clastogenic and/or mutagenic effects. Quinone metabolites participate in redox cycles leading to oxidative stress including DNA damage (O’Brien P. 1991. Molecular mechanisms of quinone cytotoxicity. *Chem-Biol Interact* 80:1-41.). In the NTP (2000) inhalation pharmacokinetic studies, naphthalene was measured in the bloodstream of rats and mice, indicating that naphthalene is systemically absorbed via inhalation exposures and circulates throughout the body. Buckpitt *et al.* (2002) reported that the primary target for the toxicity of naphthalene in mice is Clara cells in the airway epithelium, regardless of whether the mice were exposed via inhalation or intraperitoneal injection (non-inhalation). Injury to the nasal olfactory epithelium has also been observed in mice and rats exposed to naphthalene via either the
inhalation or intraperitoneal routes of exposure (NTP, 1992; NTP, 2000; Buckpitt et al., 2002). These data demonstrate that naphthalene, or a metabolite(s), reaches the mouse lung and the rat and mouse nose even by non-inhalation exposure, that is, even if direct site contact at the portal of entry does not occur. Therefore, the tumors observed in the nasal and lung regions in rodents could arise both from direct contact of naphthalene at the portal of entry and from naphthalene, or its metabolites, circulating in the bloodstream to the target site.

Naphthalene has also been shown to exert systemic nonneoplastic effects distant from the site of exposure in humans. In particular, inhalation and ingestion exposures to naphthalene induce hemolytic anemia in humans (IARC, 2002; Agency for Toxic Substances and Disease Registry [ATSDR], 1995. Toxicological Profile for Naphthalene, 1-Methylnaphthalene, and 2-Methylnaphthalene. ATSDR, U.S. Department of Health and Human Services, Public Health Service, Research Triangle Park). There are also reports that infants in dermal contact with diapers, clothes or blankets treated with naphthalene have developed hemolytic anemia (ATSDR, 1995; IARC, 2002). The above data indicate that naphthalene is absorbed systemically to produce biologically effective internal doses in humans exposed orally, dermally or via inhalation. Any internal dose of naphthalene will be associated with a nonzero cancer risk, regardless of the route by which exposure occurred.

The carcinogenic effects observed in the available rodent inhalation studies occurred in the lung and nose. Tumor site concordance between rodents and humans is not necessarily expected. Chemicals shown to cause tumors at one site in rodents may cause tumors at a different site in humans (e.g., benzene) or at the same site (e.g., vinyl chloride) (U.S. EPA, 2005). The carcinogenic effects of naphthalene have not been adequately studied in humans, so the target site(s) is not known and may be different from the target sites in rodents. Hemolytic anemia, a noncancer effect associated with inhalation and non-inhalation exposures to naphthalene, has been observed in humans and dogs but rodents do not appear to be sensitive to this effect (NTP, 1992; ATSDR, 1995).

With regard to the quotation from the U.S. EPA 1996 guidelines, OEHHA could not locate a statement in the current version (U.S. EPA, 2005) specifying that “if a chemical can be shown to be carcinogenic by one route of exposure it should no longer be automatically assumed that the chemical is carcinogenic by other routes of exposure.” In the U.S. EPA’s 2005 Guidelines discussion of route extrapolation, the quotation reads (as compared to the 1996 version cited by the commenter), “In certain situations, an assessment based on studies of one exposure route may be applied to another exposure route. Route-to-route extrapolation has both qualitative and quantitative aspects. For the qualitative aspect, the assessor should weigh the degree to which positive results by one exposure route support a judgment that similar results would be expected by another route. In general, confidence in making such a judgment is strengthened when tumors are observed at a site distant from the portal of entry and when absorption is similar through both routes. In the absence of contrary data, a qualitative default option can be used: if the agent is absorbed through an exposure route to give an internal dose, it may be
Based on OEHHA’s scientific judgment of the available data, as discussed in detail above, naphthalene is clearly absorbed by routes other than the inhalation route to give an internal dose. In addition, there is no data either from bioassays or from mechanistic studies that cancer occurs only by the inhalation route. Thus, OEHHA’s conclusion that the carcinogenicity of naphthalene should not be assumed to be limited only to the inhalation route of exposure is consistent with the U.S. EPA guidelines. Further, OEHHA’s conclusion is also consistent with the California cancer guidelines (Guidelines for Chemical Carcinogen Risk Assessment and Their Scientific Rationale. California Department of Health Services, Health and Welfare Agency, Sacramento, CA, 1985), which state that “in the absence of data with which to make an evaluation, it is prudent risk assessment policy to assume that if a substance causes cancer when administered by ingestion, it will cause cancer when inhaled, and vice versa.”

With regard to the assessment of the carcinogenic potency of naphthalene, the 1992 and 2000 NTP inhalation studies are the only adequate data available for dose-response assessment. If in the future new data from cancer studies conducted by routes other than inhalation become available, these data can be evaluated to determine if route-specific differences in cancer potency exist, and if these differences can be reliably quantified. In the absence of such data, the naphthalene human cancer potency and the associated NSRL as derived by OEHHA based on the inhalation cancer bioassays are reasonable estimates to apply to all routes of exposure.

