FOREWORD INTRODUCITON

AMMONIUM CHLORIDE

CAS N°: 12125-02-9

SIDS Initial Assessment Report

For

SIAM 17

Arona, Italy, 11-14 November 2003

1. Chemical Name:	Ammonium chloride
2. CAS Number:	12125-02-9
3. Sponsor Country:	Japan
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4. Shared Partnership with:	Mr. Tadaaki Komatsu CENTRAL GLASS CO., LTD.
5. Roles/Responsibilities of the Partners:	See below
• Name of industry sponsor /consortium	CENTRAL GLASS CO., LTD., The Dallas Group of America, BASF AG/ Ammonium chloride-Consortium
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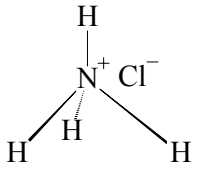
11. Comments:	None

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	12125-02-9
Chemical Name	ammonium chloride
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

The toxicity of ammonium chloride depends on ammonia which enters the living organism and thence the cell. This substance is readily absorbed by the gastrointestinal tract, and utilized in the liver to form amino acids and proteins.

The acute oral LD_{50} was 1,630 mg bw/kg in male rats and 1,220 mg/kg bw in female rats. The acute oral LD_{50} was 1,300 mg/kg bw in male mice. No data for inhalation and dermal acute toxicity are available.
This substance is considered to be moderately irritant to the skin and eye. In a study on sensitization, ten percent of the animals of a treatment group demonstrated a positive reaction after the challenge exposure (below the limit value of 30 percent). The study showed that the substance had no sensitising potential.

A repeated dose toxicity study was conducted using Sprague-Dawley rats (10 males/group) fed a diet containing this substance at 684 mg/kg bw/day (12,300 ppm) for 70 days. This substance had no effect on clinical signs, body weights, food consumption or necropsy findings. The urine pH was approximately 6.0 compared to a pH of 7.56 or greater in the control group, and the concentration of urinary calcium was increased. However no crystals were found in the urine. The other urinary chemistries (the concentration of magnesium, creatinine, phosphate, protein, and osmolality) were unchanged. Also no histopathological changes ascribable to this substance were found. The NOAEL for oral repeated dose toxicity is considered to be 684 mg/kg bw/day (12,300 ppm) in male rats. No data on repeated dose toxicity by inhalation and dermal exposure are available.

A reverse mutation study in bacteria [OECD TG 471] gave negative result. An *in vitro* chromosomal aberration test with Chinese hamster lung cells (CHL/IU) without metabolic activation was positive. This result is ascribable to the acidity of this substance. An *in vivo* micronucleus assay up to the maximum tolerance dose was negative. Based on the weight of evidence, this substance is considered to be not genotoxic.

Sprague-Dawley rats were administered 1 mL/kg bw of a solution at 1/6 M (8.9 mg/kg bw/day) by gavage on days 7 to 10 of gestation. Neither maternal toxicity nor developmental toxicity including teratogenicity was found.

There are three studies in which this substance was tested for carcinogenicity and for promotion effect on the initiator-induced carcinogenesis in the urinary system. These studies showed negative results on carcinogenicity of this substance in rats and mice.

Environment

Ammonium chloride is highly soluble in water and is dissociated to its respective ions (283 g/L at 25 °C). Depending on pH and temperature of water, these ions exist in the following equilibrium, $NH_4^+ + Cl^- + H_2O \Leftrightarrow H_3O^+ + Cl^- + NH_3 \Leftrightarrow HCl + NH_4^+ + OH^-$. Melting point, boiling point, and vapour pressure are 338 °C (decomposition), 520 °C (sublimation), and 0.0065 Pa at 35 °C, respectively. That indicates that this substance released into the environment is distributed into the water compartment in the form of ammonium ion and chloride ion. This substance is not expected to be adsorbed in soil. It is subjected to ion exchange to form inorganic or

organic salts with other counter ions in soil and water. It is known that ammonia (NH_3 or NH_4^+) is easily mineralized to nitrite (NO_2^-) by numerous species of bacteria. This substance is not expected to undergo photolysis. The fugacity model cannot be applied to estimate the distribution of this substance in environment because this substance is beyond the application limit of these models. Based on its physical-chemical properties, it can be assumed that water is the preferred compartment of the substance. Considering its propertiesit is not likely to accumulate in living organisms.

