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.

Reliability: (2) valid with restrictions
no information about GLP
25-MAR-2003 (80) (115)

Type: other: single-strand DNA-breaks
Species: mouse Sex: male
Strain: CD-1
Route of admin.: i.p.
Exposure period: single application
Doses: 60 mg/kg bw
Result: positive
Method: other: 8 mice, 4 h post appl. nuclei were isolated from liver and kidney cells, DNA damage was evaluated by alkaline elution technique was used, coupled with a microfluorometric method for DNA assay
Year: 1982
GLP: no data
Test substance: other TS: no data on purity
Result: effects: an increased elution rate in alkali of DNA from liver and kidney was obtained
Reliability: (2) valid with restrictions
no data on purity and GLP, only 1 dose used
Flag: Critical study for SIDS endpoint
25-MAR-2003 (19)

5.7 Carcinogenicity

Species: rat Sex: male
Strain: other: CD
Route of administration: oral feed
Exposure period: 18 months
Frequency of treatment: daily
Post exposure period: 6 months
Doses: 0, 500, 1000 or 2000 ppm (= ca. 0, 37.5, 75 or 150 mg/kg bw/d) ; see method
Control Group: yes, concurrent no treatment

Method: other: s. freetext
Year: 1978
GLP: no data
Test substance: other TS: purity: 97-99 %

Method: 25 rats/group,1000 or 2000 ppm for 6 mo., 500 or 1000 ppm for another 12 mo; complete gross necropsy and histology on certain organs (lung, liver, spleen, kidney, adrenal, heart, bladder, stomach, intestines, reproductive organs, pituitaries), on all grossly abnormal organs and tumour masses, statistical methods: Fisher Exact Test, Bonferroni correction
Remark: pathological examination was not performed of animals that died within the first six months
Result: no information on body weight gain
multiple tumours at the low dose only and late in life: usually a pituitary adenoma along with either a stomach papilloma, adrenal tumour, thyroid adenocarcinoma, lymphosarcoma, choliangosarcoma of the liver or subcutaneous fibroma
incidences: low dose level:7/22, high dose level:1/19, simultaneous control: 1/22, pooled control: 14/111

Reliability: (2) valid with restrictions
study doesn't meet the criteria of today (number of animals too low, time of duration too short, doses too high), reported in brief
Flag: Critical study for SIDS endpoint
16-JUN-2003 (110)

Species: mouse Sex: male/female
Strain: CD-1
Route of administration: oral feed
Exposure period: 18 months
Frequency of treatment: daily
Post exposure period: 3 months
Doses: 0, 1500, 3000 or 6000 ppm (= ca.0, 225, 450 or 900 mg/kg bw/d)
Control Group: yes, concurrent no treatment

Method: other: s. freetext
Year: 1978
GLP: no data
Test substance: other TS: purity: 97-99 %

Method: 25 mice/sex/group,3000 or 6000 ppm for 8 mo., 1500 or 3000 ppm for another 10 mo; complete gross necropsy, histology on certain organs (lung, liver, spleen, kidney, adrenal, heart, bladder, stomach, intestines, reproductive organs), on all grossly abnormal organs and tumour masses , statistical methods: Fisher-Exact Test, Bonferroni correction
Remark: pathological examination was not performed of animals that died within the first six months
Result: no information on body weight gain
significant increase in hepatocellular carcinomas in female mice at both dose levels and in male mice at the low dose level
incidences of hepatocellular carcinomas:
male mice:
low dose level: 7/17, high dose level: 3/16, simultaneous control: 3/18, pooled control: 7/99;
female mice:
low dose level: 5/22, high dose level: 5/19, simultaneous control: 0/20, pooled control: 1/102
Reliability: (2) valid with restrictions
study doesn't meet the criteria of today (number of animals too low, time of duration too short, doses too high), reported in brief
Flag: Critical study for SIDS endpoint
16-JUN-2003 (110)

5.8.1 Toxicity to Fertility

Type: Two generation study
Species: mouse
Sex: male/female
Strain: other: Swiss CD-1
Route of administration: gavage
Exposure Period: see type and remarks
Frequency of treatment: daily
Premating Exposure Period
male: 7 d
female: 7d
Duration of test: 34 weeks

