18 ppm, esp. males: hypoactivity, abnormal posture, dyspnea
mortality, 18 ppm: 1/5 male on day 2 (diffusely dark,
discoloured liver, severe centrilobular congestion,
necrosis)
body weight gain was not affected,
pathology:
concentration-related increases in liver weights,
18 ppm, all rats: increased spleen and kidney weights
histopathologic findings:
18 ppm, all rats: liver: coagulative necrosis with
associated inflammation; spleen: haemosiderin deposition
18 ppm, esp. males: haematopoietic cell proliferation,
increased haematopoietic activity
9,18 ppm: hepatocytomegaly of the centrilobular cells
4.5, 9, 18 ppm, females: increasing incidence and severity
of haematopoietic activity
Reliability: (2) valid with restrictions
dose-range finding study
21-MAR-2003 (80)

Species: mouse Sex: male/female
Strain: B6C3F1
Route of administration: oral feed
Exposure period: 5 weeks
Frequency of treatment: daily
Post exposure period: no
Doses: 0, 50, 500, 5000 ppm (calc. intake: (m):0,16,167,1120
mg/kg bw; (f):0,24,220,1310 mg/kg bw)
Control Group: yes, concurrent no treatment
NOAEL: ca. 50 ppm

Method: other: according to OECD Guideline 407, 1981; 12
mice/sex/group and additional 6 mice/sex/group for the interim
sacrifice
Year: 1990
GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Result: except one male in the low dose group no deaths,
5000 ppm(m)/500, 5000 ppm(f): reduced food intake,
sign. clin. findings only in the male 5000 ppm gr.: narrowed
palpebral fissure and corneal opacity;
500/5000 ppm, m/f: centrilobular hepatocytomegaly
5000 ppm, m/f: reduced body weight gain, increased spleen
weight, discolored spleen, deposition of hemosiderin in the
spleen; increased liver weight (differences up to 89% were
noted in females)
5000 ppm,m: reduced tested weight, decreased urea;
5000 ppm, m/f: reduced erythrocyte count(change in morphology:
anisocytosis, poiklocytosis and polychromasie), reduced HK-
and HB-content, increased MetHb (2.8 % f; 1.7% m), MCV, MCH,
MCHC, bilirubin,
500 and 5000 ppm, after 1 week, m/f: increased cholesterin
content, sign. changes in the activity of cytochrome
450-dependent EOD (7-Ethoxycoumarin deethylase), EH (Epoxide
Hydroxylase) and ALD (Aldrin epoxidase) and Phase II enzymes:
GSH-T(Glutathion-S-transferase), GLU-T
(UDP-Glucuronyltransferase), and decreased gluconeogenesis
and glycogen;
after 5 weeks:
f: normal ALD activity, increased activity of EOR, EH,
Glu-T, slight increase in EOD, strong increase in GSH-T
activity; m: increased activities of EOD, EOR, GLU-T, ALD,

GSH-T, EH
5000 ppm: increased activity of ASAT, ALAT, alkaline phosphatase(m), activated pentose phosphate cycle, increased glycolysis
no signs of nephrotoxicity
Reliability: (1) valid without restriction
Flag: Critical study for SIDS endpoint
30-AUG-2001 (4) (5)

Species: mouse Sex: male/female
Strain: other: Swiss CD-1
Route of administration: gavage
Exposure period: 14 d
Frequency of treatment: daily
Post exposure period: no data
Doses: 0, 20, 40, 80, 160 or 320 mg/kg bw/d dissolved in corn oil
Control Group: yes, concurrent vehicle
NOAEL: ca. 40 mg/kg bw

Method: other: 8 mice/sex/dose, statistical analysis
Year: 1992
GLP: yes
Test substance: other TS: purity: > 99 %

Remark: type: dose-setting study
Result: mortality due to gavage trauma: control, f: 2/8, 20 mg-group, f: 1/8, 40-mg-group, f: 1/8
20 and 40 mg/kg bw/d: no clinical signs
80 mg/kg bw/d: all animals were inactive after the first two daily doses but appeared normal post-dosing throughout the rest of the exposure period
160 mg/kg bw/d: during the first week, animals were slightly weak and inactive; during the second week, these animals became slightly cyanotic, but remained active
320 mg/kg bw/d: during the first 2 days of treatment, all mice died or were moribund and sacrificed; clinical signs of toxicity: recumbency, trembling, inactivity, weakness and cyanosis
Reliability: (2) valid with restrictions
dose-setting study, histopathologic examination not performed
21-MAR-2003 (75) (80)