Comment: Gary K. Whitmyre asserts that Title 22, Cal. Code of Regs. specifies that NSRLs should be promulgated only for the routes for which there is adequate evidence of carcinogenicity. In support of this statement, the commenter cites Title 22, Cal. Code of Regs., §12703(a)(4) and §12707(a). The commenter also lists the following reasons for promulgating an inhalation only NSRL: (1) absence of federal and state regulatory standards for non-inhalation routes based on potential carcinogenicity; (2) the lack of treatment-related tumors at sites other than the exposure site (nasal/respiratory); and (3) the use of the inhalation route in the key study identified by OEHHA.

Response: OEHHA does not agree with the commenter. OEHHA’s position that the NSRL for naphthalene should be applied to all routes of exposure is fully in accordance with Title 22, Cal. Code of Regs., §12703(a)(4) and §12707(a). Title 22, Cal. Code of Regs., §12703(a)(4) states that “the results obtained for the most sensitive study deemed to be of sufficient quality shall be applicable to all routes of exposure for which the results are relevant.” As discussed in detail above, the results of the NSRL analyses based on the NTP inhalation bioassays are considered relevant to all routes of exposure since naphthalene is absorbed by other routes of exposure, produces internal doses by other routes of exposure, induces systemic toxicity by other routes of exposure and there are no adequate bioassays for those other routes. Title 22, Cal. Code of Regs., §12707(a) states that “where scientifically valid absorption studies conducted according to generally accepted standards demonstrate that absorption of a chemical through a specific route of exposure can be reasonably anticipated to present no significant risk of cancer at levels of exposure not in excess of current regulatory levels, the lead agency may identify the
chemical as presenting no significant risk by that route of exposure.” There are no data to support a conclusion that absorption of naphthalene through a specific route of exposure can be reasonably anticipated to present no significant risk of cancer. The available data indicate that the opposite is true, as discussed in detail above. Currently, naphthalene has been adequately tested for carcinogenicity in animals only by the inhalation route. Naphthalene is readily absorbed via other routes, including the oral and dermal routes, circulates in the bloodstream throughout the body and is metabolized at multiple sites to form genotoxic compounds. After non-inhalation exposures, naphthalene has been shown to induce systemic toxicity in humans and rodents. In particular, naphthalene induces nasal toxicity in rats and mice and respiratory toxicity in mice (NTP, 2000; Buckpitt et al., 2002) and hemolytic anemia in humans (ATSDR, 1995) by both non-inhalation and inhalation exposures.

The other reasons that the commenter lists for promulgating an inhalation-only NSRL are also insufficient. The absence of route-specific regulatory standards for naphthalene is simply a reflection of the lack of information on relevant routes of exposure other than inhalation. There is no evidence to indicate that the tumors observed in the NTP bioassays should be considered to arise solely through a site of contact mechanism. Naphthalene is known to be internally absorbed after inhalation exposure, to circulate throughout the body via the bloodstream, and to undergo metabolism at multiple sites to form genotoxic compounds. Further, inhalation of naphthalene results in systemic toxicity in humans (hemolytic anemia). Finally, OEHHA based the NSRL on data derived from inhalation bioassays because currently these are the only bioassays suitable for quantitative cancer dose-response assessment. The fact that the only adequate studies available are inhalation studies does not indicate that inhalation is the only exposure route of concern for the carcinogenicity of naphthalene.

Comment: Gary K. Whitmyre notes that there are precedents where OEHHA has developed route-specific NSRLs and excluded routes for which data are negative or equivocal.

Response: When data are available to indicate that route-specific NSRLs are warranted OEHHA reviews the data and promulgates route-specific NSRLs as appropriate. The available data do not indicate that naphthalene presents an inhalation-only risk of cancer. As discussed in detail above, naphthalene is absorbed by the inhalation and non-inhalation routes of exposure to produce an internal dose. Once absorbed into the bloodstream, naphthalene circulates throughout the body, and is metabolized at multiple sites to genotoxic compounds. Currently, there are no adequate bioassay data for routes other than the inhalation route. Given the information on the absorption, distribution and metabolism of naphthalene by multiple routes of exposure and the absence of adequate bioassay data for routes other than inhalation, naphthalene can be reasonably anticipated to pose a risk of cancer by all routes of exposure. Thus, OEHHA has developed an NSRL for naphthalene that applies to all routes of exposure.

Comment: Gary K. Whitmyre suggests that OEHHA should adjust the NSRL for chemical-specific metabolic differences between humans and rodents. The commenter
cites data from Buckpitt et al. (2002) in which the rates of metabolism of naphthalene to certain reactive intermediates in lung microsomes from non-human primates were 10-fold and 100-fold lower than in lung microsomes from rats and mice respectively.

Response: OEHHA does not agree that the available data on naphthalene dose-response, metabolism, pharmacokinetics, and mechanism of action support adjusting the NSRL to account for chemical-specific metabolic differences between humans and rodents. OEHHA reviewed the available data on metabolism and pharmacokinetics of naphthalene. The mechanism of naphthalene carcinogenesis, including the precise identity of the key carcinogenic metabolites, the key metabolic pathways, and the key cellular events is not known. Because tumor site concordance is not necessarily expected between rodents and humans, the lung may not be the only or the primary target site for naphthalene carcinogenesis in humans. Studies of metabolism in the lung of rodents and primates may not provide sufficient data to draw conclusions regarding the potential carcinogenic effects of naphthalene in humans.