Doses: 0, 40, 80 or 160 mg/kg bw/d dissolved in corn oil
Control Group: yes, concurrent vehicle
NOAEL F1 Offspring: ca. 160 mg/kg bw
NOAEL F2 Offspring: ca. 160 mg/kg bw

Method: other: NTP Continuous Breeding Protocol, see also ME
Year: 1992
GLP: yes
Test substance: other TS: purity: > 99 %
Method: NTP Continuous Breeding Protocol: 20 ps/group, 40 ps (contr.), exposure period: F0: 7d prior to cohousing, 98d of continuous breeding. Last litter from F0, control and high dose groups were reared, weaned, and kept until mating. Siblings received the same treatment as their parents. At sexual maturity, 20 non-sibling males and females were cohabited for 7 days and housed singly through delivery, until sacrifice. Exam.: symtoms, bw gain, water consumption; F0,F1: contr,160 mg-gr.: spleen weight, methb; F0,F1:

fertility indices; F1(m): testes,epididymis, F1(f): vaginal cytolo
Result: Conclusion:
In the presence of altered somatic and selected organ weights 2-chloronitrobenzene (2CNB) did not alter reproductive function in either generation (NOEL 160 mg/kg bw); thus, 2CNB is not a selective reproductive toxicant.
F0 mice:
Mortality: 2,2,2,3 control to high dose gr., 160 mg-group: increased terminal bw and spleen weights; 80 mg-gr.(1m), 160 mg-gr.(3m): with hepatocellular degeneration;
160 mg-gr.: methaemoglobinaemic, during the first 10 d mice were slightly inactive post dosing, 3 lactating females were cyanotic for up to 2 weeks; no other signs of clin.l toxicity
F0-fertility and reproductive parameters were not affected
F1-pups:
in the final litter of the holding period following the continuous breeding phase, F1 pup weight gain during suckling was lower in all treated groups;
at weaning, F1 pups in the 160 mg/kg bw/d group weighed 10-13% less than controls, all other fertility and reproductive parameters were not affected;
F1 mice (only control and high dose group):
no signs of clin. tox. observed, 160 mg/kg bw/d:
significantly lowered body weights at weaning but sign. heavier than controls at mating and at terminal necropsy;
right epididymis, kidney/adrenals(m), spleen and liver weights increased, seminal vesicle-to-body weight ratio was sign. decreased, sign. methaemoglobinaemia;
none of the fertility and reproductive parameters examined were affected in F1 mice, i.e., epididymal sperm parameters (motility, count and percentage of abnormal sperms) and estrous cycle length and estrual cyclicity
Reliability: (1) valid without restriction
Flag: Critical study for SIDS endpoint
27-AUG-2001 (20) (76) (80)

Type: other:
Species: rat
Sex: male/female
Strain: other: F344/N
Route of administration: inhalation

Exposure Period: 13 w
Frequency of treatment: 6 h/d, 5 d/w
Doses: 0, 4.5, 9 or 18 ppm (approx. 0, 28.8, 57.6, 115.2 mg/m3)
Control Group: yes, concurrent no treatment

Method: other: 10 rats/sex/group, reproduct. system evaluation: vaginal cytology, sperm morphology, necropsy body and reproductive tissue weights, sperematozoal data, spermatogenesis, oestrous cycle length, percent of cycle spent in various
Year: 1993
GLP: yes
Test substance: other TS: purity: 99 %

Remark: see chapter 5.4.
Result: females: no effects observed
males, 18 ppm: decreases in cauda epididymis weights (6.8%), and in the spermatid count and spermatid heads/testis (ca. 13%)
Reliability: (1) valid without restriction
Flag: Critical study for SIDS endpoint
25-MAR-2003 (44) (80)

Type: other:
Species: rat
Sex: male
Strain: Fischer 344
Route of administration: gavage
Exposure Period: single application
Frequency of treatment: once
Doses: 150 mg/kg bw
Control Group: yes

Method: other: 5or 6 rats, sacrifice on d1 and d25 post application, evaluation of testes weight, testicular histopathology, sperm production
Year: 1988
GLP: no data
Test substance: other TS: no data