Species: rabbit Sex: no data
Strain: no data
Route of administration: inhalation
Exposure period: up to 18 d
Frequency of treatment: 8 h/d
Post exposure period: no
Doses: 0.1 mg/l
Control Group: other: no data

Method: other: no information
Year: 1910
GLP: no
Test substance: other TS: no data on purity

Result: deaths occurred after exposure for 8-18 d (no further data)
Reliability: (3) invalid
lack of information

16-JUN-2003 (26)

Species: cat Sex: no data
Strain: no data
Route of administration: inhalation
Exposure period: up to 14 d
Frequency of treatment: 8 h/d
Post exposure period: no
Doses: 0.1 mg/l
Control Group: other: no data

Method: other: no data
Year: 1910
GLP: no
Test substance: other TS: no data on purity

Result: deaths occurred after exposure for 8-14 d (no further data); 1 animal survived (total number of animals not mentioned)
Reliability: (3) invalid
lack of information

16-JUN-2003 (26)

Species: cat Sex: no data
Strain: no data
Route of administration: inhalation
Exposure period: all together 17.5 h during 3 consecutive d
Frequency of treatment: no data
Post exposure period: no
Doses: 0.05-0.18 mg/l
Control Group: other: no data

Method: other: no details given
Year: 1908

Result: mortality: 100 % (no further data)
Reliability: (3) invalid
lack of information: secondary literature

16-JUN-2003 (96)

5.5 Genetic Toxicity 'in Vitro'

Type: Ames test
System of testing: S. typhimurium TA 98, TA 100, TA 1535, TA 1537
Concentration: 0, 833.3, 1000.0, 1200.0, 1440.0, 1728.0, 2073.6 ug/plate in DMSO; from 1000 ug/plate bacteriotoxicity
Metabolic activation: with and without
Result: positive

Method: other: s. freetext
Year: 1984
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: suspensions of bacterial cells were incubated with the TS with and without S9-mix from rat liver for 48 hours at 37 celsius, the number of revertant colonies were counted; positive (2-aminoanthrazene, trypaflavine, endoxan) and negative controls

Remark: on strain TA 100, a marked dose-dependent increase in mutation rate (up to 4 times higher than in control) was found with metabolic activation
Reliability: (2) valid with restrictions
only 4 strains used
Flag: Critical study for SIDS endpoint
25-MAR-2003 (3)

Type: Ames test
System of testing: S. typhimurium TA 100
Concentration: no data
Metabolic activation: with
Result: positive

Method: other: no data
Year: 1981
GLP: no data
Test substance: other TS: no data on purity
Reliability: (4) not assignable
documentation insufficient for assessment
16-JUN-2003 (21)

Type: Ames test
System of testing: S. typhimurium TA 78, TA 100, TA 1535, TA 1538
Concentration: no data
Metabolic activation: with and without
Result: negative

Method: other: no data
Year: 1983
GLP: no data
Test substance: no data

Reliability: (4) not assignable
documentation insufficient for assessment
25-MAR-2003 (30)

Type: Ames test
System of testing: S. typhimurium TA 98, TA 100, TA 1535, TA 1537
Concentration: (1): 0.0, 6.0, 20.0, 60.0, 200.0, 600.0:
TA98,TA100,TA1535,TA1537
(2): 0.0, 6.0, 20.0, 60.0, 200.0, 600.0: TA100,TA98
(3): 0.0, 62.5, 125.0, 250.0, 500.0, 1000.0: TA100
see RM
Metabolic activation: with and without
Result: positive

Method: other: s. freetext
Year: 1983
GLP: no data
Test substance: other TS: purity 99 %
Method: preincubation method, solvent: DMSO, S9 prepared from rat liver and hamster liver, positive controls (2-AA, NOPD, 9-AAD), solvent control, performed in triplicate and repeated twice, highest dose: cytotoxic, statistical method according to Margolin et al. 1981

