REPORT ON ETHYLENE DIBROMIDE TO THE SCIENTIFIC REVIEW PANEL

PART C - PUBLIC INPUT REQUESTS, COMMENTS, AND RESPONSES

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

April 1985

REPORT ON ETHYLENE DIBROMIDE TO THE
SCIENTIFIC REVIEW PANEL

PART C - PUBLIC INPUT REQUESTS, COMMENTS, AND RESPONSES

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STATE OF CALIFORNIA GEORGE DEUKMEJIAN, Governor

AIR RESOURCES BOARD
1102 Q STREET
P.O. BOX 2815
SACRAMENTO, CA 95812

March 30, 1984

Dear Sir or Madam:

Subject: Request for Information Regarding Ethylene Dibromide

I am writing to request information on the health effects of ethylene dibromide as part of our toxic air contaminant program. This program is based on legislation enacted in September 1983, Assembly Bill 1807 (Tanner). AB 1807 (Health and Safety Code Sections 39650, et seq.) requires the ARB to identify compounds as toxic air contaminants and once identified to develop and adopt control measures for such compounds. After consultation with the staff of the Department of Health Services (DOHS), we have selected ethylene dibromide as a candidate toxic air contaminant to be evaluated in accordance with the provisions of AB 1807.

Before the ARB can formally identify a compound as a toxic air contaminant, several steps must be taken. First, the ARB must request the Department of Health Services to evaluate the health effects of candidate compounds. Second, the ARB staff must prepare a report which includes the health effects evaluation and then submit the report to a Scientific Review Panel for its review. The report submitted to the Panel will be made available to the public. Any person may also submit information to the Panel for its consideration. The Panel reviews the sufficiency of the information, methods, and data used by the DOHS in its evaluation. Lastly, after review by the Scientific Review Panel, the report with the written findings of the Panel will be considered by the Air Resources Board and will be the basis for any regulatory action by the Board to officially identify a compound as a toxic air contaminant.

Prior to formally requesting the DOHS to prepare a health effects evaluation of ethylene dibromide, we are providing, pursuant to the provisions of Section 39660(e) of the Health and Safety Code, an opportunity to interested parties to submit information on the health effects of ethylene dibromide which he or she believes would be important in DOHS's evaluation of ethylene dibromide as a candidate toxic air contaminant.

In March 1984, ARB staff received a reference search on ethylene dibromide health effects using the MEDLARs II and DIALOG Information Services. These information services include material available to the public on or before September 1983. The attached bibliography lists the references from this information search. We are requesting pertinent information on ethylene dibromide health effects, including any material that may not be available to the public, that is not included in the attached bibliography.

I would appreciate receiving any relevant information you wish to submit by May 1, 1984. To expedite the review process, we ask that any information which you believe should be regarded as "trade secret" be clearly marked and separated from other information. Your help in expediting our review will be greatly appreciated.

Health and Safety Code Section 39660(e) provides that you may identify portions of the information you submit as "trade secret." The ARB may later request that you provide documentation to support any claim of trade secret. In addition, information other than trade secrets may be identified as confidential in accordance with the provisions of Section 91011, Title 17, California Administrative Code. The information which you provide pursuant to this request may be released "(1) to the public upon request, except trade secrets, which is exempt from disclosure or the disclosure of which is prohibited by law, and (2) to the federal Environmental Protection Agency, which protects trade secrets as provided in Section 114(c) of the Clean Air Act and amendments thereto (42 USC 7401 et seq.) and in federal regulations." (Section 91010, Title 17, California Administrative Code.) The information, including trade secret and other confidential information, may also be released to other public agencies, which are also required to preserve the protections accorded to trade secret and confidential information.

Please send the information to the attention of:

William V. Loscutoff, Chief
Toxic Pollutants Branch
Re: Ethylene Dibromide
California Air Resources Board
P. O. Box 2815
Sacramento, CA 95812

If you have any further questions regarding health effects information, please contact Mr. John Batchelder at (916) 323-1505. For any other questions, please contact Mr. Don Ames at (916) 322-8285.

If you are not the person to whom this request should be addressed, please forward it to the appropriate person in your organization. Also please let us know whether you would like to continue to receive information inquiries for

other candidate compounds, and if not, if there is anyone in your organization to whom such requests should be sent.

Sincerely,

Peter D. Venturini, Chief
Stationary Source Division

cc: Alex Kelter, DHS
Lori Johnston, DFA
Wayne Morgan, President CAPCOA
Jan Bush, Executive Secretary CAPCOA
David Howekamp, EPA Region IX
Assemblywoman Tanner
APCO's

Attachment

adcoat, inc.
172 East La Jolla Road, Placentia, California 92670 – (714) 630–7311

April 3, 1984

Mr. William V. Loscutoff, Chief
Toxic Pollutants Branch
California Air Resources Board
P.O. Box 2815
Sacramento
CA 95812

Re: Ethylene Dibromide

Dear Mr. Loscutoff:

Adcoat does not use or sell products containing ethylene dibromide. For this reason we are unable to provide you with the information you seek.

We would like to be kept on your mailing list, however, since one of our products, AC-770-2 Farmers Film Adhesive, is used to bond the polyfilm used to contain the gaseous EDB.

Very truly yours,
ADCOAT, INC.

Hugh Muller

HUGH H. MULLER
PRESIDENT

HHM/mw

BARNES-HIND HYDROCURVE INC.
A Revlon Vision Care Company

895 Kifer Road
Sunnyvale, California 94086
408 736-6482

April 7, 1984

William V. Loscutoff, Chief
Toxic Pollutants Branch
California Air Resources Board
P.O. Box 2815
Sacramento, CA 95812

Dear Mr. Loscutoff:

Reference: Ethylene Dibromide

Regarding March 30, 1984 ARB request for information on the health effects of Ethylene Dibromide. We have no data to submit at this time. Presently, we only purchase and use less than 1 gallon of Ethylene Dibromide per year for QC lab testing purposes.

We would like to continue to receive information inquiries, etc. for other potential toxic air contaminants.

Sincerely,

Dale B. Hanson

Dale B. Hanson
Director, Engineering

DBH/dpc

cc: P. Charley
G. Sweeney

CALIFORNIA STATE UNIVERSITY, HAYWARD

HAYWARD, CALIFORNIA 94542

OFFICE OF EXECUTIVE DEAN
(415) 881-3688

April 5, 1984

Mr. William V. Løscutoff, Chief
Toxic Pollutants Branch
California Air Resources Board
P.O. Box 2815
Sacramento, CA 95812

Dear Mr. Loscutoff:

California State University, Hayward does not regularly use Ethylene Dibromide. The Department of Chemistry, however, does store a limited amount of 1,2-dibroma ethane, which is a similar substance. This substance is labeled as a carcinogen, and use is severely restricted in accord with existing regulations.

Should further information be needed, please contact me.

Sincerely,

W.G. Vandenburgh
Environmental Health &
Safety Officer

WGV:sw

cc President Ellis E. McCune
J. Shelton
V. Smith

Chevron

Chevron Environmental Health Center, Inc.
A Chevron Research Company Subsidiary
15299 San Pablo Avenue, Richmond, California
Mail Address: P.O. Box 4054, Richmond, CA 94804

R. D. Cavalli
Manager
Product Evaluation

May 2, 1984

Ethylene Dibromide
Health Effects Information

Mr. William V. Loscutoff
Toxic Pollutants Branch
California Air Resources Board
P.O. Box 2815
Sacramento, California 95812

Dear Mr. Loscutoff:

This letter is in response to your recent request for information on the health effects of ethylene dibromide. Although we do not have any in-house information on the toxicity of ethylene dibromide, several literature references were identified upon review of our files, which you may wish to consider for inclusion in your bibliography on this chemical (see attached reference list). While several of these references are 10 to 20 years old, they have served as the foundation for much of the recent research on ethylene dibromide and are, therefore, worthy of your review.

Should you have any questions concerning the information we are submitting, please contact R. M. Wilkenfeld of my staff at (415) 231-6018.

Sincerely,

Attachment

CALIFORNIA STATE UNIVERSITY
LONG BEACH

Office of Associate Vice President for
Academic Affairs--Academic Personnel
(213) 498-5157

April 16, 1984

Mr. William V. Loscutoff, Chief
Toxic Pollutants Branch
RE: Ethylene Dibromide
California Air Resources Board
P.O. Box 2815
Sacramento, CA 95812

Dear Mr. Loscutoff:

California State University, Long Beach is not conducting any scientific evaluations involving the health effects of ethylene dibromide and its impact on the environment. Therefore, I am unable to provide you with any information that could be submitted to the Scientific Review Panel for its consideration.

I have reviewed your bibliography on ethylene dibromide and cannot add to it. I appreciate you providing the opportunity to review and comment on the study being conducted.

Sincerely,

June M. Cooper
Associate Vice President
for Employee Relations

JMC:pj
cc: President Horn
Environmental Health &
Safety Officer Hunt

LONG BEACH CALIFORNIA 90840
THE CALIFORNIA STATE UNIVERSITY AND COLLEGES

COUNTY OF SAN DIEGO

DEPARTMENT OF HEALTH SERVICES
1700 Pacific Highway, San Diego, CA 92101
JAMES A. FORDE, Director

DIVISION OF ENVIRONMENTAL HEALTH PROTECTION
(619) 236-2243

April 10, 1984

William V. Loscutoff, Chief
Toxic Pollutants Branch
Re: Ethylene Dibromide
California Air Resources Board
P.O. Box 2815
Sacramento, CA 95812

Dear Mr. Loscutoff:

This letter is in response to your recent request for information regarding the health effects of ethylene dibromide as part of your Toxic Air Contaminant Program. After a thorough reference search, we were unable to locate supplemental information to the bibliography list you provided.

Thank you for allowing us the opportunity to assist you in your program.

Very truly yours,

GARY STEPHANY, Chief
Division of Environmental Health Protection

GS:LM:dmc

Memorandum

To : William V. Loscutoff, Chief
Toxic Pollutants Branch
California Air Resources Board
P.O. Box 2815
Sacramento, CA 95812

Date : April 13, 1984

Place : Sacramento

From : **Department of Food and Agriculture**

Subject: Response to Request for Information Relevant to DOHS Evaluation of EDB as a Candidate Toxic Air Contaminant

HISTORY: EDB is a major industrial chemical with 85 percent of production being used as an additive in leaded gasoline. Production of EDB was first reported in the United States in 1923. By 1977, 300 million pounds were produced annually. In 1982, 2 million pounds were sold in California for pesticidal use, while 874,000 pounds were reported used. Through the second quarter of 1983, 604,000 pounds were reported used.

Before December 31, 1983, the major agricultural and related uses of EDB included soil fumigation, stored grains and fruit fumigation, spot fumigation in grain mills, and termite fumigation.

Three departments in the executive branch have jurisdiction over major areas affected by EDB use. The California Department of Food and Agriculture (CDFA), is responsible for pesticide sales and use including all fumigation uses. The Department of Health Services (DOHS) has general responsibility for public health protection, including food products processed and consumed in the State. Cal-OSHA has jurisdiction over workplace health and safety including chemicals, such as EDB, found in the workplace. Cal-OSHA's jurisdiction includes pesticide manufacture and formulation, but does not extend to the use of pesticides which is vested in CDFA.

EDB has been used extensively for many years throughout the U.S. including California as a soil fumigant against the nematodes that attack plant roots. Concern that EDB may be reaching groundwater supplies prompted CDFA to begin an extensive testing program of water wells in 1982. By this time, CDFA testing sophistication had developed to the point when 50 parts per trillion (ppt) of EDB residue could be detected.

Levels of EDB detected by CDFA in well water in four California counties promoted suspension of EDB use as a soil fumigant by the Director of Food and Agriculture in affected counties.

SURNAME SO-106						

CDFA cancelled the use of EDB as a termiticide on an emergency basis and later proposed to cancel EDB use as a fumigant on stored grains and on milling machinery, and for use as a beehive fumigant. The proposed regulations were published and public comments received.

Before final adoption of California cancellation, EPA gave clear indications that it would take the necessary national action the Department had sought. On September 28, 1983, EPA announced the emergency suspension of EDB as a soil fumigant and the cancellation of nearly all other major pesticidal uses of EDB.

In addition, the Director of Food and Agriculture ordered the suspension of all permits for EDB use as a fumigant on stored grains and as a spot fumigant on milling machinery effective December 31, 1983.

Present EDB Activity

Through various mechanisms, virtually all agricultural use of EDB in California has been halted. California still maintains the post-harvest fruit fumigation use but, since there are currently no production areas under quarantine, no treatments are taking place.

In response to your request for additional research information, several CDFA publications on worker occupation exposure to EDB are attached.

Lori Johnston

Lori Johnston, Assistant Director
Pest Management, Environmental
Protection and Worker Safety
(916) 322-6315

Attachments

cc Hans Van Nes
Olaf Leifson

Memorandum

To : William V. Loscutoff, Chief
Toxic Pollutants Branch
California Air Resources Board
P.O. Box 2815
Sacramento, CA 95812

Date : July 25, 1984

Place : Sacramento

From : **Department of Food and Agriculture**

Subject: Additional Response to Request for Information Relevant to DOHS Evaluation of Ethylene Dibromide as a Candidate Toxic Air Contaminant

In addition to our earlier response, I am enclosing a copy of the print-out of references in the Department of Food and Agriculture's Registration Library. Please be advised that some of these references may be confidential access and as such may fall under the Department's policy on such matters.

Lori Johnston

Lori Johnston, Assistant Director
Pest Management, Environmental
Protection & Worker Safety
(916) 322-6315

Attachment

cc Hans Van Nes
Olaf Leifson

SURNAME SC-106						

DEPARTMENT OF THE ARMY
U. S. ARMY ENVIRONMENTAL HYGIENE AGENCY
ABERDEEN PROVING GROUND, MARYLAND 21010

April 27, 1984

REPLY TO
ATTENTION OF

Occupational and Environmental
Medicine Division

Mr. William V. Loscutoff
Chief, Pollutants Branch
California Air Resources Board
P. O. Box 2815
Sacramento, California 95812

Dear Mr. Luscutoff:

This Agency does not have any additional health information on file regarding Ethylene Dibromide which is not included in your bibliography.

