FINAL STATEMENT OF REASONS
TITLE 27, CALIFORNIA CODE OF REGULATIONS

SECTION 25805. SPECIFIC REGULATORY LEVELS: CHEMICALS CAUSING REPRODUCTIVE TOXICITY

MAXIMUM ALLOWABLE DOSE LEVEL: METHANOL

This is the Final Statement of Reasons for the adoption of Maximum Allowable Dose Levels (MADLs) for methanol, a chemical known to the State of California to cause reproductive toxicity (developmental endpoint) under Proposition 65[1]. On March 16, 2012, the Office of Environmental Health Hazard Assessment (OEHHA) issued a Notice of Proposed Rulemaking to adopt the proposed levels of 47,000 micrograms per day by the inhalation route and 23,000 micrograms per day by the oral route for methanol in Title 27, California Code of Regulations, section 25805(b)[2]. The Initial Statement of Reasons set forth the grounds for the amendment to the regulation. A public comment period was provided from March 16 to April 30, 2012. A subsequent notice was published on April 20, 2012 announcing that a public hearing would be held on May 7, 2012 and the comment period would be extended until May 21, 2012. OEHHA received a request for an additional extension and extended the public comment period on this proposed amendment to Monday, June 25, 2012. Four written public comments were received by OEHHA.

On March 14, 2012, OEHHA provided the notice of proposed rulemaking and the Initial Statement of Reasons for the proposed MADLs for methanol to the members of the Developmental and Reproductive Toxicant Identification Committee for their review and comment as required by Section 25801(f). No comments were received from any committee members.

SUMMARY AND RESPONSE TO COMMENTS

Table 1 provides the names of commenters, who submitted written comments on the March 16, 2012 Notice of Proposed Rulemaking. After the table, the submitters' comments are summarized and responses are provided.

[1] The Safe Drinking Water and Toxic Enforcement Act of 1986 (Health and Safety Code, section 25249.5 *et seq.*)
[2] All further references are to sections of Title 27 of the California Code of Regulations, unless otherwise noted.

Table 1. Commenters on the Notice of Proposed Rulemaking (OAL Notice File No. Z-2012-0305-04)

Commenter/Affiliation	Representing	Date Received
Paul Noe and Robert Glowinski	American Forest & Paper Association, and American Wood Council	May 21, 2012
Gregory Dolan	Methanol Institute	June 22, 2012
Haley Curtis Stevens, Ph.D.	International Food Additives Council (IFAC)	June 25, 2012
Arthur L. Lawyer, Ph.D.	Technology Sciences Group, Inc. (TSG) on behalf of (1) Methanol Institute, (2) International Food Additive Council (IFAC), (3) Consumer Specialty Products Association	June 25, 2012

In addition to the aforementioned comments received by OEHHA during the comment period, several emails were received from Mr. Rich Murray. None of the emails from Mr. Murray stated an objection to or made any recommendation regarding the proposed action. The emails contained website URLs and quotes from websites that discuss aspartame, an artificial sweetener. Methanol is known to be a metabolite of aspartame. Because Mr. Murray did not indicate how the information pertains to the methanol MADL, and did not otherwise comment on the methanol MADL, no formal response is being provided. However, the anticipated exposure to methanol from consumption of aspartame would not be considered an exposure within the meaning of Proposition 65 because aspartame is not listed under Proposition 65. Further, the level of exposure to methanol from aspartame metabolism among pregnant women that consume aspartame can be calculated to fall below the oral MADL using information from the National Toxicology Program's report on methanol[3].

