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## **Eastman Chemical Company**

### **Robust Summaries for Methyl 4-formylbenzoate**

**Methyl 4-formylbenzoate**

**CAS No. 001571-08-0**

### **Registration Number**

**Submitted to the EPA under the HPV Challenge Program by:**

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# The Flavor and Fragrance High Production Volume Consortia

## Robust Summaries for Methyl 4-formylbenzoate

The data summarized in the test plan and data recorded in the robust summaries for structurally related substances have been previously submitted to the Office of Economic and Community Development (OECD) and the U.S. Environmental Protection Agency (EPA). Data for terephthalic acid and dimethyl terephthalate were submitted in the form of Safety Information Data Sheets (SIDS) to the OECD by the EPA. The test plans and robust summaries were accepted with no requests for additional testing. Robust summaries used in the preparation of these SIDS submissions have been included in this document.

In addition, the Flavor and Fragrance High Production Volume Consortia (FFHPVC) has submitted (12/01) a test plan and robust summaries for the chemical category named “Benzyl Derivatives” including data for ten benzyl derivatives. EPA commented (12/02) on this test plan and robust summaries. The robust summaries for methyl benzoate, benzaldehyde, benzoic acid and sodium benzoate for which no revisions or additional information were requested or ones in which requested information has been added are also included in this document.

The evaluation of the quality of the following data uses a systematic approach described by Klimisch [Klimisch *et al.*, 1996]. Based on criteria relating to international testing standards for categorizing data reliability, four reliability categories have been established. The following categories are:

- Reliability code 1. Reliable without restrictions
- Reliability code 2. Reliable with restrictions
- Reliability code 3. Not reliable
- Reliability code 4. Not assignable

# 1 CHEMICAL AND PHYSICAL PROPERTIES

## 1.1 Melting Point

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Method/guideline</b>	Measured
<b>Melting Point</b>	60-62 °C
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restriction.
<b>Remarks for Data Reliability</b>	Code 1. Comparable to guideline study.
<b>References</b>	Aldrich Chemical Co. (1986) Aldrich Catalog/Handbook of Fine Chemicals. Aldrich Chemical Co., Inc. Milwaukee, WE. P. 906#24, 474-0.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Method/guideline</b>	Calculated
<b>Melting Point</b>	40.11 °C
<b>Data Qualities Reliabilities</b>	Reliability code 4. Not assignable.
<b>Remarks for Data Reliability</b>	Code 4. Calculated.
<b>References</b>	MPBPVP EPI Suite (2000) US Environmental Protection Agency.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance terephthalic acid
<b>Method/guideline</b>	Measured
<b>Melting Point</b>	Greater than 300 °C
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restriction.
<b>Remarks for Data Reliability</b>	Code 2. Basic data given: comparable to guidelines/standards.
<b>References</b>	Bemis, Dindorf, Harwood, Samans. (1982) Kirk-Othmer

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Method/guideline</b>	Measured
<b>Remarks for Substance</b>	Data are for structurally related substance terephthalic acid
<b>Melting Point</b>	402 °C
<b>Data Qualities Reliabilities</b>	Reliability code 3. Not reliable.
<b>Remarks for Data Reliability</b>	Code 3. Documentation insufficient for assessment.
<b>References</b>	Anon (1988) Dangerous Properties of Industrial Materials Report 8, 68-71.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance terephthalic acid
<b>Method/guideline</b>	Measured
<b>Melting Point</b>	425 °C
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restriction.
<b>Remarks for Data Reliability</b>	Code 1. Comparable to guideline study.
<b>References</b>	ICI Chemicals & Polymers Limited (1991) Product Safety Data: Pure Terephthalic Acid, Jan 1991.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance terephthalic acid
<b>Method/guideline</b>	Measured
<b>Melting Point</b>	Greater than 300 °C
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restriction.
<b>Remarks for Data Reliability</b>	Code 1. Comparable to guideline study.
<b>References</b>	CRC Handbook of Chemistry and Physics (2000) 82nd edition, David R. Lide, editor, The Chemical Rubber Co. Press, Inc., Boca Raton, FL.

## 1.2 Boiling Point

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Method/guideline</b>	Measured
<b>Boiling Point</b>	265 °C
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restriction.
<b>Remarks for Data Reliability</b>	Code 1. Comparable to guideline study.
<b>References</b>	Aldrich Chemical Co. (1986) Aldrich Catalog/Handbook of Fine Chemicals. Aldrich Chemical Co., Inc. Milwaukee, WE P. 906#24, 474-0.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Method/guideline</b>	Calculated
<b>Boiling Point</b>	261.31 °C
<b>Data Qualities Reliabilities</b>	Reliability code 4. Not assignable.
<b>Remarks for Data Reliability</b>	Code 4. Calculated.
<b>References</b>	MPBPVP EPI Suite (2000) US Environmental Protection Agency.

## 1.3 Vapor Pressure

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance dimethyl

	terephthalate
<b>Method/guideline</b>	Measured
<b>Vapor Pressure</b>	0.00133 kPa
<b>Temperature</b>	25 °C
<b>Remarks for Results</b>	Input parameters: BP - 179 °C. The vapor pressure of methyl 4-formylbenzoate is expected to be in the same range as that of dimethyl terephthalate.
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restriction.
<b>Remarks for Data Reliability</b>	Code 2. Basic data given: comparable to guidelines/standards.
<b>References</b>	Eastman Chemical Co., Material Safety Data Sheet.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance methyl benzoate
<b>Method/guideline</b>	Measured
<b>Year</b>	1986
<b>Vapor Pressure</b>	0.0507 kPa (0.38 mm Hg)
<b>Temperature</b>	25 °C
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restriction.
<b>Remarks for Data Reliability</b>	Code 1. Comparable to guideline study.
<b>References</b>	Daubert T.E. and Danner, R.P. (1986) US EPA EPI Suite (2000) MPBPVPWIN.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for the structurally related substance benzaldehyde
<b>Method/guideline</b>	Measured
<b>Year</b>	1975
<b>Vapor Pressure</b>	0.169 kPa (1.27 mm Hg)
<b>Temperature</b>	25 °C
<b>Remarks for Results</b>	Vapor pressure for methyl 4-formylbenzoate is expected to be significantly lower than that for benzaldehyde.

<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Code 2. Acceptable, well-documented publication/study report, which meets basic scientific principles.
<b>References</b>	Ambrose D., Connett, J., Green, J., Hales, J., Head, A., and Martin, J. (1975) Thermodynamic properties of organic oxygen compounds. 42 Physical and thermodynamic properties of benzaldehyde. J. Chem. Therm., 7,1143-57.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Method/guideline</b>	Calculated
<b>Vapor Pressure</b>	0.00088 kPa (0.00662 mm Hg)
<b>Temperature</b>	25 °C
<b>Remarks for Results</b>	Input parameters: BP - 265 °C, MP - 61 °C
<b>Data Qualities Reliabilities</b>	Reliability code 4. Not assignable.
<b>Remarks for Data Reliability</b>	Code 4. Calculated.
<b>References</b>	MPBPVWIN EPI Suite (2000) US Environmental Protection Agency.

## 1.4 n-Octanol/Water Partition Coefficients

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Method/guideline</b>	Calculated
<b>Log Pow</b>	1.55
<b>Temperature</b>	25 °C
<b>Data Qualities Reliabilities</b>	Reliability code 4. Not assignable.
<b>Remarks for Data Reliability</b>	Code 4. Calculated.

**References** KOWWIN EPI Suite (2000) US Environmental Protection Agency.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for substance</b>	Data are for structurally related substance terephthalic acid
<b>Method/guideline</b>	Measured
<b>Log Pow</b>	1.16
<b>Data Qualities Reliabilities</b>	Reliability code 3. Not reliable.
<b>Remarks for Data Reliability</b>	Code 3. Documentation insufficient for assessment.
<b>References</b>	Church C. Unpublished analysis Zeneca Brixham Environmental Laboratory.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance terephthalic acid
<b>Method/guideline</b>	Measured
<b>Log Pow</b>	1.19
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restriction.
<b>Remarks for Data Reliability</b>	Code 2. Acceptable, well-documented publication/study report, which meets basic scientific principles.
<b>References</b>	Leo A.J. (1978) Report on the calculation of octanol/water log P values for structures in EPA files.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for substance</b>	Data are for structurally related substance terephthalic acid
<b>Method/guideline</b>	Measured
<b>Log Pow</b>	1.25
<b>Temperature</b>	25 ° C
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restriction.
<b>Remarks for Data Reliability</b>	Code 2. Basic data given: comparable to guidelines/standards.
<b>References</b>	Tomida, Yotsiyang, Ikeda. (1978) Chem Pharm Bull, 261,

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for substance</b>	Data are for structurally related substance terephthalic acid
<b>Method/guideline</b>	Measured
<b>Log Pow</b>	1.96
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restriction.
<b>Remarks for Data Reliability</b>	Code 2. Basic data given: comparable to guidelines/standards.
<b>References</b>	Dunn and Johnson (1983) Plank Struct Act Relat 2 156-163, Verschueren Handbook of Environmental Data on Organic Chemicals, 3rd Ed.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for substance</b>	Data are for structurally related substance terephthalic acid
<b>Method/guideline</b>	Measured
<b>Year</b>	1985
<b>Log Pow</b>	2.0
<b>Data Qualities Reliabilities</b>	Reliability code 3. Not reliable.
<b>Remarks for Data Reliability</b>	Code 3. Documentation insufficient for assessment.
<b>References</b>	Chan and Hansch, C. (1985) Pomona College Unpublished report.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for substance</b>	Data are for structurally related substance dimethyl terephthalate
<b>Method/guideline</b>	Measured
<b>Year</b>	1995
<b>Log Pow</b>	2.25
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restriction.

<b>Remarks for Data Reliability</b>	Code 2. Acceptable, well-documented publication/study report, which meets basic scientific principles.
<b>References</b>	Hansch C., Leo, A., and D. Hoekman (1995) Exploring QSAR - Hydrophobic, Electronic, and Steric Constants. Washington, DC: American Chemical Society; 69.

## 1.5 Water Solubility

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Method/Guideline</b>	Calculated
<b>Value (mg/L) at Temperature</b>	3136 mg/L at 25 °C
<b>Data Qualities Reliabilities</b>	Reliability code 4. Not assignable.
<b>Remarks for Data Reliability</b>	Code 4. Calculated.
<b>References</b>	WSKOWWIN EPI Suite (2000) US Environmental Protection Agency.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for substance</b>	Data are for structurally related substance terephthalic acid
<b>Method/guideline</b>	Measured
<b>Value (mg/L) at Temperature</b>	15 mg/L at 10 °C
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Code 2. Acceptable, well-documented publication/study report, which meets basic scientific principles.
<b>References</b>	ICI Chemicals & Polymers Limited Product Safety Data: Pure Terephthalic Acid Jan. 1991.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for substance</b>	Data are for structurally related substance terephthalic acid
<b>Method/Guideline</b>	Measured
<b>Value (mg/L) at Temperature</b>	19 mg/L at 25 °C
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restriction.
<b>Remarks for Data Reliability</b>	Code 2. Basic data given: comparable to guidelines/standards.
<b>References</b>	Bemis, Dindorf, Harwood, Samans. (1982) Kirk-Othmer Encyclopedia of Chemical Technology 3rd Ed Vol 17, 734.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for substance</b>	Data are for structurally related substance dimethyl terephthalate
<b>Value (mg/L) at Temperature</b>	28.7 mg/L at 20 °C
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restriction.
<b>Remarks for Data Reliability</b>	Code 2. Acceptable, well-documented publication/study report, which meets basic scientific principles.
<b>References</b>	Montefibre Spa (undated) Unpublished report.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for substance</b>	Data are for structurally related substance dimethyl terephthalate
<b>Value (mg/L) at Temperature</b>	19 mg/L at 25 °C
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restriction.
<b>Remarks for Data Reliability</b>	Code 2. Acceptable, well-documented publication/study report, which meets basic scientific principles.
<b>References</b>	Kuhne R. <i>et al.</i> (1995) Chemosphere, 30, 2061-77; HSDB No. 2580.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0

<b>Remarks for substance</b>	Data are for structurally related substance dimethyl terephthalate
<b>Value (mg/L) at Temperature</b>	37.2 mg/L at 25 °C
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restriction.
<b>Remarks for Data Reliability</b>	Code 2. Acceptable, well-documented publication/study report, which meets basic scientific principles.
<b>References</b>	Eastman Kodak Co. Environmental Safety Data Sheet; HAEL No. 77-0311 and 80-0056. Unpublished report.

## 2 ENVIRONMENTAL FATE AND PATHWAYS

### 2.1 Photodegradation

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Method/guideline</b>	Calculated
<b>Test Type</b>	AOPWIN
<b>Half-life t<sub>1/2</sub></b>	7.371 hours
<b>Data Qualities Reliabilities</b>	Reliability code 4. Not assignable.
<b>Remarks for Data Reliability</b>	Code 4. Calculated.
<b>References</b>	AOPWIN EPI Suite (2000) US Environmental Protection Agency.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance dimethyl terephthalate
<b>Half-life t<sub>1/2</sub></b>	Approximately 3 days
<b>Remarks for results</b>	Substance was unreactive with ozone treatment.
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restriction.
<b>Remarks for Data Reliability</b>	Code 2. Basic data given: comparable to guidelines/standards.
<b>References</b>	Brown, S.L., Chan, F.Y., Jones, J.L., Liu, D.H. and McCaleb, K.E. (1975) Research program on hazard priority ranking of manufactured chemicals (chemicals 21-40). U.S. NTIS, PB-263162, p.195. Health and Environmental Effects Profile for Dimethyl Terephthalate (1984) EPA/600/X-84/152.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance dimethyl terephthalate
<b>Half-life t<sub>1/2</sub></b>	4.7 to 46.6-days

<b>Data Qualities Reliabilities</b>	Reliability code 3. Not reliable.
<b>Remarks for Data Reliability</b>	Code 3. Documentation insufficient for assessment.
<b>References</b>	Howard, P.H., Boethling, R.S., Jarvis, W.F., Meylan, W.M., and Michalenko, E.M. editors, Handbook of Environmental Degradation Rates Lewis Publishers, p 465.

## 2.2 Stability in Water

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for hydrolysis of methyl benzoate
<b>Method/guideline</b>	Measured
<b>Remarks for Test Conditions</b>	Solutions of test compound (0.001 to 0.22M) were incubated in solution of freshly prepared human plasma diluted to 80% with 0.05 M phosphate buffer at pH=7.4. Samples were withdrawn at regular time intervals, deproteinated with zinc sulphate and analyzed by HPLC
<b>Halflife t1/2</b>	108 minutes at 37 °C .
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restriction.
<b>Remarks for Data Reliability</b>	Code 2. Acceptable, well-documented publication/study report, which meets basic scientific principles.
<b>References</b>	Nielsen N.M. and Bundgaard H (1987) Chemical and plasma-catalyzed hydrolysis of various esters of benzoic acid. A reference system for designing pro-drug esters of carboxylic acids. <i>Int. J. of Pharmaceutics</i> , <b>39</b> , 75-85

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Method/guideline</b>	Measured/OECD Guideline 111
<b>Test Type</b>	Abiotic Degradation-Hydrolysis as Function of pH
<b>GLP</b>	Yes

<b>Year</b>	2003
<b>Duration (days)</b>	Up to 194 hours
<b>Analytical procedures</b>	GC(FID)
<b>Remarks for Test Conditions</b>	Test concentration was approximately 500 mg/L in 1% dimethylformamide for all experiments. In preliminary test hydrolysis was measured at 50 °C at pH=4,7, or 9. Based on preliminary test (greater than 10% hydrolysis after 120 hours), Test 1 was performed on pH=7 test solution. Based on results of Test 1 (not first order reaction kinetics), Test 2 was performed. Test 2 was performed at buffered pH=7 at 60, 70, and 80 C. Natural log of the test concentration 9mg/L versus time (hours) was plotted. Linear regression analysis was performed to calculate observed reaction rate. As Arrhenius plot of log k versus 1/T was used to determine k(observed) and half life at 25 C.
<b>Nominal</b>	500 mg/L
<b>Degradation %</b>	In preliminary test, approximately 10% hydrolysis at 120-194 hours at pH=4, 66% hydrolysis at 2.4 hours at pH=9, and greater than 10% hydrolysis at 120 hours at pH=7. In Test 1 at pH=7, reaction rate was determined to not be pseudo first order. In Test 2 at pH=7 and at 60, 70, and 80 °C hydrolysis data was generated to determine hydrolysis rate and half-life at 25 °C.
<b>Halflife t1/2</b>	The estimated half-life of the test substance was at pH=7 and 25 °C was 3286 hours. In the preliminary test at pH=9, the half-life was estimated to be less than 2.4 hours at 50 °C. Under environmental conditions hydrolysis should occur at half-lives closer to those achieved at pH=9.
<b>Breakdown products</b>	4-formylbenzoic acid and methanol
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restriction.
<b>Remarks for Data Reliability</b>	Code 1. Guideline study.
<b>References</b>	Hoffman C. (2003) Abiotic Degradation: Hydrolysis as a function of pH. Eastmen Chemical Company Report no. 1667-HYD. Unpublished report to Chemintox Inc.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance dimethyl terephthalate
<b>Method/guideline</b>	Measured
<b>Halflife t1/2</b>	1 to 4-weeks for surface water and 2 to 8-weeks for ground water.
<b>Data Qualities Reliabilities</b>	Reliability code 3. Not reliable.

**Remarks for Data Reliability** Code 3. Documentation insufficient for assessment.

**References** Howard P.H., Boethling, R.S., Jarvis, W.F., Meylan, W.M., and Michalenko, E.M. editors Handbook of Environmental Degradation Rates" Lewis Publishers, p 464.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance dimethyl terephthalate
<b>Method/guideline</b>	Measured
<b>Half-life t<sub>1/2</sub></b>	321 days in neutral water at 25 °C
<b>Data Qualities Reliabilities</b>	Code 3. Documentation insufficient for assessment.
<b>Remarks for Data Reliability</b>	Code 3. Documentation insufficient for assessment.
<b>References</b>	Mabey W. and Mill, T. (1978) Critical review of hydrolysis of organic compounds in water under environmental conditions" J. Phys. Chem. Ref. Data. 7(2):383-415. Health and Environmental Effects Profile for Dimethyl Terephthalate (1984) EPA/600/X-84/152.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance dimethyl terephthalate
<b>Method/guideline</b>	Calculated
<b>Half-life t<sub>1/2</sub></b>	23.9 days at pH=8 and 239 days at pH=7.
<b>Data Qualities Reliabilities</b>	Reliability code 4. Not assignable.
<b>Remarks for Data Reliability</b>	Code 4. Calculated.
<b>References</b>	HYDROWIN EPI Suite (2000) US Environmental Protection Agency.

## 2.3 Biodegradation

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Method</b>	OECD Guide-line 301 B "Ready Biodegradability: Modified Sturm Test (CO2 evolution)"
<b>Innoculum</b>	Domestic sewage, non-adapted
<b>Total degradation</b>	Greater than 60 % after 10 days
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restriction.
<b>Remarks for Data Reliability</b>	Code 2. Acceptable, well-documented publication/study report, which meets basic scientific principles.
<b>Reference</b>	Amoco Chemicals Co. (1992) Data cited in a letter with enclosures from Amoco Chemicals Co. to ICI Chemicals & Polymers Limited. Dated January 29, 1993.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Method</b>	Calculated
<b>Results</b>	Probability of rapid biodegradation by the linear and non-linear model approaches or exceeds 1.
<b>10 day window criteria</b>	Yes
<b>Conclusion remarks</b>	Ultimate survey model predicts biodegradation of 2.99 weeks and primary survey model predicts in 4.03 days.
<b>Data Qualities Reliabilities</b>	Reliability code 4. Not assignable.
<b>Remarks for Data Reliability</b>	Code 4. Calculated.
<b>Reference</b>	BIOWIN EPI Suite (2000) US Environmental Protection Agency.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance terephthalic acid
<b>Method</b>	OECD Guide-line 301 B "Ready Biodegradability: Modified Sturm Test
<b>Year</b>	1991
<b>Contact time (units)</b>	16 days

<b>Innoculum</b>	Activated sludge
<b>Results</b>	Readily biodegradable
<b>Total degradation</b>	16 days = 85.2% (10 mg/l) 82.6% (20 mg/l)
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restriction.
<b>Remarks for Data Reliability</b>	Code 1. Guideline study.
<b>Reference</b>	Amoco Corporation (1991) Study on the ready biodegradability (Modified Sturm Test) of terephthalic acid. Conducted by Battelle Europe; Study # BE-EA-128-91-01-STT-03

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance terephthalic acid
<b>Method</b>	OECD Guide-line 301 B "Ready Biodegradability: Modified Sturm Test (CO2 evolution)"
<b>Innoculum</b>	Activated sludge
<b>Total degradation</b>	91 % after 28 days
<b>Data Qualities Reliabilities</b>	Reliability code 3. Not reliable.
<b>Remarks for Data Reliability</b>	Code 3. Documentation insufficient for assessment.
<b>Reference</b>	Gerike P. and Fischer WK. (1979) A correlation study of biodegradability determinations with various chemicals in various tests. Ecotox Environ Safety 3, 159-73.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance terephthalic acid
<b>Test Type</b>	Chemical oxygen demand
<b>GLP</b>	No
<b>Year</b>	1976
<b>Contact time (units)</b>	Up to 120 hours
<b>Innoculum</b>	From activated sludge
<b>Remarks for Test Conditions</b>	The concentration of test material is increased during activation until it reaches 200 mg/L COD. Degradation is carried out on an initial concentration equivalent to 200 mg/L COD and continues until there is no measured decrease in COD.

<b>Degradation % After Time</b>	99% at less than 120 hours
<b>Results</b>	Total degradation
<b>Kinetic</b>	119 mg COD/L
<b>Time required for 10% degradation</b>	Less than 120 hours
<b>10 day window criteria</b>	Yes
<b>Total degradation</b>	Yes
<b>Conclusion remarks</b>	Terephthalic acid is classified to be readily degradable.
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Code 2. Acceptable, well-documented publication/study report, which meets basic scientific principles.
<b>Reference</b>	Pitter P. (1976) Determination of biological degradability of organic substrates. Water Research, 10, 231-235.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance methyl benzoate
<b>Method</b>	OECD Guideline 301B
<b>Test Type</b>	Sealed vessel test (CO <sub>2</sub> production test)
<b>Year</b>	1995
<b>Contact time (units)</b>	28 days
<b>Innoculum</b>	10% by volume of secondary effluent from an unacclimatized activated sludge
<b>Remarks for Test Conditions</b>	The test concentration was nominal 10 mg/L organic carbon with a test temperature range of 17-22 C. The mean percentage biodegradation was calculated from 4 vessels on day 28
<b>Degradation % After Time</b>	95.3% at 28 days
<b>10 day window criteria</b>	Yes
<b>Total degradation</b>	Yes
<b>Conclusion remarks</b>	Methyl benzoate is classified as readily and ultimately biodegradable.
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restriction.
<b>Remarks for Data Reliability</b>	Code 1. Guideline study.
<b>Reference</b>	Quest International Ltd. (1995) The biodegradability of methyl benzoate in the sealed vessel test. Unpublished report.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance methyl benzoate
<b>Method</b>	OECD Guideline 301B CO2 evolution test (Modified Sturm) and EPA's Ready Biodegradability: Modified Sturm Test
<b>Test Type</b>	Aerobic
<b>GLP</b>	Yes
<b>Year</b>	1995
<b>Contact time (units)</b>	28 days
<b>Innoculum</b>	Activated sludge (microbial content: 8.4 million CFU/mL) mixed liquor collected from the Downingtown Regional Water Pollution Control Center (Downingtown, PA)
<b>Remarks for Test Conditions</b>	In separate 4-L Erlenmeyer flasks containing 2 L modified biochemical oxygen demand water and supplied with CO2-free air, control (no methyl benzoate), glucose (20 mg/L0 and methyl benzoate (10 and 20 mg/L) were tested. Evolved CO2 was trapped in 3 bottles containing Ba(OH)2 and connected to each flask. Test substances were added by direct weight. During the study, the flasks were shaken at ~110 ppm and temperature ranged from 23-23.6 C. Airflow through rate was regulated to provide 1-2 bubbles/second into the CO2 traps. Trapped CO2 was precipitated as BaCO3 by reacting it with 0.024 N Ba(OH)2. To determine the amount of CO2 produced, the remaining Ba(OH)2 was titrated with 0.05 N standardized HCl. At the end of the study (28 days), concentrated H2SO4 was used to acidify the flasks' contents and after overnight aeration, the concentration of soluble organic carbon (SOC) was determined by final titration.
<b>Degradation % After Time</b>	Greater than 80% after 15 days
<b>Results</b>	Biodegradation was similar between both methyl benzoate concentrations and the glucose positive control (% SOC removed: 96.2, 100, and 99.3 for 20 mg glucose/L, 10 mg methyl benzoate/L, and 20 mg methyl benzoate/L, respectively). CO2 production by 10 days in the methyl benzoate flasks was approximately 80% and at the end of the study, the SOC content was approximately 1% at both concentrations.
<b>10 day window criteria</b>	Yes
<b>Total degradation</b>	Yes
<b>Conclusion remarks</b>	Methyl benzoate was considered readily biodegradable.
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restriction.

**Remarks for Data Reliability** Code 1. Guideline study.

**Reference** Corby J. E. (1995) EPA: CO2 Production Test C-2000. Hoechst Celanese Corporation. Unpublished report.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance sodium benzoate
<b>Method</b>	OECD 301B Guideline CO2 evolution test - modified sealed vessel
<b>Test Type</b>	Aerobic
<b>Year</b>	1991
<b>Contact time (units)</b>	28 days
<b>Innoculum</b>	10% secondary effluent from sludge from local STP
<b>Remarks for Test Conditions</b>	2-10 mg DOC/L at 20 °C for 28 days; modification to OECD guidelines was the use of infra-red analyzers to measure CO2; 6 replicates
<b>Degradation % After Time</b>	85.7% at 21 days
<b>Results</b>	Mean biodegradation of 85.7% after 21 days (CI 82.4-89.2) and the authors concluded that the modification produced similar results to the standard protocol but was simpler and more readily replicated. In addition, there was no practical difference between a concentration of 2 mg/L and 10 mg/L.
<b>Time required for 10% degradation</b>	1 day
<b>10 day window criteria</b>	Not reported
<b>Total degradation</b>	Yes
<b>Conclusion remarks</b>	Sodium benzoate was readily biodegradable.
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restriction.
<b>Remarks for Data Reliability</b>	Code 1. Guideline study.
<b>Reference</b>	Birch R.R. and Fletcher, R.J. (1991) The application of dissolved inorganic carbon measurements to the study of aerobic biodegradability. Chemosphere, 23(4), 507-524.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance benzoic acid

<b>Test Type</b>	Chemical oxygen demand
<b>GLP</b>	No
<b>Year</b>	1976
<b>Contact time (units)</b>	Up to 120 hours
<b>Innoculum</b>	From activated sludge
<b>Remarks for Test Conditions</b>	The concentration of test material is increased during activation until it reaches 200 mg/L COD. Degradation is carried out on an initial concentration equivalent to 200 mg/L COD and continues until there is no measured decrease in COD.
<b>Degradation % After Time</b>	99% at less than 120 hours
<b>Results</b>	Total degradation
<b>Kinetic</b>	88.5 mg COD/L
<b>Time required for 10% degradation</b>	Less than 120 hours
<b>10 day window criteria</b>	Yes
<b>Total degradation</b>	Yes
<b>Conclusion remarks</b>	Material is readily degradable.
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Code 2. Acceptable, well-documented publication/study report, which meets basic scientific principles.
<b>Reference</b>	Pitter P. (1976) Determination of biological degradability of organic substrates. Water Research, 10, 231-235.

