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(Attn: Section 8(e) Coordinator)
Office of Toxic Substances
U.S. Environmental Protection Agency
401 "M" Street S.W.
Washington, DC 20460

A

Dear Mr. Williams,

Please find enclosed a copy of "Review of Toxicology Data and Derivation of Occupational Exposure Levels on Methyl-3-Methoxypropionate". JSR Electronics Inc. received this review article on September 1, 1993 from our parent company JSR, Tokyo, Japan.

JSR Electronics Inc. was not able to verify whether all new information referred to in this report had been reported to EPA (See table 1 and references).

Since all information in the report is used to set new manufacturer proposed exposure levels for Methyl-3-methoxypropionate, JSR Electronics wishes to notify under TSCA 8(e) to EPA the existence of this review report and its referred into studies .

Sincerely,

Jan Vandendriessche, Ph.D.
Vice President

Enclosure
Review report Showa Denko (7/27/93)

RECEIVED 9-30-93

31 pgs.

REVIEW OF TOXICOLOGY DATA AND DERIVATION OF OCCUPATIONAL EXPOSURE LEVELS ON METHYL-3-METHOXYPROPIONATE

CAS # 3852-09-3

Prepared for

Showa Denko K.K.
Tokyo, Japan

Prepared by

ENVIRON Corporation
Arlington, Virginia

July 27, 1993

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I. INTRODUCTION

At the request of Showa Denko, K.K., ENVIRON reviewed the available toxicology data on methyl-3-methoxypropionate (MMP). The purpose of this review was to develop the toxicity section of a material safety data sheet and to propose occupational exposure limits for this chemical. The data relied upon for this review were primarily provided by Showa Denko K.K. A literature search was also conducted to identify any additional scientific papers on the toxicity of MMP.

Section II of this report contains a review of the toxicity data on MMP. Section III documents the derivation of proposed occupational exposure limits for MMP. Finally, Appendix A contains a table that summarizes the toxicity studies on MMP that were reviewed.

II. REVIEW OF METHYL-3-METHOXYPROPIONATE TOXICITY

Toxicity data for methyl-3-methoxyproprionate (MMP) are limited to several short-term and less-than chronic duration exposure studies in laboratory animals. These studies are presented in Table 1 and briefly summarized below.

A. Short-term Exposure

Single-dose exposure studies indicate that MMP has very low acute toxicity by both inhalation and oral exposure. High median lethal concentrations (LC_{50}) and median lethal doses (LD_{50}) have been reported in rodents. For inhalation, an LC_{50} (exposure duration not reported) of 40 g/m^3 has been reported for mice (RTECS 1993). In rats, the 6-hour LC_{50} was 2,776 ppm, about 13.4 g/m^3 (Kodak 1986b). Oral LD_{50}s of 2,300 mg/kg and 4,900 mg/kg have been reported for mice and male rats, respectively (SDKK 1993).

Effects in the nervous system also have been reported in rats exposed to high doses of MMP for short exposure durations. Signs of neurotoxicity included lethargy, defective muscular coordination, and hindlimb weakness in rats exposed to air concentrations of 1,900 ppm MMP and above or administered a single gavage dose of 5 g/kg (Kodak 1986a,b). Histopathology in rats orally dosed with MMP showed necrotic lesions in the spinal cord and brain stem, suggesting that neurological effects may be secondary to decreased blood supply and oxygen deficiency.

MMP caused irritation in two experimental animals when exposed by either inhalation, oral administration, or direct contact to the skin or eyes. Rats exhibited partial closing of the eyes and slow respiratory movements upon inhalation and increased salivation following a single oral dose (HRC 1990a,b). In rabbits, direct contact resulted in mild skin irritation and moderate to severe eye reactions, which were less severe and reversible when eyes were rinsed with water (HRC 1990c,d,e).

B. Repeat Exposure

Effects observed in subchronic toxicity studies are similar to those reported in single-dose, short-term exposure studies. Minimal effects in rats following inhalation for 6 hours/day for 10 days included eye irritation from 290 to 2,945 ppm and respiratory

irritation at 945 ppm and above (HRC 1991). Repeat exposure to rats for 6 hours/day, 5 days/week for 4 weeks to 1,000 and 2,000 ppm MMP caused lethargy and respiratory irritation (Kodak 1986d). Salivation was reported in rats administered 600 mg/kg/day MMP for three months and in some rats treated with 200 mg/kg/day (SDKK 1990).

C. Mutagenicity

MMP caused no reverse mutations in bacteria in the Ames assay or chromosomal aberrations in Chinese hamster ovary (CHO) cells (HRC 1990f,g).

D. Reproductive and Developmental Toxicity

A preliminary reproductive toxicity study in which rats were exposed to 0, 100, 300, or 1,000 ppm for 6 hours/day during days 6 to 15 of pregnancy indicated slight maternal toxicity at all doses (slightly lower mean body weight gain and increased water consumption) and a slight reduction in mean fetal body weight at 1,000 ppm (HRC 1991b). An increased incidence of fetal skeletal anomalies (lumbar ribs) was reported at all doses.

Potential developmental toxicity also was investigated in rats exposed to 0, 5, 50, or 500 ppm for 6 hours day from days 6 to 15 of pregnancy (HRC 1993). No significant adverse effects were noted in rats treated with 50 ppm or below. Only hair loss, red/brown facial staining, and a suggested increase in water intake were observed in some rats exposed to 50 ppm. Exposure to 500 ppm caused a significant decrease in maternal body weight gain and effects to the fetus, including decreased fetal body weight and litter weight and increased skeletal anomalies. Skeletal anomalies reported in this study were consistent with those reported in the preliminary reproductive toxicity study described above.

E. Identification of No-Observable-Adverse-Effect Level

Survey of the available toxicity data shows that only a small number of studies assess the potential toxic effects of MMP following short-term, repeat exposures. Review of these limited studies shows that the study designed to investigate MMP toxicity at the lowest dose levels is the main reproductive and developmental toxicity study. As described above, damage to the developing fetus was demonstrated in pregnant rats exposed to at least 500 ppm (HRC 1993). The study also tested concentrations lower than 500 ppm (0, 5, and 50 ppm) and found no significant adverse effects in either dams or fetuses at 50 ppm or below. Based on this study, 50 ppm is considered the maximum air concentration to which an

individual may be exposed without experiencing adverse health effects of MMP and is identified as the highest no-observable-adverse-effect level (NOAEL).

III. DERIVATION OF PROPOSED OCCUPATIONAL EXPOSURE LIMITS FOR METHYL-3-METHOXYPROPIONATE (MMP)

A. Methodology

When deriving exposure limits for occupational exposure to a chemical, the most appropriate source of information is from human experience of exposure to the chemical. For many chemicals that have been in commercial use for many years, the exposure limits are based on such human data. For new chemicals, however, data from human exposure are rarely available, and it becomes necessary to rely on data from experimental animal studies. This is the case with MMP.

Deriving an exposure limit from experimental animal data involves two conservative steps that tend to result in an exposure limit that is very protective of human health. The first step involves identification of the most sensitive animal study. This is the study showing effects at the lowest exposure level. The no-observable-adverse-effect level (NOAEL) from that study represents an estimate of the threshold dose level below which adverse effects are not expected to occur. Because the NOAEL represents a dose level at which no adverse effects are seen, it is, by definition, below the experimental threshold dose. This is the first conservative step.

The second conservative step involves application of one or more uncertainty or safety factors to this exposure level. This is done because there is some uncertainty regarding the relative sensitivity of humans and of the experimental animals in the study from which the NOAEL was derived, and because there is some limitation in the sensitivity of the animal studies because of the relatively small numbers of animals that can be studied. Because regulatory agencies tend to err on the side of safety, it is normal regulatory practice to assume that humans may be more sensitive than the experimental animals in the study from which the NOAEL was derived.

