Strain: Wistar
Sex: female
Vehicle: other: polyethylene glycol 400
Value: ca. 1320 mg/kg bw
Method: other: 10 or 20 rats/dose, 3 doses, subst.(solved in polyethylene glycol 400) appl. on the shaved back for 24 hours, covered by alu and a plaster, then rinsed with water and soap, post exposure observ.-time: 14 d
Year: 1976
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Remark:

dosis mg/kg	conc. %	result m /s /n	signs of intoxication start	signs of intoxication end	time of death
750	50	0/10/10	24 h	6 d	-
1000	50	5/20/20	18 h	14 d	2 - 3 d
1500	75	6/10/10	18 h	10 d	2 - 6 d

m: number of rats which died;
n: number of animals in test
s: number of animals with signs of intoxication: reduced general condition, difficulties in breathing, cyanotic appearance, some animals showed lacrimation
Reliability: (2) valid with restrictions
no pathologic examination performed, individual animal data and information on GLP are missing
Flag: Critical study for SIDS endpoint
21-MAR-2003 (6)

Type: LD50
Species: rat
Sex: female
No. of Animals: 6
Vehicle: other: diluted in sesame oil to give a concentration of 40 %
Value: = 1796 mg/kg bw

Method: other: 6 rats/dose, single application to the clipped intact skin, covered by alu and a plaster, exposure time: 24 h, then rinsing, postexposure observation time: 14 d
Year: 1975
GLP: no
Test substance: other TS: no data on purity

Remark: doses and mortality:
500 mg/kg: 0/6 ; 1000 mg/kg: 1/6 ; 1600 mg/kg: 3/6;
2000 mg/kg: 3/6
no signs of toxicity, necropsy of the survivors: no pathological findings
Reliability: (2) valid with restrictions
no data on purity and information on GLP is missing
21-MAR-2003 (42)

Type: LD50
Species: rabbit
Value: = 450 mg/kg bw

Method: other: 5 rabbits/dose, trunks were clipped free of hair, 3 doses (warm to melting point), exposure time 24 h (rabbits immobilized during exposure), then rinsing and wiping dry, observation time: 14 d
Year: 1975

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

Remark: dose / mortality / individual reactions
330 mg/kg/ 20 % / slight discoloration of the skin and eyes; normal < 48 hrs
560 mg/kg/ 80 % / death 48 to 96 hours preceded by lethargy, loss of motor coordination, sometimes coma
750 mg/kg/ 80 % / death 2 to 5 days, other reaction similar

general reaction:
manifestation of methaemoglobinaemia symptoms evident in < 20 minutes
Reliability: (2) valid with restrictions
no data on purity, no pathologic examination, information on GLP is missing
16-JUN-2003 (104)

Type: LD50
Species: rabbit
Sex: male/female
No. of Animals: 2
Vehicle: other: undissolved
Value: = 400 mg/kg bw
Method: other: 2 rabbits/sex/dose, 5 doses, single dermal application (intact skin), undiluted (warmed to make suitable for dosing), no further information, exposure time: 24 hrs, post exp.observation time: 14 d
Year: 1983
GLP: yes
Test substance: other TS: purity: no data
Remark: Dose and mortality: 251 mg/kg: Males: 0/2; Females: 0/2
316 mg/kg: 0/2 1/2
398 mg/kg: 0/2 2/2
501 mg/kg: 2/2 1/2
631 mg/kg: 2/2 2/2

observations: toxic signs: lethargy (lasting up to 3 days); increasing weakness; collapse; death
Gross necropsy:
decedents: haemorrhagic areas of the lungs;
liver, kidney, spleen discoloration; enlarged gall bladder, gastrointestinal inflammation
survivors(14 d): viscera appeared normal
LD50 (male): 445 mg/kg bw
LD50 (female): 355 mg/kg bw
Reliability: (2) valid with restrictions
no data on purity, no individual pathologic data
Flag: Critical study for SIDS endpoint
21-MAR-2003 (69) (112)

Type: LD50
Species: rabbit
Sex: male/female
No. of Animals: 1
Vehicle: other: none
Value: > 79.4 mg/kg bw
Method: other:1 rabbit/dose, 6 doses, single application of undiluted, warmed substance, exposure time. 24 hrs, postexposure observation time: 14 d (no further information)
Year: 1975
GLP: no