## 2.4 Fugacity

<b>Substance</b>	Methyl 4-formylbenzoate
<b>CAS</b>	001571-08-0
<b>Model Conditions</b>	25 C, 1000 lbs.
<b>Test Type</b>	Environmental Equilibrium Partitioning Model
<b>Method</b>	Mackay

<b>Model Used (title, version, date)</b>	EQC Fugacity Level III
<b>Input parameters</b>	MW, VP(0.00662 mm Hg), log Kow (1.55), water solubility (20 mg/L), estimated MP, 60-62 °C, BP, 265 °C
<b>Year</b>	2000
<b>Media</b>	Air-Water-Soil-Sediment Partition Coefficients
<b>Model data and results</b>	Compartment half-lives, hours: Air=14.7; Water=360;Soil=360;Sediment=1440
<b>Estimated Distribution and Media Concentration</b>	Air=3.38% Water=46.5% Soil=50% Sediment=0.101%
<b>Conclusion remarks</b>	Substance is predicted to persist in the environment for 235 hours.
<b>Reliabilities</b>	Reliability code 4. Not assignable.
<b>Remarks for Data Reliability</b>	The data are obtained by a recognized fugacity calculation method. Data are considered reliable with restriction because this method does not allow for biodegradation or metabolism.
<b>References</b>	Mackay D., A.DiGuardo, S.Paterson and C.E.Cowan (1996b) Evaluating the fate of a variety of types of chemicals using the EQC model. Environmental Toxicology and Chemistry, 15(9), 1627-1637.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Model Conditions</b>	25 °C, 1000 lbs.
<b>Test Type</b>	Environmental Equilibrium Partitioning Model
<b>Method</b>	Mackay
<b>Model Used</b>	EQC V 2.11 Level I
<b>Input Parameters</b>	MW, log Kow, water solubility, MP & VP
<b>Media</b>	Air-Water Partition Coefficient
<b>absorption coefficient</b>	0.0000197
<b>Data Qualities Reliabilities</b>	Reliability code 4. Not assignable.
<b>Remarks for Data Reliability</b>	Code 4. Calculated.
<b>References</b>	Trent University (1999) Level 1 Fugacity-based Environmental Equilibrium Partitioning Model Version 2.11. Based on Mackay, Donald (1991) Multimedia environmental models: The fugacity approach. Lewis Publications, CRC Press, Boca

Raton, FL.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Model Conditions</b>	25 °C, 1000 lbs.
<b>Test Type</b>	Environmental Equilibrium Partitioning Model
<b>Method</b>	Mackay
<b>Model Used</b>	EQC V 2.11 Level I
<b>Input Parameters</b>	MW, log Kow, water solubility, MP & VP
<b>Media</b>	Soil-Water Partition Coefficient
<b>absorption coefficient</b>	0.698
<b>Data Qualities Reliabilities</b>	Reliability code 4. Not assignable.
<b>Remarks for Data Reliability</b>	Code 4. Calculated.
<b>References</b>	Trent University (1999) Level 1 Fugacity-based Environmental Equilibrium Partitioning Model Version 2.11. Based on Mackay, Donald (1991) Multimedia environmental models: The fugacity approach. Lewis Publications, CRC Press, Boca Raton, FL.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Model Conditions</b>	25 °C, 1000 lbs.
<b>Test Type</b>	Environmental Equilibrium Partitioning Model
<b>Method</b>	Mackay
<b>Model Used</b>	EQC V 2.11 Level I
<b>Input Parameters</b>	MW, log Kow, water solubility, MP & VP
<b>Media</b>	Sediment-Water Partition Coefficient
<b>absorption coefficient</b>	1.40
<b>Data Qualities Reliabilities</b>	Reliability code 4. Not assignable.
<b>Remarks for Data Reliability</b>	Code 4. Calculated.
<b>References</b>	Trent University (1999) Level 1 Fugacity-based Environmental Equilibrium Partitioning Model Version 2.11. Based on Mackay, Donald (1991) Multimedia environmental models: The fugacity approach. Lewis Publications, CRC Press, Boca

Raton, FL.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Model Conditions</b>	25 °C, 1000 lbs.
<b>Test Type</b>	Environmental Equilibrium Partitioning Model
<b>Method</b>	Mackay
<b>Model Used</b>	EQC V 2.11 Level I
<b>Input Parameters</b>	MW, log Kow, water solubility, MP & VP
<b>Media</b>	Suspended Sediment-Water Partition Coefficient
<b>absorption coefficient</b>	4.36
<b>Data Qualities Reliabilities</b>	Reliability code 4. Not assignable.
<b>Remarks for Data Reliability</b>	Code 4. Calculated.
<b>References</b>	Trent University (1999) Level 1 Fugacity-based Environmental Equilibrium Partitioning Model Version 2.11. Based on Mackay, Donald (1991) Multimedia environmental models: The fugacity approach. Lewis Publications, CRC Press, Boca Raton, FL.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Model Conditions</b>	25 °C, 1000 lbs.
<b>Test Type</b>	Environmental Equilibrium Partitioning Model
<b>Method</b>	Mackay
<b>Model Used</b>	EQC V 2.11 Level I
<b>Input Parameters</b>	MW, log Kow, water solubility, MP & VP
<b>Media</b>	Fish-Water Partition Coefficient
<b>absorption coefficient</b>	1.77
<b>Data Qualities Reliabilities</b>	Reliability code 4. Not assignable.
<b>Remarks for Data Reliability</b>	Code 4. Calculated.
<b>References</b>	Trent University (1999) Level 1 Fugacity-based Environmental Equilibrium Partitioning Model Version 2.11. Based on Mackay, Donald (1991) Multimedia environmental models: The fugacity approach. Lewis Publications, CRC Press, Boca

Raton, FL.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Model Conditions</b>	25 °C, 1000 lbs.
<b>Test Type</b>	Environmental Equilibrium Partitioning Model
<b>Method</b>	Mackay
<b>Model Used</b>	EQC V 2.11 Level I
<b>Input Parameters</b>	MW, log Kow, water solubility, MP & VP
<b>Media</b>	Aerosol-Air Partition Coefficient
<b>absorption coefficient</b>	2,870,000
<b>Data Qualities Reliabilities</b>	Reliability code 4. Not assignable.
<b>Remarks for Data Reliability</b>	Code 4. Calculated.
<b>References</b>	Trent University (1999) Level 1 Fugacity-based Environmental Equilibrium Partitioning Model Version 2.11. Based on Mackay, Donald (1991) Multimedia environmental models: The fugacity approach. Lewis Publications, CRC Press, Boca Raton, FL.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Model Conditions</b>	25 °C, 1000 lbs.
<b>Test Type</b>	Environmental Equilibrium Partitioning Model
<b>Method</b>	Mackay
<b>Model Used</b>	EQC V 2.11 Level I
<b>Input Parameters</b>	MW, log Kow, water solubility, MP & VP
<b>Media</b>	Air
<b>Estimated Distribution and Media Concentration</b>	0.944%
<b>Data Qualities Reliabilities</b>	Reliability code 4. Not assignable.
<b>Remarks for Data Reliability</b>	Code 4. Calculated.
<b>References</b>	Trent University (1999) Level 1 Fugacity-based Environmental Equilibrium Partitioning Model Version 2.11. Based on Mackay, Donald (1991) Multimedia environmental models: The fugacity approach. Lewis Publications, CRC Press, Boca

Raton, FL.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Model Conditions</b>	25 °C, 1000 lbs.
<b>Test Type</b>	Environmental Equilibrium Partitioning Model
<b>Method</b>	Mackay
<b>Model Used</b>	EQC V 2.11 Level I
<b>Input Parameters</b>	MW, log Kow, water solubility, MP & VP
<b>Media</b>	Water
<b>Estimated Distribution and Media Concentration</b>	95.97%
<b>Data Qualities Reliabilities</b>	Reliability code 4. Not assignable.
<b>Remarks for Data Reliability</b>	Code 4. Calculated.
<b>References</b>	Trent University (1999) Level 1 Fugacity-based Environmental Equilibrium Partitioning Model Version 2.11. Based on Mackay, Donald (1991) Multimedia environmental models: The fugacity approach. Lewis Publications, CRC Press, Boca Raton, FL.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Model Conditions</b>	25 °C, 1000 lbs.
<b>Test Type</b>	Environmental Equilibrium Partitioning Model
<b>Method</b>	Mackay
<b>Model Used</b>	EQC V 2.11 Level I
<b>Input Parameters</b>	MW, log Kow, water solubility, MP & VP
<b>Media</b>	Soil
<b>Estimated Distribution and Media Concentration</b>	3.0156%
<b>Data Qualities Reliabilities</b>	Reliability code 4. Not assignable.
<b>Remarks for Data Reliability</b>	Code 4. Calculated.
<b>References</b>	Trent University (1999) Level 1 Fugacity-based Environmental Equilibrium Partitioning Model Version 2.11. Based on Mackay, Donald (1991) Multimedia environmental models: The

fugacity approach. Lewis Publications, CRC Press, Boca Raton, FL.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Model Conditions</b>	25 °C, 1000 lbs.
<b>Test Type</b>	Environmental Equilibrium Partitioning Model
<b>Method</b>	Mackay
<b>Model Used</b>	EQC V 2.11 Level I
<b>Input Parameters</b>	MW, log Kow, water solubility, MP & VP
<b>Media</b>	Sediment
<b>Estimated Distribution and Media Concentration</b>	0.067%
<b>Data Qualities Reliabilities</b>	Reliability code 4. Not assignable.
<b>Remarks for Data Reliability</b>	Code 4. Calculated.
<b>References</b>	Trent University (1999) Level 1 Fugacity-based Environmental Equilibrium Partitioning Model Version 2.11. Based on Mackay, Donald (1991) Multimedia environmental models: The fugacity approach. Lewis Publications, CRC Press, Boca Raton, FL.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Model Conditions</b>	25 °C, 1000 lbs.
<b>Test Type</b>	Environmental Equilibrium Partitioning Model
<b>Method</b>	Mackay
<b>Model Used</b>	EQC V 2.11 Level I
<b>Input Parameters</b>	MW, log Kow, water solubility, MP & VP
<b>Media</b>	Suspended Sediment
<b>Estimated Distribution and Media Concentration</b>	0.0021%
<b>Data Qualities Reliabilities</b>	Reliability code 4. Not assignable.
<b>Remarks for Data Reliability</b>	Code 4. Calculated.
<b>References</b>	Trent University (1999) Level 1 Fugacity-based Environmental Equilibrium Partitioning Model Version 2.11. Based on

Mackay, Donald (1991) Multimedia environmental models: The fugacity approach. Lewis Publications, CRC Press, Boca Raton, FL.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Model Conditions</b>	25 °C, 1000 lbs.
<b>Test Type</b>	Environmental Equilibrium Partitioning Model
<b>Method</b>	Mackay
<b>Model Used</b>	EQC V 2.11 Level I
<b>Input Parameters</b>	MW, log Kow, water solubility, MP & VP
<b>Media</b>	Fish
<b>Estimated Distribution and Media Concentration</b>	0.00017%
<b>Data Qualities Reliabilities</b>	Reliability code 4. Not assignable.
<b>Remarks for Data Reliability</b>	Code 4. Calculated.
<b>References</b>	Trent University (1999) Level 1 Fugacity-based Environmental Equilibrium Partitioning Model Version 2.11. Based on Mackay, Donald (1991) Multimedia environmental models: The fugacity approach. Lewis Publications, CRC Press, Boca Raton, FL.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Model Conditions</b>	25 °C, 1000 lbs.
<b>Test Type</b>	Environmental Equilibrium Partitioning Model
<b>Method</b>	Mackay
<b>Model Used</b>	EQC V 2.11 Level I
<b>Input Parameters</b>	MW, log Kow, water solubility, MP & VP
<b>Media</b>	Aerosol
<b>Estimated Distribution and Media Concentration</b>	0.0000542%
<b>Data Qualities Reliabilities</b>	Reliability code 4. Not assignable.
<b>Remarks for Data Reliability</b>	Code 4. Calculated.

## References

Trent University (1999) Level 1 Fugacity-based Environmental Equilibrium Partitioning Model Version 2.11. Based on Mackay, Donald (1991) Multimedia environmental models: The fugacity approach. Lewis Publications, CRC Press, Boca Raton, FL.

### 3 ECOTOXICITY

#### 3.1 Acute Toxicity to Fish

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Method/guideline</b>	Calculated
<b>Species/Strain/Supplier</b>	Fish
<b>Exposure Period</b>	96 hours
<b>Conclusion remarks</b>	The 96 hour LC50 was 19.0 mg/L.
<b>Remarks for Test Conditions</b>	Based on aldehyde ECOSAR Class, 96 hour LC50 was calculated to be 19 mg/L. Based on ester ECOSAR Class, 96 hour LC50 was calculated to be 43 mg/L
<b>Data Qualities Reliabilities</b>	Reliability code 4. Not assignable.
<b>Remarks for Data Reliability</b>	Code 4. Calculated.
<b>Reference</b>	ECOSAR EPI Suite (2000) US Environmental Protection Agency.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance terephthalic acid
<b>Method/guideline</b>	OECD Guideline 203 "Fish, Acute Toxicity Test"
<b>GLP</b>	Yes
<b>Year</b>	1991
<b>Species/Strain/Supplier</b>	Golden orfe ( <i>Leuciscus idus melanotus</i> )
<b>Exposure Period</b>	96 hours
<b>Remarks for Test Conditions</b>	Fish were held for 21 days in a 376 liter glass vessels containing 327 liters of reconstituted water (19 °C, 85-95% oxygen). Fish density was 0.51 g/liter. They were fed five times a week with 50% Tetra Special Mix and 50% IBL Novo food tablets prior to study. The study was conducted in 16 liter stainless steel vessels that contained 10 liters of test solution. Test solution was not renewed. At the time of the test, fish were an average of 4.86 ± 0.47 cm in length and weighed 1.028 ± 0.246 g. Ten fish were placed in each vessel (for a loading rate

of 1.028 g/l). Fish were not fed during the test. The test article was diluted with reconstituted purified water to yield nominal concentrations of 130, 220, 350, 600 and 1000 ppm. The actual concentration of the highest exposure level was 999.3 ppm at time 0, and 922.2 ppm at 96 hours. Fish were maintained at  $22.0 \pm 0.07$  °C, a pH of  $7.57 \pm 0.26$ , conductivity of  $1026.9 \pm 367.74$  microS/cm, alkalinity of  $41.68 \pm 1.14$  mg/l CaCO<sub>3</sub>, hardness of  $193.86 \pm 75.0$  mg/l CaCO<sub>3</sub>, and a light/dark photoperiod of 16/8 hours. The dissolved oxygen content was  $8.33 \pm 0.22$  mg/l and was maintained through aeration. Parameters were determined at time 0 and every 24 hours thereafter.

Under the test conditions it was believed that some of the terephthalic acid was converted to a salt form. Fish loading was slightly above the 1.0 g/l recommended level, but was not believed to impact the results.

**Remarks for results**

Dissolved oxygen, temperature, conductivity, alkalinity, and hardness did not vary between groups. The pH of the water decreased slightly as a function of time and increasing concentration of test material (i.e. the pH of the vessel containing 1000 mg/l at 96 hours was 7). All test condition values were within acceptable limits. No mortalities or behavioral changes were noted at any concentration during the study.

**Data Qualities Reliabilities**

Reliability code 1. Reliable without restriction.

**Remarks for Data Reliability**

Code 1. Guideline study.

**Reference**

Amoco Corporation (1993a) A Study of the Acute Toxicity to Fish (*Leuciscus idus melanotus*) of Terephthalic Acid. Conducted by Battelle Europe; Study # BE-EA-128-91-01-F3A-3; Reference no. 21

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance terephthalic acid
<b>Method/guideline</b>	OECD Guideline 203 "Fish, Acute Toxicity Test"
<b>Test Type</b>	Semistatic
<b>GLP</b>	Yes
<b>Year</b>	1991
<b>Species/Strain/Supplier</b>	<i>Salmo gairdneri</i>
<b>Exposure Period</b>	96 hours
<b>Remarks for Test Conditions</b>	LC0 - 500 mg/L; LC50 - 798-1640 mg/L; LC100 - 1500 mg/L. Mean value 1157 mg/L.
<b>Conclusion remarks</b>	The LC50 was 798 - 1640 mg/L.

<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restriction.
<b>Remarks for Data Reliability</b>	Code 1. Guideline study.
<b>Reference</b>	ICI Chemicals & Polymers Ltd. (1991) Internal report, BLS 1200/B.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance dimethyl terephthalate
<b>Test Type</b>	Static test
<b>Species/Strain/Supplier</b>	Minnow/flathead
<b>Exposure Period</b>	96 hours
<b>Remarks for Test Conditions</b>	100% mortality at 30 mg/L
<b>Conclusion remarks</b>	LC50 = 9.6 mg/L, NOEC = 3 mg/kg.
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restriction.
<b>Remarks for Data Reliability</b>	Code 2. Acceptable, well-documented publication/study report, which meets basic scientific principles.
<b>Reference</b>	Eastman Kodak Co. (1984) Unpublished data.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance dimethyl terephthalate
<b>Test Type</b>	Static test
<b>Species/Strain/Supplier</b>	Minnow/flathead
<b>Exposure Period</b>	96 hours
<b>Conclusion remarks</b>	LC50 = 45 mg/L
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restriction.
<b>Remarks for Data Reliability</b>	Code 2. Acceptable, well-documented publication/study report, which meets basic scientific principles.
<b>Reference</b>	Eastman Kodak Co. (1984) Unpublished data.

<b>Substance Name</b>	Methyl 4-formylbenzoate
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<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance methyl benzoate
<b>Method/guideline</b>	TSCA Environmental Effects Testing Guideline 797.1400
<b>Test Type</b>	Acute Fish Toxicity
<b>GLP</b>	Yes
<b>Year</b>	1997
<b>Species/Strain/Supplier</b>	Bluegill sunfish ( <i>Lepomis macrochirus</i> )
<b>Exposure Period</b>	96 hours
<b>Analytical monitoring</b>	
<b>Remarks for Test Conditions</b>	Groups of 10 juvenile bluegill fish (average length 22 mm and weight 0.19 g) from Northeastern Biologists (Rhinebeck, NY) were exposed to solvent control (acetone), 5.0, 10, 20, 40 or 80 mg methyl benzoate/L for 96 hours in 10 L glass tanks containing 9 L of test media (methyl benzoate dissolved in acetone and diluted with reconstituted water). The reconstituted freshwater had an initial hardness of 80 mg/L (as CaCO <sub>3</sub> ) and alkalinity of 11. Each test was conducted in duplicate. Oxygen content, and pH were measured at the beginning of the test and at 24, 48, 72, and 96 hours. Test temperatures ranged from 20.3 to 23.9 C. Fish were observed for signs of toxicity every 24 hours.
<b>Observations on precipitation</b>	Undissolved test substance was noted at the 2 highest concentrations.
<b>Nominal concentrations as mg/L</b>	5.0, 10, 20, 40 or 80 mg/L
<b>Remarks fields for results</b>	No deaths occurred in controls and at concentrations up to and including 10 mg/L. Mortality was 100% at the highest concentration. Loss of equilibrium was reported in fish exposed to 20 mg/L or higher and dose-related pigmentation darkening was seen in all treatment groups. Undissolved test substance was noted at the 2 highest concentrations. The undissolved substance may have effected lethality and LC50 determinations. Certainly since no deaths were observed at 10 and 20 mg/L, the LC50 should exceed 20 mg/L.
<b>Conclusion remarks</b>	The 96 hour LC50 was 28.3 mg/L and the NOEC was 10 mg/L based on mortality and loss of equilibrium. The NOEC for color change was not determined but was expected to be less than 5.0 mg/L.
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restriction.
<b>Remarks for Data Reliability</b>	Code 2. Basic data from study using sound scientific guidelines.
<b>Reference</b>	Cunningham F.J. (1997a) C-2000 (Methyl benzoate) Acute toxicity to Bluegill, <i>Lepomis macrochirus</i> , under static conditions. Project No. J9605001a. Private communication to FFHPVC. Unpublished report.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance methyl benzoate
<b>Method/guideline</b>	Calculated
<b>Species/Strain/Supplier</b>	Fish
<b>Exposure Period</b>	96 hour
<b>Conclusion remarks</b>	The 96 hour LC50 was 18.0 mg/L.
<b>Data Qualities Reliabilities</b>	Reliability code 4. Not assignable.
<b>Remarks for Data Reliability</b>	Code 4. Calculated.
<b>Reference</b>	ECOSAR EP Suite (2000) US Environmental Protection Agency.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance benzaldehyde
<b>Method/guideline</b>	Experimental
<b>Test Type</b>	Larval survival and growth test
<b>GLP</b>	Yes
<b>Year</b>	1996
<b>Species/Strain/Supplier</b>	Fathead minnow ( <i>Pimephales promelas</i> )
<b>Exposure Period</b>	1, 4, and 7 days
<b>Analytical monitoring</b>	HPLC with an ultraviolet detector at 254 nm
<b>Nominal concentrations as mg/L</b>	1st test: 0.9, 1.8, 3.6, 7.2, 14.3; 2nd test: 0.11, 0.22, 0.45, 0.9, 1.8, 3.6, 7.2
<b>Measured concentrations as mg/L</b>	Not detectable at 2 lowest concentrations, 0.02, 0.13, 0.20 for 3 highest concentrations.
<b>Remarks for Test Conditions</b>	Each test concentration had 4 replicates with 10 larvae each. Larvae were fed once on the 1st day and 2x/day on days 1-6. Dead and surviving larvae were counted and survivors were prepared for dry weight determination.
<b>Remarks for results</b>	The NOEC for growth of 7-d larvae was 1.8 mg/L. The NOEC for 1- and 4- day larvae was less than 0.9 mg/L. NOEC for survival of 1- and 4-d larvae was 3.6 mg/L (first test). NOEC for survival in second test was 0.22 mg/L for 1-d larvae and 1.8 mg/L for 4- and 7-d.

<b>Conclusion remarks</b>	1-d larvae more sensitive than older larvae to benzaldehyde.
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restriction.
<b>Remarks for Data Reliability</b>	Code 1. Guideline study.
<b>Reference</b>	Pickering Q. H., Lazorchak, J. M. and Winks. K. L. (1996) Subchronic sensitivity of one-, four-, and seven-day-old-fathead minnow ( <i>Pimephales promelas</i> ) larvae to five toxicants. Environmental Toxicology and Chemistry, 15(3), 353-359.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance benzaldehyde
<b>Method/guideline</b>	Experimental
<b>Species/Strain/Supplier</b>	Guppy ( <i>Poecilia reticulata</i> )
<b>Exposure Period</b>	14 days
<b>Analytical monitoring</b>	Tracor 550 gas chromatograph
<b>Remarks for Test Conditions</b>	Experiments were conducted under semi-static conditions with daily renewal of test solutions. A minimum of 5 concentrations of benzaldehyde were tested. The guppies were acclimated for 12 days prior to testing and 10 guppies/concentration were tested. The control group consisted of 12 guppies exposed to the test substance carrier solvent, acetone. Logit transformation was used to calculate the LC50.
<b>Measured concentrations as mg/L</b>	Not reported
<b>Conclusion remarks</b>	The 14-day LC50 for benzaldehyde was reported to be 1.57 umoles/L. The log P was calculated to be 1.49 (Rekker, 1977).
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restriction.
<b>Remarks for Data Reliability</b>	Code 2. Acceptable, well-documented publication/study report, which meets basic scientific principles.
<b>Reference</b>	Deneer J.W., Seinen, W., and Hermens, J.L.M. (1988) The acute toxicity of aldehydes to the guppy. Aquatic Toxicol., 12, 185-192.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance benzaldehyde
<b>Method/guideline</b>	Calculated
<b>Species/Strain/Supplier</b>	Fish

<b>Exposure Period</b>	96 hour
<b>Conclusion remarks</b>	The 96 hour LC50 was 13.0 mg/L.
<b>Data Qualities Reliabilities</b>	Reliability code 4. Not assignable.
<b>Remarks for Data Reliability</b>	Code 4. Calculated.
<b>Reference</b>	ECOSAR EP Suite (2000) US Environmental Protection Agency.

### 3.2 Acute Toxicity to Aquatic Invertebrates

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Method/guideline</b>	Calculated
<b>Species/Strain/Supplier</b>	<i>Daphnia magna</i>
<b>Conclusion remarks</b>	The 48-hour LC50 was 16.4 mg/L.
<b>Data Qualities Reliabilities</b>	Reliability code 4. Not assignable.
<b>Data Reliability Remarks</b>	Code 4. Calculated.
<b>Reference</b>	ECOSAR EPI Suite (2000) US Environmental Protection Agency.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance terephthalic acid
<b>Method/guideline</b>	OECD Guideline 202
<b>Test Type</b>	Static test
<b>GLP</b>	Yes

<b>Year</b>	1991
<b>Species/Strain/Supplier</b>	<i>Daphnia magna</i>
<b>Test Details</b>	48 hours
<b>Remarks for Test Conditions</b>	<p>Adult <i>Daphnia</i> (approx. 20/vessel) were kept in 3.5 liter vessels containing 2 liters of Elendt M 7 medium (22 °C) and were fed with algae. <i>Daphnia</i> were placed in reconstituted water 24 hours prior to test. New-born <i>Daphids</i> were collected and held for 6 hours. The study was conducted in quadruplicate using 5 new-born <i>Daphnia</i> (6-20 hours)/concentration in each 300 ml test vessel. The test article was diluted with purified reconstituted water to yield nominal concentrations of 0, 80, 130, 220, 350, 600 and 1000 ppm in a total volume of 200 ml. The actual concentration of the highest exposure level was 951.5 ppm at time 0, and 982 ppm at 48 hours. A group of <i>Daphnids</i> was also exposed to water that contained 1.57 g NaOH that was pH adjusted by adding HCl (salinity control). Vessels were not aerated. <i>Daphnia</i> were maintained at 22.07 ± 0.11 °C, a pH of 7.79 ± 0.06, dissolved oxygen content of 8.31 ± 0.15 mg/l, conductivity of 929.38 ± 369.64 microS/cm, alkalinity of 42.91 ± 1.55 mg/l CaCO<sub>3</sub>, hardness of 232.64 ± 12.61 mg/l CaCO<sub>3</sub>, and a light/dark photoperiod of 16/8 hours. The number of immobilized fleas was noted at 0, 24 and 48 hours.</p> <p>Under the test conditions it was believed that some of the terephthalic acid was converted to a salt. Immobilization at the highest dose was only noted in 1 of the 20 fleas.</p>
<b>Remarks for results</b>	Water quality parameters of pH, oxygen concentration, temperature and alkalinity remained within acceptable limits throughout the study and did not differ significantly with time or increasing concentration of test material. Conductivity of the saline control group (1660 at time 0) was higher than most other groups. Conductivity increased with increasing concentration of test material (from 570 to 1230 microS/cm at time 0 for 1000 ppm). Lethality was 1/20 (5%) in the salinity control group and 1/20 in <i>Daphnia</i> exposed to 1000 ppm
<b>Conclusion remarks</b>	The NOEC = 600 mg/L (nominal); EC0 = 600 mg/L (nominal); EC50 = greater than 1000 (nominal)
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restriction.
<b>Data Reliability Remarks</b>	Code 1. Guideline study.
<b>Reference</b>	Amoco Corporation (1993b) A study of the acute immobilization to <i>daphnia</i> of terephthalic acid. Conducted by Battelle Europe; Study # BE-EA-128-91-02-DAK-3.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance dimethyl terephthalate

<b>Test Type</b>	Static test
<b>Species/Strain/Supplier</b>	<i>Daphnia magna</i>
<b>Test Details</b>	96 hour
<b>Conclusion remarks</b>	The LC50 = to or greater than 100 mg/L
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restriction.
<b>Data Reliability Remarks</b>	Code 2. Acceptable, well-documented publication/study report, which meets basic scientific principles.
<b>Reference</b>	Eastman Kodak Co. (1977) Unpublished report.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance dimethyl terephthalate
<b>Test Type</b>	Static test
<b>Species/Strain/Supplier</b>	<i>Dugesia tigrina</i> (Flatworm)
<b>Test Details</b>	96 hour
<b>Conclusion remarks</b>	The LC50 = to or greater than 100 mg/L
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restriction.
<b>Data Reliability Remarks</b>	Code 2. Acceptable, well-documented publication/study report, which meets basic scientific principles.
<b>Reference</b>	Eastman Kodak Co. (1977) Unpublished report.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance dimethyl terephthalate
<b>Test Type</b>	Static test
<b>Species/Strain/Supplier</b>	<i>Helisoma trivolvis</i> (Snail)
<b>Conclusion remarks</b>	The LC50 = to or greater than 100 mg/L
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restriction.
<b>Data Reliability Remarks</b>	Code 2. Acceptable, well-documented publication/study report, which meets basic scientific principles.
<b>Reference</b>	Eastman Kodak Co. (1977) Unpublished report.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data is for structurally related substance dimethyl terephthalate
<b>Test Type</b>	Static test
<b>Species/Strain/Supplier</b>	<i>Helisoma trivolvis</i> (Snail)
<b>Test Details</b>	96 hour
<b>Conclusion remarks</b>	The LC50 = to or greater than 30 mg/L and NOEC 3 mg/L.
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restriction.
<b>Data Reliability Remarks</b>	Code 2. Acceptable, well-documented publication/study report, which meets basic scientific principles.
<b>Reference</b>	Eastman Kodak Co. (1984) Unpublished data.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data is for structurally related substance dimethyl terephthalate
<b>Test Type</b>	Static Test
<b>Species/Strain/Supplier</b>	<i>Daphnia magna</i>
<b>Test Details</b>	48 hours
<b>EC50, EL50, LC0, at 24,48 hours</b>	EC50 = to or greater than 30 mg/L
<b>Conclusion remarks</b>	Exposure to 30 mg/L induced 40% immobility
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restriction.
<b>Data Reliability Remarks</b>	Code 2. Acceptable, well-documented publication/study report, which meets basic scientific principles.
<b>Reference</b>	Eastman Kodak Co. (1984) Unpublished report.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data is for structurally related substance dimethyl terephthalate
<b>Species/Strain/Supplier</b>	<i>Daphnia magna</i>
<b>Test Details</b>	48 hours