The commenter states that the rates of metabolism of naphthalene to certain reactive intermediates in lung microsomes from non-human primates were 10-fold and 100-fold lower than in lung microsomes from rats and mice respectively. The commenter did not include data on primate and rodent differences in the metabolite elimination rate, which would be a key parameter in judging whether the differences in the rate of metabolism would translate to differences in sensitivity to the carcinogenic effects of naphthalene between rodents and non-human primates. Further, the active metabolite for naphthalene carcinogenesis is not yet known, so currently it is not possible to use data on differences in rates of metabolism and metabolite elimination, if available, to adjust the interspecies extrapolation factor. In a more recent publication from the same group of researchers, Boland and coauthors (Boland B, Lin CY, Morin D, Miller L, Plopper C and Buckpitt A. 2004. Site-specific metabolism of naphthalene and 1-nitronaphthalene in dissected airways of rhesus macaques. *J Pharmacol and Exp Therapeutics* 310[2]:546-554) reported that while the overall rate of naphthalene metabolism was found to be lower in non-human primates than in rodents, based on studies using airway incubations, these authors also showed that the amounts of metabolites covalently bound to proteins was only 2 to 3 fold lower in non-human primates than in rodents. Because the toxicity and carcinogenicity of naphthalene is likely to be mediated through covalently bound toxic metabolites of naphthalene, these data suggest that primates are at substantial carcinogenic risk from exposure to naphthalene. Moreover, the studies of Buckpitt et al. (2002) and Boland et al. (2004) indicate that given the current lack of understanding regarding the mechanism of naphthalene carcinogenesis, it is not possible to infer species differences in naphthalene dose-response based upon species differences in metabolic rate for a particular metabolic pathway.

Comment: Gary K. Whitmyre asserts that OEHHA combined the incidences for different tumor types in a way that is inconsistent with NTP’s evaluation of the data. OEHHA combined tumor incidences for benign tumors (respiratory epithelial adenomas) and malignant tumors (olfactory epithelial neuroblastosomas) that are derived from two different cells of origin. The commenter notes that NTP (2000) did not combine these
two tumor types in its evaluation of the naphthalene study data. The commenter states that OEHHA did not adequately explain why combining these two tumor types is valid. The commenter further states that OEHHA may have overestimated the cancer potency and may have double counted animals in which both a respiratory epithelial adenoma and an olfactory epithelial neuroblastoma occurred. The commenter suggests that OEHHA reexamine the individual animal data and make appropriate adjustments.

Response: The commenter has incorrectly interpreted the OEHHA analysis. OEHHA agrees with the commenter and with NTP that since the nasal respiratory epithelial adenomas and nasal olfactory epithelial neuroblastoma tumors arise from different cell types, it is inappropriate to combine the incidences in the way that is done for tumor types of common origin, *i.e.* to go to the individual animal data and determine a combined incidence (individuals affected/individuals at risk). OEHHA therefore did not combine tumors in this way for naphthalene. In the case where tumors occur at more than one site, the public health question is "what is the overall risk of cancer, on a per individual (human or animal) basis?" In other words, independent risks (at different sites or of different origins) each contribute to the overall risk of cancer to the individual. Calculating cancer potency based on the incidence of each tumor type separately and then taking the larger potency value, or averaging the potency values, when there are two or more independent sites at which tumor induction occurs to a substantial degree, does not adequately address the question of overall risk. Further, one cannot simply add the upper 95% confidence bounds for the two significant sites; that approach would over predict the likely range of risks. Thus, OEHHA used a procedure that statistically adds the cancer slopes, represented by probability distributions, for the independent sites using Monte Carlo sampling. The upper 95% confidence bound of the resulting distribution is taken as the cancer potency value. OEHHA believes that this is a mathematically appropriate way of determining overall risk of tumor induction in the case where treatment-related tumors independently arise from different cell types. U.S. EPA (2005) similarly recommends considering all datasets in estimating human cancer risk and presents various options for doing so, including adding risk estimates from different tumor sites.

Comment: Gary K. Whitmyre suggests that OEHHA should delay implementation of the NSRL for naphthalene until the U.S. EPA has completed its re-evaluation of the potential carcinogenicity of naphthalene, and updated its Integrated Risk Information System database, which is expected to occur by August 30, 2004.

Response: OEHHA has the responsibility for implementing Proposition 65, a California statute. It is in the interest of the business community to have an NSRL for naphthalene to provide greater certainty in complying with the requirements of Proposition 65. The approach OEHHA has taken to develop an NSRL is fully in accordance with applicable regulations (Title 22, Cal. Code of Regs., §12703). The U.S. EPA process for publishing a cancer potency analysis on the Integrated Risk Information System is lengthy and the timeline uncertain. The U.S. EPA has not yet completed its re-evaluation of naphthalene.

