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PART V

ENVIRONMENTAL PROTECTION AGENCY

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TOXIC SUBSTANCES CONTROL

Second Report of the Interagency Testing Committee; Receipt and Request for Comments

[6560-01]

ENVIRONMENTAL PROTECTION AGENCY

[FRL 884-7]

TOXIC SUBSTANCES CONTROL

Second Report of the Interagency Testing Committee; Receipt and Request for Comments

AGENCY: Environmental Protection Agency (EPA).

ACTION: This Notice requests comments on the Interagency Testing Committee's recommendations of chemicals for priority consideration for testing.

SUMMARY: The Interagency Testing Committee established under section 4(e) of the Toxic Substances Control Act (TSCA) has transmitted to the EPA its Second Official Report. This Report identifies additional chemical substances and mixtures which the Committee recommends to EPA for priority consideration for promulgation of testing rules under section 4 of the Act. The Committee's recommendations revise and update recommendations made in the Committee's Initial Report. The Second Report appears in its entirety following this Notice. The Agency invites interested persons to submit comments on the Report.

BACKGROUND: Section 4 of TSCA authorizes the EPA Administrator to promulgate regulations requiring testing of chemicals to develop data relating to the risks which such chemicals may present to human health and the environment.

Section 4(e) established an Interagency Testing Committee and directed the Committee to recommend to the Administrator chemical substances and mixtures for priority consideration for test rule promulgation by October 1, 1977. The Committee's initial recommendations were published in the FEDERAL REGISTER on October 12, 1977 (42 FR 55026). Section 4(e) also directs the Committee to revise the list every six months as necessary. The Second Report recommends the addition of chemicals and groups of chemicals to the Committee's initial list and includes the Committee's reasons for each addition. The Agency is required to initiate rulemaking for these chemicals within 12 months of their inclusion on the priority list or to publicly state its reasons for not doing so.

AVAILABILITY

The Committee's report making these revisions appears in the FEDERAL REGISTER following this notice. Those persons who received the Committee's initial report will be mailed this report automatically within two weeks. Other persons wishing to receive copies should call or write to: John B. Ritch, Jr., Director, Industry Assistance Office, Office of Toxic Substances, EPA, Washington, D.C. 20460. Call toll free 800-424-9065; in Washington, D.C. call 554-1404.

In developing its recommendations, the Committee relied almost exclusively on published or other generally available information. A number of general references were given in the Committee's initial report.

In addition, references for specific chemicals being added to the list at this time will be included in the dossiers which the Committee will transmit to EPA in the next few weeks.

REQUEST FOR COMMENTS

EPA invites interested persons to submit comments on the Committee's new recommendations. In view of the statutory deadline for initiating rulemaking (or stating reasons for not doing so), the Agency requests that comments be submitted no later than July 21, 1978.

Comments should bear the identifying notation OTS-040004 and should be submitted to Joan Urquhart; U.S. Environmental Protection Agency, Office of Toxic Substances (TS-788), Federal Register Section, 401 M Street SW., Washington, D.C. All written comments will be available for public inspection in Room 623 East Tower, at the same address, between 8:30 a.m. and 4:30 p.m., weekdays.

Dated: April 14, 1977.

WARREN R. MUIR,
Acting Assistant Administrator for Toxic Substances.

TOXIC SUBSTANCES CONTROL ACT,
INTERAGENCY TESTING COMMITTEE,
Washington, D.C., April 10, 1978.

HON. DOUGLAS M. COSTLE,
Administrator,
Environmental Protection Agency,
Washington, D.C.

DEAR MR. COSTLE: In accordance with the requirements of the Toxic Substances Control Act, the TSCA Interagency Testing Committee is now recommending the addition of eight designated entries to the Section 4(e) Priority List. These revisions and the Committee's reasons for recommending them are presented in the enclosed document entitled, "Second Report of the TSCA Interagency Testing Committee to the Administrator, Environmental Protection Agency." The representatives of the statutory member agencies are in consensus on these revisions.

Also, the report contains two special recommendations which bear on the activities of the Environmental Protection Agency. First, it is recommended that EPA consider taking the initiative in the development of a comprehensive survey of health and environmental effects testing facilities in the United States. And secondly, your agency is encouraged to join in the effort to provide increased training support in the fields of mammalian and environmental toxicology, pathology, occupational health and epidemiology as these fields relate to the need for greater numbers of qualified personnel to meet the increasing demand for testing.

