

REPORT ON ETHYLENE DIBROMIDE  
TO THE SCIENTIFIC REVIEW PANEL

Prepared by the Staffs of the  
Air Resources Board and  
the Department of Health Services

April 1985

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## OVERVIEW

### I. INTRODUCTION

Under the provisions of Division 26, Chapter 3.5 of the Health and Safety Code, the Air Resources Board (ARB or the Board) is responsible for the identification and control of toxic air contaminants, except in their pesticidal use. The Department of Food and Agriculture is responsible for the regulation of toxic air contaminants in their pesticidal use (Health and Safety Code sections 39650(9) and 39655; Food and Agriculture Code Section 14021 et seq.). Health and Safety Code section 39650<sup>1/</sup> et seq., and Food and Agriculture Code Section 14021 et seq., enacted in September 1983, (Assembly Bill 1807; Stats. 1983, ch. 1047) sets forth a procedure for the identification and control of toxic air contaminants (TAC) in California.

We are proposing, in accordance with these provisions, that ethylene dibromide (EDB) be identified as a toxic air contaminant. This overview reviews briefly our report on the uses of, and the extent of emissions of and public exposure to EDB in California (Part A of this report), and the Department of Health Services' (DHS) evaluation of the health effects of EDB (Part B of this report). The findings in these reports comprise the rationale for the selection of EDB as a candidate substance for listing as a toxic air contaminant. Health and Safety Code section 39655 defines a "toxic air contaminant" as an air pollutant which may cause or

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<sup>1/</sup> All statutory references are to the Health and Safety Code unless otherwise indicated.

contribute to an increase in mortality or an increase in serious illness, or which may pose a present or potential hazard to human health."

Health and Safety Code section 39650 sets forth the Legislature's findings with respect to substances which may be toxic air contaminants. The Legislature has declared:

"That public health, safety, and welfare may be endangered by the emission into the ambient air of substances which are determined to be carcinogenic, teratogenic, mutagenic, or otherwise toxic or injurious to humans."

The findings also include directives with respect to the consideration of scientific evidence and the basis for regulatory action. With respect to the control of toxic air contaminants, the Legislature has declared:

"That it is the public policy of this state that emissions of toxic air contaminants should be controlled to levels which prevent harm to the public health."

The Legislature has further declared that, "while absolute and undisputed scientific evidence may not be available to determine the exact nature and extent of risk from toxic air contaminants, it is necessary to take action to protect public health."

With respect to the evaluation of substances, the Legislature has declared that the best available scientific evidence, gathered from both public agencies and private sources, including industry, should be used. The Legislature has also determined that this information should be reviewed by a Scientific review panel and by members of the public.

Under the procedures established in the Health and Safety Code to implement the Legislature's findings, the determination by the Board as to whether a substance is a toxic air contaminant includes several steps. First, we request the DHS to evaluate the health effects of a substance (section 39660). The evaluation includes a comprehensive review of all available scientific data. Second, upon receipt and in consideration of the DHS evaluation and recommendation, we prepare and submit a health effects report to the scientific Review Panel (SRP) for its review (section 39661). The report is prepared in a form which may serve as the basis for future regulatory action by the Board. The report is also made available to the public, which may submit comments on the report to the SRP. After receiving the written findings of the SRP, concerning the report, the Board issues a public hearing notice and proposed regulation which includes the proposed determination as to whether the substance is a toxic air contaminant. The Board's determination, after a public hearing and other procedures to comply with applicable provisions of Government Code Section 11340 et seq., that a substance is a toxic air contaminant must be set forth in a regulation (section 39662). The Health and Safety Code also includes procedures for the development and adoption of control measures for substances identified by regulation as toxic air contaminants (sections 39665-39667).

## II. EVALUATION OF ETHYLENE DIBROMIDE

Consistent with the provisions of Chapter 5, Division 26 of the Health and Safety Code, the ARB and the DHS first prioritized candidate substances for evaluation and regulation as "toxic air contaminants" pursuant to section 39660(f). Briefly, the selection of a substance for the Board's evaluation and consideration as a toxic air contaminant is to be based on the risk to the public from exposure to the substance, amount or potential amount of emissions from use of the substance, manner of usage in California, atmospheric persistence, and ambient concentrations. After consulting with DHS, we selected EDB for the Board's consideration for listing as a TAC. We selected EDB because it is a known animal

carcinogen, it is ubiquitously emitted from evaporation and burning of leaded gasoline, it is persistent in the atmosphere, and its presence in the atmosphere has been documented. Pertinent data for California are summarized below. The emissions estimates show pesticide applications represented 96 percent of statewide emissions in 1983. Since nearly all pesticidal uses of EDB are now prohibited, the marketing and use of leaded gasoline will be the primary EDB emission sources in California.