<b>EC50, EL50, LC0, at 24,48 hours</b>	LC50 = 30.4 mg/L
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restriction.
<b>Data Reliability Remarks</b>	Code 2. Acceptable, well-documented publication/study report, which meets basic scientific principles.
<b>Reference</b>	DuPont Chemicals; Material Safety Data Sheet.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance methyl benzoate
<b>Method/guideline</b>	Experimental
<b>Test Type</b>	Static freshwater toxicity test
<b>GLP</b>	Yes
<b>Year</b>	1996
<b>Species/Strain/Supplier</b>	<i>Daphnia magna</i>
<b>Test Details</b>	Ten <i>Daphnia magna</i> were added in pairs to 300 mL glass test chambers containing methyl benzoate dissolved in acetone and diluted with freshwater to a volume of 250 mL. The test concentrations were 9.38, 18.8, 37.5, 75, 150, and 300 mg/L. <i>Daphnia</i> were exposed for 48 hours. Freshwater and solvent controls were also tested. Treatments were performed in duplicate. Survival and water temperature were monitored daily; whereas pH and dissolved oxygen concentrations were measured at the beginning and end of the test.
<b>Nominal concentrations as mg/L</b>	9.38, 18.8, 37.5, 75, 150, and 300 mg/L
<b>EC50, EL50, LC0, at 24,48 hours</b>	48 hour EC50 = 32.1 mg/L
<b>Biological observations</b>	No deaths in controls and exposures up to and including 18.8 mg/L. At higher exposures, approximately 75% of the <i>Daphnia</i> were dead or immobilized. Also at these higher concentrations, undissolved methyl benzoate was initially reported, but was no longer observed at 24 hours.
<b>Conclusion remarks</b>	The 48-hour EC50 for methyl benzoate in <i>Daphnia</i> was 32.1 mg/L and the no-observed-effect concentration was 18.8 mg/L.
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restrictions.
<b>Data Reliability Remarks</b>	Code 1. Comparable to guideline study.
<b>Reference</b>	Cunningham F.P. (1997b) C-2000 (Methyl Benzoate): Acute toxicity to the water flea, <i>Daphnia magna</i> , under static conditions. Project No. J9605001b. Unpublished report.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance methyl benzoate
<b>Method/guideline</b>	Calculated
<b>Species/Strain/Supplier</b>	<i>Daphnia magna</i>
<b>Conclusion remarks</b>	48 hour LC50 = 84.0 mg/L
<b>Data Qualities Reliabilities</b>	Reliability code 4. Not assignable.
<b>Data Reliability Remarks</b>	Code 4. Calculated.
<b>Reference</b>	ECOSAR EPI Suite (2000) US Environmental Protection Agency.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance benzaldehyde
<b>Method/guideline</b>	Experimental
<b>Test Type</b>	24 hour LC50
<b>GLP</b>	No
<b>Year</b>	1977
<b>Species/Strain/Supplier</b>	<i>Daphnia magna</i>
<b>Test Details</b>	<i>Daphnia magna</i> (30/group, 24 hours old) were maintained in chlorine free tap water saturated with oxygen, pH of 7.7-7.7 and temperature of 20-22 C. The LC50, LC0 and LC100 were determined.
<b>EC50, EL50, LC0, at 24,48 hours</b>	24 hour LC50 = 50, LC0 = 6.3 and LC100 = 100 mg/L
<b>Conclusion remarks</b>	LC50 = 50 mg/L; LC0 = 6.3 mg/L; LC100 = 100 mg/L
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Data Reliability Remarks</b>	Code 2. Acceptable, well-documented publication/study report, which meets basic scientific principles.
<b>Reference</b>	Bringmann G. and Kuehn, R. (1977) Befunde der Schadwirkung wassergefaehrdender Stoffe gegen <i>Daphnia magna</i> . [Results of the damaging effects of water pollutants on <i>Daphnia magna</i> .] A Wasser Abwasser Forsch., 10(5, :161-166.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance benzaldehyde
<b>Method/guideline</b>	Calculated
<b>Species/Strain/Supplier</b>	<i>Daphnia magna</i>
<b>Conclusion remarks</b>	48 hour LC50 = 12.0 mg/L
<b>Data Qualities Reliabilities</b>	Reliability code 4. Not assignable.
<b>Data Reliability Remarks</b>	Code 4. Calculated.
<b>Reference</b>	ECOSAR EPI Suite (2000) US Environmental Protection Agency.

### 3.3 Acute Toxicity to Aquatic Plants

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Method/guideline</b>	Calculated
<b>Species/Strain/Supplier</b>	Green algae
<b>Exposure Period</b>	96 hour
<b>Conclusion remarks</b>	The EC50 = 204 mg/L
<b>Data Qualities Reliabilities</b>	Reliability code 4. Not assignable.
<b>Remarks for Data Reliability</b>	Code 4. Calculated.
<b>Reference</b>	ECOSAR EPI Suite (2000) US Environmental Protection Agency.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0

<b>Remarks for Substance</b>	Data are structurally related substance terephthalic acid
<b>Method/guideline</b>	OECD Guideline 201
<b>Test Type</b>	Static test
<b>Year</b>	1991-1992
<b>Species/Strain/Supplier</b>	Green algae
<b>Exposure Period</b>	96 hour
<b>Remarks for Test Conditions</b>	<p>The study was conducted in quadruplicate using 104 cells/ml per test concentration. A total of 100 ml of test solution was used. The age of the stock and pre-cultures were 13 and 4 days, respectively. Test vessels consisted of 300 ml Erlenmeyer flasks containing 100 ml of test solution and were capped with a cotton plug. Flasks were shaken at a rate of 80 oscillations/minute. Room temperature was <math>23 \pm 1</math> °C, pH ranged from 8.1- 10.2, and a light/dark photoperiod of 24/0 hours was used. The quantum flux density was 120uE/sec-m-2. Nominal test concentrations were 62.5, 125, 250, 500 and 1000 ppm. The actual concentration of the highest exposure level was 927.05 ppm at time 0 and 408.85 ppm at 96 hours. Lower concentrations were within 70-105% nominal levels at time 0, but less than 10 ppm after 96 hours. Growth inhibition was determined daily by counting the number of cells per volume of test solution (cell concentration).</p> <p>Under the test conditions it was believed that some of the terephthalic acid was converted to a salt. The decrease in concentration was believed to be due to adsorption of the material by the algae. Cells in all replicates treated with 125 – 1000 ppm were noted to have appeared paler than controls or those treated with 62.5 ppm between 48-72 hours.</p>
<b>NOEC, LOEC or NOEL, LOEL</b>	NOEC is greater than 1000 (nominal); EC50 is greater than 1000 (nominal)
<b>Remarks for results</b>	The pH and temperature of flasks containing test material remained within acceptable limits throughout the study and did not vary with time or concentration of test material. The pH of the control medium increased from 8.2 to 10.2. There was no effect of test material on algal growth. The test was considered valid, as the concentration of control algae increased by a factor of 93.3 within 3 days (at least a factor of 16 is required).
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restriction.
<b>Remarks for Data Reliability</b>	Code 1. Guideline study.
<b>Reference</b>	Amoco Corporation (1993c) A study of the toxicity to algae ( <i>Scenedesmus subspicatus</i> ) of terephthalic acid. Conducted by Battelle Europe; Study # BE-EA-128-91-02-ALG-3.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0

<b>Remarks for Substance</b>	Data are for structurally related substance dimethyl terephthalate
<b>Method/guideline</b>	Directive 88/302 EEC
<b>Species/Strain/Supplier</b>	Green algae
<b>Exposure Period</b>	72 hour
<b>NOEC, LOEC or NOEL, LOEL</b>	EC50 greater than 32.3 mg/L; NOEC = 10.8 mg/L
<b>Remarks for results</b>	No analytical monitoring, concentrations were nominal. For the growth rate endpoint, an EC50 was not reached at the highest concentration tested (32.3 mg/L). At test beginning pH was 7.7-8.0 and it was 8.2-9.1 at conclusion. The estimated algal toxicity EC50 using ECOTOX software is 1.5 mg/L (96-hr).
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restriction.
<b>Remarks for Data Reliability</b>	Code 2. Acceptable, well-documented publication/study report, which meets basic scientific principles.
<b>Reference</b>	Huls AG (1993) Report AW-301. Unpublished data.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance methyl benzoate
<b>Method/guideline</b>	Calculated
<b>Species/Strain/Supplier</b>	Green algae
<b>Conclusion remarks</b>	The 96 hour EC50 = 1.4 mg/L
<b>Data Qualities Reliabilities</b>	Reliability code 4. Not assignable.
<b>Remarks for Data Reliability</b>	Code 4. Calculated.
<b>Reference</b>	ECOSAR EPI Suite (2000) US Environmental Protection Agency

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance benzaldehyde
<b>Method/guideline</b>	Respiration of photosynthesizing cells
<b>GLP</b>	No
<b>Year</b>	1971
<b>Species/Strain/Supplier</b>	<i>Chlorella vulgaris</i>

<b>Endpoint basis</b>	Stimulation of cell respiration (oxygen uptake)
<b>Exposure Period</b>	5 hours
<b>Analytical monitoring</b>	Warburg respirometer
<b>Remarks for Test Conditions</b>	Cells were maintained in the dark at 25 °C in 20 ml flasks and oxygen uptake was measured over a period of 5 hours at a pH of 5.6 or pH of 7.2.
<b>Nominal concentrations as mg/L</b>	0.00005, 0.0001, and 0.001 M
<b>Biological observations</b>	Stimulation of respiration of 0, 10, and 90% at pH 5.6 and 5, 50, and 60% at pH 7.2 at 0.00005, 0.0001, and 0.001 M, respectively.
<b>Control response satisfactory?</b>	Unknown
<b>Appropriate statistical evaluations?</b>	None reported
<b>Conclusion remarks</b>	In a dose-dependent manner, benzaldehyde stimulated the respiration of cells from <i>Chlorella vulgaris</i> .
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Code 2. Acceptable, well-documented publication/study report, which meets basic scientific principles.
<b>Reference</b>	Dedonder A. and Van Sumere, C.F. (1971) The effect of phenolics and related compounds on the growth and the respiration of <i>Chlorella vulgaris</i> . Z Pflanzenphysiol Bd., 65, 70-80.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance benzaldehyde
<b>Method/guideline</b>	Growth and cell division
<b>GLP</b>	No
<b>Year</b>	1971
<b>Species/Strain/Supplier</b>	<i>Chlorella vulgaris</i>
<b>Endpoint basis</b>	Inhibition of cell growth
<b>Exposure Period</b>	80 and 160 hours
<b>Remarks for Test Conditions</b>	Cell growth was determined by direct cell counting using a Burkner counting chamber.
<b>Nominal concentrations as mg/L</b>	0.00005, 0.0001, and 0.001 M

<b>Biological observations</b>	Growth inhibition of 30, 30 and 95% after 80 hours and 7, 10 and 90% after 160 hours at 0.00005, 0.0001, and 0.001 M (8.5, 17, and 170 mg/L), respectively.
<b>Control response satisfactory?</b>	Unknown
<b>Appropriate statistical evaluations?</b>	None reported
<b>Conclusion remarks</b>	In a dose-dependent manner, benzaldehyde inhibited growth of <i>Chlorella vulgaris</i> .
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Code 2. Acceptable, well-documented publication/study report, which meets basic scientific principles.
<b>Reference</b>	Dedonder A. and Van Sumere, C.F. (1971) The effect of phenolics and related compounds on the growth and the respiration of <i>Chlorella vulgaris</i> . <i>Z Pflanzenphysiol Bd.</i> , 65, 70-80.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance benzaldehyde
<b>Method/guideline</b>	Calculated
<b>Species/Strain/Supplier</b>	Green algae
<b>Exposure Period</b>	96 hour
<b>Conclusion remarks</b>	The 96 hour EC50 = 152.0 mg/L
<b>Data Qualities Reliabilities</b>	Reliability code 4. Not assignable.
<b>Remarks for Data Reliability</b>	Code 4. Calculated.
<b>Reference</b>	ECOSAR EPI Suite (2000) US Environmental Protection Agency

## 4 HUMAN HEALTH TOXICITY

### 4.1 Acute Toxicity

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance terephthalic acid
<b>Method/guideline</b>	Oral LD50
<b>Test Type</b>	Acute oral toxicity
<b>GLP</b>	Yes
<b>Year</b>	1990
<b>Species/strain</b>	Rat/Sprague-Dawley
<b>Sex</b>	Male and Female
<b># of animals per sex per dose</b>	5/sex
<b>Vehicle</b>	Water
<b>Route of Administration</b>	Oral
<b>Remarks for Test Conditions</b>	A single dose of 5000 mg/kg test material (diluted with water to form a 50% w/v suspension) was administered by oral gavage at a rate of 10 ml/kg. At initiation of dosing rats were approximately 9 weeks of age and weighed an average of 310 g (M) and 183 g (F). Body weights were assessed at dosing, and on Days 7 and 14. Animals were observed daily for 14 days at which time they were killed and necropsied
<b>Value LD50 or LC50 with confidence limits</b>	LD50 = greater than 5,000 mg/kg bw
<b>Remarks for Results</b>	No deaths were noted in either sex. Clinical signs consisted of diarrhea (M 5/5; F 5/5), redness around nose (M 3/5; F 2/5), and discolored inguinal fur (M 4/5; F 1/5). Signs diminished in most animals by 48 hours and all were normal at study termination. Mean body weights increased during the study. No alterations were noted during gross necropsy.
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restriction.
<b>Remarks for Data Reliability</b>	Code 1. Comparable to guideline study.
<b>References</b>	Amoco Corporation (1990) Acute oral toxicity study of terephthalic acid in rats. Conducted by IIT Research Institute. IITRI Study #1557.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance dimethyl terephthalate
<b>Method/guideline</b>	Oral LD50
<b>Test Type</b>	Acute oral toxicity
<b>GLP</b>	No
<b>Year</b>	1973
<b>Species/strain</b>	Rat/Long-Evans Hooded
<b>Sex</b>	Male and Female
<b># of animals per sex per dose</b>	3-6/sex
<b>Vehicle</b>	None
<b>Route of Administration</b>	Oral
<b>Remarks for Test Conditions</b>	Oral doses of 0, 3000, 3900, 5020 or 6590 mg/kg DMT were administered to groups of 3-6 male rats as a 20% solution in corn oil. The animals were observed for clinical signs of toxicity and mortality for 14-days. After 14-days of observations, the animals were euthanized, autopsied, and examined for gross pathology and histopathology.
<b>Value LD50 or LC50 with confidence limits</b>	LD50 = to or greater than 6590 mg/kg bw
<b>Number of deaths at each dose level</b>	None
<b>Remarks for Results</b>	No mortality was observed during the 14-day post-treatment period. Clinical signs of toxicity were limited to slight to moderate weakness at all dose levels and slight tremors and ataxia at the 5,020 and 6,590 mg/Kg dose levels. No signs of gross or histopathological changes due to systemic toxicity were noted at necropsy.
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restriction.
<b>Remarks for Data Reliability</b>	Code 2. Acceptable, well-documented publication/study report, which meets basic scientific principles.
<b>References</b>	Krasavage, W.J., Yanno, F.J., and Terhaar, C.J. (1973) "Dimethyl terephthalate (DMT): Acute Toxicity, Subacute Feeding and Inhalation Studies in Male Rats." J. Amer. Ind. Hyg. Assoc., 34(10):455-462
<b>Substance Name</b>	Methyl 4-formylbenzoate

<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance benzaldehyde
<b>Method/guideline</b>	Oral LD50
<b>Test Type</b>	Acute oral toxicity
<b>GLP</b>	No
<b>Year</b>	1967
<b>Species/strain</b>	Rat/white
<b>Sex</b>	Not reported
<b># of animals per sex per dose</b>	Not reported
<b>Vehicle</b>	Not reported
<b>Route of Administration</b>	Oral
<b>Remarks for Test Conditions</b>	Total of 70 rats orally administered benzaldehyde and observed for 7 days.
<b>Value LD50 or LC50 with confidence limits</b>	LD50 = 2850 mg/kg bw (no confidence limits reported)
<b>Number of deaths at each dose level</b>	Not reported
<b>Data Qualities Reliabilities</b>	Reliability code 4. Not assignable.
<b>Remarks for Data Reliability</b>	Code 4. Only short abstract available.
<b>References</b>	Sporn A., Dinu, I., and Stanclu, V. (1967) Cercetari cu privire la toxicitatea aldehydei benzoice. [Research regarding the toxicity of benzaldehyde.] Igiene, 16(1), 23.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance benzaldehyde
<b>Method/guideline</b>	Oral LD50 (calculated by using the Litchfield and Wilcoxon, dose range is 95 confidence interval)
<b>Test Type</b>	Acute oral toxicity
<b>GLP</b>	No
<b>Year</b>	1964
<b>Species/strain</b>	Rat/Osborne-Mendel
<b>Sex</b>	Male and Female

<b># of animals per sex per dose</b>	5
<b>Vehicle</b>	Not reported
<b>Route of Administration</b>	Gavage
<b>Remarks for Test Conditions</b>	Five male and five female young adult Osborne-Mendel rats were fasted for 18 hours prior to treatment. Animals were observed for toxic signs and death. The observation period was up to 2 weeks.
<b>Value LD50 or LC50 with confidence limits</b>	LD50 = 1300 mg/kg bw (95% C.L. 1110-1540)
<b>Number of deaths at each dose level</b>	Not reported
<b>Remarks for Results</b>	Slope function: 1.4 (95% C.L. 1.2-1.6). Depression and coma were observed at higher doses. Time of deaths was between 4 and 18 hours.
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Code 2. Acceptable, well-documented publication/study report, which meets basic scientific principles.
<b>References</b>	Jenner P.M., Hagen, E.C., Taylor, J.M., Cook, E.L., and Fitzhugh, O.G. (1964) Food flavourings and compounds of related structure. I. Acute oral toxicity. <i>Fd Cosmet Toxicol.</i> , 2, 327-343.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance benzaldehyde
<b>Method/guideline</b>	Oral LD50 (calculated by using the Litchfield and Wilcoxon, dose range is 95 confidence interval)
<b>Test Type</b>	Acute oral toxicity
<b>GLP</b>	No
<b>Year</b>	1964
<b>Species/strain</b>	Guinea pig
<b>Sex</b>	Male and Female
<b># of animals per sex per dose</b>	Not reported
<b>Vehicle</b>	Not reported
<b>Route of Administration</b>	Gavage
<b>Remarks for Test Conditions</b>	Groups of guinea pigs consisting of both males and females were fasted for 18 hours prior to treatment. Animals were observed for toxic signs and death. The observation period was

up to 2 weeks.

<b>Value LD50 or LC50 with confidence limits</b>	LD50 = 1000 mg/kg bw (95% C.L. 800-1250)
<b>Number of deaths at each dose level</b>	Not reported
<b>Remarks for Results</b>	Slope function: 1.4 (95% C.L. 1.2-1.8). Diuresis, tremors, intestinal irritation and haemorrhage were observed. Time of deaths was between 1 hour and 4 days.
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Code 2. Acceptable, well-documented publication/study report, which meets basic scientific principles.
<b>References</b>	Jenner P.M., Hagen, E.C., Taylor, J.M., Cook, E.L., and Fitzhugh, O.G. (1964) Food flavourings and compounds of related structure. I. Acute oral toxicity. <i>Fd Cosmet Toxicol.</i> , 2, 327-343.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance methyl benzoate
<b>Method/guideline</b>	Oral LD50 (calculated by using the Thompson method and tables of Weil)
<b>Test Type</b>	Acute oral toxicity
<b>GLP</b>	No
<b>Year</b>	1954
<b>Species/strain</b>	Rat/Carworth-Wistar
<b>Sex</b>	Male
<b># of animals per sex per dose</b>	5
<b>Vehicle</b>	Not specified
<b>Route of Administration</b>	Gavage
<b>Remarks for Test Conditions</b>	Groups of 5 unfasted male rats were given a single dose of test substance in a logarithmic series. The animals were observed for up to 14 days.
<b>Value LD50 or LC50 with confidence limits</b>	LD50 = 3430 mg/kg bw (2.83-4.15 s.d.)
<b>Number of deaths at each dose level</b>	Not reported
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.

**Remarks for Data Reliability** Code 2. Acceptable, well-documented publication/study report, which meets basic scientific principles.

**References** Smyth H.F., Carpenter, C.P., Weil, C.S., and Pozzani, U.C. (1954) Range-finding toxicity data: List V. Arch Ind Hyg Occupat Med 10(1), 61-68.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance methyl benzoate
<b>Method/guideline</b>	Oral LD50 (calculated by using the Berens method)
<b>Test Type</b>	Acute oral toxicity
<b>GLP</b>	No
<b>Year</b>	1970
<b>Species/strain</b>	Rat
<b>Sex</b>	Not reported
<b># of animals per sex per dose</b>	24
<b>Vehicle</b>	2% starch solution
<b>Route of Administration</b>	Gavage
<b>Remarks for Test Conditions</b>	Groups of 24 rats were intragastrically administered 1000, 2000, 3000, 4000, or 5000 mg methyl benzoate/kg bw and were observed until death (within 14 days). The results were analyzed using the Berens method. Following death, the internal organs were macroscopically and pathologically examined.
<b>Value LD50 or LC50 with confidence limits</b>	LD50 = 3500 mg/kg bw
<b>Number of deaths at each dose level</b>	Not reported
<b>Remarks for Results</b>	Animals receiving the absolute lethal dose died within 2-3 hours. Initially following methyl benzoate administration, the animals became stimulated and slowly became uncoordinated, and breathing became rapid, spasms occurred and death due to cessation of respiration occurred. Animals receiving doses below the absolute lethal dose died within 14 days. There were no macroscopic lesions on the internal organs; however, the authors reported "severe expansion of the vessels in the liver" and "a plethora in the pulmonary tissue, expansion of the vessels, there were patches of vesicular emphysema with membrane rupture" in animals receiving the absolute lethal dose. The brain and adrenal gland showed no pathological changes.

<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Code 2. Basic data given: comparable to guidelines/standards.
<b>References</b>	Kravets-Bekker A.A., and Ivanova., O.P. (1970) Toxicological characteristics of methyl benzoate and potassium benzoate. Faktory Vneshn. Sredy Ikh Znach. Zdorov'ya Naseleniya, 1970(2), 125-129.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance methyl benzoate
<b>Method/guideline</b>	Oral LD50 (calculated by using the Berens method)
<b>Test Type</b>	Acute oral toxicity
<b>GLP</b>	No
<b>Year</b>	1970
<b>Species/strain</b>	Guinea pig
<b>Sex</b>	Not reported
<b># of animals per sex per dose</b>	6
<b>Vehicle</b>	2% starch solution
<b>Route of Administration</b>	Gavage
<b>Remarks for Test Conditions</b>	Groups of 6 guinea pigs were intragastrically administered 2000, 3000, 4000, 5000, or 6000 mg methyl benzoate/kg bw and were observed until death (within 14 days). The results were analyzed using the Berens method. Following death, the internal organs were macroscopically and pathologically examined.
<b>Value LD50 or LC50 with confidence limits</b>	LD50 = 4100 mg/kg bw
<b>Number of deaths at each dose level</b>	Not reported
<b>Remarks for Results</b>	Animals receiving the absolute lethal dose died within 2-3 hours. Initially following methyl benzoate administration, the animals became stimulated and slowly became uncoordinated, and breathing became rapid, spasms occurred and death due to cessation of respiration occurred. Animals receiving doses below the absolute lethal dose died within 14 days. There were no macroscopic lesions on the internal organs; however, the authors reported "severe expansion of the vessels in the liver" and "a plethora in the pulmonary tissue, expansion of the vessels, there were patches of vesicular emphysema with membrane rupture" in animals receiving the absolute lethal dose. The brain and adrenal gland showed no pathological

changes.

<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Code 2. Basic data given: comparable to guidelines/standards.
<b>References</b>	Kravets-Bekker A.A., and Ivanova., O.P. (1970) Toxicological characteristics of methyl benzoate and potassium benzoate. Faktory Vneshn. Sredy Ikh Znach. Zdorov'ya Naseleniya, 1970(2), 125-129.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Chemical assay: 60-65% Methyl 4-formylbenzoate; 18% methyl p-methylbenzoate
<b>Method/guideline</b>	Oral LD50
<b>Test Type</b>	Acute oral toxicity
<b>GLP</b>	No
<b>Year</b>	1970
<b>Species/strain</b>	Rat
<b>Sex</b>	Not reported
<b># of animals per sex per dose</b>	10
<b>Vehicle</b>	10% in 0.5% aqueous guar gum
<b>Route of Administration</b>	Gavage
<b>Remarks for Test Conditions</b>	Groups of rats of unspecified strain were given dose levels of 200 to 3200 mg/kg orally by gavage. Time to death was 2 to 24 hours after dosing. Animals were observed for 2 weeks after dosing.
<b>Value LD50 or LC50 with confidence limits</b>	LD50 = 1600-3200 mg/kg
<b>Number of deaths at each dose level</b>	Not reported
<b>Remarks for Results</b>	Time to death 2 to 24 hours. Surviving animals showed slight weight gain 2 weeks after dosing. White crystals were observed in the urine.
<b>Conclusion remarks</b>	The acute oral LD50 of methyl 4-formylbenzoate in rats is in the range from 1600 to 3200 mg/kg bw.
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Code 2. Basic data given: comparable to guidelines/standards.
<b>References</b>	Clark R.B. (1970) Toxicity Report to Eastman Kodak Co. Laboratory of Industrial Medicine. Report No 15928706. Private

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Chemical assay: 60-65% Methyl 4-formylbenzoate; 18% methyl p-methylbenzoate
<b>Method/guideline</b>	Oral LD50
<b>Test Type</b>	Acute oral toxicity
<b>GLP</b>	No
<b>Year</b>	1970
<b>Species/strain</b>	Mouse
<b>Sex</b>	Not reported
<b># of animals per sex per dose</b>	10
<b>Vehicle</b>	10% in 0.5% aqueous guar gum
<b>Route of Administration</b>	Gavage
<b>Remarks for Test Conditions</b>	Groups of mice of unspecified strain were given dose levels of 200 to 3200 mg/kg orally by gavage. Animals were observed for 2 weeks after dosing.
<b>Value LD50 or LC50 with confidence limits</b>	LD50 = 1600-3200 mg/kg
<b>Number of deaths at each dose level</b>	Not reported
<b>Remarks for Results</b>	Time to death 2 hours. Surviving animals showed slight weight gain 2 weeks after dosing. Animals showed slight to moderate weakness after dosing.
<b>Conclusion remarks</b>	The acute oral LD50 of methyl 4-formylbenzoate in mice is in the range from 1600 to 3200 mg/kg bw.
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Code 2. Basic data given: comparable to guidelines/standards.
<b>References</b>	Clark R.B. (1970) Toxicity Report to Eastman Kodak Co. Laboratory of Industrial Medicine. Report No 15928706. Private Communication to Chemintox Inc. Unpublished Report.
<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance methyl benzoate

<b>Method/guideline</b>	Oral LD50 (calculated)
<b>Test Type</b>	Acute oral toxicity
<b>GLP</b>	No
<b>Year</b>	1945
<b>Species/strain</b>	Rat
<b>Sex</b>	Not reported
<b># of animals per sex per dose</b>	Not reported
<b>Vehicle</b>	Not reported
<b>Route of Administration</b>	Gavage
<b>Remarks for Test Conditions</b>	A total of 25 rats were used to determine the LD50. Not less than 3 groups of 5 rats were tested. Rats were fasted 24 to 48 hours prior to administration of test substance. Rats were observed for 2 weeks or until death.
<b>Value LD50 or LC50 with confidence limits</b>	LD50 = 2170 mg/kg bw
<b>Number of deaths at each dose level</b>	Not reported
<b>Remarks for Results</b>	Overall intoxicated rats showed signs of central nervous system stimulation including: piloerection, muscular incoordination, progressive paralysis of the hind limbs and violent spastic convulsions, dyspnea and death (often preceded by respiratory paralysis).
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Code 2. Basic data given: comparable to guidelines/standards.
<b>References</b>	Graham B.E. and Kuizenga, M.H. (1945) Toxicity studies of benzyl benzoate and related benzyl compounds. J Pharm Exp Ther., 84, 358-62.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance methyl benzoate
<b>Method/guideline</b>	Oral LD50 (calculated)
<b>Test Type</b>	Acute oral toxicity
<b>GLP</b>	No
<b>Year</b>	1945
<b>Species/strain</b>	Rabbit

<b>Sex</b>	Not reported
<b># of animals per sex per dose</b>	Not reported
<b>Vehicle</b>	Not reported
<b>Route of Administration</b>	Gavage
<b>Remarks for Test Conditions</b>	A total of 12 rabbits were used to determine the LD50. Not less than 3 groups of 3 rabbits were tested. Rabbits were fasted 24 to 48 hours prior to administration of test substance. Rabbits were observed for 2 weeks or until death.
<b>Value LD50 or LC50 with confidence limits</b>	LD50 = 2170 mg/kg bw
<b>Number of deaths at each dose level</b>	Not reported
<b>Remarks for Results</b>	Overall intoxicated rabbits showed signs of central nervous system stimulation similar to that reported in rats [including: piloerection, muscular incoordination, progressive paralysis of the hind limbs and violent spastic convulsions, dyspnea and death (often preceded by respiratory paralysis)] followed by a 12- to 24-hour period of prostration prior to death.
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Code 2. Acceptable, well-documented publication/study report, which meets basic scientific principles.
<b>References</b>	Graham B.E. and Kuizenga, M.H. (1945) Toxicity studies of benzyl benzoate and related benzyl compounds. J Pharm Exp Ther., 84, 358-62.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance methyl benzoate
<b>Method/guideline</b>	Oral LD50 (calculated by using the Berens method)
<b>Test Type</b>	Acute oral toxicity
<b>GLP</b>	No
<b>Year</b>	1970
<b>Species/strain</b>	Mouse/white
<b>Sex</b>	Not reported
<b># of animals per sex per dose</b>	20
<b>Vehicle</b>	2% starch solution
<b>Route of Administration</b>	Gavage

<b>Remarks for Test Conditions</b>	Groups of 20 white mice were intragastrically administered 500, 1000, 2000, 3000, 3500, or 4000 mg methyl benzoate/kg bw and were observed until death (within 14 days). The results were analyzed using the Berens method. Following death, the internal organs were macroscopically and pathologically examined.
<b>Value LD50 or LC50 with confidence limits</b>	LD50 = 3000 mg/kg bw
<b>Number of deaths at each dose level</b>	Not reported
<b>Remarks for Results</b>	Animals receiving the absolute lethal dose died within 2-3 hours. Initially following methyl benzoate administration, the animals became stimulated and slowly became uncoordinated, and breathing became rapid, spasms occurred and death due to cessation of respiration occurred. Animals receiving doses below the absolute lethal dose died within 14 days. There were no macroscopic lesions on the internal organs; however, the authors reported "severe expansion of the vessels in the liver" and "a plethora in the pulmonary tissue, expansion of the vessels, there were patches of vesicular emphysema with membrane rupture" in animals receiving the absolute lethal dose. The brain and adrenal gland showed no pathological changes.
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Code 2. Basic data given: comparable to guidelines/standards.
<b>References</b>	Kravets-Bekker A.A., and Ivanova., O.P. (1970) Toxicological characteristics of methyl benzoate and potassium benzoate. Faktory Vneshn. Sredy Ikh Znach. Zdorov'ya Naseleniya, 1970(2), 125-129.

