REVISED FINAL STATEMENT OF REASONS

TITLE 27, CALIFORNIA CODE OF REGULATIONS

AMENDMENT TO SECTION 25805. SPECIFIC REGULATORY LEVELS: CHEMICALS CAUSING REPRODUCTIVE TOXICITY

MAXIMUM ALLOWABLE DOSE LEVEL: Chromium (hexavalent compounds)

This is the Final Statement of Reasons for the adoption of a maximum allowable dose level (MADL) for chromium (hexavalent compounds). Chromium (hexavalent compounds) is listed as known to the State to cause reproductive toxicity under Proposition 65[1]. On August 13, 2010, the Office of Environmental Health Hazard Assessment (OEHHA) issued a Notice of Proposed Rulemaking to adopt the proposed level for this chemical in Title 27, California Code of Regulations, section 25805[2]. The Initial Statement of Reasons set forth the grounds for the proposed amendment to the regulation.

The Notice of Proposed Rulemaking opened a public comment period that commenced on August 13, 2010 and ended on September 27, 2010. The Notice stated that a public hearing would be held only on request. No request for a public hearing was received by OEHHA. One written public comment was received by OEHHA.

On March 8, 2011, OEHHA submitted the regulatory package to the Office of Administrative Law (OAL) for review and approval. The regulatory package was withdrawn from OAL review on April 18, 2011 in order for OEHHA to provide sufficient time for the OEHHA Science Advisory Board's Developmental and Reproductive Toxicant (DART) Identification Committee to review and comment on the proposed MADL. No written comment was received by OEHHA from the Committee members. Therefore, OEHHA is re-submitting the regulatory package for OAL review and approval.

[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.

SUMMARY AND RESPONSE TO COMMENTS

Table 1 below provides the name of the single commenter on the August 13, 2010, Notice of Proposed Rulemaking. After the table, the submitter's comments are summarized and responses are provided.

Table 1. Commenter on the Notice of Proposed Rulemaking (OAL Notice File No. Z-2010-0803-12)

Commenter/Affiliation	Representing	Date Received
Frank T. Sheets III	California Cement Manufacturers Environmental Coalition (CCMEC)	Sept. 27, 2010

Comment 1

The commenter objects to expression of the MADL as µg/day, as opposed to µg/kg body weight/day.

Response

As described in Sections 25803(a)(2) and (b) of our regulations, the MADL is expressed in units of amount/day (and not amount per unit bodyweight per day):

> "The no observable effect level (NOEL) shall be the highest dose level which results in no observable reproductive effect expressed in milligrams of chemical per kilogram of bodyweight per day."
>
> "The NOEL shall be converted to a milligram per day dose level by multiplying the assumed human body weight by the NOEL. When the applicable reproductive effect is upon the male, human body weight of 70 kilograms shall be assumed. When the applicable reproductive effect is upon the female or conceptus, human body weight of 58 kilograms shall be assumed."

In the context of Proposition 65's requirement for warning about exposure to a listed chemical, the MADL specifies the largest amount of a chemical to which a responsible party can cause exposure without being required to provide a warning. Expressing the MADL in units of milligrams of chemical per kilogram of bodyweight per day would require that the responsible party know the body weight of every individual to whom they were causing an exposure in order to determine on a person-by-person basis whether a warning was required. This is not feasible and is not required by Proposition 65. The MADL document identifies the milligrams of chemical per kilogram of bodyweight per day value from which the MADL is derived. That document is

available at
http://www.oehha.ca.gov/prop65/law/pdf_zip/081210DraftMADLChromVI.pdf

Comment 2

The commenter recommends using an average body weight for all adults of 71.8 kg instead of a body weight of 58 kg for a female.

Response

Although chromium (hexavalent compounds) is listed under Proposition 65 for developmental, male reproductive, and female reproductive effects, the commenter recognizes that "the most sensitive study of health effects involved female mice." Per Section 25803(a)(2), "where multiple reproductive effects provide the basis for the determination that a chemical is known to the state to cause reproductive toxicity, the reproductive effect for which studies produce the lowest NOEL shall be utilized for the determination of the NOEL." This provision is intended to ensure that the dose which results from exposure at the MADL will not exceed one one-thousandth of the NOEL for any exposed individual. Using the average bodyweight for men and women suggested by the commenter to calculate the MADL would not be consistent with this provision and is not scientifically appropriate.

Comment 3

The commenter notes that the MADL is specific to oral exposure, but that the supporting document for the MADL gives guidance in interpreting the MADL relative to inhalation and dermal exposures. The commenter asserts that there is no basis for the guidance provided.

