NIOSH

A Recommended Standard for Occupational Exposure to.....

DIBROMOCHLOROPROPANE

The National Institute for Occupational Safety and Health (NIOSH) recommends that employee exposure to dibromochloropropane in the workplace be controlled so that no worker will be exposed to dibromochloropropane in excess of 10 ppb (0.1 mg/cu m) in air. The NIOSH recommendations is to restrict exposure to very low levels that can still be reliably measured in the workplace. The recommended exposure limit of 10 ppb is above the lowest level at which a reliable estimate of occupational exposure to dibromochloropropane can be determined at this time. The recommended standard contains recommendations for medical surveillance, informing employees of hazards, sanitation, work practices, labeling and posting, personal protective clothing and equipment, monitoring and recordkeeping.

The recommended standard is designed to protect the health and provide for the safety of employees for up to a 10-hour shift, 40-hour workweek, over a working lifetime. Compliance with all sections of the standard should, at the minimum, substantially reduce adverse effects of exposure to dibromochloropropane in the workplace. The employer should regard the recommended workplace environmental limit as the upper bondary for exposure and make every effort to keep the exposure as low as possible.

The possible effects on the health of employees chronically exposed to DBCP may include sterility, diminished renal function, and degeneration and cirrhosis of the liver. In addition, ingestion of daily doses of DBCP by mice and rats has been found to result in the appearance of gastric cancers in both sexes of both species and in mammary cancers in female rats. Although an increased risk for cancer has not been seen with inhalation exposures, these results are not definitive, therefore the risk of cancer due to occupational exposure to DBCP remains a continuing concern. There are indications from *in vitro* experiments that mutagenic effects may occur also, but there has been no study yet of this possibility with mammalian subjects. Employees should be told of these possible effects and informed that some 20-25 years of experience in the manufacture and formulation of DBCP has not yet called such effects in employees of the pesticide industry to the notice of physicians and epidemiologists. A more detailed review of the known health effects are given in Enclosure 1.

The recommended standard is part of a continuing series of recommendations developed by NIOSH in accordance with the Occupational Safety and Health Act of 1970. The recommended standard is being transmitted to the Department of Labor, September 2, 1977, for review and consideration in the preparation of an emergency temporary standard. If research by NIOSH results in the development of improved methods for sampling and analysis of dibromochloropropane in air from the occupational environment, information regarding the new methods will be forwarded to the Department of Labor.

U. S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
Public Health Service
Center for Disease Control
National Institute for Occupational Safety and Health

I. RECOMMENDATIONS FOR A TEMPORARY EMERGENCY STANDARD FOR OCCUPATIONAL EXPOSURE TO DIBROMOCHLOROPROPANE

The National Institute for Occupational Safety and Health (NIOSH) recommends that employee exposure to dibromochloropropane (DBCP) in the workplace be controlled by adherence to the following sections. The standard is designed to protect the health and provide for the safety of employees for up to a 10-hour work shift, 40-hour workweek, over a working lifetime. Compliance with all sections of the standard should, at the minimum, substantially reduce the effects of DBCP on the health of employees and provide for their safety. The employer should regard the recommended workplace environmental limit as the upper boundary for exposure and make every effort to keep the exposure as low as possible. The criteria and standard will be subject to review and revision as necessary.

The possible effects on the health of employees chronically exposed to DBCP may include sterility, diminished renal function, and degeneration and cirrhosis of the liver. In addition, ingestion of daily doses of DBCP by mice and rats has been found to result in the appearance of gastric cancers in both sexes of both species and in mammary cancers in female rats. Although an increased risk for cancer has not been seen with inhalation exposures, these results are not definitive, therefore the risk of cancer due to occupational exposure to DBCP remains a continuing concern. There are indications from *in vitro* experiments that mutagenic effects may occur also, but there has been no study yet of this possibility with mammalian subjects. Employees should be told of these possible effects and informed that some 20-25 years of experience in the manufacture and formulation of DBCP has not yet called such effects in employees of the pesticide industry to the notice of physicians and epidemiologists. A more detailed review of the known health effects are given in Enclosure 1.

Sampling methods utilizing both charcoal and Florisil® tubes have been reported to NIOSH as acceptable for measurements at the recommended environmental limit. However, an evaluation of the suggested methods has not yet been completed by NIOSH. Such a laboratory evaluation should be completed in the first part of FY 78.

"Occupational exposure to dibromochloropropane" refers to any workplace situation in which DBCP is manufactured, formulated, or stored. All sections of the standard shall apply where there is occupational exposure to DBCP.

Section 1 — Environmental (Workplace Air)

(a) Concentration

Dibromochloropropane shall be controlled in the workplace so that no employee is exposed to airborne dibromochloropropane, at a concentration greater than 10 parts per billion (approximately 0.1 mg/cu m) determined as a time weighted average (TWA) concentration for up to a 10-hour work shift, 40-hour workweek.

(b) Sampling and Analytical Methods

The environmental limit represents a concentration of dibromochloropropane measurable by reported sampling and analytical methods.

Section 2 — Medical

Medical surveillance shall be made available to employees as outlined below:

(a) Comprehensive preplacement or initial medical and work histories with emphasis on reproductive experience and menstrual history.

(b) Comprehensive physical examination with emphasis on the genito-urinary tract including testicle size and consistency in males.

(1) Semen analysis to include sperm count, motility and morphology.

(2) Other tests, such as serum testosterone, serum follicle stimulating hormone (FSH), and serum lutenizing hormone (LH) may be carried out if, in the opinion of the responsible physician, they are indicated. In addition, screening tests of the renal and hepatic systems may be considered.

(3) A judgment of the worker's ability to use positive pressure respirators.

(c) Employees shall be counseled by the physician to ensure that each employee is aware that DBCP has been implicated in the production of effects on the reproductive system including sterility in male workers. In addition, they should be made aware that cancer has been produced in some animals. While the relevancy of these findings are not yet clearly defined, they do indicate that both employees and employers should do everything possible to minimize exposure to DBCP.