Result: no effect on testicular histopathology (at 1 d) or testes weight and daily sperm production (at 25 d)
Reliability: (4) not assignable
lack of information
25-MAR-2003 (65)

Type: other:
Species: mouse
Sex: male/female
Strain: B6C3F1
Route of administration: inhalation
Exposure Period: 13 w
Frequency of treatment: 6 h/d, 5 d/w
Doses: 0, 4.5, 9 or 18 ppm (approx. 0, 28.8, 57.6, 115.2 mg/m3)
Control Group: yes, concurrent no treatment

Method: other: 10 rats/sex/group, reproductive system evaluation: vaginal cytology, sperm morphology, necropsy body and reproductive tissue weights, spermatozoal data, spermatogenesis, estrous cycle length, percent of cycle spent in various
Year: 1993
GLP: yes
Test substance: other TS: purity: 99 %

Remark: see chapter 5.4
Result: male, 4.5, 9, 18 ppm: decreased sperm motility
females: increased terminal body weight; no reproductive effects observed
Reliability: (1) valid without restriction
Flag: Critical study for SIDS endpoint
03-SEP-2001 (20) (44) (80)

5.8.2 Developmental Toxicity/Teratogenicity

Species: rat Sex: female
Strain: Sprague-Dawley
Route of administration: gavage
Exposure period: days 6-15 of gestation
Frequency of treatment: daily
Duration of test: 21 d
Doses: 0, 25, 75, or 150 mg/kg bw/d dissolved in corn oil
Control Group: yes, concurrent vehicle
NOAEL Maternal Toxity: ca. 25 mg/kg bw

Method: other: 25 females/group, due to severe mat. tox. and mortality the 150 mg-level was terminated prior to scheduled sacrifice
Year: 1986
GLP: yes
Test substance: other TS: purity: commercial

Result: mortality:
150 mg-gr.: due to severe toxicity and high mortality rate of the dams, all females were terminated prior to sheduled sacrifice, 75 mg-group: 1/25;
general toxicity:
75 mg/kg bw/d: gest.-d. 6-10: reduced body weight gain (slight but not significant) and
reduced food consumption; recovery later in gestation;
urinary staining, alopecia; maternal reproductive parameters comparable to controls, mean number of early resorptions and post implantation loss slightly increased (post implantation loss in the respective control very low when compared to historical control; values range: 0-0.9)
25 mg/kg bw/d: no evidence of maternal toxicity
developmental toxicity:
fetal body weight comparable to control
variations: cervical #7 ribs at 25 mg-gr (1.1%) and sign. at 75 mg-gr (2%); 13 full pair of ribs with lumbar #1 rudimentary ribs in controls, at 25 mg-, 75 mg-gr increased, but not sign.;
12 full pair of ribs with #13 unilateral full rib and/or rudimentary rib(s) in controls and in 25 mg-gr. increased, but not sign.
Reliability: (2) valid with restrictions
highest dose was too high
Flag: Critical study for SIDS endpoint
25-MAR-2003 (67) (105)

Species: rat Sex: female
Strain: Sprague-Dawley
Route of administration: gavage
Exposure period: d6-d15
Frequency of treatment: daily
Doses: 0, 100 mg/kg bw in corn oil
Control Group: yes, concurrent vehicle
other: NOAEL developmental toxicity : ca. 100 mg/kg bw

Method: other: 25 females/group, only one dose
Year: 1984
GLP: yes
Test substance: other TS: purity: commercial

Remark: The study was intended to clarify the observations of the study of Monsanto,1986
Result: d6-10: slight maternal body weight loss accompanied by reduction in food consumption for d6-16, maternal reproductive parameters were not affected, fetal body weight comparable to the respective controls; no teratogenic effects were observed
Reliability: (2) valid with restrictions
only one dose used
Flag: Critical study for SIDS endpoint
25-MAR-2003 (49)

