

Environmental Protection Agency

Wednesday
November 16, 1988

Part V

Environmental Protection Agency

**Twenty-Third Report of the Interagency
Testing Committee to the Administrator;
Receipt of Report and Request for
Comments**

40 CFR Parts 712 and 716

**Preliminary Assessment Information and
Health and Safety Data Reporting; Final
Rule**

**ENVIRONMENTAL PROTECTION
AGENCY**
[OPTS-41030; FRL-3476-6]
**Twenty-Third Report of the
Interagency Testing Committee to the
Administrator; Receipt of Report and
Request for Comments Regarding
Priority List of Chemicals**
AGENCY: Environmental Protection
Agency (EPA).

ACTION: Notice.

SUMMARY: The Interagency Testing Committee (ITC), established under section 4(e) of the Toxic Substances Control Act (TSCA), transmitted its Twenty-Third Report to the Administrator of EPA on November 1, 1988. This report, which revises and updates the Committee's priority list of chemicals, adds six chemicals to the list for priority consideration by EPA in promulgation of test rules under section 4(a) of the Act. The Twenty-Third Report is included with this notice. The new chemicals are tris(2-chloroethyl)-phosphate (CAS No. 115-96-8), three tris(2-chloropropyl)-phosphate, (CAS Nos. 6145-73-9, 13674-84-5, and 13674-87-8), tetrakis(2-chloroethyl)-ethylene diphosphate (CAS No. 33125-86-9) and butyraldehyde (CAS No. 123-72-8). These chemicals are not designated for response within 12 months. Crotonaldehyde (CAS No. 4170-30-3), which was recommended with intent-to-designate by the ITC in its Twenty-Second Report (53 FR 18196; May 20, 1988), now is designated for response within 12 months. In response to ITC's designation, EPA will either initiate rulemaking under section 4(a) of TSCA, or publish a Federal Register notice explaining the reasons for not initiating such rulemaking within 12 months. EPA invites interested persons to submit written comments on the report, and to attend Focus Meetings to help narrow and focus the issues raised by the ITC's recommendations.

Additionally, EPA is soliciting interest in public participation in the consent agreement process for tris(2-chloroethyl)-phosphate, three tris(2-chloropropyl)-phosphates, and tetrakis(2-chloroethyl)-ethylene diphosphate.

The ITC also has removed two chemicals, ethylbenzene and methyl ethyl ketoxime, from the priority list.

DATES: Written comments should be submitted by December 16, 1988. Submit written notice of interest in being designated an "interested party" to development of consent agreements for tris(2-chloroethyl)-phosphate, three

tris(2-chloropropyl)-phosphates and tetrakis(2-chloroethyl)-ethylene diphosphate by December 16, 1988.

Focus Meetings will be held on December 13, 1988.

ADDRESS: Send written submissions to: TSCA Public Docket Office (TS-793), Office of Toxic Substances, Environmental Protection Agency, Rm. NE G-004, 401 M Street SW., Washington, DC 20460.

Submissions should bear the document control number (OPTS-41030).

The public record supporting this action, including comments, is available for public inspection in Rm. NE G-004 at the address noted above from 8 a.m. to 4 p.m., Monday through Friday, except legal holidays.

The Focus Meetings will be held at EPA Headquarters, Rm. 103 NE Mall, 401 M Street SW., Washington, DC. Persons planning to attend the Focus Meetings, and/or seeking to be informed of subsequent public meetings on these chemicals, should notify the TSCA Assistance Office at the address listed below. To ensure seating accommodations at the Focus Meetings, persons interested in attending are asked to notify EPA at least one week ahead of the schedule date.

FOR FURTHER INFORMATION CONTACT: Michael M. Stahl, Director, TSCA Assistance Office (TS-799), Office of Toxic Substances, Environmental Protection Agency, 401 M Street, SW., Washington, DC 20460, (202) 554-1404, TDD (202) 554-0551.

SUPPLEMENTARY INFORMATION: EPA has received the TSCA Interagency Testing Committee's Report to the Administrator.

I. Background

TSCA (Pub. L. 94-469, 90 Stat. 2003 *et seq.*; 15 U.S.C. 2601 *et seq.*) authorizes the Administrator of EPA to promulgate regulations under section 4(a) requiring testing of chemical substances and mixtures in order to develop data relevant to determining the risks that such chemical substances and mixtures may present to health and the environment. Section 4(e) of TSCA established an Interagency Testing Committee to make recommendations to the Administrator of EPA on chemical substances and mixtures to be given priority consideration in proposing test rules under section 4(a). Section 4(e) directs the ITC to revise its list of recommendations at least every 6 months as necessary. The ITC may "designate" up to 50 substances and mixtures at any one time for priority consideration by the Agency. Crotonaldehyde is a designated

chemical. For such designations, the Agency must within 12 months either initiate rulemaking or issue in the Federal Register its reasons for not doing so. The ITC's Twenty-Third Report was received by the Administrator on November 1, 1988, and follows this Notice. The Report adds six substances to the TSCA section 4(e) priority list.

**II. Written and Oral Comments and
Public Meetings**

EPA invites interested persons to submit detailed comments on the ITC's new recommendations. The Agency is interested in receiving information concerning additional or ongoing health and safety studies on the subject chemicals as well as information relating to the human and environmental exposure to these chemicals.

A notice is published elsewhere in today's Federal Register adding the substances recommended in the ITC's Twenty-Third Report to the TSCA section 8(d) Health and Safety Data Reporting Rule (40 CFR Part 716), which requires the reporting of unpublished health and safety studies on the listed chemicals. These chemicals also will be added to the TSCA section 8(a) Preliminary Assessment Information Rule (40 CFR Part 712) published elsewhere in this issue. The section 8(a) rule requires the reporting of production volume, use, exposure, and release information on the listed chemicals.

Focus Meetings will be held to discuss relevant issues pertaining to these chemicals and to narrow the range of issues/effects which will be the focus of the Agency's subsequent activities in responding to the ITC recommendations. The Focus Meetings will be held on December 13, 1988, as follows:

9:30 a.m. Tris(2-chloroethyl)-phosphate, three tris(chloropropyl)-phosphates, and tetrakis(2-chloroethyl)-ethylene diphosphate

1:00 p.m. Butyraldehyde

They will be held at EPA Headquarters, Rm. 103 NE Mall, 401 M St., SW., Washington, DC. These meetings are intended to supplement and expand upon written comments submitted in response to this notice.

Persons wishing to attend these meetings, or subsequent meetings on these chemicals, should call the TSCA Assistance Office at the telephone number listed above at least one week in advance.

This notice also serves to invite persons interested in participating in or monitoring negotiations for consent agreements for tris(2-chloroethyl)-

phosphate, three tris(chloropropyl)-phosphates, and tetrakis(2-chloroethyl)-ethylene diphosphate to notify EPA no later than December 16, 1988. The procedures for negotiations are described in 40 CFR 790.22. All written submissions should bear the identifying docket number (OPTS-41030).

III. Status of List

In addition to adding the six recommendations to the priority list, the ITC's Twenty-Third Report notes the removal of two chemicals from the list. Ethylbenzene has been removed from the list because the data gaps previously identified by the ITC have been satisfactorily resolved. Subsequent to ITC's preparation of its Twenty-Second Report, EPA responded to the ITC's recommendation for methyl ethyl ketoxime by publishing a Notice of Proposed Rulemaking in the Federal Register (53 FR 35838; September 15, 1988). The current list contains two designated substances, five chemicals recommended with intent-to-designate, and fourteen recommended substances.

Authority: 15 U.S.C. 2603.

Dated: November 4, 1988.

Joseph J. Merenda,

Director, Existing Chemical Assessment Division.

TWENTY-THIRD REPORT OF THE TSCA INTERAGENCY TESTING COMMITTEE TO THE ADMINISTRATOR, ENVIRONMENTAL PROTECTION AGENCY

Summary

Section 4 of the Toxic Substances Control Act of 1976 (TSCA, Pub. L. 94-469) provides for the testing of chemicals in commerce that may present an unreasonable risk of injury to health or the environment. It also provides for the establishment of a Committee (ITC), composed of representatives from eight designated Federal agencies, to recommend chemical substances and mixtures (chemicals) to which the Administrator of the U.S. Environmental Protection Agency (EPA) should give priority consideration for the promulgation of testing rules.

Section 4(e)(1)(A) of TSCA directs the Committee to recommend to the EPA Administrator chemicals to which the Administrator should give priority consideration for the promulgation of testing rules pursuant to section 4(a). The Committee is required to designate those chemicals, from among its recommendations, to which the Administrator should respond within 12 months by either initiating a rulemaking proceeding under section 4(a) or

publishing the Administrator's reason for not initiating such a proceeding. At least every 6 months, the Committee makes those revisions in the TSCA section 4(e) Priority List that it determines to be necessary and transmits them to the EPA Administrator.

As a result of its deliberations, the Committee is revising the TSCA section 4(e) Priority List by the addition of 6 chemicals.

The Priority List is divided into three parts: Part A contains those recommended chemicals and groups designated for priority consideration and response by the EPA Administrator within 12 months. Part B contains chemicals and groups of chemicals recommended with intent-to-designate. This category was established by the Committee in its seventeenth report (50 FR 47603; November 19, 1985) to take advantage of rules promulgating automatic reporting requirements for non-designated ITC recommendations under the section 8(a) Preliminary Assessment rule and the TSCA section 8(d) Health and Safety Data Reporting rule. Information received following recommendation with intent-to-designate may influence the Committee to either designate or not designate the chemicals or groups of chemicals in a subsequent report to the Administrator. Part C contains chemicals and groups of chemicals that have been recommended for priority consideration by EPA without being designated for response within 12 months. The changes to the Priority List are presented, together with the types of testing recommended, in the following Table 1:

TABLE 1.—ADDITIONS TO THE SECTION 4(E) PRIORITY LIST

[November 1988]

Chemical/Group	Recommended studies
A. Designated for response within 12 months: Crotonaldehyde ¹ CAS No. 4170-30-3.	Chemical Fate: Volatilization rate from water; aerobic aquatic biodegradation rate. Health Effects: None. Ecological Effects: Acute toxicity to algae, fish and aquatic invertebrates.
B. Recommended with Intent-to-Designate: Tris(2-chloroethyl)-phosphate ² CAS No. 115-96-8.	Chemical Fate: Environmental monitoring; vapor pressure; biodegradation. Health Effects: None.