Sincerely,

for Rockwell W. Utech LTC

Joel C. Gaydos, M.D.
Colonel, Medical Corps
Director, Occupational and
Environmental Health

DETREX CHEMICAL INDUSTRIES, INC.

P.O. BOX 501, DETROIT, MICHIGAN 48232

TWX 810-224-4756

TELEPHONE
(313)358-5800

April 5, 1984

Mr. Peter B. Venturini, Chief
Stationary Source Division
Air Resources Board
1102 Q Street
P. O. Box 2815
Sacramento, CA 95812

Re: Request for Information Regarding Ethylene Dibromide

Dear Sir:

We have no information on the health effects of Ethylene Dibromide which would supplement or add to the information contained in the bibliography attached to your request.

Please keep us on your mailing list to receive information inquiries for other candidate compounds as they appear on your candidate list.

Very truly yours,

W. L. McCracken

W. L. McCracken, Ph.D

WLM/smb

cc: L. Schlossberg
F. J. Chmielnicki

DOW CHEMICAL U.S.A.

MIDLAND, MICHIGAN 48640

2020 W. H. DOW CENTER
April 9, 1984

Mr. William V. Loscutoff, Chief
Toxic Pollutants Branch
RE: Ethylene Dibromide
California Air Resources Board
P. O. Box 2815
Sacramento, CA 95812

Dear Mr. Loscutoff:

Your March 30, 1984, letter requesting any new information on ethylene dibromide (EB) was forwarded to my attention. I have reviewed the attached bibliography and have concluded that it is quite complete and we cannot add any further information pertaining to the health effects of EDB.

If we can be of any further assistance, please do not hesitate to contact us.

Sincerely,

T. I. Betts
SCFP Government and
Public Affairs

lr

JAMES RIVER CORPORATION
P O Box 6000 RiverPark Norwalk CT 06856-6000
(203) 854-2000

JOHN C. CUTHBERTSON
Director
Environmental Affairs
Operations Technology
(203) 854-2052

April 11, 1984

Mr. Peter D. Venturini, Chief
Stationary Source Division
State of California
Air Resources Board
1102 Q Street
Sacramento, CA 95812

Dear Mr. Venturini:

We recently received from your office a letter dated March 30, 1984 requesting information regarding Ethylene Dibromide.

All requests for information involving other candidate compounds under your toxic air contaminant program should continue to be sent to me at the above address.

Your assistance in this matter is very much appreciated.

Sincerely,

John C. Cuthbertson

JCC/pah

LAKE COUNTY AIR POLLUTION
CONTROL DISTRICT

— OFFICE —
Courthouse - 255 N. Forbes Street
Lakeport, California 95453
Telephone: 707/263-2391
Laboratory: 707/263-2348
Burn Info.: 707/263-3121

ROBERT L. REYNOLDS
Air Pollution Control Director

April 5, 1984

William V. Loscutoff
Toxic Pollutants Branch
California Air Resources Board
P. O. Box 2815
Sacramento, CA 95812

Re: Ethylene Dibromide

Dear Mr. Loscutoff:

After review of the list of references submitted to me on the above referenced item, I did not see the Science Applications, Incorporated (SAI) Study on which I was project officer while employed at the ARB. The approaches and conclusions, while being 5-6 years old, are still relevant and should be considered.

I would suggest you also include this study in your review process for information regarding Ethylene Dibromide as it was identified at that time as an airborne carcinogen of concern in California. The staff at SAI, R. Ziskind and M. Rogozen, would be excellent people to include and seek advice from in this consideration.

Sincerely,

Bob Reynolds

Robert L. Reynolds

RLR/jg

cc: Toxic File

Attachment: Article, JAPCA

NATIONAL AGRICULTURAL CHEMICALS ASSOCIATION
THE MADISON BUILDING
1155 Fifteenth Street, N.W., Washington, D. C. 20005
202 • 296-1585 Cable: NAGRCHEM

March 12, 1984

Mr. Peter D. Venturini, Chief
Stationary Source Division
Air Resources Board
P.O. Box 2815
Sacramento, CA 95812

Dear Mr. Venturini:

We received your letter 30 March requesting information on Etylene Dibromide.

As a national trade association, we do not maintain on any specific chemical, the kind of information you are seeking. Our source is always the manufacturer of the product or the Environmental Protection Agency.

Since David Howekamp of EPA Region IX has received a copy of your request, perhaps he can provide you with sufficient information.

Sincerely,

Arthur T. Hart
Director, State Legislative Affairs

cc: William V. Loscutoff
John Browning
David Howekamp

New York State Department of Environmental Conservation
50 Wolf Road, Albany, New York 12233-0001

Henry G. Williams
Commissioner

May 15, 1984

Mr. William V. Loscutoff
Chief, Toxic Pollutants Branch
California Air Resources Board
P.O. Box 2815
Sacramento, California 95812

Re: Ethylene dibromide

Dear Mr. Loscutoff:

Your request of March 30, 1984 for information regarding Ethylene dibromide (EDB) has been forwarded to me for reply.

Ethylene dibromide (dibromo ethane) is a compound exhibiting carcinogenic potential (suspect of carcinogenic potential to man). In the Department of Environmental Conservation, Division of Air, we have classified EDB as a high toxicity air contaminant - see enclosed Air Guide - 1, page 25.

The New York State Department of Health has established a safety level for EDB. They are recommending a safety factor of no less than one thousand to the no effect level established in experimental animals. This results in tolerable limits such as 30 parts per billion (p.p.b.) for intermediate level products and 6 p.p.b. for ready to eat products. These values are more restricted than the EPA levels, such as 150 p.p.b. for intermediate level products and 30 p.p.b. for ready to eat products.

I have been informed recently that New York plans to propose a regulation to limit EDB to 10 p.p.b. in ready to eat foods. In the interim, the state is following EPA's tolerance standards.

I suggest you contact the New York State Department of Health for any additional information you may want. Contact:

Dr. Nancy Kim
Bureau of Toxic Substances Management
Tower Building - Room 359
New York State Department of Health
Empire State Plaza
Albany, New York 12237
Telephone: (518) 473-3798
7238

If I can be of further help, do not hesitate to contact me.

Sincerely,

Moises M. Riano, Ph.D.
Section of Toxics
Bureau of Abatement Planning
Division of Air

Enc.

PPG Industries, Inc. One PPG Place Pittsburgh, Pennsylvania 15272 (412) 434-2801

A. Philip Leber, Ph.D.
Manager of Industrial Toxicology
Environmental Affairs
Industrial Chemical Division

April 26, 1984

Mr. William V. Loscutoff, Chief
Toxic Pollutants Branch
Re: Ethylene Dibromide
California Resources Board
P.O. Box 2815
Sacramento, CA 95812

Dear Mr. Loscutoff:

At PPG, we appreciate having the opportunity to contribute to your efforts on developing risk assessments for ethylene dibromide (EDB).

Our EDB files in Environmental Affairs have been checked against your list of references. Five published articles were found that were not included in your compilation. I am not aware of any further information that PPG may possess that would pertain to this issue.

Parenthetically, the Chemical Manufacturer's Association EDB Panel submitted extensive comments to California's OSHA Standards Board back in December 1981 on this compound. You may want to refer to these.

Best regards,

A. Philip Leber/mec

A. Philip Leber

mec

Attachments (6)

STANFORD
UNIVERSITY

DEPARTMENT OF HEALTH AND SAFETY
Encina Annex
Stanford, CA 94305
(415) 497-0448

Alain DeCleve, M.D., Director

25 April 1984

William V. Loscutoff, Chief
Toxic Pollutants Branch
Re: Ethylene Dibromide
California Air Resources Board
P. O. Box 2815
Sacramento, California 95812

Dear Mr. Loscutoff:

The Department of Health and Safety has checked with various research and support departments at the University and found that

a) Ethylene dibromide has not been used on campus for more than 20 years, and whether it was used before then is not known;

b) None of the research departments contacted are conducting any research on this compound.

Consequently, Stanford University cannot be of any help to you in providing any information or data on Ethylene dibromide that is not already available to the public in the scientific or health and safety literature. However, the Department of Health and Safety would be interested in obtaining any toxicologic or health information that the Air Resources Board would make available.

Sincerely,

Alain Decleve, M.D.

AD/cmz

cc: Lawrence Crowley

UNITED STATES DEPARTMENT OF AGRICULTURE
FOREST SERVICE
Mt. Shasta Ranger District
204 West Alma Street
Mt. Shasta, CA 96067

April 17, 1984

Peter D. Venturini, Chief
Stationary Source Division
California Air Resources Board
1102 Q Street
P. O. Box 2815
Sacramento, CA 95812

Dear Mr. Venturini:

It is my understanding that we have had no occasion to use the fumigant ethylene dibromide on the Shasta-Trinity National Forest and do not anticipate using it in the future. We therefore do not have any health effects information, other than what you have already referenced.

Future requests for such information should be sent to:

Brian Sturgess
Regional Pesticide Use Coordinator
U. S. Forest Service
630 Sansome Street
San Francisco, CA 94111

Sincerely,

KENNETH V. SHOWALTER
District Ranger

UNIVERSITY OF CALIFORNIA, DAVIS

BERKELEY • DAVIS • IRVINE • LOS ANGELES • RIVERSIDE • SAN DIEGO • SAN FRANCISCO

SANTA BARBARA • SANTA CRUZ

DAVID PIERPONT GARDNER
President of the University

EMIL M. MRAK
Chancellor Emeritus

UNIVERSITY HOUSE
DAVIS, CALIFORNIA 95616

April 19, 1984

Mr. Peter Venturini
Air Resources Board
1102 Q Street
Sacramento, CA 95814

Dear Dr. Venturini:

I have been away for almost two weeks, and it is for this reason that I am slow in responding to your last letter concerning EDB.

I would like to suggest that you write a letter to Dr. Donald Crosby, Department of Environmental Toxicology, UC Davis, and ask him to comment on the material relating to the chemical. I would like to suggest, too, that you indicate in your letter that you are doing this at my suggestion. I am quite sure that Don can be helpful.

Thank you so very much for keeping me informed. Every good wish.

Kindest personal regards,

Emil M. Mrak

UNIVERSITY OF CALIFORNIA, DAVIS

BERKELEY • DAVIS • IRVINE • LOS ANGELES • RIVERSIDE • SAN DIEGO • SAN FRANCISCO SANTA BARBARA • SANTA CRUZ

DAVID PIERPONT GARDNER
President of the University

EMIL M. MRAK
Chancellor Emeritus

UNIVERSITY HOUSE
DAVIS, CALIFORNIA 95616

June 5, 1984

William V. Loscutoff, Chief
Toxic Pollutants Branch
RE: Ethylene Dichloride
California Air Resources Board
P. O. Box 2815
Sacramento, CA 95812

Dear Mr. Luscutoff:

I am sending you some material of interest with respect to the banning of EDB in certain areas.

It has been said that a good substitute for the use of EDB is irradiation. I would like to call your attention to the fact that activists are already saying that irradiation is uncertain, and should be furthered studied before use. Likewise, they talk about refrigeration, but this is a costly procedure.

In other words, agriculture may find itself in a terrible situation with the banning of EDB. I thought you might be interested in the attached reprint from the activist group, the name of which is the Northwest Coalition for Alternatives to Pesticides.

Kindest personal regards,

Emil M. Mrak

Enclosure

UNIVERSITY OF CALIFORNIA, LOS ANGELES

UCLA

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SANTA BARBARA · SANTA CRUZ

DEPARTMENT OF MEDICINE
UCLA SCHOOL OF MEDICINE
CENTER FOR THE HEALTH SCIENCES
LOS ANGELES, CALIFORNIA 90024

May 24, 1984

William V. Loscutoff, Chief
Toxic Pollutants Branch
California Air Resources Board
P.O. Box 2815
Sacramento, CA 95812

RE: Request for information regarding ethylene dibromide

Dear Mr. Lescutoff:

Your letter of March 30 has been referred to me for response. Although I cannot contribute significant new information regarding EDB, I would appreciate continuing to receive inquiries and information about other candidate compounds. Where appropriate, I will bring such requests to the attention of other members of the faculty of the UCLA School of Medicine.

Sincerely,

Philip Harber, M.D., M.P.H.
Chief, Occupational Medicine Branch

PH/jg
d27

THE
UNIVERSITY
OF
ILLINOIS
COLLEGE OF MEDICINE
AT CHICAGO

Department of Preventive Medicine
and Community Health
SPH-West, Room 324
2121 West Taylor Street
Box 6998, Chicago, Illinois 60680
(312) 996-2297

April 4, 1984

Dr. Peter D. Venturini, Chief
Stationary Source Division
Air Resources Board
1102 O Street
P. O. Box 2815
Sacramento, CA 95812

Dear Dr. Venturini:

Further to your letter of March 30, I enclose a copy of recent testimony on EDB which I hope will be helpful.

Sincerely yours,

Samuel S. Epstein, M.D.
Professor of Occupational
and Environmental Medicine

SSE/ds

Enclosure

TESTIMONY IN SUPPORT OF A ZERO TOLERANCE FOR EDB

Samuel S. Epstein

and

Joel Swartz

University of Illinois Medical Center, Chicago, Illinois

Public Hearings Panel on Final Regulations of EDB

Boston, Mass. March 19, 1984

TABLE OF CONTENTS

A. INTRODUCTION

Distinguished panel members, my name is Samuel Epstein. I am professor of occupational and environmental medicine in the Department of Preventive Medicine at the University of Illinois Medical Center, Chicago.

As an M.D. and human and experimental pathologist and toxicologist, for over three decades, I have studied the hazardous effects of chemicals and chemical pollutants, including pesticides, herbicides, industrial chemicals, drugs and food additives, in air, water, food and the workplace, with particular reference to delayed or chronic toxic effects, notably cancer, reproductive and genetic effects, and have some two hundred and fifty scientific publications and six books in these areas. Furthermore, over the past two decades, I have had substantial involvement in the interface between science and public policy, as exemplified by membership of a wide range of Federal advisory and expert committees, and by consultantships to Congress, including the Senate Committee on Public Works. Additionally, I have served on the Environmental Health Advisory Committee of EPA, and on its subcommittee on pesticide tolerances. Other committees on which I have also served include H.E.W. Secretary Finch's 1969 Commission on Pesticides and Their Relationship to Environmental Health, and the 1973 Advisory Commitee to the Department of Labor on Standard Setting for Occupational Carcinogens. I have also testified before a wide range of Congressional Committees on problems including pesticides, food additives, food tolerances and carcinogens. Past consultantships include: To the Pesticide Board of the State of Massachusetts, to the Office of General Counsel of EPA in suspension and cancellation proceedings against carcinogenic pesticides, and to the State of California Program on Toxic Substances.