This substance has been tested in aquatic species (algae, invertebrates and fish). An acute growth inhibition test for algae was performed using algae (*Chlorella vulgaris*). The EC_{50} (biomass; 0-5 d) was 1,300 mg/L. An acute toxicity test with daphnids (*Daphnia magna*) and bivalves (*Mulinia lateralis*) reported results of 101 mg/L (survival; 48-h LC_{50}) and 42.0 mg/L (growth weight; 10-d EC_{50}), respectively. The 96-h LC_{50}s using various kinds of fish were in a range of 96.2 [the lowest; fathead minnow (*Pimephales promelas*)] to 218 mg/L. The lowest acute toxicity value of this substance was 42.0 mg/L (10-d EC_{50} for bivalves). A chronic test for algae was performed using *Navicula sp*. The NOEC (growth rate; 0-10 d) was 26.8 mg/L. A chronic reproduction toxicity test was performed using daphnids (*Daphnia magna*). The 21-d NOEC was 14.6 mg/L. And NOECs from 28-d and 44-d chronic tests for fish were in a range of 8.0 to 23.9 mg/L. The lowest chronic toxicity value of this substance was reported for a marine fish, inland silverside (*Menidia beryllina*) to be 8.0 mg/L for 28-d NOEC.
In soil organisms, a LC_{50} for earthworms (*Eisenia fetida)* was reported to be 163 mg/kg. As a conclusion of effect in the environmental organism, effects are rather mild and transient.

Exposure

The production volume of ammonium chloride in Japan was 85,600 tons in 2001. In Europe, the same range of production volume as in Japan is estimated and in the U.S., a production volume of 10,000 – 50,000 tonnes per year is presumed. This substance is mainly used (approximately 70%) as a fertilizer for water paddies in Japan. This substance is also used as an electrolyte for dry cell batteries, flux agent for coating sheet iron with zinc, agents for tinning, food additives, therapeutic drugs etc. In the U.S., this substance is mainly used as a feed additive to prevent the formation of calculi for cattle. This substance has been ingested for a long time by humans. This substance can be added directly to human food in the U.S. and is Generally Recognized As Safe (GRAS) [US FDA]. Bottled water containing this substance as chloride up to 250.0 mg/L is allowed as potable [US Federal Food, Drug and Cosmetic Act]. This substance is approved as drug in several countries for electrolyte replenishment or expectorants and as food additive (fermentation and blowing agent) without use restrictions in Japan. This substance is also used as food additive (flavors) in Germany. This substance has been available as a therapeutic agent in Canada since its introduction in 1925. It has been used as a mild diuretic, an expectorant, a weight-reducing agent and a urine-acidifying agent.
This substance released into the environment is distributed into the water compartment in the form of ammonium ion and chloride ion, and exposure to aquatic biota is possible. Occupational exposure is possible by inhalation (as dust) and dermal routes. In the case, the workers wear protective equipments. Consumer exposure is also possible by inhalation (as dust) and dermal routes. It should be noted that the use of ammonium chloride as a fertiliser may cause a concern when assessing the potential eutrophication hazard including drinking water quality in certain regions.

RECOMMENDATION

The chemical is currently of low priority for further work.

RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

The chemical possesses properties indicating a hazard for human health (acute toxicity and irritation) and the environment. Although the hazard do not warrant further work (as they are related to transient or non-lasting effects or to acute toxicity which may become evident only at very high exposure level), they should nevertheless be noted by chemical safety professionals and users.
Although the substance has a low inherent hazard potential for the environment, it degrades in the environment to nitrite. It is recommended that the use of ammonium chloride as a fertiliser is taken into account when assessing the exposure of nitrite and nitrate to humans through drinking water.

SIDS Initial Assessment Report

1 IDENTITY

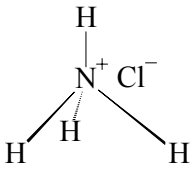
1.1 Identification of the Substance

CAS Number: 12125-02-9

IUPAC Name: Ammonium chloride

Molecular Formula: ClH_4N

Structural Formula: See below



Molecular Weight: 53.49

Synonyms: Acide ammonium chloride
Amchlor
Ammoneric
Ammonium chlorid
Ammonium muriate
Chlorid ammony
Chlorihydrate d'ammoniaque
Chlorure d'ammonium
Darammon
Sal ammonia
Sal ammoniac
Sal ammonite
Salmiac

1.2 Purity/Impurities/Additives

Purity: ≥ 99.5 (w/w)

Impurities: water ≤ 0.2 (w/w)

iron ≤ 0.0005 (w/w)

heavy metal (as Pb) ≤ 0.0006 (w/w)

sulfate salt ≤ 0.02 (w/w)

residue on ignition ≤ 0.2 (w/w)