Commenters 1

Paul Noe and Robert Glowinski for the American Forest & Paper Association and the American Wood Council

Comment 1.1

The commenters state that the proposed MADL for methanol fails a "reality test". To support that statement, the commenters used a physiologically-based pharmacokinetic (PBPK) model to calculate the blood methanol concentration that would result from

[3] National Toxicology Program – Center for the Evaluation of Risks to Human Reproduction (NTP-CERHR) Monograph on the Potential Human Reproductive and Developmental Effects of Methanol, 2003, page 4, Table 2).

exposure to inhaled methanol at the MADL. The commenters compared that level to background blood methanol concentrations in humans reported in the National Toxicology Program – Center for the Evaluation of Risks to Human Reproduction (NTP-CERHR) Monograph on the "Potential Human Reproductive and Developmental Effects of Methanol", the authoritative body document that provided the basis for addition of methanol to the Proposition 65 list. On that basis, the commenters suggest that OEHHA should revise the MADL to take into consideration background blood methanol concentrations. The commenters also suggest that if OEHHA chooses to stay with the proposed MADL for inhalation, OEHHA should provide justification for setting a MADL at a level much less than normal levels of methanol found in human blood. Finally, the commenters state that the legislative mandate for a 1,000-fold exposure multiplier is inconsistent with the use of the best available science.

Response 1.1

As acknowledged by the commenters, the 1,000-fold factor is established by statute (Health and Safety Code section 25249.10(c)) as a mandatory factor. The MADL is derived pursuant to the provision of Proposition 65 relating to Exemptions from Warning Requirements (Health and Safety Code, section 25249.10) that no warning is required for "an exposure for which the person responsible can show that.…the exposure will have no observable effect assuming exposure at one thousand (1,000) times the level in question for substances known to the state to cause reproductive toxicity". The party causing an exposure is responsible only for the exposure it causes to any given individual and is unlikely to have knowledge of or control over exposures to methanol occurring from other sources that contribute to the background level for that individual.

Regarding the "reality test", OEHHA agrees that an exposure at the MADL would likely result in a blood concentration that is lower than background levels. The NTP-CERHR Monograph on methanol reports background blood-methanol levels of 0.57 to 1.9 milligrams per liter (mg/L) in studies of small groups (3 to 22 people) of unexposed humans (NTP-CERHR Table 7.2A, page II-137). However, the NTP-CERHR document cited the need for further research to obtain better data on methanol concentrations in human blood[4].

A rough estimate of the increase in blood levels was provided by the commenters using a pharmacokinetic model. They calculated a blood level of 0.073 mg/L from exposure to the inhalation MADL alone. OEHHA calculates a slightly different number using the equation provided by the commenters – 0.0814 mg/L[5]. Without endorsing the model,

[4] NTP-CERHR, page II-120: "Studies are needed to assess total exposure to methanol from all sources, including foods, food additives, occupational and environmental exposures. Such studies would allow better quantification of human blood methanol concentrations that, in turn, would improve estimations of human risk. Including methanol as one of the chemicals assessed in a NHANES survey could be a means for characterizing the range of methanol blood levels in the U.S. population."

[5] The value for exhalation rate used by Starr and Festa (2003) is correctly cited by the commenter as 5.1×10^{-2} h^{-1}. However, Starr and Festa (2003) incorrectly state in their paper that this was the human parameter value utilized by Bouchard et al. (Bouchard M, Brunet RC, Droz PO, and Carrier G. A Biologically Based Dynamic Model for Predicting the Disposition of Methanol and Its Metabolites in

OEHHA notes that these rough estimates are consistent with OEHHA's determination that exposures at the MADL should not pose a concern for developmental toxicity in humans. The MADL was developed by identifying a no observable effect level in an animal model and then dividing that level by 1,000, as required by Proposition 65.

Commenter 2

Gregory Dolan for the Methanol Institute

Comment 2.1

The commenter reiterates arguments, originally made in opposition to listing of methanol, about whether methanol itself causes developmental toxicity in rodents or whether the effects are caused by reactive oxygen species created by the metabolism of high doses of methanol by catalase in rodents, citing a series of studies referenced during the listing procedure. The commenter also recommends that OEHHA adopt an oral MADL of 40,000 micrograms/day based on mouse inhalation data or 116,000 micrograms/day based on rabbit oral data.