## 4.2 Genetic Toxicity

### 4.2.1 *In vitro* Genotoxicity

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance dimethyl terephthalate
<b>Method/guideline</b>	Ames reverse mutation

<b>Year</b>	1982, 1985
<b>Species/Strain</b>	<i>Salmonella typhimurium</i> TA98, TA100, TA1535, and TA1537
<b>Metabolic Activation</b>	With and without
<b>Doses/Concentration</b>	3.3 to 333 micrograms/plate
<b>Results</b>	With metabolic activation: 666 ug Without metabolic activation: 666 ug
<b>Genotoxic Effects</b>	None
<b>Remarks for Results</b>	Procedure: Pre-incubation Plates/test: Unknown Activation system: S-9 was from Aroclor 1254-induced male SD rats and Syrian hamsters. Media: Histidine selective Number of replicates: 2
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restriction.
<b>Remarks for Data Reliability</b>	Code 2. Basic data given: comparable to guidelines/standards.
<b>References</b>	Zeiger, E., Haworth, S., Speck, W., and Mortelmans, K. (1982) "Phthalate Ester Testing in the National Toxicology Program's Environmental Mutagenesis Test Development Program", <i>Environmental Health Perspectives</i> , 45:99-101.  Zeiger, E., Haworth, S., Mortelmans, K., and Speck, W. (1985) "Mutagenicity Testing of Di(2-ethylhexyl)phthalate and Related Chemicals in Salmonella", <i>Environmental Mutagenesis</i> , 7:213-232.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance dimethyl terephthalate
<b>Method/guideline</b>	Chromosomal aberration and Sister chromatid exchange
<b>Year</b>	1990
<b>Species/Strain</b>	Chinese Hamster Ovary (CHO) cells
<b>Remarks for Test Conditions</b>	CHO cells were grown and treated under conditions similar to those described by Galloway et al., (1985). Aroclor-induced rat liver microsomal preparations were combined with cofactors and added as the metabolic activation system. Medium and solvent controls were used with each assay. Positive controls (Mitomycin C for use without the metabolic activation system and cyclophosphamide for use with the activation system) were also included. For sister chromatid exchange (SCE)

experiments without metabolic activation, bromodeoxyuridine (BRDU) was added 2-hours after the addition of the control or test substance and the culture continued for 24-hours. Fresh medium with BRDU and colcemid replaced the previous media and the cultures continued for 2.5-hours. For SCE experiments with metabolic activation, serum free medium with cofactors, S9 fraction, and chemical were used for 2-hours and replaced with medium containing BRDU and the culture continued for 24-hours. Colcemid was added to the media and the cultures continued for 2.5-hours. The cells were then examined for cytotoxicity, harvested and fixed. Fluorescence-microscopy was then used to assess the frequency of metaphase cells and SCE. For experiments examining chromosomal aberrations without metabolic activation, media with either the control or test substance was used for 8-hours and then removed. Media containing colcemid replaced the previous media and the cultures continued for 2.5-hours. For experiments with metabolic activation, serum free medium with cofactors, S9 fraction, and chemical were used for 2-hours, then the media removed and fresh media used for 8-hours. Colcemid was then added and incubations continued for 2-hours. Cells were harvested and slides prepared using a 5% Giemsa stain for five minutes. Two hundred cells per dose were scored for chromosomal aberrations.

<b>Cytotoxic concentration</b>	With metab. activ.: >10 ug/ml Without metab. activ.: >10 ug/ml
<b>Genotoxic Effects</b>	None
<b>Remarks for Results</b>	Procedure: CHO cells Plates/test: Unknown Activation system: Aroclor 1254-treated male SD rats Media: McCoy's 5A (modified media) buffered with 20 mM HEPES and supplemented with 10% FBS, 2 mM L-glutamine, 50 IU penicillin, and 50 µg/ml streptomycin.
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restriction.
<b>Remarks for Data Reliability</b>	Code 2. Acceptable, well-documented publication/study report, which meets basic scientific principles.
<b>References</b>	Loveday, K.S., Anderson, B.E., Resnick, M.A., and Zeiger, E. (1990) Chromosome Aberration and Sister Chromatid Exchange Tests in Chinese Hamster Ovary Cells In Vitro. V: Results with 46 Chemicals, Environmental and Molecular Mutagenesis, 16:272-303.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance dimethyl terephthalate

<b>Test Type</b>	DNA single-strand breaks
<b>Year</b>	1989,1991
<b>Species/Strain</b>	Rat\Hepatocytes
<b>Metabolic Activation</b>	With
<b>Doses/Concentration</b>	0, 3.75, 7.50, or 15.00 µmole/ml equivalent to 0, 727.5, 1,455, or 2,910 µg/ml
<b>Remarks for Test Conditions</b>	DMT was dissolved in a mixture of DMSO and Tween 20 (29:1). Rat hepatocytes were isolated by conventional methods. Cytotoxicity (trypan blue exclusion) was measured following a 1-hour incubation period. The remaining cells were lysed and DNA was isolated on filters and eluted at alkaline pH. DNA was measured in the eluted fractions by fluorometric determinations using a Hoechst 33258 dye. A positive finding is designated when the percent DNA retained on the control filter minus the percent DNA retained on the filters from each treatment group is greater than 20% at dose levels with greater than 70% viability.
<b>Results</b>	Dimethyl terephthalate treatment did not produce any evidence of an increase in DNA single strand breaks.
<b>Cytotoxic concentration</b>	With metabolic activation: greater than 2,910 micrograms/ml Without metabolic activation: NA
<b>Genotoxic Effects</b>	None
<b>Remarks for Results</b>	Procedure: Primary rat hepatocytes were used Plates/test: Unknown Activation system: Primary rat hepatocytes Media: Unknown No. replicates: Unknown
<b>Conclusion Remarks</b>	Within the limitations of the test, dimethyl terephthalate is not genotoxic
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restriction.
<b>Remarks for Data Reliability</b>	Code 2. Basic data given: comparable to guidelines/standards.
<b>References</b>	Monarca, S., Pool-Zobel, B.L., Rizzi, R., Klein, P., Schmezer, P., Piatti, E., Pasquini, R., De Fusco, R., and Biscardi, D. (1991) In vitro Genotoxicity of Dimethyl Terephthalate. Mutation Research, 262:85-92.  Monarca, S., Rizzi, R., Pasquini, R., Pool, B.L., De Fusco, R., Biscardi, D., Gervasoni, M., and Piatti, E. (1989) Studies on the Genotoxic Properties of Precursors of Polyethyleneterephthalate Plastics, Mutation Research, 216:314-315.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance dimethyl terephthalate
<b>Method/guideline</b>	Gene Mutation
<b>Year</b>	1991
<b>Species/Strain</b>	Mouse/L5178Y lymphoma cells (clone 3.7.2C.)
<b>Doses/Concentration</b>	0-100 ug/ml
<b>Remarks for Test Conditions</b>	Increases in the frequency of 5-trifluorothymidine(TFT)-resistant cells due to mutational events occurring at the thymidine kinase locus following DMT exposure (50 µg/ml) was determined with and without S9 fraction. Dimethylformamide (1%) was used as the solvent carrier. The treatment period was 4 hours at 37 °C in a roller drum (10-15 rpm). Cells were retrieved by centrifugation and washed twice with growth media. The two-day expression and growth period was conducted with cell densities of 3x10 <sup>5</sup> cells/ml (20 ml of media on roller drum). After two-days, the cells were added to 90 ml of cloning media. Dishes containing the cells and cloning media were incubated for 11 to 12-days at 37 °C with 5% CO <sub>2</sub> /humidified air for colony development.
<b>Cytotoxic concentration</b>	With metabolic activation greater than 100 ug/ml Without metabolic activation greater than 100 ug/ml
<b>Genotoxic Effects</b>	None
<b>Remarks for Results</b>	Procedure: L5178Y mouse lymphoma cells (clone 3.7.2C.) Plates/test: Unknown Activation system: Aroclor 1254-induced male F344 rats Growth media: RPMI 1640 medium supplemented with heat-treated horse serum (10% v/v), 220 µg/ml sodium pyruvate, 2 mM L-glutamine, 0.05% Pluronic F68 and gentamycin (50 micrograms/ml) Treatment media: Fischer's growth medium with 5% heat-treated horse serum. Cloning media: Growth media plus 0.35-0.40% agar and 3 µg/ml TFT
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restriction.
<b>Remarks for Data Reliability</b>	Code 2. Acceptable, well-documented publication/study report, which meets basic scientific principles.
<b>References</b>	Myhr, B.C. and Caspary, W.J. (1991) Chemical Mutagenesis at the Thymidine Kinase Locus in L5178Y Mouse Lymphoma Cells: Results for 31 Coded Compounds in the National Toxicology Program, Environmental and Molecular Mutagenesis, 18:51-83.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance dimethyl terephthalate
<b>Test Type</b>	DNA single-strand breaks
<b>Year</b>	1989,1991
<b>Species/Strain</b>	SV40-transformed Chinese Hamster Embryo cell line (CO60 cells)
<b>Metabolic Activation</b>	Without
<b>Doses/Concentration</b>	0, 3.75, 7.50, or 15.00 µmole/ml equivalent to 0, 727.5, 1,455, or 2,910 micrograms/ml.
<b>Remarks for Test Conditions</b>	DMT was dissolved in a mixture of DMSO and Tween 20 (29:1). Cytotoxicity (trypan blue exclusion) was measured following a 1-hour incubation period. Cells were lysed and DNA was isolated on filters and eluted at alkaline pH. DNA was measured in the eluted fractions by fluorometric determinations using a Hoechst 33258 dye. A positive finding is designated when the percent DNA retained on the control filter minus the percent DNA retained on the filters from each treatment group is greater than 20% at dose levels with greater than 70% viability.
<b>Results</b>	Dimethyl terephthalate treatment did not produce any evidence of an increase in DNA single strand breaks.
<b>Cytotoxic concentration</b>	Without metabolic activation: greater than 2,910 micrograms/ml
<b>Genotoxic Effects</b>	None
<b>Remarks for Results</b>	Procedure: SV40-transformed Chinese Hamster Embryo cell line (CO60 cells). Plates/test: Unknown Activation system: None Media: Unknown No. replicates: Unknown Other: Results of this test were not fully reported.
<b>Conclusion Remarks</b>	Dimethyl terephthalate was not genotoxic within the limitations of this test.
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restriction.
<b>Remarks for Data Reliability</b>	Code 2. Basic data given: comparable to guidelines/standards.
<b>References</b>	Monarca, S., Pool-Zobel, B.L., Rizzi, R., Klein, P., Schmezer, P., Piatti, E., Pasquini, R., De Fusco, R., and Biscardi, D. (1991) In vitro Genotoxicity of Dimethyl Terephthalate, Mutation Research, 262:85-92.

Monarca, S., Rizzi, R., Pasquini, R., Pool, B.L., De Fusco, R., Biscardi, D., Gervasoni, M., and Piatti, E. (1989) "Studies on the Genotoxic Properties of Precursors of Polyethyleneterephthalate Plastics", Mutation Research, 216:314-315.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance dimethyl terephthalate
<b>Test Type</b>	Unscheduled DNA synthesis
<b>Species/Strain</b>	Human/Hela
<b>Metabolic Activation</b>	With and Without S-9 Activation
<b>Doses/Concentration</b>	5, 50, 500, 5,000 micrograms/ml
<b>Remarks for Test Conditions</b>	Induction of unscheduled DNA synthesis was measured in HeLa cells exposed to varying concentrations of DMT dissolved in a mixture of DMSO and Tween 20 (29:1). DMT exposures were conducted in PBS with or without S9 liver fractions. Following treatment and rinsing to remove residual material, the cells were incubated with or without hydroxyurea (HU) in culture media. Tritiated methylthymidine was added after 15 minutes and the incubations continued for three-hours. Radioactivity was then counted to determine the incorporation of the radiolabeled thymidine. Inhibition of DNA replication and synthesis by HU in the control and treated cultures was determined by comparing the ratio of counts from 1) control w/o HU, control plus HU, and 2) treated w/o HU, treated plus HU. Inhibition of DNA replication and synthesis by DMT exposure was determined by the ratio of treated w/o HU, control w/o HU. The effect of HU on the induction of DNA repair in the presence of DMT was determined by the ratio of (treated plus HU, treated w/o HU) divided by (control plus HU, control w/o HU).
<b>Results</b>	Dimethyl terephthalate treatment did not produce any evidence of an increase in unscheduled DNA synthesis.
<b>Cytotoxic concentration</b>	With metabolic activation: Unknown Without metabolic activation.: Unknown
<b>Genotoxic Effects</b>	Dimethyl terephthalate did not induce any evidence
<b>Remarks for Results</b>	Procedure: Hela cells Plates/test: Unknown Activation system: S-9 was from Aroclor induced SD rats Media: Phosphate-buffered saline No. replicates: Unknown

<b>Conclusion Remarks</b>	Within the limitations of the test, dimethyl terephthalate is not genotoxic.
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restriction.
<b>Remarks for Data Reliability</b>	Code 2. Basic data given: comparable to guidelines/standards.
<b>References</b>	<p>Monarca, S., Pool-Zobel, B.L., Rizzi, R., Klein, P., Schmezer, P., Piatti, E., Pasquini, R., De Fusco, R., and Biscardi, D. (1991) "In vitro Genotoxicity of Dimethyl Terephthalate", Mutation Research, 262:85-92.</p> <p>Monarca, S., Rizzi, R., Pasquini, R., Pool, B.L., De Fusco, R., Biscardi, D., Gervasoni, M., and Piatti, E. (1989) "Studies on the Genotoxic Properties of Precursors of Polyethyleneterephthalate Plastics", Mutation Research, 216:314-315</p>

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance methyl benzoate
<b>Method/guideline</b>	Paper disk method (Lyer and Szybalski, 1958)
<b>Test Type</b>	Reverse mutation test
<b>System of Testing</b>	Bacterial
<b>GLP</b>	No
<b>Year</b>	1958
<b>Species/Strain</b>	Sd-4-73 <i>E. coli</i>
<b>Metabolic Activation</b>	No
<b>Doses/Concentration</b>	Not reported
<b>Statistical Methods</b>	Not reported
<b>Remarks for Test Conditions</b>	<i>E. coli</i> was cultured overnight at 36 °C in an aerated nutrient broth containing 20 ug/ml streptomycin. Plates were prepared and methyl benzoate was added by applying to a paper disk, which was then placed on the agar. Relative mutagenicity, defined as "an approximate ratio of the number of colonies on the plate containing the mutagen to the number of colonies on the control plate", was calculated. "Potent" mutagens had relative mutagenicities of greater than 3 and "weak and doubtful" mutagens had relative mutagenicities between 1.5 and 3.
<b>Results</b>	Methyl benzoate produced no increase in the frequency of reversion from streptomycin dependence to independence in Sd-4-73 <i>E. coli</i> .

<b>Cytotoxic concentration</b>	Not reported
<b>Genotoxic Effects</b>	None
<b>Conclusion Remarks</b>	Methyl benzoate was non mutagenic in this assay.
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Study was conducted prior to establishment of GLP guidelines.
<b>References</b>	Szybalski W. (1958) Special microbiological systems. II. Observations on chemical mutagenesis in microorganisms. Annals New York Academy of Sciences. Pp 475-489.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance methyl benzoate
<b>Method/guideline</b>	Ames assay (Haworth et al., 1983)
<b>Test Type</b>	Reverse mutation test
<b>System of Testing</b>	Bacterial
<b>GLP</b>	Not reported
<b>Year</b>	1992
<b>Species/Strain</b>	<i>Salmonella typhimurium</i> TA100, TA1535, TA1537, TA97, TA98
<b>Metabolic Activation</b>	S9 fractions of Aroclor 1254-induced male Sprague-Dawley rats and male Syrian hamster livers
<b>Doses/Concentration</b>	0, 10, 33, 100, 333, 666, 1000, 1666, 3333, or 6666 ug/plate
<b>Statistical Methods</b>	
<b>Remarks for Test Conditions</b>	Sodium azide (TA1535 and TA100), 4-nitro-o-phenylenediamine (TA98 and 1538), mitomycin C (TA102), methyl methanesulfonate (TA104) and 9-aminoacridine (TA97 and TA1537) were used as positive controls for the specific Salmonella strains without S9. 2-Aminoanthracene was used with all strains incubated with S9 and either sterigmatocystin or 2-aminoanthracene was used for TA102. DMSO was used as the solvent control. Nine concentrations of the methyl benzoate (in triplicate) were incubated with or without S9 for 20 minutes after which plates were prepared and incubated at 37 °C for 48 hours. The number of revertants was machine counted. If a chemical was not active (with or without metabolic activation) in all Salmonella strains tested, it was considered non mutagenic.
<b>Results</b>	Methyl benzoate showed no mutagenic activity in any of the strains tested with or without S9.
<b>Cytotoxic concentration</b>	Not reported

<b>Genotoxic Effects</b>	None
<b>Conclusion Remarks</b>	Methyl benzoate was non mutagenic.
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restriction.
<b>Remarks for Data Reliability</b>	Assay was conducted by standard methodology and published in a peer-reviewed journal. Tabulated results.
<b>References</b>	Zeiger E., Anderson, B., Haworth, S., Lawlor, T., and Mortelmans, K. (1992) Salmonella mutagenicity tests: V. Results from the testing of 311 chemicals. Environ Mol Mut., 19 (Suppl 21), 2-141.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance benzaldehyde
<b>Method/guideline</b>	Ames assay
<b>Test Type</b>	Reverse mutation test
<b>System of Testing</b>	Bacterial
<b>GLP</b>	Not reported
<b>Year</b>	1992
<b>Species/Strain</b>	<i>Salmonella typhimurium</i> TA100, TA102, TA104
<b>Metabolic Activation</b>	Rat liver microsome fraction S9 from Aroclor induced F344 rats and B6C3F1 mice
<b>Doses/Concentration</b>	Not reported
<b>Statistical Methods</b>	The data were evaluated using Wahrendorf ranking and Dunnett's t-test.
<b>Remarks for Test Conditions</b>	Cells were tested with and without S9.
<b>Results</b>	Benzaldehyde was non mutagenic with or without S9 in all <i>Salmonella</i> strains tested.
<b>Cytotoxic concentration</b>	Not reported
<b>Genotoxic Effects</b>	None
<b>Conclusion Remarks</b>	Benzaldehyde was non mutagenic in this assay.
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Data from abstract only but method appears to be standard and results are consistent with chemical structure and other results.
<b>References</b>	Dillon D.M., McGregor, D.B., Combes, R.D. and Zeiger, E. (1992) Detection of mutagenicity in Salmonella of some aldehydes and peroxides. Environ. Molec. Mutagen., 19(suppl

20), 15.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance benzaldehyde
<b>Method/guideline</b>	Ames assay
<b>Test Type</b>	Reverse mutation (spot test)
<b>System of Testing</b>	Bacterial
<b>GLP</b>	Not reported
<b>Year</b>	1980
<b>Species/Strain</b>	<i>Salmonella typhimurium</i> TA1535, TA1537, TA98, TA100
<b>Metabolic Activation</b>	With and without rat liver microsomes fraction S9 from Aroclor induced rats
<b>Doses/Concentration</b>	3 umol/plate
<b>Remarks for Test Conditions</b>	For each experiment viable count was determined, the number of spontaneous revertants was measured, the presence of the rfa-mutation was determined by crystal violet inhibition, the presence of the plasmid pKM 101 in strains TA98 and TA100 was determined by resistance to ampicillin, and the response to positive controls N-methyl-N-nitrosoquandin (without metabolic activation) and 2-aminoanthracene (with activation) was determined. Spectroscopic-grade ethanol was used as the solvent. The test substance was tested at 3 umol/plate in TA98, TA100, TA1535, and TA1537 with or without S9. If there was no background lawn of bacteria, the tests were redone using lower concentrations. Uncertain results prompted the conduction of the tests at 4 concentration levels (0.03, 0.3, 3 and 30 umol/plate).
<b>Results</b>	Benzaldehyde produced a negative response in this assay.
<b>Cytotoxic concentration</b>	Not reported
<b>Genotoxic Effects</b>	None
<b>Remarks for Results</b>	Spot tests are less sensitive than quantitative experiments. Also, the results from strain TA100 are difficult to interpret because the high growth background (150-200 colonies per plate); however, spot tests provide a good "screening" method for large numbers of chemicals.
<b>Conclusion Remarks</b>	Benzaldehyde is non-mutagenic in the Ames assay using <i>Salmonella typhimurium</i> strains TA98, TA100, TA1535, and TA1537 with or without S9.
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restriction.

**Remarks for Data Reliability** Study is published in a peer-reviewed journal with adequate description and follows standard procedures.

**References** Florin I., Rutberg, L., Curvall, M. and Enzell, C.R. (1980) Screening of tobacco smoke constituents for mutagenicity using the Ames' test. *Toxicology*, 18, 219-232.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance benzaldehyde
<b>Method/guideline</b>	Ames assay
<b>Test Type</b>	Reverse mutation test
<b>System of Testing</b>	Bacterial
<b>GLP</b>	Not reported
<b>Year</b>	1989
<b>Species/Strain</b>	<i>Salmonella typhimurium</i> TA1535, TA1537, TA1538, TA98, TA100
<b>Metabolic Activation</b>	With and without rat liver microsome fraction S9 from Aroclor induced rats
<b>Doses/Concentration</b>	37500 ug/plate
<b>Statistical Methods</b>	Not reported
<b>Remarks for Test Conditions</b>	Following 2 days of incubation at 37 °C, revertant colonies were counted electronically.
<b>Results</b>	Benzaldehyde was inactive in the Ames assay using <i>Salmonella typhimurium</i> TA1535, TA1537, TA1538, TA98, TA100 with or without S9 activation.
<b>Cytotoxic concentration</b>	Not reported
<b>Genotoxic Effects</b>	None
<b>Conclusion Remarks</b>	Benzaldehyde was non-mutagenic in this assay.
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Assay was conducted by standard methodology, but there was limited description of the study and the results were tabulated.
<b>References</b>	Heck J.D., Vollmuth, T.A., Cifone, M.A., Jagannath, D.R., Myhr, B. and Curren, R.D. (1989) An evaluation of food flavoring ingredients in a genetic toxicity screening battery. <i>The Toxicologist</i> , 9(1), 257.
<b>Substance Name</b>	Methyl 4-formylbenzoate

<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance benzaldehyde
<b>Method/guideline</b>	Ames assay
<b>Test Type</b>	Reverse mutation test
<b>System of Testing</b>	Bacterial
<b>GLP</b>	Not reported
<b>Year</b>	1979
<b>Species/Strain</b>	<i>Salmonella typhimurium</i> TA98, TA100
<b>Metabolic Activation</b>	With rat liver microsome fraction S9
<b>Doses/Concentration</b>	Urinary metabolites assayed ranged from 0.05 to 100 ul/plate
<b>Remarks for Test Conditions</b>	0.5 ml benzaldehyde was administered by gavage to 2 Sprague-Dawley rats, which were kept in metabolism cages. Urine and feces were collected for 24 hours. Urine was separated from the feces and was prepared for mutagenicity screening. Bacterial cells were incubated with benzaldehyde in the presence of S9 for 48 hours at 37 C. Sodium azide and picrolonic acid were used as positive controls for TA100 and TA98, respectively. Enzyme activation by S9 was confirmed with plates containing aflatoxin B1.
<b>Results</b>	The urinary metabolites of benzaldehyde did not increase the number of revertants.
<b>Cytotoxic concentration</b>	Not reported
<b>Genotoxic Effects</b>	None
<b>Remarks for Results</b>	The urinary metabolites of benzaldehyde were non mutagenic in this assay.
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Limited description of study and results.
<b>References</b>	Rockwell P. and Raw, I. (1979) A mutagenic screening of the various herbs, spices, and food additives. Nutrition and Cancer, 1(4), 10-16.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance benzaldehyde
<b>Method/guideline</b>	Ames assay
<b>Test Type</b>	Reverse mutation test

<b>System of Testing</b>	Bacterial
<b>GLP</b>	Not reported
<b>Year</b>	1998
<b>Species/Strain</b>	<i>Salmonella typhimurium</i> TA100, TA102, TA104
<b>Metabolic Activation</b>	With and without rat liver microsome fraction S9 (from Aroclor 1254-induced F344 rats and male B6C3F1 mice)
<b>Doses/Concentration</b>	33-3333 ug/plate
<b>Statistical Methods</b>	Dunnett's t-test, Wahrendorf ranking and linear regression
<b>Results</b>	Benzaldehyde produced no increase in reverse mutations.
<b>Cytotoxic concentration</b>	Not reported
<b>Genotoxic Effects</b>	None
<b>Appropriate statistical evaluations?</b>	Yes
<b>Conclusion Remarks</b>	Benzaldehyde was non mutagenic with or without metabolic activation.
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restriction.
<b>Remarks for Data Reliability</b>	Assay was conducted using standard methodology and was published in a peer-reviewed journal.
<b>References</b>	Dillon D., Combes, R. and Zeiger, E. (1998) The effectiveness of <i>Salmonella</i> strains TA100, TA102 and TA104 for detecting mutagenicity of some aldehydes and peroxides. <i>Mutagen.</i> , 13(1), 19-26.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance benzaldehyde
<b>Method/guideline</b>	Ames assay
<b>Test Type</b>	Reverse mutation test
<b>System of Testing</b>	Bacterial
<b>GLP</b>	Not reported
<b>Year</b>	1982
<b>Species/Strain</b>	<i>Salmonella typhimurium</i> TA98, TA100
<b>Metabolic Activation</b>	Rat liver microsome fraction S9 from Aroclor induced rats
<b>Doses/Concentration</b>	0.05-500 ug/plate

<b>Remarks for Test Conditions</b>	DMSO was used as the solvent and control. The results were considered positive if a reproducible, dose-related increase in the number of revertants and a greater than 2-fold increase in spontaneous mutation rate was observed.
<b>Results</b>	Benzaldehyde did not increase the incidence of mutation as compared to the vehicle controls, either with or without S9 mix.
<b>Cytotoxic concentration</b>	Not reported
<b>Genotoxic Effects</b>	None
<b>Conclusion Remarks</b>	Benzaldehyde was non-mutagenic.
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Assay was conducted by standard methodology and published in a peer-reviewed journal. Tabulated results.
<b>References</b>	Kasamaki A., Takahashi, H., Tsumura, N., Niwa, J., Fujita, T. and Urasawa, S. (1982) Genotoxicity of flavoring agents. <i>Mutat. Res.</i> , 105, 387-392.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance benzaldehyde
<b>Method/guideline</b>	Ames assay
<b>Test Type</b>	Reverse mutation test
<b>System of Testing</b>	Bacterial
<b>GLP</b>	Not reported
<b>Year</b>	1983
<b>Species/Strain</b>	<i>Salmonella typhimurium</i> TA98 and TA1535
<b>Metabolic Activation</b>	Not reported
<b>Doses/Concentration</b>	0, 0.1, 0.5, 1.0, 2.5, or 5.0 umol/plate
<b>Statistical Methods</b>	Mean of 3 values with extremes never removed from the means by greater than 5-10%.
<b>Remarks for Test Conditions</b>	The test substance was tested at 5 concentrations with 3 plates per concentration. The positive control for TA1535 was 2 ug sodium azide and for TA98 was 3 ug 2-nitrofluorene.
<b>Results</b>	There was no detectable mutagenic activity.
<b>Cytotoxic concentration</b>	Not reported
<b>Genotoxic Effects</b>	None
<b>Conclusion Remarks</b>	Benzaldehyde was non-mutagenic in this assay.