Regulatory agencies in the United States, such as the Environmental Protection Agency and the Food and Drug Administration have commonly used an uncertainty factor of 100-fold when extrapolating from an animal NOAEL to an acceptable exposure level for the general population. This 100-fold factor is commonly thought of as comprising two ten-fold factors, one for extrapolating from the animals to the average human, and one to cover the possible

range of differential sensitivity within the entire human population, including the very young, the very old, and other unusually sensitive groups. For the reasons documented below, however, such a large uncertainty factor is unnecessary in the context of occupational exposure limits, and has generally not been applied in the past in setting occupational limits.

First, there is no reason to believe that humans are, in general, ten times more sensitive than the most sensitive experimental animal species, particularly when the comparison is based on the concentration of the substance in the air. Dourson and Stara (1983) have suggested that humans may be more sensitive than rats by a factor of about six-fold when the dose they receive is expressed on a mg/kg body weight scale. However, when exposed by inhalation, rats receive a much higher dose of a chemical than do humans because of the rats' higher inhalation rate in relation to their body weight. When exposed to a chemical in the air at a concentration of 1 mg/m^3, a human will inhale about 10 mg of the chemical in an 8-hour work day, for a dose of 10/70 = 0.14 mg/kg. A rat, with a body weight of 300 g and a minute volume of 0.225 liters/minute (Leong et al. 1964) would inhale a dose of:

$$\frac{0.225\ (liters/min) \times 60\ (min/hr) \times 8\ (hr)}{1000\ (liters/m^3) \times 0.3\ (kg)} = 0.36\ mg/kg.$$

Thus, at the same air concentration, a rat would receive a dose 0.36/0.14 = 2.6-times higher than a human. Even if a human were ten times more sensitive than a rat on a mg/kg basis, he would be only 10/2.6 = about four-times more sensitive when compared on the basis of the air concentration, and based on Dourson and Stara (1983), a human would be only 6/2.6 = 2.3-fold more sensitive. Hence an uncertainty factor of 4 is more than adequate for interspecies extrapolation of an acceptable air concentration from rats to the <u>average</u> human.

In addition, the full range of potential human sensitivity is not represented in the occupational setting because the work-force does not include the very young and the very old. Hence, a smaller factor (perhaps five-fold) will provide adequate protection. Based on a different argument, Calabrese and Gilbert (1993) also recently proposed that a factor of five-fold is appropriate for inter-individual variability when extrapolating from animal data. They noted that if the standard 10-fold factor is thought to represent the range of human sensitivity from the most sensitive to the least sensitive, then the range from <u>average</u> human sensitivity to the most sensitive would be half of this, or five-fold. As a result, a total uncertainty factor of about 20-fold (4-fold from the average rat to the average human and 5-

fold from the average human to the most sensitive human, or at least to the most sensitive worker) will provide adequate protection of healthy workers when extrapolating from a rat inhalation study.

B. Selection of NOAEL for Derivation of Time Weighted Average (TWA) Exposure Limit

The proposed TWA exposure limit is based on a no-observed-adverse-effect level (NOAEL) of 50 ppm for developmental toxicity in rats (HRC 1993). This represents the most sensitive toxicity endpoint of those examined. In the study, rats were exposed to concentrations of 0, 5, 50, or 500 ppm MMP by inhalation during days 6 through 15 of pregnancy. A significant decrease in maternal body weight gain and effects on the fetus, including decreased fetal body weight and litter weight and increased skeletal anomalies, were observed at 500 ppm. No significant adverse effects were observed in pregnant rats or fetuses exposed to 50 ppm or below. Hair loss, red/brown facial staining, and a suggested increase in water intake were observed in some rats exposed to 50 ppm, but these are not considered to represent significant adverse effects. Therefore, the TWA exposure limit was derived using 50 ppm as the highest NOAEL.

C. Derivation of Proposed TWA Exposure Limit

To derive a TWA exposure limit appropriate for occupational exposure eight hours per day, the NOAEL concentration was adjusted by a factor of 6/8 because the rats were exposed just 6 hours/day, and divided by an uncertainty factor of 20. The calculation is as follows:

$$\textit{TWA Exposure Limit} = \frac{\textit{NOAEL Concentration} \times \textit{Exposure Adjustment}}{\textit{Safety Factor}}$$

$$= \frac{50 \times 6/8}{20}$$

$$= 2\ ppm$$

As discussed above, an uncertainty factor of 20 is appropriate for the derivation of an occupational exposure limit based on a rat inhalation study.

Further support for the use of an uncertainty factor of 20 in the derivation of an exposure limit for MMP comes from its reproductive and developmental toxicity relative to glycol ethers. In a Federal Register notice on March 23, 1993, the OSHA proposed to lower the permissible exposure limit (PEL) for two glycol ethers (2-ethoxyethanol, 2-EE and 2-ethoxyethanol acetate, 2-EEA) from 5 ppm to 0.5 ppm (55 FR 15526-15632). The proposed PEL for these glycol ethers also is based on a NOAEL of 50 ppm but OSHA proposed using an uncertainty factor of 100 to derive the PEL. 2-EE and 2-EEA caused severe developmental toxicity with no maternal toxicity at doses only slightly above the 50 ppm NOAEL. MMP, however, caused only mild developmental effects and only at maternally toxic doses. Hence, the reproductive and developmental effects of MMP are less serious than those associated with exposure to 2-EE and 2-EEA and it is appropriate to use a smaller uncertainty factor and derive a higher exposure limit for MMP than that proposed by OSHA for 2-EE and 2-EEA.

D. Derivation of Short-Term Exposure Limit (STEL)

Insufficient data are available to support the independent derivation of a STEL for MMP. The information indicating that MMP has irritant properties by all routes of exposure (inhalation, oral and dermal) strongly suggests that a STEL would be useful to avoid irritant reactions. In the absence of human studies, it is not possible to determine accurately what the STEL should be to avoid irritation. Rather than derive an independent STEL based on data on MMP itself, we have examined other chemicals that have had TWA exposure limits (Threshold Limit Values, TLV-TWAs) and STELs assigned by the American Conference of Governmental Industrial Hygienists (ACGIH) to determine what is the range of factors separating the TLV-TWA and the STEL for substances with irritant properties (excluding non-irritant substances like carbon dioxide and carbon monoxide that have a very wide margin between the TLV-TWA and the STEL — 6-fold and 8-fold, respectively). Based on a review of current values, this range is 1.25-fold (e.g., 1,1-dichloroethane, ethyl benzene, ethyl ether, heptane, isoamyl alcohol, methyl acetate) to 4-fold (e.g., perchloroethylene, toluene-2,4-diisocyanate, trichloroethylene). Based on the range of values reported, and the relatively low degree of irritancy of MMP, a factor of 2 seems appropriate for MMP, giving a STEL of $2 \times 2 = 4$ ppm.

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Toxicity Studies Provided by Showa Denko K.K.

Showa Denko K.K. (SDKK). 1993. *Material safety data sheet.* (English translation of MSDS used in Japan.)

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APPENDIX A

Toxicological Studies for Methyl-3-Methoxypropionate Provided by Showa Denko K.K.

TABLE 1
Toxicological Studies for Methyl-3-methoxypropionate
Provided by Showa Denko K.K.