I attach as Appendix 1 my curriculum and that of my colleague, Dr. Joel Swartz.

B. THE CARCINOGENICITY OF EDB

EDB has been tested for carcinogenicity in three strains of rats and two strains of mice by gavage, inhalation, cutaneous and percutaneous exposures. The carcinogenicity of EDB has been unequivocally established in all these tests, in which a wide range of tumors involving a wide range of organs, have been induced irrespective of the route of exposure. (Table 1). Evidence for the extremely high carcinogenic potency of EDB is based on the very high incidence of tumor induction, illustratively over 80% in rats and over 90% in mice in the lower does gavage test, with animals dying from tumors exceptionally and unusually early, as soon as 12 weeks for rats and 24 weeks for mice. Such evidence, moreover, clearly underestimates the carcinogenic potency of EDB in view of the competing risks of high premature mortality due to toxicity, apart from the obvious fact that tumor induction must have occurred a substantial period of time prior to death.

Of further significance is the evidence of very marked synergistic interactions following inhalation exposure of rats to EDB in combination with dietary administration of disulfiram, a non-carcinogenic drug closely related to a wide range of food crop fungicides in common use. (Wong et al, 1980). The combined exposure resulted in a more than 10 - fold increased incidence of liver cancer and angiosarcomas, besides an increased incidence of tumors at other sites including kidney, thyroid and lung. The very high carcinogenic potency of EDB has been well recognized for over a decade. The following quotations are illustrative:

> (as EDB produced) "a high incidence of squamous cell carcinomas (in rats), --- there is considerable doubt that any tolerance for EDB can be approved" (EPA, 1973).

Table 1: Multi-system Carcinogenicity of EDB

	GAVAGE (1)		INHALATION (2,3)		CUTANEOUS AND PERCUTANEOUS
TARGET ORGAN	MICE	RATS	MICE	RATS	MICE
FORESTOMACH	+	+			
NASAL CAVITY			+	+	
LUNG	+		+	+	+
LIVER		+		+	
KIDNEY				+	
PITUITARY			+	+	
ADRENAL				+	
THYROID				+	
BREAST			+	+	
TESTIS				+	
SKIN					+
SUB-CUTANEOUS			+	+	
ANGIOSARCOMA		+	+	+	

(1) NCI, 1978

(2) NCI and NTP, 1980.

(3) Wong (NIOSH), 1980.

(4) Van Duuren et al, 1979

"Quantitative data that indicate a non-hazardous concentration for exposure to EDB have not been found" (NIOSH, 1977).

"EDB is a potent animal oncogen" (EPA, 1980).

"---the request for a 1 ppb tolerance on soybeans should be denied" (EPA, 1981a).

(EDB is) "probably the most potent and toxic carcinogenic substance used as a pesticide today.---I find the data (used for risk assessment by EPA in 1980) to show that the risk is one in a thousand or possibly 50-70 per thousand" (EPA, 1981b).

"EDB is a potent animal oncogen and is a likely human oncogen ---. EDB may (also) pose a risk with respect to heritable mutations" (EPA, 1984).

It is of particular interest to note that, using toxicological criteria developed in a recent regulatory approach to the ranking of animal carcinogens proposed by the former Director of Carcinogenesis Testing at the NCI and now a well-known industry consultant, EDB scores in the highest possible class of carcinogenic potency (Squire, 1981); carcinogens in this class "would represent the greatest potential hazard and may, in the case of an intentional food additive, trigger a total ban."

Apart from carcinogenicity, there is evidence on the potent mutagenicity of EDB in a broad range of test systems, including germ cells in vivo, and its reproductive toxicity in a wide range of species (for summary, see EPA, 1980).

It is of interest to note that Rodricks, the consultant on whose views industry places great reliance, appears unimpressed by the carcinogenicity of EDB, which he seems to attribute to chronic irritation (Rodricks, 1984). "These tumors (stomach and forestomach) it is suggested, would not have arisen unless there had been prolonged and substantial irritation at the site of EDB contact (an expected consequence of EDB dosing), and, most significantly, that there is no condition of human (dietary) EDB exposure

under which such irritation would arise." Apart from the fact that EDB induced tumors at a wide range of distant sites in the various studies (Table 1), the resurrection of the chronic irritation theory of carcinogenesis is inconsistent with an extensive body of historical data, including the fact that a wide range of irritant chemicals are not carcinogenic when administered by gavage of inhalation (Federal Panel Report, 1982).

C. SAFE THRESHOLDS OR TOLERANCES CAN NOT BE SET FOR CARCINOGENS

There is an overwhelming concensus in the scientific literature, as also reflected in regulatory precedent, that there is no scientifically valid method of setting or estimating safe levels for carcinogens. This principle has been repeatedly re-iterated by a wide range of expert bodies and qualified scientific authorities over the last few decades.

In 1960 hearings on the 1958 Delaney Amendment, HEW Secretary Flemming stated that:

> "Scientifcally, there is no way to determine a safe level for a substance known to produce cancer in animals" (Flemming, 1960).

This position was unequivocally endorsed one decade later by an Ad Hoc Committee, composed of recognized authorities in chemical carcinogenesis, in a report to the Surgeon General (Ad Hoc Committee Report, 1970)

> "The scientific basis on which the Government's position was established in 1958 remain valid. The progress of knowledge in carcinogenesis in the last decade has only strengthened the points made in Secretary Flemming's testimony".

Numerous authoritative reports have more recently confirmed our scientific inability to set thresholds. Illustrative are the following:

> "Because there is no currently recognized method for determining no-effect level for a carcinogen in an exposed population, substances identified as carcinogens will be considered capable of causing or contributing to the development of cancer even at the lowest doses of exposure" (Regulatory Council, 1979).

> "The self-replicating nature of cancer, the multiplicity of causative factors to which individuals can be exposed, the additive and possibly synergistic combination of effects, and the wide range of individual susceptibilities work together in making it currently unreliable to predict a threshold below which human cancer population exposure to a carcinogen has no effect on cancer risk. --- There is no presently acceptable way to determine a threshold for a carcinogen for an entire population" (Inter Agency Regulatory Liaison Group, 1979).

"Because there is not definitive evidence of the existence of thresholds and because not all cancer variables have been identified, prudence requires that no safe level of thresholds be assumed to exist ---. Exposure to any amount of a carcinogen, however small, must be regarded as an addition to the total carcinogenic risk" (Toxic Substances Strategy Committee Report, 1980).

The threshold problem was examined in great detail at 1978 OSHA hearings on occupational carcinogens and testimony was received from numerous qualified scientists and scientific bodies (Federal Register, 1980). OSHA concluded that:

"---its proposed position that there is no presently acceptable way to reliably determine a threshold for a carcinogen for any given population is amply supported by the evidence presented and also represents, to a large extent, a consensus of scientific opinion.---The evidence proposed for the existence of thresholds for specific carcinogens was inconclusive or erroneous. In short, there is much scientific evidence that thresholds do not exist for carcinogenesis; even if they do, there is no scientific way to establish what they are for any specific carcinogen and for any specific population."

D. EPIDEMIOLOGICAL STUDIES ON EDB

The mortality experience of workers exposed to EDB in two Dow Chemical production units was examined (Ott, et al. 1980). Only 161 employees were included in the total study, rendering it virtually useless for the purpose of detecting EDB-induced cancer deaths (NIOSH, 1977; EPA, 1980; Federal Register, 1981). However, even this scant study strongly suggests that EDB induced excess cancer deaths.

Two separate production units were included in the study population, encompassing a period from the mid 1920's to 1976, and a total of 39 deaths were recorded among the entire study population. In unit 1, there were 2 cancer deaths versus 3.6 expected, and in unit 2, there were 5 cancer deaths versus 2.2 expected.

The relative risk for all cancers would have had to be between 2 and 3 in order to be detected in this study, if in fact, all workers were really at risk; only 46 of the 161 workers had six or more years of exposure to EDB. When attention is restricted to the group with 6 or more years exposure and 15 years since initial exposure, then 4 cancer deaths were found compared to 1.4 expected. This result is significant by itself, and is also indicative of a strong carcinogenic dose-response effect with exposure duration.

In compiling the data, workers with concomitant exposure to arsenicals were excluded. The justification for this is that excess mortality in this group could have been caused by arsenic exposure. Among the 5 people with arsenic exposure, there were 3 deaths compared to .62 expected, including 2 from respiratory cancer versus .1 expected. The grounds for exclusion of this group were extremely tenuous, since the 2 respiratory cancer deaths in this group occurred in persons with only 1.5 and 20 months

exposure to arsenic, respectively.

Overall, this study is based on far too small a population sample with too brief duration of exposure to give any definitive indication of the carcinogenicity of EDB. What results there are, however, are strongly supportive of the carcinogenicity of EDB.

A small study was performed by Octel on workers exposed to EDB at a plant in southwest England (Ter Haar, 1980). The mortality experience of the workers in the plant was compared to that of the general population in the surrounding area of England. There were only four cancer deaths in the test population and the total study had fewer than 3500 person years, far less than the number generally required to detect cancer excess. Moreover, most of the person years were contributed by young people, over half by people under 44 years old. No data are presented concerning the duration of exposure or time since first exposure. The study is far too small to allow for any conclusions whatsoever concerning the carcinogenicity of EDB.

E. LIMITATION IN QUANTITATIVE RISK ASSESSMENT FOR CARCINOGENS

There are a wide range of major, critical problems with current techniques for quantitative risk assessment of carcinogens. They result from: limited knowledge of the carcinogenesis process; the sparse data and the design of NCI bioassay and other studies from which risk assessment data are generally derived; and the use of biologically indefensible or questionable principles in creating risk models. These various problems, reflecting inherent limitations in the entire concept and practice of quantitative risk assessment, quite apart from fundamental methodological errors, will generally result in the underestimation of risk by many orders of magnitude. For illustrative supportive statements and quotations on such limitations, see Appendix II and III.

1. Differences in Species Sensitivity

There is sometimes a wide variation in sensitivity to particular carcinogens between different species. Illustratively, wide differences in sensitivity between humans and rodents have been found for beta-naphthylamine, asbestos, and tobacco smoke (Federal Register, 1980).

2. Dose-Response Relationships

The major problem with most risk assessment techniques is their use of a multi-stage model with a lifetime risk of cancer depending on dose to a power greater than or equal to 1. In practice, this generally leads to a linear relationship between the proportion of subjects with cancer and dose over most dose ranges. The rationale for this procedure is that carcinogenesis is a multi-stage process, with one or more stages affected by the carcinogen, and therefore, the chance of developing cancer must depend on carcinogen dose at least to the first power.

Such linear extrapolation has often been made in an effort to estimate the effect of relatively low doses of carcinogens. For example, the effects of exposure to atmospheric levels of polycyclic aromatic hydrocarbon (PAH) carcinogens and heavy metals have been estimated by linear extrapolation from workers with high exposure to the general population with 20-200 times lower exposure levels (Doll, 1978). "General knowledge of carcinogenesis suggests that at low doses the carcinogenic effect is likely to be linearly proportional to the dose received... the combined effect of all such atmospheric (PAH and heavy metals) agents cannot be responsible for more than about 5 cases of lung cancer per 100,000 population per year in the European populations." Similar calculations, using the same assumption, have been made by others, including EPA's Carcinogen Assessment Group, for a number of carcinogens including benzene and coke oven emissions (Pike, 1975; EPA, 1978).

The argument that use of the linear extrapolation is accurate or conservative is contradicted by a wide range of data from animal and human studies which demonstrate that dose-reponse curves for carcinogens almost universally become plateaued or flattened at "high" doses (Scherer and Emmelot, 1979; Maltoni, 1975, Davies et at., 1974 Hulse et al. 1968, Hooper et al. 1979); this is especially true when there is substantial life shortening from competing toxicity at high doses. As demonstrated in a recent analysis of experimental and epidemiological studies, carcinogenesis dose-reponse curves tend to flatten at high doses, so that linear extrapolation through the origin from such high doses will cause substantial underestimation of the tumor induction level at low doses (Swartz et al., 1982). These analyses indicate that, in general, the slope of a carcinogenesis bioassay curve tends to decrease, frequently sharply,

with increasing dose. This sharp decrease in slope is generally far greater than would result from the decline in population at risk with an increasing percentage of responders and cannot be attributed to this effect. Linear extrapolations may thus lead to substantial underestimation by a factor of over 50, and in some cases by factors of greater than 100,000.

3. Time and Age Effects

Most risk assessment models ignore the importance of the time and age effects noted in a wide range of animal and human studies. Illustrative is the observation that for some carcinogens, cessation of exposure is accompanied by a rapid decline in relative cancer risks (Whittemore, 1977). This cessation effect has been noted particularly in persons who stop smoking, and is taken to imply that the tobacco carcinogens are acting in a late stage of a multi-stage process. However, it has so far not been possible to generalize whether most carcinogens act in early or late stages or both. For example, 2-AAF acts as an early stage carcinogen in one organ, and a late stage carcinogen in another organ in the same strain of mice (Day and Brown, 1980).

This phenomenon has pronounced consequences for carcinogenic risk assessment, particularly in the case of short term exposures. For example, if a carcinogen acts at an early stage, then a short exposure early in life may be sufficient to induce cancer, and all later exposures may well be irrelevant. Additionally, pronounced differences have been noted in the effect of a carcinogen depending on the age of the subject at exposure, quite apart from the enhanced sensitivity of fetuses and neonates (Gofman, 1972).

4. Exposure of Neonates and Fetuses

While some risk assessments attempt to reflect effects of

age at exposure, however, rarely, if ever, is exposure or neonates and fetuses even considered. Neonates and fetuses have generally been shown to be far more susceptible to cancer induction by carcinogens, than adults of the same species. Illustratively, human fetuses are about five times as susceptible to the carcinogenic effects of irradiation as are neonates, who in turn are ten or more times susceptible than adults (Gofman, 1972). Similar enhanced sensitivity is well recognized in animal studies.