Comment: The *ad hoc* Naphthalene Coalition states that the weight of evidence indicates that naphthalene is not genotoxic and that linear extrapolation is inappropriate. To
support this conclusion, the Coalition cited a review by Dr. Byron Butterworth on the genotoxicity of naphthalene, which was submitted to the Air Resources Board’s Scientific Review Panel for consideration at their May 19, 2004 meeting and provided to OEHHA as an attachment to the Coalition’s comments. The Coalition states that OEHHA sets such a high standard for deviating from the default assumption of linearity that this departure would never occur, even if a chemical posed no significant cancer risk to humans.

in DNA repair-deficient strains of *E. coli* (Suter W and Jaeger I. 1982. Comparative evaluation of different pairs of DNA repair-deficient and DNA repair-proficient bacterial tester strains for rapid detection of chemical mutagens and carcinogens. *Mutat Res* 97[1]:1-18) and *Bacillus subtilis* (Tanooka, H. 1977. Development and applications of *Bacillus subtilis* test systems for mutagens, involving DNA-repair deficiency and suppressible auxotrophic mutations. *Mutat Res* 42[1]:19-31; Kawachi T, Yahagi T, Kada T, Tazima Y, Ishidate M, Sasaki M, Sugiyama T. 1980. Cooperative programme on short-term assays for carcinogenicity in Japan. *IARC Sci Publ* 27:323-330). 1,2-Naphthoquinone was positive in the *Salmonella* reverse mutation assay (test strains TA97a, TA98, TA100 and TA104) in the absence of metabolic activation (Flowers-Geary L, Bleczinki W, Harvey RG and Penning TM. 1996. Cytotoxicity and mutagenicity of polycyclic aromatic hydrocarbon ortho-quinones produced by dihydrodiol dehydrogenase. *Chem Biol Interact* 99:55-72), induced SCEs in human lymphocytes (Wilson AS, Davis CD, Williams DP, Buckpitt AR, Pirmohamed M and Park BK. 1996. Characterisation of the toxic metabolite(s) of naphthalene. *Toxicology* 114:233-242) and was shown to induce *p53* mutations in a yeast reporter system in the presence of cupric chloride (CuCl₂) and NADPH, conditions which simulate redox-cycling conditions (Yu D, Berlin J, Penning TM, Field J. 2002. Reactive oxygen species generated by PAH o-quinones cause change-in-function mutations in *p53*. *Chem Res Toxicol* 15:832-842). 1,4-Napthoquinone induced SCEs in human lymphocytes (Wilson et al., 1996), and caused a significant increase in the frequency of both CREST™ (indicative of chromosomal loss) and total micronuclei in the human B-lymphoblastoid MCL-5 cell line (Sasaki et al., 1997). Naphthalene-1,4-diol induced mutations in *Salmonella* strain TA2637 in the presence of rat liver S9, and in TA104 (an oxidative mutagen-sensitive strain) in the absence of rat liver S9 (Hakura A, Tsutsui Y, Mochida H, Sugihara Y, Mikami T, Sagami F. 1996. Mutagenicity of dihydroxybenzenes and dihydroxynaphthalenes for Ames Salmonella tester strains. *Mutat Res* 371[3-4]:293-299). The positive results in genotoxicity assays of naphthalene and of multiple metabolites of naphthalene support the conclusion that naphthalene is genotoxic, possibly acting through one or more metabolic pathways. While the carcinogenic mechanism of naphthalene is unknown, the data summarized above clearly indicate that a genotoxic mechanism of action is plausible and that linear extrapolation is therefore appropriate. Further, in the absence of principles and assumptions scientifically more appropriate, based upon the available data, Title 22, Cal Code of Regs., §12703(a)(5) requires application of the default assumption of linearity.

Comment: The *ad hoc* Naphthalene Coalition states that the weight of evidence indicates that it is unlikely that nasal tumors in rats are relevant to humans. The Coalition comments that rats are obligate nose breathers, making the rat uniquely sensitive to nasal damage produced by naphthalene.

Response: Mice are also obligate nose breathers, yet naphthalene caused tumors in the mouse lung. Since naphthalene induced tumorigenic effects in the rat nose and the mouse lung, the carcinogenicity of naphthalene is neither species nor site specific. Further, the human cancer potencies of naphthalene estimated based on tumor incidence data in rat nose compared to data in mouse lung are similar (0.12 [mg/kg-day]⁻¹ based on
rat nose data compared to 0.059 [mg/kg-day]$^{-1}$ based on mouse lung data). Also, the
difference between rats and humans regarding the sensitivity to naphthalene in the nasal
cavity or at other respiratory sites has not been ascertained. The carcinogenic effects of
naphthalene may occur in humans at a different location in the respiratory tract or at other
sites. For example, humans have been shown to be more sensitive than rodents to
naphthalene’s hematological effects. Because the carcinogenicity of naphthalene has not
been adequately studied in humans, the prudent public health policy is to apply the results
in animal studies to humans, as recommended by the California carcinogen guidelines
(CDHS, 1985).

**SUMMARY AND RESPONSE TO COMMENTS RECEIVED DURING THE NOTICE
PERIOD OF JUNE 21 THROUGH JULY 6, 2005**

Comments were received regarding the revised technical support document for
naphthalene from Gary K. Whitmyre, risksciences, LLC, on behalf of the BASF
Corporation.

**Comment:** The commenter asserts that the references cited by OEHHA do not support
the application of the NSRL for naphthalene to multiple exposure routes, and goes on to
discuss how OEHHA (2004), Buckpitt et al. (2002) and NTP (2004) do not provide
information regarding cancer risks associated with dermal or ingestion exposures to
naphthalene.