Study Type (Test Code Number)	Study Design				Reported Effects	Comments and Author's Conclusions	Study Conductor*
	Species	MMP	Route	Exposure Frequency and Duration			
Acute Toxicity Studies: Inhalation							
Submitted to USEPA, OTS (8EHQ-0486-0599; 88-8600074)	LC_{50} study: ♂ & ♀ rats (no. & species not reported)	Not reported	Inhalation (whole-body)	Single exposure 965, 1,968, or 3,656 ppm vapor, 6 hrs	All ♂ & all but 1 ♀ dead during exposure to high dose. Ataxia & signs of hindlimb weakness in surviving ♀.	Reported preliminary results of inhalation LC_{50}. Kodak not aware of any adverse health effects related to compound. Concluded no substantial risk of exposure.	Kodak 1986a[15]
Interim Report: Acute Inhalation Toxicity Study in Rats (230765Y TX-86-134) [Submitted by Kodak for 8EHQ-0486-0599]	20 ♂ & 20 ♀ weanling (CRL:CD® (SD) BR) rats (5 rats/sex/ group), ♂ 221-257 g bw & ♀ 188-211 g bw (Charles River, MA, U.S.A.)	Lot no. 002371586 (>99.9% purity)	Inhalation (whole-body)	0, 950, 1,900, or 3,800 ppm vapor, 6 hrs	♂ & ♀ at 950 & 1,900 ppm survived with no clinical signs of toxicity. Reversible lethargy in ♂ & ♀ during exposure to 1,900 ppm. Moderate lethargy in 5/5 ♂ & 4/5 ♀ at 3,800 ppm prior to dying. Hindlimb weakness/paralysis in surviving ♀.	Describes studies & results for LC_{50} studies above (8EHQ-0486-0599; 88-8600074). In compliance with GLP; no QA statement since interim. Observed for 14 days. No significant effects at 1,900 ppm. LC_{50} 2,776 ppm with 95% CI 2,372-3,250 ppm.	Kodak 1986b[15]
Acute Inhalation Toxicity in Rats - 4-Hour Exposure (SHD 97/90389)	10 ♂ & 10 ♀ Albino Sprague-Dawley rats (5 rats/sex/ group), 200 g bw (Charles River U.K.)	Lot no. 89227-M3 (99.7% purity)	Inhalation (whole-body)	Mean 5.83 mg/ℓ vapor & droplets, 4 hrs (continuous)	Partial closing of eyes (2-4 hrs), slow respiratory movements (1-4 hrs), & reduced response to external stimuli (0.25-4 hrs) during exposure.	In compliance with GLP & QA statement. No effects during 14-day observation period. No macro or micro pathological effects. Effects indicated a mildly irritant vapor (ocular & respiratory).	Huntingdon Research Centre Ltd. 1990a[7]

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Study Type (Test Code Number)	Study Design				Reported Effects	Comments and Author's Conclusions	Study Conductor*
	Species	MMP	Route	Exposure Frequency and Duration			
Acute Toxicity Studies: Oral							
Acute Neurotoxicity Study in Rats (598-003)	25 ♂ & 25 ♀ Charles River CD rats (5 rats/sex/ group), ♂ 377-485 g bw & ♀ 205-240 g bw (Charles River Labs, MI, U.S.A.)	Lot no. 26001	Oral (gavage)	Single dose 10 mℓ/kg of 0, 200, 600, or 2,000 mg/kg MMP in w/v solution in water or 5,000 mg/kg MMP in w/v suspension * Suspension at that level due to insolubility	High mortality in high dose group. Increased or labored respiration 1 hr post-dose & on days 2-4 in 1-2 rats at 2,000 mg/kg & 1 surviving rat at 5,000 mg/kg 1 hr post-dose. Increased salivation in 1 rat each at 2,000 & 5,000 mg/kg at 1 hr post-dose. Gasping, convulsions, & increased salivation at 5,000 mg/kg; abnormal vocalization in 2 ♂, & lethargy in 1 ♂ 4 hrs post-dose.	In compliance with GLP & QA statement. Observed 14 days. No pathological changes (macro in lungs or lymph nodes or micro) considered to be treatment-related. Other neuropharmacological signs observed periodically: rearing, urination, & defecation in all groups throughout study, vocalization in 1 ♂ at 200 mg/kg 1 hr post-dose, piloerection in 1 control ♂ & 1 ♂ at 2,000 mg/kg 1 hr post-dose, & lacrimation in 1 ♀ at 2,000 mg/kg 1 hr post-dose.	International Research and Development Corporation 1991[10]

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Study Type (Test Code Number)	Study Design				Reported Effects	Comments and Author's Conclusions	Study Conductor*
	Species	MMP	Route	Exposure Frequency and Duration			
Submitted to USEPA, OTS (8EHQ-0486-0599; 88-8600074)	LD_{50} study: 15 ♂ & 15 ♀ rats (5 rats/sex/group) (species not reported) Additional test: 5 ♂ & 5 ♀ rats	Not reported	Oral	Single dose 1,250, 2,500, or 5,000 mg/kg Single dose 3,500 mg/kg (♂) & 1,700 mg/kg (♀)	No mortality at 1,250 mg/kg. At 2,500 mg/kg, 3/5 ♂ normal & death in 1/5 ♂ & 4/5 ♀ after 1 day. 4/5 ♂ & 5/5 ♀ dead at 5,000 mg/kg. Hindlimb weakness in 1/5 ♂ (severe) & 1/5 ♀ at 2,500 mg/kg & 1/5 ♂ at 5,000 mg/kg. Death of 3/5 ♂ & 2/5 ♀. Hindlimb weakness in 1 ♂. No effects in 2/5 ♂ & 3/5 ♀.	Reported preliminary results of oral LD_{50} study. Kodak not aware of any adverse health effects related to compound. Concluded no substantial risk of exposure. Histopathology of 1 ♂ & 1 ♀ with hindlimb weakness in LD_{50} study showed necrotic lesions in spinal cord & brain stem (possibly related to decreased blood supply and oxygen deficiency).	Kodak 1986a[15]
Final Report: Acute Oral Toxicity Study (230818R TX-86-177) [Submitted by Kodak for 8EHQ-0486-0599]	15 ♂ & 15 ♀ rats (CRL:CD® (SD) BR), ♂ 174-211 g bw & ♀ 157-212 g bw (Charles River, MA, U.S.A.) Additional test: 5 ♂ & 5 ♀ rats	Lot no. 002371586 (>99.9% purity)	Oral (gavage)	Single dose 1,250, 2,500, & 5,000 mg/kg Single dose 3,500 mg/kg (♂) & 1,700 mg/kg (♀)	1,250 mg/kg caused slight to severe weakness in all rats but no abnormal neurological signs. Majority of animals died at 2,500 & 5,000 mg/kg & had lesions, which were not seen in rats who survived 2-wk observation period.	Describes studies & results for LD_{50} studies above (8EHQ-0486-0599; 88-8600074). In compliance with GLP. Observed 24 hrs & for 14-15 days. LD_{50} (mg/kg) determined based on results: Group / LD_{50} / 95% CI ♂ / 2,973 / 1,807-4,891 ♀ / 1,768 / 1,340-2,333	Kodak 1986c[15]

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Provided by Showa Denko K.K.