<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restriction.
<b>Remarks for Data Reliability</b>	Assay was conducted by standard methodology and published in a peer-reviewed journal.
<b>References</b>	Wiessler M. Romruen, K. and Pool, B.L. (1983) Biological activity of benzylating N-nitroso compounds. Models of activated N-nitrosomethylbenzylamine. <i>Carcinogenesis</i> , 4(7), 867-871.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance benzaldehyde
<b>Method/guideline</b>	Ames assay (Haworth et al., 1983)
<b>Test Type</b>	Reverse mutation test
<b>System of Testing</b>	Bacterial
<b>GLP</b>	Yes
<b>Year</b>	1990
<b>Species/Strain</b>	<i>Salmonella typhimurium</i> TA102, TA104, TA100, TA98, TA1535, and TA1537
<b>Metabolic Activation</b>	S9 mix from livers of Aroclor 1254-incude male SD rat or Syrian hamster
<b>Doses/Concentration</b>	TA102 (trial 1 and 2): 0, 33, 100, 333, 1,000 or 3,333 ug/plate; TA100 (trial 1): 0, 33, 100, 333, 1,000, or 3,333 ug/plate; TA100 (trial 2): 0, 10, 33, 100, 333, or 1,000 ug/plate; TA1535, TA1537 and TA98: 0, 10, 33, 100, 333, or 1,000 ug/plate
<b>Remarks for Test Conditions</b>	Tester strains and test substance or solvent were incubated with or without S9. Cytotoxicity limited highest concentration tested, but test concentration did not exceed 10 mg/plate. Positive controls used were 2-aminoanthracene, 4-nitro-o-phenylenediamine, sodium azide, and 9-aminoacridine. Tests with TA102, TA104 and TA100 were conducted at Inveresk Research International and with TA1535, TA1537 and TA98 at EG&G Mason Research Institute.
<b>Results</b>	All tester strains produced negative results. Cytotoxicity was observed at 1,000 and 3,333 ug/plate for TA100, at 3,333 ug/plate for TA102 and TA104, and at 1,000 ug/plate for TA98, TA1535 and TA1537.
<b>Cytotoxic concentration</b>	1,000 to 3,333 ug/plate
<b>Genotoxic Effects</b>	None
<b>Conclusion Remarks</b>	Benzaldehyde was non-mutagenic in this assay.
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restriction.

**Remarks for Data Reliability** NTP study

**References** National Toxicology Program (1990) Toxicology and carcinogenesis studies of benzaldehyde (CAS No. 100-52-7) in F344/N rats and B6C3F1 mice. Technical Report Series 378.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance benzaldehyde
<b>Method/guideline</b>	Ames assay (modified)
<b>Test Type</b>	Reverse mutation test
<b>System of Testing</b>	Bacterial
<b>GLP</b>	No
<b>Year</b>	1978
<b>Species/Strain</b>	<i>Salmonella typhimurium</i> TA100, TA98
<b>Metabolic Activation</b>	Liver microsomal enzymes from KC-500 treated rats and "certain co-factors"
<b>Doses/Concentration</b>	Not reported
<b>Statistical Methods</b>	Not reported
<b>Remarks for Test Conditions</b>	The slight modification of the Ames assay was a preincubation of the samples for 15 min at 37 °C prior to plating. Benzaldehyde was tested with and without metabolic activation.
<b>Results</b>	No mutagenicity was reported.
<b>Cytotoxic concentration</b>	Not reported
<b>Genotoxic Effects</b>	None
<b>Conclusion Remarks</b>	Benzaldehyde was non-mutagenic in this assay.
<b>Data Qualities Reliabilities</b>	Reliability code 4. Not assignable.
<b>Remarks for Data Reliability</b>	The data were published in a brief abstract with limited detail and the study was conducted prior to GLP and OECD guidelines.
<b>References</b>	Sasaki Y. and Endo, R. (1978) Mutagenicity of aldehydes in Salmonella. <i>Mutat Res.</i> , 54(2), 251.
<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance benzaldehyde

<b>Method/guideline</b>	Ames assay
<b>Test Type</b>	Reverse mutation test
<b>System of Testing</b>	Bacterial
<b>GLP</b>	No
<b>Year</b>	1980
<b>Species/Strain</b>	<i>Salmonella typhimurium</i> TA100
<b>Metabolic Activation</b>	None
<b>Doses/Concentration</b>	Not reported
<b>Remarks for Test Conditions</b>	The test was not conducted in duplicate and was part of a larger study examining the mutagenicity of aqueous chlorination of organic compounds.
<b>Results</b>	No mutagenicity was reported.
<b>Cytotoxic concentration</b>	Not reported
<b>Genotoxic Effects</b>	None
<b>Conclusion Remarks</b>	Benzaldehyde was non-mutagenic in this assay.
<b>Data Qualities Reliabilities</b>	Reliability code 3. Not reliable.
<b>Remarks for Data Reliability</b>	Assay was not conducted in accordance with current standards (lack of duplicates) and was not well described.
<b>References</b>	Rapson W.H., Nazar, M.A. and Butsky, V.V. (1980) Mutagenicity produced by aqueous chlorination of organic compounds. J Bull of Environ Contamination and Toxicology, 24(4), 590-596.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance benzaldehyde
<b>Method/guideline</b>	<i>Bacillus subtilis</i> recessive assay
<b>Test Type</b>	Reverse mutation test
<b>System of Testing</b>	Bacterial
<b>GLP</b>	No
<b>Year</b>	1978
<b>Species/Strain</b>	<i>Bacillus subtilis</i> M45 (Rec-) and H17 (Rec+)
<b>Metabolic Activation</b>	None

<b>Doses/Concentration</b>	21 ug/disk
<b>Remarks for Test Conditions</b>	The results were considered negative if the zone of inhibition was less than 2 mm, weakly positive if greater than or equal to 2 mm, and positive if greater than or equal to 5mm.
<b>Results</b>	Benzaldehyde produced negative results.
<b>Genotoxic Effects</b>	None
<b>Conclusion Remarks</b>	Benzaldehyde was non-mutagenic in this assay.
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Code 2. Acceptable, well-documented publication/study report, which meets basic scientific principles.
<b>References</b>	Oda Y., Hamano, Y., Inoue, K., Yamamoto, H., Niihara, T. and Kunita, N. (1978) Mutagenicity of food flavours in bacteria. <i>Obaka-Furitsu Koshu Eisei Kenyu</i> , 9, 177.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance benzaldehyde
<b>Method/guideline</b>	<i>Bacillus subtilis</i> recessive assay
<b>Test Type</b>	Reverse mutation test
<b>System of Testing</b>	Bacterial
<b>GLP</b>	Not reported
<b>Year</b>	1989
<b>Species/Strain</b>	<i>Bacillus subtilis</i> M45 (arg-, trp-, recE-) and H17 (arg-, trp-, recE+)
<b>Metabolic Activation</b>	S9 mixture (not described)
<b>Doses/Concentration</b>	Not reported
<b>Remarks for Test Conditions</b>	Benzaldehyde was tested with and without metabolic activation. The data were evaluated several ways: (1) calculation of the 50% survival concentration from the benzaldehyde concentration giving 50% survival turbidity of Rec+ over benzaldehyde concentration giving 50% survival turbidity of Rec-; (2) probit analysis of the area enclosed (S-probit) between the plotted survival lines of Rec+ and Rec-; (3) mathematical calculation of "repaired survival" from a plot of mean lethal hits of Rec- against survival as the difference between Rec- and Rec+ curves; and (4) quantitative evaluation of DNA damaging potential expressed as Rec-gram=S-probit/benzaldehyde concentration giving 50% survival turbidity of Rec-.

<b>Results</b>	Without metabolic activation, benzaldehyde did not show any DNA damaging potential; however, when metabolically activated, benzaldehyde was considered to show DNA damaging potential. The authors conclusion was based only on the evaluation of the S-probit which was at the low end of the range of values considered to have DNA damaging potential. The repaired survival value calculated for benzaldehyde was well below the range considered to have DNA damaging potential.
<b>Remarks for Results</b>	The reviewer does not agree with the authors' conclusion of benzaldehyde's DNA damaging potential for several reasons: (1) the S-probit value (0.258) on which the conclusion was based just barely fell into the value range (0.200-0.592) listed in the criteria as having DNA damaging potential. Chemicals with strong DNA damaging potential had S-probit values of more than 0.593. (2) The value for "repaired survival" indicated no DNA damaging potential. (3) Chemicals tested by the authors as positive controls produced calculated values several fold higher than any calculated for benzaldehyde.
<b>Conclusion Remarks</b>	Benzaldehyde was reported to show DNA damaging potential based on one parameter examined. The weight of evidence indicates that benzaldehyde does not have DNA damaging potential.
<b>Data Qualities Reliabilities</b>	Reliability code 4. Not assignable.
<b>Remarks for Data Reliability</b>	Although the study was well documented, the methodology used was not standard and the results were open to interpretation.
<b>References</b>	Matsui S., Yamamoto, R., and Yamada, H. (1989) The <i>Bacillus subtilis</i> /microsome Rec-assay for the detection of DNA damaging substances which may occur in chlorinated and ozonated waters. Wat Sci Tech., 21, 875-887.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance benzaldehyde
<b>Method/guideline</b>	Mouse lymphoma assay
<b>Test Type</b>	Forward mutation test
<b>System of Testing</b>	Non bacterial
<b>GLP</b>	Not reported
<b>Year</b>	1991
<b>Species/Strain</b>	L5178Y mouse lymphoma cell line
<b>Metabolic Activation</b>	Rat liver microsome fraction S9
<b>Doses/Concentration</b>	Trial #1: 0, 50, 100, 200, 400 or 800 ug/ml; Trial #2: 0, 80, 160,

320, 480, or 640 ug/ml

<b>Statistical Methods</b>	The data were evaluated using the dose-trend test (Barlow et al., 1972) and a variance of analysis of pair-wise comparisons.
<b>Remarks for Test Conditions</b>	DMSO was used as the solvent and control (4 cultures). Methanesulphonate at 15 ug/ml was used as the positive control (2 cultures). Four cultures for each concentration were prepared. Colonies were counted using an automated counter. If relative growth and/or cloning efficiency did not meet the predetermined quality control criteria, then the culture was rejected.
<b>Results</b>	Benzaldehyde significantly increased mutant fractions in both experiments without S9 but at concentrations close to cytotoxic levels. The lowest-observed-effective dose (LOED) was 400 ug/ml and concentrations of 640 ug/ml were lethal.
<b>Cytotoxic concentration</b>	640 ug/ml
<b>Genotoxic Effects</b>	Increase in mutational frequency at 640 ug/ml
<b>Appropriate statistical evaluations?</b>	Yes
<b>Conclusion Remarks</b>	Benzaldehyde increased mutant fractions but only at concentrations nearing lethal levels.
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restriction.
<b>Remarks for Data Reliability</b>	NTP study guideline study
<b>References</b>	McGregor D.B., Brown, A.G., Howgate, S., McBride, D., Riach, C. and Caspary, W.J. (1991) Responses of the L5178Y mouse lymphoma cell forward mutation assay. V: 27 coded chemicals. Environ. Molec. Mutagen., 17, 196-219.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance benzaldehyde
<b>Method/guideline</b>	Mouse lymphoma assay (Clive <i>et al.</i> , 1979)
<b>Test Type</b>	Forward mutation test
<b>System of Testing</b>	Non bacterial
<b>GLP</b>	Not reported
<b>Year</b>	1989
<b>Species/Strain</b>	L5178Y mouse lymphoma cell line
<b>Metabolic Activation</b>	With and without rat liver microsome fraction S9 and cofactors
<b>Doses/Concentration</b>	12.5-800 nl /ml (with and without S9), 25-600 nl/ml (without S9), 400-600 nl/ml (with S9)

<b>Statistical Methods</b>	Not reported
<b>Remarks for Test Conditions</b>	Cells were exposed to benzaldehyde for 4 hours, washed, incubated for 48 hours and then cloned. After 10-14 days, colonies were automatically counted. The ratio of mutant to viable colonies cloned without selective medium was considered to be the mutant frequency.
<b>Results</b>	No increase in mutagenesis (as compared to the negative controls) except at 400-600 nl/ml (with S9) where a 2.8-5.2 fold increase was observed.
<b>Cytotoxic concentration</b>	Not reported
<b>Genotoxic Effects</b>	Increased mutations with S9
<b>Conclusion Remarks</b>	Although benzaldehyde produced an increase in mutagenic activity at concentrations ranging from 400-600 nl/ml (with S9), no change in mutagenic activity was reported at the other concentration ranges (12.5-800 and 25-600 nl/ml) that also cover the range reportedly showing an effect. Without further detail regarding the study design, it is difficult to interpret the significance of the positive finding.
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Assay was conducted by standard methodology, but there was limited description of the study and the results were tabulated.
<b>References</b>	Heck J.D., Vollmuth, T.A., Cifone, M.A., Jagannath, D.R., Myhr, B. and Curren, R.D. (1989) An evaluation of food flavoring ingredients in a genetic toxicity screening battery. <i>The Toxicologist</i> , 9(1), 257.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance benzaldehyde
<b>Method/guideline</b>	Sister chromatid exchange (Galloway <i>et al.</i> , 1985)
<b>Test Type</b>	Clastogenic assay
<b>System of Testing</b>	Non bacterial
<b>GLP</b>	Ambiguous
<b>Year</b>	1987
<b>Species/Strain</b>	Chinese hamster ovary cells
<b>Metabolic Activation</b>	With and without rat liver microsome fraction S9 and cofactors
<b>Doses/Concentration</b>	5-160 ug/ml (without S9); 160-1600 ug/ml (with S9)
<b>Statistical Methods</b>	Linear regression analysis was used to test trend. A 20% absolute increase over the control, at each dose, was considered to be significant.

<b>Remarks for Test Conditions</b>	Chemical treatment periods were approximately 25 hours without S9 (after 2 hours of test chemical exposure, 5-bromodeoxyuridine was added) and 2 hours with S9 (after which 5-bromodeoxyuridine was added). After treatment with hypotonic KCl, cells were fixed, stained and examined with fluorescent microscopy. 50 cells per dose were scored from the three highest concentrations when sufficient M2 cells were available, from the control groups.
<b>Results</b>	Benzaldehyde induced sister chromatid exchanges with and without metabolic activation.
<b>Cytotoxic concentration</b>	Not reported
<b>Genotoxic Effects</b>	Induction of sister chromatid exchanges
<b>Remarks for Results</b>	The induction of sister chromatid exchanges was positive without S9 and weakly positive with S9.
<b>Conclusion Remarks</b>	Benzaldehyde was an inducer of sister chromatid exchanges, but the effect was weak in the presence of metabolic activation.
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restriction.
<b>Remarks for Data Reliability</b>	Assay was conducted by standard methodology and published in a peer-reviewed journal.
<b>References</b>	Galloway S.M., Armstrong, M.J., Reuben, C., Colman, S., Brown, B., Cannon, C., Bloom, A.D., Nakamura, F., Ahmed, M., Duk, S., Rimpo, J., Margolin, B.H., Resnick, M.A., Anderson, B. and Zeiger, E. (1987) Chromosomal aberrations and sister chromatid exchanges in chinese hamster ovary cells: Evaluations of 108 chemicals. <i>Env. Molec. Mutagen.</i> , 10(10), 1-175.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance benzaldehyde
<b>Method/guideline</b>	Sister chromatid exchange (Jansson <i>et al.</i> , 1986)
<b>Test Type</b>	Clastogenic assay
<b>System of Testing</b>	Non bacterial
<b>GLP</b>	Not reported
<b>Year</b>	1988
<b>Species/Strain</b>	Human lymphocytes
<b>Metabolic Activation</b>	Phytohemagglutinin-stimulated
<b>Doses/Concentration</b>	0-2.0 mM
<b>Statistical Methods</b>	The data were analyzed using linear regression by least squares and significance was tested at p less than 0.05, 0.01,

and 0.001.

<b>Remarks for Test Conditions</b>	DMSO and ethanol were used as solvents and negative controls. The positive control used was styrene-7,8-oxide. After an exposure of 88 hours, the lymphocytes were treated with colchicine (50 ng/ml for 2 hours) and hypotonic KCl (0.075 M for 5-10 minutes). For each concentration tested (not specified), 25 metaphases from one culture were analysed.
<b>Results</b>	Statistically significant increase in sister chromatid exchanges ( $p$ less than 0.01) as compared to the vehicle control. The regression coefficient was 4.0 SCE/cell/mM.
<b>Cytotoxic concentration</b>	Not reported
<b>Genotoxic Effects</b>	Induction of sister chromatid exchanges
<b>Appropriate statistical evaluations?</b>	Significant at $p$ less than 0.01, correlation coefficient of 0.93
<b>Conclusion Remarks</b>	Benzaldehyde induced sister chromatid exchanges in this assay.
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restriction.
<b>Remarks for Data Reliability</b>	Assay was conducted by standard methodology and published in a peer-reviewed journal.
<b>References</b>	Jansson T., Curvall. M., Hedin, A. and Enzell, C. (1988) In vitro studies of the biological effects of cigarette smoke condensate. III. Induction of SCE by some phenolic and related constituents derived from cigarette smoke. <i>Mutat Res.</i> , 206, 17-24.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance benzaldehyde
<b>Method/guideline</b>	Sister chromatid exchange
<b>Test Type</b>	Clastogenic assay
<b>System of Testing</b>	Non bacterial
<b>Year</b>	1989
<b>Species/Strain</b>	Chinese hamster K-1 ovary cells (ATCC)
<b>Metabolic Activation</b>	Mitomycin C (induction of SCEs)
<b>Doses/Concentration</b>	0, 3.3, 10, 33.3, 100, 333, or 1000 uM
<b>Statistical Methods</b>	Student's t-test
<b>Remarks for Test Conditions</b>	Chinese hamster ovary cells were exposed to mitomycin C for 21 hours and then cells were exposed to benzaldehyde for 1 cell cycle followed by addition of 5-bromodeoxyuridine 2 cell cycles prior to fixation. Fifty metaphases per culture were analyzed for sister chromatid exchanges with and without

treatment with mitomycin C for SCE induction.

<b>Results</b>	Benzaldehyde did not induce sister chromatid exchanges at concentrations up to 333 uM. The highest concentration was reported to be cytotoxic.
<b>Cytotoxic concentration</b>	1000 uM
<b>Genotoxic Effects</b>	None
<b>Conclusion Remarks</b>	Benzaldehyde produce any evidence of an increase in sister chromatid exchanges in this assay.
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Published in peer review journal but limited description of protocol and tabulated results.
<b>References</b>	Sasaki Y.F., Imanishi, H., Ohta, T. and Shirasu, Y. (1989) Modifying effects of components of plant essence on the induction of sister-chromatid exchanges in cultured Chinese hamster ovary cells. <i>Mutat. Res.</i> , 226, 103-110.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance benzaldehyde
<b>Method/guideline</b>	Chromosomal aberrations
<b>Test Type</b>	Clastogenic assay
<b>System of Testing</b>	Non-bacterial
<b>GLP</b>	Not reported
<b>Year</b>	1982
<b>Species/Strain</b>	Chinese hamster ovary cells
<b>Metabolic Activation</b>	Rat liver microsome fraction S9
<b>Doses/Concentration</b>	50 nM
<b>Statistical Methods</b>	Chi square test
<b>Remarks for Test Conditions</b>	DMSO was used as the solvent and control. Cells were exposed to the flavoring agent for 24 hours and then incubated another 24 hours without the flavor after which the cells were treated with colchicine for 2-3 hours. Cells were stained using Giemsa staining method. The scoring of about 200 metaphase spreads, containing 20-26 chromosomes was used to calculate the percentage of chromosomal aberrations.
<b>Results</b>	Benzaldehyde produced a significant difference in chromosomal aberrations compared to the vehicle control (p less than 0.001).

<b>Cytotoxic concentration</b>	Not reported
<b>Genotoxic Effects</b>	Induction of chromosomal aberrations
<b>Appropriate statistical evaluations?</b>	p less than 0.001
<b>Conclusion Remarks</b>	Benzaldehyde induced an increase in chromosomal aberrations in Chinese hamster ovary cells.
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Assay was conducted by standard methodology and published in a peer-reviewed journal. Tabulated results.
<b>References</b>	Kasamaki A., Takahashi, H., Tsumura, N., Niwa, J., Fujita, T. and Urasawa, S. (1982) Genotoxicity of flavoring agents. <i>Mutat. Res.</i> , 105, 387-392.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance benzaldehyde
<b>Method/guideline</b>	Chromosomal aberrations (Galloway <i>et al.</i> , 1985)
<b>Test Type</b>	Clastogenic assay
<b>System of Testing</b>	Chinese hamster ovary cells
<b>GLP</b>	Not reported
<b>Year</b>	1987
<b>Species/Strain</b>	Chinese hamster ovary cells
<b>Metabolic Activation</b>	With and without rat liver microsome fraction S9 and cofactors
<b>Doses/Concentration</b>	50-500 ug/ml (without S9); 160-1600 ug/ml (with S9)
<b>Statistical Methods</b>	Linear regression analysis, binomial sampling assumption, and Dunnett's method for multiple dose comparison were used to evaluate the data.
<b>Remarks for Test Conditions</b>	Positive controls consisted of treatment with mitomycin C, triethylenemelamine, or cyclophosphamide and negative controls were solvents used to dissolve the test chemical. Tests were carried out with (2-hr test substance exposure) or without S9 (exposure throughout incubation) activation (male Sprague-Dawley rat hepatocytes induced with Aroclor 1254). Cells were harvested 8-12 hours after the beginning of the treatment, yielding cells in mitosis. 100 cells were scored from each of the three highest dose groups having sufficient metaphases for analysis and from positive and solvent controls. All types of aberrations were recorded and they were grouped as either "simple", "complex", or "other" and "total".
<b>Results</b>	No aberration induction was observed.

<b>Cytotoxic concentration</b>	Not reported
<b>Genotoxic Effects</b>	None
<b>Remarks for Results</b>	Benzaldehyde was negative for chromosomal aberration induction.
<b>Conclusion Remarks</b>	Benzaldehyde did not induce chromosomal aberrations in this assay.
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restriction.
<b>Remarks for Data Reliability</b>	Assay was conducted by standard methodology and published in a peer reviewed journal.
<b>References</b>	Galloway S.M., Armstrong, M.J., Reuben, C., Colman, S., Brown, B., Cannon, C., Bloom, A.D., Nakamura, F., Ahmed, M., Duk, S., Rimpo, J., Margolin, B.H., Resnick, M.A., Anderson, B. and Zeiger, E. (1987) Chromosomal aberrations and sister chromatid exchanges in chinese hamster ovary cells: Evaluations of 108 chemicals. <i>Env. Molec. Mutagen.</i> , 10(10), 1-175.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance benzaldehyde
<b>Method/guideline</b>	Chromosomal aberrations
<b>Test Type</b>	Clastogenic assay
<b>System of Testing</b>	Non bacterial
<b>GLP</b>	No
<b>Year</b>	1985
<b>Species/Strain</b>	Chinese hamster cells
<b>Metabolic Activation</b>	S9 mixture (not described)
<b>Doses/Concentration</b>	0, 0.8, or 1.0 mg/ml without S9; 0, 0.8, 1.0, 1.2 mg/ml with S9
<b>Remarks for Test Conditions</b>	The solvent used was DMSO and the tests were conducted with and without S9. The percent of polyploid cells was reported, as was the frequency of aberrant cells.
<b>Results</b>	At 0, 0.8 and 1.0 mg/ml without S9, the percent polyploid was 0, 11 and 3 and the frequency of total aberrant cells was 2, 2, and 24%, respectively. At 0, 0.8, 1.0, and 1.2 mg/ml with S9, the percent polyploid was 0, 11, 5, and 0 and the frequency of total aberrant cells was 0, 2, 9, and 9%, respectively.
<b>Genotoxic Effects</b>	Induction of chromosomal aberrations without S9
<b>Conclusion Remarks</b>	Benzaldehyde was judged by the authors to be positive only without metabolic activation at the highest dose tested.

<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Although the data were presented in Japanese with English summary tables, the data were generated by a reputable group of researchers and it appeared that standard procedures were followed. The data were considered reliable.
<b>References</b>	Sofuni T., Hayashi, M., Matsuoka, A., Sawada, M., Hatanaka, M. and Ishidate, M. (Jr.). (1985) Mutagenicity tests on organic chemical contaminants in city water and related compounds. II. Chromosome aberration tests in cultured mammalian cells. Bull Nat Inst Hyg Sci, 103, 64.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance benzaldehyde
<b>Method/guideline</b>	Unscheduled DNA synthesis (Williams, 1977, 1980 and Butterworth <i>et al.</i> , 1987)
<b>Test Type</b>	DNA damage
<b>System of Testing</b>	Rat hepatocyte
<b>GLP</b>	Not reported
<b>Year</b>	1989
<b>Species/Strain</b>	Rat/Fischer and Sprague-Dawley
<b>Doses/Concentration</b>	251 ug/ml
<b>Statistical Methods</b>	Not reported
<b>Remarks for Test Conditions</b>	Rat hepatocytes were incubated in culture dishes for 18-20 hours with benzaldehyde. Concurrent cell counting or measurement of LDH release was used to determine relative cell survival. UDS was measured by electronically counting nuclear grains and calculating the net nuclear grain count (NNG). At each test concentration, 75-150 cells were analyzed. An increase in NNG of "at least 6 grains per nucleus above the concurrent solvent control value and/or an increase in the percent of nuclei having 6 or more net grains to at least 10% above the concurrent negative control" was considered a positive UDS response.
<b>Results</b>	Benzaldehyde treatment did not increase UDS compared to controls.
<b>Cytotoxic concentration</b>	Not reported
<b>Genotoxic Effects</b>	None
<b>Conclusion Remarks</b>	Benzaldehyde was not genotoxic in this assay.
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.

<b>Remarks for Data Reliability</b>	Assay was conducted by standard methodology, but there was limited description of the study and the results were tabulated.
<b>References</b>	Heck J.D., Vollmuth, T.A., Cifone, M.A., Jagannath, D.R., Myhr, B. and Curren, R.D. (1989) An evaluation of food flavoring ingredients in a genetic toxicity screening battery. <i>The Toxicologist</i> , 9(1), 257.