1.3 Physico-Chemical properties

Table 1 Summary of physico-chemical properties

Property	Value	Reference
Physical state	Solid	Merck Index 2001
Melting point	Decomposition at 338 °C	IPCS CEC
Boiling point	Sublimation at 520 °C	IPCS CEC
Relative density	1.53 at 20°C	Ullmann's Encyclopedia of Industrial Chemistry, 2000
Vapour pressure	1.3 hPa at 160 °C 0.0065 Pa at 35 °C	IPCS CEC Wagner, 1961
Water solubility	283 g/L at 25 °C	IPCS CEC, Merck Index 2001
Partition coefficient n-octanol/water (log value)	The log Kow for this substance cannot be experimentally determined. It is expected to be very low.	
Henry's law constant	3.88 X 10^{-13} atm-m^3/mole	HENRYWIN version 1.90, Syracuse Research Co.
Appearance	almost white and odorless solid (powder or flake)	Merck Index 2001

2 GENERAL INFORMATION ON EXPOSURE

2.1 Production Volumes and Use Pattern

The production volume of ammonium chloride in Japan was 85,600 tonnes in 2001. In Europe, the same range of production volume as in Japan is estimated and in the U.S., a production of 10,000 – 50,000 tonnes per year is estimated. This substance is mainly used (approximately 70%) as a fertilizer for water paddies in Japan. This substance is also used as an electrolyte for dry cell batteries, a flux agent for coating sheet iron with zinc, a tinning agent, a food additive, therapeutic drug and so on. In the U.S., this substance is mainly used as feed additive to prevent the formation of calculi for cattle.

2.2 Environmental Exposure and Fate

2.2.1 Sources of Environmental Exposure

This substance is used for various uses and exposure to the environment is possible. This substance is directly released into the environment, when used as fertilizer in water paddies and as feed additive.

2.2.2 Photodegradation

Direct photodegradation is not expected because this substance has no absorption band in the UV and visible region.

2.2.3 Stability in Water

This substance is highly soluble in water and is dissociated to the ions, NH_4^+ and Cl^-. These ions exist in the following equilibrium.

$$NH_4^+ + Cl^- + H_2O \Leftrightarrow H_3O^+ + Cl^- + NH_3 \Leftrightarrow HCl + NH_4^+ + OH^-$$

This equilibrium is affected by temperature and pH of the solution.

2.2.4 Transport between Environmental Compartments

The substance is not expected to be adsorbed in soil. However it is subjected to ion exchange to form inorganic or organic salts with other counter ions in soil and water. Based on its physical-chemical properties, it can be assumed that water is the preferred compartment of the substance.

2.2.5 Biodegradation

Although quantitative data are not available, it is known that ammonia (NH_3 or NH_4^+) is easily mineralized to nitrite ion (NO_2^-) by numerous species of bacteria such as *Nitrosomonas europea, Nitrosococcus, Nitrosospira*.

2.2.6 Bioaccumulation

Because NH_3 and/or NH_4^+ or Cl^- is common component of the living organism, pertinent data are not available.

2.2.7 Other Information on Environmental Fate

It should be noted that the use of ammonium chloride as a fertilizer may cause a concern when assessing the potential eutrophication hazard as well as drinking water quality in certain regions.

2.3 Human Exposure

2.3.1 Occupational Exposure

Under conditions of use in Japan, occupational exposure of this substance to the user may occur from the application as a fertilizer to water paddies during bagging off and emptying bags, during spreading on land and from the production of dry cell batteries. During maintainance of the production system, occupational exposure is possible by inhalation (as dust) and by the dermal route. In this case, the workers wear protective equipments.

In ACGIH, TLV-TWA and STEL/C in the state of dust are determined as 10 and 20 mg/m^3, respectively [ACGIH, 1999].

2.3.2 Consumer Exposure

Consumer exposure is possible by inhalation (as dust) and by the dermal route because of use as fertilizer in water paddies. This substance has been ingested for a long time. This substance can be added directly to human food and is considered in the U.S. as Generally Recognized As Safe (GRAS) [US FDA]. Bottled water containing this substance not exceeding 250.0 mg(as chloride)/L is allowed as potable [US Federal Food, Drug and Cosmetic Act]. This substance is approved as a drug in several countries for electrolyte replenishment or expectorants and as food additive (fermentation and blowing agent) without usage restrictions in Japan. This substance is also used as food additive (flavors) in Germany. This substance has been available as a therapeutic agent in Canada since its introduction in 1925. It has been used as a mild diuretic, an expectorant, a weight-reducing agent and a urine-acidifying agent [Levene and Knight, 1974]. Usually the dose is 4 to 12 grams a day orally [Service-drug Inform., 1988]. These doses correspond to 57 mg/kg and 171 mg/kg for a body weight of 70 kg..