Remark: (4): 0.0, 10.0, 33.3, 100.0, 333.3, 1000.0 : TA98,TA100,TA1535,TA1587
(5): 0.0, 10.0, 33.3,100.0, 333.3, 1000.0: TA100
the test substance was mutagenic only in strain TA 100 with metabolic activation from hamster and rat
Reliability: (2) valid with restrictions
only 4 strains used, no information about GLP
Flag: Critical study for SIDS endpoint
25-MAR-2003 (33) (80)

Type: Ames test
System of testing: S. typhimurium TA 98, TA 100
Concentration: no information
Metabolic activation: with and without
Result: negative

Method: other: preincubation method (only engl. abstract available)
Year: 1987
GLP: no data
Test substance: no data

Reliability: (4) not assignable
documentation insufficient for assessment
25-MAR-2003 (54)

Type: Ames test
System of testing: S. typhimurium TA 97, TA 98, TA 100, TA 102, TA 1535, TA 1537, TA 1538
Concentration: no data
Metabolic activation: with and without
Result: positive
Method: other: no data
Year: 1985
GLP: no data
Test substance: no data
Remark: the strain(s) on which the test substance induced an increase in the mutant count is (are) not mentioned in the description of the test results
Reliability: (4) not assignable
documentation insufficient for assessment
25-MAR-2003 (55)

Type: Cytogenetic assay
System of testing: Chinese Hamster Ovary cells
Concentration: without: 0, 16, 50, 160 ug/ml DMSO;
with: 0, 50, 160, 500 ug/ml DMSO
Metabolic activation: with and without
Result: ambiguous
Method: other: protocol in Galloway Environm. Mol. Mutagen. 10 [Suppl 10],1-175, 1987; solvent control, positive control, harvest time: 14 hours
Year: 1993
GLP: no data
Test substance: other TS: purity: 99 %

Remark: type: chromosomal aberration test
Result: without S9: equivocal, cell with aberrations (control, low to high doses): 2, 7, 8, 9%
with S9: negative
Reliability: (2) valid with restrictions
no information about GLP

Flag: Critical study for SIDS endpoint
25-MAR-2003 (77) (80)

Type: Sister chromatid exchange assay
System of testing: Chinese Hamster Ovary cells
Concentration: without S9:
(1) 0, 5, 16, 50 ug/ml DMSO
(2) 0,30, 40, 50, 60, 75ug/ml DMSO;
with S9:
0, 50,160,500 ug/ml DMSO
Metabolic activation: with and without
Result: positive

Method: other: s. freetext
Year: 1993
GLP: no data
Test substance: other TS: purity: 99 %

Method: protocol in Galloway Environm. Mol. Mutagen. 10 [Suppl 10],1-175, 1987; solvent control, positive control (mitomycin C, cyclophosphamide), S9-mix of induced rat liver, incubation time without S9: 26 hours, with S9: 2 hours, after removal of TS 26 hours
Remark: the test substance exhibited a mutagenic response only in the absense of S9-mix (up to 29% increase over solvent control)
Reliability: (1) valid without restriction
Flag: Critical study for SIDS endpoint
25-MAR-2003 (77) (80)

Type: other: mutation assay in Actinobacteria
System of testing: spores of Actinomyces sphaeroides
Concentration: 0, 0.63 g/l (= 0.004 M)
Metabolic activation: no data
Result: positive

Method: other: no details given
Year: 1971
GLP: no
Test substance: no data

Reliability: (4) not assignable
documentation insufficient for assessment
25-MAR-2003 (87)

Type: Ames test
System of testing: S. typhimurium TA 98, TA 100, TA 1535, TA 1537, TA 1538
Concentration: 0, 25.6, 51.2, 102.4, 204.8, 409.6, 819.2, 1638.4, 3276.8 ug/plate in DMSO
Metabolic activation: without
Result: positive

Method: other: according to: OECD Guide-line 471: pour plate method, highest dose cytotoxic, performed in duplicate and repeated at least 2 times, solvent and positive control
Year: 1983
GLP: no data
Test substance: other TS: purity: 99 %

Remark: increased mutation rate only in strains TA 98 and TA 1538

Reliability: (2) valid with restrictions
study meets criteria of today but is only performed without metabolic activation, no information about GLP
25-MAR-2003 (92)