Test substance: other TS: no data on purity

Remark: dose, sex, mortality, time to death:
31.6 mg/kg, male, 0/1, -; 50.0 mg/kg, female, 0/1, -;
79.4 mg/kg, male, 0/1, -; 126.0 mg/kg, female, 1/1, 2 d;
200.0 mg7kg, male, 1/1, 1 d; 398.0 mg/kg, female, 1/1, 1 d

signs of intoxication: slight lethargy (1-2 d in survivors), increasing weakness, collapse, death

gross autopsy: decedents: haemorrhagic areas of the lungs, slight liver discoloration, enlarged gall bladder, gastrointestinal inflammation;
survivors: viscera appeared normal

Reliability: (2) valid with restrictions
no data on purity, information on GLP is missing, only 1 animal/dose, no individual pathologic data

16-JUN-2003 (113)

Type: LDLo
Species: rabbit
Sex: male/female
No. of Animals: 1
Vehicle: other: none
Value: 316 mg/kg bw

Method: other: 1 rat /dose, single application of undiluted substance, exposure time: 24 hrs, post exposure observation time: 14 d
Year: 1975
GLP: no
Test substance: other TS: orthonitrobenzene residue

Remark: dose, sex, mortality, time to death:
126 mg/kg, male, 0/1, -; 200 mg/kg, female, 0/1, -;
316 mg/kg, male, 1/1, 2 days; 794 mg/kg, 1/1, 3 days
signs of intoxication: reduced appetite and activity (2-4 days in survivors), increasing weakness, collapse, death
gross autopsy: decedents: haemorrhagic areas of the lungs, mottled liver, slight enlarged gall bladder, blackened spleen, gastrointestinal inflammation
survivors: viscera appeared normal

Reliability: (4) not assignable
o-chloronitrobenzene residue used, no information of o-chloronitrobenzene itself

21-MAR-2003 (111)

5.1.4 Acute Toxicity, other Routes

5.2 Corrosiveness and Irritation

5.2.1 Skin Irritation

Species: rabbit
Concentration: 500 other: mg
Exposure Time: 24 hour(s)
No. of Animals: 2
Result: not irritating

Method: other: ear, dose: 500 mg/animal, undissolved TS, covered by cellulose pads and plaster, a rolled gauze pad was put on it, all together was bandaged, exposure time: 24 h, semi-occlusive, observation time 7 d
Year: 1976
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Reliability: (2) valid with restrictions
only a few animals used, no information on GLP
Flag: Critical study for SIDS endpoint
21-MAR-2003 (6)

Species: rabbit
Concentration: 10 %
Exposure: Semiocclusive
Exposure Time: 24 hour(s)
No. of Animals: 6
Result: not irritating

Method: other: appl. to intact and abraded skin, flank, test substance diluted in sesame oil, dose: 0.5 ml/animal, observation time: 72 hrs, reading: 24, 48 and 72 hours, evaluated according Fed.Reg.38, No.187, p.27019, 1973, § 1500.41
Year: 1975
GLP: no
Test substance: other TS: no data on purity

Remark: intakt skin (score 0-4):
24 hrs: 4/6 erythema: score: 1; 0/6 oedema
48 hrs: 0/6 erythema: score: ; 0/6 oedema
72 hrs: 0/6 erythema: score: ; 0/6 oedema
abraded skin:
24 hrs: 4/6 erythema: score: 1; 0/6 oedema
48 hrs: 0/6 erythema: score: ; 0/6 oedema
72 hrs: 0/6 erythema: score: ; 0/6 oed
Reliability: (2) valid with restrictions
sesame oil as vehicle, no data on purity
16-JUN-2003 (41)

Species: rabbit
Concentration: undiluted
Exposure: no data
Exposure Time: 24 hour(s)
No. of Animals: 3
Result: corrosive

Method: other: 0.5 ml undiluted, exposure: 24 hrs
Year: 1974
GLP: no
Test substance: other TS: o-nitrochlorobenzene residue (not the original substance, no further information on chemical characteristics)