(d) Periodic examinations containing the elements of the preplacement or initial examination shall be made available on at least an annual basis.

(e) Examinations of current employees shall be made available as soon as practicable after the promulgation of a standard for DBCP.

(f) Medical surveillance shall be made available to any worker suspected of having been exposed to DBCP.

(g) Pertinent medical records shall be maintained for all employees subject to exposure to DBCP in the workplace. Such records shall be maintained for

at least 30 years after termination of employment. These records shall be made available to the designated medical representatives of the Secretary of Health, Education, and Welfare, of the Secretary of Labor, of the employer, the employee, or former employee.

Section 3 — Labeling and Posting

A label shall be placed on each shipping and storage container of dibromochloropropane and all areas where there is occupational exposure to dibromochloropropane shall be posted.

All warning signs shall be printed both in English and in the predominant language of non-English-reading workers. Illiterate workers and workers reading languages other than those used on labels and posted signs shall be informed of the hazardous areas and shall be informed of the instructions printed on labels and signs.

(a) Labeling

Each container of dibromochloropropane shall carry in a readily visible location a label stating:

DIBROMOCHLOROPROPANE

(Trademark, Common Name, or Chemical Name)

WARNING!!

BREATHING VAPOR MAY BE HAZARDOUS TO HEALTH
CAN BE FATAL IF SWALLOWED
HARMFUL IF ABSORBED THROUGH SKIN

Avoid breathing vapor.
Use only with adequate ventilation.
Keep containers closed when not in use.
Wash thoroughly before eating, drinking, smoking, or using toilet.
If swallowed, induce vomiting immediately if patient is conscious. Call a physician.

(b) Posting

Warning placards shall be affixed in readily visible locations in or near areas where there is occupational exposure to dibromochloropropane. The information shall be arranged as in the following example:

DIBROMOCHLOROPROPANE

HARMFUL IF INHALED
CAN BE FATAL IF SWALLOWED

If respiratory protection is required in accordance with Section 4, the following statement in large letters shall be added to the required sign:

RESPIRATORY PROTECTION REQUIRED IN THIS AREA

Section 4 — Personal Protective Equipment and Clothing

(a) Respiratory Protection

(1) Engineering controls shall be used wherever needed to keep airborne dibromochloropropane concentrations below the recommended occupational exposure limit. Compliance with this limit may be achieved by the use of respirators under the following conditions only:

(A) During the time necessary to install or test the required engineering controls.

(B) For nonroutine operations, such as emergency maintenance or repair activities.

(C) During emergencies when air concentrations of dibromochloropropane may exceed the recommended occupational exposure limit.

(2) When a respirator is permitted by paragraph (a)(1) of this section, it shall be selected and used pursuant to the following requirements:

(A) The employer shall ensure that no employee is exposed to dibromochloropropane because of improper respirator selection, fit, use, or maintenance.

(B) The employer shall establish and enforce a respirator program meeting the requirements of 29 CFR 1910.134 as amended.

(C) The employer shall provide respirators in accordance with Table I-1 and shall ensure that the employee uses the respirator provided when necessary.

(D) Respiratory protective devices described in Table I-1 shall be those approved under the provisions of 30 CFR 11.

(E) Respirators specified for use in higher concentrations of dibromochloropropane may be used in atmospheres of lower concentrations.

(F) The employer shall ensure that respirators are adequately cleaned and maintained, and that employees are instructed and drilled, at least annually, in the proper use and testing for leakage of respirators assigned to them.

(G) Respirators shall be easily accessible and employees shall be informed of their location.

(b) Eye protection

Eye protection shall be provided by the employer and used by the employees where eye contact with liquid dibromochloropropane is likely. Selection, use, and maintenance of eye protective equipment shall be in accordance with the provisions of the American National Standard Practice for Occupational and Educational Eye and Face Protection, ANSI Z87.1-1968. Unless eye protection is afforded by a respirator hood or facepiece, protective goggles [splash-proof safety goggles (cup-cover type dust and splash safety goggles) which comply with 29 CFR 1910.133(a)(2)—(a)(6)] or a face shield (8-inch minimum) shall

TABLE I-1
RESPIRATOR RECOMMENDATIONS FOR
1,2-DIBROMO-3-CHLOROPROPANE

CONCENTRATION	PERMISSIBLE RESPIRATORY PROTECTION
Up to 50 times the PEL	Any supplied-air respirator with a full facepiece, helmet or hood (30 CFR 11.110(A)).
	Any self-contained breathing apparatus with a full facepiece (30 CFR 11.70(A)).
50—2,000 times the PEL	A Type C supplied-air respirator with a full facepiece operated in pressure-demand or other positive pressure mode with a full facepiece, hood or helmet operated in continuous flow mode (30 CFR 11.110(A)).
50—10,000 times the PEL	Self-contained breathing apparatus with a full facepiece operated in pressure-demand or other positive pressure mode (30 CFR 11.70(A)).
	A combination respirator which includes a Type-C supplied-air respirator with a full facepiece operated in pressure-demand or other positive pressure or continuous flow mode and an auxiliary self-contained breathing apparatus operated in pressure-demand or positive pressure mode (30 CFR 11.70(B)).
Escape	Any self-contained breathing apparatus (30 CFR 11.70(A)).
	Any gas mask providing protection against organic vapors (30 CFR 11.90).

be worn at operations where there is danger of contact of the eyes with liquid dibromochloropropane because of spills or splashes. If there is danger of liquid dibromochloropropane striking the eyes from underneath or around the sides of the face shield, safety goggles shall be worn as added protection.

