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31. Januar 2018

Product Safety Basel
BASF Schweiz AG
Switzerland

Summary of toxicological investigations with CAS 81-33-4

1. BASF Report XXV/454, 1975

1.1 Acute oral toxicity with rats

Corresponds to study #9 in Attachment A of transmittal memo on CBI
HERO ID:4731529

Method: The study was conducted according to an internal protocol comparable to OECD Guideline 401. A test group consisting of 5 animals/sex was treated by single gavage application with an aqueous solution of the test substance. The animals were observed for mortality and for clinical symptoms of toxicity. At the end of the observation period of 14 days, the surviving animals were sacrificed for necropsy; animals that died during the observations period also were subjected to necropsy.

Test animals: Sprague-Dawley rats, male and female
Average weights at study initiation: males: 250 g, females: 160 g
Diet: Altromin R 1324, Altromin GmbH Lage
Application: gavage
Vehicle: water, 50% aqueous suspension
Dose level: 10000 mg/kg body weight

Results: None of the animals died. Dark red coloring of the skin and dark red coloring of the feces. No effects were reported regarding body weight. No abnormal observations during gross necropsy. The NOAEL was derived at >10000 mg/kg body weight.

Data Table:

Dose level (mg/kg body weight)	Animals used	Animals died within				
		1 hour	24 hours	48 hours	7 days	14 days
10000	5 males	0/5	0/5	0/5	0/5	0/5
10000	5 females	0/5	0/5	0/5	0/5	0/5

1.2 Acute inhalation toxicity with rats

Corresponds to study #5 in Attachment A of transmittal memo on CBI
HERO ID:4731525

Method: The conducted Inhalation Risk Test demonstrates the toxicity of an atmosphere saturated with vapors of the volatile components of a test substance at the temperature chosen for vapor generation. Young adult laboratory rats, 6 per sex, were exposed sequentially to the vapors generated by bubbling 200 L/h air through a substance column of about 5 cm above a fritted glass disc in a glass cylinder for 8 h. No analytical determination of the atmosphere concentrations was performed. The nominal concentration usually can be calculated as quotient of the amount of the test substance weight loss during exposure. Group-wise documentation of clinical signs was performed over a 7 day study period. Body weight of groups was determined before the start of the study and at the end of the observation period in surviving animals. However, the inhalation hazard test is insufficient for non-volatile substances.

Test animals: Rats, male and female
Average weights at study initiation: 182 g
Application: inhalation of dust
Duration of exposure: 8h
Vehicle: unchanged (no vehicle)
Dose levels: 14.74 mg/l (calculated)

Results: None of the animals died during the exposure period. Slight irritation of the mucous membrane. No effects on body weight were reported. No abnormal observations during gross pathology. Average concentration of substance in the atmosphere as stated in the report: 14.74 mg/l

Data Table:

Dose level (mg/kg body weight)	Animals used	Exposure time				
		3 min	10 min	1 hour	3 hours	8 hours
		Animals died				
Saturated atmosphere	6 males					0/6
Saturated atmosphere	6 females					0/6
Air control	3 males					0/3
Air control	3 females					0/3

1.3 Acute intraperitoneal toxicity with mice

Corresponds to study #7 in Attachment A of transmittal memo on CBI
HERO ID: 4731527

Method: The study was conducted according to an internal protocol. A test group consisting of 5 animals/sex was treated by single intraperitoneal application with an aqueous suspension of the test substance. The animals were observed for mortality and for clinical symptoms of toxicity. At the end of the observation period of 14 days, the surviving animals were sacrificed for necropsy; animals that died during the observations period also were subjected to necropsy.

Test animals: NMRI-Ivanovas mice
Average weights at study initiation: males: 22.6 g, females: 20.6 g
Diet: Altromin R 1324, Altromin GmbH Lage
Application: intraperitoneal
Vehicle: 0.5% aqueous carboxymethyl cellulose, 21.5%, 46.4% or 50% aqueous suspension.
Dose levels: 2150, 4640 and 10000 mg/kg

Results: At 10000 mg/kg, all animals died within 7 days. At 4640 mg/kg, 2/5 males and 1/5 females died; 1/5 males died when treated with 2150 mg/kg. Dyspnea, apathy, agitation, lying on the stomach, tumbling, bradykinesia, paresis of the hind extremities, spastic walk, shivering, tremors, roll cramps, flexing cramps, tonic cramps, tonic-clonic cramps, systemic red coloration of the skin and bad general health. Body weight gain was normal. During gross pathology, Intra-abdominal precipitation of the substance and isolated agglutination was recorded. An LD50 of 7000 mg/kg body weight was derived.