3 HUMAN HEALTH HAZARDS

3.1 Effects on Human Health

3.1.1 Toxicokinetics, Metabolism and Distribution

Toxicity of ammonium chloride depends on the ammonia which enters the living organism and thence the cell. Cell membranes are relatively impermeable to ionized ammonia (NH_4^+), whereas un-ionized ammonia (NH_3) passes tissue barriers with ease. Following oral administration, this substance is rapidly absorbed from the gastrointestinal tract. This substance is utilized in the liver to form amino acids and proteins [Reynolds et al., 1982].

3.1.2 Acute Toxicity

Studies in Animals

Inhalation

No study was available.

Dermal

No study was available.

Oral

Many studies have been available, and two studies [BASF AG, 1983 and Takasaki et al., 1990] were considered to be most reliable and identified as key studies.

1) BASF study

Wistar rats (10 animal/group/sex) were administered by gavage at 681, 1,000, 1,470, 1,780 and 2,150 mg/kg bw. Dead male and female animals were observed in those given a dose of 1,470 mg/kg bw or higher and 1,000 mg/kg bw or higher within 1 day after administration. Dyspnea, apathy, abnormal position and staggering were observed at a dose of 1,000 mg/kg bw or higher. In

necropsy findings, no abnormalities were detected in surviving animals. The LD50 for males, females and overall were 1,630, 1,220 and 1,410 mg/kg bw.

2) Takasaki study

CD-1 mice (10 male/group) were administered at 0 (control), 800, 1,000, 1,200, 1,400, 1,700 and 2,100 mg/kg bw through a stomach tube. Dead animals were observed in those dose groups given 1,200 mg/kg bw or higher. Diarrhoea, cyanosis and ataxic gait were observed. At necropsy, swelling and whitening of kidney and hemorrhage in brain were observed. The LD50 was 1,300 mg/kg bw in male mice.

Conclusion

The oral LD50 in rats was 1,410 mg/kg bw. Overt signs of toxicity (dyspnea, apathy, abnormal posture and staggering, and some deaths) occurred at doses of 1,000 mg/kg bw and above [BASF, 1983]. For male mice, the oral LD50 was 1,300 mg/kg bw. Diarrhoea, cyanosis, ataxia gait and some deaths were seen at 1,200 mg/kg bw [Takasaki et al., 1990].

Other Routes of Exposure

Although several studies were available, these studies were not reliable.

Studies in Humans

Oral

Large doses of this substance may cause nausea, vomiting, thirst, headache, hyperventilation and progressive drowsiness, and lead to profound acidosis and hypokalemia [Reynolds et al., 1982].

3.1.3 Irritation

Skin Irritation

Studies in Animals

Two studies have been available. The study by M.B.A. LABS. (1985) was considered to be more reliable. It was conducted using six New Zealand White Albino rabbits according to the method of Draize in accordance with GLP. The only redness was observed after 24 hours and disappeared within 48 hours. The result indicates that this substance is a moderate skin irritant.

A second study by BASF AG (1968) reported also that this substance is moderately irritant to skin in rabbits.

Eye Irritation

Studies in Animals

Two studies have been available. The study by BASF AG (1968) was considered to be reliable and identified as the key study. About 50 mg of the powdery product was applied to the conjunctival sac of the rabbit's eye. Both powder and aqueous solution of this substance caused moderate irritation to rabbit’s eye after 10 minutes, 1 and 24 hours. The changes such as redness, swelling or cloudy corneal opacity were reversible within 8 days without leaving any residues. There were no differences in the irritation between the powder and aqueous solution.

Conclusion

This substance is considered to be moderately irritant to the skin and eye in rabbits.

3.1.4 Sensitisation

Studies in Animals

Skin

A guinea pig maximization test conducted according to GLP [Hoechst AG, 1987b] in female guinea pigs (Pirbright-White) is available. In an attempt to induce the sensitised state the animals received an intradermal injection of a 5% solution (in saline) and the skin was also subsequently in covered contact for 24 hours with a 25% solution. When challenged 11 days after the end of the induction phase with a 24-hour covered patch of a 10% solution, two of the 20 guinea pigs (10 %) demonstrated a positive reaction after the challenge exposure (below the limit value of 30 %). The study showed that the substance had no sensitising potential.