TABLE 1.—ADDITIONS TO THE SECTION 4(E) PRIORITY LIST—Continued

[November 1988]

Chemical/Group	Recommended studies
Tris(chloropropyl)-phosphates, including the following:	Ecological Effects: Acute toxicity to aquatic and terrestrial plants; chronic toxicity to fish. Chemical Fate: Environmental monitoring; water solubility; vapor pressure; octanol/water partition coefficient; biodegradation.
Tris(2-chloro-1-propyl) phosphate ³ CAS No. 6145-73-9	Health Effects: Acute and subchronic effects, including cholinesterase inhibition, 90-day subchronic effects and reproductive effects. Health effects recommendations apply only to CAS Nos. 6145-73-9 and 13674-84-5.
Tris(1-chloro-2-propyl) phosphate ⁴ CAS No. 13674-84-5; and	
Tris(1,3-dichloro-2-propyl) phosphate ⁵ CAS No. 13674-87-8.	Ecological Effects: Acute toxicity to fish, aquatic invertebrates and algae; chronic toxicity to fish.
Tetrakis(2-chloroethyl)-ethylene diphosphate ⁶ CAS No. 33125-86-9.	Chemical Fate: Environmental monitoring; water solubility; vapor pressure; octanol/water partition coefficient; biodegradation. Health Effects: None. Ecological Effects: Acute toxicity to fish, algae and aquatic invertebrates.
C. Recommended Without Being Designated for Response Within 12 Months: Butyraldehyde ⁷ CAS No. 123-72-8.	Chemical Fate: Monitoring in the vicinity of major manufacturing and use sites. Health Effects: In depth toxicology evaluation if warranted by monitoring data. Ecological Effects: Toxicity studies with representative biota if warranted by monitoring data.

CA Index Names (9 CI)

- 2-Butenal
- Ethanol, 2-chloro-, phosphate (3:1)
- 1-Propanol, 2-chloro-, phosphate (3:1)
- 2-Propanol, 1-chloro-, phosphate (3:1)
- 2-Propanol, 1,3-dichloro-, phosphate (3:1)
- Phosphoric acid, 1,2-ethanediy l tetrakis(2-chloroethyl) ester
- Butanal

Note: Crotonaldehyde was recommended with intent-to-designate by the Committee in the twenty-second report (53 FR 18196; May 20, 1988).

TSCA Interagency Testing Committee

Statutory Member Agencies and Their Representatives

Council on Environmental Quality

William Mills, Member¹

Department of Commerce

Patrick D. Cosslett, Member

Raimundo Prat, Alternate

Environmental Protection Agency

John D. Walker, Member

Laurence S. Rosenstein, Alternate

National Cancer Institute

Richard Adamson, Member

Elizabeth K. Weisburger, Alternate

National Institute of Environmental Health Sciences

James K. Selkirk, Member and

Chairperson

National Institute for Occupational

Safety and Health

Bryan D. Hardin, Member and Vice

Chairperson

Rodger L. Tatken, Alternate

National Science Foundation

Rodger W. Baier, Member

Jarvis L. Moyers, Alternate

Occupational Safety and Health

Administration

Robert Turnage, Member

Stephen Mallinger, Alternate

Liaison Agencies and Their Representatives

Consumer Product Safety Commission

Lakshmi C. Mishra

Department of Agriculture

Richard M. Parry, Jr.

Elise A. B. Brown

Department of Defense

Harry Salem²

Melvin E. Anderson²

Department of the Interior

Gregory J. Smith³

Martha L. Gay⁴

Food and Drug Administration

Arnold Borsetti

National Library of Medicine

Vera Hudson

National Toxicology Program

Dorothy Canter

Committee Staff

Robert H. Brink, Executive Secretary

Norma Williams, ITC Program Specialist

Support Staff

Alan Carpien—Office of the General

Counsel, EPA

Notes

(1) Appointed on July 27, 1988.

(2) Appointed on September 9, 1988.

(3) Appointed on April 29, 1988.

(4) Appointed on June 3, 1988.

The Committee acknowledges and is grateful for the assistance and support

given the ITC by the staff of Dynamac Corporation (technical support contractor) and personnel of the EPA Office of Toxic Substances.

Chapter 1—Introduction

1.1 *Background.* The TSCA Interagency Testing Committee (Committee) was established under section 4(e) of the Toxic Substances Control Act of 1976 (TSCA, Pub. L. 94-469). The specific mandate of the Committee is to recommend to the Administrator of the U.S. Environmental Protection Agency (EPA) chemical substances and mixtures in commerce that should be given priority consideration for the promulgation of testing rules to determine their potential hazard to human health and/or the environment. TSCA specifies that the Committee's recommendations shall be in the form of a Priority List, which is to be published in the Federal Register. The Committee is directed by section 4(e)(1)(A) of TSCA to designate those chemicals on the Priority List to which the EPA Administrator should respond within 12 months by either initiating a rulemaking proceeding under section 4(a) or publishing the Administrator's reason for not initiating such a proceeding. There is no statutory time limit for EPA response regarding chemicals that ITC has recommended but not designated for response within 12 months.

At least every 6 months, the Committee makes those revisions in the section 4(e) Priority List that it determines to be necessary and transmits them to the EPA Administrator.

The Committee is composed of representatives from eight statutory member agencies and seven liaison agencies. The specific representatives and their affiliations are named in the front of this report. The Committee's chemical review procedures and priority recommendations are described in previous reports (Refs. 1 through 7).

1.2 *Committee's previous reports.* Twenty-two previous reports to the EPA Administrator have been issued by the Committee and published in the Federal Register (Refs. 1 through 7). Ninety-six entries (seventy-six chemicals and twenty groups of chemicals) were recommended for priority consideration by the EPA Administrator and designated for response within 12 months. In addition, 24 chemicals and one group of chemicals were recommended without being so designated. Overall, in the 22 reports to the EPA Administrator, the Committee has recommended testing for 100 chemicals and 21 groups of chemicals. A

complete list of recommended chemicals may be obtained by contacting the ITC Executive Secretary at the following address/telephone number: Robert Brink, U.S. Environmental Protection Agency (TS-792), 401 M St., SW., Washington, DC 20460, (202) 382-3820.

1.3 *Committee's activities during this reporting period.* Between April 22, 1988 and October 20, 1988, the Committee continued to review chemicals from its fifth and sixth scoring exercises, and from nominations by Member Agencies, Liaison Agencies and State Agencies.

The Committee contacted chemical manufacturers and trade associations to request information that would be of value in its deliberations. Most of those contacted provided unpublished information on current production, exposure, uses, and effects of chemicals under study by the Committee.

During this reporting period, the Committee reviewed available information on 54 chemicals. Six were selected for addition to the section 4(e) Priority List, and twenty-one were deferred indefinitely. The remaining chemicals are still under study.

In its twentieth report to the EPA Administrator (Ref. 5, ITC, 1987), the Committee placed ethylbenzene (CAS No. 100-41-4) on the Priority List in the "Recommended with Intent-to-Designate" category. The Committee recommended that ethylbenzene be tested for acute toxicity to freshwater algae and invertebrates and to saltwater algae, invertebrates and fish. Subsequently, the Committee learned that acute toxicity testing of ethylbenzene with freshwater invertebrates had recently been completed at the University of Wisconsin. As noted in the twenty-first and twenty-second reports, the Committee also was informed that a consortium of ethylbenzene producers, the Styrene and Ethylbenzene Association, voluntarily sponsored studies on the other acute toxicity tests recommended by the Committee. The Committee deferred a decision on whether or not to designate ethylbenzene pending a review of the data developed during the above studies. The Committee has reviewed the data developed in those studies and has concluded that all of the data gaps identified in the twentieth report have been satisfactorily resolved. Therefore, the Committee has decided that ethylbenzene should be removed from the Priority List.

1.4 *The TSCA section 4(e) Priority List.* Section 4(e)(1)(B) of TSCA directs the Committee to: " * * * make such revisions in the [priority] list as it

determines to be necessary and * * * transmit them to the Administrator together with the Committee's reasons for the revisions." Under this authority, the Committee is revising the Priority List by adding six chemicals: tris(2-chloroethyl)phosphate (CAS No. 115-96-8), tris(2-chloro-1-propyl)-phosphate (CAS No. 6145-73-9), tris(1-chloro-2-propyl)phosphate (CAS No. 13674-84-5), tris(1,3-dichloro-2-propyl)phosphate (CAS No. 13674-87-8), tetrakis(2-chloroethyl)ethylene diphosphate (CAS No. 33125-86-9), and butyraldehyde (CAS No. 123-72-8). In addition, the Committee is designating, for response within 12 months, crotonaldehyde, which was recommended with intent-to-designate in the twenty-second report. Two chemicals are being removed from the Priority List at this time. Methyl ethyl ketoxime (CAS No. 96-29-7) was the subject of a Notice of Proposed Rulemaking (53 FR 35838; September 15, 1988) and ethylbenzene (CAS No. 100-41-4) is being removed for the reasons given in section 1.3.