#### 4.2.2 *In vivo* Genotoxicity

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Test Substance</b>	Data are for structurally related substance terephthalate acid
<b>Method/guideline</b>	OECD Guideline 474
<b>Test Type</b>	Mammalian Erythrocyte Micronucleus assay
<b>Year</b>	2001
<b>Species/Strain</b>	Mouse/ICR
<b>Sex</b>	Male and Female
<b>Route of Administration</b>	Intraperitoneal
<b>Doses/Concentration</b>	200, 400, and 800 mg/kg
<b>Exposure Period</b>	24 and 48 hours
<b>Remarks for Test Conditions</b>	Animals were about 6-8 weeks of age at study initiation. Animals (5/sex/group) were dosed ip with vehicle (negative control), 200, 400 or 800 mg/kg TPA, or 50 mg/kg cyclophosphamide (positive control) in corn oil in a volume of 20 ml/kg body weight and were sacrificed at 24 hours. Additional animals (5/sex/group) were treated with vehicle or 800 mg/kg TPA and sacrificed at 48 hours. An additional group of 5 males and 5 females were dosed with 800 mg/kg TPA as a replacement group in case of mortality. Bone marrow samples from animals sacrificed at 24 and 48 hours were scored under oil immersion (2000 polychromatic erythrocytes (PCE) per animal) for the presence of micronuclei. The number of micronucleated normocytes per 2000 PCE was also assessed. The proportion of PCE to total erythrocytes was also recorded on a per 1000 erythrocyte basis. Statistical significance for the

<b>Remarks for Results</b>	<p>incidence of micronucleated polychromatic erythrocytes was determined using Kastenbaum-Bowman Tables.</p> <p>Mortality was observed in 1/15 male mice that had been treated with 800 mg/kg TPA. One mouse from the replacement group was used in place of the animal that died. Clinical signs following treatment with either dose of TPA included lethargy and piloerection. Negative and positive control animals appeared normal during the course of the study.</p> <p>The total number of micronuclei observed per 20000 PCE in animals treated with vehicle, 200, 400 or 800 mg/kg for 24 hours was 4, 8, 5, and 4, respectively. The incidence of micronuclei in animals treated with 800 mg/kg also did not differ from the vehicle control at 48 hours (2/20000 vs. 8/20000, respectively). There was no difference between males and females. TPA was negative in the test.</p> <p>The test was valid, as the incidence of micronuclei in the vehicle control was not greater than 5/1000 PCE and the number of micronucleated cells in the positive controls (382/20000) was significantly different (p less than 0.05) from the vehicle control. Reductions (up to 9%) in the ratio of polychromatic erythrocytes to total erythrocytes were observed in some of the treated groups relative to the vehicle control, suggesting that the test article did not inhibit erythropoiesis. Greater reductions in this ratio were observed in animals treated with cyclophosphamide (25-29%).</p>
<b>Conclusion Remarks</b>	<p>Criteria for a valid test: The mean incidence of micronucleated polychromatic erythrocytes must not exceed 5/1000 polychromatic erythrocytes (0.5%) in the negative control vehicle. The incidence rate in the positive control group must be significantly increased relative to the negative control (p less than 0.05, Kastenbaum-Bowman Tables).</p>
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restriction.
<b>Remarks for Data Reliability</b>	Code 1. Comparable to guideline study.
<b>References</b>	<p>Bioreliance</p> <p>(2001) Mammalian erythrocyte micronucleus test. Study No. AA41MJ.123.BTL for BP Amoco.</p>

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Test Substance</b>	Data are for structurally related substance dimethyl terephthalate
<b>Test Type</b>	Chromosomal aberration (micronucleus assay)
<b>Year</b>	1993
<b>Species/Strain</b>	Mouse/B6C3F1
<b>Sex</b>	Male and Female

<b>Route of Administration</b>	Intraperitoneal
<b>Doses/Concentration</b>	438 to 1,750 mg/kg
<b>Exposure period</b>	3 days
<b>Remarks for Test Conditions</b>	Mice (5-7) were exposed by ip injection to DMT (in a corn oil vehicle) over 3 consecutive days. The dose level used was the highest practical given the solubility problems with the test material. Animals were euthanized with CO2 24-hours after their last exposure. Bone marrow smears (2 per mouse) were prepared and fixed with absolute methanol and stained with acridine orange. Each slide was evaluated for the number of micronuclei in polychromatic erythrocytes among 2,000 polychromatic erythrocytes and percentage of polychromatic erythrocytes among 200 erythrocytes.
<b>Effect on mitotic index or PCE/NCE ratio by dose level and sex</b>	Control= 65% and 1,750mg/kg = 72%
<b>Genotoxic effects</b>	None
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restriction.
<b>Remarks for Data Reliability</b>	Code 2. Basic data given: comparable to guidelines/standards.
<b>References</b>	Shelby, M.D., Erexson, G.L., Hook, G.J. and Tice R.R. (1993) Evaluation of a Three-Exposure Mouse Bone Marrow Micronucleus Protocol: Results with 49 Chemicals. Environmental and Molecular Mutagenesis, 21:160-179.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance dimethyl terephthalate
<b>Test Type</b>	Chromosomal aberration (micronucleus assay)
<b>Year</b>	1988
<b>Species/Strain</b>	Mouse/(C57Bl/6j x CBA)F1
<b>Sex</b>	Male and Female
<b>Route of Administration</b>	Intraperitoneal
<b>Doses/Concentration</b>	0.20 to 1.00 mmole/kg
<b>Exposure Period</b>	1 day
<b>Remarks for Test Conditions</b>	A single 0.2 ml solution of DMT (dissolved in a DMSO vehicle) was injected intraperitoneally. The highest dose level used was limited due to the toxicity of the vehicle. Fifteen mice per exposure group were used, although lethality occurred in some animals, thereby reducing the sample sizes. Negative control groups (distilled water, or 0.2 ml DMSO) and a positive control

group (methylnitrosourea) were included. Mice were killed by cervical dislocation at 24, 48 and 72-hours post-treatment. Slides were prepared according to the method of Schmid (1976), dried at room temperature, and stained with May-Gruenwald and Giemsa stains. Polychromatic erythrocytes (1,000/mouse) were scored for the presence of micronuclei. After identifying 200 erythrocytes, the ratio of polychromatic erythrocytes to normochromatic erythrocytes was determined.

Control= 41%, DMSO = 43% and 1 mmol/kg= 37%

**Effect on mitotic index or PCE/NCE ratio by dose level and sex**

**Remarks for results**

The results of this study are particularly difficult to interpret. The data is not presented on a per mouse basis, but instead all of the data from the animals are lumped together as a group. Therefore, there is no mean and standard deviation for each group value. The distilled water negative control group (n=24) had a reported micronuclei frequency of 1.5%, although the time after treatment when this was determined was not reported. The use of DMSO as a solvent caused mortality in 21 of 270 mice after receiving either DMSO or DMSO and test material. The remaining live animals within each group were randomly selected to evaluate the micronucleus endpoint. The frequency of micronuclei in the DMSO negative control group decreases from 2.5% at 24-hours to 1.17% at 48-hours and further to 0.83% at 72-hours. The percentage of polychromatic erythrocytes in the DMSO solvent control group was significantly increased over the distilled water control group at 24-hours. Clearly the toxicity of DMSO was affecting the number of polychromatic erythrocytes and micronuclei in the DMSO solvent control group. All dose levels of DMT tested increased the frequency of micronuclei, although these findings were primarily restricted to the 24-hour observation point, coincidentally the time of greatest increase in micronuclei frequency due to the DMSO vehicle. The increased frequency of micronuclei at 48-hours were limited to the 3 highest dose levels tested and at 72-hours, the two highest dose levels tested. The highest dose was also considered to have caused bone marrow suppression. The pattern of the time course for micronuclei formation in the treated groups mimicked that observed for the DMSO vehicle control, suggesting an interaction between the two chemicals (DMSO and DMT) may have occurred. Therefore, poor study design and reporting along with solvent toxicity makes interpretation of this study problematic. The dose levels tested were much lower than those used in other mouse micronuclei studies with a corn oil vehicle (3 injections over 3-days; above) and the increased frequency of micronuclei due to DMT treatment is in contrast to the other negative mutagenicity and clastogenicity findings for this material.

**Data Qualities Reliabilities**

Reliability code 2. Reliable with restriction.

**Remarks for Data Reliability**

Code 2. Basic data given: comparable to guidelines/standards.

**References**

Goncharova, R.I., Zabrejko, S., Kozachenko, V.I. and Pashin, Y.V. (1988) Mutagenic Effects of Dimethyl Terephthalate on

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Test Substance</b>	Data are for structurally related substance benzaldehyde
<b>Method/guideline</b>	Sex-linked recessive lethal (SLRL) assay
<b>Test Type</b>	Lethal mutation test
<b>GLP</b>	Not reported
<b>Year</b>	1985
<b>Species/Strain</b>	Drosophila melanogaster
<b>Sex</b>	Male
<b>Route of Administration</b>	Feed
<b>Doses/Concentration</b>	1,150 ppm
<b>Exposure Period</b>	3 days
<b>Remarks for Test Conditions</b>	Glass fiber discs, saturated with the test compound carried a 5% sucrose solution were used to expose day-old males (Canton-S) for 3 days in glass shell vials. Males were mated immediately after treatment with 3 new females for each of 3 broods. If no wild-type males were identified among 20 or more Basc males or Basc1 +/- females, then it was considered a lethal mutation. If a few F2 or F3 wild-type males survived at less than 5% of Basc males or Basc1 +/- females then it was considered a lethal mutation.
<b>Genotoxic effects</b>	None
<b>Appropriate statistical evaluations</b>	Yes. Cluster analysis by Poisson distribution; normal test of lethal frequencies after clusters removed.
<b>Conclusion Remarks</b>	No induction of SLRL in Drosophila melanogaster.
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restriction.
<b>Remarks for Data Reliability</b>	Code 1. Comparable to guideline study.
<b>References</b>	Woodruff R.C., Mason, J.M., Valencia, R. and Zimmering, S. (1985) Chemical mutagenesis testing in Drosophila. V. Results of 53 coded compounds for the national testing program. Environ Mutagen., 7, 677-702.
<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0

<b>Remarks for Test Substance</b>	Data are for structurally related substance benzaldehyde
<b>Method/guideline</b>	Sex-linked recessive lethal (SLRL) assay
<b>Test Type</b>	Lethal mutation test
<b>GLP</b>	Not reported
<b>Year</b>	1985
<b>Species/Strain</b>	Drosophila melanogaster
<b>Sex</b>	Male
<b>Route of Administration</b>	Injection
<b>Doses/Concentration</b>	2,500 ppm
<b>Exposure Period</b>	Single dose
<b>Remarks for Test Conditions</b>	Males (Canton-S) aged 2-3 days were intraperitoneally injected with a 0.7% NaCl solution containing benzaldehyde. At 24-48 hours post injection males were mated with 3 new females for each of 3 broods. If no wild-type males were identified among 20 or more Basc males or Basc1 +/- females, then it was considered a lethal mutation. If a few F2 or F3 wild-type males survived at <5% of Basc males or Basc1 +/- females then it was considered a lethal mutation.
<b>Genotoxic effects</b>	None
<b>Appropriate statistical evaluations</b>	Yes. Cluster analysis by Poisson distribution; normal test of lethal frequencies after clusters removed.
<b>Conclusion Remarks</b>	No induction of SLRL in Drosophila melanogaster.
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restriction.
<b>Remarks for Data Reliability</b>	Code 1. Comparable to guideline study.
<b>References</b>	Woodruff R.C., Mason, J.M., Valencia, R. and Zimmering, S. (1985) Chemical mutagenesis testing in Drosophila. V. Results of 53 coded compounds for the national testing program. Environ Mutagen., 7, 677-702.

### 4.3 Repeated Dose Toxicity

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Method/guideline</b>	90-Day dietary study
<b>GLP</b>	No
<b>Year</b>	1972
<b>Species/strain</b>	Rat/Wistar
<b>Sex</b>	Male and Female
<b>Route of Administration</b>	Diet
<b>Doses/concentration Levels</b>	3% (30,000 ppm) in diet
<b>Exposure Period</b>	90 days
<b>Frequency of Treatment</b>	Daily
<b>Control Group</b>	Basal diet
<b>Post exposure observation period</b>	No
<b>Remarks for Test Conditions</b>	Animals were fed 5% terephthalic acid in the diet for 1 week, which was then reduced to 3% for the remainder of the study.
<b>Toxic Response/effects by Dose Level</b>	Formation of bladder stones and hyperplasia of the bladder urothelium
<b>Remarks for Results</b>	Pathological effects were limited to the kidney and bladder. Terephthalic acid induced bladder stones in 11/18 males and 3/19 females. Mild to moderate hyperplasia of the bladder urothelium was diagnosed in 13/18 males and 3/19 females. A strong correlation was found between the presence of uroliths and the development of bladder hyperplasia: 62% of the TPA males (8/13) and 100% of the TPA females (3/3) diagnosed as having transitional cell hyperplasia also had bladder stones. It is possible that microscopic calculi were passed or were lost during sectioning of bladder tissue for histopathology. This could explain the failure to detect uroliths in all of the hyperplastic bladders.
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Comparable to guideline study with acceptable restrictions.
<b>References</b>	Amoco Corporation (1972) Subacute Feeding Studies (13 Week) In Rats with Dimethylterephthalate (DMT), Isophthalic Acid (IA) and Terephthalic Acid (TA). Conducted by Food and Drug Research Laboratories. FDRL Study #0411.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Test Substance</b>	Data are for terephthalic acid, a structural analog.
<b>Method/guideline</b>	28-Day inhalation study
<b>GLP</b>	No
<b>Year</b>	1973
<b>Species/strain</b>	Rat
<b>Sex</b>	Male and Female
<b>Route of Administration</b>	Inhalation
<b>Doses/concentration Levels</b>	0, 0.52, 1.2, 3.3 mg/m <sup>3</sup>
<b>Exposure Period</b>	28 days
<b>Frequency of Treatment</b>	6 hours per day for 4 weeks
<b>Post exposure observation period</b>	3 days
<b>Toxic Response/effects by Dose Level</b>	Minimal irritation and degeneration of tracheal epithelium at 3.3 mg/m <sup>3</sup>
<b>Remarks for Results</b>	No deaths occurred in the study. No differences were observed in clinical chemistry, hematology, body or organ weight changes. Histopathological findings consisted of minimal tracheal epithelial lining degeneration observed in 19/20 high-exposure rats, compared to 1/20 in control rats. There were no differences in any measured physiological parameters between control and high-exposure groups. In follow-up work, the incidence of minimal degeneration changes in the epithelial lining of the trachea was 5%, 30%, 65%, and 95% at exposures of 0, 0.52, 1.2, and 3.3 mg/m <sup>3</sup> , respectively.
<b>Conclusion Remarks</b>	Except for tracheal irritation from particulate terephthalic acid, no other effects were observed.
<b>Data Qualities Reliabilities</b>	Reliability code 3. Not reliable.
<b>Remarks for Data Reliability</b>	Methodology was unconventional and there was only use of 1 dose. No statistical analyses were conducted and results were not clearly described.
<b>References</b>	Amoco Corporation (1973) 4-Week Inhalation Toxicity Study of Terephthalic Acid (TA) In Rats. Conducted by IIT Research Institute. IITRI Study #1104.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0

<b>Remarks for Test Substance</b>	Data are for in vivo metabolite terephthalic acid
<b>Method/guideline</b>	Carcinogenicity
<b>GLP</b>	No
<b>Year</b>	1974
<b>Species/strain</b>	Rat/Wistar
<b>Sex</b>	Male and Female
<b>Route of Administration</b>	Diet
<b>Doses/concentration Levels</b>	1% (500 mg/kg/day) & 2% (1000 mg), 5% (2500 mg)
<b>Exposure Period</b>	2 years
<b>Frequency of Treatment</b>	Daily
<b>Control Group</b>	Basal diet
<b>Post exposure observation period</b>	No
<b>NOAEL(NOEL)</b>	There was no statistically significant increase in bladder tumors at 500 mg/kg bw/day
<b>LOAEL(LOEL)</b>	1000 mg/kg bw/day
<b>Toxic Response/effects by Dose Level</b>	Significant increase in bladder tumors at 5%
<b>Remarks for Results</b>	Reduced body weight gain occurred at in the 5% dose level (males and females) and in the 2% dose level (males). At 1%, reduced relative liver weight in females and reduced relative kidney size in males and females. At 2%, reduced liver, kidney, and heart weights (females only). At 5%, there was increased kidney weight in males, and increased adrenal weights in males and females; as well as increased mortality, mainly as a result of increased incidence of bladder stones (at 5%: males, 42/47; females, 39/42; at 1%: females, 1/48). There was increased incidence of bladder and ureter tumors (at 5%: males, 21/37; females, 21/34; at 2%: males, 1/48; females, 2/48; at 1%: males, 1/43.). There was increased incidence of bladder and ureter tumors.
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Comparable to guideline study with acceptable restrictions.
<b>References</b>	Gross J. (1974) The effects of prolonged feeding of terephthalic acid (TPA) to rats. Project FG-IS-175. Submitted to US Dept. of Agriculture, Agriculture Research Service, Washington D.C.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0

<b>Remarks for Test Substance</b>	Data are for in vivo metabolite terephthalic acid
<b>Method/guideline</b>	15-Week dietary study
<b>GLP</b>	No
<b>Year</b>	1970
<b>Species/strain</b>	Rat/albino
<b>Sex</b>	Male and Female
<b>Route of Administration</b>	Diet
<b>Doses/concentration Levels</b>	0.05, 0.16, 0.50, 1.6, and 5.0% in the diet
<b>Exposure Period</b>	15 weeks
<b>Frequency of Treatment</b>	Daily in the diet
<b>Control Group</b>	Basal diet
<b>Post exposure observation period</b>	None
<b>Remarks for Test Conditions</b>	Animals (66-79 gram range) were divided into 7 groups of 60 each (30/sex) that corresponded to 2 control groups and 5 test groups (0.05, 0.16, 0.50, 1.6 and 5.0% test material in diet). Food and water were supplied ad libitum. Parameters assessed included: survival, clinical observations, growth, food consumption, hematology, serum clinical chemistries, urinalysis, gross pathology, and weights and histology of a full range of organs. Sacrifices were completed on 6 rats (3/sex) on Days 30, 60, and 90. All remaining animals were terminated on Day 105. Data were analyzed using analysis of variance and Duncan multiple range tests.
<b>NOAEL(NOEL)</b>	1.6% (approximately 1220 mg/kg in males and 1456 mg/kg in females)
<b>LOAEL(LOEL)</b>	5.0% (approximately 3837 mg/kg in males and 4523 mg/kg in females)
<b>Toxic Response/effects by Dose Level</b>	<p>Survival: 4 animals (one male at 0.5% (Day 56) and three females in the highest dose (Days 54, 87, and 90) died of unknown etiology.</p> <p>Clinical signs: Hematuria was noted on a sporadic basis in the latter two thirds of the study in males treated with 5.0%.</p> <p>Growth: Body weights from both sexes treated with 5.0% were mildly depressed.</p> <p>Food Intake: No effects were noted.</p> <p>Hematology: No effects were noted.</p> <p>Clinical Chemistry: No effects were noted.</p> <p>Urinalysis: The only noteworthy finding was evidence of occult blood. Positive values were sporadically observed in males of all dose groups (except the lowest level) and in females at all treatment levels (number of animals affected was not listed).</p>

Occult blood was noted primarily at the 3 month examination time point except in the high dose animals of both sexes which showed evidence at 30, 60, and 90 days. It was usually noted as small.

Gross Pathology: Findings of interest were limited to the urinary bladder. Calculi were noted in males treated with 5% (3/3 at 30 days, 2/3 at 60 days, 2/3 at 90 days, and 9/17 at 105 days).

Organ Weights: No differences were noted that were deemed attributable to exposure to test material.

Microscopic Pathology: Proliferative changes (hyperplasia) were noted in the urinary bladder and occasionally the kidney pelvis epithelium of all test groups and controls. These changes were significantly increased in both their incidence and severity in high dose (5%) males. This observation was deemed inconclusive in high dose females.

**Appropriate statistical evaluations?**

Duncan multiple range test

**Remarks for Results**

The hyperplastic change noted in the bladder is believed to be secondary to the chronic irritation induced by the presence of calculi. The bladder calculi and subsequent inflammation and hyperplasia seem to be threshold effects in that only animals in the high dose group (5%) displayed this pattern of pathology.

**Conclusion Remarks**

The NOAEL listed is for the critical effect (bladder calculi and subsequent hyperplasia). Doses of 0.05%, 0.16%, 0.5%, 1.6% and 5% corresponded to approximately 37.9, 122, 393, 1220 and 3837 mg/kg in males and 46, 147, 447, 1456 and 4523 mg/kg in females, respectively (based on average body weight and food intake).

**Data Qualities Reliabilities**

Reliability code 2. Reliable with restriction.

**Remarks for Data Reliability**

Code 2. Comparable to guideline study with acceptable restrictions.

**References**

Amoco Corporation (1970) Fifteen Week Oral Toxicity of Terephthalic Acid – Albino Rats. Conducted by Toxicological Evaluations. LSL Study#1358.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Test Substance</b>	Data are for in vivo metabolite terephthalic acid
<b>GLP</b>	No
<b>Year</b>	1981
<b>Species/strain</b>	Rat
<b>Sex</b>	Male and Female
<b>Route of Administration</b>	Diet

<b>Doses/concentration Levels</b>	0.5, 1.5, 3.0, 4.0, or 5.0%
<b>Exposure Period</b>	14 days
<b>Frequency of Treatment</b>	Daily
<b>Control Group</b>	Basal diet
<b>Post exposure observation period</b>	No
<b>Remarks for Test Conditions</b>	Rats (13-18/sex/dose group) were fed DMT diets for a period of two-weeks. Individual body weights and total feed and water intake per cage were collected. At necropsy, urine was collected directly from the bladder for pH measurement, and concentrations of "stone-forming" materials were determined. The urinary system was examined grossly for presence of macroscopic calculi. Any calculi were collected, dried, weighed and analyzed. This study also evaluated terephthalic acid (TPA) at similar dietary levels
<b>NOAEL(NOEL)</b>	3% in the diet
<b>LOAEL(LOEL)</b>	5% in diet
<b>Toxic Response/effects by Dose Level</b>	Formation of urinary bladder calculi at 5% dietary levels
<b>Remarks for Results</b>	Exposure resulted in a 93.3% incidence of bladder calculi in male pups receiving 5% dietary terephthalic acid (TPA). Female pups also developed stones, but at a lower frequency. The dose-response curves for stone induction were extremely steep: no stones were induced at dietary concentrations below 1.5%. Histological examination of the urinary tract revealed extensive hyperplasia of the transitional epithelium only in the urinary bladders that contained calculi. Analysis of calculi indicated a heterogeneous chemical composition. The principal components (by weight) were: TPA, calcium, phosphate, and protein in the TPA-induced stones. Concentrations of calcium, TPA, and phosphate, as well as pH, were determined in the urine of weanling rats at study termination. TPA induced urinary acidosis and hypercalciuria in the range of doses used. Results indicate that critical saturating urinary concentrations of TPA and calcium are necessary for stones to develop following TPA exposure, and that calculus formation appears to be a prerequisite for the induction of TPA-induced bladder hyperplasia.
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Comparable to guideline study with acceptable restrictions.
<b>References</b>	Chin T.Y., Tyl, R.W., Popp, J.A. and Heck, H. d'A. (1981) "Chemical Urolithiasis: 1. Characteristics of Bladder Stone Induction by Terephthalic Acid and Dimethyl Terephthalate in Weanling Fischer-344 Rats." Tox. and Appl. Pharm. 58:307-321.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Test Substance</b>	Data are for in vivo metabolite terephthalic acid
<b>GLP</b>	No
<b>Year</b>	1967
<b>Species/strain</b>	Rat/White
<b>Sex</b>	Male and Female
<b>Route of Administration</b>	Gavage
<b>Doses/concentration Levels</b>	10/rat on alternate days (approximately 20 mg/kg bw/d)
<b>Exposure Period</b>	12 weeks
<b>Frequency of Treatment</b>	Alternate days
<b>Control Group</b>	Not described
<b>Post exposure observation period</b>	None
<b>Remarks for Test Conditions</b>	Benzaldehyde was administered orally to adult white rats at doses of 10 mg diluted in 0.1 ml of oil on alternate days for a period of 12 weeks. 32 rats were divided into 4 groups, 2 of which were administered benzaldehyde in 2 different diet blends (18 or 8% casein). The other 2 groups were not described.
<b>Actual dose received by dose level and sex</b>	Approximately 20 mg/kg bw/d
<b>Toxic Response/effects by Dose Level</b>	There were no effects on growth, liver or adrenal gland weight.
<b>Data Qualities Reliabilities</b>	Reliability code 4. Not assignable.
<b>Remarks for Data Reliability</b>	Study translated from foreign article with very limited description.
<b>References</b>	Sporn A., Dinu, I., and Stanclu, V. (1967) Cercetari cu privire la toxicitatea aldehidei benzoice. [Research regarding the toxicity of benzaldehyde.] Igiene, 16(1), 23.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Test Substance</b>	Data are for in vivo metabolite terephthalic acid
<b>Method/guideline</b>	Carcinogenicity study
<b>GLP</b>	No

<b>Year</b>	1983
<b>Species/strain</b>	Rat/Wistar
<b>Sex</b>	Male and Female
<b>Route of Administration</b>	Diet
<b>Doses/concentration Levels</b>	20, 142, 1000 mg/kg/day
<b>Exposure Period</b>	2 years
<b>Frequency of Treatment</b>	Daily
<b>Control Group</b>	Basal diet
<b>NOAEL(NOEL)</b>	142 mg/kg bw/day
<b>LOAEL(LOEL)</b>	1000 mg/kg bw/day
<b>Toxic Response/effects by Dose Level</b>	Induction of bladder stones in high dose females
<b>Remarks for Results</b>	Terephthalic acid induced bladder stones were seen in 13/126 females in the high dose group. At the scheduled 6 and 12-month sacrifices, no bladder calculi were detected. At the 18-month sacrifice sand like particle or bladder calculi were only seen in two of the high dose females. The high-dose corresponds to an approximate dietary concentration of 2.0 to 2.8% in adult F-344 rats.
<b>Conclusion Remarks</b>	A NOAEL was established as 142 mg/kg bw/day for female rats and 1000 mg/kg bw/day for male rats
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Comparable to guideline study with acceptable restrictions.
<b>References</b>	Chemical Industry Institute of Technology (CIIT) (1983) Chronic Dietary Administration Of Terephthalic Acid. CIIT Docket 20124

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Test Substance</b>	Data are for in vivo metabolite terephthalic acid
<b>Method/guideline</b>	3-month gavage study
<b>GLP</b>	Not reported
<b>Year</b>	1970
<b>Species/strain</b>	Mouse/White
<b>Sex</b>	Male and Female
<b>Route of Administration</b>	Gavage

<b>Doses/concentration Levels</b>	80 mg/kg bw/d
<b>Exposure Period</b>	3 months
<b>Frequency of Treatment</b>	Daily
<b>Control Group</b>	Not reported
<b>Post exposure observation period</b>	Not reported
<b>Remarks for Test Conditions</b>	Groups of 50 male and 50 female crossbred white mice (strain not specified) were administered 80 mg benzoic acid/kg bw/d by oral intubation for 3 months.
<b>Toxic Response/effects by Dose Level</b>	Weight gain of the treated animals was reduced compared to control animals.
<b>Remarks for Results</b>	The reduced body weight gain was reported not to be due to reduced feed intake, but it may have been due to stress factors such as food restriction, low temperature, swimming test, centrifugation, carbon tetrachloride detoxication test or kidney function testing.
<b>Data Qualities Reliabilities</b>	Reliability code 4. Not assignable.
<b>Remarks for Data Reliability</b>	Very limited description of study and results.
<b>References</b>	Shtenberg A.J. and Ignat'ev A.D. (1970) Toxicological evaluation of some combinations of food preservatives. Food and Cosmetics Toxicology, 8, 369-380.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Test Substance</b>	Data are for dimethyl terephthalate
<b>GLP</b>	No
<b>Year</b>	1981
<b>Species/strain</b>	Rat
<b>Sex</b>	Male and Female
<b>Route of Administration</b>	Diet
<b>Doses/concentration Levels</b>	0, 0.5, 1.0, 1.5, 2, or 3% (females: 638, 1277, 1790, 2290, and 3020 mg/kg; males: 660, 1320, 1890, 2260, and 2590 mg/kg)
<b>Exposure Period</b>	14 days
<b>Frequency of Treatment</b>	Daily
<b>Control Group</b>	Basal diet
<b>Post exposure observation period</b>	No