5. Assumption of Lifetime Exposure

A very crucial error in risk assessment is the common assumption that tumors which appear early in animal bioassays have resulted from lifetime exposure to the carcinogen. Tumors which are observed early, say within 3 to 6 months, in a rodent bioassay certainly result from exposure for a period far shorter than lifetime. It is further possible that tumors occurring as early as even 3 months could have been induced by much shorter exposures, possibly for even 1 day or less; carcinogenic effects in mice and rats have been induced by only 1 hour exposure to vinyl chloride (Hehir et al., 1979).

It is highly unlikely that the effects of a short term exposure can be predicted unless specific test data are available for different periods of exposure, and ages of exposure. A simple fitting of a model to lifetime exposure data will not supply appropriate information for short term exposure.

6. Background and Synergistic Effects

The effect of any particular carcinogen is likely to depend very strongly on background cancer rates, and on the concomitant presence of other carcinogens; background rates could, of course, be indicative of the presence of other, but undetected carcinogens. Studies on humans exposed to radiation have demonstrated an effect proportional to background

cancer incidence (Kneale et al. 1982), in addition to synergistic effects with other carcinogens, particularly smoking (Whittemore and McMillan, 1983). It must be emphasized that no methods of quantitative risk assessment take such critical effects into account.

7. Incomplete Data

In many cases, risk assessments are made from data which are so scant that they are inadequate for even qualitative assessment. The commonest deficiency relates to the use of too few doses, which are usually restricted to high doses where there is substantial lifeshortening from competing causes of death. In general, there should be at least five doses, and clear evidence that the linear portion of the dose-response curve has been reached. Other deficiencies relate to the absence of data on short term exposures and on cessation of exposure. It is not feasible to make inferences on the effects of short term, interrupted, or halted exposures, without specific data from experiments in which such exposure patterns were used. In extreme cases, tumors attributed to lifetime exposure could have resulted from only the very briefest of exposure.

8. Failure to Fit Models to Data

In many cases, no attempt is made to fit a risk assessment model to data, and/or to evaluate the model. A typical example is the assumption of linear dose dependence, when the experiments actually show pronounced flatterning. Frequently, the slope of the dose response curve is determined by linear extrapolation through the origin, ignoring other possible points. Another example is the use of a model for the effects of short term exposure, without any attempt to fit the model to data from such exposures. Frequently, it is assumed that the cancer risk for short term exposure is equal to the lifetime risk multiplied by the

ratio of the duration of exposure to lifetime. There is no general justification for this procedure.

9. Variations in Risk Assessments Using Different Models

The application to any particular carcinogenicity data set of a range of accepted models for quantitative risk assessment can result in massively divergent results. As emphasized in the 1978 OSHA hearings on regulation of occupational carcinogens (FR, 1980), different models yield more than a million-fold variation in lifetime risk estimates for exposure to 1 ppm of vinyl chloride (from 10^{-8} to less than 10^{-2}), and more than 10-million fold variations in estimates for daily ingestion of saccharin (Table 2, from Federal Register, 1980). A review by the Canadian Food Directorate of existing models and their biological bases, using twenty sets of quantal response data, yielded widely different and inconclusive results (Munro and Krewski, 1980).

Table 2 Estimates of Lifetime Risk From Exposure to 1 ppm Vinyl Chloride

Source	Estimate of lifetime risks	Method of extrapolation	Source of data
Wilson (S. 53)	2.5×10^{-4}	Linear	Epidemiological unspecified source.
Wilson (Exh. 251 B)	5×10^{-4}	Linear	Epidemiological and Maltoni (unspecified).
Crump and Guess (1977), exhibit to Hoel statement.	2×10^{-4}	Multi-stage, upper confidence limit.	Maltoni (1975).
Guess *et al.* (1977), exhibit to Hoel statement.	2×10^{-4}	Multi-stage, upper confidence limit.	Maltoni (1975).
	1×10^{-4}	Mantel-Bryan, upper confidence limit.	Maltoni (1975).
Claus (S. 38)	0	Assumption of threshold at 10^{8} molecules per cell, calculated to occur at exposure level of 4.9 ppm.	
Nisbet (post-hearing comment, p. 8)	4×10^{-8} to 1×10^{-1}	Linear	Maltoni (1977), Table 12.
Gehring *et al.* (1978), p. 590	10^{-4}	Log-probit, extrapolation of observed dose-response curve.	Gehring *et al.* (1978), dose-response curve based on unmetabolized VC.
Hooper and Ames (1979)	Greater than 10^{-3} (rats)	Linear	Maltoni (1977), liver angiosarcomas.
	Greater than 10^{-3} (rats)	Linear	Maltoni (1977), mammary tumors.
	10^{-1} to 10^{-3} (humans)	Linear, extrapolated to humans.	Maltoni (1977).
Food Safety Council (1978)	10^{-3}	Multi-hit	Maltoni (1975).
Do	2×10^{-3}	Multi-hit, upper confidence limit.	Maltoni (1975).
Do	5×10^{-4}	Multi-stage	Maltoni (1975).
Do	8×10^{-4}	Multi-stage, upper confidence limit.	Maltoni (1975).
NAS (1977), exhibit to Hoel and Rall statements, p. 794.	2×10^{-4} [a]	Multi-stage, upper confidence limit.	Maltoni (1975).

[a] Assuming breathing rate of 15 m^3/day to convert from oral intake to inhalation exposure.

Estimated Human Risks From Saccharin Ingestion of 0.12 g/Day (From NAS 1978, p. 3-72)

	Lifetime cases/million exposed	Cases per 50 million/yr
Rat dose adjusted to human dose by surface area rule:		
Method of high- to low-dose extrapolation:		
Single-hit model (Hoel, 1977)	1,200	840
Multi-stage model (with quadratic term (Hoel, 1977)	5	3.5
Multi-hit model (Scientific Committee of the Food Safety Council, 1978)	.001	0.0007
Mantel-Bryan probit model (Brown, 1978)	450	315
Rat dose adjusted to human dose by mg/kg/day equivalence:		
Method of high- to low-dose extrapolation:		
Single-hit model (Saccharin and its Salts, 1977)	210	147
Multi-hit model (Scientific Committee of the Food Safety Council, 1978)	.001	0.0007
Mantel-Bryan probit model (Brown, 1978)	21	14.7
Rat dose adjusted to human dose by mg/kg/lifetime equivalence:		
Method of high- to low-dose extrapolation:		
Single-hit model (Brown, 1977)	5,200	3,640
Multi-hit model (Scientific Committee of the Food Safety Council, 1978)	.001	0.0007
Mantel-Bryan probit model (Brown, 1978)	4,200	2,940

10. Conclusions by Different Authorities on the Utility of Quantitative Risk Assessment.

In view of the wide range of inherent limitations and problems in quantitative risk assessment and the massive differences in results from the use of different models, it is not surprising to note that a wide range of scientific authorities have expressed opinions on the validity of this technique and on its regulatory utility which range from the unenthusiastic to the frankly disparaging.

A memorandum to the National Toxicology Program by A.C. Upton, former Director of NCI (Appendix II), succinctly critiques and dismisses the technique as "not yet sufficiently developed." Even more explicit critiques were offered by various experts in the 1978 OSHA hearings on regulation of occupational carcinogens, on the basis of which OSHA concluded that the uncertainties in quantitative risk assessment were so great that its use could not be justified (Appendix III).

Other authorities are in accord with such criticisms:

> "---it is impractical---to make quantitative exposure or risk estimates---(particularly) when regulatory action is concerned with substances to which the population is exposed through a multitude of sources or products at different levels and in different ways (Regulatory Council, 1979).

> "A particular problem in quantitative extrapolation arises from the fact that different extrapolation models produce estimates of cancer incidence that differ by factors of 1,000 or more at levels of human exposure. Given such uncertainty, some labor and environmental organizations and many individuals refuse to choose one model or another for estimating the impact of a carcinogen on humans, and oppose the use of quantitative extrapolation" (OTA, 1981).

> "It is felt by many that quantified risk assessment is more an art than a science; that estimates must be based on numerous and questionable assumptions, extrapolations, and uncertainties." (Ruttenberg & Bingham, 1981).

"The quantification of human risk on the basis of the results of laboratory studies in animals should be approached with great caution. We must not lose sight of the fact that animal studies serve primarily as a qualitative surrogate for humans and that any attempts to quantify responses beyond the realm of biological certainty are open to serious question." (Munro & Krewski, 1981).

F. LIMITATIONS IN THE QUANTITATIVE RISK ASSESSMENTS FOR EDB

Apart from fundamental problems in quantitative risk assessment, the risk analyses by EPA and Rodricks are so flawed that they cannot possibly be used as a basis for regulatory policy.

1. Nature of Experiments and Linear Extrapolation

The risk assessments of EPA and Rodricks share one major and crucial error which results in extrapolations of tumor incidences at lower exposure doses which are both inaccurate and also substantial underestimates; they reflect the specifics of the studies on which the estimates are based, and the assumption that a linear extrapolation through the origin is accurate and conservative. All the estimates use the assumption of a linear dose-response; the two points for the straight line being the highest and zero doses with an assumed zero response.

However, this one hit or linear model is neither accurate nor conservative. In general, dose-response curves flatten at high doses, and a further increase in dose by several orders of magnitude may not induce any increase in the proportion of animals with tumors; in some cases, an increase in dose brings about a decrease in the proportion of animals with tumors due to toxicological factors such as competing toxicity.

It is clear from examining the bioassays used for risk assessment, that the doses tested were so high as to be in the flat or possibly inverted portion of the dose-response curve. In fact, for the gavage study (NCI, 1978), the tumor incidence at the high dose was lower than that at the lower dose for all animal groups. Extrapolation based on this study alone would thus yield higher cancer risks at lower doses.

Also, the incidence of forestomach cancers was close to 100% for all low dose groups, again confirming that the study was performed on the flat portion of the curve.

To estimate risks from inhalation exposure, EPA based their analyses on the rat inhalation bioassay data (NCI, 1980); it is not clear whether risk estimates were based on total tumors or tumors of a particular site. Regardless, it is apparent that the doses used were again so high as to yield responses on the flat part of the curve. For example, a four-fold increase in dose induced less than a 50% increase in nasal cancers. This problem alone is more than sufficient to invalidate the use of all these bioassays for the purpose of risk estimates, and to ensure that the risk estimates for lower doses are major underestimates, probably by several orders of magnitude,

In addition, there are a wide range of problems with the use of the NCI Bioassay data for any form of risk assessment. The lifespan of the test mice and rats was generally very short. In many experimental sub-groups the median lifespan for all test animals, was in the 30 to 50 week range; nearly half of the deaths in all high dose gavage groups were due to competing toxicity. Since the tumors appeared in such a short time, there is no way that the data can be used to provide information on the results of lifetime exposures. The EDB studies provide no information on the effects of shorter exposures. Single exposures of one month, week, day or even hour could conceivably have yielded the same tumor response as that observed in any of the bioassays.

2. Extrapolation to Conditions of Less than Lifetime Exposures

In the Rodricks risk assessment, it is assumed that for less than lifetime human exposure, the cancer risk is multiplied by the fraction $\frac{l}{T}$, where T is lifetime, and l is exposure duration. There is absolutely no justification for such a procedure. Given that the tumors in the gavage study appeared so early, this correction is likely to be erroneous.

The EPA PD 4 risk assessment employs a factor aimed at correcting for the short tumor induction period, called the one hit model with Weibul timing. The only justification given for the model is that it fits the data, i.e., it presumably predicts the time incidence of the tumors at a dose used in the experiment. But this model still assumes a linear dose dependence, a dependence which is unwarranted, and leads to an underestimate at low doses. Furthermore, the model cannot even fit the data for the two measured points, as the dose dependence is far less than linear in both NCI experiments used for the risk assessment, and in one case is inverted.

3. Other Limitations

Both the EPA and Rodricks'assessments ignore or discount three further important factors which can critically affect risk assessments and result in very major underestimates of risk. First, no consideration is given to high risk sub-groups, such as fetuses and neonates, Second, no consideration is given to interactive or synergistic effects, such as those clearly demonstrated in the Wong et al (1980) studies. Finally, no justification is given for the treatment of background cancer. In the Rodricks'risk assessment, EDB-induced tumors are assumed to be independent of background. However, induced tumors are frequently proportional to background cancer rates.

G. PARADOXES IN THE POSITIONS OF PROTAGONISTS OF INSIGNIFICANT RISKS FROM EDB RESIDUES

The food industry has placed great emphasis on the reassuring views of two scientists, Joseph Rodricks of Environ Corp, consultant to the Grocery Manufacturers of America, and Bruce Ames, a bacterial geneticist at the University of California, Berkeley, in support of their contention that EDB residues in food represent trivial and insignificant cancer risks.

Rodricks bases his position on a quantitative risk assessment which concludes that the upper bound limits of lifetime cancer risks from EDB residues in grain products are.1 in 4 million for children and 1 in 12 million for adults (Rodricks, 1984). Apart from a wide range of critically limiting assumptions in such estimates, which are not even discussed, Rodricks' current confidence in their reliability appears oddly at variance with his recent emphatic warnings to the contrary.

> "---it must not be forgotten that we are estimating animal, not human, risks. We do not know how to estimate the latter. We resolve this uncertainty by imposing the policy decision that animal risks will be taken to represent human risks. We could be wrong (emphasis added). --- segments of the human population are likely to be more sensitive than test animals." (Rodricks, 1981).

In 1977, Ames argued forcefully for a ban on the flame retardant Tris for reasons including the fact that it is contaminated with "the potent carcinogen EDB" (Blum & Ames (1977). Ames also warned that there are "enormous possible (carcinogenic) risks" from inadequately tested industrial chemicals, such as flame retardants; that a "steep increase in the human cancer rate from (industrial) chemicals may soon occur (especially) --- as the 20- to 30- year lag time for chemical carcinogenesis in humans is almost over"; "the tens of thousands of manmade chemicals have been introduced into the environment

in the last few decades, with widespread human exposure, to low but disturbing doses of these carcinogens," and that such chemicals be tested for mutagenicity and carcinogenicity; and that priorities must be established to minimize human exposure to these chemicals (Ames, 1979).