Study Type (Test Code Number)	Study Design				Reported Effects	Comments and Author's Conclusions	Study Conductor*
	Species	MMP	Route	Exposure Frequency and Duration			
Acute Oral Toxicity to Rats (891483D/ SHD 94/AC) - Preliminary Study	2 ♂ & 2 ♀ CD rats [Cr1:CD®(SD)BR VAF plus] (Charles River U.K.)	Lot no. 89227-M3 (99.7% purity)	Oral (gavage)	Single dose 2.5 g/kg	No mortality observed.	In compliance with GLP & QA statement. Observed 5 days. LD_{50} >2.5 g/kg bw.	Huntingdon Research Centre Ltd. 1990b[2]
Acute Oral Toxicity to Rats (891483D/ SHD 94/AC) - Main Study	15 ♂ & 15 ♀ rats [Cr1:CD®(SD)BR VAF plus], 101-150 g bw (5 rats/sex/group) (Charles River U.K.)	Lot no. 89227-M3 (99.7% purity)	Oral (gavage)	Single dose 2.0, 3.2, or 5.0 g/kg (2.0, 3.2, or 5.0 mℓ/kg)	Mortality in ♂ & ♀ at 5.0 g/kg & in 1 ♀ at 3.2 g/kg (within 1 hr to day 2). Slight lung congestion in 1 ♂ & 1 ♀ at autopsy. Hair stiffening within 5 mins & hunched posture in all rats; salivation & abnormal gait in all groups; & lethargy, pallor of extremities, reduced respiratory rate, & ptosis at mid & high doses. Ataxia in 2 ♂ & 3 ♀ at 5.0 g/kg, & 1 ♂ & 3 ♀ at 5.0 g/kg prostrate.	In compliance with GLP & QA statement. Observed 14 days. Recovery by day 3. Reported LD_{50} & 95% CI (g/kg) values: Group / LD_{50} / 95% CI ♂ & ♀ / 4.2 / 3.6-5.0 ♂ / 4.9 / 3.9-6.1 ♀ / 3.7 / 3.1-4.4	Huntingdon Research Centre Ltd. 1990b[2]

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Toxicological Studies for Methyl-3-methoxypropionate
Provided by Showa Denko K.K.

Study Type (Test Code Number)	Study Design				Reported Effects	Comments and Author's Conclusions	Study Conductor*
	Species	MMP	Route	Exposure Frequency and Duration			
Dermal Toxicity Studies							
Irritant Effects on Rabbit Skin (90125D/SHD 95/SE)	1 ♂ & 5 ♀ New Zealand White (albino) rabbits, 2.4-3.0 kg bw (Froxfield Farms U.K.)	Lot no. 89227-M3 (99.7% purity)	Dermal Contact	0.5 mℓ applied to shaved & intact skin under dressing for 4 hrs	Very slight erythema in 1 ♂ & 2 ♀ after 30 mins that resolved on day 4 (1 on scale of 0-4).	In compliance with GLP & QA statement. Observed after 30 mins & on days 2-4. Single application caused transient mild dermal irritation. No edema or eschar formation.	Huntingdon Research Centre Ltd. 1990c[4]
Ocular Toxicity Studies							
Irritant Effects on Rabbit Eye (90126D/SHD 96/SE)	1 ♂ New Zealand White (albino) rabbit, 2.96 kg bw (Froxfield Farms U.K.)	Lot no. 89227-M3 (99.7% purity)	Ocular Contact	0.1 mℓ in lower everted lid of 1 eye (other eye left untreated as control)	Dulling of cornea after 1 hr; very slight to well defined corneal opacity from day 1-7 (1-2 on scale of 0-4); iridial inflammation from days 3-4 (1 on scale of 0-2); moderate redness of conjunctivae from day 1-7 (1-2 on scale of 0-3); & slight to moderate swelling of conjunctivae from day 1-4 (1-2 on scale of 0-4).	In compliance with GLP & QA statement. Observed after 1 hr & days 1-4, 7, & 14. Instillation into the eye of 1 rabbit caused moderate to severe ocular reactions. No other animals tested due to intensity of response.	Huntingdon Research Centre Ltd. 1990d[5]

TABLE 1
Toxicological Studies for Methyl-3-methoxypropionate
Provided by Showa Denko K.K.

Study Type (Test Code Number)	Study Design				Reported Effects	Comments and Author's Conclusions	Study Conductor*
	Species	MMP	Route	Exposure Frequency and Duration			
Irritant Effects on the Rabbit Eye Following Irrigation (90551D/SHD 99/SE)	3 ♀ New Zealand White (albino) rabbits, 2.4-3.3 kg (Froxfield Farms U.K.)	Lot no. 89227-M3 (99.7% purity)	Ocular Contact	0.1 mℓ in lower everted lid of 1 eye (other eye left untreated as control); treated eye rinsed with water 30 sec after instillation for 30 sec	Dulling of cornea after 1 hr in 2 animals. Corneal opacities from day 1 up to 7. Extent of corneal opacities: very slight to slight for density (1-2 on scale of 0-4) & very slight to well-defined for area (1-4 on scale of 0-4). From day 1 up to 7, slight to moderate redness of conjunctivae (1-2 on scale of 0-3) & very slight to slight swelling of conjunctivae (1-2 on scale of 0-4).	In compliance with GLP & QA statement. Observed after 1 hr & days 1-4, 7, & 14. Corneal opacification & slight to well defined conjunctival reactions observed. Irrigation of the eyes 30 secs after instillation slightly reduced the irritant potential of MMP. Corneal opacities & all conjunctival reactions resolved by day 7 or 14.	Huntingdon Research Centre Ltd. 1990e[9]

TABLE 1
Toxicological Studies for Methyl-3-methoxypropionate
Provided by Showa Denko K.K.

Study Type (Test Code Number)	Study Design				Reported Effects	Comments and Author's Conclusions	Study Conductor*
	Species	MMP	Route	Exposure Frequency and Duration			
Subacute and Subchronic Toxicity Studies: Inhalation							
Interim Report: 4-Week Inhalation Toxicity in Rats (230813L TX-86-172) [Submitted by Kodak for 8EHQ-0486-0599]	20 ♂ & 20 ♀ weanling rats (CRL:CD® (SD) BR) (5 rats/sex/group) (species not reported), ♂ 229-247 g bw & ♀ 191-216 g bw (Charles River, MA, U.S.A.)	SRID or Lot no. 002371586 (>99.9% purity)	Inhalation (whole-body)	0, 500, 1,000, or 2,000 ppm vapor, 6 hrs/day, 5 days/wk, for 4 wks (22 exposures in 32 days)	Minimal lethargy at 1,000 ppm on days 15, 21, 28, & 29. Slight lethargy during most exposures to 2,000 ppm. Clinical signs of irritation (brown discoloration of face hair in 2 ♀, & excessive salivation in 1 of these ♀) that resolved within a few days. Alkaline phosphatase values 2x's compared in control in ♀ but not ♂.	In compliance with GLP; no QA statement since interim. Preliminary results indicate that up to 2,000 ppm for 4 wks caused minimal effects in rats, including lethargy & irritation.	Kodak 1986d[15]

TABLE 1
Toxicological Studies for Methyl-3-methoxypropionate
Provided by Showa Denko K.K.

