Supplemental Table S2. Genetic and related effects of styrene and styrene-7,8-oxide in non-human mammals in vitro

End-point	Species, tissue, cell line	Results		Agent, concentration (LEC or HIC)	Reference
		Without metabolic activation	With metabolic activation		
Styrene					
DNA strand breaks	Rat, primary hepatocytes	+	NT	312 μg/mL	Sina et al. (1983)
DNA strand breaks (comet assay)	Mouse albino Swiss male, isolated hepatocytes	+		2.5 mM [260 μg/mL]	Fontaine et al. (2004)
Hprt	Chinese hamster, lung V79	–	NT	1771 μg/mL	Loprieno et al. (1976)
Hprt	Chinese hamster, lung V79	–	+	6250 μg/mL	Beije & Jenssen (1982)
Chromosomal aberrations	Chinese hamster, lung cells	–	(+)	100 μg/mL	Ishidate & Yoshikawa (1980)
Chromosomal aberrations	Chinese hamster, lung cells	–	(+)	250 μg/mL	Matsuoka et al. (1979)
Sister-chromatid exchange	Chinese hamster, ovary cells	–	+	455 μg/mL	de Raat (1978)
Sister-chromatid exchange	Rat, lymphocytes	+	NT	50 μg/mL	Norppa et al. (1985)
Styrene-7,8-oxide					
DNA strand breaks (alkaline elution)	Rat, primary hepatocytes	+	NT	36 μg/mL	Sina et al. (1983)
DNA strand breaks (alkaline elution assay, SSB)	Rat, adrenal gland, pheochromocytoma/PC 12	+	NT	30 μM [3.6 μg/mL]	Dypbukt et al. (1992)
DNA strand breaks (alkaline elution assay, SSB)	Wistar rat, testicular cells	+	NT	12 μg/mL	Bjørge et al. (1996)
DNA strand breaks (alkaline elution assay, SSB)	Chinese hamster, V79 cells	+	NT	6 μg/mL	Herrero et al. (1997)
DNA strand breaks (alkaline elution)	Chinese hamster, lung V79	+		50 μM [6 μg/mL]	Oesch et al. (2000)
DNA strand breaks (alkaline elution)	Chinese hamster, lung V79 expressing human mEH	+		200 μM [24 μg/mL]	Oesch et al. (2000)

Supplemental Table S2. Genetic and related effects of styrene and styrene-7,8-oxide in non-human mammals in vitro

End-point	Species, tissue, cell line	Results		Agent, concentration (LEC or HIC)	Reference
		Without metabolic activation	With metabolic activation		
Tk locus mutation	Mouse, L5178 lymphoma cells	+	–	13.80 µg/mL	Amacher & Turner (1982)
Hprt mutation	Chinese hamster, lung V79	+	NT	1020 µg/mL	Loprieno et al. (1976)
Hprt mutation	Chinese hamster, lung V79	+	NT	504 µg/mL	Loprieno et al. (1978)
Hprt mutation	Chinese hamster, lung V79	+	–	240 µg/mL	Beije & Jenssen (1982)
Sister-chromatid exchange	Chinese hamster, ovary cells	+	+	50 µg/mL	de Raat (1978)
Sister-chromatid exchange	Chinese hamster, lung V79	+	NT	20 µg/mL	Nishi et al. (1984)
Sister-chromatid exchange	Chinese hamster, lung V79	+	NT	15 µg/mL	von der Hude et al. (1991)
Chromosomal aberration and micronuclei	Chinese hamster, lung V79	+	NT	90 µg/mL	Turchi et al. (1981)

+, positive; –, negative; (+), positive/negative in a study of limited quality (e.g. only a single dose tested; data or methods not fully reported); the level of significance was set at $P < 0.05$ in all cases.

HIC, highest ineffective concentration; LEC, lowest effective concentration, mEH, microsomal epoxide hydrolase; NT, not tested; SSB, single-strand break

Supplemental Table S3. Genetic and related effects of styrene and styrene-7,8-oxide in non-mammalian experimental systems