The Committee has not yet completed its review of all of those chemical substances and categories of substances identified during our initial activities in 1977. This review is to continue and will be a subject of future Committee reports. In addition, candidate chemicals recommended by the Committee members or public comment will be reviewed by the Committee as such information is made available.

We trust that this report will be of value to EPA as it continues to carry out the Toxic Substances Control Act.

Sincerely,

MARVIN E. STEPHENSON,
Chairperson, TSCA Interagency Testing Committee.

SECOND REPORT OF THE TSCA INTERAGENCY TESTING COMMITTEE TO THE ADMINISTRATOR, ENVIRONMENTAL PROTECTION AGENCY

APRIL 1978

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Joseph McLaughlin

Committee Staff

Executive Secretary: Carol A. Mapes
Secretary: Phyllis D. Tucker

ACKNOWLEDGMENTS

The Committee wishes to acknowledge the important contributions of the many individuals and groups who have significantly aided us in our work. These include:

The Federal agencies who have cooperated by providing support through the liaison members;

Clement Associates, Inc., technical support contractor;

The National Science Foundation, for funding and managing the technical support contract and the National Institute of Environmental Health Sciences, for assisting in that funding;

Former Committee members: Sidney R. Galler, Department of Commerce; William M. Upholt, Environmental Protection Agency; Norbert P. Page, National Institute for Occupational Safety and Health; Grover C. Wrenn, Occupational Safety and Health Administration.

EPA staff members who assisted the Committee in a variety of activities, and particularly: Donald G. Barnes, Office of Toxic Substances; John W. Lyon, Office of General Counsel; Ralph C. Northrop, Jr., Office of Toxic Substances.

The numerous experts who prepared presentations and materials for the Committee; and

The many individuals and organizations who responded to the Committee's Initial Report to the Administrator, Environmental Protection Agency.

SUMMARY

A central provision of the Toxic Substances Control Act (TSCA, Pub. L. 94-469) concerns the testing of chemical substances and mixtures which are used in commerce or may represent an unreasonable risk of injury to human health or the environment. The Act provides for continuing advice from certain Federal agencies having common interests in identifying chemical substances or mixtures for testing. Accordingly, the TSCA Interagency Testing Committee, which is composed of representatives from those concerned Federal agencies, regularly provides to the Administrator of the Environmental Protection Agency (EPA) recommendations on chemicals and mixtures to which the Administrator should give priority consideration for the promulgation of testing rules.

As a result of its deliberations during the past six months, the Committee has elected to revise the TSCA Section 4(e) Priority List by the addition of four individual substances and four categories of substances. The Committee considers these additions to be of the same priority as the previously designated entries. The chemical substances or categories being designated for addition to the Priority List and the testing recommendations are presented alphabetically as follows:

Substance or Category and Testing Recommended

Acrylamide—Carcinogenic- ity, mutagenicity, teratogenicity, environmental effects and epidemiological study.

Aryl phosphates—Carcinogenicity, mutagenicity, teratogenicity, other chronic effects, environmental effects and epidemiological study.

Chlorinated naphthalenes—Carcinogenicity, mutagenicity, teratogenicity, other chronic effects, environmental effects and epidemiological study.

Dichloromethane—Carcinogenicity, mutagenicity, teratogenicity, other chronic effects, environmental effects and epidemiological study.

Halogenated alkyl epoxides—Carcinogenicity, mutagenicity, teratogenicity, other chronic effects, and epidemiological study.

Polychlorinated terphenyls—Carcinogenicity, mutagenicity, teratogenicity, other chronic effects, and environmental effects.

Pyridine—Carcinogenicity, mutagenicity, teratogenicity, other chronic effects, environmental effects and epidemiological study.

1,1,1-Trichloroethane — Carcinogenicity, mutagenicity, teratogenicity, other chronic effects, and epidemiological study.

A set of dossiers containing information on the additional entries designated to the Priority List will be forwarded to the EPA Administrator within a few weeks.