Type: Ames test
System of testing: S. typhimurium TA 98, TA 100
Concentration: 0, 1, 5, 10, 15, 20 ug/plate in DMSO
Metabolic activation: with and without
Result: positive

Method: other: according to OECD Guide-line 471, preincubation method, without S9-mix, and with S9-mix and 200 ug/plate Norharman
Year: 1983
GLP: no data
Test substance: other TS: chromatographically pure

Remark: the test substance exhibited no mutagenicity to the tester strains in the absence of S9 mix, without norharman;
in the presence of S9 mix, without norharman, o-chloronitrobenzene was not mutagenic to S. typhimurium TA 98;
in the presence of norharman and S9-mix, the test substance exhibited mutagenicity only to S. typhimurium TA
Reliability: (3) invalid
special study, only performed in the presence of metabolic activation, cytotox concentration not determined, no information on GLP, no exact data on purity
25-MAR-2003 (98)

Type: Ames test
System of testing: S. typhimurium TA 98, TA 98 NR and TA 98/1,8-DNP6
Concentration: 0, 5, 10, 15, 20 ug/plate in DMSO
Metabolic activation: with
Result: positive

Method: other: according to OECD Guide-line 471, preincubation method, addition of S9-mix and norharman
Year: 1987
GLP: no data
Test substance: other TS: no dataon purity

Remark: the test substance exhibited weak mutagenicity towards TA 98 NR; the mutagenic activity, however, was much lower than that of o-chloronitrobenzene towards TA 98; the difference in the mutagenicities (test results: positive) of the test compound towards TA 98 and TA 98/1,8-DNP6 could not be regarded as significant
Reliability: (3) invalid
special study, only performed in the presence of metabolic activation, cytotox concentration not determined, no information on GLP, no exact data on purity
16-JUN-2003 (97) (99)

Type: other: SOS chromotest
System of testing: E. coli PQ 37
Concentration: 3-5 different concentrations (no further information)
Metabolic activation: with and without
Result: negative

Method: other
Year: 1988

GLP: no data
Test substance: other TS: no data on purity

Remark: o-chloronitrobenzene did not induce SOS-repair in the chromotest with and without S9 mix (without norharman); it was tried to increase the sensitivity of the SOS chromotest by addition of norharman to the S9 mix: a negative result was obtained again with the test substance
Reliability: (4) not assignable
documentation insufficient for assessment
25-MAR-2003 (108)

Type: HGPRT assay
System of testing: V 79 Chinese Hamster lung cells
Concentration: without S9-mix: 0,100,300,400,500,600,700,800,900 ug/ml DMSO;
with S9-mix: 0,100,200,450,600,750,900,1050,1200 ug/ml DMSO
Cytotoxic Concentration: without: 800 ug/ml; with: 750 ug/ml
Metabolic activation: with and without
Result: negative

Method: other: OECD Guide-line 476, rat liver S9-mix (induced), toxicity test prior to testing, exposure duration 5 hours, positive controls (EMS, DMN)
Year: 1989
GLP: yes
Test substance: other TS: purity: 99.8%

Reliability: (1) valid without restriction
Flag: Critical study for SIDS endpoint
25-MAR-2003 (101)

Type: Cytogenetic assay
System of testing: Chinese hamster ovary cells
Concentration: without S9-mix: 0, 10, 50, 100 ug/ml DMSO; with S9-mix: 0, 25, 125, 250 ug/ml DMSO
Metabolic activation: with and without
Result: negative
Method: other: OECD Guide-line 473, harvest time: 8, 12, 21 hours, cytotoxicity was tested prior to testing, positive controls: mitomycin C, cyclophosphamide
Year: 1988
GLP: yes
Test substance: other TS: purity: 99.8 %

Remark: type: chromosomal aberration test
Reliability: (1) valid without restriction
Flag: Critical study for SIDS endpoint
25-MAR-2003 (47)

Type: Ames test
System of testing: Salmonella typhimurium TA 100, TA 1535, TA 1537, TA 1538, TA 98, Escherichia coli WP2uvrA
Concentration: 0, 4, 20, 100, 500, 2500 ug/plate, dissolved in 100 ul DMSO, additionally:TA100 with S9-mix: 2000 ug/plate, dissolved in 100 ul DMSO
Metabolic activation: with and without
Result: positive
Method: other: OECD Guideline 471, rat S9-mix, positive controls
Year: 1984