Reliability: (4) not assignable
o-chloronitrobenzene residue used, no information of o-chloronitrobenzene itself
21-MAR-2003 (111)

Species: rabbit
Concentration: other: undissolved
Exposure: no data

Exposure Time: 24 hour(s)
No. of Animals: 6
Result: not irritating

Method: other: 0.5 ml/rabbit, warmed, observation time: 168 hours (no further information)
Year: 1973
GLP: no
Test substance: other TS: purity: 99.71 %

Remark: time of reading up to 168 hours: no erythema or oedema
Reliability: (2) valid with restrictions
no GLP, no information on exposure
Flag: Critical study for SIDS endpoint
21-MAR-2003 (113)

5.2.2 Eye Irritation

Species: rabbit
Dose: 50 other: mg
No. of Animals: 2
Result: not irritating

Method: other: undissolved test substance, dose: 50 mg/animal,observation period: 7 d
Year: 1976
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Remark: Slight redness (score 1/3) observed in 1/2 animals, disappeared within 24 hours, the other animal was without effects
Reliability: (2) valid with restrictions
no GLP, only a few animals used
Flag: Critical study for SIDS endpoint

21-MAR-2003 (6)

Species: rabbit
Concentration: other: undissolved
Dose: 100 other: mg
Exposure Time: 24 hour(s)
Comment: no data
No. of Animals: 6
Result: slightly irritating

Method: other: according Fed.Reg.38, No.187, 1973: undissolved test substance, dose: 100 mg/animal, observation time: 24 hrs
Year: 1975
GLP: no
Test substance: other TS: no data on purity

Remark: 1 hr post appl: 4/6 with conjunctival injections, score: 1/0-3; and 2/6 with conjunctival injections, score: 2/0-3; 7 hr post appl: 2/6 with conjunctival injections, score: 1/0-3; 24 hr post appl: no findin
Reliability: (2) valid with restrictions
no data on purity, no GLP
Flag: Critical study for SIDS endpoint
16-JUN-2003 (41)

Species: rabbit

Concentration: undiluted
Dose: .1 ml
Exposure Time: 24 hour(s)
No. of Animals: 3
Result: corrosive

Method: other: 0.1 ml, undiluted, 24 hrs exposure
Year: 1974
GLP: no
Test substance: other TS: o-nitrochlorobenzene residue (not the original substance, no further information on chemical characteristics)

Reliability: (4) not assignable
o-chloronitrobenzene residue used, no information of o-chloronitrobenzene itself
21-MAR-2003 (111)

Species: rabbit
Concentration: undiluted
Dose: .1 ml
Exposure Time: 24 hour(s)
No. of Animals: 6
Result: not irritating

Method: other: 0.1 ml/rabbit, warmed, observation time: 168 hours
Year: 1973
GLP: no
Test substance: other TS: purity: 99.71 %

Remark: Time of reading:
24 hrs: 6/6 slight erythema, Score 9.6/110
48 hrs: 5/6 slight erythema, Score 2.3/110
72 hrs: 1/6 slight erythema, Score 0.3/110
168 hrs: no findings
Reliability: (2) valid with restrictions
no GLP
21-MAR-2003 (113)

Species: rabbit
Concentration: 10 %
Dose: .1 ml
No. of Animals: 6
Result: slightly irritating
Method: other: according Fed.Reg.38, No.187, 1973: observation time: 24 hrs
Year: 1975
GLP: no
Test substance: other TS
Remark: 1 hr post appl: 3/6 conjunctival injection, score: 1/0-3; 7 and 24 hrs post appl: no findings
Reliability: (2) valid with restrictions
no data on purity, no GLP
21-MAR-2003 (41)

5.3 Sensitization

Type: no data
Species: human

Remark: experience with human exposure: o-chloronitrobenzene

has been used for decades, but there have been no indications of an allergenic potential in man

(16)

Type: other: modified Draize test
Species: guinea pig
Concentration 1st: Induction 1 %
2nd: Challenge 1 %
No. of Animals: 10
Vehicle: other: Aceton
Result: not sensitizing