With the six new recommendations and two removals noted in this report, twenty-one entries now appear on the section 4(e) Priority List. The Priority List is divided in the following Table 2 into three parts; namely, A. Chemicals and Groups of Chemicals Designated for Response Within 12 Months, B. Chemicals and Groups of Chemicals Recommended with Intent-to-Designate, and C. Chemicals and Groups of Chemicals Recommended Without Being Designated for Response Within 12 Months. Table 2 follows:

TABLE 2—THE TSCA SECTION 4(E) PRIORITY LIST, NOVEMBER 1988

Entry	Date of designation
A. Chemicals and Groups of Chemicals Recommended and Designated for Response Within 12 Months:	
1. 1,6-Hexamethylene diisocyanate.	May 1988
2. Crotonaldehyde.....	Nov. 1988
B. Chemicals and Groups of Chemicals Recommended with Intent-to-Designate:	
1. Tris(2-chloroethyl phosphate).	Nov. 1988
2. Tris(2-chloro-1-propyl) phosphate.	Nov. 1988
3. Tris(1-chloro-2-propyl) phosphate.	Nov. 1988
4. Tris(1,3-dichloro-2-propyl) phosphate.	Nov. 1988
5. Tetrakis(2-chloroethyl) ethylene diphosphate.	Nov. 1988
C. Chemicals and Groups of Chemicals Recommended Without Being Designated for Response Within 12 Months:	
1. Diisodecyl phenyl phosphite.	Nov. 1985
2. C.I. Disperse Blue 79.....	Nov. 1986

TABLE 2—THE TSCA SECTION 4(E) PRIORITY LIST, NOVEMBER 1988—Continued

Entry	Date of designation
3. N-[5-[bis[2-(acetyloxy)ethyl]amino]-2-[(2-bromo-4,6-dinitrophenyl)azo]-4-methoxy phenyl]-acetamide.	May 1987
4. N-[5-[bis[2-(acetyloxy)ethyl]amino]-2-[2-chloro-4,6-dinitrophenyl)azo]-4-methoxy phenyl]-acetamide.	May 1987
5. N-[5-[bis[2-(acetyloxy)ethyl]amino]-2-[(2-chloro-4,6-dinitrophenyl)azo]-4-ethoxy phenyl]-acetamide.	May 1987
6. Imidazolium compounds, 4,5-dihydro-1-methyl-2-nortallow alkyl-1-(2-tallow amidoethyl), Me sulfates.	May 1988
7. Ethanaminium,2-amino-N-(2-aminoethyl)-N-(2-hydroxyethyl)-N-methyl-N,N'-ditallow acyl derivs., Me sulfates (salts).	May 1988
8. Poly(oxy-1,2-ethanediyl)-α-[2-[bis(2-aminoethyl)-methylammonio]-ethyl]-ω-hydroxy-, N,N'-dicoco acyl derivs., Me sulfates (salts).	May 1988
9. Poly(oxy-1,2-ethanediyl)-α-[2-[bis(2-aminoethyl)-methylammonio]-ethyl]-ω-, N,N'-bis(hydrogenated tallow acyl) derivs., Me sulfates (salts).	May 1988
10. Poly(oxy-1,2-ethanediyl)-α-[2-[bis(2-aminoethyl)-methylammonio]-ethyl]-ω-hydroxy-, N,N'-ditallow acyl derivs., Me sulfates (salts).	May 1988
11. Poly[oxy(methyl-1,2-ethanediyl)]-α-[2-[bis(2-aminoethyl)-methylammonio]-methyl ethyl]-ω-hydroxy-, N,N'-ditallow acyl derivs., Me sulfates (salts).	May 1988
12. Poly(oxy-1,2-ethanediyl)-α-[3-[bis(2-aminoethyl)-methylammonio]-2-hydroxypropyl]-ω-hydroxy-, N-coco acyl derivs., Me sulfates (salts).	May 1988
13. Poly(oxy-1,2-ethanediyl)-α-[2-[bis(2-aminoethyl)-methylammonio]-ethyl]-ω-hydroxy-, N,N'-di-C ₁₄₋₁₈ acyl derivs., Me sulfates (salts)D May 1988.	May 1988
14. Butyraldehyde.....	Nov. 1988.

REFERENCES

- (1) Sixteenth Report of the TSCA Interagency Testing Committee to the Administrator, Environmental Protection Agency. TSCA Interagency Testing Committee, May 21, 1985, 50 FR 20930-20939. Includes references to Reports 1 through 15 and an annotated list of removals.
- (2) Seventeenth Report of the TSCA Interagency Testing Committee to the Administrator, Environmental Protection Agency. TSCA Interagency Testing Committee, November 19, 1985, 50 FR 47803-47812.

(3) Eighteenth Report of the TSCA Interagency Testing Committee to the Administrator, Environmental Protection Agency. TSCA Interagency Testing Committee, May 19, 1986, 51 FR 18368-18375.

(4) Nineteenth Report of the TSCA Interagency Testing Committee to the Administrator, Environmental Protection Agency. TSCA Interagency Testing Committee, November 14, 1986, 51 FR 41417-41432.

(5) Twentieth Report of the TSCA Interagency Testing Committee to the Administrator, Environmental Protection Agency. TSCA Interagency Testing Committee, May 20, 1987, 52 FR 19020-19026.

(6) Twenty-first Report of the TSCA Interagency Testing Committee to the Administrator, Environmental Protection Agency. TSCA Interagency Testing Committee, November 20, 1987, 52 FR 44830-44837.

(7) Twenty-second Report of the TSCA Interagency Testing Committee to the Administrator, Environmental Protection Agency. TSCA Interagency Testing Committee, May 20, 1988, 53 FR 18196-18210.

Chapter 2—Recommendations of the Committee

2.1 Chemicals recommended for priority consideration by the EPA Administrator. As provided by section 4(e)(1)(B) of TSCA, the Committee is adding the following chemical substances to the section 4(e) Priority List: tris(2-chloroethyl)phosphate (CAS No. 115-96-8), tris(2-chloro-1-propyl)phosphate (CAS No. 6145-73-9), tris(1-chloro-2-propyl)phosphate (CAS No. 13674-84-5), tris(1,3-dichloro-2-propyl)phosphate (CAS No. 13674-87-8), tetrakis(2-chloroethyl)ethylene diphosphate (CAS No. 33125-86-9), and butyraldehyde (CAS No. 123-72-8). In addition, the Committee is designating for response within 12 months one chemical that was recommended with intent-to-designate in the twenty-second report. The designated chemical is crotonaldehyde (CAS No. 4170-30-3). The recommendation of these chemicals is made after considering the factors identified in section 4(e)(1)(A) and other relevant information, as well as the professional judgment of Committee members.

2.2 Chemicals designated for response within 12 months—2.2.a

Crotonaldehyde. In the twenty-second report to the Administrator of EPA (53 FR 18196) crotonaldehyde was recommended with intent-to-designate. The rationale for that recommendation appears in the twenty-second report. Information reviewed by the Committee in response to the twenty-second report includes any public comments on the Committee's recommendations; production volume, use, exposure and release information reported by

manufacturers of crotonaldehyde under the TSCA section 8(a) Preliminary Assessment rule; health and safety studies submitted under TSCA 8(d) Health and Safety Data Report rule; and any unpublished and published data available to the Committee.

After reviewing the information, the Committee concluded that data are still lacking on certain chemical fate factors and ecological effects. For these reasons and for the reasons previously presented

(53 FR 18196) the Committee is now designating crotonaldehyde for response within 12 months and recommending that it be tested for the following:

1. *Chemical fate.* Volatilization rate from water; aerobic aquatic biodegradation rate.
 2. *Health effects.* None.
 3. *Ecological effects.* Acute toxicity to algae, fish and aquatic invertebrates.
- 2.3 *Chemicals recommended with intent-to-designate*—2.3.a *Tris(2-*

chloroethyl)phosphate—*Summary of recommended studies.* It is recommended that tris(2-chloroethyl)phosphate (TCEP) be tested for the following:

1. *Chemical Fate.* Environmental monitoring; vapor pressure; biodegradation.
2. *Health Effects.* None.
3. *Environmental Effects.* Acute toxicity to aquatic and terrestrial plants; chronic toxicity to fish.

PHYSICAL AND CHEMICAL INFORMATION

CAS No. 115-96-8	
Synonyms:.....	Ethanol, 2-chloro, phosphate (3:1) (9CI); Tris (2-chloroethyl) phosphate; FYROL CEF; FYROL PCF; Celluflex CEF; Disflamol TCA; Niax Flame Retardant 3CF. TCEP.
Acronym:.....	
Structural Formula:	
$ \begin{array}{c} \text{O} \\ \parallel \\ \text{O} = \text{P} \begin{cases} \text{---} \text{O} \text{---} \text{CH}_2 \text{CH}_2 \text{Cl} \\ \text{---} \text{O} \text{---} \text{CH}_2 \text{CH}_2 \text{Cl} \\ \text{---} \text{O} \text{---} \text{CH}_2 \text{CH}_2 \text{Cl} \end{cases} \end{array} $	
Empirical Formula.....	C ₁₂ H ₉ O ₄ P.
Molecular Weight.....	285.5.
Melting Point (°C).....	-55 (Ref. 25, Sandmeyer and Kirwin, 1981).
Boiling Point (°C).....	330 (Ref. 2, Aldrich, 1986).
Vapor Pressure (mmHg).....	No information was found.
Solubility in Water (mg/L).....	7,943 (Ref. 31, Yoshioka et al., 1986).
Specific Gravity.....	1.425 @ 20/20° (Ref. 28, Sax and Lewis, 1987).
Log Octanol/Water Partition Coefficient (log P).....	1.7 (Ref. 31, Yoshioka et al., 1986).
Henry's Law Constant.....	1.81 x 10 ⁻⁷ atm m ³ /mol (Ref. 21, Muir, 1984).
Adsorption Coefficient (Koc).....	5.2 (Estimated; Ref. 4, CHEMEST, 1988).
Description of Chemical:.....	Colorless liquid with slight odor (Ref. 17, Lefaux, 1968).

Rationale for Recommendations

I. Exposure Information

A. *Production/use/release to the environment.* Tris (2-chloroethyl) phosphate (TCEP) is produced in substantial but CBI annual amounts in the U.S. Actual production volumes are considered to be confidential business information. It is used as a flame retardant additive for flexible and rigid polyurethane and polyisocyanurate foams, carpet-backing, flame-retardant paints and lacquers, various resins, coatings and adhesives (Ref. 15, Kirk-Othmer, 1980). The major use appears to be in foams such as the flexible foams used in automobiles and furniture and rigid foams for building insulation materials. It is unlikely that there is any natural production of TCEP. Most of the production eventually will be released to the environment as furniture, and

landfills. Some may be released during thermal decomposition (accidental fires and waste incineration). Muir (Ref. 21, 1984) cited a report by Cho and Klaus (1980) stating that 41 percent of TCEP remains intact after thermal oxidation in air at 370°C. However, Paciorek et al. (Ref. 23, 1978) reported that 85 percent of the TCEP chlorine was accounted for in volatile products of degradation at 370°C, which indicates that no more than 15 percent of the TCEP was left undegraded.