SECOND REPORT OF THE TSCA INTERAGENCY TESTING COMMITTEE TO THE ADMINISTRATOR, ENVIRONMENTAL PROTECTION AGENCY, APRIL 1978

CHAPTER 1. INTRODUCTION

1.1 *Committee Establishment and Responsibilities.* The Toxic Substances Control Act (Pub. L. 94-469) establishes the TSCA Interagency Testing Committee under Section 4(e). The Committee has the continuing responsibility to identify and recommend to the Administrator of the Environmental Protection Agency (EPA) chemical substances or mixtures which should be tested to determine their hazard to human health or the environment. The statute requires that the Committee consider revisions to its previous recommendations at least every six months.

The Committee has eight statutory members appointed by the Federal agencies identified for membership in Section 4(e)(2)(A) of the Act, a number of alternate members as permitted by Section 4(e)(2)(B)(i), and liaison members from several Federal agencies with programs related to the control of toxic substances. Current Committee members, alternates, and liaison representatives are identified at the beginning of this report.

1.2 *Initial Report.* In July 1977, the Committee published a Preliminary List of 330 chemical substances and categories of such substances including background information describing the methods used by the Committee in making those selections (Reference No. 1). The Preliminary List contains substances and categories selected primarily on the basis of their potential for human exposure and environmental release. Subsequently, the chemicals on the Preliminary List and chemicals added to the Preliminary List on the basis of public comments and Committee recommendations were screened further by the Committee. The screening process was based primarily on the chemicals' potential for causing adverse human and/or environmental effects but also considered their exposure potential. Available data on these chemicals were reviewed with regard to: potential for carcinogenic, mutagenic, teratogenic, and chronic toxic effects; their ability to bioaccumulate or cause deleterious environmental effects; and possible toxic impurities. A scoring system was used in this process which took into account both available information and the lack of it for these factors. The Committee further narrowed the list of substances and categories under consideration on the basis of its scientific judgment and the scoring results, and requested its technical contractor to prepare dossiers on these chemicals. The Committee was able to review about one-half of these substances and categories aided by information in the dossiers. Four individual chemicals and six categories of chemical substances were selected for inclusion in the Initial Report to the Administrator, Environmental Protection Agency (Reference No. 2) dated October 1, 1977.

In addition to the listing of the chemicals designated by the Committee for consideration by EPA, the report contains a detailed description of the methods used in developing the Committee's initial recommendations including data sources and methods used for production, release and exposure scores, as well as biological and environmental scores. Later, on February 7, 1978, a finalized set of supporting dossiers on the designated entries on the Priority List was officially transmitted to the Administrator.

1.3 *Committee Activities During This Reporting Period.* Since completion of its initial recommendations in October 1977, the Committee has continued to consider individual chemical substances and mixtures identified for in-depth consideration by the screening process mentioned in the preceding section.

This review has given specific consideration to the factors described in TSCA Section 4(e)(1)(A) and other relevant factors identified by the Committee. Readily available information on these factors and the knowledge and professional judgment of the Committee members have been employed to select additional entries to the TSCA Section 4(e) Priority List. On the basis of the review of more, but not all, of the previously requested dossiers, the Committee is now recommending the addition of four chemical substances and four categories of chemical substances to the 4(e) Priority List.

1.4 *Future Activities of the Committee.* In the course of developing its third report, the

Committee expects to continue reviewing those dossiers in hand and consider new dossiers on additional chemicals and groups.

CHAPTER 2. CONSIDERATION OF AVAILABILITY OF TESTING FACILITIES AND PERSONNEL

Section 4(e)(1)(A) of TSCA requires that the Committee consider, among other factors, the reasonably foreseeable availability of facilities and personnel for carrying out the testing on the substances or mixtures recommended to the Administrator for priority consideration. The Committee concludes that testing capabilities are presently adequate to carry out the recommended health effects and environmental tests on the chemicals listed in Table 1. However, the concerns expressed by the Committee in its first report (Reference No. 2, p. 55043) regarding the limited national capability for conducting long-term tests for environmental effects are reiterated.

The expansion of testing facilities by industry, contracting laboratories, and universities seems to be proceeding at a satisfactory rate, especially in the area of health effects testing. Estimates indicate a significant increase in facilities over the next five years. While this is encouraging, the Committee is aware that the increasing requirements of various government agencies are creating competition for the same testing facilities and personnel. Therefore, the projected need and capacity for health and environmental effects testing is somewhat uncertain and should be more accurately surveyed. The Committee recommends that EPA assume the leadership in the development of a comprehensive survey of availability of current Federal and private health effects testing facilities in the United States and the projected annual capacity of such facilities during the next five years. In those cases where testing is likely to involve animal bioassay, the survey should include an evaluation of the capacity to provide appropriate and sufficient populations of test species.