Method: other: 3 drops of a 1 % solution to the clipped area of the skin for 5 d; on the 7th d 3 drops of the 1 % solution to an untreated area of the skin; reading time not mentioned
Year: 1973
GLP: no
Test substance: other TS: no data on purity

Remark: The study documentation is incomplete and the methology employed is no longer in use.
Reliability: (3) invalid
no data on purity, study documentation incomplete, no data on GLP
16-JUN-2003

(88)

Type: other: modified Freunds complete adjuvant test
Species: guinea pig
Concentration 1st: Induction 10 %
2nd: Challenge 10 %
No. of Animals: 10
Vehicle: other: aceton
Result: sensitizing

Method: other: 3 drops(10% sol.) to the clipped area of the skin;22nd inj.of Freund-adjuvans and TS into the hind paw (0.5 mg/kg bw), 28th d 3 drops(10 % sol.) to an untreated clipped area of the skin; reading time not mentioned
Year: 1973
GLP: no
Test substance: other TS: no data on purity

Remark: The allergenic activity of o-chloronitrobenzene is less marked than that of p-chloronitrobenzene; 2,4-dinitro-chlorobenzene provokes even stronger sensitization effects than p-chloronitrobenzene
The study documentation is incomplete and the methology employed is no longer in use.
Reliability: (3) invalid
no data on purity, study documentation incomplete, no data on GLP
16-JUN-2003

(88)

Type: other: the rats were exposed via inhalation to o-chloronitrobenzene for 5 months
Species: rat
Result: sensitizing
Year: 1973
GLP: no
Test substance: other TS: no data on purity

Reliability: (3) invalid
no data on purity, study documentation incomplete, no data

on GLP
16-JUN-2003 (88)

5.4 Repeated Dose Toxicity

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	
Post exposure period:	no	
Doses:	0, 1.1, 2.3, 4.5, 9 or 18 ppm (approx. 0, 7, 14.7, 28.8, 57.6, 115.2 mg/m3)	
Control Group:	yes	
LOAEL:	ca. 1.1 ppm	

Method: other: see freetext: method
Year: 1993
GLP: yes
Test substance: other TS: purity: 99 %

Method: 10 rats/sex/group, whole body expos., clin.chem., hematol., bw., org.weight, compl. histopathol. in all control rats and 18ppm gr. and rats that died, gross lesions and selec. organs of rats < 18-ppm-groups, add. 10 rats/sex/conc: clin. pathol. at d1, d4, d23

histopathol. evaluations on reproductive organs: see chapter 5.8

Remark: although a no-observed-effect level (NOEL) for histopathological findings was not found in this study, observations among rats exposed to 4.5 ppm or less were limited to minimal effects on nasal tissues

Result: clinical signs:
no clear signs of toxicity (no other information), no deaths, no differences in body weight gain or terminal body weight compared to controls;
haematology, male and female:
concentration-related increase in methaemoglobinaemia (m sign: from 1.1 ppm at d23; from 2.3 ppm at all time points with max of 1.14 g/dl at 18 ppm; f sign.: from 1.1 ppm at week 13 and from 2.3 ppm at all time points with max of 1.04 g/dl at 18 ppm), reticulocyte count (sign. at all dose groups at week 13), nucleated erythrocytes, leucocyte count (predominantly at the highest dose groups of male and females); concentration-related decrease in haematocrit, haematoglobin, RBC (m. sign.: 1.1 ppm(d23), 4.4 ppm (week13), 9 ppm (d4,week13),18 ppm (at all time points); f. sign.: at every dose group at week13), MCH and MCHC (only in females)
clinical chemistry, male and female:
increase in serum activities of sorbitol dehydrogenase and alanine aminotransferase in different male and female exposure groups at various time points, decrease in alkaline phosphatase
pathology: dark spleen (1 female, 2 males, 18 ppm)
concentration-related increases in liver, spleen and right kidney weight
Histopathologic changes:
liver: basophilia of centrilobular hepatocytes, kidney: pigmentation and regeneration of the proximal convoluted

tubules, spleenic congestion was observed in all exposed and control rats: in males with dose-dependent increase in severity and in females with dose-dependent increase in incidences; nose: hyperplasia of the nasal cavity respiratory epithelium
Reliability: (1) valid without restriction
Flag: Critical study for SIDS endpoint
21-MAR-2003 (45) (80) (102)