**Response:** The three references that the commenter is discussing, OEHHA (2004),
Buckpitt et al. (2002) and NTP (2004) were added as support for very specific points.
OEHHA never claims that these three references are the entire support for applying the
NSRL to multiple exposure routes. The three points that these references support are as
follows:

**OEHHA (2004):** OEHHA (2004) was added to refer to a discussion of the plausibility of
a genotoxic mechanism as the justification for applying the default linear approach to
potency analysis. The sentence from the NSRL document in which OEHHA (2004) is
cited is as follows: “This default linear approach is used for naphthalene because a
genotoxic mechanism of action is plausible, as discussed in OEHHA (2004), and an
alternative mechanism of action has not been established.”

**Buckpitt et al. (2002):** The Buckpitt reference was added to support the fact that
naphthalene is absorbed and distributed in the body via a noninhalation route of exposure
(*i.e.*, intraperitoneal exposure), and that biologically effective doses reach the lung and
nasal tissues, target sites for cancer, via a noninhalation route of exposure. Internal doses
of naphthalene will pose a nonzero cancer risk, regardless of the route by which exposure
occurs. The sentence from the NSRL document that cites Buckpitt et al. (2002) is as
follows: “Naphthalene induces nasal toxicity in rats and mice and respiratory toxicity in
mice by intraperitoneal exposures (Buckpitt et al., 2002), demonstrating that biologically
effective doses are achieved via non-inhalation exposures at the target sites for cancer in
rodents.”
NTP (2004): The NTP (2004) reference was added to support the statement that
naphthalene was listed as “reasonably anticipated to be a human carcinogen” in the
Eleventh Report on Carcinogens. The sentence from the NSRL document that cites NTP
(2004) is as follows: “The National Toxicology Program (NTP, 2004) has listed
naphthalene as “reasonably anticipated to be a human carcinogen” based on sufficient
evidence from studies in experimental animals.

OEHHA is in agreement with the commenter that there are no adequate data from
carcinogenicity bioassays in experimental animals via the ingestion and dermal routes of
exposure for naphthalene. It is the absence of this route-specific cancer bioassay data,
coupled with evidence that naphthalene is systemically absorbed via the inhalation, oral
and dermal routes of exposure, distributed throughout the body, and metabolized at
multiple sites to produce biologically effective internal doses posing a nonzero risk of
cancer that requires OEHHA to conclude that naphthalene should be considered a
carcinogen regardless of the exposure route. Because there are no adequate cancer
bioassays via routes other than the inhalation route, OEHHA must rely on the NTP
inhalation cancer bioassays to calculate a cancer potency. In the absence of more specific
information, the cancer potency derived by OEHHA for naphthalene is a reasonable
estimate to apply to all routes of exposure. If route-specific data become available,
OEHHA could reevaluate the cancer potency for naphthalene.

Comment: The commenter asserts that OEHHA’s use of the NSRL for naphthalene for
all exposure routes violates the principles of the U.S. EPA’s cancer risk assessment
guidelines. The commenter cites the 1996 version of the U.S. EPA guidelines as stating
that: (1) full use should be made of all biological and mechanistic data; and (2) if a
chemical can be shown to be carcinogenic by one route of exposure, it should no longer
be automatically assumed that the chemical is carcinogenic by other routes of exposure.
The commenter states that “one indisputable fact is that no conclusive data exist that
associate dermal exposure to purified naphthalene with actual tumor formation at any
site.” The commenter quotes Rennen et al. (Rennen MAJ, Bouwmann T, Wilschut A,
Bessems JGM, and De Heer C. 2004. Oral-to-inhalation route extrapolation in
5-11) as stating that “…route-to-route extrapolation…is not generally reliable and
certainly not valid for substances inducing local effects.”

Response: OEHHA did not automatically assume that naphthalene is carcinogenic by
routes of exposure other than inhalation. OEHHA analyzed the available biological and
mechanistic data and found no basis to conclude that naphthalene is carcinogenic by only
the inhalation route of exposure. The commenter’s statement that there are “no
conclusive data…that associate dermal exposure to purified naphthalene with actual
tumor formation at any site” is merely a consequence of the fact that the dermal route of
exposure has not been studied in an adequate cancer bioassay. However, there are data
that show that naphthalene is absorbed by all routes of exposure, including the dermal
route, to produce a biologically effective internal dose of naphthalene. Any internal dose
of naphthalene will be associated with a nonzero risk of cancer.
OEHHA’s treatment of naphthalene as being carcinogenic by multiple routes is consistent with the current U.S. EPA (2005) guidelines, which state that, “In the absence of contrary data, a qualitative default option can be used: if the agent is absorbed through an exposure route to give an internal dose, it may be carcinogenic by that route.” OEHHA’s conclusion is also consistent with the California cancer guidelines (CDHS, 1985) which state that, “in the absence of data with which to make an evaluation, it is prudent risk assessment policy to assume that if a substance causes cancer when administered by ingestion, it will cause cancer when inhaled, and vice versa.” Rennen et al. (2004) is not a recognized authority on carcinogen policy. Further, the quoted text from Rennen et al. does not apply here since inhalation tumorigenicity of naphthalene is not likely to be a “local effect.” As discussed in detail above in response to earlier comments, naphthalene is absorbed by all routes of exposure (oral, dermal, inhalation and intraperitoneal) and is metabolized at multiple sites in the body to toxic compounds that have been shown to be mutagenic and/or clastogenic and that can participate in redox cycles resulting in oxidative DNA damage. The NTP (2000) pharmacokinetic studies showed that naphthalene administered via inhalation can be measured in the bloodstream of rats and mice, demonstrating systemic absorption. Both respiratory and nasal toxicity has been shown to occur when naphthalene is administered via either the inhalation or intraperitoneal (i.e., noninhalation) routes of exposure. These data show that naphthalene can reach target sites of carcinogenesis in the rodent even when there is no direct contact at the target site. Thus, the tumors observed in the nasal and lung regions in rodents could arise both from direct contact of naphthalene at the portal of entry and from naphthalene, or its metabolites, circulating in the bloodstream to the target site. Further, inhalation, oral and dermal exposures to naphthalene have all been linked to the induction of hemolytic anemia in humans. The data in humans demonstrate that systemic absorption of naphthalene occurs and results in a biologically effective internal dose regardless of the route of exposure. Thus, naphthalene poses a carcinogenic risk to humans by all routes of exposure. OEHHA has derived a human cancer potency and associated NSRL for naphthalene based on the inhalation bioassays conducted by NTP (2000). These are reasonable estimates to apply to all routes of exposure. If route-specific data become available, OEHHA will review these data and promulgate route-specific NSRLs if appropriate.