Ames now seems to have changed his mind on these issues, quite apart from EDB. He now maintains that there is no evidence of any generalized increase in US cancer rates other than that due to tobacco, and that cancer prevention strategies should be based on recognition of "natures pesticides" and trace natural carcinogenic components in US diets, rather than regulation of industrial carcinogens, which he considers unimportant except for restricted "high-dose exposure" groups (Ames, 1973). For a detailed rebuttal of Ames' latest (1973) position, see Appendix IV.

While Weisburger now seems unimpressed by the potential hazards of EDB, even challenging the human relevance of the NCI bioassay data, he has recently classified the closely related carcinogen DBCP, which if anything appears less potent than EDB in bioassay tests, as a "powerful carcinogen" (Weisburger & Williams, 1982). Further in his suggested classification of carcinogens into "epigenetic" and "genotoxic", EDB clearly falls into the latter category which is characterized by Weisburger as having high potency, and the ability to induce carcinogenic effects after a single exposure, and for which "zero exposure" must be the goal , according to Weisburger.

H. THE BASIS FOR A ZERO TOLERANCE FOR EDB

The only appropriate tolerance for EDB is zero. Any tolerance in excess of zero contributes further to the carcinogenizing of the nation's food supplies, and results in incremental cancer risks of a magnitude which cannot possibly be predicted with any reasonable degree of certainty or confidence. Following three decades of unregulated dietary contamination with EDB, the goal of zero tolerance is now ostensibly shared both by industry and government, as reflected in statements such as:

> "I want to emphasize that the goal of eliminating EDB as soon as possible from the food supply is an objective that is shared by all major food manufacturers" (Schwecke, 1984).
>
> "---in the long run, the major uses of EDB pose unacceptable risks and should be cancelled." (Ruckelshaus, 1984).

The zero tolerance goal is based on the following range of scientific and public policy considerations.

1. The U.S. population, in general, is at risk from ingestion of grains, fruit and vegetables contaminated with varying levels of EDB, quite apart from incremental exposures from contaminated groundwater and contaminated air due to the use of EDB in leaded gasoline. Another source of potentially serious exposure, which does not appear to have been considered as yet, is inhalation by housewives and cooks of EDB volatilized from food during cooking; such losses are estimated by industry to range from 78 to 99% (Quaker Oats, 1984).

2. Various population sub-groups are at still higher risk, reflecting higher exposure levels due to particular dietary habits and marketing factors, incremental occupational exposures, synergistic interactions with disulfiram, structurally related fungicides and possibly other

carcinogens, and enhanced carcinogenic sensitivity of infants and fetuses.

3. As recognized by industry and government since 1973, EDB is a highly potent carcinogen whose potency can be still further increased by synergistic interaction with the non-carcinogenic disulfiram, quite apart from the untested and unpredictable interaction with a wide range of other carcinogenic dietary contaminants and environmental carcinogens. Concerns on the carcinogenicity of EDB are still further emphasized by its induction of heritable genetic damage (mutagenicity) in a wide range of test systems, and by its reproductive toxicity in a wide range of species.

4. There is an overwhelming consensus in the scientific literature, as properly reflected in regulatory practice, that carcinogenicity data derived from valid, well-designed animal tests can be extrapolated with reasonable confidence to human risk.

5. There is an overwhelming consensus in the scientific literature, as properly reflected in regulatory practice, that there is no valid method for determining or estimating thresholds, safe levels or tolerances for carcinogens.

6. The quantitative risks assessments now used by EPA and industry to trivialize the carcinogenic risks from EDB food residues and to attempt to justify tolerances well in excess of 1 ppb are substantially flawed and rest on a wide range of assumptions which are likely to underestimate risks by many orders of magnitude.

7. The industry-sponsored occupational studies, allegedly providing epidemiological evidence as to the non-carcinogenicity of EDB, are so methodologically flawed and grossly insensitive as to preclude any possible inferences on safety or otherwise.

8. There are practical and non-carcinogenic alternatives to all current uses of EDB.

I. ALTERNATIVES TO EDB

Practical alternatives to EDB which do not result in carcinogenic food residues include aluminum phosphide, carbon disulfide and controlled atmospheres of carbon dioxide, nitrogen and combustion products of natural gas for grain fumigation (EPA, 1980), and aluminum phosphide, cold storage and sterile fruit flies for quarantine fumigation of fruits and vegetables (EPA, 1984 a & b); occupational hazards from the use of carbon disulfide and aluminum phosphide must be recognized and prevented by rigorous implementation of appropriate work practices. EPA has further determined that use of these alternatives either results in net savings or in no substantial economic losses to farmers and the food industry. (EPA, 1980).

Unacceptable alternatives which leave carcinogenic residues in food include carbon tetrachloride used in association with carbon disulfide, and methylbromide, which in recent rat feeding tests has been shown to induce a similar pattern of carcinogenicity to EDB (Danse et al, 1984). Irradiation is an equally unacceptable alternative, but for different reasons. While not radioactive, irradiated food contains stable radiolytic products whose chemical identify and toxicology are poorly defined. Industry claims for the safety of irradiated food largely depend on insensitive conventional animal feeding tests, rather than the more critical long term tests of concentrated extracts of irradiated food for carcinogenic and other chronic toxic effects which have still to be undertaken (Epstein & Goffman, 1984).

The use of EDB is leaded fuel would be eliminated, with a wide range of significant savings to the U.S. public besides reducing the toll of lead poisoning in urban children, by the alternative of unleaded fuel. As pointed out in a recent petition to EPA,

"much of the capital equipment needed to produce unleaded fuel is already on line as a result of existing federal lead-in-gas regulations, (besides) cost-effective alternative octane enhancers such as alcohol fuels (which) are or could shortly be made available" (NRDC, 1984).

J. CONCLUSIONS

1. The State of Massachusetts is to be commended for taking the lead in replacing the three tiered Federal guidelines for EDB, ranging from 30 to 900 ppb, with a single 1 ppb standard. Given a choice, it would seem likely that consumers in this state would prefer to be guided by the prudent conservatism of the Massachussetts Department of Public Health, rather than by the temporizing policies of the Federal Government and the self-interested policies of the food and chemical industries which have recklessly disregarded these public health problems for over a decade.

2. Consistent with a wide range of scientific and public policy considerations, the State of Massachusetts should move expeditiously to replace the 1 ppb standard with a zero tolerance.

3. On an interim basis, pending the promulgation of a zero tolerance, all food contaminated by EDB should be clearly labelled to allow consumers the right to exercise informed and free choice as to whether they wish to incur incremental cancer risks. This would seem preferable to imposing on the consumer carcinogenic tolerances that reflect highly dubious statistical manipulations, that shift the burden of uncertainty from industry and government to the consumer, and that appear to reflect pre-determined economic and political considerations.

4. All uses of EDB still allowed, including as a fruit fumigant and fuel additive, should be banned immediately or on an expedited phase-out, in favor of practical non-carcinogenic alternatives. The State should take immediate action to preclude the replacement of EDB by the carcinogenic methyl bromide or by the poorly tested technology of food irradiation.

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STATE OF CALIFORNIA
GEORGE DEUKMEJIAN, Governor

AIR RESOURCES BOARD
1102 Q STREET
P.O. BOX 2815
SACRAMENTO, CA 95812

December 7, 1984

Dear Sir/Madam:

Subject: Reports on 1,2-Dibromoethane (EDB)

In my March 30, 1984, letter requesting health effects information on EDB, I indicated that we would prepare a report on EDB for review by the Scientific Review Panel (SRP). Also in that letter, I stated that the report submitted to the Panel will be made available to the public upon its submittal to the Panel.

This letter is to inform you of an opportunity we are providing to review and comment on the report on EDB prior to its submittal to the SRP. The report will have two parts. Part A, by the ARB staff, will discuss the use, emissions, and ambient air concentrations of EDB. Part B, by the Department of Health Services (DHS) will discuss the effects of EDB on health and the risks from breathing ambient EDB. A draft Part A is expected to be available by December 14, 1984 and the DHS Part B is available now.

I am issuing this notice now to facilitate distribution and review of the report. Due to the holidays we will provide forty-five days for review. Therefore, reviewers will have until January 28, 1985 to submit written comments to:

Mr. William V. Loscutoff, Chief
Toxic Pollutants Branch
Air Resources Board
P. O. Box 2815
Sacramento, CA 95812

Within 30 days after January 28, we plan to send the report to the Scientific Review Panel for their review. The report will contain all comments by reviewers, responses by the ARB staff to comments on Part A, our revisions to the text of Part A, responses by DHS to comments on Part B, and DHS' revisions to Part B.

Please indicate on Attachment I which reports you wish to receive by mail, or you may pick up a copy of the appropriate reports in person at our

Public Information Office. As I stated, the draft of Part A should be available December 14. Part B is available now. Please call Don Ames at 916-322-8285 if you have any questions.

Sincerely,

Ronald O. Hansen

Peter D. Venturini, Chief for
Stationary Source Division

Attachment

cc: Alex Kelter, DHS
Raymond Neutra, DHS

Attachment 1

Request for EDB Reports

Please send me the indicated number of reports regarding EDB:

	Preliminary Draft	Report to SRP	Final Report (to Board)
Part A (only)	_____	_____	_____
Part B (only)	_____	_____	_____
Both parts	_____	_____	_____

I understand that I may be billed $15.00 for each set of Parts A and B in excess of 2 sets.

_____
(Signature)

Agency or Company:

Address:

City, State, Zip:

Attention:

Title:

Mail this request to:

Toxic Pollutants Branch
Air Resources Board
Attn: EDB Requests
P. O. Box 2815
Sacramento, Ca 95812

Chevron U.S.A. Inc.
575 Market Street, San Francisco, California • Phone (415) 894-2242
Mail Address: P.O. Box 7643, San Francisco, CA 94120-7643

W. T. Danker
Manager, Environmental Programs
Environment, Safety, Fire and Health

January 28, 1985

Draft Reports
on Ethylene Dibromide

Mr. William V. Loscutoff, Chief
Toxic Pollutants Branch
Air Resources Board
P. O. Box 2815
Sacramento, CA

Dear Sir:

We appreciate the opportunity to comment on the early draft reports on ethylene dibromide (EDB), the second compound to enter the State's toxic air contaminant program. The following summarizes our observations on both "Part A - A Review of Ethylene Dibromide Uses, Emissions, and Public Exposure" and "Part B - Health Effects of Ethylene Dibromide". More detailed comments on Parts A and B prepared by our experts at Chevron Research Company and the Chevron Environmental Health Center are included as attachments.

1. As noted in the Part A report, the EPA's planned phase out of lead as a motor gasoline additive will result in a like reduction in EDB emissions. The EPA lead phase out, which is anticipated to be announced in late January or early February of 1985, will reduce lead levels in California from the current 0.8 gm/gal to 0.1 gm/gal by 1986. This reduced use of lead will result in an approximate 90% reduction in EDB emissions from all gasoline related uses. This reduction, along with the existing ban on agricultural uses, will essentially eliminate the air emissions of EDB in California.

2. In the Part A report, sampling error should not be dismissed as a possible explanation for the discrepancy between estimated EDB emissions and observed ambient concentrations in the South Coast Air Basin. Only 30% of the samples analyzed were above the 5 ppt lower detection level of the analytical method used. In addition, the 7.4 ppt average level measured by the Air Resources Board is only one third to one half the quantification level of the measurement technique. This, along with potential errors in the calibration method used (see Attachment I), makes the 7.4 ppt ambient concentration essentially meaningless.

3. In reviewing the Department of Health Service's (DOHS) Part B report, it is apparent that the DOHS has incorporated many of the positive ideas generated by the Scientific Review Panel and industry during the formal review process for the DOHS's earlier report on benzene. We think this speaks positively for the AB 1807 process and the Department of Health Services. We do have several minor comments on Part B that are discussed in detail in Attachment II.

We hope these comments will be of value in revising your draft documents. If you have any questions, please contact Mark Nordheim at (415) 894-6107.

Sincerely,

W. T. Danker

ATTACHMENT I

CHEVRON U.S.A. COMMENTS ON THE AIR RESOURCES BOARD DRAFT "PART A" REPORT ON EDB

1. Calibration Procedure (pp. D-11 through D-14) Calibration is done using a gas mixture containing 10 ppb EDB. Four different volumes of this standard, corresponding to sample concentrations of 1, 3, 7, and 10 ppb EDB, are analyzed. A straight line is fitted to these points, which is then used as a calibration "curve" down to 5 ppt. Therefore, the lowest point used to determine the calibration curve is a factor of 200 greater than the detection limit. We recommend that CARB prepare standard gases with EDB concentrations closer to expected ambient levels to avoid errors in calibration.

2. Calculation of Evaporative Emissions (pp. F-3 through F-5) The volatility of EDB relative to gasoline is estimated using Raoult's Law. 25 degC (77 degF) is used as a reference temperature (note typo "77 degC" on p. F-3), but the vapor pressure of EDB at 30 degC is used in the calculation because it was the only data point available. This is not true. In fact, the same reference book (Verschueren, 1983) also lists EDB's vapor pressure at 20 degC. Simple linear interpolation gives a good estimate at 25degC. The result is a volitilization rate some 18% lower than calculated in the report.

3. Emission Estimates for Gasoline Production Facilities (pp. 1-4, 5) Table I-1 and Reference 1 state that the EDB emission estimates for gasoline production facilities are discussed in Appendix F. We cannot find this discussion, and therefore have no way of reviewing the ARB's calculations. We suspect an adjustment to the estimates may be required due to the over-statement of relative EDB volatility noted above.

4. A comparison of the ratio of "estimated EDB emission/mean ambient EDB concentration" to that of other non-reactive pollutants (CO and Pb) was used as a rough consistency check on the emissions estimate. From this, the hypothesis was developed that unknown sources may be contributing to peak summer concentrations, and that year-round emissions may be several times greater than estimated. While the former hypothesis has some merit, the latter is based on ambient concentrations which were simply too low to quantify.