5.8.3 Toxicity to Reproduction, Other Studies

5.9 Specific Investigations

5.10 Exposure Experience

Remark: based on clinical and laboratory evaluation of cyanosis cases during a 10-year period a number of cyanogenic aromatic nitro compounds were ranked in descending order of relative hazard relating to their cyanogenic potential observed in exposed industrial workers (rank 1 = most potent, rank 13 = least potent): o-chloronitrobenzene was classified in rank 7; laboratory evaluation showed that total oxygenatable haemoglobin in some cases, notably after be expected from methaemoglobin analysis (unspecified route of absorption)
Flag: Critical study for SIDS endpoint
(59)

Remark: experience with human exposure: a number of the more important aromatic nitrocompounds were ranked showing their commparative hazard ratings for cyanosis, anaemia and overall toxicity (the degree of hazard ranges from 1 = slight hazard to 6 = severe hazard): for o-chloronitro-benzene, the degree of hazard is 4 concerning cyanosis hazard, 2 concerning anaemia hazard and 3 concerning over-all toxic hazard (no further data)
(60)

Remark: all 325 records of industrial chemical cyanosis poisoning in Britain notified to the inspectorate from 1961 to 1980 were scrutinised: the cases occurred mainly during chemical or dyestuff manufacture; a total of 50 cases of chemical cyanosis syndrome due to chloronitrobenzene were reported; 23 (46 %) cases were "early cases", i.e., the symptoms developed while at work on the same day of exposure, and 27 (54 %) cases were "delayed cases", i.e., the symptoms developed insidiously or some definite time after the "working" day on which the poisoning occurred (the route of absorption is not described in detail for each test compound, the most cases resulted from skin absorption and/or inhalation; in this study, the isomer(s) of chloronitrobenzene is/are not clearly specified)
Flag: Critical study for SIDS endpoint
14-AUG-2001 (91)

Remark: experience with human exposure: in chloronitrobenzene poisoning cardiac complications appear to be more frequent and more serious than in aniline poisoning and gastrointestinal irregularities (anacidity) also appear to be quite common (no further data, isomer(s) of chloronitrobenzene not specified)
(13) (14)

Remark: experience with human exposure: four workmen were reported who were hospitalized as the result of exposure to a mixture of o- and p-chloronitrobenzene; these cases resulted from two to four days exposure and all were cyanotic; headache and weakness accompanied the cyanoses
Flag: Critical study for SIDS endpoint
(84)

Remark: The exposition against a mixture of 2-chloro- and 4-chloronitrobenzene caused severe intoxications which exceeds the signs of intoxication during repair of a unit for isolation of the isomers. As symtoms cyanotic appearance and collapse were described. Hb-content was decreased up to 65 % of the normal value. During the recovery period the patients suffered from difficulty in breathing and sensation of dizziness. Within 7 weeks Hb content increased to 80 % of the normal value.
Flag: Critical study for SIDS endpoint
14-AUG-2001 (28)

5.11 Additional Remarks

Type: other

Remark: the level of lipid peroxidation, content of vitamine E and its metabolites as well as antioxidative activity in the blood serum, liver and spleen of white rats were studied. Toxicological efects of nitrochlorobenzenes were decreased by vitamine E (no further information) .

23-FEB-1998 (82) (83)

Type: other: Haematotoxizitaet

Remark: Ergebnis: 10 mg/kg Kgw. zeigte (2 Katzen): keine Letalitaet, leichte Veraenderungen im weissen Blutbild, leichten Anstieg der Zahl der Heinz'schen Innenkoerper und leichte Methaemoglobinaemie, nach 48 Stunden p.a. weitgehend reversibel.
Source: Hoechst AG Frankfurt/Main
Test substance: technisch rein

(36)

Remark: an attempt to vaporize o-chloronitrobenzene by passing air (2 l of air/min. for 1 h) through a tower of dust was not successful in that no weighable amounts of the test substance were vaporized; rats and mice in an inhalation chamber were exposed to the generated atmosphere for 1 h: no symptoms of toxicity were observable and no deaths occurred at the end of the exposure period or within an observation period of 7 d

(6)