Study Type (Test Code Number)	Study Design				Reported Effects	Comments and Author's Conclusions	Study Conductor*
	Species	MMP	Route	Exposure Frequency and Duration			
10-Day Preliminary Inhalation Study in Rats (SHD 100/91150)	20 ♂ & 20 ♀ Albino Sprague-Dawley CD rats (5 rats/ sex/group), ♂ 169 g bw & ♀ 142-145 g bw (Charles River U.K.)	SDKK	Inhalation (whole-body)	0, 290, 945, or 2,953 ppm (0, 1.40, 4.56, or 14.25 mg/ℓ) vapor, 6 hrs/day for 10 days * Single dose only of high dose due to mortality	Blinking and hunched posture at 290 ppm. Blinking & closed eyelids, reduced breathing rate, & prone posture at 945 ppm. Hunched posture during early exposure, & slight lacrimation near end of exposures. Testes weight significantly increased. High mortality following first exposure to 2,953 ppm. Prone posture, blinking, slight lacrimation, closed eyelids, reduced breathing rate, & pronounced & irregular breathing pattern. Congested and "not" collapsed lungs, pale spleen, congested adrenal glands, & distended urinary bladder. Convulsions & paralysis in hind limbs of 1 ♀ after day 1; paralysis persisted to end of study.	In compliance with GLP & QA statement. Observed for 2 days post exposure. Effects indicated irritation (ocular & respiratory). Difference in testicular weights in mid-dose group considered small. Slight increase in low-dose group. Toxicological significance unclear. No statistical analyses of macroscopic changes in high-dose group due to small sample size. Some abnormalities may have been related to death or agony. None in surviving high-dose animals or those killed at termination. Determined exposure levels suitable for proposed 28-day inhalation study: Low dose 100 ppm Intermediate dose 300 ppm High dose 1,000 ppm	Huntingdon Research Centre Ltd. 1991a[6]

TABLE 1
Toxicological Studies for Methyl-3-methoxypropionate
Provided by Showa Denko K.K.

Study Type (Test Code Number)	Study Design				Reported Effects	Comments and Author's Conclusions	Study Conductor*
	Species	MMP	Route	Exposure Frequency and Duration			
Subacute and Subchronic Toxicity Studies: Oral							
3-Month Subacute Toxicity Study by Oral Administration in Rats (T89-23)	48 ♂ & 48 ♀ Sprague- Dawley ([Crj:CD(SD)] rats (12 rats/ sex/group), 152-190 g bw (Charles River Japan)	Lot no. 89227-M3 (99.9% purity)	Oral (gavage)	0, 60, 200, or 600 mg/kg/day in water, 1 time/day for 3 mos	Salivation in 600 mg/kg group starting around day 9 & sporadically in 200 mg/kg group.	Study not necessarily in compliance with GLP. High dose is ¼ LD_{50} reported in Kodak studies. Salivation attributed to irritation of tongue & mucosa of oral cavity. No treatment-related testicular, hematological, or nervous system effects or organ weight changes. NOEL 200 mg/kg for both ♂ & ♀.	Showa Denko K.K. 1990[1]
Mutagenicity Studies							
Bacterial Mutation Assay (SHD 93/891799)	*Salmonella typhimurium* (TA 1535, TA 1537, TA 1538, TA 98, & TA 100) & *Escherichia coli* (WP2 uvrA)	Lot no. 89227-M3 (99.7% purity)	*In vitro*	312.5, 625, 1,250, 2,500, & 5,000 μg/plate +/- S-9 metabolic activation, incubated at 37° for 3 days	No mutagenicity observed.	In compliance with GLP & QA statement. Dose levels ≤5,000 μg/plate in water was not mutagenic in this bacterial system.	Huntingdon Research Centre Ltd. 1990f[3]

TABLE 1
Toxicological Studies for Methyl-3-methoxypropionate
Provided by Showa Denko K.K.

Study Type (Test Code Number)	Study Design				Reported Effects	Comments and Author's Conclusions	Study Conductor*
	Species	MMP	Route	Exposure Frequency and Duration			
Analysis of Metaphase Chromosomes Obtained from CHO Cells Cultured *In Vitro* and Treated in MMP (SHD 98/90271)	Cultured Chinese hamster ovary (CHO) cells, strain K_1-BH_4	Lot no. 89227-M3 (99.7% purity)	*In vitro*	0, 2.3, 4.6, 9.2, 18.4, 36.9, 73.8, 148, 295, 590, 1,180 μg/mℓ +/- S-9 metabolic activation (2 flasks each concentration & 4 flasks each control), incubated at 37° for 21 hrs 148, 490, & 1,180 μg/mℓ chosen as concentrations for metaphase analysis	Mitotic activity: MMP + S-9: 1,180 μg/mℓ reduced mitotic index (57%) when MMP + S-9 but not significant when MMP - S-9. Metaphase analysis: • MMP - S-9: Significant increase in chromosomal aberrations at 590 μg/mℓ. • MMP + S-9: Significant increase in chromosomal aberrations at 148 or 1,180 μg/mℓ. • Significantly increased chromosomal aberrations in both + controls.	In compliance with GLP & QA statement. Increased chromosomal aberrations MMP +/- S-9 was not considered to be indicative of clastogenic activity due to poor reproducibility between replicates and the mean frequency of aberrations was within the historical control range of the lab. *In vitro* studies in CHO cells showed no evidence of clastogenic activity of MMP.	Huntingdon Research Centre Ltd. 1990g[8]

TABLE 1
Toxicological Studies for Methyl-3-methoxypropionate
Provided by Showa Denko K.K.

Study Type (Test Code Number)	Study Design				Reported Effects	Comments and Author's Conclusions	Study Conductor*
	Species	MMP	Route	Exposure Frequency and Duration			
Reproductive and Developmental Toxicity Studies							
Preliminary Study of the Effect of MMP on Pregnancy of the Rat by Inhalation Exposure (SHD 101/901708)	40 ♀ Specific Pathogen Free [Crl:CD®(SD) BR VAF plus] rats (10 ♀ rats/ group), 215-248 g bw, time mated to ♂ of same strain (Charles River U.K.)	Lot no. 1.5.90/8 (99.75 purity)	Inhalation (whole-body)	0, 100, 300, or 1,000 ppm (0, 0.48, 1.45, or 4.83 mg/ℓ), 6 hrs/day from days 6-15 of pregnancy (inclusive)	Slightly lower mean bw gain from day 6 in all groups. Increased incidence of fetal skeletal anomalies at all doses (lumbar ribs). Partially closed eyes & increased mean water consumption at 300 & 1,000 ppm. At 1,000 ppm also blinking of eyelids, rubbing of snout, licking inside of mouth, & failure to respond to knock on chamber door. Fetal effects at high dose also included slightly lower mean fetal bw & increased incidence visceral anomalies (abnormal lobulation of liver). Skeletal anomalies (reduced ossification crania, vertebral arches, pelvic, & digital) & variant sternebrae (unossified, reduced) possibly related to lower mean fetal weight.	Compliance with GLP & QA statement not reported. Test concentrations selected based on study results reported above (10-Day Preliminary Inhalation Study in Rats - SHD 100/91150). Observed until sacrificed on day 20 of pregnancy. No statistical analyses due to low group size. Slight maternal toxicity in all groups & slight reduction in mean fetal bw at 1,000 ppm. Embryofetal development was impaired at all concentrations (increased incidence of skeletal anomalies; incidence of visceral anomalies & variant sternebrae at 1,000 ppm). Lumbar ribs considered treatment-related. Determined 1,000 ppm for main study of effects on embryofetal development.	Huntingdon Research Centre Ltd. 1991b[11]

TABLE 1
Toxicological Studies for Methyl-3-methoxypropionate
Provided by Showa Denko K.K.