ATTACHMENT II

CHEVRON U.S.A. COMMENTS ON THE DEPARTMENT OF HEALTH SERVICES DRAFT "PART B" REPORT ON EDB

1. While the DOHS demonstrated that risk estimates calculated using the linearized multistage, Weibull or Probit models are compatible with the available epidemiological results, the Department excluded from their final assessment (of the potential risks associated with ambient levels of ethylene dibromide) the risk estimate calculated by the Probit model. We do not believe that the risk estimates based on this model are any less realistic or reliable than those based on the other two models cited. Thus, we believe it would be scientifically defensible for the ARB to use estimates from all three models in the case of ethylene dibromide.

2. It is not clear in the report what, if any, interspecies extrapolation the DOHS used in converting from animal exposure data to humans. If simple exposure equivalency (i.e., 1 ppm-hour in rodents equals 1 ppm-hour in humans) was assumed, this should be stated.

3. The DOHS states (page 18) that the potential lifetime carcinogenic risk associated with ambient levels of ethylene dibromide is in the range of 10^{-4} (one in 10,000). This statement is incorrect, as it assumes an ambient airborne concentration of 1 ppb. Based on the ARB's estimate of an average ambient level of ethylene dibromide in the South Coast Air Basin of 0.0074 ppb (see the ARB's Part A report) the estimated risk ranges from 3×10^{-8} (MLE, Probit model) to 4×10^{-6} (UCL, Weibull model).

STATE OF CALIFORNIA
GEORGE DEUKMEJIAN, Governor

AIR RESOURCES BOARD
1102 Q STREET
P.O. BOX 2815
SACRAMENTO, CA 95812

February 28, 1985

Mr. W. T. Danker, Manager
Environmental Programs
Chevron, USA
575 Market Street
San Francisco, CA 94120-7643

Dear Mr. Danker:

Subject: Comments on Ethylene Dibromide Report

Thank you for your comments on our draft report on ethylene dibromide (EDB). This letter contains our responses to your comments on Part A. The Department of Health Services (DHS) will respond to comments on Part B. Your comments and corresponding responses from ARB and DHS will be included in Part C of the EDB report to the Scientific Review Panel.

Our responses to your Part A comments follow.

Comment 1 - regarding effects of reduced lead in gasoline and the ban on EDB as a pesticide:

We agree that a phase out of lead in gasoline along with the current ban of agricultural EDB use will eliminate the major sources of EDB emissions. The summary and Chapter I. state that the ban of EDB as a pesticide has, and reduced lead in gasoline would, strongly reduce EDB emissions.

Comment 2 - regarding possible effect of sampling error on monitoring results:

You are correct that the prevalence of data below the quantitation limit creates a relatively large uncertainty in the calculated annual average concentration of 7.4 ppt. However, the calculated average is about one and one-half times the limit rather than "one-third to one-half the quantitation limit" as stated in your letter. Accordingly, we believe that the uncertainty due to data below the quantitation limit probably does not account for the five-fold discrepancy between inventoried emissions and emissions predicted from monitoring data.

Comment 1 in Attachment 1 - regarding calibration procedure:

You are correct that measured data fall far below the calibration curve described by Appendix D. This introduces considerable uncertainty in the

measurements. However, considering the lack of certified EDB calibration gas at concentrations near ambient, we believe that some degree of downward extrapolation of the calibration curve is preferrable to dilution of available standards to ambient air levels. We are currently updating our sampling and analysis procedures for EDB. Improved procedures will be used when developing information for the EDB regulatory needs report.

Comment 2 in Attachment 1 - regarding evaporative emissions from gasoline marketing:

You are correct that 30°C was inappropriate for calculating EDB's vapor pressure. Our revised report will use new calculations using an activity coefficient of 2.1 for EDB as suggested by EPA. Applied at 70°F to all marketing sources of EDB (underground tanks, vehicle refueling, bulk terminals, and bulk plants), our new calculations show total marketing emissions of 0.32 ton per year. The methodology will be explained in Appendix F.

Comment 3 in Attachment 1 - regarding gasoline production emissions:

The material referenced as being in Appendix F was omitted by oversight. A review of the calculations has lead to a reduction of the estimated emissions from 0.9 to 0.19 ton per year. The method of estimation will be added to Appendix F.

Comment 4 in Attachment 1 - regarding consistency of estimated emissions with measured concentrations:

Please see our response to your second comment.

Thank you again for your comments. If you have any questions, please contact William Loscutoff at (916) 322-6023.

Sincerely,

Peter D. Venturini, Chief
Stationary Source Division

cc: W. Loscutoff, ARB
R. Neutra, DHS
A. Kelter, DHS

1/ EPA, 1984. Evaluation of Air Pollution Regulatory Strategies for Gasoline Marketing Industry, EPA 450/3-84-0120, Washington, D.C.

Southern California Edison Company

P. O BOX 800
2244 WALNUT GROVE AVENUE
ROSEMEAD, CALIFORNIA 91770

January 31, 1985

Mr. William V. Loscutoff, Chief
Toxic Pollutants Branch
California Air Resources Board
P.O. Box 2815
Sacramento, California 95812

Dear Mr. Loscutoff:

Subject: Report on the Health Effects of Ethylene Dibromide

Southern California Edison Company has reviewed the report entitled "Health Effects of Ethylene Dibromide (EDB)" and would like to submit these brief comments on the methods used to assess and communicate the health risks of this chemical. SCE believes that estimates of the carcinogenic risk of EDB and other chemicals which are provided to the Board are very important because they will influence decisions which are made on the listing and control measures for toxic air pollutants in California.

We have concerns, however with the methods by which the uncertainty of a risk assessment are being communicated to those who will ultimately make risk management decisions. The provisions of H & S Code Section 39660.(c) provide the board with an indication of how this uncertainty should be expressed. Specifically, the State Department of Health Services' evaluation of health effects must assess the availability and quality of data on health effects, and for substances where there is no threshold of significant adverse health effects, the range of risk must be provided. As discussed below, mathematical models are available which can estimate the health risk posed by a carcinogen and the uncertainty around that estimate in the form of confidence intervals which convey the potential range for that risk. We feel that the requirements for the state board to participate in the evaluation of health

effects (Section 39660.(a)) gives the board the prerogative to request the DOHS to convey this information in its health evaluation.

The EDB report serves as an example. Uncertainty caused by the choice of model is demonstrated by observing that the choice of dose/response (extrapolation) model can greatly influence the risk estimates derived for EDB. Similarly, the influence by the choice of animal tumor data, used to estimate risk, is also seen to contribute to risk estimate uncertainty.

We feel that another component of the risk assessment uncertainty should also be presented; uncertainty in the risk estimates once the choice of an appropriate model and data set have been made. The report demonstrates this to some degree by showing both the maximum likelihood estimate (MLE) and the 95 percent upper confidence limit (UCL) on risk for certain sets of data. What is missing is the lower confidence limit on risk (e.g., a 95 percent LCL) to show the full range in the uncertainty of these estimates. Only by communicating this complete range can a decision maker (risk manager) gain an understanding of how large or, conversely, how small the potential health impacts might be for a toxic air pollutant.

Figure 1 shows risk estimates calculated for nasal malignancies in male rats using the data from the DOHS Report on EDB with a recent version of the multistage model developed by Crump and Howe (2). Using a lifetime airborne exposure to 1.0 ppb EDB it can be shown than the MLE for risk is about 243 per million persons exposed and this risk may be as high as 303 per million (3). However it should also be noted that this risk might also be as low as 186 per million exposed. From a statistical standpoint the number describing the lower confidence limit is equally likely as an interpretation of the data as the number describing the upper limit.

SCE feels that it is important for a public official making risk management decisions on a chemical be fully informed on all the uncertainties associated with risk estimates which can influence these choices. We recommend that DOHS incorporate the full range of risk estimates into this report and future reports to the SRP and the ARB concerning the health impact of toxic air pollutants by including lower as well as upper confidence bounds on risk.

Sincerely,

E. J. Faeder

E. J. Faeder, Ph.D.
Manager of Environmental Operations

Attachments

REFERENCES

1. Health Effects of Ethylene Dibromide (EDB), Epidemiological Studies Section, Department of Health Services, Berkeley, California, November 30, 1984. (Data provided on page D-2)

2. GLOBAL 82 : A Computer Program to Extrapolate Quantal Animal Toxicity Data to Low Doses. R. B. Howe and K. S. Crump, May, 1982 (A more recent version of this model, GLOBAL85, was used to calculate the risk estimates used in these comments. This version calculates both upper and lower confidence limits).

3. The risk estimates given in the DOHS report on EDB are slightly higher than those presented here. These differences are probably due to slightly different computational techniques.

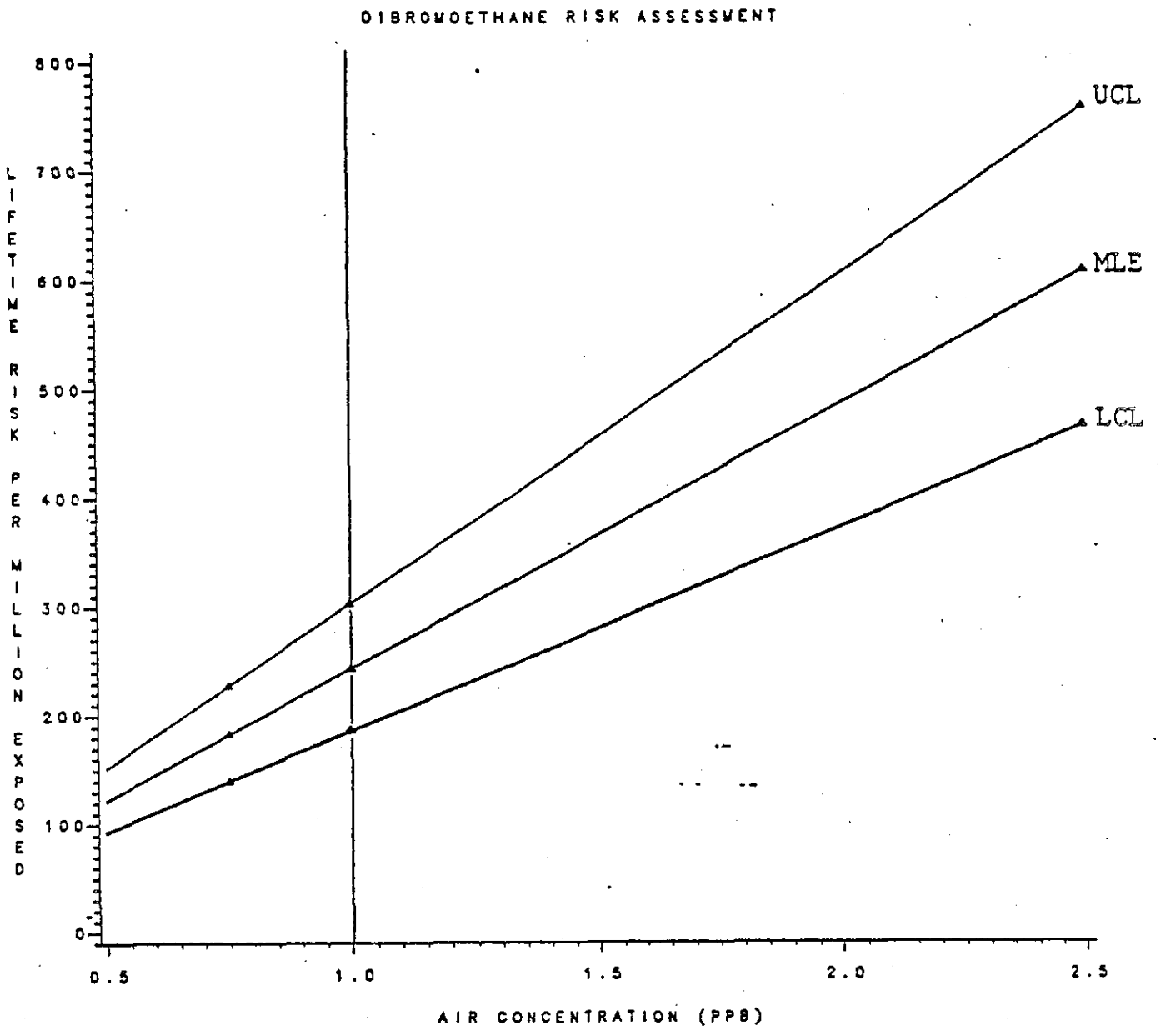


FIGURE 1. Lifetime Risk Estimates in Terms of Cancers per Million Persons Exposed at Various Airborne Concentrations of Ethylene Dibromide. UCL = 95% Upper Confidence Limit on Risk. MLE = Maximum Likelihood Estimate of Risk. LCL = 95% Lower Confidence Limit on Risk. [Data are for nasal cavity malignancies in male rats as reported in reference 1.]

Western Oil and Gas Association
727 West Seventh Street, Los Angeles, California 90017
(213) 627-4866

February 14, 1985

William V. Loscutoff
Chief, Toxic Pollutants Branch
Stationary Source Division
Post Office Box 2815
Sacramento, California 95812

Re: EDB Health Effects Assessment Report

Dear Mr. Loscutoff:

WOGA member company experts have reviewed your report on "The Health Effects of Ethylene Dibromide (EDB)" dated November 30, 1984. Our review was not able to be as detailed as we would like, but we offer the following comments.

1. The Report Characterizes Risks and Recommends Specific Risk Numbers But Does Not Present the Full Range of Estimates and Their Attendant Uncertainties.

WOGA recognizes the improvements that have been made in DHS' dose-response assessment procedures since publication of the first draft of the benzene health effects report last summer. We continue to be concerned, however, that DHS is stepping outside the boundaries of its role as an objective risk assessor by offering a range that consists of only conservative estimates. WOGA maintains that it is the ARB's role to decide how conservative to be in these matters and that as much information as possible should be presented to the Board to guide their decisions. This information must include a sensitivity analysis and a detailed discussion of the pros and cons of each assumption needed in the dose-response assessment. Only in this way can the ARB know how much confidence to place in the estimates.

We recognize that the EDB report evaluates the effects on the risk estimates of using different tumor data sets. However, more needs to be done to combine different assumptions and to present lower confidence limits along with UCLs and MLEs. The lower bound is often zero (assuming non-negativity) and should be presented as such.