Test system (species, strain)	End-point	Results		Concentration (LEC or HIC)	Reference
		Without metabolic activation	With metabolic activation		
Styrene					
Fish *Symphodus melops* (corkwing wrasse)	DNA strand breaks	+	NA	0.2 mg/L 7 days in seawater	Mamaca et al. (2005)
Mussels *Mytilus edulis* (blue mussels)	DNA strand breaks	+	NA	0.2 mg/L 7 days in seawater	Mamaca et al. (2005)
Drosophila melanogaster	Sex-linked recessive lethal mutations	+	NA	182 µg/mL, feed	Donner et al. (1979)
Drosophila melanogaster null	Aneuploidy	–	NA	500 µg/mL, feed	Penttilä et al. (1980)
Drosophila melanogaster	Somatic mutation and recombination test (SMART)	–		1040 µg/mL, feed	Rodriguez-Arnaiz (1998)
Plant *Allium cepa*	Chromosomal aberrations	+	NA	0.01%, 90 µg/mL	Linnainmaa et al. (1978a, b)
Saccharomyces cerevisiae D7	Gene conversion and reverse mutation	+	NT	104 µg/mL	Del Carratore et al. (1983)
Saccharomyces cerevisiae D7	DNA damage (homozygosis)	+	NT	104 µg/mL	Del Carratore et al. (1983)
Saccharomyces cerevisiae D7	Mitotic crossing over	NT	–*	12.5 mM [1300 µg/mL]	Paolini et al. (1988)
Saccharomyces cerevisiae D7	Mitotic crossing over	NT	+**	12.5 mM [1300 µg/mL]	Paolini et al. (1988)
Saccharomyces cerevisiae D7	Gene conversion and reverse mutation	NT	–*	12.5 mM [1300 µg/mL]	Paolini et al. (1988)
Saccharomyces cerevisiae D7	Gene conversion and reverse mutation	NT	+**	12.5 mM [1300 µg/mL]	Paolini et al. (1988)
Saccharomyces pombe P1	Forward mutation	–	–	10 400 µg/mL	Loprieno et al. (1976)
Saccharomyces pombe P1	Forward mutation	NT	–	2080 µg/mL	Bauer et al. (1980)

Supplemental Table S3. Genetic and related effects of styrene and styrene-7,8-oxide in non-mammalian experimental systems

Test system (species, strain)	End-point	Results		Concentration (LEC or HIC)	Reference
		Without metabolic activation	With metabolic activation		
Escherichia coli PQ37	SOS induction	–	–	10 000 µg/mL	Brams et al. (1987)
Escherichia coli PQ37	SOS induction	+/–	NT	100 µg/mL	Głośnicka & Dziadziuszko (1986)
Salmonella typhimurium TA100	Reverse mutation	(+)	(+)	52 µg/mL	Vainio et al. (1976)
Salmonella typhimurium TA100, TA1537, TA1538, and TA98	Reverse mutation	–	–	100 µmol/plate [5200 µg/mL]	de Meester et al. (1977)
Salmonella typhimurium TA100, TA1535, TA1537, TA1538, and TA98	Reverse mutation	–	–	500 µg/mL	Stoltz & Whitey (1977)
Salmonella typhimurium TA100, TA1535, TA1537, TA1538, and TA98	Reverse mutation	NT	–	250 µg/mL	Watabe et al. (1978)
Salmonella typhimurium TA100, TA1535, TA1537, TA1538, and TA98	Reverse mutation	–	–	104 µg/mL	Busk (1979)
Salmonella typhimurium TA100, TA1535, TA1538, and TA98	Reverse mutation	–	–	250 µg/mL	De Flora (1979)
Salmonella typhimurium TA100, TA1535, TA1537, and TA98	Reverse mutation	–	–	312 µg/mL	Florin et al. (1980)
Salmonella typhimurium TA100	Reverse mutation	–	+	1000 µg/mL	de Meester et al. (1981)
Salmonella typhimurium TA100 and TA98	Reverse mutation	–	–	500 µg/mL	Brams et al. (1987)
Salmonella typhimurium TA1530	Reverse mutation	+	+	0.02 µg/mL	de Meester et al. (1981)
Salmonella typhimurium TA1535	Reverse mutation	–	+	0.5 µg/mL	Vainio et al. (1976)
Salmonella typhimurium TA1535	Reverse mutation	–	+	52 µg/mL	de Meester et al. (1977)
Salmonella typhimurium TA1535	Reverse mutation	NT	+	521 µg/mL	Poncelet et al. (1980)
Salmonella typhimurium TA1535	Reverse mutation	–	+	1000 µg/mL	de Meester et al. (1981)

Supplemental Table S3. Genetic and related effects of styrene and styrene-7,8-oxide in non-mammalian experimental systems