Data Table:

Dose level (mg/kg body weight)	Animals used	Animals died within				
		1 hour	24 hours	48 hours	7 days	14 days
10000	5 males	2/5	4/5	4/5	5/5	5/5
10000	5 females	0/5	4/5	4/5	5/5	5/5
4640	5 males	0/5	0/5	0/5	2/5	2/5
4640	5 females	0/5	0/5	1/5	1/5	1/5
2150	5 males	0/5	1/5	1/5	1/5	1/5
2150	5 females	0/5	0/5	0/5	0/5	0/5

1.4 Skin irritation study

Corresponds to study #12 in Attachment A of transmittal memo on CBI
HERO ID:4731532

Method: Animals were treated for 20 hours using occlusive conditions. An application site of 2.5x2.5 cm was covered with a 50% suspension of test substance. The animals were observed for 8 days and skin changes were recorded daily. The report describes findings after 24 hours and at the end of the observation period (8 days). Scores at additional timepoints are given in the raw data.

Test animals: White Vienna rabbits, 2 females
Average weights at study initiation: 3.41 kg and 3.38 kg
Application: intact skin, occlusive
Exposure Duration: 20 hours
Vehicle: water, the test substance was given as a 50% aqueous suspension
Amount applied: not specified
Washing of test site at the end of exposure: not specified

Results: The test item was found to have no irritation potential, however the exact determination of erythema scores at 24 and 72 hours was not possible due to coloring by the test substance which persisted until the 4th day pf the study.

Data Table:

Score	Timepoint	Animal 1	Animal 2
Erythema Score	24h	#	#
	72h	#	#
	4 days	#	#
	7 days	0	0
	8 days	0	0
Edema Score	24h	0	0
	72h	0	0
	4 days	0	0
	7 days	0	0
	8 days	0	0

Score not readable due to coloring by the test substance

1.5 Eye irritation study

Corresponds to study #1 in Attachment A
of transmittal memo on CBI
HERO ID: 4731519

Method: 50 µL of the test substance were applied to the conjunctival sac of the right eyes in two female rabbits. The animals were observed after 10 min, 1 and 3 h on the day of treatment and up to 8 days afterwards. The report describes findings after 1 and 24 hours and at the end of the observation period. More timepoints were available in the raw data. Talcum powder was used as negative control (left eyes).

Test animals: rabbits, 2 females
Average weights at study initiation: 3.38 and 3.44 kg
Application: single application, no washing was performed
Vehicle: unchanged (no vehicle)
Amount applied: volume of 50 µl

Results: After 1 hour, secretion and substance residues were observed. Remaining substance and smear were observed after 24 hours. The irritation caused by the test substance was not different from the control substance talcum powder. In animal 2, the redness apparently returned on day 8 after having disappeared on day 7 (similar findings for the talcum treated control eyes). All values were, however, well below the threshold of significance.

Data Table:

Score	Timepoint	Animal 1		Animal 2	
		Test substance	Talcum (control)	Test substance	Talcum (control)
Conjunctiva score	10 min	1	1	1	1
	1 h	1	1	1	1
	3 h	1	1	1	1
	24 h	1	1	1	1

	4 days	1	1	1	0
	7 days	1	1	0	0
	8 days	1	1	1	1
Chemosis Score	10 min	0	0	0	0
	1 h	1	1	1	1
	3 h	1	1	1	1
	24 h	1	0	0	0
	4 days	0	0	0	0
	7 days	0	0	0	0
	8 days	0	0	0	0
Iris Score	10 min	0	0	0	0
	1 h	0	0	0	0
	3 h	0	0	0	0
	24 h	0	0	0	0
	4 days	0	0	0	0
	7 days	0	0	0	0
	8 days	0	0	0	0
Cornea Score	10 min	0	0	0	0
	1 h	0	0	0	0
	3 h	0	0	0	0
	24 h	0	0	0	0
	4 days	0	0	0	0
	7 days	0	0	0	0
	8 days	0	0	0	0

Until day 7 substance residues were observed in both animals

2. BASF Report 77/360, 1978

2.1 Acute oral toxicity with rats

Corresponds to study #10 in Attachment A of transmittal memo on CBI
HERO ID:4731530

Method: The study was conducted according to an internal protocol comparable to the OECD Guideline 401. A test group consisting of 5 animals/sex was treated by single gavage application with an aqueous solution of the test substance. The animals were observed for mortality and for clinical symptoms of toxicity. At the end of the observation period of 14 days, the surviving animals were sacrificed for necropsy; animals that died during the observations period also were subjected to necropsy.