3.1.5 Repeated Dose Toxicity

Studies in Animals

Oral

Four studies have been available. The study by Arnold et al. (1997) was considered to be the most reliable and identified as the key study, because this test was reported with most details.

Sprague-Dawley rats (10 males/group) were fed a diet containing this substance at 12,300 ppm (equivalent to 684 mg/kg bw/day) for 70 days.

This substance had no effect on clinical signs, body weights, food consumption or necropsy findings. The urine pH was approximately 6.0 compared with a pH of 7.56 or greater in the control group, and the concentration of urinary calcium increased. However the crystals in urine were not found. The other urinary chemistries (the concentration of magnesium, creatinine, phosphate, protein, and osmolality) were unchanged. Histopathlogical examination was conducted on stomach kidneys and bladder. The study is consistent with the result of a study conducted in similar dose duration and method (580 mg/ kg bw/day, 58 days, with histopathlogy of bladder) [Shibata, et al 1989], revealing no adverse effect.No histopathological changes ascribable to this substance were found. The NOAEL for repeat dose toxicity is considered to be 12,300 ppm (equivalent to 684 mg/kg bw/day).

Studies in Humans

Oral

Two cases were shown below.

A 58-year-old woman with a long history of renal stone disease and urinary tract infection presented to the emergency room with exhaustion and air hunger. She had been taking six grams daily of this substance as a urine-acidifying agent for a period of six months in addition to agents directed against urinary tract infection. The combination of impaired renal function and effective hydrogen ion loading resulted in profound systemic acidosis [Levene and Knight, 1974].

An 18-year-old photographer's model who had always been in good health, was taken to the hospital by her parents because of hyperventilation and confusion of 1 day's duration. It was learned that for the past 6 months, in an effort to stay slim and photogenic, she had been taking up to 15 enteric-coated tablets of this substance daily for short periods, each tablet containing 1 gram,. No ill-effects had been noted except on 1 occasion, 4 weeks earlier, when she became nauseated and weak, with transient hyperventilation. During a period of 48 hours, ending 2 days before

admission, she took 82 grams of this substance. Thereafter, although she took no more medication, headache and nausea developed; she vomited once or twice and was noted to become progressively drowsy and confused. Soon after admission the patient lapsed into a comatose state. Large amounts of sodium bicarbonate solution were administrated intravenously. There was a steady rise in serum carbon dioxide content, which reached normal levels in 20 hours and then became higher than normal thereafter [Relman, 1961].

3.1.6 Mutagenicity

In vitro Studies

Bacterial test

Two studies have been available, the study by Hoechst AG (1987a) was considered to be more reliable and identified as the key study. The study was conducted according to OECD TG 471 and in compliance with GLP. Strains used were *Salmonella typhimurium* TA98, TA100, TA1535, TA1537, TA1538 and *Escherichia coli* WP2uvrA, and doses were 0, 4, 20, 100, 500, 2,500, 5,000 ug/plate. This test was conducted with and without metabolic activation. No increase of revertants was observed at any dose in any strains, indicating a negative result for this substance. Toxic effects were not observed at any dose. Another study [Ishidate et al., 1984] also gave a negative result.

Non-bacterial in vitro test

A chromosomal aberration test in Chinese hamster lung cells (CHL/IU) was conducted without metabolic activation at 0, 0.25, 0.3 and 0.4 mg/mL. Positive results were observed at concentrations of 0.3 mg/mL at 24 hrs and at 0.3 mg/mL and 0.4 mg/mL at 48 hrs [Ishidate et al., 1984]. This result is ascribable to the acidity of this substance, considering the physico-chemical properties of this substance.

In vivo Studies

A micronucleus assay was conducted with bone marrow in ddY male mice [Hayashi et al., 1988]. Animals had received by intraperitoneal injection either a single dose or four doses spaced 24 hours apart. The single dose test and the 4 times dose test were dosed with 62.5 - 500 mg/kg bw and 31.3 - 250 mg/kg bw as MTD (maximum tolerance dose), respectively, with mitomycin C as positive control. No increase of erythrocytes with micronuclei was observed in any group.

Conclusion

A reverse mutation study in bacteria [OECD TG 471] gave negative results. An *in vitro* chromosomal aberration test with Chinese hamster lung cells (CHL/IU) without metabolic activation was positive. This result is ascribable to the acidity of this substance. An *in vivo* micronucleus assay up to the maximum tolerance dose was negative. Based on the weight of evidence, this substance is considered to be not genotoxic.