(c) Protective Clothing

Protective clothing shall be resistant to the penetration and to the chemical action of dibromochloropropane. Additional protection, including gloves, bib-type aprons, boots, and overshoes, shall be provided for, and worn by, each employee during any operation that may cause direct contact with liquid dibromochloropropane. Supplied-air hoods or suits resistant to penetration by dibromochloropropane shall be worn when entering confined spaces, such as pits or storage tanks. In situations where heat stress is likely to occur, supplied-air suits, preferably cooled, are recommended. The employer shall ensure that all personal protective clothing is inspected regularly for defects and is maintained in a clean and satisfactory condition by the employee.

Section 5 — Informing Employees of Hazards from Dibromochloropropane

(a) All new and present employees working where occupational exposure to dibromochloropropane may occur shall be informed orally and in writing of the hazards, relevant signs and symptoms of exposure, appropriate emergency procedures, and proper conditions and precautions concerning safe use and handling of dibromochloropropane. This information should be readily available to all employees involved in the manufacture, formulation, or storage of dibromochloropropane and shall be posted in prominent positions within the workplace.

(b) All employees involved with the manufacture, formulation, or storage of dibromochloropropane shall be informed that it has been implicated in human reproductive abnormalities and has induced gastric cancers in animals following oral intubation.

(c) Employers shall institute a continuing education program to ensure that all employees have current knowledge of job hazards, maintenance procedures, cleanup methods, emergency procedures, and evacuation procedures. This program shall include at least:

Emergency procedures and drills.
Instruction in handling spills and leaks.

Decontamination procedures.
Location and use of firefighting equipment.
First-aid procedures, equipment location, and use.
Rescue procedures.
Confined space entry procedures.

Records of such training shall be kept for inspection by authorized personnel as required. This program shall be held for all employees with occupational exposure to dibromochloropropane at intervals not greater than quarterly, or whenever there is a process change.

(d) Information as required shall be recorded on the "Material Safety Data Sheet," or on a similar form approved by the Occupational Safety and Health Administration, U.S. Department of Labor.

Section 6 — Work Practices

(a) Emergency Procedures

For all work areas where emergencies may occur, the employer shall take all necessary steps to ensure that employees are instructed in and follow the procedures specified below and any others appropriate to the specific operation or process.

(1) Procedures shall include at least prearranged plans for re-entry into areas where dibromochloropropane leaks or spills have occurred for clean-up, decontamination, or maintenance purposes.

(2) Evacuation alarm systems shall be provided by the employer.

(3) Personal protective equipment and clothing as specified in Section 4 shall be used by trained personnel essential to emergency operations.

(4) Nonessential employees shall be evacuated from hazardous areas during emergencies. Perimeters of these areas shall be delineated, posted, and secured. The employees in adjacent areas shall be trained in evacuation procedures if these work areas become involved.

(5) Only personnel trained in the emergency procedures and protected against the attendant hazards shall shut off sources of dibromochloropropane, clean up spills, control and repair leaks, and fight fires in dibromochloropropane areas.

(6) Firefighting procedures shall be established for areas where flammable materials are used with dibromochloropropane. Chemical foam, carbon dioxide, or dry chemicals shall be used for fighting fires in areas where dibromochloropropane is present. Proper protective respirators and clothing shall be worn by all personnel in the hazard area until concentrations of airborne dibromocholorpropane have been demonstrated by monitoring to be below the recommended occupational exposure limit.

(7) Showers, eyewash fountains, and washroom facilities shall be provided and so located as to be readily accessible to workers in all areas where skin or eye contact with liquid dibromochloropropane is likely. If liquid dibromochloropropane is splashed on the clothing or skin, contaminated clothing shall be promptly removed and the skin washed thoroughly with soap and water. If liquid dibromochloropropane gets into the eyes, they shall be irrigated immediately with copious quantities of running water.

(8) Medical attention shall be provided promptly for any affected worker. Such exposures shall be reported to the immediate supervisor by the affected worker or by a fellow employee.

(b) Control of Airborne Dibromochloropropane

(1) Suitable engineering controls designed to limit exposure to dibromochloropropane to that prescribed in Section 1(a) shall be used. The use of completely enclosed processes is the recommended method of control for dibromochloropropane. Local exhaust ventilation may also be effective, used alone or in combination with process enclosure. When a local exhaust ventilation system is used, it shall be designed to prevent the accumulation or recirculation of ventilation control or process air in the workroom, to maintain dibromochloropropane concentrations below the limit of the recommended standard, and to remove dibromochloropropane from the breathing zones of employees. Exhaust systems discharging into outside air must conform with applicable local, state, and federal air pollution regulations. Ventilation systems shall be subjected to regular preventive maintenance and cleaning to ensure effectiveness, which shall be verified by periodic airflow measurements at least every 3 months. Measurements of system efficiency shall also be made immediately by personnel properly attired in specific protective equipment when any change in production, process, or control might result in increased concentrations of airborne dibromochloropropane. Tempered makeup air shall be provided to work areas in which exhaus ventilation is operating.

(c) Handling of Dibromochloropropane and General Work Practices

(1) Written operating instructions and emergency medical procedures shall be formulated and posted where dibromochloropropane is handled or used.

(2) Prompt medical attention shall be provided if there is known or suspected exposure to dibromochloropropane, whether or not symptoms are present.

(3) The employer shall ensure that safety showers, eyewash fountains, and other emergency equipment is in proper working order through reg-

ularly scheduled inspections performed by qualified maintenance personnel.

(4) Dibromochloropropane operating systems shall be inspected daily for signs of leaks by personnel attired in specified protective equipment. All equipment including valves, fittings, and connections shall be checked for tightness and good working order. All newly made connections shall be checked for leaks immediately after dibromochloropropane is introduced by trained personnel attired in prescribed personal protective equipment.

(5) If there is a leak, the leak shall be corrected immediately. Work shall resume normally only after necessary repair or replacement has been completed, the area has been ventilated, and the concentration of dibromochloropropane has been determined by monitoring to be below the recommended occupational exposure limit.