GLP: yes
Test substance: other TS: purity: 99 %
Remark: mutagen with metabolic activation in TA100 and without in TA 1538
Source: Hoechst AG Frankfurt/Main
Reliability: (1) valid without restriction
25-MAR-2003 (43)

Type: Unscheduled DNA synthesis
System of testing: Rat Hepatocytes
Concentration: 0, 1.0, 5.0, 10, 50, 75, 100 ug/ml DMSO, 500 ug/ml DMSO was cytotoxic
Metabolic activation: with and without
Result: negative
Method: other: in accordance with OECD Guide-line 482, no detailed data available
Year: 1983
GLP: yes
Test substance: other TS: as prescribed in 1.1-1.4 of the Monsanto dataset

Remark: Cytotoxicity observed at 100 ug/ml in preliminary, but not replicate assay
Cytotoxicity at 500 ug/ml
Source: Monsanto
Reliability: (2) valid with restrictions
no details on results given
25-MAR-2003 (72)

Type: other: UMU test
System of testing: Salmonella typhimurium TA1535/pSK1002
Concentration: 100 ug/ml
Metabolic activation: with and without
Result: negative

Method: other: incubation time: 4 hours; determination of ß-galactosidase activity
Year: 1992
GLP: no data
Test substance: no data

Reliability: (4) not assignable
documentation insufficient for assessment
25-MAR-2003 (81)

Type: Bacterial reverse mutation assay
System of testing: S. typhimurium TA98, TA100, TA1530, TA1532, TA1535, TA1537, TA1538, TA1950, TA1975, G46
Concentration: no data
Metabolic activation: with and without
Result: negative

Method: other: OECD guideline 471: plate incorporation method: aerobic and anaerobic condition; fluctuation method
Year: 1980
GLP: no data
Test substance: other TS: purest grade available
Reliability: (3) invalid
no details given, special study
25-MAR-2003 (29)

Type: Sister chromatid exchange assay
System of testing: Chinese Hamster Ovary cells

Concentration: without S9:
0,5,16,50 ug/ml DMSO;
with S9:
(1): 0, 50, 167, 500 ug/ml DMSO
(2): 0, 63, 125, 250 ug/ml DMSO
Metabolic activation: with and without
Result: positive

Method: other: s. freetext
Year: 1993
GLP: no data
Test substance: other TS: purity: 99 %

Method: protocol in Galloway Environm. Mol. Mutagen. 10 [Suppl 10],1-175, 1987; solvent control, positive control (mitomycin C, cyclophosphamide), S9-mix of induced rat liver, incubation time without S9: 26 hours, with S9: 2 hours, after removal of TS 26 hours
Result: without S9-mix: negative; with S9-mix: positive (up to ca. 40% increase over solvent control)
Reliability: (2) valid with restrictions
no information about GLP
Flag: Critical study for SIDS endpoint
25-MAR-2003 (80)

Type: Cytogenetic assay
System of testing: Chinese Hamster Ovary (CHO) cells
Concentration: without S9: 0,47,101,216 ug/ml DMSO; with S9: 0, 101,125,216,250,465,500 ug/ml DMSO
Metabolic activation: with and without
Result: positive

Method: other: protocol in Galloway Environm. Mol. Mutagen. 10 [Suppl 10],1-175, 1987; solvent control, positive control, harvest time: without S9: 18.5 hours, with S9: 13.6 hours
Year: 1993
GLP: no data
Test substance: other TS: purity: 99 %

Result: with S9-mix: poitive;
without S9-mix: negative
Reliability: (2) valid with restrictions
no information about GLP
Flag: Critical study for SIDS endpoint
25-MAR-2003 (80)

Type: HGPRT assay
System of testing: Chinese Hamster Ovary cells
Concentration: with S9-mix: 0, 10,30,100,300,400 ug/ml DMSO; without S9-mix: 0, 6.6, 20, 66.6, 200, 300 ug/ml DMSO
Metabolic activation: with and without
Result: negative
Method: other: in accordance with OECD Guide-line 476
Year: 1984
GLP: yes
Test substance: other TS: as prescribed in 1.1-1.4 of the Monsanto dataset
Reliability: (2) valid with restrictions
only summarized report available
16-JUN-2003 (71)