3.1.7 Carcinogenicity

Three studies were reported where this substance was tested for carcinogenicity or potential enhancement of the carcinogenicity of other substances [ex. N-butyl-N-(4-hydroxybutyl) nitrosamine] by acidification of the urinary system . The decrease of urine pH was observed, however the incidences of bladder tumour, hyperplasia and calculi were not increased. These

studies showed negative results on carcinogenicity of this substance in rats and mice [Flaks and Clayson, 1975; Hagiwara et al., 1994].

3.1.8 Toxicity for Reproduction

Because the component chloride and ammonium ion is ubiquitous in the living organism, the number of experiments for inherent toxicity is limited [Goldman and Yakovac, 1964].

For humans, there is no restriction to medication to a pregnant woman according to the appending document of the medical drugs using this substance in Japan. Moreover, it is also used as medical drug and classified into Category A in Australia. Category A means that it is a medicine which has been used for many pregnant women and women of conceiving age, and that there is no proof of increase in the frequency of deformation and the frequency of direct or indirect detrimental action to the embryo.

Studies in Animals

Developmental Toxicity

The teratogenicity was tested using Sprague-Dawley rats (10 female) [Goldman and Yakovac, 1964]. Rats were administered by gavage once a day at 1 mL/kg b.w. of 1/6 M (equivalent to 8.9 mg/kg bw/day) solution on days 7 to 10 of gestation. The fetuses were obtained by Cesarean section and examined on day 20 of gestation. Maternal effect was supposely to be acidosis, no teratogenic toxicity was found. The effects of this substance on fetal growth noted were considered a consequence of maternal acidosis. No fetus with malformations was observed in this substance-treated group. This substance has no teratogenicity at this dose level.

3.2 Initial Assessment for Human Health

Ammonium chloride has been ingested for a long time by humans. This substance can be added directly to human food and is considered in the U.S. as Generally Recognized As Safe (GRAS) [US FDA]. Bottled water containing chloride not in excess of 250.0 mg/L is allowed as potable [US Federal Food, Drug and Cosmetic Act]. This substance is approved as a drug in several countries for electrolyte replenishment or expectorants and as food additive (fermentation and blowing agent) without usage restrictions in Japan. This substance is also used as food additive (flavors) in Germany. This substance has been available as a therapeutic agent in Canada since its introduction in 1925. It has been used as a mild diuretic, an expectorant, a weight-reducing agent and as in the case, a urine-acidifying agent.

The toxicity of this substance depends on ammonia which enters the living organism and thence the cell. This substance is readily absorbed by the gastrointestinal tract, and utilized in the liver to form amino acids and proteins.

The acute oral LD50 was 1,630 mg/kg bw in male rats and 1,220 mg/kg bw in female rats. The acute oral LD50 was 1,300 mg/kg bw in male mice. No data for inhalation and dermal acute toxicity are available.

This substance is considered to be moderately irritant to the skin and eye. In a study on sensitization, ten percent of the animals of a treatment group demonstrated a positive reaction after the challenge exposure (below the limit value of 30 percent). The study showed that the substance had no sensitising potential.

A repeated dose toxicity study was conducted using Sprague-Dawley rats (10 males/group) fed a diet containing this substance at 684 mg/kg bw/day (12,300 ppm) for 70 days. This substance had no effect on clinical signs, body weights, food consumption or necropsy findings. The urine pH was approximately 6.0 compared to a pH of 7.56 or greater in the control group, and the concentration of urinary calcium was increased. However no crystals were found in the urine. The other urinary chemistries (the concentration of magnesium, creatinine, phosphate, protein, and osmolality) were unchanged. Also no histopathological changes ascribable to this substance were found. The NOAEL for oral repeated dose toxicity is considered to be 684 mg/kg bw/day (12,300 ppm) in male rats. No data on repeated dose toxicity by inhalation and dermal exposure are available.

A reverse mutation study in bacteria [OECD TG 471] gave negative result. An in vitro chromosomal aberration test with Chinese hamster lung cells (CHL/IU) without metabolic activation was positive. This result is ascribable to the acidity of this substance. An in vivo micronucleus assay up to the maximum tolerance dose was negative. Based on the weight of evidence, this substance is considered to be not genotoxic.

Sprague-Dawley rats were administered 1 mL/kg bw of a solution at 1/6 M (8.9 mg/kg bw/day) by gavage on days 7 to 10 of gestation. Neither maternal toxicity nor developmental toxicity including teratogenicity was found.