Response

Data cited in the Hazard Identification Materials prepared by OEHHA (OEHHA 2008) indicate that chromium and chromium compounds are absorbed by the oral, inhalation, and dermal routes of exposure. Although the internal doses resulting from equivalent exposures by different routes may vary, there are no data indicating that the effects of the absorbed dose will vary depending on route of exposure. The MADL document provides the empirical MADL for exposure by the oral route, and additionally provides guidance for interpreting that MADL relative to exposures by other routes.

Comment 4

The commenter asserts that the oral route data used to determine the MADL are not relevant to inhalation exposure, and that therefore inhalation exposure to hexavalent chromium should not be subject to the MADL.

Response

As noted in the previous response, data cited in the Hazard Identification Materials prepared by OEHHA (OEHHA 2008) indicate that chromium and chromium compounds are absorbed both by the oral and inhalation routes of exposure. There is no indication that the effects of any absorbed dose differ depending on the route of exposure. Thus, the internal dose resulting from oral exposure to the MADL is relevant to the inhalation route of exposure.

Comment 5

The commenter challenges the scientific principles and assumptions used in deriving the MADL for hexavalent chromium, as follows:

Comment 5a: The commenter requests, "Discussion of the nature of the scientific concern over the appropriateness of the basis of the safety factor of 1,000," pertaining to uncertainty in the data.

Response to 5a: The 1,000 factor is established by statute (Health and Safety Code section 25249.10(c)). Use of the 1,000 factor is mandatory. It is not a variable "uncertainty factor" as that term is used in other contexts.

Comment 5b: The commenter requests discussion of range of doses used by Murthy et al. (1996), in the study used to derive the MADL. In particular, the commenter notes the order of magnitude difference between the LOEL of 5 ppm in that study, and the NOEL of 0.5 ppm.

Response to 5b: The doses used in the study are specified in the MADL document. A 10-fold difference between doses is not unusual, particularly when subtle effects at low doses are under consideration. In any event, the choice of doses does not alter the evidence that 5 ppm was the LOEL dose and 0.5 ppm was the NOEL dose in the Murthy et al. (1996) study.

Comment 5c: The commenter challenges the use of the Murthy et al. (1996) study in

deriving the MADL on the grounds that it presents dose information as concentrations in drinking water, without providing data on water consumption. On this basis, the commenter requests inclusion of the definition of "sufficient quality" under Section 25803(a)(5).

Response to 5c: Section 25803(a)(5) states that “the NOEL shall be based on the most sensitive study deemed to be of sufficient quality.” No single definition of “sufficient quality” has been adopted, because the large number of potentially relevant study designs and the numerous and varying factors to be considered under each design precludes adopting such a definition. Rather, OEHHA’s scientific judgment in the selection of a study being considered of sufficient quality is explained on a case-by-case basis in the supporting document for each MADL.

Section 25803(a) also requires that "the assessment shall be based on evidence and standards of comparable scientific validity to the evidence and standards which form the scientific basis for listing the chemical as known to the state to cause reproductive toxicity." The Murthy et al. (1996) study was one of the studies in animals considered by the Developmental and Reproductive Toxicant Identification Committee, along with the epidemiological evidence, to determine that chromium (hexavalent compounds) was clearly shown through scientifically valid testing according to generally accepted principles to cause reproductive toxicity, including female reproductive toxicity. The data used to calculate the consumed doses of hexavalent chromium in the Murthy et al. (1996) study came from another study (Junaid et al., 1996) conducted in the same laboratory, by the same investigators, using the same strain of mice with the same starting weight, during the same year.

Finally, Section 25801(a) states that “nothing in this article shall preclude a person from using risk assessment methodologies or levels not described in this article to establish that a level of exposure to a listed chemical would produce no observable effect within the meaning of the Act.” Thus, the MADL adopted by OEHHA does not preclude the commenter from calculating a different MADL.

Comment 5d: The commenter questions the relevance of the 90-day exposure period in the Murthy et al. (1996) study to likely human exposure, and asserts that this period in mice would be equivalent to "three plus years" of human exposure.

Response to 5d: The data from the study by Murthy et al. (1996) do not provide information on exposure to the NOEL or LOEL for periods shorter than 90 days. While the commenter may be specifically concerned about exposures of shorter duration, OEHHA considers the MADL applicable to exposures of any duration. Exposures to

hexavalent chromium, for example as a contaminant of drinking water, could occur at any point during an individual's lifetime and for any length of time. Shorter exposures are unlikely to pose a greater risk than longer exposures.

Comment 5e: The commenter states that the averaging periods for MADLs are not specified in the regulations, but should be. The commenter also requests discussion of the age range to which the MADL applies.