Response 2.1

The commenter's arguments regarding the proximate cause of developmental toxicity were considered by OEHHA in the listing process. In the one study cited by the commenter where developmental toxicity was assessed[6], the authors themselves concluded only that "It is not clear if the human risk for MeOH [methanol] developmental toxicity can be accurately estimated using sensitive rodent strains." The commenter expands on the basis for his recommendation that OEHHA adopt an oral MADL of 40,000 micrograms/day based on mouse inhalation data or 116,000 micrograms/day based on the cited rabbit oral developmental toxicity data later in his comments. The recommendations and the basis for them are addressed below in the responses to comments 2.3 and 2.4.

Comment 2.2

The commenter states that the standard OEHHA procedures used to produce the proposed MADL purport to identify safe exposure levels where there is essentially no risk, and that setting a proposed MADL that is well within normal background levels for methanol in all humans significantly risks damaging the credibility of OEHHA and the Proposition 65 program.

Animals and Humans. Toxicological Sciences. (2001). 64: 169-184.). In fact, the value provided for human exhalation rate by Bouchard et al. is 5.1 x 10^{-3} h^{-1} (page 173 of the publication). Given the results presented by the commenters, they apparently used the correct value of 5.1 x 10^{-3} h^{-1} in their calculations.

[6] Sweeting, J. N., Siu, M., Wiley, M. J. and Wells, P. G. Species- and strain-dependent teratogenicity of methanol in rabbits and mice. Reproductive Toxicology. (2011). 31(1): 50-58.

Response 2.2

The pertinent provision of the statute is that there will be “no observable effect assuming exposure at one thousand (1,000) times” the MADL. Thus, as discussed above, under Proposition 65, an exposure level 1,000 times the MADL must be determined not to cause any observable effects. The MADL for methanol meets this requirement of Proposition 65.

Comment 2.3

The commenter correctly notes that the oral MADL is based on a single level of oral exposure in the study by Rodgers et al. (1993), but considers that not to be a robust data set. The commenter says that the oral MADL should be extrapolated from the data resulting from inhalation exposures at several levels in the same study. This extrapolation would yield an oral MADL of 40,000 micrograms per day (µg/d) by adjusting the unrounded inhalation MADL of 47,248 µg/d on the basis of a mouse inhalation absorption rate of 85% for methanol (Perkins et al., 1995), and an assumed 100% human oral absorption rate (which the commenter states is based on several citations that were not identified in the comments).

Response 2.3

The commenter’s calculation combines a methanol inhalation absorption rate for a mouse and an assumed methanol oral absorption rate for a human. The commenters did not consider the differences in methanol absorption and blood levels between the inhalation and oral routes exhibited in the Rogers et al. (1993) study. In that study, the oral exposure level of 4,000 milligrams per kilogram of body weight per day (mg/kg-d) was expressly selected to result in a blood level approximating the high end of the range of maternal blood levels seen in the inhalation component of the study. The authors of the study noted that blood concentrations resulting from the oral exposure were slightly lower than the mean blood methanol concentration following inhalation exposure to 10,000 parts per million (ppm) methanol. The authors of the study did not calculate the dose of methanol in units of mg/kg-d that resulted from that inhalation exposure. However they did note that:

> “The severity of the developmental toxicity observed following this oral dosing regimen [of 4000 mg/kg-d] was similar to that seen in the 10,000-ppm inhalation exposure group.”

Using the method for calculating the level of exposure to a given concentration of methanol laid out in the Initial Statement of Reasons for this regulation, OEHHA determined that exposure of mice to 10,000 ppm methanol by inhalation will result in a dose of approximately 8,100 mg/kg-d, which is about twice the oral dose of 4,000 mg/kg that resulted in about the same blood concentration and similar severity of effects. The 15% difference proposed by the commenter (85% inhalation absorption in mice

compared to 100% oral absorption in humans) is therefore not consistent with the oral and inhalation data from the Rogers et al. (1993) study.

Although the data on oral exposure are available only for one dose level, the data are from the same well-designed and well-conducted study that provided the data on inhalation exposures. Those oral data are consistent with the inhalation data in terms of induced effects at similar blood concentrations, but differ in the external doses that resulted in those blood concentrations. It is therefore more appropriate to use the available empirical data on oral exposure to methanol as the basis for the oral MADL rather than extrapolating from inhalation exposure data.