Of paramount concern to the Committee is the availability of qualified personnel. All indices contained in the *Report of the Second Task Force for Research Planning in the Environmental Health Sciences* (Reference No. 3) indicate a current and future shortage of research professionals in the fields of mammalian and environmental toxicology, pathology, occupational health, and epidemiology. There will be a dearth of professionals and supporting technical personnel in these various skills for many years unless increased training efforts occur at the national level. The Committee notes that several Federal agencies are involved in augmenting training support and recommends that EPA join in these efforts in a significant way.

There is also a need to maintain viable basic research programs in toxicology and other related health fields. This basic need should not be neglected in order to assure short-term gains in the practical application of the present state of the art. Because of the interdisciplinary nature of toxicology and environmental health research, the educational training for some of the disciplines can be provided only by facilities with personnel engaged in this type of research.

The Committee believes that the Civil Service Commission could do much to stimulate interest in these professions by creating professional series and registers for such scarce categories as toxicologists, pathologists, epidemiologists and other scientific fields in environmental protection. Recognition of these environmental health professions by the Commission could encourage students to investigate careers in fields thus far hidden as Federal employment opportunities. It is concluded that such an action by the Commission would have the effect of increasing the available scientific manpower in these specialty fields both in the Government and in industry where the demand for such personnel exists.

CHAPTER 3. RECOMMENDATIONS OF THE COMMITTEE

3.1 *Substances and Categories of Substances Recommended for Testing.* On the basis of the review and evaluation of chemical substances which was carried out according to the methods and procedures described in Sections 1.2 and 1.3, the Committee is revising the TSCA Section 4(e) Priority List to add certain substances and categories of substances for which specific testing is recommended. The Priority List and the date each item was placed on the List are given in Table 1. The testing recommendations and reasons for such recommendations are indicated in Section 3.2 for the new entries. Supporting dossiers of information are being prepared in final form and will be forwarded to the Administrator, EPA, at an early date.

All additions to the List are designated chemical substances and categories of chemical substances which the Committee has determined require the Administrator's action under TSCA Section 4(a) within twelve months. The Committee considers these additions to be of the same priority as the previously designated entries. In recommending a category of chemical substances for testing (e.g., the aryl phosphates), the Committee recognizes that certain chemicals which are members of the category may have been tested previously for an effect of concern. For those chemicals no additional testing may be warranted if the results of previously completed tests are judged adequate for assessing the effect of concern. The Committee also recognizes that the definition and inclusive limits of a given listed category of substances may require additional specification or change in specification as the testing rule is developed. Unless stated otherwise, the chemical substance recommended for testing should be the product to which the population is exposed.

3.2 *Reasons for Recommending Testing of the Additional Substances and Categories of Substances.* In accordance with the reporting requirements of the Act, the Committee has listed in the following sections the test recommendations and reasons for recommending testing for those entries being placed on the Priority List at this time. Table 2 presents a summary of the testing recommendations for each addition to the List.

TABLE 1.—*The TSCA Section 4(e) Priority List, by Alphabetical Arrangement*

Designated entry	Date of entry
Acrylamide	April 1978.
Alkyl epoxides	October 1977.
Alkyl phthalates	October 1977.
Aryl phosphates	April 1978.
Chlorinated benzenes, mono- and di-	October 1977.
Chlorinated naphthalenes	April 1978.
Chlorinated paraffins	October 1977.
Chloromethane	October 1977.
Cresols	October 1977.
Dichloromethane	April 1978.
Halogenated alkyl epoxides	April 1978.
Hexachloro-1,3-butadiene	October 1977.
Nitrobenzene	October 1977.
Polychlorinated terphenyls	April 1978.
Pyridine	April 1978.
Toluene	October 1977.
1,1,1-trichloroethane	April 1978.
Xylenes	October 1977.