B. *Evidence for environmental exposure.* TCEP, in common with many similar tris(haloalkyl)phosphates, has been found in numerous environmental samples throughout the world, at very low concentrations. TCEP was found in river waters in Japan at 17 to 350 ng/L at 14 of 16 sites at Kitakyushu (Ref. 12, Ishikawa et al., 1985b) and in Canadian rivers at 13 sites, with a mean

concentration of 8.7 ng/L (Ref. 29, Williams and LeBel, 1981). TCEP was detected in the Netherlands in the river Waal (Ref. 19, Meijers and Van der Leer, 1976) and the Rhine (Ref. 24, Piet et al., 1987). TCEP was present in ground water from two wells at Fort Devens, MA at concentrations of 0.28 and 0.81 ug/L (Ref. 3, Bedient et al., 1983; Ref. 10, Hutchins et al., 1984). Water from the Great Lakes contained TCEP at a mean concentration of 1.7 ng/L at ten Canadian sites (Ref. 30, Williams and LeBel, 1981) and at concentrations of 3 to 9.6 ng/L at 4 of 5 sites in a later report (Ref. 16, LeBel et al., 1987). Samples from 10 coastal sites in Japan contained 14 to 60 ng/L in the seawater (Ref. 12, Ishikawa et al., 1985b). Sewage treatment facilities in Japan contained from 540 to 1,200 ng/L TCEP in the influent to the plants and 500 to 1,200

ng/L in the effluents. Similarly, at night soil treatment facilities, the influent contained 190 to 1,500 ng/L TCEP and the effluents were found to have 190 to 1,500 ng/L (Ref. 13, Ishikawa et al., 1985c). Five river and ocean sediment samples from Japan contained 13 to 28 ng TCEP/g of sediment. None was detected in a sixth sample (Ref. 12, Ishikawa et al., 1985b). TCEP was detected but not quantified in ambient air at Kitakyushu, Japan (Ref. 9, Haraguchi et al., 1985).

In a survey of infant and toddler dietary intake from October 1978 through September 1979, Gartrell et al. (Ref. 7, 1985a) reported finding TCEP in composite U.S. drinking water at an average concentration of 0.3 ug/L. Drinking water in Japan, examined over a 1-year period, contained 2 to 60.5 ng/L TCEP, with a mean concentration of 17.4 ng/L (Ref. 1, Adachi et al., 1984). Fifteen pooled U.S. drinking water samples contained an average of 2.6 ng/L TCEP (Ref. 18, Lucas, 1984) and Millington et al. (Ref. 20, 1983) reported finding TCEP on activated carbon filter beds used at 40 U.S. drinking water treatment plants. In a study of drinking water samples in England, Fielding et al. (Ref. 6, 1981) found TCEP in one of fourteen samples. LeBel et al. (Ref. 16, 1987) found TCEP at 0.3 to 9.2 ng/L in duplicate drinking water samples from six sites in eastern Ontario. Drinking water from 22 other Canadian cities contained TCEP at 0.3 to 52 ng/L while water from 7 other cities contained no detectable TCEP (Ref. 29, Williams and LeBel, 1981). In a survey of drinking water from the Great Lakes at twelve Canadian cities, Williams et al. (Ref. 30, 1982) found concentrations of TCEP at 0.3 to 13.8 ng/L in water at 11 of the cities. In a survey of infant and toddler diets from October 1979 through September 1980, Gartrell et al. (Ref. 8, 1985b) reported TCEP in composite fruit and fruit juice samples at an average concentration of 0.2 ug/L. It was not detected in other foods tested. Fish from the Okayama Prefecture in Japan contained from less than 0.005 ug/g up to 0.019 ug/g TCEP (Ref. 14, Kenmochi et al., 1981).

TCEP and other widely used tris(chloroalkyl)phosphate flame retardants appear to be widely distributed in the environment, especially in water, at low concentrations. It is not known whether the environmental concentrations are increasing with time or whether these anthropogenic phosphates have attained some steady-state, low-level concentrations.

II. Chemical Fate Information

A. Transport. The water solubility of TCEP is reported to be from 7,000 (Ref. 17, LeFaux, 1968) to 8,300 mg/L (Ref. 11, Ichikawa et al., 1985a). A measured value of 7,943 mg/L was reported by Yoshioka et al. (Ref. 31, 1986). A measured value for the log octanol/water partition coefficient was reported as 1.7 (Ref. 31, Yoshioka et al., 1986). These data indicate that TCEP, following release to the environment, will partition largely to water with little accumulation in sediments or biota. Vapor pressure data at environmentally relevant temperatures were not found, but the Henry's Law constant reported by Muir (Ref. 21, 1984) indicates no significant volatilization from water. The monitoring evidence (see preceding paragraph I.B.) demonstrates widespread occurrence of TCEP in water with some partitioning to air, sediments and biolipids.

B. Persistence. The trialkylphosphates, in general, are resistant to hydrolysis and free-radical oxidations although hydrolysis at the pH of sea water (approximately 8.5) may be significant. TCEP is expected to demonstrate similar resistance to hydrolysis and oxidation, although no data were found. Biodegradation is probably the major degradation mechanism in nature but the available data, which indicate that biodegradation is slow, are mostly circumstantial. There are reports of very little biodegradation of TCEP as it passes through drinking water sand filtration units (Ref. 24, Piet et al., 1981) and through sewage treatment and night soil treatment facilities (Ref. 11, Ishikawa et al., 1985a). TCEP was reported to be hardly degraded after 50 hours in activated sludge (Ref. 11, Ishikawa, et al., 1985a).

C. Rationale for chemical fate recommendations. There is widespread contamination of the environment by TCEP (and other tris(chloroalkyl)phosphates) at very low concentrations. There is some evidence that TCEP may be resistant to biodegradation. Based on its water solubility and octanol/water partition coefficients, TCEP released to the environment is expected to partition largely to water. No data were found on its vapor pressure at ambient temperatures. Since TCEP has been and will continue to be released to both water and soil (landfill) environments, there is a need to obtain measured vapor pressure data and to evaluate its biodegradability in natural waters. It also is recommended that appropriate follow-on monitoring studies be conducted at sites sampled in the 1970's

and early 1980's in an attempt to determine whether environmental concentrations are increasing with time.

III. Biological Effects of Concern to Human Health

A two-year gavage study with rats and mice has recently been completed under the National Toxicology Program (Ref. 22, NTP, 1988) and is currently in the histopathology stages. Given this information, the Committee has deferred its review of TCEP for health effects pending receipt and review of data from the NTP study.

IV. Ecological Effects of Concern

A. Acute and subchronic (short-term) effects. The 96-hour LC50 of TCEP was reported to be 210 mg/L with killifish (*Orizias latipes*) and 90 mg/L with goldfish (*Carassius auratus*) (Ref. 26, Sasaki et al., 1981). These authors also reported spine deformations (caused by convulsive muscle contractions) in killifish with exposure to 200 mg/L of TCEP for 72 hours and protrusion of killifish eyes after 24 to 72 hours exposure to 200 mg/L. Yoshioka et al. (Ref. 31, 1986) reported LC50 values of 251 mg/L with red killifish (*Orizias latipes*), 1,000 mg/L with a daphnia species (*Moina macrocopa*) and 158 mg/L with a flatworm (*Dugesia japonica*). Another literature report (Ref. 5, Eldefrawi et al., 1977) stated that 5 mg/L TCEP had no observable effects on goldfish after 7 days exposure.

B. Chronic (long-term) effects. No information on chronic effects was found. Sasaki et al. (Ref. 26, 1981), as noted in the preceding paragraph, reported spine deformations and eye bulging in killifish exposed to 200 mg/L for 72 hours. Eldefrawi et al. (Ref. 5, 1977) reported that TCEP is a weak inhibitor of acetylcholinesterase and this may produce some chronic effects.

C. Other ecological effects (biological, behavioral, or ecosystem processes). No information was found.

D. Bioconcentration and food-chain transport. The bioconcentration of TCEP was examined by Sasaki et al. (Ref. 26, 1981 and Ref. 27, 1982) in both static and continuous-flow studies. Static tests with killifish and goldfish showed bioconcentration factors (BCFs) of 2 and 1, respectively. A BCF of 1 was observed for killifish in continuous-flow studies over a 10-day period. When the fish were placed in clean water there was rapid depuration with half gone in 0.7 hours after cessation of exposure.

E. Rationale for ecological effects recommendation. The widespread occurrence of TCEP in environmental samples raises concerns for its

ecological effects. On the other hand, the available data indicate that acute toxicity levels for fish and aquatic invertebrates are 1,000 times or more greater than observed environmental concentrations. However, there were no data on plants and it is recommended that TCEP be tested for acute toxicity to aquatic and terrestrial plants. There appear to be chronic exposures to low concentrations of TCEP in aquatic environments and reports of spine deformations raise concerns for chronic effects. Therefore, it is recommended that TCEP also be tested for chronic toxicity to fish.

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2.3.b Tris(chloropropyl)phosphates— Summary of recommended studies. It is recommended that tris(2-chloro-1-propyl)phosphate (CAS No. 6145-73-9) and tris(1-chloro-2-propyl)phosphate (CAS No. 13674-84-5) be tested for the following:

1. **Chemical fate.** Environmental monitoring; water solubility; vapor pressure; octanol/water partition coefficient; biodegradation.
2. **Health effects.** Acute and subchronic effects; including cholinesterase inhibition, 90-day subchronic effects and reproductive effects.
3. **Ecological effects.** Acute toxicity to fish, aquatic invertebrates and algae; chronic toxicity to fish. It is further recommended that tris(1,3-dichloro-2-propyl)phosphate (CAS No. 13674-87-8) be tested for the following:
 1. **Chemical fate.** Environmental monitoring; water solubility; vapor pressure; octanol/water partitioning coefficient; biodegradation.
 2. **Health effects.** None.
 3. **Ecological effects.** Acute toxicity to fish, aquatic invertebrates and algae; chronic toxicity to fish.

PHYSICAL AND CHEMICAL INFORMATION

CAS No. 6145-73-9	
9 CI Name	1-Propanol, 2-chloro-, phosphate (3:1).
Synonyms	2-Chloro-1-propanol phosphate; Tris(beta-chloropropyl)-phosphate; Tris(2-chloropropyl)phosphate; FYROL PCF.
Acronym.....	TCPP.
Structural Formula:	
Empirical Formula.....	C ₉ H ₁₈ Cl ₃ O ₄ P.
Molecular Weight.....	327.55.
Melting Point (°C).....	No information was found.
Boiling Point (°C).....	No information was found.
Vapor Pressure (mmHg).....	No information was found.
Solubility in Water (mg/L).....	No information was found.
Specific Gravity.....	No information was found.
Log Octanol/Water Partition Coefficient	No information was found.