Comment 2.4

The commenter also suggests that because human metabolism of methanol is dissimilar from rodents, rabbit data should be used. As an alternative to the MADL calculation he proposed in Comment 2.3, the commenter proposes using a NOEL in rabbits exposed to 2,000 mg/kg methanol by intraperitoneal injection as the basis for the MADL.

Response 2.4

The recommendation for use of rabbit data is based on the same study noted in response 2.1[7]. As also noted in the response to that comment, OEHHA considered that and other related studies in determining whether methanol should be added to the Proposition 65 list.

In the study by Sweeting et al. (2011) proposed by the commenter as the basis for the MADL, rabbits were exposed by intraperitoneal injection to 2,000 milligrams per kilogram (mg/kg) of methanol twice daily, for a total daily dose of 4,000 mg/kg-d (the commenter incorrectly identifies the dose in rabbits as 2,000 mg/kg-d). There was not a clear no observable effect level (NOEL) in rabbits. As noted by the authors of the study:

> "There was an apparent, but non-significant, 4-fold increase in the incidence of tail abnormalities (short or absent tails) in MeOH-exposed rabbit fetuses. While this occurrence was not significantly different from saline treated fetuses, it suggests the potential for species-specific differences in the spectrum of teratogenic anomalies following MeOH [methanol] exposure."

It appears that biologically-significant developmental effects occurred in rabbits at this level of exposure. Thus, this dose may be considered a LOEL. This dose is the same as the LOEL in mice in the study by Rogers et al. (1993) that forms the basis for the

[7] Sweeting, J. N., Siu, M., Wiley, M. J. and Wells, P. G. Species- and strain-dependent teratogenicity of methanol in rabbits and mice. Reproductive Toxicology. (2011). 31(1): 50-58.

proposed MADL. The route of exposure in the Sweeting et al. study is not one by which humans will potentially be exposed, so empirical data from the Rogers et al. (1993) study on oral exposure to methanol remain the appropriate basis for the oral MADL, particularly since the mouse and rabbit LOELs appear to be the same.

Commenter 3

Haley Curtis Stevens, Ph.D. for the International Food Additives Council (IFAC)

Comment 3.1

The comment states that Proposition 65 requires the Office of Environment Health Hazard Assessment (OEHHA) to establish safe harbor levels for all chemicals listed on Proposition 65. The comment further states that, beginning in March 2013, products containing methanol above an OEHHA-established safe harbor level will be required to display warning labels.

Response 3.1

Neither of these statements is correct. OEHHA develops safe harbor numbers as an aid to businesses in complying with Proposition 65, but is not required to do so under the statute. Also, it is the exposure to methanol from use of a product by the average consumer that determines whether a warning is required, rather than the amount of methanol contained in the product. It should also be noted that naturally occurring methanol in foods does not constitute an exposure for purposes of Proposition 65[8]. Finally, any party that does not agree with the MADL established by OEHHA may select a different no observable effect level (NOEL), and hence a MADL, by application of the procedures specified in regulations[9]. Any party doing so would assume responsibility for defending the scientific validity of that MADL.

Comment 3.2

The commenter criticized the data and the methodology that were used in the development of the proposed MADLs for methanol because significant differences exist in the way that humans and rodents process and metabolize methanol. The commenter cites statements by the Organization for Economic Co-operation (OECD) that “at a higher inhalation exposure (6.5 mg/L), humans show the lowest blood methanol level (at 140 mg/L), followed by monkeys, rats, and mice, with the level in mice being more than 10 times higher than humans”, and by the Health Council of the Netherlands that methanol blood levels could be 13-to 18-fold higher in mice than in humans for comparable exposures. On the basis of those statements, the commenter concludes that humans are also less vulnerable than rodents to methanol’s developmental effects.