Study Type (Test Code Number)	Study Design				Reported Effects	Comments and Author's Conclusions	Study Conductor*
	Species	MMP	Route	Exposure Frequency and Duration			
The Effect of Inhalation Exposure on Pregnancy of the Rat (SHD 144/931031)	100 ♀ Specific Pathogen Free (Crl:CD®(SD) BR VAF/plus) rats (25 ♀ rats/group), 193-248 g bw, time mated to ♂ of same strain (Charles River U.K.)	Batch no. 03684202 (99.9% purity)	Inhalation (whole-body)	0, 5, 50, or 500 ppm, 6 hrs/day from days 6-15 (inclusive)	Red/brown facial staining and marginally increased water consumption and loss of hair at 50 ppm. Transient red/brown facial staining in 15/25 animals during first half treatment period at 500 ppm. Significantly decreased bw gain & lower food consumption & significantly higher mean water consumption during treatment; food & water consumption not significantly different post-treatment. Mean fetal weight was lower (slightly lower mean litter weight). Significantly increased no. fetuses & litters with skeletal anomalies. Significant no. malformations not considered treatment-related (no consistent type observed).	Compliance with GLP & QA statement not reported ("final draft" to be audited). Test concentrations selected based on study above (Preliminary Study of the Effect of MMP on Pregnancy of the Rat by Inhalation Exposure - SHD 101/901708). Observed until sacrificed on day 20 of pregnancy. Treatment-related skeletal anomalies in high-dose group included reduced ossification, irregular ossification of vertebral centra, minimally distorted ribs (2 malformed fetuses also had rib defects), & additional thoracolumbar vertebra. Percentage fetuses with extra ribs & variant sternebrae higher. Lower mean fetal & litter weights & skeletal anomalies consistent with preliminary study (SHD 101/901708) at maternally toxic dose of 500 ppm.	Huntingdon Research Centre Ltd. 1993[13]

TABLE 1
Toxicological Studies for Methyl-3-methoxypropionate
Provided by Showa Denko K.K.

Study Type (Test Code Number)	Study Design				Reported Effects	Comments and Author's Conclusions	Study Conductor*
	Species	MMP	Route	Exposure Frequency and Duration			
Report to USEPA based on TSCA 8(e)			Inhalation (whole-body)	0, 100, 300, or 1,000 ppm, 6 hrs/day from days 6-15 of gestation.	Increased fetotoxicity & visceral anomalies in the presence of maternal toxicity at 1,000 ppm. Fetotoxicity included delayed skeletal ossification & slightly decreased fetal weights, which are generally considered reversible & should not interfere with normal development. Visceral anomalies were predominantly abnormal lobulation of the liver, which was not reported in control fetuses but historically have been observed at low incidences in control animals. Slight trend of delayed skeletal ossification & low frequency of abnormal liver lobulations observed at 100 & 300 ppm, but no apparent toxicological findings in any fetuses.	Submitted information for TSCA 8(e) "substantial risk notification." Report preliminary study on pregnancy of the rat by inhalation exposure (Study no. SHD 101/901708 - Huntingdon Research Centre Ltd.) that suggested MMP may cause reproductive/developmental toxicity. Evaluation that since MMP did not adversely affect other parameters at this or other doses (i.e., corpora lutea, implantations, embryonic deaths, pre- & post-implantation loses, live births, & litter weights) & abnormal lobulation of the liver has been reported in historical controls, the biological significance is unclear. Concluded that inhalation of 1,000 ppm during sensitive periods of gestation resulted in apparent significant increase of fetotoxicity over control animals. Identified NOAEL of 300 ppm.	Olin Corporation, Environmental Hygiene & Toxicology Department 1993[14]

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TABLE 1
Toxicological Studies for Methyl-3-methoxypropionate
Provided by Showa Denko K.K.

Study Type (Test Code Number)	Study Design				Reported Effects	Comments and Author's Conclusions	Study Conductor*
	Species	MMP	Route	Exposure Frequency and Duration			
Other Studies and Documents Provided by Showa Denko K.K.							
• **Pharmacology**							
General Pharmacology (SR-9033)	20 ♂ Jcl:ICR mice (5 mice/ group), 25.9-28.2 g bw	Batch no. 25001 & 004025	Oral (gavage) (?)	0, 20, 200, or 2,000 mg/kg	Grooming behavior significantly different from control at high dose.	Compliance with GLP & QA statement not reported. Written in Japanese. Evaluated behavior, neurology, & autonomic system 30, 60, 120, 180, & 240 mins & 24 hrs.	Not reported n.d.[12]
• **Additional Documents Submitted by Eastman Kodak Company[15]**							
Status Report of 8EHQ-0486-0599						Describes oral LD_{50} & inhalation LC_{50} studies submitted by Kodak (above). No conclusion from data if MMP is a primary neurotoxic agent or if observed neurotoxic effects occurred secondarily, such as from lack of oxygen	USEPA 1986
Letter Submitted to USEPA, OTS (8EHQ-0586-0599, followup to 89-86-00008)						Reports that LD_{50} studies are still in progress. Currently planned study includes a repeated dose, 28-day inhalation toxicity study (in the in-life phase).	Kodak 1986e

TABLE 1
Toxicological Studies for Methyl-3-methoxypropionate
Provided by Showa Denko K.K.

Study Type (Test Code Number)	Study Design				Reported Effects	Comments and Author's Conclusions	Study Conductor*
	Species	MMP	Route	Exposure Frequency and Duration			
Submitted Final & 2 Interim Reports for 8EHQ-0486-0599						Final report: oral LD_{50}. Interim reports: inhalation LC_{50}; repeated dose inhalation study. [Also includes hard-to-read German paper & interim report for inhalation LC_{50} study for EMP.]	Kodak 1986f

* Footnotes correspond to MMP Toxicity Data List provided by Showa Denko K.K.

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

Jan Vandendriessche, Ph.D.
Vice President
JSR Electronics, Inc.
725 North Pastoria Avenue
Sunnyvale, California 94086

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

APR 12 1994

EPA acknowledges the receipt of information submitted by your organization under Section 8(e) of the Toxic Substances Control Act (TSCA). For your reference, copies of the first page(s) of your submission(s) are enclosed and display the TSCA §8(e) Document Control Number (e.g., 8EHQ-00-0000 Initial) assigned by EPA to your submission(s). Please cite this number when submitting follow-up or supplemental information and refer to the enclosure on the reverse side "EPA Information Requests".

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Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
Washington, D.C. 20460-0001

EPA looks forward to continued cooperation with your organization in its ongoing efforts to evaluate and manage potential risks posed by chemicals to health and the environment.

Sincerely,

Terry R. O'Bryan

Terry R. O'Bryan
Risk Analysis Branch

Enclosure

12427 A

Recycled/Recyclable
Printed with Soy/Canola Ink on paper that contains at least 50% recycled fiber

CATS DATA:
mission # 8EHQ 0993-12427 SEQ A

PE INT SUPP FLWP

BMITTER NAME JSR Electronics, Inc.

INFORMATION REQUESTED: FLWP DATE
0501 NO INFO REQUESTED
0502 INFO REQUESTED (TECH)
0503 INFO REQUESTED (VOL ACTIONS)
0504 INFO REQUESTED (REPORTING RATIONALE)

DISPOSITION:
0629 REFER TO CHEMICAL SCREENING
0678 CAP NOTICE

VOLUNTARY ACTIONS:
0401 NO ACTION REPORTED
0402 STUDIES PLANNED/UNDERWAY
0403 NOTIFICATION OF WORKER/OTHERS
0404 LABEL/MSDS CHANGES
0405 PROCESS/HANDLING CHANGES
0406 APP./USE DISCONTINUED
0407 PRODUCTION DISCONTINUED
0408 CONFIDENTIAL