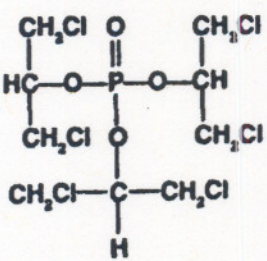
Physical and Chemical Information

CAS No. 13674-84-5	
9 CI Name	2-Propanol, 1-chloro-, phosphate (3:1).
Synonyms	1-Chloro-2-propanol phosphate; Tris(2-chloroisopropyl)-phosphate; Phosphoric acid, tris(2-chloro-1-methylethyl) ester; Tris(1-chloromethylethyl)-phosphate.
Acronym.....	TCIP.
Structural Formula:	
Empirical Formula.....	C ₉ H ₁₈ Cl ₃ O ₄ P.
Molecular Weight.....	327.55.
Melting Point (°C).....	No information was found.
Boiling Point (°C).....	No information was found.
Vapor Pressure (mmHg).....	No information was found.
Solubility in Water (mg/L).....	No information was found.
Specific Gravity.....	No information was found.
Log Octanol/Water Partition Coefficient	No information was found.

Physical and Chemical Information

CAS No. 13674-87-8	
9 CI Name	2-Propanol, 1,3-dichloro-, phosphate (3:1)

PHYSICAL AND CHEMICAL INFORMATION—Continued

Synonyms.....	1,3-Dichloro-2-propanol phosphate; Tris(1,3-dichloro-2-propyl)-phosphate; Tris(1,3-dichloroisopropyl)-phosphate; Tris(1-chloromethyl-2-chloroethyl)phosphate; FYROL FR2; PF38 TDCP; TDCPP.
Acronyms.....	
Structural Formula:	
	
Empirical Formula.....	C ₉ H ₁₅ Cl ₆ O ₄ P.
Molecular Weight.....	430.88.
Melting Point (°C).....	26.7 (Ref. 18, Stauffer, 1979).
Boiling Point (°C).....	No information was found.
Vapor Pressure (mmHg).....	No information at environmentally relevant temperatures and pressures was found.
Solubility in Water (mg/L).....	7 at 24°C (Ref. 2, Hollifield 1979); 100 at 25°C (Ref. 11, Muir, 1984); 1000 at 30°C (Ref. 18, Stauffer, 1979).
Specific Gravity.....	1.515 at 20/20° (Ref. 18, Stauffer, 1979).
Log Octanol/Water Partition Coefficient (log P).....	3.8 (Ref. 13, Sasaki et al., 1981).

Rationale for Recommendations

I. Exposure Information

A. *Production/use/release to environment.* TCPP, TCIP and TDCP are each produced in substantial annual amounts in the U.S. but actual production volumes are classified as confidential business information. TCPP and TDCP are used as additive flame retardants in various plastic materials. TDCP is known to be used primarily in flexible polyurethane foams. No information was found on the use of TCIP but it appears likely that it too is used as an additive flame retardant. Most of the production eventually will be released to the environment as the plastic materials containing them are scrapped or disposed of in dumps and landfills. Some may be released during thermal decomposition (accidental fires and waste incineration). A report by Cho and Klaus (1980) stating that 32 percent of TDCP remains intact after thermal oxidation in air at 370° C was cited by Muir (Ref. 11, 1984). It was reported by Paciorek et al. (Ref. 12, 1978) that TDCP underwent 68 percent thermal oxidation at 370° C. It is unlikely that there is any natural production of these phosphates.

B. *Evidence for environmental exposure.* No information was found on TCPP or TCIP and there was no indication that they have been looked for in the environment. TDCP, in common with many similar tris(haloalkyl)phosphates, has been found in many environmental samples throughout the world, at very low concentrations. TDCP was found in Great Lakes water at 4 of 5 Canadian sites (Ref. 9, LeBel et al., 1987). TDCP was found by LeBel et al. (Ref. 7, 1981) at 0.2 to 1.8 ng/L in drinking water at six eastern Ontario sites. Drinking water from 15 other Canadian cities contained TDCP at 0.3 to 23 ng/L while water from 14 other cities contained no detectable TDCP (Ref. 21, Williams and LeBel, 1981). In a survey of drinking water from the Great Lakes at twelve Canadian Cities, Williams et al. (Ref. 22, 1982) found concentrations of TDCP at 0.1 to 15.7 ng/L. A study of activated carbon filter beds used at 40 U.S. drinking water treatment plants found tris(chloropropyl)phosphate (not further identified) on the carbon (Ref. 11, Millington et al., 1983).

Fish and shellfish from the Okayama prefecture in Japan were reported to contain tris(2, 3-

dichloropropyl)phosphate (Ref. 6, Kenmochi et al., 1981).

In an examination of Swedish products thought to contain additive flame retardants (Ref. 16, Sellestroem and Jansson, 1987), 11 of 104 samples were found to contain TDCP. It was most common in polyurethane products such as sound absorbing materials and liners for cars and buses. These same authors also examined the contents of vacuum cleaner bags from one new and one older (15-year old) house and found TDCP in the dust from the older house.

In analyses of human adipose tissues, LeBel and Williams (Ref. 8, 1983) found TDCP in 5 of 16 samples at 0.5 to 110 ng/g. TDCP also was found at 5 to 50 ppb in 34 of 123 human seminal plasma samples (Ref. 3, Hudec et al. 1981).

Japanese studies have reported finding tris(chloropropyl)-phosphate (CAS No. 26248-87-3) and tris(dichloropropyl)phosphate (CAS No. 26604-51-3) (Ref. 1, Haraguchi et al., 1985) and tris(3-chloropropyl)phosphate (CAS No. 1067-98-7) and tris(2, 3-dichloropropyl)phosphate (CAS No. 78-43-3) (Ref. 4, Ishikawa et al., 1985a) in air and treatment plant influents and effluents in Japan. The first three CAS numbers are not listed in the TSCA Inventory and the fourth CAS number is

a compound that is produced in low amounts in the U.S. It may be that Japanese industry uses tris(chloropropyl)phosphate flame retardants not commonly used in the U.S. and that those compounds may be introduced into the U.S. environment from imported products.

TDCP and other widely used tris(chloroalkyl)phosphate flame retardants appear to be widely distributed in the environment. When they are looked for, they often are found. No information was found on monitoring studies designed to look for TCPP or TCIP and monitoring should be conducted if continued high production and use are confirmed. Additional monitoring studies to evaluate the concentrations of TDCP in the environment should be conducted to determine whether its concentration in the environment is increasing with time.

I. Chemical Fate Information

A. Transport. The water solubility of TDCP is reported to be from 7 to 1,000 mg/L (Ref. 2, Hollifield, 1981, Ref. 11, Muir, 1984, Ref. 18, Stauffer, 1979). The log octanol/water partition coefficient is reported to be 3.8 (Ref. 14, Sasaki et al., 1981). No information was found for TCPP and TCIP. The monitoring evidence (see I.B., above) for TDCP demonstrates widespread occurrence of TDCP in water with some partitioning to sediments and biolipids. TCPP and TCIP are expected to behave similarly.

B. Persistence. No information was found for TCPP, TCIP or TDCP. However, Ishikawa et al. (Ref. 5, 1985b) reported that influent and effluent data for activated sludge treatment showed no biodegradation of tris(chloropropyl)phosphate (CAS No. 1067-98-7) and tris(2,3-dichloropropyl)phosphate (CAS No. 78-43-3).

C. Rationale for chemical fate recommendations. There is widespread contamination of the environment by TDCP. There may be persistent background levels of TCPP and TCIP in the environment but this is unknown. There is a need to conduct appropriate monitoring studies to determine if TCDD and TCIP, like similar tris(chloroalkyl)phosphate flame retardants, are present in the environment at low concentrations and whether the environmental concentrations of TDCP are increasing. There also is a need to obtain reliable, measured water solubility, vapor pressure and octanol/water partition coefficient data on these flame retardants to better estimate their transport in the environment and to

evaluate their biodegradability in natural waters.

III. Biological Effects of Concern to Human Health

The Committee determined that tris(1,3-dichloro-2-propyl)phosphate (CAS No. 13674-87-8) has been studied extensively for health effects and concluded that additional studies are not required. Therefore, health effects testing is not being recommended at this time.

A. Metabolism and toxicokinetics. No information was found for TCPP or TCIP.

B. Acute (short-term) effects. No information was found for TCPP. An LD50 of 56 mg/kg, administered intravenously in mice, was found for TCIP (U.S. Army data, cited in Ref. 13, RTECS, 1988). The reliability of this information cannot be assessed since experimental details are not available.

Stauffer (cited in Ref. 20, USEPA, 1981) reported studies on the neurotoxic potential of TDCP, a structurally similar phosphate, on adult hens. At 10 g/kg, the maximum tolerated dose, there was 7 percent inhibition of brain neurotoxic esterase. In positive controls, treated with tri-*o*-cresyl phosphate at 0.5 g/kg, there was an 85 percent inhibition.

No subchronic effects data were found for TCIP. The neurotoxic potential of TCPP in adult white Leghorn hens was evaluated by Sprague et al. (Ref. 17, 1981). A group of 18 hens received an initial oral dose of 13.23 g TCPP/kg, followed by the same treatment 3 weeks later. The animals were sacrificed 3 weeks after the second dose. Loss of body weight, transient reductions in food consumption and one death were reported for the treated animals. Egg production ceased shortly after the first dose and there was severe feather loss. No behavioral or histological evidence of delayed neurotoxicity was observed.

C. Genotoxicity. No information was found for TCPP or TCIP.

D. Oncogenicity. No information was found for TCPP or TCIP. A structurally similar compound, TDCP, was tested for oncogenicity in rats of both sexes and produced a significantly increased incidence of hepatocellular carcinoma and interstitial cell tumors of the testes (Ref. 19, Stauffer, 1981).

E. Chronic (long-term) effects. No information was found for TCPP or TCIP.

F. Reproductive and developmental effects. No information was found for TCPP or TCIP.

G. Observations in humans. No information was found for TCPP or TCIP.

H. Rationale for health effects recommendations. Three tris(chloropropyl)phosphates (TCPP, TCIP and TDCP) are produced in substantial amounts in the U.S. and used as additive flame retardants. TDCP is widely distributed in the environment at low concentrations. No exposure information (occupational, consumer or environmental) is available for TCPP or TCIP. It is assumed that use of the latter two compounds as flame retardants will eventually lead to the release of TCPP and TCIP to the environment. TDCP appears to be well studied for potential health effects but there is very little health effects information on TCIP and TCPP. The health effects information is limited to a LD50 for TCIP in mice by intravenous exposure and a subchronic evaluation of the neurotoxic potential of TCPP in hens. An evaluation of neurotoxicity should be conducted for a period of 90 days.