TABLE 2.—*Summary of testing recommendations by the TSCA Interagency Testing Committee*

Substance or category	Carcinogenicity	Mutagenicity	Teratogenicity	Other chronic effects	Environmental effects	Epidemiology study
Acrylamide	X	X	X	.....	X	X
Aryl phosphates	X	X	X	X	X	X
Chlorinated naphthalenes	X	X	X	X	X	X
Dichloromethane	X	X	X	X	X	X
Halogenated alkyl epoxides	X	X	X	X	.....	X
Polychlorinated terphenyls	X	X	X	X	X	.....
Pyridine	X	X	X	X	X	X
1,1,1-trichloroethane	X	X	X	X	.....	X

3.2.A Acrylamide.

Testing recommendations: Carcinogenicity, mutagenicity, teratogenicity, environmental effects, and epidemiology.

Substance identification: CAS No. 79-06-1.

REASONS FOR RECOMMENDATIONS

Production, release, and exposure. The 1976 U.S. production of acrylamide monomer is estimated at 64 million pounds, and indications point to a high growth rate of around 12 percent for the next decade. Eighty percent of the acrylamide produced is used captively in polymer production for water treatment, papermaking and wastewater clarification. About 5 percent is used in chemical grouts as the acrylamide monomer, for soil stabilization and sewer rehabilitation. The remainder is consumed in

other chemical syntheses. Other uses are in the paper and paperboard industry, coal industry, mining and ore beneficiation industry, and secondary oil recovery industry.

Acrylamide release to the environment (usually ending up in surface and ground water) occurs at manufacuring sites, soil grouting sites, polymer application sites and in handling. General population, low-level exposure to acrylamide is likely to occur wherever polyacrylamides are utilized. No data are available on release rates into the environment or actual concentration levels. NIOSH estimates that 20,000 workers are potentially exposed in the workplace.

Carcinogenicity. Acrylamide has not been tested for carciongenicity. Because of widespread low-level exposure to the population, acrylamide should be tested for carcinogenicity.

Mutagenicity. Although the results of two independently reported Ames tests were negative, the Committee believes that additional tests, employing other systems, are required to evaluate the mutagenic potential of this chemical.

Teratogenicity. Transplacental transport of acrylamide was demonstrated in rats; therefore, it should be tested conclusively for teratogenicity.

Environmental effects. In view of the high degree of neurotoxicity and neuropathy caused by cumulative exposure and the extensive use of this material in waste water treatment and soil grouting, studies should be initiated to determine the degree of leaching of the monomer from the polymer with water and various solvents. Further, the potential for environmental exposures to the aquatic ecosystem, movement in soil solution and leachate from soil waste must be determined for biological effects on plant and animal life.

Epidemiology. No epidemiological reports on acrylamide have been found in the literature. Studies are needed to provide information on human exposure to acrylamide and to determine the relationship between airborne concentrations and observed effects on humans.

3.2.B Aryl phosphates.

Testing recommendations: carcinogenicity, mutagenicity, teratogenicity, other chronic effects, environmental effects, and epidemiology.

Category identification: This category consists of phosphate esters of phenol or of alkyl-substituted phenols. Tri-aryl and mixed alkyl and arly esters are included, but tri-alkyl esters are excluded.

REASONS FOR RECOMMENDATIONS

Production, release, and exposure. As a category, the aryl phosphates are produced in quantities exceeding 65 million pounds/year. Several individual aryl phosphates, such as tritolyl phosphate and triphenyl phosphate, have annual production greater than 10 million pounds. Aryl phosphates are widely used as plasticizers in polymers (principally in polyvinyl chloride) and in hydraulic fluids and high pressure lubricants. Such uses provide opportunity for extensive occupational exposure to these compounds beyond that encountered in their manufacture. NIOSH estimates that over 2 million workers are so exposed. Because of the nature of their uses, most of the aryl phosphates manufactured will ultimately be released into the environment, although those used as plasticizers may be released quite slowly. Persistence of aryl phosphates in the environment for significant periods (at least on the order of months) is indicated by the available data.

Carcinogenicity. With the exception of several tests of inadequate duration using triphenyl phosphate, the carcinogenic potential of aryl pohosphates has not been assessed. Carcinogenicity testing should be performed on aryl phosphates having substantial human exposure and/or environmental release.

Mutagenicity. No mutagenicity testing has been reported for aryl phosphates. Such testing should be performed because of the potential of these substances for widespread environmental release and human exposure.

Teratogenicity. No teratogenicity testing has been reported for aryl phosphates. Such testing should be conducted for aryl phosphates having substantial human exposure and/or environmental release.