B DATE: 09/13/93 OTS DATE: 09/21/93 CSRAD DATE: 09/30/93

IEMICAL NAME:
~~Propionate, methyl 3-methoxy~~

CAS#
~~unknown~~ 3852-09-3

FORMATION TYPE:		P F C	INFORMATION TYPE:		P F C	INFORMATION TYPE:		P F C
01	ONCO (HUMAN)	01 02 04	0216	EPI/CLIN	01 02 04	0241	IMMUNO (ANIMAL)	01 02 04
02	ONCO (ANIMAL)	01 02 04	0217	HUMAN EXPOS (PROD CONTAM)	01 02 04	0242	IMMUNO (HUMAN)	01 02 04
03	CELL TRANS (IN VITRO)	01 02 04	0218	HUMAN EXPOS (ACCIDENTAL)	01 02 04	0243	CHEM/PHYS PROP	01 02 04
04	MUTA (IN VITRO)	01 02 04	0219	HUMAN EXPOS (MONITORING)	01 02 04	0244	CLASTO (IN VITRO)	01 02 04
05	MUTA (IN VIVO)	01 02 04	0220	ECO/AQUA TOX	01 02 04	0245	CLASTO (ANIMAL)	01 02 04
06	REPRO/TERATO (HUMAN)	01 02 04	0221	ENV. OCCC/REL/FATE	01 02 04	0246	CLASTO (HUMAN)	01 02 04
07	REPRO/TERATO (ANIMAL)	01 02 04	0222	EMER INCI OF ENV CONTAM	01 02 04	0247	DNA DAM/REPAIR	01 02 04
08	NEURO (HUMAN)	01 02 04	0223	RESPONSE REQEST DELAY	01 02 04	0248	PROD/USE/PROC	01 02 04
09	NEURO (ANIMAL)	01 02 04	0224	PROD/COMP/CHEM ID	01 02 04	0251	MSDS	01 02 04
10	ACUTE TOX. (HUMAN)	01 02 04	0225	REPORTING RATIONALE	01 02 04	0299	OTHER	01 02 04
11	CHR. TOX. (HUMAN)	01 02 04	0226	CONFIDENTIAL	01 02 04			
12	ACUTE TOX. (ANIMAL)	01 02 04	0227	ALLERG (HUMAN)	01 02 04			
13	SUB ACUTE TOX (ANIMAL)	01 02 04	0228	ALLERG (ANIMAL)	01 02 04			
14	SUB CHRONIC TOX (ANIMAL)	01 02 04	0239	METAB/PHARMACO (ANIMAL)	01 02 04			
15	CHRONIC TOX (ANIMAL)	01 02 04	0240	METAB/PHARMACO (HUMAN)	01 02 04			

Rtox

RIAGE DATA:	NON-CBI INVENTORY	ONGOING REVIEW	SPECIES	TOXICOLOGICAL CONCERN:	USE:	PRODUCTION:
	YES (CONTINUE)	YES (DROP/REFER)	RAT	LOW		
	NO (DROP)	NO (CONTINUE)	MUS	MED		
	~~DETERMINE~~	REFER	RBT	HIGH		

Inhalation
Maternal toxicity & fetal skeletal abnormalities at 100ppm
NOAEL = 50ppm

COMMENTS: Non-Cap

CATS DATA:
Submission # BE110 0993-12427 SEQ A

PE INT SUPP FLWP

SUBMITTER NAME JSR Electronics, Inc.

SUB DATE: 09/13/93 OTS DATE: 09/21/93 CSRAD DATE: 09/30/93

CHEMICAL NAME:
~~Propanoate, methyl 3-methoxy~~

CAS#
~~unknown~~ 3852-09-3

INFORMATION REQUESTED: FLWP DATE
0501 NO INFO REQUESTED
0502 INFO REQUESTED (TECH)
0503 INFO REQUESTED (VOL ACTIONS)
0504 INFO REQUESTED (REPORTING RATIONALE)

DISPOSITION:
0639 REFER TO CHEMICAL SCREENING
0678 CAP NOTICE

VOLUNTARY ACTIONS:
0401 NO ACTION REPORTED
0402 STUDIES PLANNED/UNDERWAY
0403 NOTIFICATION OF WORKERS/OTHERS
0404 LABEL/MSDS CHANGES
0405 PROCESS/HANDLING CHANGES
0406 APP/USE DISCONTINUED
0407 PRODUCTION DISCONTINUED
0408 CONFIDENTIAL

INFORMATION TYPE:		P F C
01	ONCO (HUMAN)	01 02 04
02	ONCO (ANIMAL)	01 02 04
03	CELL TRANS (IN VITRO)	01 02 04
04	MUTA (IN VITRO)	01 02 04
05	MUTA (IN VIVO)	01 02 04
06	REPRO/TERATO (HUMAN)	01 02 04
07	REPRO/TERATO (ANIMAL)	01 02 04
08	NEURO (HUMAN)	01 02 04
09	NEURO (ANIMAL)	01 02 04
10	ACUTE TOX. (HUMAN)	01 02 04
11	CHR. TOX. (HUMAN)	01 02 04
12	ACUTE TOX. (ANIMAL)	01 02 04
13	SUB ACUTE TOX (ANIMAL)	01 02 04
14	SUB CHRONIC TOX (ANIMAL)	01 02 04
15	CHRONIC TOX (ANIMAL)	01 02 04

INFORMATION TYPE:		P F C
0216	EPI/CLIN	01 02 04
0217	HUMAN EXPOS (PROD CONTAM)	01 02 04
0218	HUMAN EXPOS (ACCIDENTAL)	01 02 04
0219	HUMAN EXPOS (MONITORING)	01 02 04
0220	ECO/AQUA TOX	01 02 04
0221	ENV. OCCC/REL/FATE	01 02 04
0222	EMER INCI OF ENV CONTAM	01 02 04
0223	RESPONSE REQEST DELAY	01 02 04
0224	PROD/COMP/CHEM ID	01 02 04
0225	REPORTING RATIONALE	01 02 04
0226	CONFIDENTIAL	01 02 04
0227	ALLERG (HUMAN)	01 02 04
0228	ALLERG (ANIMAL)	01 02 04
0239	METAB/PHARMACO (ANIMAL)	01 02 04
0240	METAB/PHARMACO (HUMAN)	01 02 04

INFORMATION TYPE:		P F C
0241	IMMUNO (ANIMAL)	01 02 04
0242	IMMUNO (HUMAN)	01 02 04
0243	CHEM/PHYS PROP	01 02 04
0244	CLASTO (IN VITRO)	01 02 04
0245	CLASTO (ANIMAL)	01 02 04
0246	CLASTO (HUMAN)	01 02 04
0247	DNA DAM/REPAIR	01 02 04
0248	PROD/USE/PROC	01 02 04
0251	MSDS	01 02 04
0299	OTHER	

RIAGE DATA:

NON-CBI INVENTORY	ONGOING REVIEW	SPECIES	TOXICOLOGICAL CONCERN:
YES (CONTINUE)	YES (DROP/REFER.)	RAT	LOW
NO (DROP)	NO (CONTINUE)	MUS	MED
[illegible]	REFER.	RBT	HIGH

Gtox

USE:

PRODUCTION:

COMMENTS: Non-Cap

CATS DATA:
mission # 8EHQ 0993-12427 SEQ A

PE INT SUPP FLWP

BMITTER NAME JSR Electronics, Inc.