Remark: 48 h after a single oral administration of 100 mg/kg bw of o-chloronitrobenzene to rabbits, 0.3 % of the administered dose was found in faeces as unabsorbed material which was completely reduced to the chloroaniline; in the urines collected each 24 h for 48 h the following metabolites of o-chloronitrobenzene were detectable (expressed as percentages of the administered dose): ether glucuronide (42 %), ethereal sulphate (24 %), mercapturic acid (7 %), free chloroaniline (9 %) (total accounted for: 82 %)
Flag: Critical study for SIDS endpoint

(15)

Remark: metabolism in vitro: radiolabelled (14 C) o-chloronitrobenzene (concentration not specified) was incubated with isolated rat hepatocytes for up to 90 min.: after 90 min., 71 % of the o-chloronitrobenzene had been metabolized; the primary metabolic pathway for o-chloronitrobenzene was reduction to o-chloroaniline (19.2 % of the total radioactivity after 90 min.); o-chloronitrobenzene was also conjugated with glutathione; two other very polar metabolites, com- prising 14.2 % of the total 14 C from o-chloronitrobenzene, have not been identified

23-FEB-1998 (34) (35)

Remark: in order to identify the specific enzymes involved in the metabolism of o-chloronitrobenzene by isolated rat hepatocytes, hepatic subcellular fractions were isolated from rats; microsomes incubated with radiolabelled (14 C) o-chloronitrobenzene in the presence of NADPH produced o-chloroaniline under aerobic conditions and SKF 525 A and metyrapone had no effect on the metabolism to o-chloroaniline: these findings suggest that cytochrome P-450 reductase is responsible for o-chloronitrobenzene reduction; radiolabelled o-chloronitrobenzene was also incubated with or without microsomes, cytosol and/or glutathione: o-chloronitrobenzene was converted to S-(2-nitrophenyl)glutathione in the presence of cytosol and glutathione suggesting that cytosolic glutathione transferase is involved in this conjugation (concentration of the test substance un-

specified)

(34)

Remark: the effect of o-chloronitrobenzene on heme synthesis was determined in vitro by studying its influence on delta-aminolevulinic acid synthetase (ALAS) and ferrochelatase (FC) activities in rat liver homogenates; at 0.001 mol/l concentration, o-chloronitrobenzene did not significantly affect the enzyme activities

(53)

Remark: o-chloronitrobenzene was administered by gavage to adult and geriatric rats at 65 mg/kg bw/d for 11 d; 14 C-o-chloronitrobenzene was administered on days 1, 5 and 9; 14 C was determined in urine and faeces up to 96 h after each 14 C-dose and in tissues at 72 h after the day 9 dose: in adult rats, at all treatment intervals, 71-74 % of each dose was excreted in urine and 20-27 % in faeces and the rates of excretion increased with pretreatment; 5 % of the day 9 dose was in tissues, the highest concentrations were in liver and kidney; 24 urinary metabolites were found; pattern, rate and extent of excretion of 14 C were similar in geriatric and adult rats, except that urinary excretion by unpretreated geriatrics was more extensive (85 %) and the rates of urinary and faecal excretion did not increase with pretreatment; tissue distribution of 14 C was also similar and 8 % of the day 9 dose was in tissues

Flag: Critical study for SIDS endpoint

27-AUG-2001 (62)

Remark: 14 C-o-chloronitrobenzene was administered by gavage to rats at 2, 20 or 200 mg/kg bw (single administration); radioactivity was determined in urine and faeces up to 72 h and in tissues at 24 and 72 h: at 2 and 20 mg/kg bw 58-60 % of the dose was excreted in urine, 26-28 % in faeces, primarily during the first 24 h, 6 % was in 24-h and 3 % in 72-h tissues; at 200 mg/kg bw 74 % was in urine and only 7 % in faeces and it was excreted more slowly with 21 % in 24-h and 4 % in 72-h tissues; at 2 and 20 mg/kg bw o-chloronitrobenzene equivalent concentrations in tissues

were proportional to dose, whereas at 200 mg/kg bw they were disproportionately higher in all tissues, especially in fat, and disproportionately lower in liver; at all doses the highest concentrations were in liver and kidney and at 200 mg/kg bw in fat; up to 23 metabolites were in urine

Flag: Critical study for SIDS endpoint

27-AUG-2001 (63)

Remark: After a single non-occlusive, protective dermal application of 14 C-o-chloronitrobenzene at doses of ca. 0.65, 6.5 or 65 mg/kg bw to male rats, 33-40 % of the doses of o-chloronitrobenzene was absorbed from the skin within 72 h; the absorbed 14 C was excreted in urine (21-28 %) and faeces (11-15 %). The extent absorption increased with an increase in dose from 0.65 to 6.5 mg/kg bw but increased only neglibly when the dose was increased to 65 mg/kg bw.