There are three studies in which this substance was tested for carcinogenicity and for promotion effect on the initiator-induced carcinogenesis in the urinary system. These studies showed negative results on carcinogenicity of this substance in rats and mice.

4 HAZARDS TO THE ENVIRONMENT

4.1 Aquatic Effects

Special attention

Ammonium chloride entered into the environment exists in various species in the following equilibrium.

$$NH_4^+ + Cl^- + H_2O \Leftrightarrow H_3O^+ + Cl^- + NH_3 \Leftrightarrow HCl + NH_4^+ + OH^-$$

$pKa = 0.09018 + 2729.92 / T$ (T = absolute temperature in Kelvin)

$f = 1/(10^{pk_a - pH} + 1)$ where f is for fraction

This equilibrium depends on temperature, pH and ionic strength of the water in the environment. Un-ionized NH_3 species exists in the aquatic environments. and the fraction $(NH_3/(NH_3 + NH_4^+))$ steeply increases with elevated pH value or temperature. It is well known that toxicity to aquatic organisms has been attributed to un-ionized ammonia (NH_3) species, and NH_4^+ species is considered to be non-toxic, or significantly less toxic [Emerson et al., 1975].

A detailed treatment of aqueous ammonium equilibrium has been presented by the Emerson et al (1975).

A large number of the environmental toxicity studies of this substance were performed to investigate the toxicity of ammonia using this substance as a source of ammonia and the toxicity is expressed as total ammonia nitrogen (NH_3-N) or un-ionized NH_3. Therefore, we converted these values to NH_4Cl concentrations.

The ecotoxicity of this substance is low, based on these data available from different species and different trophic levels.

The reliable toxicity data of aquatic organisms are summarized in Table 2 and 3. The substance concentrations in the testing media were monitored during the course of the experiments.

Acute Toxicity Test Results

Acute toxicity data have been reported for three trophic levels of aquatic organism (algae, invertebrates and fish). One growth inhibition test for algae was performed using chlorella (*chlorella vulgaris*) [Przytocka-Jisiak et al., 1977]. The EC50 (biomass; 0-5 d) was 1,300 mg/L. Gersich and Hopkins (1986) and Huber et al. (1977) performed acute toxicity tests with daphnids (*Daphnia magna*) and bivalves (*Mulinia lateralis*), respectively. The 48-h LC50 (survival) and EC0 (immobilization) for daphnids were 101 and 39.7 mg/L, respectively. The 10-d LC50 (survival), EC50 (growth: weight), EC0 (survival) and EC0 (growth: weight) for bivalves were 82.9, 42.0, 31.3 and 8.8 mg/L, respectively. Also several acute toxicity tests for fish were reported. Various kinds of fish were used, and their 96-h LC50s were in a range of 74.2 [the lowest; bluegill (*Lepomis macrochirus*)] to 218 mg/L. The lowest acute toxicity value of this substance has been reported in a test with bivalves (10-d EC50 of 42.0 mg/L) by Huber et al. (1997).

Table 2 Summary of acute toxicity of ammonium chloride on aquatic organisms

Organism	Test duration, pH and temperature (°C)	Result (mg/L)	Reference
Algae			
Chlorella (*Chlorella vulgaris*)	5 d pH 8.0 - 8.5 26.0 °C	EC_{50} (biomass) = 1,300	Przytocka-Jisiak et al., 1977
Invertebrates			
Water flea (*Daphnia magna*)	48 h (s) pH 8.4 - 8.6 19.5 - 20.5 °C	LC_{50} (survival) = 101 EC_0 (imm) = 39.7	Gersich and Hopkins, 1986
Bivalve (*Mulinia lateralis*)	10 d (ss) pH 7.79 21.8 °C	LC_{50} (survival) = 82.9 EC_{50} (growth: weight) = 42.0 EC_0 (survival) = 31.3 EC_0 (growth: weight) = 8.8	Huber et al., 1997
Fish			
Fathead minnow (*Pimephales promelas*) Walleye (*Stizostedion vitreum*) Bluegill (*Lepomis macrochirus*)	96 h (ft) pH 7.89 - 8.39 21.4 - 22.6 °C	LC_{50} (survival) = 96.2 (fathead minnow) LC_{50} (survival) = 84.0 (walleyes) LC_{50} (survival) =74.2 (bluegill)	Mayes et al., 1986
Fathead minnow (*Pimephales promelas*)	96 h (ft) pH 8.06 22.0 °C	LC_{50} (survival) = 163	Thurston et al., 1983
Inland silverside (*Menidia beryllina*)	96 h (ft) pH 7.9- 8.1 25.0 ± 1.0 °C	LC_{50} (survival) = 174	Miller et al., 1990
Carp (*Cyprinus carpio*)	96 h (ss) pH 7.2 - 7.8 27.5 °C	LC_{50} (survival) = 209	Rao et al., 1973
Green sunfish (*Lepomis cyanellus*)	96 h (ft) pH 7.7 22.4 °C	LC_{50} (survival) = 218	McCormick et al., 1984
Rainbow trout (*Salmo gairdneri*)	96 h (ft) pH 7.84 13.8 °C	LC_{50} (survival) = 127	Thurston and Russo., 1983
Cutthroat trout (*Salmo clarki*)	96 h (ft) pH 7.8 12.8 °C	LC_{50} (survival) = 144	Thurston and Russo, 1978