(6) Transportation and use of dibromochloropropane shall comply with all applicable local, state, and federal regulations. Strict adherence to the pesticide container label requirements for application and personal protection shall be followed. Additional standards for pesticide use by agricultural workers can be found in 40 CFR 170.

(7) When dibromochloropropane containers are being moved, or when they are not in use and are disconnected, valve protection covers shall be in place. Containers shall be moved only with the proper equipment and shall be secured to prevent dropping or loss of control while moving.

(8) Process valves and pumps shall be readily accessible and should not be located in pits and congested areas.

(9) Containers and systems shall be handled and opened with care. Approved protective equipment as specified in Section 4 shall be worn while opening, connecting, and disconnecting dibromochloropropane containers and systems. Adequate ventilation shall be available to prevent exposure to dibromochloropropane when opening containers and systems.

(10) Personnel shall work in teams when dibromochloropropane is first admitted to a system, while repairing leaks, or when entering a confined or enclosed space.

(d) Work Areas

(1) Dibromochloropropane Hazard Areas

A hazard area shall be considered as any space workers may enter that has physical characteristics and sources of dibromochloropropane that could result in air concentrations exceeding the recommended limit. Exits shall be plainly marked and shall open outward. Emergency exit doors shall be conveniently located and shall open into areas which will remain free of contamination in an emergency. At least two separate means of exit shall be provided from each room or building in which dibromochloropropane is stored, handled, or used in quantities that could create a hazard.

(2) Confined or Enclosed Spaces

Entry into confined spaces, such as tanks, pits, process vessels, tank cars, sewers, or tunnels, where there may be limited egress shall be controlled by a permit system. Permits shall be signed by an authorized employer representative certifying that preventive and protective measures have been followed.

Confined spaces which have contained dibromochloropropane shall be thoroughly ventilated to ensure an adequate supply of oxygen, tested for dibromochloropropane and other contaminants, and inspected for compliance with these requirements prior to each entry. Adequate ventilation shall be maintained while workers are in the space. Leakage of dibromochloropropane into the confined space while work is in progress shall be prevented by disconnecting and blanking the dibromochloropropane supply lines. An individual entering confined spaces shall be furnished with appropriate personal protective equipment and protected by a lifeline harness tended by another worker outside the space, who shall also be equipped for entry with approved personal protective equipment and who has contact with a third party. Communication (visual, voice, signal line, telephone, radio, or other suitable means) shall be maintained by the standby person with the employee inside the confined or enclosed space. A third employee, equipped to proceed to the aid of the other two if necessary, shall have general surveillance of their activities.

(e) Storage

(1) Storage facilities shall be designed to contain spills completely within a surrounding dike and to prevent contamination of workroom air.

(2) Storage of dibromochloropropane in the same area as reactive metals, such as aluminum or magnesium, or as liquid ammonia shall be prohibited.

(3) Storage containers shall be periodically inspected for leakage.

(4) Ventilation switches and emergency respiratory equipment shall be located outside storage areas in readily accessible locations which will be free of dibromochloropropane in an emergency.

(f) Spills, Leaks, and Waste Disposal

(1) If dibromochloropropane leaks or is spilled, the following steps shall be taken:

(A) Evacuate all nonessential personnel from the area.

(B) Adequately ventilate the area of the

spill or leak to prevent accumulation of the vapor.

(C) If in liquid form, collect spilled material for reclamation or absorb in vermiculite, dry sand, earth, or similar nonreactive material.

(D) If in solid form, collect spilled material in the most convenient and safe manner for reclamation or for disposal.

(2) Personnel entering the spill or leak area shall be furnished with appropriate personal protective equipment. All other personnel shall be excluded from the area.

(3) All wastes and residues containing dibromochloropropane shall be collected in dibromochloropropane resistant containers and incinerated or buried in such a manner that no dibromochloropropane or toxic decomposition products are released to the environment.

Section 7 — Sanitation Practices

(a) Plant sanitation shall meet the requirements of 29 CFR 1910.141.

(b) Appropriate locker rooms shall be available for changing into required protective clothing in accordance with 29 CFR 1910.141(e). Clothing contaminated with liquid dibromochloropropane shall be immediately removed and placed in a closed container in a well-ventilated area for later disposal or decontamination. Employers shall require personnel who work with dibromochloropropane to shower before leaving the workplace at the end of a workday.

(c) Employers shall ensure that employees who handle dibromochloropropane wash their hands thoroughly with soap and water before eating, smoking, or using toilet facilities.

(d) The storage, dispensing, preparation, and consumption of food, beverages, or tobacco shall be prohibited in dibromochloropropane work areas.

(e) The employer shall ensure that personnel who launder and clean clothing or equipment contaminated with dibromochloropropane are provided adequate personal protective equipment to prevent exposure and shall ensure that these employees are aware of the potential hazards of exposure to dibromochloropropane.

Section 8 — Monitoring and Recordkeeping Requirements

(a) Industrial hygiene surveys shall be made in any workplace where dibromochloropropane is handled, processed, or stored. Records of these surveys, including the basis for concluding that environmental concentrations are below the recommended limit shall be maintained. Surveys shall be repeated every month or whenever a process change is made.

(b) Where exposure concentrations have not been determined, they shall be determined as soon as practicable after the promulgation of a standard based on these recommendations.

(c) Requirements set forth below apply to work areas where there is occupational exposure to dibromochloropropane.

(1) An adequate number of samples shall be collected monthly for the evaluation of the work environment with respect to the occupational exposure of the employees.

(2) Environmental samples shall be taken when a new process is installed or process changes are made which may cause an increase in environmental concentrations. Significantly increased production, relocation of existing operations, interruption of normal maintenance schedules, or other function which may increase dibromochloropropane concentrations shall require resampling and analysis.

