PUBLIC NOTICE

Initiation of Process to Update Public Health Goals for Three Chemicals in Drinking Water
September 2012

Public health goals (PHGs) are concentrations of drinking water contaminants that pose no significant health risk if consumed over a lifetime. The Office of Environmental Health Hazard Assessment (OEHHA) establishes PHGs, which are used as the health basis for the development of California's primary drinking water standards. OEHHA also reviews and updates existing PHGs. This public notice provides an update on PHG reviews in progress and announces the initiation of reviews for three chemicals: chlorobenzene, 1,1-dichloroethane, and trichloroethylene.

A. Requirements

The Calderon-Sher California Safe Drinking Water Act of 1996 requires OEHHA to post on its web site notices for the chemicals in drinking water for which it is initiating development of PHGs. The law also describes the intent and general context of the PHGs. PHGs are concentrations of chemicals in drinking water that are not anticipated to produce adverse health effects following long-term exposures. OEHHA is required to consider potential adverse effects on members of subgroups that comprise a meaningful proportion of the population, including but not limited to infants, children, pregnant women, the elderly, and individuals with a history of serious illness. The PHGs are non-regulatory in nature but are to be used as the health basis to update the state's primary drinking water standards (maximum contaminant levels, or MCLs) established by the California Department of Public Health (DPH) for chemicals subject to regulation.

The act requires PHGs to be developed for the approximately 90 chemicals for which state or federal MCLs are provided, and review and update the risk assessments that form the basis for the PHGs every five years or as appropriate. Other chemicals may be added to the list by legislative or interdepartmental request. Opportunities for public comment and peer review are provided.

B. Implementation

OEHHA has published PHGs for 89 chemicals as of September 2012. Two MCLs, for gross alpha and gross beta radionuclides, represent screening levels for contaminants rather than specific regulatory standards; for these, OEHHA has provided risk assessments and guidance memoranda. In addition, re-evaluations of the original PHG have been completed for 23 chemicals. OEHHA concluded that no new information was available on some of these that would result in changes to the PHG. The re-reviews of several other chemicals required more extensive efforts, for which complete updated documents have been published and revised PHGs provided. The updated

PHGs and supporting documents are available at http://www.oehha.ca.gov/water/phg/index.html.
PHG documents are being drafted for two groups of contaminants, trihalomethanes and haloacetic acids, that do not have PHGs, as well as updates of the PHG for several chemicals. At the initial posting of the draft document, a 45-day public comment period is provided, followed by a public workshop. All comments received are considered in the preparation of a second draft, which is then posted for a 30-day public comment period. After consideration of comments, the final PHG is then published on the OEHHA web site for public reference and use by DPH in developing California MCLs.

Evaluation is now being initiated for three more chemicals for which PHGs were developed earlier (see Section D). These are now being re-reviewed as part of the ongoing PHG update process. Information relevant to the development of PHGs is requested on each of these chemicals.

C. PHGs in progress

PHG documents are currently in progress for several chemicals for which initiation of review has previously been announced. An update of the 2004 perchlorate PHG is in preparation for its second posting following scientific peer review and public comments, and the trihalomethanes PHG is in preparation for its third posting following a second round of public comments. Listed below are other chemicals for which PHGs are being updated.

- Alachlor
- Antimony
- Atrazine/Simazine
- Cyanide
- Diethylhexylphthalate
- 1,2-Dibromo-3-chloropropane
- 1,4-Dichlorobenzene
- 1,1-Dichloroethylene
- 1,2-Dichloropropane
- Endothall
- Ethylbenzene
- Fluoride
- Haloacetic acids

- Hexachlorocyclopentadiene
- Nitrate/nitrite
- Picloram
- 1,2,4-Trichlorobenzene
- Trichlorofluoromethane
- Xylene

D. Initiation of PHGs

Updates of PHGs are being initiated for the following chemicals for which PHGs have already been released, based on the availability of new data, methodology updates, concern about environmental exposures, and/or potential significance as drinking water contaminants:

- Chlorobenzene
- 1,1-Dichloroethane
- Trichloroethylene

A brief description of these chemicals is provided below. This announcement solicits the submission of pertinent information on these contaminants that could assist our office in updating the risk assessment and deriving a revised PHG.

Information submitted to OEHHA in response to this request should not be proprietary in nature, because all information submitted is a matter of public record. Information should be submitted by November 1, 2012 to:

Michael Baes
PHG Program
Pesticide and Environmental Toxicology Branch
Office of Environmental Health Hazard Assessment
1515 Clay St., 16th floor
Oakland, California 94612

All data submitted will be considered in the development of the PHG for these chemicals. If substantive revisions to the original PHG documents are required, the draft documents will be available for discussion in a public workshop and public comment will be solicited as described above in Section B. The final risk assessments will be utilized by DPH for potential revisions to the MCLs for the chemical in drinking water, as described in more detail on the DPH Web site at http://www.cdph.ca.gov/certlic/drinkingwater/Pages/MCLsandPHGs.aspx.

E. Descriptions of chemicals or substances for review initiation:

CHLOROBENZENE

Chlorobenzene (CAS Registry Number: 108-90-7) belongs to a group of chemicals called halogenated aromatic hydrocarbons. Chlorobenzene is used in the manufacture of other organic chemicals, dyestuffs and insecticides. It is also used as a solvent for adhesives, drugs, rubber, paints and dry cleaning, and as a fiber-swelling agent in textile processing.

Historically, the major source of chlorobenzene in drinking water has been discharge from chemical and agricultural chemical factories. Chlorobenzene was once used as an intermediate in production of the pesticide DDT (p,p'-dichlorodiphenyltrichloroethane). Since the banning of DDT in 1972, the use of chlorobenzene has decreased significantly and, according to the U.S. EPA's 2010 Toxics Release Inventory (TRI) Chemical Report, 72 pounds of chlorobenzene were discharged into surface waters nationally whereas on- and off-site disposal or other releases totaled 282,256 pounds (accessed at: http://iaspub.epa.gov/triexplorer/tri_release.chemical). In moist soil, the majority of chlorobenzene should volatize to the atmosphere. Chlorobenzene is relatively mobile in sandy soil, where it biodegrades slowly or not at all, and is expected to leach into groundwater (OEHHA, 2003). Since 2009, chlorobenzene has been detected in numerous public water supply wells throughout California, with results ranging from < 0.5 ppb to < 5 ppb, well below the California MCL of 70 ppb and PHG of 200 ppb (data accessed with GeoTracker GAMA: http://geotracker.waterboards.ca.gov/gama/).

Potential health effects of chlorobenzene include headaches, nausea, sleepiness, numbness, and vomiting, as demonstrated by workers exposed to high levels of chlorobenzene. However, it is unclear whether all of these effects were due to chlorobenzene because the workers may have been exposed to other chemicals as well (OEHHA, 2003). In animal studies, exposure to chlorobenzene has been shown to affect the liver, kidney, and central nervous system (symptoms include unconsciousness, tremors, restlessness, and death from inhalation exposure) (OEHHA, 2003).

An update of the PHG is being initiated in keeping with the California Safe Drinking Water Act's mandates to review PHGs and to ensure that the risk assessment is performed using the most current principles, practices, and methods used by public health professionals. The update of the risk assessment for chlorobenzene will include a review of more recent toxicology literature since the publication of the PHG in 2003, and incorporate the application of updated risk assessment methodologies.

Selected References

Faisal Siddiqui, M., Ahmad, R., Ahmad, W., and A.U. Hasnain (2006). Micronuclei induction and chromosomal aberrations in Rattus norvegicus by chloroacetic acid and chlorobenzene. *Ecotoxicol Environ Saf* 65: 159-64.

Feltens, R., Mogel, I., Roder-Stolinski, C., Simon, J.C., Herberth, G., and I. Lehmann (2009). Chlorobenzene induces oxidative stress in human lung epithelial cells in vitro. *Toxicol Appl Pharmacol* 242: 100-8.

Lehmann, I., Roder-Stolinski, C., Nieber, K., and G. Fischader (2008). In vitro models for the assessment of inflammatory and immuno-modulatory effects of the volatile organic compound chlorobenzene. *Exp Toxicol Pathol* 60: 185-93.

Morbt, N., Tomm, J., Feltens, R., Mogel, I., Kalkhof, S., Murugesan, K., Wirth, H., Vogt, C., Binder, H., Lehmann, I., and M. von Bergen (2010). Chlorinated benzenes cause concomitantly oxidative stress and induction of apoptotic markers in lung epithelial cells (A549) at nonacute toxic concentrations. *J Proteome Res* 10: 363-78.

OEHHA (2003). Public Health Goals for Chemicals in Drinking Water: Chlorobenzene. Office of Environmental Health Hazard Assessment, California Environmental Protection Agency, Sacramento, CA.

1,1-DICHLOROETHANE

1,1-Dichloroethane (1,1-DCA, CAS Registry Number: 75-34-3) is a volatile organic compound that is used as a chemical intermediate in the synthesis of vinyl chloride and 1,1,1-trichloroethane. It is also used as a solvent and degreaser (HSDB, 2012). 1,1-Dichloroethane is anticipated to partition into the air due to its volatility and relatively low solubility in water. Since 2009, 1,1-DCA has been detected in public water supply wells across California at concentrations ranging from < 0.5 ppb to 3.4 ppb, with one sample result listed as < 10 ppb (data accessed with GeoTracker GAMA: http://geotracker.waterboards.ca.gov/gama/). California's MCL for 1,1-DCA is 5 ppb, and the current PHG is 3 ppb.

1,1-Dichloroethane was classified as group C, a possible human carcinogen, by the U.S. EPA in 1996 (U.S. EPA, 1996). 1,1-Dichloroethane was listed under Proposition 65 as a chemical known to the state of California to cause cancer in 1989 (OEHHA, 2003). The current PHG is based on carcinogenicity. The critical non-cancer effect observed in experimental animals exposed to 1,1-dichloroethane was increased kidney toxicity in cats (OEHHA, 2003). However, this endpoint is less sensitive than cancer, and requires a larger daily dose for induction. Therefore, a water concentration of 1,1-dichloroethane that is health-protective for cancer will also protect against the most sensitive non-cancer effects.

The update of the risk assessment for 1,1-dichloroethane will include a review of more recent toxicology literature since the publication of the PHG in 2003, and incorporate the application of updated risk assessment methodologies.

Selected References

HSDB (2012). 1,1-dichloroethane. Hazardous Substances Data Bank, National Library of Medicine. (http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB)

NCI (1978). Bioassay of 1,1-dichloroethane for possible carcinogenicity. Bethesda, MD, National Cancer Institute Carcinogenesis Technical Report Series 66.

OEHHA (2003). Public Health Goals for Chemicals in Drinking Water: 1,1-Dichloroethane in Drinking Water. Office of Environmental Health Hazard Assessment, California Environmental Protection Agency, Sacramento, CA.

OEHHA (2008). OEHHA Cancer Potency Values. Sacramento, CA, Office of Environmental Health Hazard Assessment, California Environmental Protection Agency.

OEHHA (2009). Technical Support Document for Cancer Potency Factors: Methodologies for Derivation, Listing of Available Values, and Adjustments to Allow for Early Life Stage Exposures. Sacramento, CA, Office of Environmental Health Hazard Assessment, California Environmental Protection Agency.

OEHHA (2012). Chemicals known to the state to cause cancer or reproductive toxicity - July 20, 2012, Office of Environmental Health Hazard Assessment, California Environmental Protection Agency.

Patlolla, B.P., Patlolla, A.K. and P.B. Tchounwou (2005). "Cytogenetic effects of 1,1-dichloroethane in mice bone marrow cells." *Int J Environ Res Public Health,* 2: 101-106.

U.S. EPA (1996). 1,1-Dichloroethane (CASRN 75-34-3) Washington, DC, Integrated Risk Information System (IRIS), U.S. Environmental Protection Agency.

TRICHLOROETHYLENE

Trichloroethylene (TCE, CAS Registry Number: 79-01-6) is a volatile organic compound that is predominantly used as a metal degreaser. It is also an adhesive and can be found in paints, lacquers, and paint strippers. TCE was previously found in dry cleaning solutions, cosmetics, foods and pesticides, but these uses have been discontinued. In the United States, TCE is a high production volume chemical, and it was estimated that 100-500 million pounds were produced in 2002 (HSDB, 2012). TCE has relatively low solubility in water, and is expected to partition into the air due to its volatility. In the past three years, TCE has been detected in 146 public supply wells throughout California at levels ranging from 5.1 to 680 ppb, well above its MCL of 5 ppb and current PHG of 1.7

ppb (data accessed with GeoTracker GAMA: http://geotracker.waterboards.ca.gov/gama/).

In its recent evaluation, U.S. EPA determined TCE to be "carcinogenic to humans" by all routes of exposure (U.S. EPA, 2011). This is stronger than U.S. EPA's 2001 characterization of TCE as "highly likely to produce cancer in humans" (U.S. EPA, 2001). The 2011 conclusion was based on human epidemiological data linking TCE exposure with increased incidences of kidney cancer (Dosemeci et al., 1999; Bruning et al., 2003; Raaschou-Nielsen et al,. 2003; Zhao et al., 2005; Charbotel et al., 2006; Moore et al., 2010) and non-Hodgkin lymphoma (Hardell et al., 1994; Hansen et al., 2001; Raaschou-Nielsen et al., 2003). There is also evidence that TCE exposure is correlated with other types of cancer, including liver, bladder, and esophageal cancer (reviewed by U.S. EPA, 2011). The human toxicity studies are supported by animal studies, where similar tumor types (kidney and liver) were observed in rats and mice chronically exposed to TCE (Maltoni et al., 1988; NTP, 1990; Anna et al., 1994; Bull et al., 2002). For the current PHG, published in 2009, OEHHA calculated a cancer slope factor of 0.0059 $(mg/kg\text{-}day)^{-1}$, which is approximately an order of magnitude lower than U.S. EPA's newly developed oral slope factor of 0.05 $(mg/kg\text{-}day)^{-1}$.

TCE exposure has also been associated with various non-cancer effects. U.S. EPA has estimated a chronic oral reference dose of 0.0005 mg/kg-day, based on observations of increased thymus weight in female mice (Keil et al., 2009), increased fetal cardiac malformations in rats (Johnson et al., 2003), and decreased plaque-forming cell response and increased delayed-type hypersensitivity in mice (Peden-Adams et al., 2006). Additional hepatic, renal, neurological, immunological, hematological, developmental, and reproductive effects have been reported in humans and experimental animals following TCE exposure.

The release of U.S. EPA's risk assessment for TCE has prompted an expedited review and update of the TCE PHG since U.S. EPA's assessment concludes that TCE is a significantly more potent toxicant than was reflected in OEHHA's 2009 PHG document and TCE is still a common groundwater contaminant. In its update, OEHHA will evaluate any recent studies that were published since the previous PHG in 2009, as well as evaluate the overall scientific evidence to determine health-protective concentrations in drinking water for cancer and non-cancer endpoints, and employ updated risk assessment methodologies.

Selected References

Anna, C.H., Maronpot, R.R., Pereira, M.A., Foley, J.F., Malarkey, D.E., and M.W. Anderson (1994). ras proto-oncogene activation in dichloroacetic acid-, trichloroethylene- and tetrachloroethylene-induced liver tumors in B6C3F1 mice. *Carcinogenesis* 15: 2255-2261.

Bruning, T., Pesch, B., Wiesenhutter, B., Rabstein, Lammert, S.M., Baumuller, A., and H.M. Bolt (2003). Renal cell cancer risk and occupational exposure to trichloroethylene: results of a consecutive case-control study in Arnsberg, Germany. *Am J Ind Med* 43: 274-285.

Bull, R.J., Orner, G.A., Cheng, R.S., Stillwell, L., Stauber, A.J., Sasser, L.B., Lingohr, M.K., and B.D. Thrall (2002). Contribution of dichloroacetate and trichloroacetate to liver tumor induction in mice by trichloroethylene. *Toxicology and applied pharmacology* 182: 55-65.

Charbotel, B., Fevotte, J., Hours, M., Martin, J.L., and A. Bergeret (2006). Case-control study on renal cell cancer and occupational exposure to trichloroethylene. Part II: Epidemiological aspects. *The Annals of occupational hygiene* 50: 777-787.

Corton, J.C. (2008). Evaluation of the role of peroxisome proliferator-activated receptor alpha (PPARalpha) in mouse liver tumor induction by trichloroethylene and metabolites. *Critical reviews in toxicology* 38: 857-875.

Cummings, B.S., Parker, J.C., and L.H. Lash (2000). Role of cytochrome P450 and glutathione S-transferase alpha in the metabolism and cytotoxicity of trichloroethylene in rat kidney. *Biochemical pharmacology* 59: 531-543.

Dosemeci, M., Cocco, P., and W.H. Chow (1999). Gender differences in risk of renal cell carcinoma and occupational exposures to chlorinated aliphatic hydrocarbons. *American journal of industrial medicine* 36: 54-59.

Hansen, J., Raaschou-Nielsen, O., Christensen, J.M., Johansen, I., McLaughlin, J.K., Lipworth, L., Blot, W.J., and J.H. Olsen (2001). Cancer incidence among Danish workers exposed to trichloroethylene. *J Occup Environ Med* 43: 133-139.

Hardell, L., Eriksson, M., and A. Degerman (1994). Exposure to phenoxyacetic acids, chlorophenols, or organic solvents in relation to histopathology, stage, and anatomical localization of non-Hodgkin's lymphoma. *Cancer research* 54: 2386-2389.