Species: rat Sex: male/female
Strain: Sprague-Dawley
Route of administration: inhalation
Exposure period: 4 w
Frequency of treatment: 6 h/d, 5 d/w
Post exposure period: no
Doses: 0, 10, 30 or 60 mg/m3
Control Group: yes, concurrent no treatment
LOAEL: ca. .01 mg/l

Method: other: 15 rats/sex/group, whole body exposure, haematology, clinical chemistry, gross and microscopic examination, statistical analysis
Year: 1986
GLP: no data
Test substance: other TS: purity: 99.71%
Result: all concentration groups:
no deaths, mean body weights comparable to controls, microscopic changes of the spleen: increased degree of haemosiderosis
0.01 mg/l: slight, but statistically significant increase in relative liver weights in male rats
0.03 and 0.06 mg/l: increases in liver, kidneys and spleen weight, significant increase in blood methaemoglobin levels and decrease in haemoglobin, haematocrit and red blood cell count values; increases in liver, kidney, and spleen weights, microscopic changes of the spleen:
slight increase in degree of extramedullary haematopoiesis
Reliability: (2) valid with restrictions
Histopathologic evaluation not performed from all animals, no information on GLP
21-MAR-2003 (73) (74)

Species: rat Sex: male/female
Strain: other: F344/N
Route of administration: inhalation
Exposure period: 2 weeks
Frequency of treatment: 6 h/d, 5 d/w
Post exposure period: no
Doses: 0, 1.1, 2.3, 4.5, 9, 18 ppm (approx. 0, 7, 14.7, 28.8, 57.6, 115.2 mg/m3)
Control Group: yes
LOAEL: ca. 1.1 ppm

Method: other: 5 rats/sex/group, whole body exposure, complete necropsies on all rats, histopatholologic evaluation of all rats in the controls and the highest exposure group
Year: 1993
GLP: yes
Test substance: other TS: purity: 99 %

Result: clinical signs:
18 ppm, males: hypoactivity, ataxia, pallor
18 ppm, males, females: dehydration, nasal discharge, decreased urination and defecation
all concentration groups:
no deaths, body weight gain was not affected
pathology:
males and females: exposure-related increases in liver weights,
18 ppm, males, females: increased spleen weights
18 ppm-group, males: slight increased relative kidney weights
histopathologic findings:
18 ppm, all rats:
hemosiderin deposition in liver (minimal) and spleen (mild severity)
Reliability: (2) valid with restrictions
dose-finding study
21-MAR-2003 (80)

Species: rat Sex: male/female
Strain: Sprague-Dawley
Route of administration: inhalation
Exposure period: 3 days
Frequency of treatment: 6 hours/day, daily
Post exposure period: none
Doses: 0.045 mg/l
Control Group: yes
NOAEL: < .045 mg/l
LOAEL: = .045 mg/l

Method: other: no information
Year: 1982
GLP: yes
Test substance: other TS: as prescribed in 1.1-1.4 of the Monsanto datasheet

Result: 0.045 mg/l blood, methaemoglobin (3%), incr.; m.f.
Source: Monsanto
Reliability: (3) invalid
information on method and no. of animals is missing
21-MAR-2003 (70)

Species: rat Sex: male
Strain: other: Crl:CD
Route of administration: inhalation
Exposure period: 2 weeks
Frequency of treatment: 6 hrs/d, 5 d/week
Post exposure period: 13 d
Doses: 0, 0.03, 0.15, 0.53 mg/l
Control Group: yes, concurrent no treatment
NOAEL: ca. .03 mg/l

Method: other
Year: 1984
GLP: no data
Test substance: other TS: purity: 99.8 %

Result: haemolytic anemia, methaemoglobinemia
Reliability: (2) valid with restrictions
no information of GLP
21-MAR-2003 (32)

Species: rat Sex: no data
Strain: no data
Route of administration: oral unspecified
Exposure period: 20 d
Frequency of treatment: daily
Post exposure period: no data
Doses: 70 mg/kg bw/d
Control Group: other: no data