<b>1983 Emissions</b>	<b>Statewide</b>	<b>South Coast Air Basin</b>
Stationary Sources		
Pesticides*	362 tons/year	4 tons/year
Gasoline evaporation	0.5   “	0.2   “
Vehicular	15   “	7   “
Atmospheric Half-Life		
(OH. attack, polluted atmosphere)	50 days	
Ambient Concentration		
Average (annual)	Unknown	.0074 part per billion
Range (24 hour)	Unknown	<.005-.18 part per billion

Pursuant to Health and Safety Code section 39660, we requested that the DHS conduct a health effects evaluation of EDB. The DHS evaluation was conducted in accordance with

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\* Under Chapter 3.5, Division 26, of the Health and Safety Code, TACs which are pesticides are to be regulated in their pesticidal use by the Department of Food and Agriculture.

the provisions of that section, which requires that the DHS consider all available scientific data, including, but not limited to, relevant data provided by the ARB, the Department of Industrial Relations, international and federal health agencies, private industry, academic researchers, and public health and environmental organizations. To facilitate the identification of all available data prior to formally requesting the DHS evaluation, we sent a letter to owners of potential sources of EDB emissions in California and other interested members of the public requesting that they submit any information they considered pertinent to the DHS evaluation. We also received a reference search on EDB health effects using the MEDLARS II and DIALOG Information Services and included a bibliography from that search in our request for information. The data compiled in the search were provided to the DHS. Also, the DHS report and our draft report were released to the public upon completion on December 14, 1984; providing additional time during our preparation of the report to the SRP for the public's preparation of comments. These reports were also provided to the SRP on that date.

Section 39660 specifies that the DHS evaluation shall assess the availability and quality of data on health effects, including potency, mode of action, and other relevant biological factors of the substance. Section 39660 also requires that the DHS evaluation contain an estimate of the levels of exposure which may cause or contribute to adverse health effects, and, in the case where there is no threshold of significant adverse health effects, the range of risk resulting from current or anticipated exposure.

Five major issues discussed in the DHS health effects evaluation of EDB are: 1) Are health effects other than cancer expected to occur at current ambient levels? 2) Is EDB an animal carcinogen? 3) Should EDB be considered a potential human carcinogen? 4) Does EDB have a threshold below which cancer does not occur? and 5) What is the range of added lifetime cancer risk for populations continuously exposed to California's urban air EDB concentrations? Based on its review of all available scientific data, the DHS evaluation

concludes that: 1) health effects other than cancer are not expected to occur at current ambient levels; 2) the DHS staff agrees with the International Agency for Research on Cancer (IARC) that EDB is an animal carcinogen; 3) since EDB is a potent animal carcinogen, it should be considered a potential human carcinogen; 4) EDB should be treated as a carcinogen without a threshold; and 5) the added lifetime cancer risk from ambient air EDB exposure ranges from 1.02 to 5.53 cases per million per 10 ppt.

The DHS report finds that the adverse health effects indicative of systemic toxicity of EDB, and reproductive effects, occur at levels of exposure to EDB which are thousands of times higher than ambient levels likely to be found in California's urban air. Thus, the DHS concludes that health effects other than cancer are not expected to occur at current ambient levels.

According to the DHS report, studies on the mutagenic potential of EDB were reviewed by the Occupational Safety and Health Administration (OSHA). EDB was shown to have genotoxic activity in artificial environments outside of living organisms (in vitro), and within living organisms (in viva). It can induce gene mutation in bacteria, fungi, plants, insects, and mammalian cells.

According to the DHS report, animal cancer bioassays show EDB is a potent carcinogen in both sexes in more than one animal species. When administered to animals, EDB caused malignancies both at the site of first contact (skin, forestomach, and nasal cavity), as well as remote sites (circulatory system, lung, and pituitary, among others). Thus, the DHS agrees with IARC's conclusion that EDB is a proven animal carcinogen.

The DHS evaluation indicates that the one published epidemiological study of 161 workers failed to show a statistically significant increase in cancer rates from exposure to EDB. However, the DHS agrees with the authors of the study that it can neither rule out nor



establish EDB as a human carcinogen because of the small size of the population studied. Since the scant human data for carcinogenicity are inconclusive, and the animal data establish EDB as a potent animal carcinogen, the DHS staff recommends that EDB be considered a potential human carcinogen.