[8] Title 27, Cal. Code of Regs., section 25501
[9] Title 27, Cal. Code of Regs., sections 25801 and 25803

Response 3.2

Methanol was added to the Proposition 65 list on the basis of formal identification as causing developmental toxicity in a final report from the NTP-CERHR, a Proposition 65 Authoritative Body[10]. In that report, the NTP stated that:

> "Species differences in methanol metabolism were noted and considered by the expert panel. In primates, including humans, methanol is converted to formaldehyde by the enzyme alcohol dehydrogenase. In rodents this conversion is made by catalase. Metabolism of methanol to formaldehyde and then to formate occurs at similar rates in rodents and primates. …The expert panel concluded that there was insufficient evidence to determine if a human fetus is more or less sensitive than rodents to the adverse effects of methanol."

OEHHA concurs with the NTP. While there are differences in metabolism of methanol between primates, including humans, and rodents, these differences are primarily in the formation and persistence of specific metabolites of methanol. Although these differences likely influence the susceptibility of different species to the acute effects of methanol, the commenter offers no data to refute NTP's finding that "it appears that methanol itself results in the developmental toxicity observed in rodents". OECD concluded that "rodent data on reproductive and developmental toxicity are relevant for humans despite the known differences in methanol metabolism between rodents and humans." OECD also stated that "air concentrations up to 1.6 mg/L [1,600 mg/m^3] resulted in similar blood methanol among rats, monkeys, and humans."

The no observable effect level upon which the MADL is based is 1,000 ppm (1,330 mg/m^3). The National Toxicology Program also states that "species differences are less obvious at lower exposure levels. … At 5,000 ppm the differences between blood methanol levels in rats and mice were generally 2-fold or less; at 1,000 ppm rat and mouse blood levels were similar. The limited data indicate that at 200 ppm rat, monkey, and human blood methanol levels were similar." Thus, at exposure levels relevant to development of the MADL, there appears to be little or no support for the commenter's argument that humans are less vulnerable than rodents to methanol's developmental effects. The inhalation exposure level identified by the OECD (6.5 mg/L, or 6,500 milligrams per cubic meter [mg/m^3]) is approximately five-fold higher than the no observable effect level that forms the basis for the inhalation MADL, and any differences in pharmacokinetic parameters between mice and humans at such high exposure levels appear to have little relevance to exposures which cause no observable effects.

Comment 3.3

Based on the commenter's assertion that humans are less vulnerable than rodents to methanol's developmental effects, and the dissimilar processing of methanol by

[10] Health and Safety Code section 25249.8(b) and Title 27, Cal. Code of Regs., section 25306(l)(3).

primates and rodents, the commenter proposed the oral MADL be raised by at least 3.5-fold from 23,000 µg/d to at least 80,000 µg/d.

Response 3.3

The commenter did not state how the proposed oral MADL of 80,000 µg/d was calculated. The statements the commenter cited to defend an increase in the oral MADL were not among the studies used to form the basis for the methanol listing[11,12]. As stated previously, methanol was listed based on formal identification as causing reproductive toxicity by a Proposition 65 authoritative body. That body considered methanol to cause developmental toxicity in rodents. As discussed in the response to comment 3.2, the materials cited by the commenter do not provide a valid scientific basis for adjusting the MADL based on differences between primates and rodents at the levels of methanol exposure relevant to the derivation of the MADL.

Commenter 4

Arthur Lawyer, Ph.D. for the Technology Sciences Group, Inc. on behalf of (1) Methanol Institute, (2) International Food Additive Council (IFAC), (3) Consumer Specialty Products Association

Comment 4.1

The commenter concurs with OEHHA's selection of the study by Rogers et al. (1993) as the most sensitive study deemed to be of sufficient quality to serve as the basis for the inhalation MADL. However, the commenter believes that the resulting oral MADL is unnecessarily conservative because the small, single point study by Rogers et al. (1993) did not result in a NOEL, and "as a consequence, OEHHA used a factor of 10 to provide a crude estimate of the oral NOEL" from the lowest observable effect level (LOEL) for methanol. The commenter proposes that an oral MADL should be extrapolated from the inhalation exposure data in the Rogers et al. (1993) and, on that basis, the commenter requests that OEHHA modify the oral MADL from 23,000 µg/d to 40,000 µg/d.