Response to 5e: Comments on the general content of the existing regulation are beyond the scope of this specific amendment adopting a MADL for chromium (hexavalent compounds). The MADL is developed based on the most sensitive effect of the chemical. In the case of hexavalent chromium, that effect was identified in adult female mice. Hexavalent chromium is, however, known to cause developmental and male reproductive toxicity in addition to female reproductive toxicity. Thus, the MADL applies to all segments of the population, including both sexes and all age groups. Nothing in the MADL documentation indicates otherwise, nor should anything in the documentation be interpreted to do so.

Comment 5f: The commenter requests that discussion of the human epidemiological data on the reproductive and developmental toxicity data for hexavalent chromium appear in the MADL document.

Response to 5f: This comment pertains mainly to the listing of hexavalent chromium, rather than to development of a MADL, and so is beyond the scope of the present rulemaking. As stated in the MADL document (OEHHA, 2010), while the human data contributed to the evidence of hazard posed by hexavalent chromium to all three reproductive endpoints, these data were not suitable for establishing quantitative dose-response relationships required for determining a MADL value.

Comment 5g: The commenter repeats his request for discussion of human epidemiological data and asserts that the data can be used to decrease by several orders of magnitude the uncertainty reflected in the MADL.

Response to 5g: The use of epidemiological data is addressed in the response to comment 5f. The relationship between the mandatory 1,000-fold factor used to derive the MADL and the degree of uncertainty in the data is addressed in the response to comment 5a.

Comment 5h: The commenter requests that discussion of naturally occurring chromium content in food be included in the MADL document.

Response to 5h: The vast majority of adverse developmental and reproductive outcomes are of unknown cause, as is the potential contribution of hexavalent chromium in food to such outcomes. Where a business can show that hexavalent chromium is present naturally in food, and was not added by any known human activity, such exposures are not subject to the warning requirements of Proposition 65.

Comment 5i: The commenter requests discussion of the Institute of Medicine's (IOM) position on the safety of chromium picolinate, stating that the IOM has no concerns about exposures to 1.6 milligrams of chromium picolinate per day for 3-6 months. The commenter also states that chromium picolinate is known to contain up to 12 parts perbillion (ppb) hexavalent chromium. The commenter asserts that there is orders of magnitude greater exposure, presumably than the MADL, in currently approved dietary supplements.

Response to 5i: Exposure to 1.6 mg of chromium picolinate that contains 12 ppb of hexavalent chromium will result in exposure to 19.2 picograms of hexavalent chromium. That exposure is more than 400,000 times lower than the MADL. The IOM's approval of an exposure level is not relevant to the proposed rulemaking.

Comment 5j: The commenter requests discussion of the magnitude of the difference between the MADL and the level of exposure that would cause adverse developmental or reproductive effects in humans, which the commenter asserts is several orders of magnitude.

Response to 5j: As required by statute, the proposed MADL is a level of exposure that is at least three orders of magnitude below a level that would be expected to cause no observable adverse effects.

Comment 6

The commenter notes that Government Code Section 11346.5(a)(13) requires that, "OEHHA must determine that no reasonable alternative...would be more effective...or as effective and less burdensome to the affected private persons than the proposed action." The commenter asks that OEHHA therefore consider taking no action, or else derive the MADL according to the points outlined in comments 1-5.

Response

The action being taken by OEHHA will provide an optional "safe harbor" value that may

be utilized by any interested party. Taking no action would mean that all interested parties would be required to make their own determinations regarding whether the exposure in question was a factor of 1000 below the exposure that produces no observable effect. Taking the action does not prevent any interested party, including the commenter, from calculating their own MADL if they disagree with that adopted by OEHHA.

Comment 7

The commenter objects to statements in the Notice of Proposed Rulemaking that characterize the proposed MADL as having no impact on businesses or jobs. Although no evidence or details are provided, the commenter anticipates "inevitable and significant adverse economic impacts created by this proposed rule."

Response

The adoption of a MADL simply identifies a level of exposure at or below which a business responsible for that exposure would not be subject to the warning requirement or discharge prohibition. Thus, the adoption of a “safe harbor” value does not impose any regulatory requirements on businesses, but instead is expected to aid affected parties in complying with the statutory requirements if they choose to use it.

ALTERNATIVES DETERMINATION

In accordance with Government Code, section 11346.5(a)(7), OEHHA has, throughout the adoption process of this regulation, considered available alternatives. OEHHA has not found any alternative more effective, or as effective and less burdensome to affected private persons than the proposed action.

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 (Title 27, California Code of Regulations, 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.

LOCAL MANDATE DETERMINATION

Proposition 65 provides an express exemption from the warning requirement and discharge prohibition for all state and local agencies. Therefore, OEHHA has determined this regulatory action will not impose 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.