2. The Per-PPB Risk Estimates Must Be Extended to the Actual Exposure Estimates Presented by the ARB (0.0074 PPB).

As was done in the benzene report, the risk estimates are calculated at the 1 ppb level for purposes of assessing the impact of commmunity exposures. However, this is misleading and confusing in the case of EDB. The ARB's exposure assessment report estimates that average exposure in the South Coast Air Basin is only 0.0074 ppb or over one hundred times lower than 1 ppb. While we recognize that your report was completed before the ARB produced its report, WOGA believes that in order to present an accurate picture of the risks future drafts should calculate the risk estimates using the ARB exposure estimate (or numbers in that range). This will show that the range of risks could be several orders of magnitude lower than the 1 ppb estimates in the current draft. It is essential that the most realistic picture of risks be presented to the decision makers and the public.

3. Risk Estimates Several Orders of Magnitude Lower Than Those Presented Are "Not Grossly Incompatible" With the Available Epidemiological Data and Should be Presented as Such.

The report concludes that the risk estimates from the animal extrapolation models "are not grossly incompatible with the results from the one small epidemiological study." This conclusion is grossly misleading. Given the small number of workers in the single available epidemiological study, risk estimates three or four orders of magnitude lower are also "not grossly incompatible" with its results. Again, good risk communication requires this fact to be presented to the ARB.

4. The Toxicological Analysis Failed to Clearly Identify Several Assumptions and Conclusions As "Science Policy."

The report does not adequately deal with the possible effect of low survival in the high dose group, which brings into question the range of doses used in the NTP inhalation bioassay.

Also, while the report presents estimates using nasal carcinomas and hemangiosarcomas, it did not deal with the issue of significant respiratory tract irritation at higher doses and did not address the uncertain significance of

contact site tumors. A better job of explaining this uncertainty and the choices made by the Department is needed.

5. Epidemiologic Analysis

In Appendix B it is preferable epidemiological practice to exclude the two arsenical cases. Therefore, the analysis should more clearly present the results with and without these deaths.

As noted above, a wide range of risk estimates from the animal data is "consistent" with the limited epidemiological information.

On page B-3, the report states that observed risk levels may underestimate risk for those employed prior to 1940. It is equally true, however, that the observed levels may overestimate risk in the post-1940 group.

We hope these comments are helpful and look forward to the next draft.

Very truly yours,

Robert Harrison /s/

Robert N. Harrison
Assistant General Manager

RNH:wm

Response to Comments on EDB Document

Comment:

DHS states that the potential lifetime carcinogenic risk associated with ambient levels of ethylene dibromide (EDB) is in the range of 10^{-4} (one in 10,000). This statement is incorrect, as it assumes an ambient airborne concentration of 1 ppb. The ARB estimated an average ambient level of EDB in the South Coast Air Basin of 0.0074 ppb ("Health Effects of Ethylene Dibromide", p. 18). (Commentor: Chevron, Western Oil and Gas Association[WOGA])

Response:

The commentor is correct. This should read, "As has been seen above, extrapolations from the animal cancers, both of first contact and remote sites, suggest theoretical lifetime risks in the 10^{-4} range from an ambient concentration of 1.0 ppb of EDB. Since the average ambient air level of EDB in the South Coast Air Basin is estimated to be 0.0074 ppb, the theoretical lifetime risk is on the order of 1-4 x 10^{-6}."

Comment:

The interspecies extrapolation from animal inhalation exposure data to that of human inhalation is not clear. (Commentor: Chevron)

Response:

The method of interspecies extrapolation for inhalation of lipid soluble substances has been described previously (Part B, "Health Effects of Benzene") and is provided in the following paragraphs. Simple exposure equivalency (ppm) was used. This is possible due to the assumption that surface area provides the best scaling factor between species. Direct

exposure equivalency is derived from this assumption since inhalation volume is a function of surface area.

"The dose in mg/kg of partially soluble vapors is proportional to oxygen consumption, which in turn is proportional to $W^{2/3}$ and is also proportional to the solubility of the gas in body fluids, which in turn can be expressed as an absorption coefficient, r, for the gas. Therefore, expressing the O_2 consumption as $O_2 = (k)\ (W^{2/3})$, where k is a constant independent of species, it follows that:

If:

m - the average dose/day in mg during administration of the agent.

v - the average lifetime concentration of benzene in the inhalation chambers.

Then:

$$m = (k) \times (W^{2/3}) \times (mg/m^3) \times r$$

$$dose = \frac{m}{W^{2/3}} = kvr$$

In the absence of experimental information or a sound theoretical argument to the contrary, the absorption fraction, r, is assumed to be the

same for all species. Therefore, for these substances a certain concentration in ppm or in mg/m^3 in experimental animals is equivalent to the same concentration in humans (Part B, "Health Effects of Benzene")".

Comment:

DOHS demonstrated the carcinogenic risk estimates using the linearized multistage, Weibull and Probit models and should have used all three models in their final risk conclusions. (Commentor: Chevron)

DHS Response:

The Weibull model referred to is not the classical Weibull model (the extreme value function model) but the time-corrected multistage model (which Howe and Crump refer to as the "Weibullized" multistage model). This model corrects for intercurrent mortality using time-to-death with and without the presence of the indicated tumor. The Probit model was included to demonstrate the large variation observed with different models for low-dose extrapolation (although at high doses the models may adequately fit the data). DHS staff disagrees with the commentor that risk estimates based on the Probit model are as realistic or reliable as those based on the multistage model.

This issue has been discussed at length in a prior document (Part B, "Health Effects of Benzene").

Comment:

To better provide risk managers with a greater understanding of the uncertainty of the low dose risk assessment, DHS should provide the 95% lower confidence limit (95% LCL) as well as the 95% upper confidence limit (95% UCL) and maximum likelihood estimates (MLE) for the multistage model. (Commentor: Southern California Edison, WOGA)

DHS Response:

The DHS staff believes that providing the lower confidence limit is misleading, and attributes a greater certainty to the risk value than is warranted. The staff believes that the linear 95% UCL of the multistage model provides a rough but plausible estimate of the upper limit of risk -- that is, with this model it is not likely that the true risk would be much more than the estimate risk, but it could be considerably lower. This lower risk estimate is not necessarily bounded by the 95% lower confidence interval.

Comment:

The report does not present the full range of estimates and their attendant uncertainties. Specifically, the report must include: a sensitivity analysis and a detailed discussion of the pros and cons of each assumption needed in the dose response assessment. (Commentor: WOGA)

DHS Response:

The report does not and could not present a full (complete) range of risk estimates. The total number of combinations for the assumptions and different tumor data is very large. The staff of DHS provide a range of risk estimates based on sound scientific judgement and consistent with protecting the health of the people of California.

Sensitivity analysis is not a formal statistical method. It evolved as a technique to determine how varying data-input effects the resultant estimates. The use of sensitivity analysis is not in general use for risk estimations. It is not used by federal regulatory agencies (EPA, FDA, CPSC, OSHA, etc.) nor has it been employed by the National Academy of Sciences in their risk documents for drinking water quality. Thus, DHS does not believe that a sensitivity analysis is warranted. It should be noted that DHS did not provide the worst estimates of risk. DHS separated contact and systemic tumors i.e., nasal and hemangiosarcomas, used only malignancies, and did not combine tumors from other

target organs as an indication of carcinogenic risk is frequently done by the Carcinogen Assessment Group of the EPA.

Comment:

Risk estimates several orders of magnitude lower than those presented are "not grossly incompatible" with the available epidemiological data and should be presented. (Commentor - WOGA)

DHS Response:

The staff of DHS did not mean to imply that the Ott et al. epidemiolgical study confirms the animal bioassay risk values. This study has been cited in the literature as evidence for the incompatability of the human and animal data. This is the primary issue that DHS was addressing. As pointed out by the commentor and in the DHS report, there is a small number of workers in this single epidemiological study and thus the statistical power of this study is low. Therefore, the staff of DHS do not believe that the Ott study should be used for quantitative risk assessment and consequantly animal bioassays must be relied upon for risk assessment. The staff of DHS futher agree with the authors of this study when the concluded, "Findings of this investigation neither rule out nor establish EDB to be a human carcinogen".

The comparison of the Ott study and the animal biossay data attempted to establish that the upper 95% confidence bound of the bioassay was consistent with the epidemiological data. As will any upper confidence limit values less than the bound are consistent.

Comment:

The toxicological analysis failed to clearly identify several assumptions and conclusions as "science policy". (Commentor - WOGA)

A. The report does not adequately deal with the possible effect of low survival in the high dose group, which brings into question the range of doses used the NTP inhalation bioassay.

B. The report does not deal the the issue of significant respiratory tract irritation at higher doses and did not address the uncertain significance of contact site tumors.

DHS Response:

A. It is not clear what the commentor means by "...brings into question the range of doses ..." If the commentor is referring to the fact that the low survival rate in the high dose group of the NTP inhalation study suggests that the dosage of the NTP bioassay was greater than the maximum tolerated dose, DHS concurs. However, this does not invalidate the study. It should be noted that the survival rate in the inhalation study was much greater that that in the gavage bioassay.

Carcinogenic risk based on the high exposure group without correcting for early mortality will underestimate the cancer incidence rate. This is because the increased mortality rate decreased the true denominator

(number of animals at risk) while not affecting the numerator (the number of tumors at neropsy). The uncorrected number of animals at risk (50, no animals were censored) was used for the cancer incidence rate for the dichotomous risk models. The time-corrected multistage (Weibullized-multistage) model was used to correct for competing causes of death (intercurrent mortality). Comparison of the Weibull-multistage model to that of the "simple" multistage model i.e., the non-time corrected model, demonstrates the effect of intercurrent mortality. Thus, DHS did address the issue of lower survival in the high dose group.

B. The staff of DHS assume that the comment " ... issue of significant respiratory tract irritation ... " refers to the concept of cytotoxicity as a mechanism of carcinogenesis. Cytotoxicity was discussed by DHS in response to comments for Part B, Health Effects for the benzene document. This "science policy" decision was based on the fact that the current knowledge of the mechanism of carcinogenesis does not provide sufficient evidence to presently allow the separation of carcinogenic mechanisms into genetic and non-genetic.

Comment: The epidemiological analysis should more clearly present the results with and without the two arsenical cases and should state that the estimated risk could overestimate the risk level in the post-1940 group. (Commentor: WOGA)

DHS Response: Table 2, which summarizes the results of Ott et al., does provide the rates with and without the two individuals who were exposed to arsenic (pg. B-16). The two arsenical cases were excluded in the data analysis.

Industrial hygiene measurements of EDB for workers exposed prior to 1949 were not available to either us or Ramsey et al. If such measurements were available and were higher than measurements made during 1949 and after, then both we and Ramsey et al., using our respective models, would have predicted a greater number of cancers among these workers. However, since worker exposure information for the period prior to 1949 was not available we followed the lead of Ramsey et al. and assumed the same worker exposure levels for the period prior to 1949 as was measured during 1949 and after.

309 Santa Monica Blvd., Suite 212
Santa Monica, CA 90401 (213) 451-0651

March 16, 1985

Mr. Richard Bode
1800 15th Street
P.O. Box 2815
Sacramento, CA 95812

Dear Mr. Bode,

The Coalition for Clean Air would like to submit the following comments concerning the health effects of ethylene dibromide (EDB).

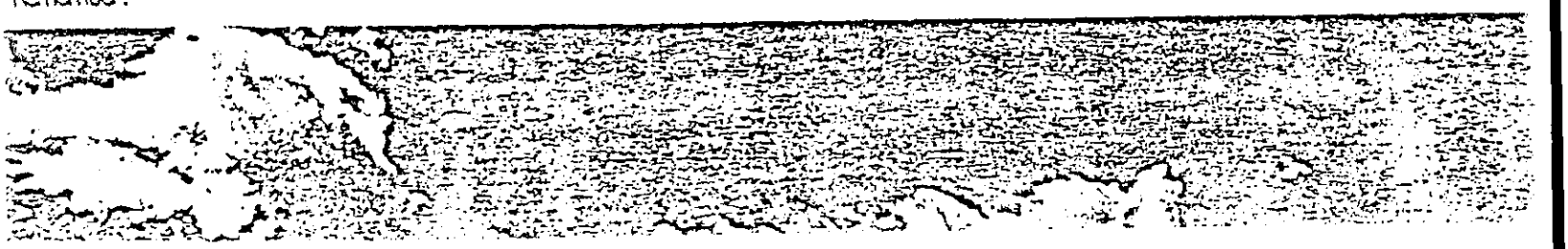
At present the lead component of gasoline is being reduced, thus the need for EDB as a lead scavenger is decreasing. Even though EDB is being slowly phased out of gasoline, and has been banned from most agricultural uses since 1983, the public is still at risk from the presence of this compound in our environment. EDB is persistent in the atmosphere, and its presence in the atmosphere has been documented.

We strongly feel that EDB should be classified as a toxic air contaminant according to AB 1807.

The International Agency for Research on Cancer (IARC) has determined that there is sufficient evidence that EDB is carcinogenic in animals and therefore should be considered a potential carcinogen in humans. The carcinogenicity of EDB has been established in multiple animal studies. A wide range of tumors involving various organ systems have been induced, regardless of the route of exposure (i.e. ingestion, inhalation, dermally).

A synergistic effect is seen when disulfiram (a noncarcinogenic drug closely related to a fungicide in common use) is induced into the diet of the test animals prior to inhalation of EDB. Following the inhalation of EDB, there was a 10-fold increased incidence of various tumors (Wong et al 1980).

As well as being carcinogenic, there is evidence that EDB is mutagenic in a wide spectrum of in vivo tests. EDB and two of its metabolite bromoacetaldehyde and N-acetyl cysteine, are positive in the Ames Salmonella assay.



EDB's carcinogenicity has been implied by epidemiological studies. These studies were based on occupationally exposed workers. While these studies were very small, and contained several methodological flaws, i.e. sample size too small, exposure period too short, and a lack of follow up for significant number of the workers, the data stil suggests that EDB may be responsible for the excess cancer that was observed.