<b>Remarks for Test Conditions</b>	Rats (13-18/sex/dose group) were fed DMT diets for a period of two-weeks. Individual body weights and total feed and water intake per cage were collected. At necropsy, urine was collected directly from the bladder for pH measurement, and concentrations of "stone-forming" materials were determined. The urinary system was examined grossly for presence of macroscopic calculi. Any calculi were collected, dried, weighed and analyzed. This study also evaluated terephthalic acid (TPA) at similar dietary levels.
<b>NOAEL(NOEL)</b>	0.5% (660 mg/kg) (males); 1.0% (1277 mg/kg) (females)
<b>LOAEL(LOEL)</b>	1.5% in diet
<b>Toxic Response/effects by Dose Level</b>	Formation of bladder calculi at 1.5, 2.0, and 3.0% dimethyl terephthalate
<b>Remarks for Results</b>	Average BW of the animals consuming the 1.5% and above was decreased on study Days 6-8 and 12-14 (postnatal Days 34-36 and 40-42) in females and 1.0% in males. Decreases in BW were accompanied by reduced feed consumption (possible palatability problems). There was no effect on water consumption at any dose. The incidence of bladder calculi in males from the 0, 0.5, 1.0, 1.5, 2.0, and 3.0% DMT dietary groups were 0, 0, 0, 35, 72, and 100%, respectively. The incidence of bladder calculi in females from the 0, 0.5, 1.0, 1.5, 2.0, and 3.0% DMT dietary groups were 0, 0, 0, 0, 36, and 47%, respectively. Grossly observable irregular thickening of the bladder wall was limited to animals having bladder calculi. The composition of the bladder calculi from the DMT treated animals was primarily calcium and terephthalic acid (TPA) with 5-7% protein. Phosphate levels were low, in contrast to bladder calculi from animals treated directly with terephthalic acid. Neither oxalate, nor uric acid, was found in the calculi. An acidic urinary pH was believed to have induced the hypercalciuria, a characteristic of urolithiasis in man. The higher urinary concentrations of TPA from DMT in the diet (when compared to similar dietary concentrations of TPA) explained the higher incidence of urinary calculi from the DMT diets than from comparable levels of TPA in the diet. Urinary phosphate levels were decreased in the animals consuming the DMT diet and explained why phosphate was present only at very low levels in the bladder calculi in those animals.
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Comparable to guideline study with acceptable restrictions.
<b>References</b>	Chin, T.Y., Tyl, R.W., Popp, J.A. and Heck, H. d'A. (1981) "Chemical Urolithiasis: 1. Characteristics of Bladder Stone Induction by Terephthalic Acid and Dimethyl Terephthalate in Weanling Fischer-344 Rats." Tox. and Appl. Pharm. 58:307-321.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0

<b>Remarks for Test Substance</b>	Data are for structurally related substance methyl benzoate
<b>Method/guideline</b>	1.5-month toxicity study
<b>GLP</b>	No
<b>Year</b>	1970
<b>Species/strain</b>	Rat/white (strain not specified)
<b>Sex</b>	Not reported
<b>Route of Administration</b>	Not specified
<b>Doses/concentration Levels</b>	111 or 500 mg/kg bw/d
<b>Exposure Period</b>	45 days
<b>Frequency of Treatment</b>	Daily
<b>Control Group</b>	Yes, but not described
<b>Remarks for Test Conditions</b>	The study was translated from a Russian study and some of the methodology was difficult to interpret. Based on the previous acute portion of the study, it appears that methyl benzoate was administered by gavage; however in a discussion of some results, the authors indicate that a "preparation" was given by intraperitoneal injection. General condition and some hematology were evaluated once every 10-11 days and at the end of the study a necropsy was performed.
<b>LOAEL(LOEL)</b>	111 mg/kg bw/d
<b>Toxic Response/effects by Dose Level</b>	At 111 mg/kg bw/d, there was a statistically significant increase in blood erythrocytes ( $p < 0.05$ ) and reticulocytes significantly increased. At 500 mg/kg bw/d there was no change in "red blood", but a significant increase in "white blood" ( $p < 0.01$ ) and in the number of reticulocytes. There was a significant increase in prothrombin time ( $p < 0.01$ ) at both doses and a tendency for a decreased phagocytic index (authors reported this to occur in mice, but the reviewer assumes this is a typographical error and "rats" was intended) at 500 mg/kg bw/d. Whole blood cholinesterase activity was significantly decreased at the high dose. No histological findings were reported, although it was reported that the level of ascorbic acid in the adrenal glands was decreased in rats given 500 mg methyl benzoate/kg bw/d.
<b>Remarks for Results</b>	The results were difficult to interpret due to the poor translation of the article. The exact administration route and schedule were not clearly indicated and it is possible that additional groups were tested.
<b>Data Qualities Reliabilities</b>	Reliability code 4. Not assignable.
<b>Remarks for Data Reliability</b>	The study was translated from a foreign article and the data were collected prior to GLP and OECD guidelines and although the acute portion of this study received a code 2, the description of the subacute portion of the study is not well documented and difficult to interpret. Therefore the data are

not considered reliable.

## References

Kravets-Bekker A.A., and Ivanova., O.P. (1970) Toxicological characteristics of methyl benzoate and potassium benzoate. Factory Vneshn. Sredy Ikh Znach. Zdorov'ya Naseleniya, 1970(2), 125-129.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Test Substance</b>	Data are for structurally related substance methyl benzoate
<b>Method/guideline</b>	6-month toxicity study
<b>GLP</b>	No
<b>Year</b>	1970
<b>Species/strain</b>	Rat/white (strain not specified) and grey rat
<b>Sex</b>	Not reported
<b>Route of Administration</b>	Not specified
<b>Doses/concentration Levels</b>	0.005 or 0.05 mg/kg bw/d
<b>Exposure Period</b>	6 months
<b>Frequency of Treatment</b>	Daily
<b>Control Group</b>	Yes, but not described
<b>Remarks for Test Conditions</b>	The study was translated from a Russian study and some of the methodology was difficult to interpret. Based on the previous acute portion of the study, it appears that methyl benzoate was administered by gavage; however in a discussion of some results, the authors indicate that a "preparation" was given by intraperitoneal injection. General condition and some hematology were evaluated once every 10-11 days and at the end of the study a necropsy was performed. In addition, the grey rats were studied for conditional reflexes using a food motive method and the white rats were studied for biochemical parameters.
<b>NOAEL(NOEL)</b>	0.005 mg/kg bw/d
<b>LOAEL(LOEL)</b>	0.05 mg/kg bw/d
<b>Toxic Response/effects by Dose Level</b>	The general condition of the animals in both dose groups did not differ from controls. At the high dose, there was decrease in the number of reticulocytes ( $p < 0.01$ ). There was no difference from controls in prothrombin time or phagocytic activity at either dose. In the grey rats, at the high dose, the latent period for response to "bell" or "light" stimulus was increased. Also, there was an increase in the number of sulfhydryl groups in cerebral tissue of high-dose grey rats. At necropsy, congestion and swelling of the hepatic central veins and capillaries was

	reported in high-dose rats. There were no histological findings in the low-dose animals.
<b>Remarks for Results</b>	The results were difficult to interpret due to the poor translation of the article. The exact administration route and schedule were not clearly indicated.
<b>Conclusion Remarks</b>	The authors reported that methyl benzoate administered at 0.005 mg/kg bw/d to rats did not produce adverse effects.
<b>Data Qualities Reliabilities</b>	Reliability code 4. Not assignable.
<b>Remarks for Data Reliability</b>	The study was translated from a foreign article and the data were collected prior to GLP and OECD guidelines and although the acute portion of this study received a code 2, the description of the chronic portion of the study is not well documented and difficult to interpret. Therefore the data are not considered reliable.
<b>References</b>	Kravets-Bekker A.A., and Ivanova., O.P. (1970) Toxicological characteristics of methyl benzoate and potassium benzoate. <i>Factory Vneshn. Sredy Ikh Znach. Zdorov'ya Naseleniya</i> , 1970(2), 125-129.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Test Substance</b>	Data are for structurally related substance sodium benzoate
<b>Method/guideline</b>	Carcinogenicity assay
<b>Year</b>	1984
<b>Species/strain</b>	Mouse/albino Swiss
<b>Sex</b>	Male and Female
<b>Route of Administration</b>	Drinking water
<b>Doses/concentration Levels</b>	2% in the drinking water (approximately 4,000 mg/kg bw/d)
<b>Exposure Period</b>	Life span (up to approximately 112 weeks)
<b>Frequency of Treatment</b>	Daily
<b>Control Group</b>	Untreated drinking water
<b>Post exposure observation period</b>	None
<b>Remarks for Test Conditions</b>	Groups of 50 male and 50 female 5-week-old albino Swiss mice were administered sodium benzoate at a concentration of 2% in the drinking water (approximately 4,000 mg/kg bw/d) for their life span (up to approximately 112 weeks). Control groups consisted of 100 untreated mice per sex. Mice were examined clinically, weighed and gross pathological changes were recorded. Complete necropsies were conducted on all mice and organs were examined macroscopically and selected

	tissues (liver, spleen, kidney, bladder, thyroid, heart, pancreas, testes, ovaries, brain, nasal turbinates, and lung) were histopathologically examined.
<b>Toxic Response/effects by Dose Level</b>	Sodium benzoate administration had no effect on survival or on tumor incidence.
<b>Conclusion Remarks</b>	Sodium benzoate at a lifetime exposure of 2% in the drinking water of mice showed no evidence of carcinogenicity.
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	The protocol and results were reported in a short communication and statistical analyses were not reported.
<b>References</b>	Toth B. (1984) Lack of tumorigenicity of sodium benzoate in mice. <i>Fundam Appl Toxicol.</i> , 4, 494-496.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Test Substance</b>	Data are for structurally related substance benzoic acid
<b>Method/guideline</b>	17-month oral toxicity study
<b>GLP</b>	Not reported
<b>Year</b>	1970
<b>Species/strain</b>	Mouse
<b>Sex</b>	Male and Female
<b>Route of Administration</b>	Oral
<b>Doses/concentration Levels</b>	40 mg/kg bw/d
<b>Exposure Period</b>	17 months
<b>Frequency of Treatment</b>	Daily
<b>Control Group</b>	Not reported
<b>Post exposure observation period</b>	Not reported
<b>Remarks for Test Conditions</b>	Groups of 25 male and 25 female mice were orally administered 40 mg benzoic acid/kg bw/d for 17 months.
<b>Toxic Response/effects by Dose Level</b>	Survival (%) at 2.5 months was greater for the benzoic acid group (68%) than that for the control group of males (60%) or female rats (62%).
<b>Data Qualities Reliabilities</b>	Reliability code 4. Not assignable.
<b>Remarks for Data Reliability</b>	Very limited description of study and results.
<b>References</b>	Shtenberg A.J. and Ignat'ev A.D. (1970) Toxicological evaluation of some combinations of food preservatives. <i>Food</i>

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Test Substance</b>	Data are for structurally related substance benzoic acid
<b>Method/guideline</b>	3-month gavage study
<b>GLP</b>	No
<b>Year</b>	1970
<b>Species/strain</b>	Mouse/cross-bred white
<b>Sex</b>	Male and Female
<b>Route of Administration</b>	Gavage
<b>Doses/concentration Levels</b>	80 mg benzoic acid/kg bw/d or 80 mg benzoic acid/kg bw/d plus 160 mg sodium bisulphite/kg bw/d
<b>Exposure Period</b>	3 months
<b>Frequency of Treatment</b>	Daily
<b>Control Group</b>	Basal diet only
<b>Remarks for Test Conditions</b>	Groups of 50 male and 50 female cross-bred white mice were administered 80 mg benzoic acid/kg bw/d by gavage for 3 months. Similarly, groups of 50 male and 50 female cross-bred white mice were administered 80 mg benzoic acid/kg bw/d in conjunction with 160 mg sodium bisulphite/kg bw/d. Observations consisted of general condition, behaviour, and survival. Food consumption and body weight gain were recorded daily. Additionally, mice were tested to determine the possible effects of hunger, physical stress, and poisoning with carbon tetrachloride (single dose of 0.1 ml/mouse). A co-carcinogenicity test was conducted with Ehrlich ascites carcinoma. A control group was used but not described.
<b>LOAEL(LOEL)</b>	80 mg/kg bw/d
<b>Toxic Response/effects by Dose Level</b>	Survival was decreased at 2.5 months in animals given the benzoic acid/sodium bisulphite combination. Percent survival was 60, 68, and 30% for control mice, benzoic acid-fed mice, and benzoic acid/sodium bisulphite combination-fed mice, respectively. Treated animals did not gain weight to the same extent as controls (no statistical analysis) and did not appear to be associated with feed intake. Under 90% feed restriction conditions, treated mice showed greater mortality and weight loss than controls. Treated mice also appeared to be more sensitive to carbon tetrachloride poisoning. In the co-carcinogenicity tests, tumor growth appeared to be increased in treated animals compared to controls (data not shown by the study authors).

<b>Conclusion Remarks</b>	It appeared that benzoic acid administered at 80 mg/kg bw/d produced a reduction in body weight gain; however, no statistical analyses were conducted. In addition, benzoic acid in combination with sodium bisulphite appeared to decrease survival.
<b>Data Qualities Reliabilities</b>	Reliability code 3. Not reliable.
<b>Remarks for Data Reliability</b>	Methodology was unconventional and there was only use of 1 dose. No statistical analyses were conducted and results were not clearly described.
<b>References</b>	Shtenberg A.J., and Ignat'ev, A.D. (1970) Toxicological evaluation of some combinations of food preservatives. Fd Cosmet Toxicol., 8, 369-380.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Test Substance</b>	Data are for structurally related substance benzoic acid
<b>Method/guideline</b>	18-month oral toxicity study
<b>GLP</b>	No
<b>Year</b>	1970
<b>Species/strain</b>	Rat/Wistar
<b>Sex</b>	Male and Female
<b>Route of Administration</b>	Oral
<b>Doses/concentration Levels</b>	40 mg benzoic acid/kg bw/d or 40 mg benzoic acid/kg bw/d plus 80 mg sodium bisulphite/kg bw/d
<b>Exposure Period</b>	18 months
<b>Frequency of Treatment</b>	Daily
<b>Control Group</b>	Basal diet only
<b>Post exposure observation period</b>	None
<b>Remarks for Test Conditions</b>	In an 18-month study, groups of 10 male and 10 female Wistar rats were fed 40 mg benzoic acid/kg bw/d in a paste prior to normal feeding. Similarly, groups of 50 male and 50 female Wistar rats were fed 40 mg benzoic acid/kg bw/d in conjunction with 80 mg sodium bisulphite/kg bw/d. Control animals received basal diet only. Parameters measured were food and water consumption, and body weight gain. Also, possible stress factors (low temperature tolerance) were recorded. Titre of serum complement, phagocytic activity of leucocytes, serum-ceruloplasmin level, blood alkalinity, blood ketones, blood morphology, erythrocyte sedimentation rate and C-reactive protein in serum were estimated.

<b>NOAEL(NOEL)</b>	40 mg/kg bw/d
<b>Toxic Response/effects by Dose Level</b>	The results were not clearly reported; however, it appeared that survival was decreased in rats fed the benzoic acid/sodium bisulphite combination and that the benzoic acid/sodium bisulphite combination-fed rats showed more of an effect in the stress tests, had increased erythrocyte sedimentation rates, and a decreased level of blood ketones compared to controls. No effects on blood alkalinity, C-reactive protein levels and blood morphology were reported in the treated rats. Apparently, small groups of benzoic acid-fed rats and benzoic acid/sodium bisulphite combination-fed rats were administered a lethal dose of sodium benzoate, to which the benzoic acid-fed rats appeared to have gained tolerance (25,100, and 100% mortality in benzoic acid-fed rats, benzoic acid/sodium bisulphite combination-fed rats, and controls, respectively).
<b>Conclusion Remarks</b>	A combination of benzoic acid and sodium bisulphite apparently decreased survival in rats; however, no statistical analysis was conducted and only 1 dose level was tested.
<b>Data Qualities Reliabilities</b>	Reliability code 3. Not reliable.
<b>Remarks for Data Reliability</b>	Methodology was unconventional and there was only use of 1 dose. No statistical analyses were conducted and results were not clearly described.
<b>References</b>	Shtenberg A.J., and Ignat'ev, A.D. (1970) Toxicological evaluation of some combinations of food preservatives. Fd Cosmet Toxicol., 8, 369-380.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Test Substance</b>	Data are for structurally related substance benzaldehyde
<b>Method/guideline</b>	14-day inhalation study
<b>Year</b>	1991
<b>Species/strain</b>	Rat/Sprague-Dawley
<b>Sex</b>	Male and Female
<b>Route of Administration</b>	Inhalation
<b>Doses/concentration Levels</b>	500, 750, or 1,000 ppm
<b>Exposure Period</b>	14 days
<b>Frequency of Treatment</b>	6 hours/day
<b>Control Group</b>	Filtered air
<b>Post exposure observation period</b>	Up to 72 hours

<b>Remarks for Test Conditions</b>	Groups of 14 male and 14 female Sprague-Dawley rats were exposed to 500, 750, or 1,000 ppm benzaldehyde, 6 hours/day for 14 consecutive days in 2.5 m <sup>3</sup> chambers with an air flow rate of 500 L/min (Laham et al., 1991). Body weights were recorded after day 2, 8 and 14. At necropsy, blood samples were collected for hematological and biochemical analyses, and gross pathological and histopathological examinations were conducted.
<b>LOAEL(LOEL)</b>	500 ppm
<b>Toxic Response/effects by Dose Level</b>	In the first week, 10 females and 1 male from the 1,000 ppm group and 1 female from the 750 ppm group died. Two more females were moribund in the second week. At all exposure groups, a mild irritation of the mucosa was reported with effects on the central nervous system including tremors, hypothermia, reduced breathing rates and decreased motor activity. At 1,000 ppm, hemoglobin and hematocrit counts were decreased in both sexes. Red blood cells also were decreased in high-dose females. A dose-related increase in monocytes was observed in females. Also in females, significant changes in total protein, albumin fraction, and serum cholinesterase were reported. Aspartate aminotransferase was significantly increased at all exposures in both males and females. In males, goblet cell metaplasia (largely confined to the respiratory epithelium lining the nasal septum) was reported; however the incidence and severity were similar in all treatment groups. There was no change in females.
<b>Appropriate statistical evaluations?</b>	Yes. Results analyzed using Duncan's multiple range test and a modified least significant difference procedure. Differences between groups determined with Student's t-test.
<b>Remarks for Results</b>	The authors suggested that the reported goblet cell metaplasia corresponded to a "mild form of adaptation during the recovery period following the inhalation exposure to benzaldehyde".
<b>Conclusion Remarks</b>	A NOAEL could not be determined, but the authors concluded that typical human exposure levels are so small (5.3-22.5 ppb) that they should not be considered hazardous.
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restrictions.
<b>Remarks for Data Reliability</b>	Although it was not reported whether this study was conducted under GLP, it was well reported and conducted by the Canadian Health Protection Branch. The data are considered reliable.
<b>References</b>	Laham S., Broxup, B., Robinet, M., Potvin, M., and Schrader, K. (1991) Subacute inhalation toxicity of benzaldehyde in the Sprague-Dawley rat. <i>Am Ind Hyg Assoc J.</i> , 52(12), 503-510.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Test Substance</b>	Data are for structurally related substance benzaldehyde

<b>Method/guideline</b>	8-week gavage study
<b>GLP</b>	No
<b>Year</b>	1967
<b>Species/strain</b>	Rat/White
<b>Sex</b>	Male and Female
<b>Route of Administration</b>	Gavage
<b>Doses/concentration Levels</b>	10 mg/rat on alternate days (approximately 20 mg/jkg bw/d)
<b>Exposure Period</b>	8 weeks
<b>Frequency of Treatment</b>	Alternate days
<b>Control Group</b>	Not described
<b>Post exposure observation period</b>	None
<b>Remarks for Test Conditions</b>	Benzaldehyde was administered orally to adult white rats at doses of 10 mg diluted in 0.1 ml of oil on alternate days for a period of 8 weeks. Animals were killed and livers were examined for biochemical changes.
<b>Actual dose received by dose level and sex</b>	Approximately 20 mg/kg bw/d
<b>Toxic Response/effects by Dose Level</b>	No hepatic enzyme activity was reported.
<b>Remarks for Results</b>	Not described
<b>Data Qualities Reliabilities</b>	Reliability code 4. Not assignable.
<b>Remarks for Data Reliability</b>	Study translated from foreign article with very limited description.
<b>References</b>	Sporn A., Dinu, I., and Stanclu, V. (1967) Cercetari cu privire la toxicitatea aldehidei benzoice. [Research regarding the toxicity of benzaldehyde.] Igiena, 16(1), 23.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Test Substance</b>	Data are for structurally related substance benzaldehyde
<b>Method/guideline</b>	Screening method used by U.S. Food and Drug Administration
<b>GLP</b>	No
<b>Year</b>	1967
<b>Species/strain</b>	Rat/Osborne-Mendel

<b>Sex</b>	Male and Female
<b>Route of Administration</b>	Diet
<b>Doses/concentration Levels</b>	10,000 ppm
<b>Exposure Period</b>	16 weeks
<b>Frequency of Treatment</b>	Daily
<b>Control Group</b>	Basal diet
<b>Post exposure observation period</b>	None
<b>Remarks for Test Conditions</b>	Groups of 5 male and 5 female Osborne-Mendel rats were provided test substance in the diet at concentrations of 0 or 10,000 ppm for 16 weeks. No vehicle was used. The diet was prepared and analyzed weekly. Measurements of body weight, food intake and general condition were recorded weekly. Hematological examinations (white cell counts, red cell counts, hemoglobins and hematocrits) were performed at the termination of the study. Macroscopic examination of all tissues was performed. Histopathological examination was performed on the liver, kidneys, spleen, heart, and testes of 6-8 animals (evenly divided by sex) from the high dose and controls.
<b>Actual dose received by dose level and sex</b>	Approximately 500 mg/kg bw/d
<b>Toxic Response/effects by Dose Level</b>	No effects were reported.
<b>Conclusion Remarks</b>	No effect reported at 10,000 ppm benzaldehyde in the diet of rats.
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	This study was performed by the Food and Drug Administration prior to the establishment of GLP and OECD. Data are considered reliable.
<b>References</b>	Hagan E.C., Hansen W.H., Fitzhugh O.G., Jenner P.M., Jones W.I., Taylor J.M., Long E.L., Nelson A.A., and Brouwer J.B. (1967) Food flavourings and compounds of related structure. II. Subacute and chronic Toxicity. Food Cosmet Toxicol 5:141-157.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Test Substance</b>	Data are for structurally related substance benzaldehyde
<b>Method/guideline</b>	Screening method used by U.S. Food and Drug Administration
<b>GLP</b>	No
<b>Year</b>	1967

<b>Species/strain</b>	Rat/Osborne-Mendel
<b>Sex</b>	Male and Female
<b>Route of Administration</b>	Diet
<b>Doses/concentration Levels</b>	1,000 ppm
<b>Exposure Period</b>	27-28 weeks
<b>Frequency of Treatment</b>	Daily
<b>Control Group</b>	Basal diet
<b>Post exposure observation period</b>	None
<b>Remarks for Test Conditions</b>	Groups of 5 male and 5 female Osborne-Mendel rats were provided test substance in the diet at concentrations of 0 or 1,000 ppm for 27-28 weeks. No vehicle was used. The diet was prepared and analyzed weekly. Measurements of body weight, food intake and general condition were recorded weekly. Hematological examinations (white cell counts, red cell counts, hemoglobins and hematocrits) were performed at the termination of the study. Macroscopic examination of all tissues was performed. Histopathological examination was performed on the liver, kidneys, spleen, heart, and testes of 6-8 animals (evenly divided by sex) from the high dose and controls.
<b>Actual dose received by dose level and sex</b>	Approximately 50 mg/kg bw/d
<b>Toxic Response/effects by Dose Level</b>	No effects were reported.
<b>Conclusion Remarks</b>	No effect reported at 1,000 ppm benzaldehyde in the diet of rats.
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	This study was performed by the Food and Drug Administration prior to the establishment of GLP and OECD. Data are considered reliable.
<b>References</b>	Hagan E.C., Hansen W.H., Fitzhugh O.G., Jenner P.M., Jones W.I., Taylor J.M., Long E.L., Nelson A.A., and Brouwer J.B. (1967) Food flavourings and compounds of related structure. II. Subacute and chronic Toxicity. Food Cosmet Toxicol., 5, 141-157.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Test Substance</b>	Data are for structurally related substance benzaldehyde
<b>Method/guideline</b>	16-day gavage study
<b>GLP</b>	Yes

<b>Year</b>	1990
<b>Species/strain</b>	Rat/F344/N
<b>Sex</b>	Male and Female
<b>Route of Administration</b>	Gavage
<b>Doses/concentration Levels</b>	0, 100, 200, 400, 800, or 1,600 mg/kg bw/d
<b>Exposure Period</b>	16 days
<b>Frequency of Treatment</b>	Daily, 5 days/week
<b>Control Group</b>	Corn oil (vehicle)
<b>Post exposure observation period</b>	No
<b>Remarks for Test Conditions</b>	Groups of 5 male and 5 female rats were administered 0, 100, 200, 400, 800, or 1,600 mg benzaldehyde/kg bw/d in corn oil by gavage, 5 days/week for a period of 16 days. Animals were housed 5 per cage. Water and feed were available ad libitum. Animals were observed 2X per day, weighed on days 1 and 8 and necropsied at study termination.
<b>NOAEL(NOEL)</b>	400 mg/kg bw/d
<b>LOAEL(LOEL)</b>	800 mg/kg bw/d
<b>Toxic Response/effects by Dose Level</b>	All high dose rats died on day 2. 2 male and 2 female rats died in the 800 mg/kg bw/d dose group. Decreased final body weights (14% in males and 11% in females) were reported in the 800 mg/kg bw/d dose group. No other compound-related effects were reported.
<b>Appropriate statistical evaluations?</b>	Yes. Methodology of Kaplan and Meier (1958), Cox (1972), and Tarone (1975).
<b>Conclusion Remarks</b>	Based on increased mortality, the NOEL was determined to be 400 mg/kg bw/day.
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restrictions.
<b>Remarks for Data Reliability</b>	NTP study
<b>References</b>	National Toxicology Program (1990) Toxicology and carcinogenesis studies of benzaldehyde (CAS No. 100-52-7) in F344/N rats and B6C3F1 mice. Technical Report Series 378.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Test Substance</b>	Data are for structurally related substance benzaldehyde
<b>Method/guideline</b>	16-day gavage study
<b>GLP</b>	Yes

<b>Year</b>	1990
<b>Species/strain</b>	Mouse/B6C3F1
<b>Sex</b>	Male and Female
<b>Route of Administration</b>	Gavage
<b>Doses/concentration Levels</b>	0, 200, 400, 800, 1,600, or 3,200 mg/kg bw/d
<b>Exposure Period</b>	16 days
<b>Frequency of Treatment</b>	Daily, 5 days/week
<b>Control Group</b>	Yes-vehicle
<b>Post exposure observation period</b>	No
<b>Remarks for Test Conditions</b>	Groups of 5 male and 5 female mice were administered 0, 200, 400, 800, 1,600, or 3,200 mg benzaldehyde/kg bw/d in corn oil by gavage, 5 days/week for a period of 16 days. Animals were housed 5 per cage. Water and feed were available ad libitum. Animals were observed 2X per day, weighed on days 1 and 8 and necropsed at study termination.
<b>NOAEL(NOEL)</b>	400 mg/kg bw/d
<b>LOAEL(LOEL)</b>	800 mg/kg bw/d
<b>Toxic Response/effects by Dose Level</b>	All mice in the 2 highest dose groups died by day 3. One male receiving 800 mg/kg bw/d died on day 10. No other compound related effects were reported.
<b>Appropriate statistical evaluations?</b>	Yes. Methodology of Kaplan and Meier (1958), Cox (1972), and Tarone (1975).
<b>Conclusion Remarks</b>	Based on increased mortality, the NOEL was determined to be 400 mg/kg bw/day.
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restrictions.
<b>Remarks for Data Reliability</b>	NTP study
<b>References</b>	National Toxicology Program (1990) Toxicology and carcinogenesis studies of benzaldehyde (CAS No. 100-52-7) in F344/N rats and B6C3F1 mice. Technical Report Series 378.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Test Substance</b>	Data are for structurally related substance benzaldehyde
<b>Method/guideline</b>	13-week gavage study
<b>GLP</b>	Yes
<b>Year</b>	1990

<b>Species/strain</b>	Rat/F344/N
<b>Sex</b>	Male and Female
<b>Route of Administration</b>	Gavage
<b>Doses/concentration Levels</b>	0, 50, 100, 200, 400, or 800 mg/kg bw/d
<b>Exposure Period</b>	13 weeks
<b>Frequency of Treatment</b>	Daily, 5 days/week
<b>Control Group</b>	Corn oil (vehicle)
<b>Post exposure observation period</b>	No
<b>Remarks for Test Conditions</b>	Groups of 10 male and 10 female rats were administered 0, 50, 100, 200, 400, or 800 mg benzaldehyde/kg bw/d in corn oil by gavage, 5 days/week for a period of 13 weeks. Animals were housed 5 per cage. Water and feed were available ad libitum. Animals were observed 2X per day, weighed on day 0, once per week and at termination. All animals were necropsied at study termination and complete histopathologic examinations were conducted on controls, and 2 highest dose groups.
<b>NOAEL(NOEL)</b>	400 mg/kg bw/d
<b>LOAEL(LOEL)</b>	800 mg/kg bw/d
<b>Toxic Response/effects by Dose Level</b>	At the highest dose, final mean body weight of male rats was 26% lower than controls and 6/10 males and 3/10 females died before the study ended. In addition, multiple histopathological effects were reported including: degeneration and necrosis of the cerebellum, necrosis of the neurons in the hippocampus, hyperplasia and/or hyperkeratosis of the forestomach (with mild to moderate thickening of the squamous epithelium, degeneration of the liver, necrosis of the liver (males only), and degeneration or necrosis of the tubular epithelium in the kidney. No other compound-related effects were reported. One female rat in the 400 mg/kg bw/day group and one female control rat died.
<b>Appropriate statistical evaluations?</b>	Yes. Methodology of Kaplan and Meier (1958), Cox (1972), Mantel -Haenszel (1959), and Tarone (1975). The Fisher exact/Cochran-Armitage trend analysis was also used.)
<b>Conclusion Remarks</b>	Based on the various lesions reported at 800 mg/kg bw/d, but not at 400 mg/kg bw/d, doses selected for the 2-yr study were 200 and 400 mg/kg bw/d.
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restrictions.
<b>Remarks for Data Reliability</b>	NTP study
<b>References</b>	National Toxicology Program (1990) Toxicology and carcinogenesis studies of benzaldehyde (CAS No. 100-52-7) in F344/N rats and B6C3F1 mice. Technical Report Series 378.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Test Substance</b>	Data are for structurally related substance benzaldehyde
<b>Method/guideline</b>	13-week gavage study
<b>GLP</b>	Yes
<b>Year</b>	1990
<b>Species/strain</b>	Mouse/B6C3F1
<b>Sex</b>	Male and Female
<b>Route of Administration</b>	Gavage
<b>Doses/concentration Levels</b>	0, 75, 150, 300, 600, or 1,200 mg/kg bw/d
<b>Exposure Period</b>	13 weeks
<b>Frequency of Treatment</b>	Daily, 5 days/week
<b>Control Group</b>	Yes-vehicle
<b>Post exposure observation period</b>	No
<b>Remarks for Test Conditions</b>	Groups of 10 male and 10 female mice were administered 0, 75, 150, 300, 600, or 1,200 mg benzaldehyde/kg bw/d in corn oil by gavage, 5 days/week for a period of 13 weeks. Animals were housed 5 per cage. Water and feed were available ad libitum. Animals were observed 2X per day, weighed on day 0, once per week, and at the end of the study. All animals were necropsied at study termination and complete histopathologic examinations were conducted on controls, and 2 highest dose groups.
<b>NOAEL(NOEL)</b>	300 mg/kg bw/d
<b>LOAEL(LOEL)</b>	600 mg/kg bw/d
<b>Toxic Response/effects by Dose Level</b>	At the highest dose, 9/10 males and 1/10 females died. At 600 mg/kg bw/d, the final mean body weight of males was 9% lower than controls. Mild to moderate renal tubule degeneration occurred in all males in the high-dose group and in 1/10 males in the 600 mg/kg bw/d group. No other compound related effects were reported.
<b>Appropriate statistical evaluations?</b>	Yes. Methodology of Kaplan and Meier (1958), Cox (1972), Mantel -Haenszel (1959), and Tarone (1975). The Fisher exact/Cochran-Armitage trend analysis was also used.
<b>Conclusion Remarks</b>	Based on the mild renal lesions and depressed body weight gain, the doses selected for the 2-yr study were 300 and 600 mg/kg bw/d.
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restrictions.