In view of the lack of health effects information on TCIP and TCPP and given the acute effects, oncogenicity and neurotoxicity of TDCP, it is recommended that TCIP and TCPP be tested for acute effects, including cholinesterase inhibition, 90-day subchronic effects and reproductive effects. Based on the results of the recommended studies, the need for long-term studies should be considered.

IV. Ecological Effects of Concern

A. Acute and subchronic (short-term) effects. No information was found for TCPP or TCIP.

The 96-hr LC50 for TDCP was reported to be 3.6 mg/L with killifish and 5.1 mg/L with goldfish (Ref. 14, Saaski et al., 1981). These authors also reported spine deformations (caused by convulsive muscle contractions) in killifish after 24 hours exposure at 3.5 mg/L TDCP.

B. Chronic (long-term) effects. No information on chronic effects was found. However, as noted in the preceding paragraph, Sasaki et al. (Ref. 14, 1981) reported spine deformations in killifish exposed to 3.5 mg/L TDCP for 24 hours.

C. Other ecological effects. No information was found.

D. Bioconcentration and food-chain transport. The bioconcentration of TDCP was examined by Sasaki et al. (Ref. 14, 1981 and Ref. 15, 1982) in both static and continuous flow studies. Static tests with killifish and goldfish showed bioconcentration factors of 47 to 107 with killifish and 3 to 5 with goldfish. In continuous-flow studies, the bioconcentration factor for TDCP was 31 to 59 for up to 32 days exposure. There

was a rapid depuration following cessation of exposure to TDCP in the continuous-flow studies, with half gone in 1.7 hours.

E. Rationale for ecological effects recommendations. The widespread occurrence of TDCP in environmental samples and the likely contamination of the environment by TCPP and TCIP raise concerns for their ecological effects. Each should be tested for acute toxicity to fish, aquatic invertebrates and algae to better evaluate the hazard associated with chronic exposures to low environmental concentrations. The observation of spine deformations in fish exposed to TDCP and the widespread occurrence of TDCP at low concentrations also raises concerns for chronic effects. It is recommended that each of these tris(chloropropyl)-phosphates be tested for chronic toxicity to fish.

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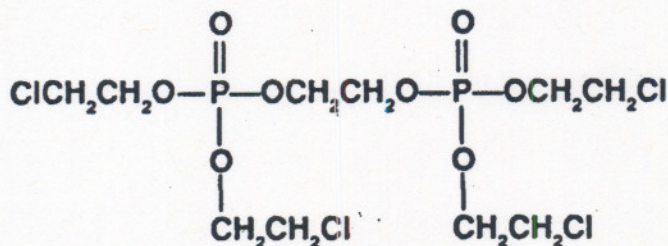
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2.3.c Tetrakis(2-chloroethyl)ethylene diphosphate—Summary of recommended studies. It is recommended that tetrakis(2-chloroethyl)ethylene diphosphate (TCEED) be tested for the following:

1. **Chemical fate.** Environmental monitoring; water solubility; vapor pressure; octanol/water partition coefficient; biodegradation.
2. **Health effects.** None.
3. **Ecological effects.** Acute toxicity to fish, algae and aquatic invertebrates.

PHYSICAL AND CHEMICAL INFORMATION

CAS No. 33125-86-9	
Synonyms.....	Phosphoric acid, 1,2-ethanediyl (2-chloro-ethyl) ester (9CI); Thermolin 101.
Acronym.....	TCEEP.
Structural Formula:	



PHYSICAL AND CHEMICAL INFORMATION—Continued

CAS No. 33125-86-9	
Empirical Formula.....	C ₁₀ H ₂₀ Cl ₂ O ₄ P ₂
Molecular Weight.....	471.9
Melting Point (°C).....	No information was found.
Boiling Point (°C).....	No information was found.
Vapor Pressure (mmHg).....	0.85 at 25°C (Ref. 3, Olin, 1987).
Solubility in Water (mg/L).....	3000 at 24°C (Ref. 3, Olin, 1987).
Specific Gravity.....	1.45 at 25°C (Ref. 3, Olin 1987).
Log Octanol/Water Partition Coefficient (log P).....	1.16, estimated (Ref. 2, CLOGP, 1987).
Henry's Law Constant.....	1.76 x 10 ⁻⁴ atm m ³ /mol (calculated)
Log Adsorption Coefficient.....	2.0 (Ref. 1, CHEMEST, 1987)
Description of Chemical.....	Dark liquid under ambient conditions. (Ref. 3, Olin, 1987).

Rationale for Recommendations

I. Exposure Information

A. Production/use. Tetrakis(2-chloroethyl)ethylene diphosphate (TCEEP) is produced in substantial annual amounts in the U.S. but actual production volumes are classified as confidential business information. TCEEP is used as an additive flame retardant in flexible polyurethane foams and may be used as a flame retardant in various resins. There is no known natural production of TCEEP.

B. Environmental release. It is likely that most of the TCEEP production is eventually released to the environment as furniture, automobiles, construction materials, etc. are scrapped and disposed of in dumps and landfills. Some TCEEP may be released during thermal decomposition (in accidental fires and incinerators) but no information was found on thermal decomposition.

C. Evidence for environmental exposure. No information was found. Related chloroalkyl phosphate flame retardants (e.g., tris(2-chloroethyl)phosphate and tris(1,3-dichloropropyl)phosphate), when looked for in the environment, have been found at low concentrations in a wide variety of environmental media in industrialized countries. It is not known whether anyone has looked for TCEEP in the environment.

II. Chemical Fate Information

A. Transport. The water solubility, vapor pressure and estimated octanol/water partition coefficient for TCEEP suggest significant transport to both air and water, with little sorption to soil or sediment. The calculated Henry's law constant, if true, would produce a half-life for volatilization from water of

about 1 to 2 days. A related phosphate, the tris(2-chloroethyl)-phosphate, has a reported Henry's constant of 1.81×10^{-7} atm m³/mol for a predicted half-life in water of about 1.4 years. It is difficult to believe that there would be such a great difference between these two phosphates and the water solubility and vapor pressure used to calculate the Henry's constants should be reliably measured. If this phosphate behaves similarly to the tris(chloroalkyl)phosphate flame retardants, it will partition largely to water following release to the environment.

B. Persistence. No information was found.

C. Rationale for chemical fate and recommendations. TCEEP, like the related tris(chloroalkyl)phosphate flame retardants, may partition largely to the aquatic environment and be relatively persistent. The related tris(chloroalkyl)phosphates have been found throughout the industrialized world in a variety of environmental media at low concentrations. There is a need for monitoring studies that look for TCEEP to determine if it also appears at low concentrations in the environment. In addition, it is recommended that studies be conducted to determine the water solubility, vapor pressure and octanol/water partition coefficient of TCEEP and to evaluate its biodegradability in natural waters.

III. Biological Effects of Concern to Human Health

The Committee, at the conclusion of its Sixth Scoring Exercise, concluded that it would not review TCEEP for health effects (52 FR 10409, April 1, 1987). Therefore, no health effects studies are being recommended at this time.

IV. Ecological Effects of Concern

A. Acute and subchronic (short-term) effects. No information was found.

B. Chronic (long-term) effects. No information was found.

C. Other ecological effects. No information was found.

D. Bioconcentration and food-chain transport. No information was found.

E. Rationale for ecological effects recommendations. It is likely that TCEEP has been and will continue to be released to the environment in significant quantities where it may persist and accumulate. Studies should be conducted to evaluate the acute toxicity of TCEEP to fish, aquatic invertebrates and algae.

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2.4 Chemicals recommended without being designated for response within 12 months—
2.4.a Butyraldehyde—Summary of recommended studies. It is recommended that butyraldehyde be tested for the following:

1. *Chemical fate.* Monitoring in the vicinity of major manufacturing and use sites.
2. *Health effects.* In depth toxicology evaluation if warranted by monitoring data.
3. *Ecological effects.* Toxicity studies with representative biota if warranted by monitoring data.

PHYSICAL AND CHEMICAL INFORMATION

CAS No. 123-72-8	
Synonyms	Butanal (9CI); Butyraldehyde (8CI); n-Butyraldehyde; Butal; Butyric aldehyde; n-Butyraldehyde; Butanaldehyde; Butyric aldehyde.
Structural Formula:	
CH₃CH₂CH₂CHO	
Empirical Formula	C ₄ H ₈ O.
Molecular Weight	72.10.
Melting Point (°C)	-99 (Ref. 61, Windholz, 1983).
Boiling Point (°C)	-74.8 (Ref. 61, Windholz, 1983).
Vapor Pressure (mmHg)	92 @ 20° (Ref. 14, Eastman, 1988).
Solubility in water (mg/L)	6,000 (Ref. 14, Eastman, 1988).
Specific Gravity	0.8016 (Ref. 61, Windholz, 1983).
Log Octanol/Water Partition Coefficient (log P)	0.88 (Ref. 15, ENVIROFATE, 1988).
Henry's Law Constant	1.4 × 10 ⁻⁴ (calculated).
Vapor Density in Air (air = 1)	2.5 (Ref. 14, Eastman, 1988).
Description of Chemicals	Colorless liquid with characteristic pungent, aldehyde odor (Ref. 25, Hawley, 1987).

Rationale for Recommendations

I. Exposure Information

A. *Production/use/release to environment.* Butyraldehyde is produced and used in the U.S. at a rate in excess of one billion pounds per year. SRI reported U.S. production of butyraldehyde in 1987 at 1.835 billion pounds by five manufacturers at six sites spread across Texas (Ref. 52, SRI International, 1987). Greater than 90 percent of the production is used as a chemical intermediate to synthesize n-butanol and 2-ethylhexanol. Domestic production of n-butanol and 2-ethylhexanol was 935 million and 638 million pounds, respectively, in 1987 (Ref. 9, C&EN, 1988). Other important uses for butyraldehyde include its use as a solvent for surface coatings and its combination with polyvinyl alcohol to form a resin in laminated safety glass (Ref. 8, CEH, 1985).