Test system (species, strain)	End-point	Results		Concentration (LEC or HIC)	Reference
		Without metabolic activation	With metabolic activation		
Salmonella typhimurium TA1537, TA1538, and TA98	Reverse mutation	–	–	52 µg/mL	Vainio et al. (1976)
Salmonella typhimurium TA1537, TA1538, and TA98	Reverse mutation	–	–	1000 µg/mL	de Meester et al. (1981)
Salmonella typhimurium TA97, TA98, TA100, TA1535, and TA1537	Reverse mutation	–	–	1666 µg/plate	Zeiger et al. (1988)
Styrene-7,8-oxide					
Drosophila melanogaster	Sex-linked recessive lethal mutations	+	NA	1000 µg/mL, inhalation	Donner et al. (1979)
Allium cepa	Chromosomal aberrations	+	NA	0.05% [500 µg/mL]	Linnainmaa et al. (1978a)
Allium cepa	Micronuclei	+	NA	0.05% [500 µg/mL]	Linnainmaa et al. (1978a)
Saccharomyces cerevisiae	Gene conversion	+	NT	1200 µg/mL	Loprieno et al. (1976)
Schizosaccharomyces pombe	Forward mutation	+	NT	600 µg/mL	Loprieno et al. (1976)
Salmonella typhimurium umu	SOS induction	+	NT	0.07 µg/mL	Nakamura et al. (1987)
Escherichia coli PQ37	SOS induction	+	NT	100 µg/mL	Głośnicka & Dziadziuszko (1986)
Escherichia coli PQ37	SOS induction	-	–	12 000 µg/mL	Brams et al. (1987)
Escherichia coli PQ37	SOS induction	+	NT	36 µg/mL	von der Hude et al. (1990)
Salmonella typhimurium TA100	Reverse mutation	+	NT	200 µg/mL	Milvy & Garro (1976)
Salmonella typhimurium TA100 and TA1535	Reverse mutation	+	+	0.6 µg/mL	Vainio et al. (1976)
Salmonella typhimurium TA100	Reverse mutation	+	+	60 µg/mL	de Meester et al. (1977)
Salmonella typhimurium TA100	Reverse mutation	+	NT	250 µg/mL	Watabe et al. (1978)

Supplemental Table S3. Genetic and related effects of styrene and styrene-7,8-oxide in non-mammalian experimental systems

Test system (species, strain)	End-point	Results		Concentration (LEC or HIC)	Reference
		Without metabolic activation	With metabolic activation		
Salmonella typhimurium TA100	Reverse mutation	+	+	120 µg/mL	Busk (1979)
Salmonella typhimurium TA100	Reverse mutation	+	+	240 µg/mL	Yoshikawa et al. (1980)
Salmonella typhimurium TA100 and TA1535	Reverse mutation	+	+	NR	De Flora (1979)
Salmonella typhimurium TA100	Reverse mutation	+	NT	144 µg/mL	Sugiura & Goto (1981)
Salmonella typhimurium TA100	Mutation	+	NT	120 µg/mL	Turchi et al. (1981)
Salmonella typhimurium TA100	Reverse mutation	+	NT	48 µg/mL	Pagano et al. (1982)
Salmonella typhimurium TA100	Reverse mutation	+	NT	60 µg/mL	Glatt et al. (1983)
Salmonella typhimurium TA100	Reverse mutation	+	+	500 µg/mL	Hughes et al. (1987)
Salmonella typhimurium TA100	Reverse mutation	+	NT	60 µg/mL	Einistö et al. (1993)
Salmonella typhimurium TA100	Reverse mutation	+	NT	120 µg/mL	Sinsheimer et al. (1993)
Salmonella typhimurium TA100	Reverse mutation	+	NT	300 µg/mL	Brams et al. (1987)
Salmonella typhimurium TA100, TA1530, and TA1535	Reverse mutation	+	+	768 µg/mL	de Meester et al. (1981)
Salmonella typhimurium TA100	Reverse mutation	+	+	100 µg/plate	Zeiger et al. (1992)
Salmonella typhimurium TA100	Reverse mutation	+	+	1200 µg/plate	Guyonnet et al. (2001)
Salmonella typhimurium TA104	Reverse mutation	+	NT	120 µg/mL	Einistö et al. (1993)
Salmonella typhimurium TA1535, TA1537, TA1538, and TA98	Reverse mutation (spot test)	+	NT	5000 µg/mL	Milvy & Garro (1976)
Salmonella typhimurium TA1535	Reverse mutation	+	+	0.60 µg/mL	Vainio et al. (1976)
Salmonella typhimurium TA1535	Reverse mutation	+	+	24 µg/mL	de Meester et al. (1977)
Salmonella typhimurium TA1535	Reverse mutation	+	+	125 µg/mL	Stoltz & Whitey (1977)