The extent of urinary excretion of radioactivity was not significantly affected by dose over the range studied. The initial rate of urinary excretion was also unaffected by dose. The initial rate of faecal exretion increased with dose over the 0.65 to 6.5 mg/kg range, but decreased notably at the high dose.

Flag: Critical study for SIDS endpoint

27-AUG-2001 (66) (79)

Remark: metabolism of o-chloronitrobenzene by hepatic subcellular fractions from rats: to determine the enzyme systems involved in the metabolism of o-chloronitrobenzene by rat isolated hepatocytes, radiolabelled (14 C) o-chloronitrobenzene (100 uM) was incubated with hepatic microsomes (incubation mixture containing microsomes and NADPH, some incubations also containing UDP-glucuronic acid) or with cytosol (incubation mixture containing GSH and cytosolic protein): reduction of o-chloronitrobenzene to o-chloroaniline occurred readily in microsomal incubations; substitution of NADH for NADPH or incubation of microsomes under a carbon monoxide atmosphere significantly inhibited nitroreduction, boiling the microsomes completely abolished reduction of o-chloronitrobenzene; addition of SKF 525-A or metyrapone significantly inhibited the microsomal reduction of o-chloronitrobenzene to o-chloroaniline (the inhibition of nitroreduction by carbon monoxide, SKF 525 A and metyrapone suggests that cytochrome P-450 catalyzes this reaction); incubation of o-chloronitrobenzene with rat hepatic cytosol and glutathione resulted in the formation of S-(2-nitrophenyl)glutathione

Flag: Critical study for SIDS endpoint

(85)

Remark: in vitro study of metabolism: after 90 min. incubation of isolated rat hepatocytes with radiolabelled (14 C) o-chloronitrobenzene (100 uM final concentration), 46.7 % of the added o-chloronitrobenzene was metabolized; the calculated half-life for disappearance of o-chloronitrobenzene from the incubations was 84 min.; a major metabolic pathway for o-chloronitrobenzene was reduction to o-chloroaniline (19.2 % of the total radioactivity after 90 min. incubation); o-chloroaniline was further metabolized to form the N-glucuronide accounting for 14.2 % of the total radioactivity; o-chloronitrobenzene was conjugated with glutathione and S-(2-nitrophenyl)glutathione accounted for 13.3 % of the total radioactivity

Flag: Critical study for SIDS endpoint

(85)

Remark: in vitro assay: the reduction of chloronitrobenzenes was investigated in purified milk xanthine oxidase-xanthine system: o-chloronitrobenzene was less readily reduced by the enzyme than the corresponding para and meta isomers, indicating the steric hindrance effect at ortho position

Flag: Critical study for SIDS endpoint

(100)

Remark: in an in vivo study, 100 umoles/kg bw (= 15.7 mg/kg bw) of o-chloronitrobenzene was given i.p. to male rats, the animals were killed 5 h after the injection to examine methaemoglobin levels: formation of methaemoglobin was observable (methaemoglobin level: 20.6 %)
Flag: Critical study for SIDS endpoint

(109)

Remark: in vitro methaemoglobin formation was studied by incubating haemolyzate (obtained from rats and containing 0.1 umole of haemoglobin) with 0.5 umole of o-chloronitrobenzene at pH 6.6 and 37 degrees centigrade for 5 h: formation of methaemoglobin (concentration: 4.8 %) was not significantly increased compared with the control

(109)

Remark: Single oral administration of 0.1 ml/100 g bw of a 0.5 M tricaprylinsolution of 1-chloro-2-nitrobenzene (o-CNB) to female Wistar rats resulted in hemoglobin binding: 2.1 (mmol TS/mol Hb)/(mmol TS/kg bw)
Flag: Critical study for SIDS endpoint