Butyraldehyde occurs naturally in many plants, including fruits and vegetables, and in cheese, meats and wines. It has FDA approval as a direct food additive for use as a synthetic flavoring substance and as an indirect food additive as a component of packaging (21 CFR 172.515; 21 CFR 175.105; and Ref. 44, Opdyke, 1979).

The major releases of butyraldehyde to the environment will occur at the manufacturing sites in Texas and at major use sites elsewhere in the U.S. This volatile water soluble chemical may be released to water and air in significant quantities. One company (Ref. 14, Eastman, 1988) reported 1987 emissions at its Texas plant of about 831,000 pounds with 90 percent of the

emissions listed as fugitive emissions to air. Toxic chemical release inventory reporting forms submitted to the EPA in response to the Toxic Chemical Release Reporting rule (53 FR 4500; February 16, 1988) provide information on substantial releases to air (from 54,000 to 836,000 lbs. per year) at six manufacturing and use sites (Ref. 55, USEPA, 1988).

B. *Evidence for human and environmental exposure.* According to the National Occupational Hazard Survey (NOHS) conducted by the National Institute for Occupational Safety and Health (NIOSH) from 1972 to 1974, 1,259 workers were potentially exposed to butyraldehyde in the workplace in 1970 (Ref. 38, NIOSH, 1976). Preliminary data available from the National Occupational Exposure Survey (NOES), conducted by NIOSH from 1980 to 1983, indicate that 5,392 workers, including 950 women, were potentially exposed to butyraldehyde in the workplace in 1980 (Ref. 39, NIOSH, 1984). Since domestic production has been increasing since 1982 (Ref. 56, USITC 1983) it is expected that more workers are exposed today.

Occupational exposure limits have not been established by the American Conference of Governmental Industrial Hygienists or the Occupational Safety and Health Administration.

One company (Ref. 14, Eastman, 1988) reported that the major points of worker exposure to n-butyraldehyde are in sampling, loading, and unloading shipping containers, and maintaining the equipment. Also, during production at its Texas plant, from 4 to 8 workers are potentially exposed daily, and from 1 to

2 maintenance workers are potentially exposed for approximately 120 days per year. The same company reported that during use of n-butyraldehyde to manufacture other chemicals, 12 to 18 workers are potentially exposed at its Tennessee plant. These processes run from 180 to 360 days per year. Personal monitoring of production workers (42 samples) indicated air concentrations of n-butyraldehyde averaging less than 1.0 ppm (8-hour TWA) with no sample above 1.25 ppm. Personal monitoring of materials handling workers (7 samples) indicated a geometric mean (8-hour TWA) of 3.7 ppm n-butyraldehyde. Five of the seven samples were under 1.0 ppm, the other two were 21.3 and 4.57 ppm. (Ref. 14, Eastman, 1988).

Another company (Ref. 26, Hoechst-Celanese, 1988) reported that 120 employees were working in the butyraldehyde unit of its Texas processing plant. It reported no monitoring data collected in previous years, and only one sample collected in 1988 which "was 1 ppm for an 8 hour period." It was not reported whether this was a personal or area sample. Its Texas purification plant (Ref. 26, Hoechst-Celanese, 1988) reported 4 to 6 workers exposed to n-butyraldehyde with monitoring data indicating exposure levels less than 10 ppm. However, no information was given concerning the collection of monitoring data.

There are no monitoring data available showing general population exposure to n-butyraldehyde. Exposures may be significant for populations living near major manufacturing sites since

toxic release information indicates substantial fugitive emissions from manufacturing and use sites (Ref. 14, Eastman, 1988; Ref. 55, USEPA, 1988). One company (Ref. 26, Hoechst-Celanese, 1988), however, reported community exposure near its Texas processing plant to be less than 0.0004 ppm n-butyraldehyde although fugitive emissions of butyraldehyde at the plant exceeded 106,000 pounds per year. Details of the sampling and other procedures used to determine this number were not reported.

Butyraldehyde was detected but not quantified in the respired air of a heterogenous nonsmoking control population living in Chicago and the surrounding suburbs; however, it was not detected in the respired air of two other populations examined in the study: A prediabetic group and a diabetic group. The total sample was 62 persons. The authors classified butyraldehyde as a physiologic volatile metabolite but did not suggest a mechanism for its generation (Ref. 34, Krotoszynski and O'Neill, 1982).

No information was found concerning drinking water exposures to n-butyraldehyde.

Many of the monitoring studies that report environmental concentrations of butyraldehyde have dealt with urban air in areas where smogs are a problem. This appears to be due to the presence of butyraldehyde in the emissions from internal combustion engines and the involvement of butyraldehyde in smog formation. Grosjean et al. have conducted several of these studies in Southern California (Ref. 17, Fung et al., 1981; Ref. 21, Grosjean, 1982; Ref. 22, Grosjean et al., 1983; Ref. 23, Grosjean and Wright, 1983; and Ref. 24, Grosjean and Fung, 1984). Similar studies have been conducted in Sweden (Ref. 31, Jonsson et al., 1985). Isodorov (Ref. 28, 1985) reported on the emissions of butyraldehyde into the atmosphere by ferns in the forests of northern Russia. Little or no monitoring data were found on the presence of butyraldehyde in the

air near major manufacturing and use sites although toxic release information reveals substantial fugitive emissions at manufacturing and use sites.

Some monitoring studies have looked for butyraldehyde in surface, ground and drinking waters and it has been found at very low concentrations in a few samples (Ref. 11, Corwin, 1969; Ref. 16, Ewing et al., 1977; and Ref. 58, Viar, 1988). No data were found on monitoring conducted on water samples obtained near manufacturing and use sites.

Ito et al. (Ref. 29, 1980) reported finding butyraldehyde in fish in Japan.

II. Chemical Fate Information

A. Transport. Based on its vapor pressure, water solubility and log P, butyraldehyde released to the environment will partition to both water and air. The Henry's law constant for butyraldehyde indicates that butyraldehyde in surface waters will volatilize rapidly with a half-life in water of about 12 hours.

B. Persistence. Butyraldehyde released to the environment will not persist. It will be rapidly degraded in the atmosphere by reaction with hydroxyl radicals with an atmospheric half-life of 4 to 9 hours (Ref. 14, Eastman, 1988). Butyraldehyde is readily biodegraded under both aerobic and anaerobic conditions by acclimated microorganisms.

C. Rationale for chemical fate recommendations. Butyraldehyde released to the environment will not persist and concerns for potential adverse effects are low in most parts of the U.S. However, the large production volumes at sites in Texas and the toxic release data on substantial releases to air at manufacturing and use site raise concerns with respect to environmental concentrations of butyraldehyde in air and water at those sites. Those emissions will occur on a nearly continuous basis and butyraldehyde may be present in the air and water at significant concentrations that represent a balance between rates of release and

rates of removal by degradation processes. It is recommended that monitoring studies be conducted to determine butyraldehyde concentrations in air and water in the vicinity of the major manufacturing and use facilities. Monitoring for the presence of low molecular weight, volatile, hydrophilic compounds in water samples, as noted by Ogawa and Fritz (Ref. 43, 1985), can be very difficult and special care should be taken to assure realistic results.

III. Biological Effects of Concern to Human Health

A. Metabolism and pharmacokinetics. Aldehydes are oxidized to the corresponding acid by the enzyme aldehyde dehydrogenase (Ref. 59, Weiner, 1980). Three isozymes have been identified from human liver, all of which oxidized several aldehydes, including butyraldehyde (Ref. 30, Jones and Teng, 1983).

Butyraldehyde has been detected in mother's milk (6 or 8 samples) obtained from urban areas in the U.S. (Ref. 45, Pellizzari et al., 1982) and in the sera of normal and diabetic patients (Ref. 62, Zlatkis et al., 1980).

In vitro studies indicate that butyraldehyde at concentrations of 0.1 to 1 mM inhibits multiplication of mouse sarcoma cells in culture (Ref. 46, Pilotti et al., 1975; Ref. 13, Curvall et al., 1984), and inhibits chemotaxis and reduces viability of human polymorphonuclear leukocytes at 90 mM (Ref. 3, Bridges et al., 1977). Other *in vitro* effects included: damage to the cell membranes of human fibroblasts at 25 mM (Ref. 54, Thelestam et al., 1980; Ref. 13, Curvall et al., 1984) and human red blood cells at 1mM (Ref. 47, Poli et al., 1987), and interference with lipolysis and glucose metabolism in adipose tissue cells at concentrations of 1 to 20 mM (Ref. 20, Giudicelli et al., 1973).

B. Acute and subchronic (short-term) effects. The acute toxicity data for butyraldehyde are summarized in the following Table 3.

TABLE 3.—TOXICITY OF BUTYRALDEHYDE IN LABORATORY ANIMALS

Species	LC50		LD50		Reference
	Duration (hours)	Concentration (mg/m ³)	Oral (mg/kg)	Dermal (mg/kg)	
Rat			2,490		Marhold (1972, as cited in RTECS, Ref. 48). Smyth et al. (1951, Ref. 51).
Rat	4	* >23,590	5,890		
Rat	0.5	174,000			
Mouse	2	44,610			Skog (1950, Ref. 50).
Rabbit				3,560	Izmerov (1982, as cited in RTECS, Ref. 48). Union Carbide Data Sheet (1967, as cited in RTECS, Ref. 48). Brabec (1981, Ref. 2).
Guinea pig				>16	

* One of six animals died.

Inhalation toxicity in males of two mouse strains was defined by a 50 percent reduction in respiratory rate (RD50) following exposure of 3 or 4 mice per dose (dose range not specified) for 10 minutes (Ref. 53, Steinhagen and Barrow, 1984). An RD50 of 1,532 ppm (4,518 mg/m³) was determined for B6C3F₁ mice, and an RD50 of 1,015 ppm (2,993 mg/m³) was determined for Swiss-Webster mice. An RD50 of 5,572 ppm (16,431 mg/m³) was determined for male rats under similar conditions (Ref. 1, Babiuk et al., 1985).

Inhalation exposure of ten Sprague-Dawley derived CD rats to measured concentrations of 1,820 ppm (5,367 mg/L) butyraldehyde for 4 hours caused irritation of the ocular and respiratory mucous membranes during the exposure and subsequent 4 hours (Ref. 26, Hoechst-Celanese, 1988). No other treatment-related effects were reported during the 14-day observation period or at necropsy.