Comment: The commenter states that there is no regulatory precedent for the assumption of the carcinogenicity of naphthalene by the dermal exposure route, indicating that he is unaware of any “cancer-based regulatory benchmark” for dermal exposure at either the State level or Federal level. The commenter asserts that OEHHA’s position is inconsistent with the position of all “relevant” regulatory agencies and that the position is “weak scientifically and is vulnerable to challenge.”

Response: A regulatory precedent is not required for OEHHA to promulgate an NSRL that applies to all routes of exposure for naphthalene. OEHHA’s position is well supported scientifically and is consistent with the U.S. EPA (2005) guidelines as well as California cancer guidelines (CDHS, 1985), as further discussed above. If there were scientifically valid data on the carcinogenicity of naphthalene by the dermal and oral
routes, OEHHA would evaluate these data, determine whether a route-specific potency for naphthalene is warranted, and promulgate route-specific NSRLs if appropriate.

Comment: The commenter states that the cytotoxicity caused by naphthalene is not a proven predictor of tumors, and goes on to elaborate that damage to the Clara cells does not constitute carcinogenicity, and that such damage has not been shown to be a required step that irreversibly commits the affected cells to tumor formation. The commenter goes on to state that respiratory toxicity by the dermal route cannot be inferred from evidence of respiratory toxicity from the intraperitoneal route and that respiratory toxicity from systemic introduction of naphthalene occurs without evidence of tumor formation. The commenter asserts that the Buckpitt et al. (2002) reference is not relevant because that study looked at chronic toxicity and not carcinogenicity and further states that using local cytotoxic damage to the respiratory epithelial (sic) as evidence of potential carcinogenicity from non-inhalation routes is scientifically unjustified.

Response: OEHHA has in no way asserted that cytotoxicity is a predictor of tumors for naphthalene, that Clara cell damage predicts tumorigenicity, that respiratory toxicity by the dermal route can be inferred from evidence of respiratory toxicity via the intraperitoneal route of exposure, nor that local cytotoxic damage to the respiratory epithelium from injection exposure is evidence of potential carcinogenicity from non-inhalation routes. Further, the commenter is incomplete in stating that “respiratory toxicity from systemic introduction of naphthalene occurs without evidence of tumor formation.” The only adequate studies of the carcinogenicity of naphthalene are the inhalation bioassays of NTP; in those studies both respiratory toxicity and tumor formation occurred. Other studies which looked at the effects of naphthalene after systemic introduction by noninhalation exposure pathways were studies of toxicity only and were not cancer bioassays. Therefore these studies of naphthalene exposure via noninhalation routes can provide information on specific issues of interest related to the potential carcinogenic risks of naphthalene, but cannot be used to support a claim that naphthalene does not produce tumors by those routes of exposure. OEHHA cited Buckpitt et al. (2002) for a very specific purpose, which was to show that naphthalene is absorbed, distributed, and metabolized and produces systemic toxicity when introduced by a noninhalation route of exposure. The observation of systemic toxicity is important because it demonstrates that biologically effective internal doses of naphthalene are produced via a noninhalation route of exposure. Internal doses of naphthalene produced by any route of exposure would be associated with a nonzero cancer risk.

Comment: The commenter asserts that OEHHA’s route-to-route extrapolation of the “inhalation NSRL” to the dermal route is flawed. The commenter asserts that it is “doubtful” that naphthalene would have the same carcinogenicity by the inhalation route as the dermal route. The commenter asserts that because of the skin barrier and the “significant metabolism and partitioning of naphthalene that occurs during distribution within the body, it is doubtful that a given external dermal exposure would produce the same effect as an equivalent potential inhalation exposure.” The commenter goes on to assert that the “rapid clearance of naphthalene from the blood in rats after brief inhalation
exposures argues against the equivalency of inhalation and dermal exposures, and against the validity of the NSRL for all routes.”