The lifetime risk number is given as 102-553/million/1 ppb of EDB exposure by the Department of Health Services. It states that this number represents the theoretical risk of cancer, accumulated over a 70 year lifetime with continuous exposure for all 70 years. It is important that this number is looked at in the context of the overall probability of developing cancer, which is on the order of 250,000/million over a 70 year lifetime. The lifetime risk number for EDB is estimated from animal data, whereas the overall probability is based on human data. With any type of risk assessment there are limita tions. Among these limitations are the following: humans are more sensitive than most test species; there is a wide variation in sensitivity to particular carcinogens between species; humans are not a homogeneous group; and most animal studies are acute in nature rather than chronic.

The risk of developing cancer from a given agent, such as EDB is dependent upon background cancer rate, the presence of other carcinogens and the potential synergistic effects they may have. The point in the lifespan at which exposure occurs can affect the risk assessment. If a carcinogen acts at an early stage, then a short exposure early in life may be sufficient to induce cancer, and any later exposu are inconsequencial. In actuality the estimated lifetime risk number for EDB may be an underestimation. This likely underestimation is thought to be due to the competing risk of premature death resulting from toxicity. A developing tumor may have gone unnoticed at the time of death.

The Department of Health Services uses the upper confidence limit (UCL) in their risk assessment. This represents the most conservative approach. We strongly agree with DOHS,because when dealing with publi health one should take the approach which maximizes public protection.

In the face of EDB's carcinogenic activity, we feel it should be treated as having no threshold. There is no safe level for carcinogen According to the Toxic Substance Strategy Report (1980):

> "Any exposure to any amount of a carcinogen however small, must be regarded as an addition to the carcinogenic risk.."

The main goal is to protect human health and welfare in every way possible and to minimize the total risk of developing cancer. In orde to accomplish this, we feel that the following issues need to be addressed:

1) EDB should be identified as a toxic air contaminant;

2) a more aggressive approach is needed toward the phasing out of all current uses of EDB still allowed, which include fuel additives and fruit fumigant, and the replacement of EDB with noncarcinogenic alternatives;

3) EDB should be recognized as a potential human carcinogen;

4) EDB should be treated as having no threshold;

The Coalition for Clean Air is a non-profit, statewide citizen's group dedicated to the elimination of air pollution. Thank you for the opportunity to submit comments on this important health issue.

Sincerely,

Kimberley Williams-Bean

Kimberley Williams-Bean
Research Analyst

References

1) Toxic Substances Strategy Committee, " Toxic Chemicals and Public Protection: A Report to the President." (May 1980)

2) Wong, L.C. , et al "Chronic Inhalation Toxicity of 1,2,-Dibromoetha in Rats with and without Dietary Disulfiram", NIOSH Contract No. 210-76-0131 (1980)

3) Testimony in Support of a Zero Tolerance for EDB Samuel S. Epstein and Joel Swartz; University of Illinois Medical Center, Chicago, Illinois Public Hearing Panel on Final Regulation of EDB Boston,Mass March 19, 1984

Southern California Edison Company

P. O BOX 800
2244 WALNUT GROVE AVENUE
ROSEMEAD, CALIFORNIA 91770

EDWARD J. FAEDER, Ph.D.
MANAGER OF ENVIRONMENTAL OPERATIONS

TELEPHONE
(818) 302-2009

March 20, 1985

Mr. Richard Bode
Air Resources Board
1800 15th Street
P. O. Box 2815
Sacramento, CA 95812

ATTENTION: MEMBERS OF THE SCIENTIFIC REVIEW PANEL

SUBJECT: CARB Report on EDB to the Scientific Review Panel

Southern California Edison (SCE) has previously submitted comments to the Air Resources Board (ARB) concerning the Department of Health Services (DHS) risk assessment of ethylene dibromide (EDB). These comments, as attached, are included in the current version of the report which has been forwarded to the SRP for review (pages 72-75). We feel that the substance of these comments has not been adequately addressed by DHS in their response (page 79 of report) and request that they be reconsidered by the SRP. Specifically, the comments concern the format used to present the results of risk assessments. This is an important issue which is relevant to all the compounds which will be examined by the DHS and SRP and should be addressed in this early phase of California's program for regulating toxic air pollutants.

The risk assessment reports prepared by DHS are tools to be used by risk managers in making decisions concerning the control of toxic air pollutants. A report must convey the degree of uncertainty in the risk estimates for a given substance in order to be useful. This is why it is necessary to present upper and lower statistical confidence limits on risk estimates. Presentation of the 95% upper confidence limits (UCLs) from several models or the UCLs derived from data at several different tumor sites is not a substitute for providing a risk manager with information regarding how high, or conversely, how low the potency of a carcinogen might be. These estimates must be considered in the context of various assumptions of the risk assessment (e.g. that humans will react in the same manner as animals and that there is no threshold.)

The DHS staff has rejected the use of a 95% lower confidence limit (LCL) because they believe the true risk estimate may be below this limit and that its presentation is "misleading, and attributes a greater certainty to the risk value than is warranted". We find this reasoning difficult to follow. Upper and lower confidence intervals are statistically derived ranges within which an estimated value for a particular parameter may lie. If DHS believes that the true lower limit of risk is far below the lower confidence limit, then this value should be presented in their evaluation as a plausible lower bound to the range of risk. The expression of such a range of risk is extremely useful to risk managers who must make decisions under conditions of uncertainty. Only if all the relevant data, with its attendant uncertainty, are presented can informed, scientifically-based decisions be made.

We have concerns that DHS is treating the subject of upper and lower bounds on risk estimates as a policy issue rather than a scientific issue. The overview of the EDB report contains the following statements:

> "The DHS recommends the MLE from the multistage model for hemangiosarcomas in female mice for calculating the lower bound of risk."
>
> "While less conservative risk estimates can also be defended as reasonable, 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."

The choice of the proper data sets and models to be used for calculating an estimate of the range of risk is clearly a scientific issue. <u>All</u> information should then be presented to risk managers so they can be fully informed when making decisions. If risk managers wish to selectively choose upper and lower bounds for regulatory purposes, it is their prerogative. However, such choices are <u>policy</u> choices and should be kept separate from the risk assessment process.

We encourage the SRP to consider these comments as well as our previous comments on the presentation of risk estimates with respect to EDB and other toxic air contaminants which will be reviewed in the future.

We appreciate being given the opportunity to provide comments to the Scientific Review Panel on this and other important issues.

Sincerely,

Edward J. Foley

Enclosure

Southern California Edison Company

P. O. BOX 800
2244 WALNUT GROVE AVENUE
ROSEMEAD, CALIFORNIA 91770

January 31, 1985

Mr. William V. Loscutoff, Chief
Toxic Pollutants Branch
California Air Resources Board
P.O. Box 2815
Sacramento, California 95812

Dear Mr. Loscutoff:

Subject: Report on the Health Effects of Ethylene Dibromide

Southern California Edison Company has reviewed the report entitled "Health Effects of Ethylene Dibromide (EDB)" and would like to submit these brief comments on the methods used to assess and communicate the health risks of this chemical. SCE believes that estimates of the carcinogenic risk of EDB and other chemicals which are provided to the Board are very important because they will influence decisions which are made on the listing and control measures for toxic air pollutants in California.

We have concerns, however with the methods by which the uncertainty of a risk assessment are being communicated to those who will ultimately make risk management decisions. The provisions of H & S Code Section 39660.(c) provide the board with an indication of how this uncertainty should be expressed. Specifically, the State Department of Health Services' evaluation of health effects must assess the availability and quality of data on health effects, and for substances where there is no threshold of significant adverse health effects, the range of risk must be provided. As discussed below, mathematical models are available which can estimate the health risk posed by a carcinogen and the uncertainty around that estimate in the form of confidence intervals which convey the potential range for that risk. We feel that the requirements for the state board to participate in the evaluation of health

effects (Section 39660.(a)) gives the board the prerogative to request the DOHS to convey this information in its health evaluation.

The EDB report serves as an example. Uncertainty caused by the choice of model is demonstrated by observing that the choice of dose/response (extrapolation) model can greatly influence the risk estimates derived for EDB. Similarly, the influence by the choice of animal tumor data, used to estimate risk, is also seen to contribute to risk estimate uncertainty.

We feel that another component of the risk assessment uncertainty should also be presented; uncertainty in the risk estimates once the choice of an appropriate model and data set have been made. The report demonstrates this to some degree by showing both the maximum likelihood estimate (MLE) and the 95 percent upper confidence limit (UCL) on risk for certain sets of data. What is missing is the lower confidence limit on risk (e.g., a 95 percent LCL) to show the full range in the uncertainty of these estimates. Only by communicating this complete range can a decision maker (risk manager) gain an understanding of how large or, conversely, how small the potential health impacts might be for a toxic air pollutant.

Figure 1 shows risk estimates calculated for nasal malignancies in male rats using the data from the DOHS Report on EDB with a recent version of the multistage model developed by Crump and Howe (2). Using a lifetime airborne exposure to 1.0 ppb EDB it can be shown than the MLE for risk is about 243 per million persons exposed and this risk may be as high as 303 per million (3). However it should also be noted that this risk might also be as low as 186 per million exposed. From a statistical standpoint the number describing the lower confidence limit is equally likely as an interpretation of the data as the number describing the upper limit.

SCE feels that it is important for a public official making risk management decisions on a chemical be fully informed on all the uncertainties associated with risk estimates which can influence these choices. We recommend that DOHS incorporate the full range of risk estimates into this report and future reports to the SRP and the ARB concerning the health impact of toxic air pollutants by including lower as well as upper confidence bounds on risk.

Sincerely,

E. J. Faeder, Ph.D.
Manager of Environmental Operations

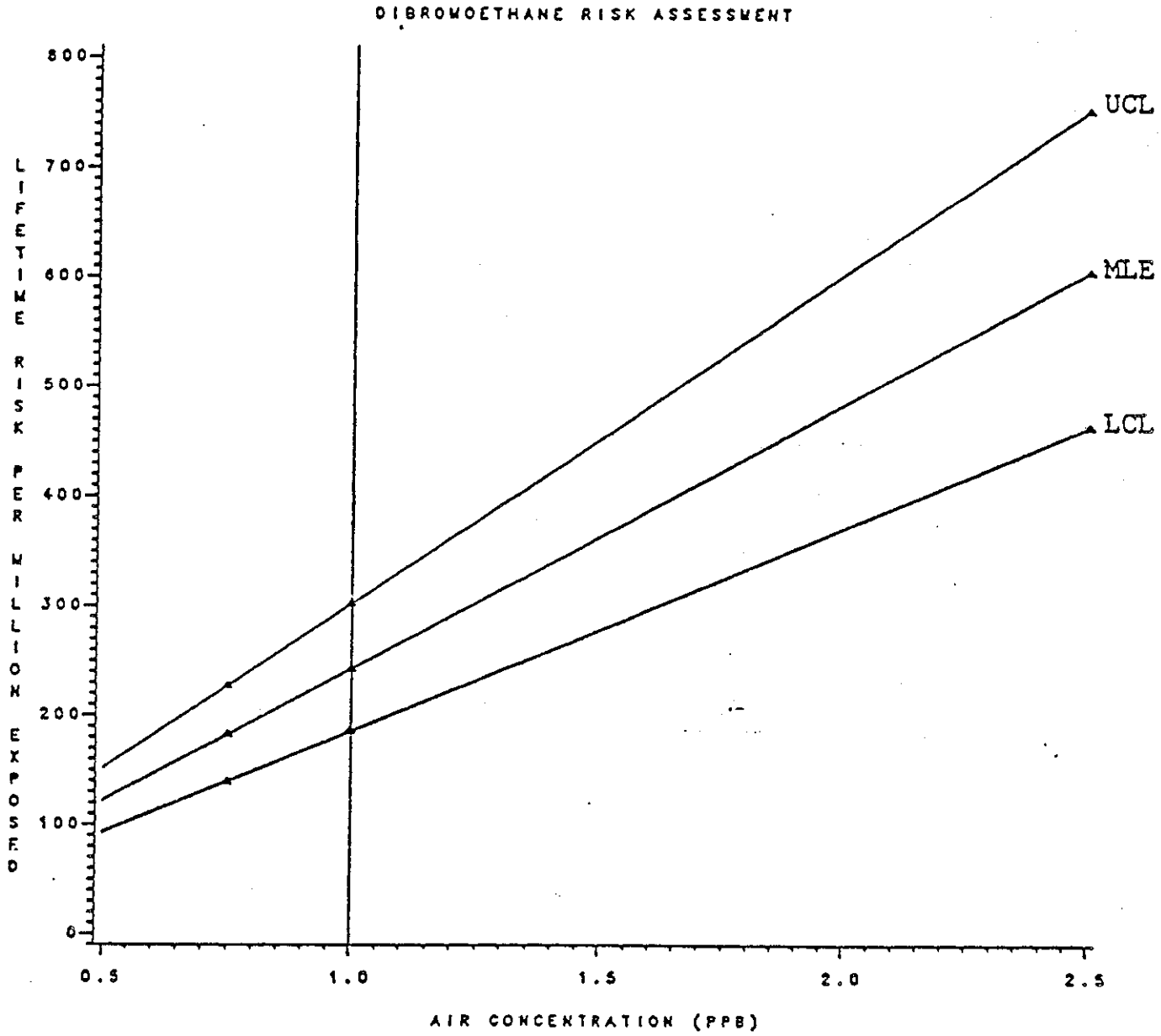


FIGURE 1. Lifetime Risk Estimates in Terms of Cancers per Million Persons Exposed at Various Airborne Concentrations of Ethylene Dibromide. UCL = 95% Upper Confidence Limit on Risk. MLE = Maximum Likelihood Estimate of Risk. LCL = 95% Lower Confidence Limit on Risk. [Data are for nasal cavity malignancies in male rats as reported in reference 1.]

REFERENCES

1. Health Effects of Ethylene Dibromide (EDB), Epidemiological Studies Section, Department of Health Services, Berkeley, California, November 30, 1984. (Data provided on page D-2)

2. GLOBAL 82 : A Computer Program to Extrapolate Quantal Animal Toxicity Data to Low Doses. R. B. Howe and K. S. Crump, May, 1982 (A more recent version of this model, GLOBAL85, was used to calculate the risk estimates used in these comments. This version calculates both upper and lower confidence limits).

3. The risk estimates given in the DOHS report on EDB are slightly higher than those presented here. These differences are probably due to slightly different computational techniques.