23-FEB-1998 (89) (90)

(1) Auergesellschaft: AUER Technikum, Ausgabe 12 (1988), p. 195

(2) Back K.C. et al, Reclassification of materials listed as tranportation Health hazard, Report No. TSA 20-72-3, Medical Aerospace Research Laboratory (AFSCS), Wright-Patterson Air Force Base, OHIO, Final Report, August 1972, At the request of Department of Transporation , Washington, D.C., PB214-270

(3) Bayer AG data, Report No. 12848: o-Nitrochlorbenzol: Salmonella/Mikrosomem-Test zur Untersuchung auf punktmutagene Wirkung, August 9, 1984

(4) Bayer AG data, Report No. 20209(F): Enzymhistochemisch darstellbare Veränderungen des Kohlenhydratstoffwechsels der Mausleber nach Gabe von o-Chlornitrobenzol, May/6/1991

(5) Bayer AG data, Report No. 22240: o-Chlornitrobenzol: Subakute Toxizitätsstudie an B6C3F1-Mäusen - Schwerpunkt Leberdiagnostic - (Verabreichung im Futter bis zu 5 Wochen),

May/7/1993 (at the request of BG-Chemie, Heidelberg)

(6) Bayer AG data, Report No. 5800, January 5, 1976

(7) Bayer AG data: Loeser, E.: o-Nitrochlorbenzol. Untersuchungen zur akuten oralen Toxizitaet an maennlichen Wistar-Ratten, April 2, 1982

(8) Bayer AG data: Loeser, E.: o-Nitrochlorbenzol. Untersuchungen zur akuten oralen Toxizitaet an weiblichen Wistar-Ratten, April 1, 1982

(9) Bayer AG, Internal studies: 1. Geschlossener Flaschen-Test (1977), 2. Test on Leuciscus idus (1974), Oxygen consumption inhibition test according to Robra (1983); no records available

(10) Bayer AG, Internal Study: GLP Final Report: vapor pressure, physical-chemical properties (2001-07-12)

(11) Bayer AG, Internal study: Identity and Material Balance of o-Chloronitrobenzene (25.08.89)

(12) Bayer AG: Safety Data Sheet (2001-07-19)

(13) Bonzanigo, A.: Deut. Z. ges. gerichtl. Med. 16, 242-255 , (1931)

(14) Bonzanigo, A.: Samml. Vergiftungsfaellen 3, A 127-128 (1932)

(15) Bray, H.G. et al.: Biochem. J. 64, 38-44 (1956)

(16) BUA Report No. 2, o-Chloronitrobenzene, VCH, Weinheim, October 1985

(17) Call, D.J. and Geiger, D.L., Subchronic toxicities of industrial and agricultural chemicals to Fathead Minnows (Pimephales promelas) Vol. I, Center for Lake Superior Environmental Studies, Lake Superior Research Institute, University of Wisconsin-Superior, USA (1992)

(18) Canton, J.H. et al., Regul. Toxicol. Pharmacol. 5, 123-131 (1985)

(19) Cesarone, C.F. et al.: New Toxicology for Old, Arch. Toxicol., Suppl. 5, 355-359 (1982)

(20) Chapin R. et al., Environm. Health Persp. 105 [Suppl 1], s 287 (1997)

(21) D'Addario, A.P. and Jagannath, D.R.: Environ. Mutagen. 3, 325 (1981) (abstr.)

(22) Davydova, S.G.: Hyg. and Sanit. 32(8), 161-166 (1967)

(23) Deneer, J.W. et al., QSAR study of the toxicity of nitrobenzene derivatives towards Daphnia magna, Chlorella pyrenoidosa and Photobacterium phosphoreum, Aquatic Toxicology, 15, 83-98 (1989)

(24) Deneer, J.W. et al., Quantitative structure-activity relationships for the toxicity and bioconcentration factor of nitrobenzene derivatives towards the guppy (Poecilia reticulata), Aquatic Toxicology, 10, 115-129 (1987)

(25) Deutsche Forschungsgemeinschaft (DFG): MAK-und BAT-Werte-Liste 2000, p. 39

(26) Dressler: Dissertation Wuerzburg 1910: cited in Flury, F. and Zernik, F.: Schaedliche Gase, Berlin (1931)