Response 4.1

The argument put forward by this commenter is essentially identical to that put forward by the Methanol Institute (see Comment 2.3). As discussed in the response to that comment, the commenter proposes combining a methanol inhalation absorption rate for a mouse and an assumed methanol oral absorption rate for a human. The commenter's calculation combines a methanol inhalation absorption rate for a mouse and an assumed methanol oral absorption rate for a human. The commenters did not consider

[11] OECD SIDS. 2004. Methanol. Page 16.
[12] Health Council of the Netherlands. 2010. Expert Committee on Occupational Safety. Methanol. Health-based recommended occupation exposure limit. Page 41. (citing conclusions by Perkins et al., 1995).

the differences in methanol absorption and blood levels between the inhalation and oral routes exhibited in the Rogers et al. (1993) study. In that study, the oral exposure level of 4,000 milligrams per kilogram of body weight per day (mg/kg-d) was expressly selected to result in a blood level approximating the high end of the range of maternal blood levels seen in the inhalation component of the study. The authors of the study noted that blood concentrations resulting from the oral exposure were slightly lower than the mean blood methanol concentration following inhalation exposure to 10,000 parts per million (ppm) methanol. The authors of the study did not calculate the dose of methanol in units of mg/kg-d that resulted from that inhalation exposure. However they did note that:

> "The severity of the developmental toxicity observed following this oral dosing regimen [of 4000 mg/kg-d] was similar to that seen in the 10,000-ppm inhalation exposure group."

Using the method for calculating the level of exposure to a given concentration of methanol laid out in the Initial Statement of Reasons for this regulation, OEHHA determined that exposure of mice to 10,000 ppm methanol by inhalation will result in a dose of approximately 8,100 mg/kg-d, which is about twice the oral dose of 4,000 mg/kg that resulted in about the same blood concentration and similar severity of effects. The 15% difference proposed by the commenter (85% inhalation absorption in mice compared to 100% oral absorption in humans) is therefore not consistent with the oral and inhalation data from the Rogers et al. (1993) study.

Although the data on oral exposure are available only for one dose level, the data are from the same well-designed and well-conducted study that provided the data on inhalation exposures. Those oral data are consistent with the inhalation data in terms of induced effects at similar blood concentrations, but differ in the external doses that resulted in those blood concentrations. It is therefore more appropriate to use the available empirical data on oral exposure to methanol as the basis for the oral MADL rather than extrapolating from inhalation exposure data.

In the inhalation study, the NOEL was 1,000 ppm, a factor of 10 below the 10,000 ppm level (that resulted in similar effects and similar blood concentration to those at the 4000 mg/kg-d oral dose). The method for estimating the NOEL when only a lowest observable effect level (LOEL) is observed is to divide by a factor of 10, following the Proposition 65 implementing regulations. This is how the NOEL of 400 mg/kg-d for the oral route was calculated – the LOEL of 4000 mg/kg-d was divided by 10. Thus the magnitude of the difference between the inhalation NOEL (1,000 ppm) and 10,000 ppm, the level of exposure that caused effects of comparable severity to those induced by the oral exposure to 4,000 mg/kg-d in the Rogers et al. (1993) study, is consistent with the assumptions made to calculate the MADL for the oral route.

Comment 4.2

In comments presented orally in a meeting with OEHHA on June 19, 2012, the commenter proposed raising the inhalation MADL to incorporate differences between the inhalation absorption rate of mice and humans. The commenter requested that OEHHA modify the inhalation MADL from 47,000 micrograms per day to 70,000 micrograms per day.

Response 4.2

The proposal to raise the inhalation MADL was not included in the subsequent written submission from this commenter. While it is therefore unclear whether the commenter intended to withdraw the proposal after discussion with OEHHA, OEHHA has considered the proposal and the rationale on which it was based. The proposed calculation by the commenter would yield an inhalation MADL of approximately 70,000 micrograms per day by adjusting the unrounded inhalation MADL of 47,248 micrograms per day on a proportional basis using a mouse inhalation absorption rate of 85% for methanol[13], and a human inhalation absorption rate of 57.7% for methanol[14].