Other chronic effects. The neurotoxicity of certain aryl phosphates is well documented. The Committee recommends that aryl phosphates be tested for chronic effects with special emphasis on neurotoxic activity.

Environmental effects. Available data, although limited, indicate a potential for persistence of aryl phosphates in the aquatic environment, as well as a potential for their bioaccumulation in aquatic species. There is evidence of chronic toxicity of aryl phosphate hydraulic fluids to fish. Several aryl phosphates potentiate the toxic effects of organophosphate pesticides on insects and one (tri-o-cresyl phosphate) has been shown to potentiate such effects in nontarget organisms including mammals. In view of this, the environmental fate and effects on aquatic and terrestrial systems should be evaluated for aryl phosphates.

Epidemiology. Because of the large-scale production and potential for substantial occupational exposure of certain aryl phosphates, the Committee recommends that epidemiological studies be conducted.

3.2.C *Chlorinated Naphthalenes.*

Testing recommendations: Carcinogenicity, mutagenicity, teratogenicity, other chronic effects, environmental effects, and epidemiology.

Category identification: This category consists of chlorinated derivatives of naphthalene (empirical formula $C_{10}H_xCl_y$, where $x+y=8$).

REASONS FOR RECOMMENDATIONS

Production, release, and exposure. Available data indicate a production volume on the order of millions of pounds annually. These products have both moderately dispersive uses (e.g., lubricating and cutting oil additives) and enclosed uses (e.g., dielectric for automotive capacitors). Although NIOSH has estimated that several thousand workers are exposed to these compounds, little is known about the ultimate release of these materials from the workplace, during product use, or as a result of disposal.

Health effects. Animal studies and analysis of human exposure reveal that these compounds are biologically active, with reports of dermatological (e.g., chloracne) and systemic (liver) effects. To date, there are no reported data on the carcinogenicity, mutagenicity, or teratogenicity of these compounds. Thus, there is a need to conduct such studies, as well as to investigate more thoroughly the chronic effects of these materials. Epidemiological studies should be undertaken where appropriate.

Environmental effects. Little information on the ecological effects of these materials is available, but the detection of chlorinated naphthalenes in stream sediments, fish, and fish-eating birds point to their dispersal, persistence, and bioaccumulation in the food chain. Therefore, testing is needed to obtain data for judging the environmental effects of these chemicals.

3.2.D *Dichloromethane.*

Testing recommendations: Carcinogenicity, mutagenicity, teratogenicity, other chronic effects, environmental effects, and epidemiology.

Substance identification: CAS NO. 75-09-2.

REASONS FOR RECOMMENDATIONS

Production, release, and exposure. The 1976 U.S. production of dichloromethane (also known as methylene chloride) exceeded 500 million pounds, a 12 percent increase over the 1972 level. An average 9 percent annual growth rate is projected over the next several years as this chemical enters markets dominated by fluorochlorocarbons in the past. Approximately ¾ of the volume produced is thought to be released to the environment through activities at industrial sites, in homes and elsewhere. NIOSH estimated that 2.5 million workers are exposed to this material at their place of work. Its use in an array of aerosol spray products and other household products brings a large fraction of the general population into contact with this chemical.

Carcinogenicity. No carcinogenicity test data were found in the searched literature. There is sufficient concern based for the Committee to recommend this chemical for such testings. The Committee is aware of two studies currently under way, however, whose results may be judged adequate to obviate the need for additional testing.

Mutagenicity. No mutagenicity test data have been reported. Such studies should be conducted in view of the widespread exposure to this chemical and its demonstrated biological activity.

Teratogenicity. One study has reported equivocal findings of abnormalities in the offspring of pregnant rats and mice exposed to this chemical. Additional testing is needed to assess this potential hazard.

Other chronic effects. Laboratory investigations and case studies have reported that dichloromethane can affect various organs (e.g., lungs and eye) and systems (blood), as well as behavior. Given the widespread use of this chemical under many different conditions, this information indicates a need for further testing.

Environmental effects. Dichloromethane is being released in large quantities and in a broad dispersion pattern throughout the environment. Low-level residues have been measured in water. The exact nature of this exposure and its chronic effects on the biota need to be determined.

Epidemiology. Epidemiological studies should be conducted to assess human risk.