(3) The minimum number of representative exposure determinations for an operation or process shall be based on variations in exposures and production schedules and in accordance with the provisions prescribed in Section 1(b).

(4) If initial, periodic, or special evaluations indicate that the recommended limit is exceeded, corrective engineering or other control measures shall be immediately instituted to ensure the safety of employees until a concentration below the occupational exposure limit is achieved. In such cases, sampling of each operation and work location shall be conducted until two consecutive employee exposure measurements, taken at least 1 week apart, reveal that the employee is not exposed to dibromochloropropane above the recommended occupational exposure limit. Employers shall notify in writing, within 5 days, every employee who is found to be exposed to dibromochloropropane above the recommended environmental limit.

(d) Employers or their successors shall maintain records which shall include sampling and analytical methods, types of respiratory protection used, concentrations found, and information concerning exposure of employees to dibromochloropropane. Each employee shall have access to data on his or her own environmental exposures. Pertinent records of occupational accidents and environmental exposures within the workplace shall be kept for at least 30 years after the worker's employment has ended. Records of occupational exposures applicable to an employee should be included in that employee's medical records. The medical representatives of the Secretary of Health, Education, and Welfare, of the Secretary of Labor, of the employee or former employee, and of the employer shall have access to all such records.

APPENDIX I

METHOD FOR SAMPLING DIBROMO-CHLOROPROPANE IN AIR

The following method is based on detailed reports from two representatives of the Shell Development Company. These reports have been communicated only by telephone. The method has not been published and has not been evaluated in NIOSH laboratories. The method has been tested by Shell with a number of field samples.

Procedure

1. An air sample is collected on a tube of Florisil.®
2. If the samples cannot be analyzed immediately after collection, the samples should be stored at —200°C. The refrigerated samples may be stored for two weeks or less.
3. The 1,2-dibromo-3-chloropropane is desorbed from the Florisil® with hexane.
4. Analysis is accomplished with a gas chromatograph equipped with an electron-capture detector.

Useful Range

The method is applicable to air concentrations ranging from 1 to 100 parts per billion (0.01 to 1 mg/cu m).

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ATTACHMENT I

LITERATURE REVIEW FOR DIBROMOCHLOROPROPANE

Background: 1,2-dibromo-3-chloropropane (DBCP) has the formula CH_2Br-$CHBr$-CH_2Cl. It has a gram molecular weight of 236.36. An amber to brown liquid with a pungent odor, DBCP has a specific gravity of 2.09 at 14°C referred to water. It has an index of refraction of 1.553 at 14°C for the D-line of the emission spectrum of sodium. DBCP has a vapor pressure of less than 1 mm of Hg at 21°C and boils at 199°C under a pressure of 760 mm of Hg. It is miscible with aliphatic and aromatic hydrocarbons, isopropyl alcohol, 1,2-dichloropropane, tetrachloroethylene, 1,1,2-trichloroethane, and oils. The undiluted material has no flash nor fire point. Because DBCP has been diluted commonly with kerosene or other flammable solvents, the preparations available in the market place may have flash points in the vicinity of 35-36°C (Tagliabue closed cup).

DBCP has been used in agriculture as a nematocide since 1955, being supplied for such use in the forms of liquid concentrate, emulsifiable concentrate, powder, granules, and solid material. Formulations of DBCP were registered for use as fumigant nematocides in 1964 on evidence that residues of the material as such would not remain on harvested raw agricultural commodities and that the only residue would consist of inorganic bromides. Newsome et al. (1977) reported, however, that substantial amounts of DBCP were found in radishes (up to 0.20 ppm) and carrots (up to 1.55 ppm in roots and 0.64 ppm in the tops) grown in soil treated with this fumigant. The estimated use of DBCP in the United States in recent years has ranged from 3.6 million pounds in 1971 to 12.3 million pounds in 1972 (USDA estimates).

In 1971, more than 59% of the DBCP used was applied in the Pacific Coast states (Andrilenas, 1974). The material is sold under such names as Nemagon, Fumazone, Nemafume, Nemaset, and Nematox.

On August 5, 1977, the National Institute for Occupational Safety and Health (NIOSH) was requested by the Oil, Chemical and Atomic Workers (OCAW) union to conduct a health hazard evaluation at the Oxidental Chemical Company plant in Lathrop, California. This request was made when representatives of OCAW learned that a number of workers at this plant had abnormally low sperm counts.

On August 9 and 10, NIOSH conducted a walk-through inspection of the Lathrop plant and met with representatives from the company, the local union, and California OSHA. NIOSH staff also met with Dr. Whorton, Univ. of Calif., Berkeley, who had consulted with the company and the union previously and who had conducted medical examinations of the affected employees. Medical examinations of a number of additional employees have subsequently been conducted by NIOSH staff in conjunction with Dr. Whorton.

On August 12, the Occupational Safety and Health Administration in a telegram alerted approximately 80 manufacturers and formulators to the potential hazard of worker exposure to DBCP. On August 23, a guideline document detailing suggested work practices was forwarded to these same affected companies.

On August 19, the Director, NIOSH, wrote to the major manufacturers of DBCP requesting information to fully evaluate the extent of the hazard posed by exposure to DBCP.

Animal Toxicity. Torkelson et al. (1961) reported that results of studies of the toxicity of DBCP for various species of animals by two different laboratories (A and B). Rakhmatulayev (1971) also has reported the results of similar studies. The various estimates of oral LD50 values for different species are listed below in mg/kg:

	Torkelson et al.		*Rakhmatulayev*
	A	*B*	
Female Mouse	260	410	
Male Rat	170	300	
Rat			350
Male Guinea Pig		210	
Guinea Pig			316
Male Rabbit		180	
Rabbit			440
Chicken		60	

Rakhmatulayev listed the effects of lethal doses as being brief central excitation followed by depression, analgesia, uncoordinated activity of skeletal muscles, and paralysis of limbs.