Inhalation exposure of rats to 1,000 ppm (2,949 mg/m³) butyraldehyde for twelve 6-hour exposures produced no observable toxic signs (Ref. 18, Gage, 1970).

Oral administration of butyraldehyde to rats at dose levels of 0.075, 0.15, 0.3, 0.6, or 1.2 g per kg, daily for 5 days per week for 13 weeks caused irritation, inflammation, necrosis, hyperplasia, and lesions in the forestomach and gastric mucosa (Ref. 40, NTP, 1988). The increased incidence of these lesions was dose-related and affected 100 percent of the males and 90 percent of females at the highest dose level, 1.2 g/kg.

Dermal exposure of rabbits to butyraldehyde (2.5 mL/kg) for 24 hours caused severe dermal lesions that became infected and led to termination of the study after 7 days (Ref. 26, Hoechst-Celanese, 1988). Extensive necrosis and severe edema were exhibited by all animals at 24 hours; eschar developed about day 4 or 5. Toxic signs evident in several animals during the 24-hour application period included ataxia, fine tremors, hypoactivity, and respiratory anomalies. Tremors, hypoactivity, hypopnea and respiratory arrhythmia persisted in a few animals for an unspecified period of time. Apart from the dermal lesions, no other treatment-induced changes were evident at necropsy.

Butyraldehyde is a severe skin and eye irritant in rabbits (Ref. 26, Hoechst-Celanese, 1988). It exhibits little or no potential to produce dermal sensitization in guinea pigs (Ref. 26, Hoechst-Celanese, 1981). After a 3-week induction period consisting of nine 6-hour applications of butyraldehyde, there was no dermal response from

guinea pigs challenged with 10 percent butyraldehyde. A second challenge at 25 percent elicited an equivocal response in only 2 of 20 animals.

C. Genotoxicity. In the *Salmonella* assay, butyraldehyde was not mutagenic in strains TA1535, TA1537, TA98, or TA100, with or without activation (Ref. 35, Mortelmans et al., 1986). No increase in chromosomal aberrations was detected in Chinese hamster ovary cells at butyraldehyde concentrations of 59 to 135 ug/mL with or without metabolic activation, but sister chromatid exchange was induced in these cells at nontoxic levels ranging from 9 to 90 ug/mL (Ref. 19, Galloway et al., 1987). The lowest effective doses were less than 9 ug/mL without activation and 30 ug/mL with activation. When butyraldehyde was administered to male mice (Q strain) in the drinking water at 0.2 mg/L for 50 days, chromosomal aberrations were evident as polyploidy at all stages of spermatogenesis and abnormal pairing of chromosomes at metaphase I (Ref. 37, Moutschen-Dahmen, 1976). Butyraldehyde did not increase sister chromatid exchange in human lymphocytes treated *in vitro* at a concentration of 2×10^{-3} percent (v/v) without metabolic activation (Ref. 42, Obe and Beck, 1979). No increase was reported in sex-linked recessive lethals of *Drosophila melanogaster* fed butyraldehyde at a concentration of 2,000 ppm in 5 percent aqueous sucrose (Ref. 57, Valencia et al., 1985).

D. Oncogenicity. No information was found on the subject compound. Plans for a chronic inhalation bioassay of butyraldehyde were dropped by NTP because of technical difficulties in generating the atmosphere for exposure (Ref. 41, NTP, 1988). A related compound, isobutyraldehyde, is scheduled for a chronic inhalation bioassay starting in February 1989 under the National Toxicology Program. Other structural analogues of n-butyraldehyde including formaldehyde and acetaldehyde have shown sufficient evidence for carcinogenicity in animal studies; the evidence in humans is considered by IARC to be limited for formaldehyde and inadequate for acetaldehyde (Ref. 27, IARC, 1987).

E. Chronic (long-term) effects. No information was found.

F. Reproductive and developmental effects. A single intraperitoneal injection of 1 mg butyraldehyde per animal produced chromosomal damage and meiotic anomalies including degenerative nuclei, multispindle cells and polyploid cells at all stages of spermatogenesis in male mice 1 month following the treatment (Ref. 36, Moutschen-Dahmen et al., 1975). In a

later study (Ref. 37, Moutschen-Dahmen et al., 1976), one group of male mice received a single intraperitoneal dose of 30 mg butyraldehyde per kg, and a second group received 0.2 mg/L in their drinking water for 50 days. Administration of butyraldehyde by either route damaged the spermatogenic cells of the seminiferous tubules. In addition to gross degeneration, polyploidy was observed at all stages of spermatogenesis and abnormal pairing of sex chromosomes occurred at metaphase I; there was increased incidence of spermatozoa without acrosomes in the vas deferens.

G. Observations in humans. Among 12 individuals of Oriental ancestry characterized as susceptible to cutaneous flushing after ingestion of ethanol, all reacted positively (with erythema) to patch testing with 75 percent butyraldehyde (Ref. 60, Wilkin and Fortner, 1985).

Butyraldehyde was found to be mildly irritating when applied in epicutaneous tests (Ref. 44, Fiser and Pokorny, 1965, as cited in Opdyke, 1979), whereas 1 percent butyraldehyde in petrolatum produced no irritation after a 48-hour closed patch test (Ref. 44, Kligman 1977, as cited in Opdyke, 1979). One out of 25 tested with 1 percent butyraldehyde in petrolatum had a positive but nonspecific sensitization reaction in a maximization test.

Butyraldehyde vapor (230 ppm) was nonirritating to the eyes of 15 men during a 30 minute exposure (Ref. 49, Sim and Pattle, 1957).

H. Rationale for health effects recommendations. Annual domestic production of n-butyraldehyde is about 1.8 billion pounds by five manufacturers at six sites in Texas. Preliminary data indicate that over 5,000 workers (including 950 women) were potentially exposed to n-butyraldehyde in the workplace in 1980. Since domestic production has been increasing since 1982, it is expected that more workers are exposed today.

Sizeable airborne fugitive emissions have been reported (from 54,000 to 836,000 lbs. per year) from six major manufacturing and use sites. Therefore, there is potential for significant community population exposure in the vicinity of manufacturing and use sites.

Structural analogues of n-butyraldehyde including formaldehyde and acetaldehyde have shown carcinogenic effects in animals. IARC considers that there is sufficient evidence from animal studies for the carcinogenicity of formaldehyde and acetaldehyde whereas the evidence in humans is limited or inadequate,

respectively. The National Toxicology Program is scheduled to perform a 2-year inhalation study with isobutylaldehyde. There are, however, no data available to assess the carcinogenicity of n/butylaldehyde itself. The Committee noted the data

indicating impaired spermatogenesis in male mice. Considering the lack of definitive data, the Committee recommends that testing addressing carcinogenicity and reproductive and developmental effects of butylaldehyde

should be conducted if warranted by monitoring data.

IV. Ecological Effects of Concern

A. *Acute and subchronic (short-term) effects.* Acute toxicity (LC50) values have been reported as shown below.

Organism	Endpoint	Butylaldehyde Conc. (mg/L)	Reference
Fathead minnow	96-hr LC50	25.8	Ref. 12, Curtis and Ward, 1981.
Golden Orfe	96-hr LC50	57 & 114	Ref. 32, Juhnke and Ludemann, 1978.
<i>Aedes aegypti</i> larva.....	4-hr LC50	2,000	Ref. 33, Kramer et al., 1983.

B. *Chronic (long-term) effects.* No information was found.

C. *Other ecological effects.* In a series of articles, Bringmann and Kuhn reported on minimum inhibitory concentrations for a large number of chemicals and a variety of aquatic organisms. The definition of minimum inhibitory concentration varied according to the organism being tested. For daphnids it was described as the maximum tested concentration at which all of the daphnids were able to retain their swimming capability following 24 hours exposure to the test chemical. For protozoa the minimum inhibitory concentration was the concentration that caused cell counts in test cultures to be 5 percent or more below the counts in control cultures with 48 hours exposure. For algae, the minimum inhibitory concentration was the concentration of test material that inhibited cell multiplication in test versus control cultures during 8 days exposure. For the bacterium, *Pseudomonas putida*, the endpoint was inhibition of cell multiplication after 24 hours exposure, as determined by turbidity measurements of test versus control cultures (Ref. 4, Bringmann, 1978; Ref. 5, Bringmann and Kuhn, 1980; Ref. 6, Bringmann and Kuhn, 1981; and Ref. 7, Bringmann and Kuhn, 1982). Their results with butylaldehyde are summarized below:

Organism	Minimum inhibitory concentration (mg/L)
<i>Microcystis aeruginosa</i> algae	19
<i>Scenedesmus quadricauda</i> algae	83
<i>Entosiphon sulcatum</i> protozoa.....	4.2
<i>Urunema paruczii</i> protozoa.....	98
<i>Chilomonas paramecium</i> protozoa	44
<i>Daphnia magna</i>	100
<i>Pseudomonas putida</i> bacterium.....	100

The butylaldehyde concentrations that inhibited the swimming capability of 50 percent and 100 percent of *Daphnia magna* populations after 24-hours exposure also were reported by Bringmann and Kuhn (Ref. 7, 1982) to be 195 and 383 mg/L, respectively.

Chou et al. (Ref. 10, 1978) reported that butylaldehyde was relatively non-toxic to methanogenic bacteria.

In a study on the use of bacteria as an indication of toxicity to fish, Curtis et al. (Ref. 12, 1981) reported a 5-minute EC50 of 16.4 mg/L for *Photobacterium phosphoreum* exposed to butylaldehyde.

D. *Bioconcentration and food-chain transport.* An examination of fish in Japan revealed the presence of butylaldehyde at low concentrations (Ref. 29, Ito et al., 1980). The significance of this information is unclear since butylaldehyde is produced naturally and is found in many food products. Based on its high water solubility and low octanol/water partitioning coefficient, butylaldehyde is not expected to bioconcentrate.

E. *Rationale for ecological effects recommendations.* Butylaldehyde is produced in very large annual quantities at several locations in Texas. There are reports of substantial emissions of butylaldehyde to air at manufacturing and use sites. There may be significant concentrations of butylaldehyde in the air and surface waters in the vicinity of one or more of the manufacturing and use sites. Few data are available on the acute toxicity of butylaldehyde to aquatic species and none were found for terrestrial plants and animals. No chronic toxicity information was found. It is recommended that appropriate toxicity studies be conducted with representative species of biota if warranted by monitoring data.

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