Test animals: male and female Sprague-Dawley rats
Average weights at study initiation: males 225 g, females 165 g
Diet: HERILAN MRH-Haltung Alleinfutter, Heinrich EGGERSMANN KG Rinteln
Application: gavage
Vehicle: 0.5% aqueous solution of carboxymethylcellulose, 50% suspension with the test item

Dose levels: 6810 and 10000 mg/kg body weight

Pre-Test: In a pre-test, two female rats per dose group were treated with dose levels of 1000 and 4640 mg/kg. No deaths occurred and no clinical symptoms were recorded except for red colored feces on the first day. No deviations from normal at autopsy.

Results main study: None of the animals died during the exposure period. At the beginning dyspnea was observed. Red colored feces observed on first day. No effects were reported regarding body weight. No abnormal observations during gross necropsy. LD50 > 10000 mg/kg body weight.

Data Table Pre-Test:

Dose level (mg/kg body weight)	Animals used	Animals died within				
		1 hour	24 hours	48 hours	7 days	14 days
4640	2 females	0/2	0/2	0/2	0/2	0/2
1000	2 females	0/2	0/2	0/2	0/2	0/2

Data Table Main Test:

Dose level (mg/kg body weight)	Animals used	Animals died within				
		1 hour	24 hours	48 hours	7 days	14 days
10000	5 males	0/5	0/5	0/5	0/5	0/5
10000	5 females	0/5	0/5	0/5	0/5	0/5
6810	5 males	0/5	0/5	0/5	0/5	0/5
6810	5 females	0/5	0/5	0/5	0/5	0/5

2.2 Acute inhalation toxicity with rats

Corresponds to study #6 in Attachment A of transmittal memo on CBI
HERO ID:4731526

Method: The conducted Inhalation Risk Test demonstrates the toxicity of an atmosphere saturated with vapors of the volatile components of a test substance at the temperature chosen for vapor generation. Young adult laboratory rats, 6 per sex, were exposed sequentially to the vapors generated by bubbling 200 L/h air through a substance column of about 5 cm above a fritted glass disc in a glass cylinder for 7 h. No analytical determination of the atmosphere concentrations was performed. The nominal concentration usually can be calculated as quotient of the amount of the test substance weight loss during exposure. Group-wise documentation of clinical signs was performed over a 14-day study period. Body weight of groups was determined before the start of the study and at the end of the observation period in surviving animals. However, the inhalation hazard test is insufficient for non-volatile substances.

Test animals: Rats, male and female
Average weights at study initiation: males 210 g, females 180 g
Application: inhalation of dust
Duration of exposure: 7h

Vehicle: unchanged (no vehicle)
Dose levels: 0.31 mg/l (calculated)

Results: None of the animals died during the exposure period. No abnormal observations during clinical investigations. No effects on body weight were reported. No abnormal observations during gross pathology. Average concentration of substance in the atmosphere as stated in the report: 0.31 mg/l.

Data Table:

Dose level (mg/kg body weight)	Animals used	Exposure time				
		3 min	10 min	1 hour	3 hours	7 hours
		Animals died				
Saturated atmosphere	6 males					0/6
Saturated atmosphere	6 females					0/6

2.3 Acute intraperitoneal toxicity with rats

Corresponds to study #8 in Attachment A of transmittal memo on CBI
HERO ID:4731528

Method: The study was conducted according to an internal protocol. A test group consisting of 5 animals/sex was treated by single intraperitoneal application with an aqueous suspension of the test substance. The animals were observed for mortality and for clinical symptoms of toxicity. At the end of the observation period of 14 days, the surviving animals were sacrificed for necropsy; animals that died during the observations period also were subjected to necropsy.

Test animals: NMRI-Wiga mice
Average weights at study initiation: males: 28.7 g, females: 28 g
Diet: HERILAN MRH-Haltung Alleinfutter, Heinrich EGGERSMANN KG Rinteln
Application: intraperitoneal
Vehicle: 0.5% aqueous carboxymethyl cellulose, 46.4% or 50% suspensions applied
Dose levels: 10000; 6810; 4640 mg/kg

Pre-Test: In a pre-test, two male mice per dose group were treated with dose levels of 215, 1000 and 4640 mg/kg. No deaths occurred, animals of the high and medium dose showed dyspnea and ruffled fur on the first day of treatment.

Results main study: 2/5 males and 5/5 females treated with 10000 mg/kg, and 1/5 females treated with 6810 mg/kg died. Dyspnea, apathy, unsteady gait and ruffled fur were reported until day 4 in mice given 10000 and 6810 mg/kg. Death occurred on day 2 and 3, bad general health until and including day 4. Mice given 4640 mg/kg showed dyspnea and ruffled fur only on the first day of treatment. Deceased animals: intra-abdominal precipitation of the substance and coloration. Euthanized animals: intra-abdominal precipitation of the substance and coloration, thickening of the edges of the liver. An LD50 of 9000 mg/kg body weight was derived.