Torkelson et al. (1961) reported also that DBCP as a 1% solution in propylene glycol or as undiluted liquid dropped into conjunctival sacs of rabbits' eyes produced slight irritation and pain of the conjunctivae and iris. These effects disappeared after 1-2 days. Washing the eyes with water 30 seconds after contact with DBCP did not alter the conjunctival and iridial responses.

Applications of 0.5 ml of DBCP to the shaven backs of 4 rabbits produced slight erythema in abraded areas of skin and no signs of irritation in intact skin (Torkelson et al., 1961). Repetition of such applications resulted in only a slight crustiness of the skin after 20 applications. The dermis and subcutaneous tissue at the site of application in one rabbit had extensive necrosis and infiltration with polymorphonuclear leucocytes upon microscopic examination. An unspecified number of other rabbits subjected to repeated, covered applications of a 10% solution of DBCP in the methylether of dipropylene glycol to their shaven bellies, the applications being renewed every 24 hours up to a total of 10 applications, had no lesions other than slight hyperemia and scaliness of the skin at the site of application. Percutaneous LD50's for the rabbit were 1400 mg/kg when undiluted DBCP was applied for 24 hours and 500 mg/kg when DBCP was applied as a 10% solution in propylene glycol.

Rats reported by Torkelson et al. (1961) to have been exposed to vaporized DBCP were observed to become apathetic, sluggish and ataxic but not to be completely narcotized. Clouding of the cornea or lens was seen with exposures to the higher concentrations (up to about 400 ppm). Laboratory A found that the LC50 fell from about 400 ppm with a 1-hour exposure to one of about 110 ppm for a 7-hour exposure. Laboratory B did not estimate LC50's but obtained mortalities in groups of rats that suggest a relationship between duration of exposure and LC50 fairly similar to that found by laboratory A within the range of durations of exposure used by the latter group. Laboratory B found that a concentration of about 290 ppm killed 2/12 rats at an exposure duration of 12 minutes, 3/12 rats at one of 30 minutes, and 3/12 rats at one of 60 minutes. These values suggest, but do not demonstrate, that the same straight line relationship between log concentration and duration of exposure found by Laboratory A for durations of 1 to 7 hours may not obtain with durations of exposure less than 1 hour.

Fifty inhalation exposures lasting for 7 hours, 5 days/week, of male rats to a concentration of DBCP of 5 ppm killed 0/15 animals, one to 10 ppm killed 2/15, and one to 20 ppm killed 10/15. Even the lowest of these concentrations produced a decrease of 18.6% in the mean weight of the testes. This was not a statistically significant decrease. Exposure to the next higher concentration (10 ppm) produced a statistically significant decrease (49.0%) in the mean weight of the testes. Exposure to that concentration also resulted in a significant increase in the weight of the kidney (31.7%). These studies were performed by Laboratory A (Torkelson et al., 1961).

Laboratory B (Torkelson et al., 1961) exposed male and female rats to 50 7-hour exposures to 12 ppm of DBCP. These exposures resulted in the deaths of 8/20 male and of 10/20 female rats, degenerative changes in the seminiferous tubules, reduction in the number of sperm cells, increase in the proportion of abnormal sperm cells, increase in the number of Sertoli cells in the males, significant increases in the weights of the kidneys in both sexes with cloudy swelling of the epithelium of the proximal convoluted tubules and increased amounts of interstitial tissue in the kidneys of the males, and dilatation of the sinusoids and centrilobular congestion in the livers of both sexes.

Laboratory B (Torkelson et al., 1961) also gave to guinea pigs and rabbits 66 7-hour exposures to vaporized DBCP in a concentration of 12 ppm. These exposures killed no animals but did result in statistically significant decreases in the mean weights of the testes in both species. Two female monkeys exposed for 50 and 60 times, respectively, to 12 ppm of DBCP developed severe leukopenias and anemias. The concentrations of bromide in the sera of the exposed rats, guinea pigs, and rabbits ranged between 6.7 and 12.8 mg/100 ml whereas those of the control animals of these 3 species ranged from 0 to 7.8 mg/100 ml.

Torkelson et al. (1961) reported also the results from a 90-day feeding study with rats of both sexes. The concentrations of DBCP in the diet were 0, 5, 20, 50, 150, 450, and 1350 ppm. The kidneys of female rats fed diets with concentrations of 20 or more ppm of DBCP and the livers of those fed diets containing 450 or more ppm were significantly heavier than those of the controls. Only those males fed the diet including 1350 ppm of DBCP had kidneys and livers significantly heavier than those of the controls.

These studies revealed that DBCP had two outstanding toxic effects in subacute exposures: an antispermiogenic effect in the male and a nephrotoxic effect that occurred in both sexes of the rat, but especially in the female. Laboratory B was able to show that neither the adrenocorticotropic hormone (ACTH), cortisone, nor testosterone altered beneficially the effect of DBCP on the testes. Indeed, testosterone enhanced the atrophic effect of DBCP.

The final bit of information in the paper by Torkelson et al. (1961) was that men given brief exposure to a concentration of 1.7 ppm of DBCP described a definite, not unpleasant, odor. The authors recommended that occupational exposure to DBCP be controlled to hold the airborne concentration of the nematocide below 1 ppm.

Rakhmatulayev (1971) also reported results from a subacute (2½ months' duration) and a chronic (8 months' duration) experiment using rats and

administering DBCP by mouth in doses of 17.5-70 mg/kg (subacute) and .0005-5 mg/kg (chronic). The most sensitive indicators of toxic activity by DBCP in these experiments were reductions in the weight of the testes and in duration of motility of spermatozoa, decreased avidity of leucocytes for engulfing bacteria and decreased rate of positive conditioning. These effects were present with the dose of 0.05 mg/kg, but not with that of 0.005 mg/kg, in the chronic exposure study.