3.2.E *Halogenated Alkyl Epoxides.*

Testing recommendations: Carcinogenicity, mutagenicity, teratogenicity, other chronic effects, epidemiology.

Category identification: This category consists of halogenated noncyclic aliphatic hydrocarbons with one or more epoxy functional groups.

REASONS FOR RECOMMENDATIONS

Production, Release, and Exposure. The 1975 U.S. production of epichlorohydrin (1-chloro-2,3-epoxypropane) exceeded 500 mil-

lion pounds. NIOSH estimates that between 50,000 and 140,000 workers are exposed to epichlorohydrin annually. While epichlorohydrin is currently the only widely used halogenated alkyl epoxide, advertising and trends in the chemical industry lead the Committee to the conclusion that chemicals of this type may find wider use in the future.

Carcinogenicity. Halogenation of an alkyl epoxide enhances its activity as an alkylating agent and hence its biological activity. Halogenated alkyl epoxides also may inhibit detoxifying enzymes in mammals. Equivocal results of recent carcinogenicity studies on epichlorohydrin further point out the need for testing this chemical category for potential carcinogenicity.

Mutagenicity. Epichlorohydrin has been shown to be mutagenic to mice and bacteria. The potential human toxicity of this and other halogenated alkyl expoxides should be evaluated.

Teratogenicity. No information could be found on the potential for teratogenicity of the halogenated alkyl epoxides and they should be studied for this effect.

Other Chronic Effects. Epichlorohydrin has been reported to penetrate human skin and cause systemic effects. This raises concern for other toxic effects and target organ toxicity of all the halogenated alkyl epoxides. Appropriate studies for these effects are recommended.

Epidemiology. No epidemiological studies of any of the halogenated alkyl epoxides were found in the literature. Studies are needed to provide information on the effects of human exposure to these compounds.

3.2.F *Polychlorinated terphenyls.*

Testing recommendations: Carcinogenicity, mutagenicity, teratogenicity, other chronic effects, environmental effects.

Category identification: This category consists of the polychlorinated *ortho-*, *meta-* and *para*-terphenyls.

REASONS FOR RECOMMENDATIONS

Production, Release and Exposure. Although the production of polychlorinated terphenyls was discontinued in the United States in 1972, there has been an increase in imports of polychlorinated terphenyls from 160,000 pounds in 1973 to 400,000 pounds in 1975. Polychlorinated terphenyls are presently used in waxes for investment casting and this use leads to wide environmental dispersion. Residues of polychlorinated terphenyls have been found in human fat and milk and in samples of water and sludge. In a group of 27 individuals tested for blood levels of polychlorinated terphenyls and polychorinated biphenyls, the average concerntration of polychlorinated terphenyls in the blood was greater than that of polychlorinated biphenyls, despite a far greater industrial use of polychlorinated biphenyls in the area of study.

Carcinogenicity. No reports of long-term carcinogenicity studies of polychlorinated terphenyls were found in the searched literature. The Committee recommends that polychlorinated terphenyls be tested for carcinogenicity.

Mutagenicity. No information on the mutagenicity of polychlorinated terphenyls was found in the searched literature. The Committee recommends that mutagenicity tests be conducted.

Teratogenicity. No information on the teratogenicity of polychlorinated terphenyls was found in the searched literature. The Committee recommends that teratogenicity tests be conducted.

Other Chronic Effects. Liver, skin and hematopoietic effects have been observed at high level exposures. Effects at lower levels cannot be characterized from existing data. Chronic studies to evaluate the effects of prolonged exposures are recommended.

Environmental Effects. The limited available data indicate a potential for bioaccumulation. No adequate information is available on the ecological effects of these chemicals.

3.2.G *PYRIDINE.*

Testing recommendations: Carcinogenicity, mutagenicity, teratogenicity, other chronic effects, environmental effects, epidemiology.

Substance identification: CAS No. 110-86-1.

REASONS FOR RECOMMENDATIONS

Production, Release, and Exposure. The annual production of pyridine is estimated to be in excess of 60 million pounds, based on production amounts for 1976. Although the amount of pyridine released into the environment is unknown, its production volume and variety of uses raise concern with respect to human exposure. NIOSH estimates that 249,000 workers may be exposed to pyridine.