Method: other: 20 rats, no further information
Year: 1967
GLP: no
Test substance: other TS: no data on purity

Result: no deaths (thus, the test substance may be regarded as lacking any marked cumulative properties)
Reliability: (3) invalid
only one dose used, lack of information (e.g. unspecified route of oral administration)
16-JUN-2003 (22)

Species: rat Sex: no data
Strain: no data
Route of administration: oral unspecified
Exposure period: 7 months
Frequency of treatment: daily
Post exposure period: no data
Doses: 0.0025, 0.005, 0.025. 0.25 or 5 mg/kg bw/d
Control Group: yes
NOAEL: ca. .25 mg/kg bw

Method: other: CNS function evaluated according Cherkinskii, 1949: method of conditioned reflexes (time required for appearance, establishment,latent period,magnitude, frequency of occurrence), no further information
Year: 1967
GLP: no
Test substance: other TS: no data on purity
Remark: o-, m-, and p-chloronitrobenzene were tested: the para-isomer was found to be most toxic
Result: 0.0025, 0.005, 0.025, 0.25 mg/kg bw/d: no toxic effects

5 mg/kg bw/d:
hemapoetic system, last month of the experiment:
increase in the methaemoglobin content in the blood,
decrease of the haemoglobin content,
increase in the reticulocyte count (up to 78 %) and presence of Heinz bodies in the erythrocytes(up to 47 %);

liver function test: slight increase in blood alkaline phosphatase (no detail given)
effects on CNS function: some slowing down of fixation of the positive conditioned reaction and of the development of the differentiation reaction; liver function tests: increase in the blood alkaline phosphatase activity; rise in the level of bilirubin in the urine

urine: slight increase in bilirubin level
Reliability: (4) not assignable
lack of relevant information
16-JUN-2003 (22)

Species: mouse Sex: male/female
Strain: B6C3F1
Route of administration: inhalation
Exposure period: 13 w
Frequency of treatment: 6 h/d, 5 d/w
Post exposure period: no
Doses: 0, 1.1, 2.3, 4.5, 9 or 18 ppm (0, 7, 14.7, 28.8, 57.6,115.2 mg/m3)
Control Group: yes

Method: other: 10 mice/sex/group, whole body exposure, body/organ weight, gross and microscopic pathology , statistical analysis; histopathological evaluations on reproductive organs: see chapter 5.8
Year: 1993
GLP: yes
Test substance: other TS: purity: 99 %

Result: No clinical signs related to 2-chloronitrobenzene exposure
Mortality: 18 ppm, week 12, 2/10 males (livers darkly discoloured, defuse, severe sinusoidal congestion with hepatocellular degeneration and necrosis);
males: no significant different in body weight gain between control and treated mice; females: from 2.3 ppm body weight greater than in control mice
pathology:
2.3, 4.5, 9 and 18 ppm: increases in right kidney weight and liver weight (all groups, females)
9 and 18 ppm: increase in liver weights(males), hepatocytomegaly in all males; spleen enlargement among females due to hematopoietic cell proliferation
18 ppm: incidence of mild hepatic mineralization and/or necrosis, pale discoloration of the liver (1/10 females, 6/10 males), chronic inflammation in the liver (especially males), incidence of hematopoietic cell proliferation in the spleens of the males; histopathologic changes in the liver, notably hepatocytomegaly observed among females
NOAEL: 4.5 ppm (histopathological injury)
Reliability: (1) valid without restriction
Flag: Critical study for SIDS endpoint
30-AUG-2001 (44) (80) (102)

Species: mouse Sex: male/female
Strain: B6C3F1
Route of administration: inhalation
Exposure period: 2 weeks
Frequency of treatment: 6 h/d, 5 d/w
Post exposure period: no
Doses: 0, 1.1, 2.3, 4.5, 9, 18 ppm (approx. 0, 7, 14.7, 28.8, 57.6, 115.2 mg/m3)
Control Group: yes
NOAEL: ca. 2.3 ppm

Method: other: 5 mice/sex/group, whole body exposure, complete necropsy on all mice, histopathological evaluation on all mice
Year: 1993
GLP: yes
Test substance: other TS: purity: 99 %

Result: clinical signs: