TECHNICAL SUPPORT DOCUMENT

PROPOSED IDENTIFICATION OF VINYL CHLORIDE AS A TOXIC AIR CONTAMINANT

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HEALTH EFFECTS OF AIRBORNE VINYL CHLORIDE

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1.0 EXECUTIVE SUMMARY

Vinyl chloride is a short-chain halogenated hydrocarbon used predominantly in the manufacture of polyvinyl chloride and various packaging and construction products. Vinyl chloride has a very low degree of acute toxicity, with two-hour inhalation LD_{50} values ranging from 27,419 ppm in mice to 236,215 ppm in rabbits and guinea pigs. Exposure to high concentrations can lead to narcosis, cardiovascular and respiratory irregularity, convulsions, cyanosis and death. Several human deaths have been attributed to occupational exposure to very high levels of vinyl chloride. Autopsies of these patients revealed congestion of the liver, spleen and kidneys. Acute toxicity symptoms are thought to occur above 100 ppm.

Chronic exposure of workers to vinyl chloride has been shown to lead to "vinyl chloride disease", characterized by occupational acro-osteolysis, vasospasm of the hands similar to Raynaud's syndrome, dermatitis, circulatory and central nervous system alterations, thrombocytopenia, splenomegaly and changes in liver function. Eight symptoms commonly reported by workers exposed to vinyl chloride (including dizziness, headaches and nausea) were observed even at dose levels below 50 ppm.

Vinyl chloride has been shown to induce cancer in animals in utero, but has not been shown to cause any other reproductive or developmental effects in rats, mice and rabbits. Epidemiologic studies of families of vinyl chloride workers or communities having vinyl chloride processing facilities

suggested the possibility of an increased incidence of birth defects and spontaneous abortions among people at risk; however, subsequent reviews of these studies have concluded that there is inadequate evidence to link environmental or paternal exposure to vinyl chloride with birth defects or spontaneous abortions in humans.

The noncarcinogenic effects occur at concentrations near or above 10 ppm, which is greater than four orders of magnitude above possible general ambient levels in California (0.5 ppb). The noncarcinogenic effects also occur at concentrations greater than 3 orders of magnitude above the highest concentrations measured near landfills (10 ppb). Consequently, DHS staff do not expect noncarcinogenic adverse health effects to occur from acute or chronic exposures to vinyl chloride in ambient air.

The International Agency for Research on Cancer (IARC), the United States Environmental Protection Agency (EPA) and the California Department of Health Services (CDHS) have identified vinyl chloride as a chemical for which there is sufficient evidence of carcinogenicity in both humans and experimental animals. Chronic inhalation and oral exposures of rats, mice and hamsters to vinyl chloride have been associated with an increased incidence of malignant and benign tumors at several sites including the liver, lung, mammary gland and the nervous system. In humans, epidemiological studies of occupationally exposed workers have linked vinyl chloride exposure to development of a rare cancer, liver angiosarcoma, and have suggested a relationship between exposure and lung and brain cancers.

Although pharmacokinetic studies in humans exposed to vinyl chloride are rare, limited evidence indicates that, following inhalation of low levels of vinyl chloride (3 to 24 ppm), up to 71% (with a mean value of 42%) of the given dose may be absorbed. Vinyl chloride absorption appears to depend on its metabolism, which is a dose-dependent, saturable process. Due to saturation of the enzyme systems responsible for the metabolism of vinyl chloride (cytochrome P-450 and alcohol dehydrogenase), exposure to concentrations above approximately 250 ppm would not necessarily be expected to lead to a perceptibly increasing incidence of tumor development. Metabolism of vinyl chloride leads to formation of chloroethylene oxide and chloroacetaldehyde, two reactive intermediates which undergo covalent binding to cellular macromolecules and are thought to be responsible for the toxic effects of vinyl chloride. These and other metabolites may be further metabolized and excreted in the urine. Unmetabolized vinyl chloride is eliminated primarily in exhaled air.

Vinyl chloride is mutagenic in both prokaryotic and eukaryotic test systems, with significantly greater genotoxicity seen after metabolic activation. DHS staff have found no evidence of a carcinogenic threshold level and the staff recommends that vinyl chloride be considered as not having a threshold for carcinogenicity.

Several studies of carcinogenicity of vinyl chloride in animals and in occupationally exposed workers have been analyzed for risk assessment purposes. The lowest lifetime equivalent concentration associated with an increased incidence of tumors in laboratory animals is 0.06 ppm or 6 to 60-fold above potential human exposure concentrations. Although measurements

of actual exposure levels are not available for vinyl chloride, worker exposure estimates have been used to evaluate the Waxweiler et al. (1976) study. Based on these estimates, the present analysis calculates that the 95% upper confidence limit (UCL) on lifetime unit risk of contracting cancer from vinyl chloride, assuming liver, brain and lung cancer are all related to vinyl chloride exposure, is 4.5×10^{-5} ppb^{-1}. In the case that only liver cancer is assumed to be linked to exposure, the UCL on unit risk is 2.5×10^{-5} ppb^{-1}. These predictions are uncertain due to inadequate exposure data, follow-up time and other methodological problems. Evaluation of animal experiments by the linearized multistage model yields predictions of UCLs on unit risks for humans to be in the range of 3.7×10^{-5} to 20×10^{-5} ppb^{-1}. Evaluation of animal tumorigenicity data indicates that vinyl chloride's carcinogenic potency is dependent on sex, tumor site and age of exposure. Taking all these factors into account, DHS staff conclude that the best estimate to use in order to assure the public health is the top of the range of animal UCLs of unit risk, 20×10^{-5} ppb^{-1}. The overall range of UCLs on unit risk suitable for regulatory purposes is 2.5×10^{-5} to 20×10^{-5} ppb^{-1}.

Vinyl chloride has not been detected in the ambient air of California (limit of detection - 0.5 ppb) except at certain "hot spots". Air Resources Board (ARB) staff has monitored vinyl chloride emissions from the BKK hazardous waste site in West Covina and the OII landfill in Monterey Park. Estimates of peak exposure concentrations for maximally exposed receptors range from 2 to 10 ppb at the BKK landfill and from 0.6 t 9 ppb at the OII site. Air Resources Board staff has estimated that between 17,000 and 131,000 individuals may be exposed to 1 ppb at the BKK site.

The model predicts that the 95% upper confidence limit on cancers due to lifetime exposure of 131,000 residents to 1 ppb would be in the range of 3 to 36. Based on the finding of vinyl chloride-induced carcinogenicity and the results of the risk assessment, DHS staff finds that vinyl chloride is an air pollutant which may cause or contribute to an increase in mortality or an increase in serious illness, or which may pose a present or potential hazard to human health.

1.1 Vinyl Chloride Highlights

I. National and International Evaluation (Other Agencies' Evaluation)

A. International Agency for Research on Cancer (IARC)

1. Short-Term Tests: Sufficient evidence of mutagenic activity exists, both with and without an exogenous metabolic activation system,

2. Animal carcinogenicity bioassays: Sufficient evidence of animal carcinogenicity by oral administration or inhalation exists.

3. Human evidence: Sufficient evidence of carcinogenicity to humans exists. Occupational exposure to vinyl chloride has been linked with development of angiosarcoma of the liver, and has been associated with tumors of the brain and lung and of the hematopoietic and lymphatic

systems. Vinyl chloride is grouped under IARC category 1, meaning that it is causally associated with cancer in humans.

B. U.S. Environmental Protection Agency (EPA)

1. Short-Term Tests: Sufficient evidence of mutagenic activity exists, both with and without an exogenous metabolic activation system, for both DNA damage and mutation.

2. Animal carcinogenicity bioassays: Sufficient evidence of animal carcinogenicity by administration orally or by inhalation exists.

3. Human data: A number of epidemiological studies have linked vinyl chloride with angiosarcoma and other forms of neoplasms. Sufficient evidence exists to indicate that vinyl chloride is a human carcinogen by inhalation.

C. Conclusions: Both EPA and IARC have concluded there is ample evidence that vinyl chloride is genotoxic and is carcinogenic in both animals and humans.

II. Exposure Sources

A. Air Levels

1. Throughout 1987 the South Coast Air Quality Maintenance District monitored near two landfill sites in the Los Angeles area. The highest annual average obtained at any of three stations near the BKK site was 2.6 ppb, and the highest annual average at any of three stations near the OII site was 2.0 ppb.

III. Quantitative Risk Assessment

A. Range of Extrapolation: Animal to human exposures in air for calculated lifetime daily exposure.

1. Experimental to ambient: Vinyl chloride has not been detected in ambient air, except at "hot spots".

2. Experimental to "hot spots": The lowest exposures in the animal studies are approximately 10- to 20-fold higher than the highest residential exposures.

B. Range of Risks:

The human risks associated with the equivalent of a continuous, lifetime exposure to vinyl chloride have been estimated using the linearized multistage model from both animal

carcinogenicity bioassays and epidemiological studies of exposed workers. The current DHS analysis obtained UCLs on unit risks for humans estimated from animal data in the range from 3.7×10^{-5} ppb^{-1} to $20. \times 10^{-5}$ ppb^{-1}, depending on experimental exposure levels, tumor type observed, and sex, species, and age of animal evaluated. The DHS analysis also obtained a UCL on unit risk of 4.5×10^{-5} for liver, lung, and brain cancer and 2.5×10^{-5} for liver cancer only from an occupational study.