HSDB. (2012). Trichloroethylene. Hazardous Substances Data Bank, National Library of Medicine. (http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB)

Johnson, P.D., Goldberg, S.J., Mays, M.Z., and B.V. Dawson (2003). Threshold of trichloroethylene contamination in maternal drinking waters affecting fetal heart development in the rat. *Environ Health Perspect* 111: 289-292.

Keil, D.E., Peden-Adams, M.M., Wallace, S., Ruiz, P., and G.S. Gilkeson (2009). Assessment of trichloroethylene (TCE) exposure in murine strains genetically-prone and non-prone to develop autoimmune disease. *J Environ Sci Health A Tox Hazard Subst Environ Eng* 44: 443-453.

Lash, L.H., Putt, D.A., Brashear, W.T., Abbas, R., Parker, J.C., and J.W. Fisher (1999). Identification of S-(1,2-dichlorovinyl)glutathione in the blood of human volunteers exposed to trichloroethylene. *Journal of toxicology and environmental health. Part A* 56: 1-21.

Lash, L.H., Putt, D.A., and J.C. Parker (2006). Metabolism and tissue distribution of orally administered trichloroethylene in male and female rats: identification of glutathione- and cytochrome P-450-derived metabolites in liver, kidney, blood, and urine. *Journal of toxicology and environmental health. Part A* 69: 1285-1309.

Maltoni, C., Lefemine, G., Cotti, G., and G. Perino (1988). Long-term carcinogenicity bioassays on trichloroethylene administered by inhalation to Sprague-Dawley rats and Swiss and B6C3F1 mice. *Annals of the New York Academy of Sciences* 534: 316-342.

Moore, L.E., Boffetta, P., Karami, S., Brennan, P., Stewar, P.S., Hung, R., Zaridze, D., Matveev, V., Janout, V., Kollarova, H., Bencko, V., Navratilova, M., Szeszenia-Dabrowska, N., Mates, D., Gromiec, J., Holcatova, I., Merino, M., Chanock, S., Chow,

NTP (1990). Carcinogenesis studies of trichloroethylene (without epichlorohydrin) (CAS No. 79-01-6) in F344/N rats and B6C3F1 mice (gavage studies), U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health.

OEHHA (2009). Public Health Goals for Chemicals in Drinking Water: Trichloroethylene. Office of Environmental Health Hazard Assessment, California Environmental Protection Agency, Sacramento, CA.

Peden-Adams, M.M., Eudaly, J.G., Heesemann, L.M., Smythe, J., Miller, J., Gilkeson, G.S., and D.E. Keil (2006). Developmental immunotoxicity of trichloroethylene (TCE): studies in B6C3F1 mice. *J Environ Sci Health A Tox Hazard Subst Environ Eng* 41: 249-271.

Raaschou-Nielsen, O., Hansen, J., McLaughlin, J.K., Kolstad, H., Christensen, J.M., Tarone, R.E., and J.H. Olsen (2003). Cancer risk among workers at Danish companies using trichloroethylene: a cohort study. *Am J Epidemiol* 158: 1182-1192.

Robbiano, L., Mereto, E., Migliazzi Morando, A., Pastore, P., and G. Brambilla (1998). Increased frequency of micronucleated kidney cells in rats exposed to halogenated anaesthetics. *Mutation research* 413: 1-6.

Rothman, W.H. and N. Rothman (2010). Occupational trichloroethylene exposure and renal carcinoma risk: evidence of genetic susceptibility by reductive metabolism gene variants. *Cancer Res* 70: 6527-6536.

U.S. EPA (2001). Trichloroethylene health risk assessment: Synthesis and characterization (External Review Draft) August 2001. Accessed at: http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=23249.

U.S. EPA (2011). Toxicological review of trichloroethylene (CAS No. 79-01-6). Integrated Risk Information System (IRIS), United States Environmental Protection Agency, Washington, D.C.

Vamvakas, S., Elfarra, A.A., Dekant, W., Henschler, D. and M.W. Anders (1988). Mutagenicity of amino acid and glutathione S-conjugates in the Ames test. *Mutation research* 206: 83-90.

Zhao, Y., Krishnadasan, A., Kennedy, N., Morgenstern, H. and B. Ritz (2005). Estimated effects of solvents and mineral oils on cancer incidence and mortality in a cohort of aerospace workers. *American journal of industrial medicine* 48: 249-258.