Response: The commenter is speculating about the dermal carcinogenicity of naphthalene but provides no supporting data. OEHHA is applying the cancer potency estimate derived from inhalation bioassays of naphthalene to all routes of exposure because that is a reasonable cancer potency estimate in the absence of route-specific data. If relevant data become available, OEHHA would review such data and promulgate route-specific NSRLs if appropriate.

Comment: The commenter asserts that differences between test species and humans require further adjustment of the NSRL. The commenter discusses the many uncertainties regarding the mechanism whereby naphthalene causes nasal/respiratory tumors in animals. The commenter repeats a comment he previously submitted regarding data indicating that the levels of cytochrome P450 monooxygenases in rodent lungs are 10 to 100 times greater compared to nonhuman primates and humans, citing Buckpitt et al. (2002). The commenter states that OEHHA did not make adjustments to the potency based on relative species differences in P450 enzymes. The commenter suggests that OEHHA should multiply the NSRL by 10 to account for the Buckpitt et al. (2002) data.

Response: The commenter emphasizes the uncertainties in the mechanism of naphthalene carcinogenesis; OEHHA agrees with his conclusions that it is not possible to describe the steps leading from naphthalene exposure to tumor formation. As discussed in detail in OEHHA’s responses to earlier comments above, the data cited by the commenter is insufficient to make any conclusions regarding the potential differences in susceptibility between rodents and humans to tumor formation related to naphthalene exposure. Multiplying the NSRL by 10 is clearly not warranted, because the mechanism is uncertain and the Buckpitt et al. (2002) data may or may not be significant in terms of differences in susceptibility. Other important factors, such as differences in elimination rates of the key metabolite(s) between rodents and humans, cannot be accounted for, as discussed in detail above. In the absence of scientifically valid data that would support an alternative approach, the default method for interspecies extrapolation is used by OEHHA, as specified in Title 22, Cal Code of Regs., §12703(a)(6).

Comment: The commenter asserts that intraperitoneal studies are likely to overstate the effects of dermal administration. The commenter states that the potency of a chemical is highly dependent on the route of exposure, how the chemical is distributed in the body, metabolism of the chemical at the site of administration and in transit during distribution in the body, and the nature of elimination. The commenter states that toxic agents that produce toxic effects at sites distal to the site of administration are most likely to produce more severe, and potentially more rapid, responses when injected via the intraperitoneal route than when applied dermally. The commenter states that because of the vapor pressure of naphthalene, one would expect volatilization from the skin in dermally-exposed individuals, resulting in lower effective doses at internal sites compared to those obtained from inhalation and intraperitoneal doses. The commenter asserts that naphthalene is metabolized in the liver at a relatively rapid rate and that naphthalene has
a propensity to partition to fat, which the commenter interprets as suggesting that a significant portion of dermally-absorbed naphthalene may be lost and effectively unavailable to circulate to nasal and lung tissues.

Response: The commenter’s statements are in agreement with OEHHA’s position that naphthalene is a toxic agent that produces effects at sites distal to the site of administration, and that dermal exposure to naphthalene produces doses at internal sites. OEHHA does not take the position that intraperitoneal studies can be used to assess the quantitative extent of dermal effects for naphthalene and does not do so; in fact there are no adequate cancer bioassays for naphthalene via either the dermal or the intraperitoneal routes so this is not a useful extrapolation to consider. What is known is that naphthalene is absorbed dermally, distributed throughout the body, and metabolized at multiple sites. It is also known that dermal exposures to naphthalene contribute to inducing systemic toxic effects, indicating that dermal exposures produce biologically effective doses of naphthalene and/or its toxic metabolites in the body. Naphthalene is a carcinogen and any internal dose of naphthalene and/or its toxic metabolites carries a carcinogenic risk. Thus, dermal exposures to naphthalene pose carcinogenic risk; the extent of this risk cannot be quantified at this time, because currently there are no adequate dermal cancer bioassays and insufficient pharmacokinetic data from dermal studies of naphthalene to derive a dermal-specific cancer potency.

The commenter is incorrect in suggesting that dermal exposures to naphthalene would necessarily be metabolized first by the liver. Dermal absorption results in direct systemic distribution without initial distribution to the liver. Thus, there is no basis to conclude that dermal exposures would be “lost and unavailable to circulate to nasal and lung tissues.”

Comment: The commenter states that there are serious uncertainties that limit the understanding of the mechanism of carcinogenicity by naphthalene. The commenter goes on to discuss uncertainties in the metabolic pathways for naphthalene and concludes that “it is highly speculative at this time to attempt to link exposures to naphthalene and reactive intermediates in lung tissues to tumor formation.”

Response: OEHHA is in agreement with the commenter that the mechanism of carcinogenesis of naphthalene is unknown at this time. OEHHA has stated that a genotoxic mechanism involving reactive metabolites of naphthalene is plausible, as discussed in detail above and in OEHHA (2004). Naphthalene is known to be metabolized to compounds that have been shown to induce clastogenic and/or mutagenic effects and quinone metabolites can participate in redox cycles leading to oxidative stress including DNA damage. Thus, although the mechanism has not been established, a genotoxic mechanism for naphthalene carcinogenesis is plausible and cannot be ruled out.