Data Table Pre-Test:

Dose level (mg/kg body weight)	Animals used	Animals died within			
		1 hour	24 hours	48 hours	7 days
4640	2 males	0/2	0/2	0/2	0/2
1000	2 males	0/2	0/2	0/2	0/2
215	2 males	0/2	0/2	0/2	0/2

Data Table Main Test:

Dose level (mg/kg body weight)	Animals used	Animals died within				
		1 hour	24 hours	48 hours	7 days	14 days
10000	5 males	0/5	0/5	1/5	2/5	2/5
10000	5 females	0/5	0/5	3/5	5/5	5/5
6810	5 males	0/5	0/5	0/5	0/5	0/5
6810	5 females	0/5	0/5	1/5	1/5	1/5
4640	5 males	0/5	0/5	0/5	0/5	0/5
4640	5 females	0/5	0/5	0/5	0/5	0/5

2.4 Skin irritation study

Corresponds to study #13 in Attachment A
of transmittal memo on CBI
HERO ID:4731533

Method: According to Federal Register 38, No. 187, § 1500.41, S. 27019, 27.09.73. Three rabbits (two male, one female) were treated with a 50% suspension of test substance on intact and scarified skin. The animals were observed for 8 days and skin changes were recorded on days 1, 2, 3, 6 and 8.

Test animals: White Vienna rabbits, 2 males, 1 female
Average weights at study initiation: average weight 3.0 kg
Application: intact and damaged skin
Exposure Duration: not specified in the report
Vehicle: water, the test substance was given as a 50% aqueous preparation
Amount applied: not specified

Results: The test item was found to have no irritation potential, however the exact determination of erythema scores at 24, 48 and 72 hours (except animal #1 intact skin) was not possible due to coloring by the test substance. All edema scores for intact skin were 0.

Data Table:

Score	Skin Type	Timepoint	Animal 1	Animal 2	Animal 3
	Intact skin	24h	#	#	#

Erythema Score		48h	#	#	#
		72h	0	#	#
		6 days	0	0	0
		8 days	0	0	0
	Scarified Skin	24h	#	#	#
		48h	#	#	#
		72h	#	#	#
		6 days	0	0	0
		8 days	0	0	0
Edema Score	Intact skin	24h	0	0	0
		48h	0	0	0
		72h	0	0	0
		6 days	0	0	0
		8 days	0	0	0
	Scarified Skin	24h	1	0	2
		48h	1	0	1
		72h	0	0	0
		6 days	0	0	0
		8 days	0	0	0

Score not readable due to coloring by the test substance

2.5 Eye irritation study

Corresponds to study #2 in Attachment A of transmittal memo on CBI
HERO ID: 4731520

Method: According to Federal Register 38, No. 187, § 1500.42, S. 27019, 27.09.73. Three male rabbits were treated with 100 µL of the test substance. Scores were recorded after 1, 24, 48 and 72 hours. Talcum was used as negative control substance in the left eyes (scores for talcum available in raw data only).

Test animals: rabbits, 3 males
Average weights at study initiation: average weight 2.75 kg
Application: single application, no washing was performed
Vehicle: unchanged (no vehicle)
Amount applied: 100 µl

Results: Minimal redness of the conjunctivae observed in all animals, reversible after 72 hours. One animal still showed redness on day 3 (the last day of observation), which is expected to be reversible upon longer observation.

Data Table:

Score	Timepoint	Animal 1		Animal 2		Animal 3	
		Test substance	Talcum (control)	Test substance	Talcum (control)	Test substance	Talcum (control)

Conjunctiva Score	1 h	1	2	2	2	2	2
	24 h	1	1	1	1	1	1
	48 h	1	1	1	1	1	0
	72 h	0	1	0	0	1	0
Chemosis Score	1 h	1	0	1	0	0	1
	24 h	0	0	0	0	0	0
	48 h	0	0	0	0	0	0
	72 h	0	0	0	0	0	0
Iris Score	1 h	0	0	0	0	0	0
	24 h	0	0	0	0	0	0
	48 h	0	0	0	0	0	0
	72 h	0	0	0	0	0	0
Cornea Score	1 h	0	0	0	0	0	0
	24 h	0	0	0	0	0	0
	48 h	0	0	0	0	0	0
	72 h	0	0	0	0	0	0

Substance residues were observed in all animals after 1 hour.