Supplemental Table S3. Genetic and related effects of styrene and styrene-7,8-oxide in non-mammalian experimental systems

Test system (species, strain)	End-point	Results		Concentration (LEC or HIC)	Reference
		Without metabolic activation	With metabolic activation		
Salmonella typhimurium TA1535	Reverse mutation	+	+	60 μg/mL	Loprieno et al. (1978)
Salmonella typhimurium TA1535	Reverse mutation	(+)	NT	250 μg/mL	Wade et al. (1978)
Salmonella typhimurium TA1535	Reverse mutation	+	NT	50 μg/mL	Watabe et al. (1978)
Salmonella typhimurium TA1535	Reverse mutation	+	+	60 μg/mL	Busk (1979)
Salmonella typhimurium TA1535	Reverse mutation	+	NT	60 μg/mL	El-Tantawy & Hammock (1980)
Salmonella typhimurium TA1535	Reverse mutation	+	+	NR	De Flora (1981)
Salmonella typhimurium TA1535	Reverse mutation	+	+	768 μg/mL	de Meester et al. (1981)
Salmonella typhimurium TA1537, TA1538, and TA98	Reverse mutation (spot test)	–	NT	5000 μg/mL	Milvy & Garro (1976)
Salmonella typhimurium TA1537	Reverse mutation	–	–	600 μg/mL	Vainio et al. (1976)
Salmonella typhimurium TA1537	Reverse mutation	–	–	6000 μg/mL	de Meester et al. (1977)
Salmonella typhimurium TA1537 and TA98	Reverse mutation	–	NT	NR	Wade et al. (1978)
Salmonella typhimurium TA1537	Reverse mutation	(+)	NT	250 μg/mL	Watabe et al. (1978)
Salmonella typhimurium TA1537 and TA98	Reverse mutation	–	NT	500 μg/mL	El-Tantawy & Hammock (1980)
Salmonella typhimurium TA1537	Reverse mutation	–	–	1150 μg/mL	de Meester et al. (1981)
Salmonella typhimurium TA1538	Reverse mutation	–	+	6 μg/mL	Vainio et al. (1976)
Salmonella typhimurium TA1538 and TA98	Reverse mutation	–	–	6000 μg/mL	de Meester et al. (1977)
Salmonella typhimurium TA1538 and TA98	Reverse mutation	–	NT	250 μg/mL	Watabe et al. (1978)
Salmonella typhimurium TA1537, TA1538, and TA98	Reverse mutation	–	–	NR	De Flora (1981)

Supplemental Table S3. Genetic and related effects of styrene and styrene-7,8-oxide in non-mammalian experimental systems

Test system (species, strain)	End-point	Results		Concentration (LEC or HIC)	Reference
		Without metabolic activation	With metabolic activation		
Salmonella typhimurium TA1538 and TA98	Reverse mutation	–	–	1150 µg/mL	de Meester et al. (1981)
Salmonella typhimurium TA98	Reverse mutation	–	–	600 µg/mL	Vainio et al. (1976)
Salmonella typhimurium TA98	Reverse mutation	–	–	250 µg/mL	Ueno et al. (1978)
Salmonella typhimurium TA98	Reverse mutation	–	–	3333 µg/plate	Zeiger et al. (1992)
Salmonella typhimurium TA97	Reverse mutation	+	NT	300 µg/mL	Brams et al. (1987)
Salmonella typhimurium TA4001	Reverse mutation	+	NT	240 µg/mL	Einistö et al (1993)
Salmonella typhimurium TA4006	Reverse mutation	(+)	NT	960 µg/mL	Einistö et al. (1993)
Escherichia coli WP2 *uvr*A	Reverse mutation	+	NT	720 µg/mL	Sugiura et al. (1978)
Escherichia coli WP2 *uvr*A	Reverse mutation	+	NT	480 µg/mL	Sugiura & Goto (1981)
Klebsiella pneumoniae	Forward mutation	+	NT	120 µg/mL	Voogd et al. (1981)

* Liver S9 from mice given 1 injection of chemical inducers (phenobarbital and β-naphthoflavone)

** Liver S9 from mice given 2 injections of inducers (phenobarbital and β-naphthoflavone) 4 or 5 weeks apart

+, positive; –, negative; +/–, equivocal (variable response in several experiments within an adequate study); (+), positive/negative in a study of limited quality (e.g. only a single dose tested; data or methods not fully reported); the level of significance was set at $P < 0.05$ in all cases.

HIC, highest ineffective concentration; LEC, lowest effective concentration, NA, not applicable; NT, not tested

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