Comment: The commenter states that OEHHA should designate the NSRL for the inhalation route only. The commenter asserts that the case for the carcinogenicity of naphthalene by the dermal route is “weak to nonexistent,” and that there is a lack of
conclusive evidence for either treatment site or distal tumors via the dermal route of exposure. The commenter asserts that it would be unlikely for any carcinogen to have identical potencies by the inhalation and dermal routes. The commenter claims that “Title 22 specifies that NSRLs should be promulgated only for exposure route(s) for which there is adequate evidence of carcinogenicity. Promulgated NSRLs must be based on, and account for, route-specific differences in carcinogenic potency.” The commenter states that OEHHA has previously designated certain NSRLs as inhalation only and that OEHHA should similarly designate the naphthalene NSRL as inhalation only.

Response: As discussed above, there are no adequate dermal cancer bioassays for naphthalene. However, there are data indicating that naphthalene is readily absorbed by the dermal route, distributed in the body, and metabolized at multiple sites to form toxic metabolites. Further, there are studies reporting that dermal exposure to naphthalene can contribute to systemic toxicity, indicating that biologically effective doses can be introduced into the body via the dermal route. Given the fact that naphthalene is a carcinogen, any internal dose of naphthalene will pose a carcinogenic risk. These qualitative data are sufficient to conclude that naphthalene should be considered a carcinogen by all routes of exposure, since all routes of exposure produce internal doses of naphthalene. In the absence of adequate route-specific data, the cancer potency estimate and NSRL derived based on inhalation studies of naphthalene are reasonable to apply to all routes of exposure. If route-specific data become available, OEHHA will evaluate these data and promulgate route-specific NSRLs if appropriate.

OEHHA’s conclusion that naphthalene should be treated as a carcinogen by all routes of exposure is consistent with Title 22. Title 22, Cal Code of Regs., §12703(a)(4) states that “The results obtained for the most sensitive study deemed to be of sufficient quality shall be applicable to all routes of exposure for which the results are relevant.” Naphthalene is absorbed systemically by the dermal, oral and inhalation routes of exposure, producing biologically effective internal doses. The carcinogenicity of naphthalene has been studied in inhalation bioassays, which have demonstrated that internal doses of naphthalene are associated with tumor formation. The results of the inhalation bioassays are applicable to all routes of exposure that produce internal doses of naphthalene, e.g., the oral, dermal and inhalation routes. Title 22, Cal Code of Regs., §12703(a)(7) states that “When available data are of such quality that physiologic, pharmacokinetic and metabolic considerations can be taken into account with confidence, they may be used in the risk assessment for inter-species, inter-dose, and inter-route extrapolations.” There are no available data of sufficient quality that can be used to make route-specific adjustments for naphthalene. If these data become available, OEHHA will evaluate them and promulgate route-specific NSRLs if appropriate.
SUMMARY AND RESPONSE TO COMMENTS RECEIVED DURING THE NOTICE PERIOD OF JULY 1, 2005 THROUGH JULY 18, 2005

No comments were received regarding the addition to the rulemaking file of documents and information relied upon by OEHHA in adopting the proposed regulatory level for naphthalene.

ALTERNATIVES DETERMINATION

In accordance with Government Code section 11346.5(a)(7), OEHHA has, throughout the adoption process of this regulation, considered available alternatives to determine whether any alternative would be more effective in carrying out the purpose for which the regulations were proposed, or would be as effective and less burdensome to affected private persons than the proposed action. OEHHA has determined that no alternative considered would be more effective, or as effective and less burdensome to affected persons, than the proposed regulation.

For chemicals listed under the Act as known to cause cancer, the Act exempts discharges to sources of drinking water and exposures of people without provision of a warning if the exposure poses “no significant risk” of cancer (Health and Safety Code section 25249.10(c)). The Act does not specify numerical levels of exposure that represent no significant risk of cancer.

The purpose of this regulation is to provide a “safe harbor” level for a particular chemical exposure. In other words, this regulation establishes the numerical no significant risk level for one carcinogen, naphthalene. At or below this level, the Act does not require a warning regarding cancer or prohibit discharges to sources of drinking water based on carcinogenicity concerns associated with naphthalene. Thus, this level will allow persons subject to the Act to determine whether a given discharge to sources of drinking water or exposure to people involving these chemicals is subject to the warning requirement and discharge prohibition provisions of the Act related to the risk of cancer or occurrence of reproductive toxicity (Health and Safety Code sections 25249.6 and 25249.5, respectively).

Many businesses subject to the Act do not have the resources to perform assessments to derive safe harbor levels. Yet each business with ten or more employees needs the ability to determine whether its activities or products are subject to the discharge prohibition or warning requirements of the Act. Given the wide use of several of the chemicals covered by this regulation, the absence of this regulation would leave numerous businesses without an efficient way of determining if they are in compliance with the Act without the expenditure of significant resources on their part.
LOCAL MANDATE DETERMINATION

OEHHA has determined this regulatory action will not pose a mandate on local agencies or school districts nor does it require reimbursement by the State pursuant to Part 7 (commencing with section 17500) of Division 4 of the Government Code. OEHHA has also determined that no nondiscretionary costs or savings to local agencies or school districts will result from this regulatory action. It should be noted that Proposition 65 provides an express exemption from the warning requirement and discharge prohibition for all state and local agencies. Thus, these regulations do not impose any mandate on local agencies or school districts.