INFORMATION REQUESTED: FLWP DATE
0501 NO INFO REQUESTED
0502 INFO REQUESTED (TECH)
0503 INFO REQUESTED (VOL ACTIONS)
0504 INFO REQUESTED (REPORTING RATIONALE)
DISPOSITION:
0539 REFER TO CHEMICAL SCREENING
0578 CAP NOTICE

VOLUNTARY ACTIONS:
0401 NO ACTION REPORTED
0402 STUDIES PLANNED/UNDERWAY
0403 NOTIFICATION OF WORKER/OTHERS
0404 LABEL/MSDS CHANGES
0405 PROCESS/HANDLING CHANGES
0406 APP/USE DISCONTINUED
0407 PRODUCTION DISCONTINUED
0408 CONFIDENTIAL

B DATE: 09/13/93 OTS DATE: 09/21/93 CSRAD DATE: 09/30/93

IEMICAL NAME:
~~Propionate, methyl 3-methoxy~~

CAS#
~~unknown~~ 3852-09-3

FORMATION TYPE:		P F C	INFORMATION TYPE:		P F C	INFORMATION TYPE:		P F C
01	ONCO (HUMAN)	01 02 04	0216	EPI/CLIN	01 02 04	0241	IMMUNO (ANIMAL)	01 02 04
02	ONCO (ANIMAL)	01 02 04	0217	HUMAN EXPOS (PROD CONTAM)	01 02 04	0242	IMMUNO (HUMAN)	01 02 04
03	CELL TRANS (IN VITRO)	01 02 04	0218	HUMAN EXPOS (ACCIDENTAL)	01 02 04	0243	CHEM/PHYS PROP	01 02 04
04	MUTA (IN VITRO)	01 02 04	0219	HUMAN EXPOS (MONITORING)	01 02 04	0244	CLASTO (IN VITRO)	01 02 04
05	MUTA (IN VIVO)	01 02 04	0220	ECO/AQUA TOX	01 02 04	0245	CLASTO (ANIMAL)	01 02 04
06	REPRO/TERATO (HUMAN)	01 02 04	0221	ENV. OCCC/REL/FATE	01 02 04	0246	CLASTO (HUMAN)	01 02 04
07	REPRO/TERATO (ANIMAL)	01 02 04	0222	EMER INCI OF ENV CONTAM	01 02 04	0247	DNA DAM/REPAIR	01 02 04
08	NEURO (HUMAN)	01 02 04	0223	RESPONSE REQEST DELAY	01 02 04	0248	PROD/USE/PROC	01 02 04
09	NEURO (ANIMAL)	01 02 04	0224	PROD/COMP/CHEM ID	01 02 04	0251	MSDS	01 02 04
10	ACUTE TOX. (HUMAN)	01 02 04	0225	REPORTING RATIONALE	01 02 04	0299	OTHER	01 02 04
11	CHR. TOX. (HUMAN)	01 02 04	0226	CONFIDENTIAL	01 02 04			
12	ACUTE TOX. (ANIMAL)	01 02 04	0227	ALLERG (HUMAN)	01 02 04			
13	SUB ACUTE TOX (ANIMAL)	01 02 04	0228	ALLERG (ANIMAL)	01 02 04			
14	SUB CHRONIC TOX (ANIMAL)	01 02 04	0239	METAB/PHARMACO (ANIMAL)	01 02 04			
15	CHRONIC TOX (ANIMAL)	01 02 04	0240	METAB/PHARMACO (HUMAN)	01 02 04			

RIAGE DATA:

NON-CBI INVENTORY	ONGOING REVIEW	SPECIES	TOXICOLOGICAL CONCERN: (Stox)	USE:	PRODUCTION:
YES (CONTINUE)	YES (DROP/REFER)	RAT	LOW		
NO (DROP)	NO (CONTINUE)	MUS	MED		
[illegible]	REFER.	RBT	HIGH		

COMMENTS: Non-Cap 3 MONTH ORAL GAVAGE STUDY IN RATS NOAEL = 60 mg/kg, BUT HIGHER DOSES ONLY DEMONSTRATED SALIVATION AND ORAL IRRITATION, BUT NO TESTICULAR, HEMATOLOGIC, ORGAN WEIGHT OR NEUROLOGIC EFFECTS. A 4 WEEK INHALATION STUDY IN 1986 (8EHQ-0486-0599) DEMONTRATED NOAEL AT 1000 ppm. AT 2000 ppm SLIGHT LETHARGY NOTED AND IRRITATION. BUT REPEAT IN 1991 OF A 10-DAY INHALATION PRELIMINARY STUDY SHOWED LETHALITY AT 2953 ppm, AND ~~[illegible]~~ EFFECTS OF BLINKING AND HUNCHED POSTURE AT 290 ppm THE LOWEST DOSE TESTED. NO NOAEL DETERMINED.

10) 8EHQ-0993-12427: Rank - low.

Chemical: Methyl-3-methoxypropionate (CAS# 3852-09-3).

Review of toxicology data and derivation of occupational exposure levels of methyl-3-methoxypropionate, Environ Corp., Arlington VA, dated July 27, 1989: Negative for gene mutations in the Salmonella typhimurium/mammalian microsomal (Ames) assay.

Negative for chromosome mutations in Chinese hamster ovary (CHO) cells in vitro.

CATS DATA:
Submission # 8EHQ-0993-12427 SEQ A

PE INT SUPP FLWP

SUBMITTER NAME JSR Electronics, Inc.

INFORMATION REQUESTED: FLWP DATE
0501 NO INFO REQUESTED
0502 INFO REQUESTED (TECH)
0503 INFO REQUESTED (VOL ACTIONS)
0504 INFO REQUESTED (REPORTING RATIONALE)
DISPOSITION:
0630 REFER TO CHEMICAL SCREENING
0678 CAP NOTICE

VOLUNTARY ACTIONS:
0401 NO ACTION REPORTED
0402 STUDIES PLANNED/UNDERWAY
0403 NOTIFICATION OF WORKERS/USERS
0404 LABEL/MSDS CHANGES
0405 PROCESS/HANDLING CHANGES
0406 APP/USE DISCONTINUED
0407 PRODUCTION DISCONTINUED
0408 CONFIDENTIAL

IH DATE: 09/13/93 OTS DATE: 09/21/93 CSRAD DATE: 09/30/93

CHEMICAL NAME: ~~Propionate, methyl 3-methoxy-~~ unknown

CAS# 3852-09-3

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15	CHRONIC TOX (ANIMAL)	01 02 04	0240	METAB/PHARMACO (HUMAN)	01 02 04			

IMAGE DATA: NON-CBI INVENTORY: YES (CONTINUE) / NO (DROP) / ~~DEFERRED~~

ONGOING REVIEW: YES (DROP/REFER.) / NO (CONTINUE) / REFER.

SPECIES: RAT, MUS, RBT

TOXICOLOGICAL CONCERN: Atox/Sbtox/Neur
LOW / MED / HIGH
Acute oral toxicity; acute inhalation toxicity; subacute inhalation toxicity; dermal irritation; ocular irritation

USE:

PRODUCTION:

COMMENTS: Non-Cap

8(e)-12427A
LOW--Acute oral toxicity; acute inhalation toxicity; subacute inhalation toxicity; dermal irritation
MODERATE--ocular irritation

Acute oral toxicity. The oral LD50 for mice is 2300 mg/kg. The oral LD50 for rats is 4900 mg/kg, with signs of neurotoxicity including lethargy, poor muscular coordination, and hindlimb weakness in rats exposed to 5000 mg/kg. Histopathology in rats showed necrotic lesions in the spinal cord and brain stem, suggesting that neurological effects were secondary to reduced oxygen supply.

Acute inhalation toxicity. Acute inhalation LC50 for mice is 40 g/m3. The inhalation 6-hour LC50 for rats is 2776 ppm (13.4 g/m3), with signs of neurotoxicity including lethargy, poor muscular coordination, and hindlimb weakness in rats exposed to 1900 ppm and above.

Subacute inhalation toxicity. Rats exposed to 290-2945 ppm for 6 hours/day for 10 days showed respiratory irritation at 945 ppm and above. Rats exposed to 1000 or 2000 ppm for 6 hours/day, 5 days/week for 4 weeks showed lethargy and respiratory irritation.

Ocular irritation. Ocular irritation in the rabbit is moderate based on moderate to severe irritation.

Dermal irritation. Dermal irritation in the rabbit is low based on mild irritation.