Type: Bacterial reverse mutation assay

System of testing: Salmonella typhimurium TA100, TA1535, TA98, TA1537, Escherichia coli WP2uvrA
Concentration: 0, 10, 20, 50, 100, 200, 500, 1000 ug/plate dissolved in DMSO, highest dose cytotoxic
Metabolic activation: with and without
Result: negative

Method: other: OECD Guide-line 471, preincubation method, S9-mix from induced rat liver, solvent and positive controls (AF2, NaN3, 9AA)
Year: 1996
GLP: no data
Test substance: other TS: purity: 99 %

Reliability: (2) valid with restrictions
no information about GLP
Flag: Critical study for SIDS endpoint
25-MAR-2003 (51)

Type: Bacterial reverse mutation assay
System of testing: S. typhimurium TA100, TA1535, WP2uvrA, TA98, TA1537
Concentration: 0, 39.1, 78.1, 156, 313, 625, 1250, 2500, 5000, 10000 ug/plate dissolved in DMSO and TA100, TA1535, WP2uvrA: 500 ug/plate dissolved in DMSO
Metabolic activation: with and without
Result: positive

Method: other: OECD Guide-line 471, preincubation method, S9-mix from rat and from hamster, highest dose cytotoxic, solvent and positive controls
Year: 1997
GLP: no data
Test substance: other TS: purity: 99 %

Result: positive: TA100 with rat and hamster S9, TA98 with hamster S9
WP2uvrA: positive and negative with hamster S9-mix
Reliability: (2) valid with restrictions
no information about GLP
25-MAR-2003 (52)

Type: Ames test
System of testing: S. typhimurium TA100, TA98
Concentration: (1)0,10,33,100,133,166,250,333,666,1000,1666 ug/plate
(2)0,3,10,33,66,100,166,333,666 ug/plate
Metabolic activation: with and without
Result: positive

Method: other: praeincubation assay, S9-mix from hamster and rat liver
Year: 1983
GLP: no data
Test substance: other TS: purity: 98 %

Remark: TS was positive only in TA98 in presence of 30 % hamster S9-mix and in TA100 in presence of induced hamster or rat mix
Reliability: (2) valid with restrictions
no information on GLP only two strains used
25-MAR-2003 (80)

5.6 Genetic Toxicity 'in Vivo'

Type: Drosophila SLRL test
Species: Drosophila melanogaster Sex: male
Strain: other: Canton-S wild type
Route of admin.: i.p.
Exposure period: once
Doses: 0, 10000 ppm in peanut oil
Result: negative

Method: other: males(1-3d old), mated with 3x with Basc virgin females brood1: 3d, brood2: 2d, brood3: 2d;
Year: 1985
GLP: no data
Test substance: other TS: purity:>99 %

Reliability: (2) valid with restrictions
no information about GLP
25-MAR-2003 (80) (116)

Type: Drosophila SLRL test
Species: Drosophila melanogaster Sex: male
Strain: other: Canton-S wild type
Route of admin.: oral feed
Exposure period: 72 hours
Doses: 0, 125 ppm in 10 % ethanol and 5 % sucrose solution
Result: negative

Method: other: males(24 hrs old), mated with 3x with Basc virgin females brood1: 3d, brood2: 2d, brood3: 2d;
Year: 1985
GLP: no data
Test substance: other TS: purity: > 99 %

Reliability: (2) valid with restrictions
no information about GLP
Flag: Critical study for SIDS endpoint
25-MAR-2003 (80) (116)

Type: Drosophila SLRL test
Species: Drosophila melanogaster Sex: male
Strain: other: Canton S wild type
Route of admin.: oral feed
Doses: 0, 60 ppm in 4 % ethanol
Result: negative

Method: other: see ME
Year: 1989
GLP: no data
Test substance: other TS: purity: > 99 %

Method: In order to obtain individuals for larval treatment Canton-S females and males were mated and eggs exposed in vials with standard cornmealfood containing the chemical plus solvent alone. Adult males emerging from the treatrment were mated at approximately 24 hours of age with two successive harems of three to five Basc females to establish two single day broods. Males were then discarded and two conventional SLRL assay were carried out.