**Remarks for Data Reliability** NTP study

**References** National Toxicology Program (1990) Toxicology and carcinogenesis studies of benzaldehyde (CAS No. 100-52-7) in F344/N rats and B6C3F1 mice. Technical Report Series 378.

<b>Substance Name</b>	Methyl 4-formylbenzoate
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**CAS No.** 001571-08-0

**Remarks for Test Substance** Data are for structurally related substance benzaldehyde

**Method/guideline** Carcinogenicity assay

**GLP** Yes

**Year** 1990

**Species/strain** Rat/F344/N

**Sex** Male and Female

**Route of Administration** Gavage

**Doses/concentration Levels** 0, 200, or 400 mg/kg bw/d

**Exposure Period** Up to 104 weeks

**Frequency of Treatment** Daily, 5 days/week

**Control Group** Corn oil (vehicle)

**Post exposure observation period** No

**Remarks for Test Conditions** Groups of 50 male and 50 female rats were administered 0, 200, or 400 mg benzaldehyde/kg bw/d in corn oil by gavage, 5 days/week for a period of 2 years. Animals were housed 5 per cage. Water and feed were available ad libitum. Animals were observed 2X per day, weighed on day 0, once per week for the first 13 weeks, once per month for the remainder of the study and at termination. All animals were necropsied at study termination and complete histopathologic examinations were conducted on controls, highest dose group, and on low-dose animals dying before study end.

**NOAEL(NOEL)** 200 mg/kg bw/d

**LOAEL(LOEL)** 400 mg/kg bw/d

**Toxic Response/effects by Dose Level** There was no effect on body weights. Survival was significantly decreased in the high-dose male group after day 373. No other effect on survival was reported. In high-dose males, hyperlasia and adenomas of the exocrine pancreas were marginally increased but the incidence of adenomas was within the range of historical corn oil vehicle controls. There was a marginal increase in the incidence of malignant mesoteliomas of the tunica vaginalis and/or peritoneum in treated male rats;

however, since there was no significant increase in high-dose males relative to historical controls, the malignant mesotheliomas were not considered related to benzaldehyde treatment. There was a positive trend for mononuclear cell leukemia in male rats thought to be due to an increase in stage 1 leukemia. The slight increases in mononuclear cell leukemia reported were not considered to be related to benzaldehyde treatment. In 2 females at the highest dose, squamous papillomas were reported but due to lack of accompanying hyperplasia and comparability with historical control incidences, these were not considered treatment related.

<b>Appropriate statistical evaluations?</b>	Yes. Methodology of Kaplan and Meier (1958), Cox (1972), Mantel -Haenszel (1959), and Tarone (1975). The Fisher exact/Cochran-Armitage trend analysis was also used.
<b>Conclusion Remarks</b>	Under the conditions of the 2-yr gavage study, there was no evidence of carcinogenic activity of benzaldehyde for male or female F344/N rats receiving 200 or 400 mg/kg bw/d.
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restrictions.
<b>Remarks for Data Reliability</b>	NTP study
<b>References</b>	National Toxicology Program (1990) Toxicology and carcinogenesis studies of benzaldehyde (CAS No. 100-52-7) in F344/N rats and B6C3F1 mice. Technical Report Series 378.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Test Substance</b>	Data are for structurally related substance benzaldehyde
<b>GLP</b>	Yes
<b>Year</b>	1990
<b>Species/strain</b>	Mouse/B6C3F1
<b>Sex</b>	Male and Female
<b>Route of Administration</b>	Gavage
<b>Doses/concentration Levels</b>	0, 300, or 600 mg/kg bw/d
<b>Exposure Period</b>	103 weeks
<b>Frequency of Treatment</b>	Daily 5 days/week
<b>Control Group</b>	Corn oil (vehicle)
<b>Post exposure observation period</b>	No
<b>Remarks for Test Conditions</b>	Groups of 50 male and 50 female mice were administered 0, 300, or 600 mg benzaldehyde/kg bw/d in corn oil by gavage, 5 days/week for a period of 103 weeks. Animals were housed 5 per cage. Water and feed were available ad libitum. Animals

were observed 2X per day, weighed on day 0, once per week for the first 13 weeks, once per month for the remainder of the study and at termination. All animals were necropsied at study termination and complete histopathologic examinations were conducted on controls, highest dose group, and on low-dose animals dying before study end.

<b>Toxic Response/effects by Dose Level</b>	There was no effect on body weight gain or survival. Focal hyperplasia characterized by increased thickness of the stratified squamous epithelium and squamous cell papillomas of the forestomach (male: control 1/50; low dose, 2/50; high dose, 5/50; female: control, 0/50; low dose, 5/50; high dose 6/50) were increased in treated animals.
<b>Appropriate statistical evaluations?</b>	Yes. Methodology of Kaplan and Meier (1958), Cox (1972), Mantel -Haenszel (1959), and Tarone (1975). The Fisher exact/Cochran-Armitage trend analysis was also used.
<b>Conclusion Remarks</b>	Under the conditions of the 2-yr gavage study, there was some evidence fo carcinogenic activity of benzaldehyde for male or female B6C3F1 mice, as indicated by increased incidences of squamous cell papillomas and hyperplasia of the forestomach.
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restrictions.
<b>Remarks for Data Reliability</b>	NTP study
<b>References</b>	National Toxicology Program (1990) Toxicology and carcinogenesis studies of benzaldehyde (CAS No. 100-52-7) in F344/N rats and B6C3F1 mice. Technical Report Series 378.

## 4.4 Reproductive Toxicity

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance terephthalic acid
<b>Test Type</b>	Oral
<b>GLP</b>	Yes
<b>Year</b>	1982
<b>Species/Strain</b>	Rat/CD and Wistar

<b>Sex</b>	Male and Female
<b>Route of Administration</b>	Oral
<b>Duration of Test</b>	Approximately 160 days
<b>Doses/Concentration</b>	0.03, 0.125, 0.5, 2.0, and 5.0%
<b>Premating Exposure period for males</b>	Paternal: 90 days prior to and throughout mating Maternal: 90 days prior to mating, throughout mating, gestation, and lactation Offspring: 51 days; from birth through lactation and 30 days post weaning
<b>Control Group and Treatment</b>	Yes; concurrent no treatment
<b>Frequency of Treatment</b>	Daily in feed
<b>Remarks for Test Conditions</b>	<p>The approximated mg/kg doses based on average feed consumption and body weight during the 90 day pre-mating period were:</p> <p>CD(M): 14, 59, 240, 930, 2499  CD(F): 17, 67, 282, 1107, 2783  Wistar(M): 14, 61, 249, 960, 2480  Wistar(F): 19, 78, 307, 1219, 3018</p> <p>This study contrasted the toxicity of TPA in two different strains of rats. Experimental conditions were identical for both. Rats 15-17 weeks of age (n=30) were grouped housed 3/cage for the first 90 days of exposure. Body weight and feed intake were determined weekly during this time period. On Day 91, breeding pairs (n=10/sex) were housed together for 2 weeks prior to being separated. On Day 0 (delivery) the number and viability of offspring were evaluated and grossly examined. Offspring were recounted, sexed, and weighed on Day 1. These measurements were repeated at weaning on Day 21. After weaning the litters were reduced to 2/sex/dose from each of 5 litters (20 pups/dose/strain) and maintained on test diets for 30 more days (Day 51) prior to sacrifice. There were only 9 pairs of CD strain rats at the 5% diet level. Remaining animals were necropsied within a few days post weaning. At termination offspring were grossly examined and necropsied. Parental and F1 generation animals were observed 2x/day for clinical signs. Body weight gain and standard reproductive indices were assessed and statistically compared using ANOVA and Dunnett's-t-test using SAS statistical programs. Parameters evaluated consisted of: fertility index, number of offspring born per dam; number and proportion of each sex born; number (Day 0, 1, and 21) and proportion (Day 1 and 21) of each sex alive; average weight at Day 1 and 21 of all offspring and of each sex.</p>
<b>NOAEL(NOEL)</b>	0.5% (CD; Wistar: 2.0%) parental – greater than 5.0% (CD and

Wistar) reproductive

## Remarks for Results

Parental Effects: Following 90 days of exposure to TPA, statistically significant decreases in food consumption were observed in CD females treated with 2% and 5%, and in both sexes of Wistars treated with 5%.

Body weights were statistically decreased after 13 weeks in both sexes of CD rats on 2% and 5% TPA diets, and in males exposed to 0.03%. This effect occurred in Wistars (both sexes) only at the 5% level. There were 5 deaths (3 CD females, 1 Wistar/sex) reported during weeks 4-13 in animals given 5% TPA in the diet.

During the one-generation component of the study 3 CD (1 male at 2.0%, 1/sex at 5.0%) and 4 Wistar female (2 at 5.0% and 2 at 0.03%) rats died.

There was no effect of treatment on fertility index and litter size.

Offspring Effects: There were no effects of treatment on litter size, sex ratio, or total number of offspring. While no control offspring were found dead on Day 0, 17 Wistar pups (1 at 0.03%, 2 at 0.125%, 1 at 0.5%, 12 at 2.0% (2 from one dam and 10 from another)) and 23 CD pups (1 at 0.5%, 7 at 2.0% (3 dams) and 15 at 5.0% (3 dams; with 11 from one of them)) were found dead. No statistical differences were noted in viability on Days 0, 1, or 21 in either strain. In CD rats, survivability on Day 21 was reduced in both sexes of offspring whose parents had been exposed to 5% TPA in the diet.

In Wistar rats, body weights of both sexes of offspring from dams given 5.0% were reduced at Day 1. On Day 21, body weight was reduced in both strains of offspring from dams that ingested 5% TPA in the diet. Increased postnatal deaths on Day 1 and decreased survivability to Day 21 were noted in the 2% and 5% groups. At these dose levels, several large litters of pups were lost to dams suffering obvious signs of toxicity. Several of these dams did not allow the pups to nurse or attend to the litters. These pups were noted not to have milk in their stomachs and presented clinically as being very weak. These dams were consuming dietary levels of TPA known to cause reduced feed consumption, diarrhea and gastric trichobezoars (hairballs) and induce the formation of renal and bladder calculi. Unscheduled deaths during the postweaning period (Day 21-51) were confined to the 5% TPA group (18 Wistar and 16 CD) and were associated with a very high incidence of renal and bladder calculi. Renal and bladder calculi were noted in all animals exposed to 5% that were necropsied at Day 21. Day 51 necropsy findings also reported a very high incidence of renal and bladder calculi and the histological sequelae of the presence of the calculi.

Other studies have demonstrated an increased incidence of renal and bladder calculi formation in weanling animals when compared to adults consuming the same dietary level of TPA. This apparent increased sensitivity can be explained by the large amount of feed consumed in relation to body weight for

young animals experiencing their initial growth spurt. Weaning animals are not more sensitive to TPA when the results are expressed on a mg/kg basis.

<b>Offspring toxicity F1 and F2</b>	0.5% (CD and Wistar)
<b>Conclusion remarks</b>	The NOAEL for reproductive toxicity was greater than 5% in the diet (approximately 2480-3018 mg/kg/day). Whereas, the NOAEL for parental toxicity and the F1 generation was 0.5% TPA in the diet (approximately 240-307 mg/kg/day).
<b>Data Reliabilities Qualities</b>	Reliability code 1. Reliable without restriction.
<b>Remarks for Data Reliability</b>	Code 1. Comparable to guideline study.
<b>References</b>	Chemical Industry Institute of Technology (CIIT) (1982) A Ninety-Day Study of Terephthalic Acid (CAS No. 100-21-0) Induced Urolithiasis and Reproduction Performance in Wistar and CD Rats. CITI Docket 11622.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance dimethyl terephthalate
<b>Test Type</b>	Oral
<b>Year</b>	1973
<b>Species/Strain</b>	Rat/Long-Evans Hooded
<b>Sex</b>	Male and Female
<b>Route of Administration</b>	Oral-Diet
<b>Duration of Test</b>	Through weaning of F1 animals
<b>Doses/Concentration</b>	0.25, 0.50, or 1.0%
<b>Premating Exposure period for males</b>	Males 115 days prior to mating throughout gestation, parturition and lactation
<b>Premating Exposure period for females</b>	Females 6 days prior to mating throughout gestation, parturition and lactation
<b>Frequency of Treatment</b>	7-Days/week (diet)
<b>Remarks for Test Conditions</b>	Males were fed DMT diets for 115-days. These males were then mated with virgin females that had been on test diets for 6 days. After mating, the pregnant females were fed the DMT diets throughout gestation, parturition and lactation
<b>NOAEL(NOEL)</b>	1.0% parental
<b>Offspring toxicity F1 and F2</b>	0.25%
<b>Remarks for Results</b>	No signs of toxicity were observed in either the male or female parental animals (P). No effects were observed on fertility,

reproductive capacity, libido, pregnancy, gestation, litter size, or offspring viability due to consumption of DMT. Pups born to parents fed 0.5 and 1.0% DMT had significantly lower average body weights at weaning when compared to the controls

**Data Reliabilities Qualities** Reliability code 2. Reliable with restriction.

**Remarks for Data Reliability** Code 2. Basic data given: comparable to guidelines/standards.

**References** Krasavage, W.J., Yanno, F.J., and Terhaar, C.J. (1973) Dimethyl terephthalate (DMT): Acute Toxicity, Subacute Feeding and Inhalation Studies in Male Rats." J. Amer. Ind. Hyg. Assoc., 34(10):455-462.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance benzaldehyde
<b>Method/Guideline</b>	Reproductive toxicity
<b>Test Type</b>	1-generation
<b>GLP</b>	No
<b>Year</b>	1967
<b>Species/Strain</b>	Rat/white
<b>Sex</b>	Male and Female
<b>Route of Administration</b>	Gavage
<b>Duration of Test</b>	32 weeks
<b>Doses/Concentration</b>	2 mg/rat, every other day (approximately 5 mg/kg bw/d)
<b>Premating Exposure period for males</b>	Not described
<b>Premating Exposure period for females</b>	Not described
<b>Control Group and Treatment</b>	Ten control animals received only the vehicle oil.
<b>Frequency of Treatment</b>	Every other day
<b>Remarks for Test Conditions</b>	Two mg benzaldehyde was administered by gavage to 10 breeding age rats every other day (approximately 5 mg/kg bw/d) for a period of 32 weeks. Ten control animals received only the vehicle oil. Two pregnancies per rat were studied, one at 75 days and one at 180 days. The parameters examined included the number of pregnant females, number of offspring born, pup body weights at days 7 and 21 postpartum, and pup vitality.
<b>Appropriate statistical</b>	Not described

## evaluations

<b>Remarks for Results</b>	There was no statistical significant difference between treatment and control groups. It was reported that fewer females in the treated group became pregnant; however, no data or statistical analyses were performed, and the authors concluded that treatment did not cause a significant change in any of the parameters measured.
<b>Actual dose received by dose level and sex</b>	Approximately 5 mg/kg bw/d
<b>Parental data and F1 as Appropriate</b>	Fewer treated females became pregnant; however, significance could not be determined.
<b>Offspring toxicity F1 and F2</b>	No effects reported.
<b>Conclusion remarks</b>	It was concluded that treatment did not affect reproduction.
<b>Data Reliabilities Qualities</b>	Reliability code 4. Not assignable.
<b>Remarks for Data Reliability</b>	Code 4. Only secondary literature (review, tables, books, etc.).
<b>References</b>	Sporn A., Dinu, I., and Stanclu, V. (1967) Cercetari cu privire la toxicitatea aldehidei benzoice. [Research regarding the toxicity of benzaldehyde.] Igiena, 16(1), 23.

## 4.5 Developmental Toxicity

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for the structurally related substance terephthalic acid
<b>Test Type</b>	Teratology
<b>GLP</b>	Yes
<b>Year</b>	1989
<b>Species/strain</b>	Rat/Sprague-Dawley
<b>Sex</b>	Female
<b>Route of Administration</b>	Inhalation

<b>Duration of Test</b>	20 days
<b>Doses/concentration Levels</b>	1.0, 5.0, and 10.0 mg/m <sup>3</sup>
<b>Exposure Period</b>	6 hours/day on days 6-15 of gestation
<b>Frequency of Treatment</b>	Daily
<b>Control Group and Treatment</b>	Yes, control group exposed to filtered room air
<b>Remarks for Test Conditions</b>	Female rats weighing 117-150 g were quarantined and housed 2/cage with 1 male. Confirmation of mating was via evidence of sperm in a vaginal smear (Day 0), after which females were housed singly. The study consisted of 26-27 timed-pregnant dams per dose level. Exposures were by whole body inhalation conducted in 2 m <sup>3</sup> chambers with an airflow rate of 305-420 l/min. Test article was ground to respirable-sized particles using a Retsch Ultra-Centrifugal Mill. Chambers were sampled 2x/exposure period and TPA levels were determined by spectrophotometric analysis. Particle size (7-10 µm) was determined using a cascade impactor. Temperature, humidity and airflow were measured hourly. Animals were observed twice daily and given detailed physical exams daily on days 0 and 6-20. Dams were weighed on Days 0, 5 (randomization into groups), 6 (exposure initiation), 11, 16, and 20 (study termination). Standard "guideline" postmortem procedures were carried out on the females and their fetuses. Data were analyzed in an appropriate statistical manner using log transformations, multivariate ANOVA, single factor ANOVA and Dunnett's-"t"-test depending on the nature and type of end-point assessed. The dam was considered to be a random factor and the pup a nested factor within the dam.
<b>NOAEL(NOEL) maternal toxicity</b>	Greater than 10.0 mg/m <sup>3</sup>
<b>NOAEL (NOEL) developmental toxicity</b>	Greater than 10.0 mg/m <sup>3</sup>
<b>Maternal data with dose level</b>	No mortalities occurred in any group. The incidences of clinical signs observed in rats exposed to TPA were similar to controls. No statistically significant differences were noted in mean dam body weight or weight gain, uterine weight, or implant number.
<b>Fetal Data with Dose Level</b>	No statistically significant differences were noted in mean litter weights, pup viability, or number of fetal malformations. External soft tissue examinations did not indicate any differences from control. However, internal examinations showed a slight increase in the incidence of rib anomalies in the middle dose (5.0 mg/m <sup>3</sup> ) group. This was only significant when all the various types of rib anomalies were added together.
<b>Appropriate statistical evaluations</b>	Yes
<b>Remarks for Results</b>	Rib anomalies were not deemed to be an indicator of teratogenesis because they were common variations, were not elevated in a dose-related manner, and occurred at a rate that was within the range of the laboratories own historical controls. Furthermore, no other signs of embryotoxicity were associated

with this change

<b>Conclusion remarks</b>	There was no evidence of maternal or developmental toxicity at atmospheric concentrations up and including 10.0 mg/m <sup>3</sup>
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Code 2. Basic data given: comparable to guidelines/standards.
<b>References</b>	Amoco Corporation (1989b) A Segment II Inhalation Teratology Study of Terephthalic Acid in Rats. Conducted by IIT Research Institute. IITRI Study #1448.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for in vivo metabolite terephthalic acid
<b>Method/Guideline</b>	Postnatal mouse screening test (Chernoff and Kavlock, 1982; Waters, 1983)
<b>Test Type</b>	Developmental
<b>GLP</b>	Yes
<b>Year</b>	1986
<b>Species/strain</b>	Mouse/CD-1
<b>Sex</b>	Female
<b>Route of Administration</b>	Gavage
<b>Duration of Test</b>	Up to day 3 postpartum
<b>Doses/concentration Levels</b>	0 or 550 mg/kg bw/d in corn oil
<b>Exposure Period</b>	Gestation days 6-15
<b>Frequency of Treatment</b>	Daily
<b>Control Group and Treatment</b>	The control group received corn oil only.
<b>Remarks for Test Conditions</b>	In a preliminary dose range-finding study, groups of 4 CD-1 mice were administered 200, 380, 720, 1,370, or 2,605 mg benzyl alcohol/kg bw/d by gavage during gestation days 6-15. No control group was used. All animals died at the highest dose and 2 animals died at the second highest dose. At 720 mg/kg bw/d, there was no signs of toxicity except for reduced
<b>NOAEL(NOEL) maternal toxicity</b>	Greater than 550 mg/kg bw/d
<b>NOAEL (NOEL) developmental toxicity</b>	Greater than 550 mg/kg bw/d
<b>Maternal data with dose level</b>	All parameters tested, including average number of live pups/litter, postnatal survival, and pup body weight, were

statistically similar for the treated and control animals.

<b>Fetal Data with Dose Level</b>	All parameters tested, including gestation index were statistically similar for the treated and control animals.
<b>Appropriate statistical evaluations</b>	Yes. Results were analyzed by Bartlett's test, F-test, ANOVA, Fischer's exact test, Mann-Whitney U-Test
<b>Conclusion remarks</b>	In this assay, benzyl alcohol did not produce evidence of developmental toxicity.
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restriction.
<b>Remarks for Data Reliability</b>	Audited study conducted under GLP.
<b>References</b>	York R.G., Barnwell, P. and Bailes, W. (1986) Final Report. Screening of Priority Chemicals for Reproductive Hazards. Environmental Health Research & Testing, Inc. No. ETOX-85-1002.

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance dimethyl terephthalate
<b>Species/strain</b>	Rat/Wistar
<b>Sex</b>	Female
<b>Route of Administration</b>	Oral-Gavage
<b>Doses/concentration Levels</b>	1000 mg/kg
<b>Exposure Period</b>	Gestation days 7-16
<b>Frequency of Treatment</b>	Single daily exposure
<b>Control Group and Treatment</b>	Yes, concurrent no treatment
<b>NOAEL(NOEL) maternal toxicity</b>	Greater than 1000 mg/kg
<b>NOAEL (NOEL) developmental toxicity</b>	Greater than 1000 mg/kg
<b>Remarks for Results</b>	Animals were sacrificed on Day 21. No abnormal developmental effects and no pre- or post-implantation losses were noted. No maternal effects were noted.
<b>Data Qualities Reliabilities</b>	Reliability code 3. Not reliable.
<b>Remarks for Data Reliability</b>	Code 3. Documentation insufficient for assessment.
<b>References</b>	Hoechst AG (1986). Dimethyl terephthalate, investigation of embryotoxic action in Wistar rats on oral administration. Unpublished report No. 86.0859. Commissioned by the Employment Accident Insurance Fund of the Chemical industry. Dimethyl terephthalate, BG Chemie Toxicological Evaluations 1

<b>Substance Name</b>	Methyl 4-formylbenzoate
<b>CAS No.</b>	001571-08-0
<b>Remarks for Substance</b>	Data are for structurally related substance benzaldehyde
<b>Method/Guideline</b>	Postnatal mouse screening test (Chernoff and Kavlock, 1982)
<b>Test Type</b>	Developmental
<b>GLP</b>	Yes
<b>Year</b>	1983
<b>Species/strain</b>	Mouse/CD-1
<b>Sex</b>	Female
<b>Route of Administration</b>	Gavage
<b>Duration of Test</b>	Up to day 3 postpartum
<b>Doses/concentration Levels</b>	750 mg/kg bw/d
<b>Exposure Period</b>	Gestation days 6-13
<b>Frequency of Treatment</b>	Daily
<b>Control Group and Treatment</b>	A control group of 50 mice gavaged with distilled water only.
<b>Remarks for Test Conditions</b>	750 mg benzyl alcohol/kg bw/day was administered by gavage to 50 mice on gestation days 6-13. A control group of 50 animals were given distilled water only. Maternal body weight gain and mortality, mating, gestation, numbers of live and dead pups per litter, total litter weight on days 1 and 2 postpartum, litter weight change between days 1 and 3 postpartum, and pup survival on days 1 and 3 postpartum were recorded. Clinical signs of maternal toxicity were reported.
<b>Maternal data with dose level</b>	Clinical signs of maternal toxicity included hunched posture, tremors, inactivity, prostration, hypothermia, ataxia, dyspnea, swollen or cyanotic abdomen, and piloerection. There was no significant difference in maternal body weight measured on days 4 and 7 of gestation between treated and control animals. However, statistically significant decreases were observed in treated females on gestation day 18 and day 3 postpartum. Maternal body weight gain during days 7-18 of gestation was also significantly lower than that of controls. Eighteen deaths were reported during the treatment period and they were all attributed to the treatment. One more death was reported the day after treatment was terminated.
<b>Fetal Data with Dose Level</b>	Significant differences were also observed in pup body weight and weight gain, including mean pup weight per litter, mean

	litter weight change, and mean pup weight change (between day 1 and 3 postpartum). No differences were observed in the mating or gestation indices, the total number of resorptions, the number of live pups per litter, or in pup survival.
<b>Appropriate statistical evaluations</b>	Yes. Results were analyzed by ANOVA, Kruskal-Wallis H test, and ANCOVA.
<b>Conclusion Remarks</b>	Although the authors concluded that benzyl alcohol was a potential reproductive hazard, the effects observed were in conjunction with significant maternal toxicity.
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	NIOSH study. Audited and found to follow SOPs, but not reported to be GLP.
<b>References</b>	Hardin B.D., Schuler R.L., Burg J.R., Booth G.M., Hazelden K.P, MacKenzie K.M., Piccirillo V.J., and Smith K.N. (1987) Evaluation of 60 chemicals in a preliminary developmental toxicity test. <i>Teratog. Carcinog. Mutag.</i> , 7, 29-48.