To determine that a substance has a carcinogenic threshold, the DHS requires strong positive evidence that the substance acts only through mechanisms which ought to have a threshold. No positive evidence exists to suggest that the carcinogenicity of EDB has a threshold. The DHS report states that EDB should be treated as a carcinogen without a threshold in humans.

The DHS estimated the carcinogenic potency of EDB at 20 ppm and 10 ppt by applying the Weibull-Multistage model, the multistage model, and the Probit model to data from animal bioassays. Table A shows the 95 percent upper confidence limit (UCL) and the maximum likelihood risk estimates (MLE) for each model based on nasal malignancies in male rats, and circulatory system malignancies (hemangiosarcomas) in female mice. The risk estimates using these models are not grossly incompatible with the results from the one small epidemiological study.

**TABLE A**

**Risk Assessment Estimates for EDB in Air**

<b>Species/Tumor</b>	<b>Model</b>	<b>UCL*/MLE* *</b>	<b>20 ppm Occupational Exposure (PEL)***</b>	<b>10 ppt Community Exposure</b>
Male Rats Nasal Malignancies	Weibull- Multistage	95% UCL MLE	985/1000 916/1000	5.35/million 2.85/million
	Multistage	95% UCL MLE	708/1000 627/1000	3/15/million 2.53/million
	Probit	95% UCL MLE	721/1000 638/1000	0 <sup>1/</sup> /million 0 <sup>1/</sup> /million
Female Rats Hemangiosarcomas	Weibull- Multistage	95% UCL MLE	732/1000 549/1000	3.23/million 2.03/million
	Multistage	95% UCL MLE	406/1000 328/1000	1.34/million 1.02/million
	Probit	95% UCL MLE	438/1000 357/1000	0 <sup>1/</sup> /million 0 <sup>1/</sup> /million

\* UCL - Upper confidence limit

\*\* MLE - Maximum likelihood estimate

\*\*\* PEL - Permissible Exposure Limit

<sup>1/</sup> Predictions for the Probit model ranged from 0-10<sup>-31</sup>

The DHS recommends the MLE from the multistage model for hemangiosarcomas in female mice for calculating the lower bound of risk. The DHS recommends the 95 percent UCL estimate from the Weibull-Multistage model for nasal malignancies in male rats for calculating the upper bound of risk. The DHS staff suggests that we consider that risk estimates between these bounds constitute the most reasonable estimates of risk from ambient EDB exposure. While less conservative risk estimates can also be defended as reasonable, the DHS staff does not feel that any can be clearly preferred, and the more

conservative of equally reasonable elements should constitute the basis for regulation. Using these bounds for the range of risk, then, the added lifetime cancer risk from exposure to EDB in urban air ranges from 1.02 to 5.53 cases per million per 10 ppt.

Using the range of risk suggested by the DHS, we estimated the added lifetime cancer risk to a population exposed continuously for 70 years to EDB at the annual average concentration of 7.4 ppt estimated for the South Coast Air Basin. The added lifetime cancer risk is in the range of 1 to 4 cases per million persons exposed. To place this in context, the comparable baseline lifetime risk of all cancers combined (SEER program, 1981, Surveillance Epidemiology and End Results Incidence and Mortality Levels, 1973-77, NCI Monograph #57), can be estimated at 23.7 percent or 237,000 cases per million persons exposed.

### III. ENVIRONMENTAL IMPACTS

The identification of EDB as a toxic air contaminant is not expected to result in any adverse environmental impacts. However, if the Board determines that EDB is a toxic air contaminant, the Board and air pollution control districts will be required to evaluate the need for, and appropriate degree of, airborne toxic control measures. Thereafter, based on this control measure evaluation, the Board and the districts may be required to adopt airborne toxic control measures. Hence, the identification of EDB as a toxic air contaminant may ultimately result in environmental benefits. Environmental impacts identified with respect to specific control measures, will be included in the consideration of such control measures pursuant to sections 39665 and 39666.

#### IV. RECOMMENDATION

Since the evidence strongly suggests that EDB is a known animal carcinogen and potential human carcinogen, and since the evidence does not warrant the assumption that carcinogenicity is confined to the dose above any threshold, we consider available evidence sufficient to recommend listing EDB as a toxic air contaminant having no threshold level.