The applicable regulation for development of the MADL specifies that "When available data are of such quality that anatomic, physiologic, pharmacokinetic and metabolic considerations can be taken into account with confidence, they may be used in the assessment"[15]. The World Health Organization International Programme on Chemical Safety (IPCS)[16] concluded that "no differences exist between the capabilities for absorption of methanol among various animal species", and that "around 60-85% of inhaled methanol is absorbed in the lung of humans". This range of human inhalation exposure levels was based on the study by Sedivec et al. (1981) and one earlier study. The 60-85% human inhalation absorption range was reiterated in the NTP-CERHR Monograph on methanol.

The mean human inhalation absorption rate of 57.7% for methanol from the Sedivec et al. study is based on only 5 adult male subjects. Thus, while the study provides relevant data, it may not be reflective of the range of absorption values in the broader population. The range of human inhalation exposures cited in the NTP-CERHR Monograph overlaps with that reported for mice. OEHHA therefore is not confident that there is a sufficient scientific basis to adjust the inhalation MADL as requested by the commenter, so has made no such adjustment.

[13] Perkins RA, Ward KW and Pollack GM. Comparative Toxicokinetics of Inhaled Methanol in the Female CD-1 Mouse and Sprague-Dawley Rat. Fundamental and Applied Toxicology. (1995). 28: 245-254.
[14] Sedivec V, Mraz M, and Flek J. Biological Monitoring of Persons Exposed to Methanol Vapours. Int Arch Occup Environ Health. (1981). 48:257-271.
[15] Title 27, Cal. Code of Regs., section 25803 (a)(7)).
[16] World Health Organization, International Programme on Chemical Safety Environmental Health Criteria 196, Methanol (Geneva, 1997).

ALTERNATIVES DETERMINATION

In accordance with Government Code, section 11346.9(a)(4), OEHHA has, throughout the adoption process for this regulation, considered available alternatives to determine whether any alternative would be more cost effective in carrying out the purpose for which the regulation was proposed, or would be as cost effective and less burdensome to affected private persons than the proposed action. OEHHA has determined that no reasonable alternative considered by OEHHA or that has otherwise been identified or brought to the attention of OEHHA would either be more effective in carrying out the purpose for which the action is proposed, or would be as effective and less burdensome to affected private persons, or would be more cost-effective to affected private persons and equally effective in implementing the statutory policy or other provision of law than the proposed regulation.

For chemicals known to the state to cause reproductive toxicity, an exemption from the warning requirement is provided by the Act when a person in the course of doing business is able to demonstrate that an exposure for which the person is responsible will have no observable reproductive effect, assuming exposure at 1,000 times the level in question (Health and Safety Code sections 25249.9, 25249.10 and 25249.11). The maximum dose level at which a chemical has no observable reproductive effect is referred to as the no observable effect level (NOEL). The Act also provides an exemption from the prohibition against discharging a listed chemical into sources of drinking water if the amount discharged does not constitute a “significant amount,” as defined, and the discharge is in conformity with all other laws and regulatory requirements (Health and Safety Code sections 25249.9 and 25249.11). Thus, these exemptions apply when the exposure or discharge in question is at a level that does not exceed the NOEL, divided by 1,000.

Regulations previously adopted by OEHHA provide guidance for determining whether an exposure to, or a discharge of, a chemical known to cause reproductive toxicity meets the statutory exemption (Sections 25801-25821). These regulations provide three ways by which a person in the course of doing business may make such a determination: (1) by conducting a risk assessment in accordance with the principles described in Section 25803 to derive a NOEL, and dividing the NOEL by 1,000; or (2) by application of the specific regulatory level adopted for the chemical in Section 25805; or (3) in the absence of such a level, by using a risk assessment conducted by a state or federal agency, provided that such assessment substantially complies with Section 25803(a). The specific regulatory levels in Section 25805 represent one one-thousandth of the NOEL.

The alternative levels proposed in the comments received by OEHHA are discussed above in the responses to comments, where OEHHA explains why the alternative calculations were not accepted.

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. 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.