(27) Eckert, J.W., Fungistatic and Phytotoxic Properties of Some Derivatives of Nitrobenzene, Phytopathology, 52, 642-649 (1962)

(28) Gerbis H., Nitrochlorbenzol-Vergiftung, gewerbliche, reperative Hyperglobulie, cited in : Führer H. (ed.). Sammlung von Vergiftungsfällen, Bd.3, 125-126, Verlag von F.W.C. Vogel, Berlin, 1932

(29) Gilbert P. et al., Arch. Environm. Contam. Toxicol. 9, 533-541 (1980)

(30) Graham, R.C. et al.: Toxicity Summary o-Chloronitrobenzene. Unpublished summary by du Pont provided by Dastur (1983): cited in Chemical Hazard Information Profile Draft report 2-Chloronitrobenzene, June 13, 1983, Office of Toxic Substances, EPA, USA

(31) Haskell laboratory, Inhalation median lethal concentration toxicity study with orthochloronitrobenzene in rats, at the request of DupOnt de Nemour, EPA OTS 0540655, 1992

(32) Haskell Labs, Subchronic inhalation toxicity study of o-chloronitrobenzene in rats, at the request of Dupont Chem Co., OTS 0546562, 1992

(33) Haworth, S. et al.: Environ. Mutagen. 5, (Suppl.1), 3-142 (1983)

(34) Held, S.D. and Rickert, D.E.: Abstracts Eleventh Annual CIIT Scientific Evening, 17-18, September 8, 1987

(35) Held, S.D. and Rickert, D.E.: Abstracts twelfth Annual CIIT Scientific Evening, 15-16, September 13, 1988

(36) Hoechst AG (1975): Unveroeffentlichte Unters. Ber. 75.0494

(37) Hoechst AG (1989): Produktinformation o-Nitrochlorbenzol der Abt. Verkauf Feinchemikalien (März 1989); document not available

(38) Hoechst AG (1993): Sicherheitsdatenblatt o-Nitrochlorbenzol TTR (26.03.1993); document not available

(39) Hoechst AG, Internal studies: 1. Zahn-Wellens-Test (1982), 2. Respirometer Test (1982), 3. Toxicity on Bacteria, Anaerobic (1982); no records available

(40) Hoechst AG, Report No. 491/75: Akute orale Toxizität von o-Nitrochlorbenzol an männlichen SPF-Wistar-Ratten, 1975/oct/01

(41) Hoechst AG, Report No. 493/75: Haut- und Schleimhautverträglichkeit von o-Nitrochlorbenzol an Kaninchen, 1975/oct./01

(42) Hoechst AG, Report no.492/75: Akute dermale Toxizität von o-Nitrochlorbenzol an weiblichen SPF-Wistar-Ratten, 1975/oct./01

(43) Hoechst AG: o-Chlornitrobenzol, Study of the mutagenic potential in strains of Salmonella typhimurium (Ames test) and Escherichia coli, unpublished Report No. 84.0410, 1984

(44) Horstman, M.G. et al.: The Toxicologist 11, 87 (1991) (abstr.)

(45) Horstman, M.G. et al.: The Toxicologist 11, 87 (1991) (abstr.)

(46) Hulzebos, E.M. et al., Environ. Toxicol. Chem. 12 (6), 1079-1094 (1993)

(47) Huntingdon Research Centre Ltd., Analysis of methaphase chromosomes obtained from CHO cells cultured in vitro and treated with o-chloronitrobenzene, HRC Report No. BGH 7/88867, 1988 (at the request of BG Chemie)

(48) Hustert, E. et al., Chemosphere 16 (4), 809-812 (1987)

(49) IRDC (International Research and Developmental Corporation): Modified teratology study in rats with o-Nitrochlorobenzene, Report no. ML-82-090A, october 1984 (at the request of Monsanto Company), EPA-OTS0522332

(50) Izmerov, N.F. et al.: "Toxicometric Parameters of Industrial Toxic Chemicals under Single Exposure", Moscow, Centre of International Projects, GKNT, p. 92 (1982)