Faydysh (1973) performed another study of the effect of prolonged administration (5 months) of DBCP in oral doses of 0.05, 0.5, and 5.0 mg/kg. The two highest doses were observed to decrease both the activity of neutrophils in engulfing and digesting bacteria and the concentration of these cells in the blood. These results confirm the report of Rakhmatulayev (1971) mentioned just above. Because phagocytically-mediated immunity is one of the defensive mechanisms of the body against conditions related to proliferation of abnormal cells, these effects of DBCP may contribute to the carcinogenic activity of this compound in experimental animals.

Faydysh et al. (1970) and Faydysh and Avkhimenko (1974) studied further the effects of DBCP on testicular function. In the first study, 10 male rats were given daily oral doses of 70 mg/kg of DBCP in sunflower seed oil. Ten other male rats were given corresponding volumes of the sunflower seed oil alone. Five of the rats given DBCP died between days 20 and 25 of the experiment; the other 5 lived through the 45 days of the experiment. At necropsy, all internal organs were pallid and the gastric mucosa was noted to have been thinned. Although the blood was not examined specifically, the authors' description of the general appearance of the internal organs and of the vascular system raises a suspicion that there was marked anemia. The major parenchymatous organs, particularly the liver and kidneys, and the testes had undergone pronounced necrotic effects. The livers contained areas of cirrhosis replacing necrotised tissue and the spleens had areas of necrosis in both the white and the red pulps. The parenchyma destroyed in the testes also was replaced by scar tissue. Some regenerative activity was visible in the parenchymatous organs. The second paper demonstrated that similar changes could be accomplished by a daily dose of 0.5 mg/kg given during a longer period of time. This suggests that DBCP exerts some relatively, or possibly completely, irreversible action that eventually accumulates to produce a deleterious effect on target organs.

Reznik and Sprinchan (1975) studied the gonadotropic actions of DBCP in both male and female rats. Single oral doses of 100 mg/kg or daily doses of 10 mg/kg, administered for 4 to 5 months, were used. The single dose produced within one week a decrease in the sperm count in the semen from 4.9±0.2 million/mg to 2.6±0.3 million/mg. At the same time, there was a decrease in the duration of mortility of the spermatozoa from about 31 minutes to about 15 minutes. In the females, the estrus cycle was prolonged, both estrus and diestrus becoming longer.

The repeated doses of DBCP eventually produced effects similar to those that followed the single large dose. By the fourth month of administration, the concentration of spermatozoa in the semen was 2.5±0.5 million/mg vs 4.9±0.3 million/mg in the controls and the duration of motility of the spermatozoa was 29 minutes whereas that of spermatozoa from control rats was 51 minutes. During the first month of daily doses, 24% of the females developed atypical estrus cycles; by the fifth month, this figure rose to 70%. At the same time, the duration of the cycles increased; 57% of the females became acyclic by the fifth month. It is apparent, therefore, that an effect on sperm count in the male may not be the only effect on human fertility from occupational exposure to DBCP and that the possibility of induction of sterility in female employees needs to be considered also.

No experimental study of teratogenic or mutagenic activities by DBCP in mammals has been found. Rosenkranz (1975) examined the effects of this substance on two strains of E. coli and on two of the tester strains of Salmonella typhimurium: TA 1530 and TA 1538. DBCP was mutagenic for the first of these tester strains but not for the second, indicating that it induces mutations of the base-substitution but not of the frame-shift type. The finding that DBCP inhibited growth of a strain of E. coli deficient in DNA polymerase to nearly 2.4x the extent of its inhibition of that of a strain with a normal complement of the polymerase indicates that its principal effect is on the DNA. These results are reminiscent of those of Vogel and Chandler (1974) in which they found that 1,2-dibromopropane was definitely mutagenic in Drosophila. As pointed out by these latter authors, the important property of vicinal 1,2-dibromides is that in solution they readily rearrange to form the very reactive bromonium ions. This ability would not be modified importantly by substitution of a chlorine atom on the third carbon of propane.

The National Cancer Institute undertook in 1972 studies of the possible carcinogenicity of DBCP, as one of a group of halogenated compounds. As early as 14 weeks after the initiation of administration by stomach tube of daily doses of 24 mg/kg of DBCP dissolved in corn oil, 5 times per week, several female rats were found to have palpable mammary tumors (Olson et al., 1973). Female rats given daily doses of 12 mg/kg of DBCP had not developed mammary tumors. After the fourteenth week, the

doses were increased to 30 and 15 mg/kg/day. These doses were continued up to a total duration of the experiment of 54 weeks. During this period, 7 males and 11 females of the 50 rats of each sex given each dose of DBCP used in the experiment died without tumors. Seventeen of the male rats and 33 of the females given the high dose developed squamous carcinomas of the forestomach and 12 of the females had adenocarcinomas of the breast. Five female rats given the low dose of DBCP developed mammary carcinomas and 4 males and 14 females developed gastric carcinomas. One male among the 20 rats of each sex used as vehicle controls developed a tumor that was not described more specifically. Groups of 50 male mice given 160 or 80 mg/kg/day of DBCP for 14 weeks, 200 or 100 mg/kg/day for the next 13 weeks, and 260 or 130 mg/kg/day for 25 weeks and numerically similar groups of female mice given 120 or 60 mg/kg/day for the first 14 weeks and thereafter given the same doses as the males developed 14 gastric carcinomas in males and 9 in females on the high dose, and 3 in each sex on the low dose of DBCP. No mammary carcinomas developed in the female mice and no tumors of any sort developed in the vehicle controls (20 of each sex for each species).

A report in abstract form (Powers et al., 1975) at a later stage of the same study (after 78 weeks) changed the results in a quantitative way only, the incidence of mammary adenocarcinoma in female rats increasing to 54% and that of squamous cell carcinoma of the stomach exceeding 60% in the rats and 90% in the mice.