Carcinogenicity. Only one limited carcinogenicity study was found in the searched literature. By current standards, the study is judged inadequate as an evaluation of the carcinogenic potential of pyridine. The Committee, therefore, recommends that appropriate carcinogenicity testing be undertaken on pyridine.

Mutagenicity. No mutagenicity studies on pyridine were found in the searched literature. Given its known biological activity, production volume, and human exposure, it is recommended that appropriate mutagenicity testing be undertaken on pyridine.

Teratogenicity. Only one limited teratogenicity study was found in the searched literature on pyridine. It indicated that pyridine produced abnormalities in chicken embryos. An evaluation of teratogenic effects should be undertaken in other species.

Other Chronic Effects. The carcinogenicity study cited above is the only investigation lasting one year or longer found in the searched literature on the possible chronic effects of pyridine. Short-term studies indicate that pyridine affects the central nervous system and causes degeneration in the liver and kidneys. Chronic effects on these and other systems should be evaluated in appropriate long-term studies.

Environmental Effects. The environmental release of pyridine may pose a hazard to aquatic biota and terrestrial life. Residues have been detected in water and uptake in plants has been reported. Although a wide range of toxicity has been measured for plant and animal life in short-term bioassay tests, the results of one longer-term exposure to *Daphnia magna* indicates a potential for chronic toxicity. More testing is needed to determine the biological significance of residues and the potential effects of long-term exposures on both plant and animal life.

Epidemiology. Pyridine has been reported to have an effect on the central nervous system in humans, as well as to produce injury to the liver and kidney. Given the large number of workers exposd, epidemiological studies should be undertaken.

3.2.H *1,1,1-Trichloroethane.*

Testing recommendations: Carcinogenicity, mutagenicity, teratogenicity, other chronic effects, epidemiology.

Substance identification: CAS No. 71-55-6.

REASON FOR RECOMMENDATIONS

Production, Release, and Exposure. This compound is produced primarily for use as a cleaning solvent for metals and other materials. 1,1,1-Tricholoroethane (methyl chloroform) has the potential to replace the chlorinated ethylenes in a variety of solvent formulations used commercially. The U.S. production of this compound totaled approximately 630 million pounds in 1976. Current release rates are not known; however, it is estimated that over 300 million pounds of this compound are employed in dispersive uses which would principally result in releases to the atmosphere. The significant adverse effects on the upper atmosphere have been evaluated. Minor amounts may also enter the acquatic and terrestrial environment. NIOSH estimates that about 3,000,000 persons may be exposed to this material in the workplace.

Carcinogenicity. The currently available information, including recent results from the NCI carcinogenesis bioassay program, indicates that data are not adequate to make a judgment on the carcinogenic potential of 1,1,1-trichloroethane. The Committee recommends that this chemical be evaluated with respect to carcinogenicity.

Mutagenicity. The absence of information on the mutagenicity of this compound indicates that such studies should be undertaken.

Teratogenicity. The Committee concludes that the current available information on teratogenic effects is insufficient to judge the hazard potential of this material. Consequently, it is recommended that appropriate teratogenesis studies be undertaken on 1,1,1-trichloro- ethane.

Other Chronic Effects. There is insufficient evidence regarding the impact of chronic, low-level exposure to 1,1,1-trichloroethane. Chronic effects, with specific attention to neurological, cardiovascular and renal systems, should be evaluated in appropriately designed studies.

Epidemiology. No investigations of health effects in occupational workers exposed to 1,1,1-trichloroethane were found during the Committee's review of this material. Given the large population of workers exposed to this compound, it is recommended that appropriate epidemiological investigations be conducted.

REFERENCES

1. *Preliminary List of Chemical Substances for Further Evaluation,* Toxic Substances Control Act Interagency Testing Committee, July 1977.

2. *Initial Report to the Administrator, Environmental Protection Agency,* TSCA Interagency Testing Committee, October 1, 1977. Published in the FEDERAL REGISTER, Vol. 42, No. 197, Wednesday, October 12, 1977, pp. 55026-55080. The report and the supporting dossiers also were published by the Environmental Protection Agency, EPA 560-10-78/001, January 1978.

3. *Human Health and the Environment—Some Research Needs,* A report of the Second Task Force for Research Planning in Environmental Health Sciences, DHEW Publication No. NIH 77-127, Chapter 16, 1977.

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