A draft of the final report of the contractor (Hazleton Laboratories America, 1977) to the National Cancer Institute reveals that male B6C3F1 mice received 160 or 80 mg/kg/day of DBCP by gavage for 11 weeks, 200 or 100 mg/kg/day for 14 weeks and 260 or 130 mg/kg/day for 22 or 33 weeks, respectively. The time weighted average daily doses were 219 mg/kg for the high-dose group and 113 mg/kg for the low-dose group. The female mice of the same strain received 120 or 60 mg/kg/day during the first 11 weeks and thereafter received the same doses as the males. The time-weighted average doses for the females were 209 mg/kg and 109 mg/kg. Osborne-Mendel rats of the two sexes were given identical doses: 24 or 12 mg/kg for the first 9 weeks, 15 mg/kg for 60 weeks (males) or 64 weeks (females), followed by a 5-week observation period for the males, for the low-dose group, and 30 mg/kg for 55 weeks for the high dose group. For both male and female rats, the time-weighted average daily doses, 5 days/week, were 15 mg/kg for the low dose group and 29 mg/kg for the high dose one.

The preliminary estimates are that the growth of male mice decreased slightly after the first 8 weeks on the high dose and after 22 weeks on the low dose. The growth of the females may have decreased after 32 weeks on the high dose. Mortality among the male mice increased after 36 weeks on the high dose and after 38 weeks on the low dose; that among the females increased after 36 weeks on the high dose and after 43 weeks on the low dose. The incidences of gastric cancer in male mice were 93.5% on the low dose and 97.9% on the high dose. No other tumors were reported in the mice but toxic nephropathy was found in 23.8% and 93.8% of male mice on the low and high doses, respectively.

The similar preliminary estimates for rats are that the growth of the females decreased slightly after 9 weeks on either the low or the high dose. Mortality among the male rats increased after 47 weeks on the high dose and after 60 weeks on the low dose; that among female rats increased after 28 weeks on the high dose and after 31 weeks on the low dose. The incidences of gastric cancer were 76% on the low dose and 59% on the high dose. In the females, adenocarcinoma of the breast appeared in 48% of the rats on the low dose and 62% of those on the high dose. In both sexes of this species, there were appreciable occurrences of other malignant and benign tumors (50% and 18% in males on the low and high doses, respectively, and 14% and 20% in the females on the low and high doses). The most common of these tumors were hemangiomas and hemangiosarcomas.

Among the control rats, mammary carcinoma occurred in 10% of the female colony controls and in none of the vehicle controls. Hemangiomas or hemangiosarcomas occurred in about 5.3% of male colony control rats and 15% of the females; they appeared in 5.0% of female vehicle control rats and in none of the male ones. Cancer of the forestomach was found in no control rats or mice.

Toxic nephropathy was found in 23.9% of male mice and 28% of female mice on the low dose and in 93.7% of male and female mice on the high dose of DBCP. Among rats, this type of lesion was found in 100% of both male and female rats on the low dose of DBCP and in 98% and 100% of the male and female rats, respectively, on the high dose of this compound.

Ward and Habermann (1974), perhaps using some of the animals from the study just summarized, reported that the squamous cell carcinomas of the forestomach induced in mice and rats by gavage of DBCP directly into the stomach invaded the wall of the stomach and metastasized in peritoneal surfaces, especially in rats. The metastatic tumors frequently were associated with peritonitis and abscesses.

On the basis of these studies with experimental animals, DBCP appears to have only slight irritative

effect on intact skin or serous surfaces of the body, but to be somewhat more irritative of respiratory mucous membranes. In two rodent species, it appears to be carcinogenic, affecting mammary tissue in the female rat and producing invasive gastric carcinomas after direct introduction into the stomachs of either sex of mice and rats. Malignant neoplasms have not been reported in rats exposed to vaporized DBCP in concentrations that killed 40 to 50% of the exposed animals and that lasted for long enough to allow the appearance of mammary carcinomas in the exposed females if a time course similar to that following gavage obtained. The likelihood of induction of malignancies by occupational exposures to DBCP is difficult to predict from these studies, therefore. It seems possible that, if ingestion of DBCP can be avoided, there will be small, if any, probability that exposure to DBCP will induce cancer. On the other hand, no one can be certain at present that this is true. In addition, the undoubted activity of this nematocide in disturbing reproductivity physiology, which has been demonstrated in the male employee but apparently has not been recognized in the female, and in producing renotoxic and hepatotoxic effects in rodents indicate that dedicated efforts to minimize exposure to this compound are necessary. There is no good quantitative basis for an occupational exposure limit, but the finding by Rakhmatulayev (1971) that repeated daily doses of 0.05 mg/kg of DBCP to male rats eventually produced decreases in the weight of the testes and in the phagocytic activity of the polymorphonuclear leucocytes indicate that the occupational exposure level should be set at a ceiling of 0.1 mg/cu m (0.01ppm). This figure is based on a daily ventilatory exchange of 18 cu m by a 70 kg man during a 10-hour work day. If all the DBCP inhaled were retained in the employee's body, this would yield a daily dose of 0.0257 mg/kg to the standard man.

The draft report of a 90-day study of the inhalation toxicity of DBCP (Hazelton Laboratories America, 1976) indicates that both rats and mice exposed for 6 hours a day, on 5 days in each of 13 weeks, to concentrations of this compound just above 1 ppm underwent slight, but definite, changes in the rate of growth and in pellation. These findings indicate that the ceiling recommended gives a probable margin of safety for man of close to 100.

Comparison of the qualitative and quantitative actions of ethylene dibromide (See NIOSH's Criteria Document for a review) and DBCP demonstrates that, although the two compounds are similar in their abilities to induce gastric cancers by gavage but apparently not by other routes of administration, DBCP has actions that have not been reported for ethylene dibromide. Furthermore, it appears to be 10 to 20 times as potent as ethylene dibromide.

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