s: static, ss: semi-static, imm: immobilization, ft: flow through, These values are calculated based on measured concentrations.

Chronic Toxicity Test Results

Chronic toxicity data have been reported for aquatic species from three trophic levels (algae, invertebrates and fish). One growth inhibition test for algae was performed using *Navicula sp*. [Admiraal, 1997]. The NOEC (growth rate; 0-10 d) was 26.8 mg/L and the LOEC (growth rate; 0-10 d) was 53.5 mg/L. One chronic toxicity test was performed using daphnids (*Daphnia magna*) on reproduction [Gersich and Hopkins, 1986]. The 21-d NOEC and LOEC for daphnids were 14.6 and 30.2 mg/L, respectively. And NOECs from 28-d and 44-d studies in fish were in a range of 8.0 to 23.9 mg/L. The lowest chronic toxicity value of this substance was reported for a marine fish, inland silverside (28-d NOEC of 8.0 mg/L) by Miller et al. (1990).

Table 3 Summary of chronic toxicity of ammonium chloride on aquatic organisms

Organism	Test duration	Result (mg/L)	Reference
Algae			
Marine diatom (*Navicula sp.*)	10 d pH 8.0 12.0 °C	NOEC (gr) = 26.8 LOEC (gr) = 53.5	Admiraal, 1977
Invertebrates			
Water flea (*Daphnia magna*)	21 d (ss) pH 8.3 - 8.6 19.5 - 20.0 °C	NOEC (rep) = 14.6 LOEC (rep) = 30.2	Gersich and Hopkins, 1986
Fish			
Fathead minnow (*Pimephales promelas*)	28 d (ft) pH 8.0 24.0 °C	NOEC = 11.8	Mayes et al., 1986
Inland silverside (*Menidia beryllina*)	28 d (ft) pH 7.36 - 7.86 23.5 - 25.0 °C	NOEC = 8.0 LOEC = 16.0	Miller et al., 1990
Green sunfish (*Lepomis cyanellus*)	44 d (ft) pH 7.9 21.0 °C	NOEC = 23.9 LOEC = 53.2	McCormick et al., 1984
Cutthroat trout (*Salmo clarki*)	36 d (ft) pH 7.8 12.8 °C	LC_{50} = 123	Thurston and Russo, 1978

ss: semi-static, ft: flow through, gr: growth rate, rep: reproduction, These values are calculated based on measured concentrations.

4.2 Terrestrial Effects

Yeardley et al. (1995) evaluated the toxicity of this substance to *Eisenia fetida* (Earth worm) according to the test guideline, EPA/600/3-88/029. Under the condition of 22 ± 2 °C and pH 7.7 in artificial soil, the LC50 was 163 mg/kg soil dw.

4.3 Other Environmental Effects

The fertilising effect of this substance has been appreciated not only in Japan but also in China, India and Southeast Asian countries such as Indonesia, Philippines, Thailand and so on. It has been said that the paddy rice manured with this substance grows healthier, hard to be lodged and good for ripening. The effect of this substance on paddy rice was shown in a study conducted at Hokuriku Agri. Experiment Station / Niigata, Japan [Fujiwara, 1976].

4.4 Initial Assessment for the Environment

This substance is highly soluble in water and is dissociated to its respective ions (283 g/L at 25 °C). Depending on pH and temperature of water, these ions exist in the following equilibrium, $NH_4^+ + Cl^- + H_2O \Leftrightarrow H_3O^+ + Cl^- + NH_3 \Leftrightarrow HCl + NH_4^+ + OH^-$. Melting point, boiling point, and vapour pressure are 338 °C (decomposition), 520 °C (sublimation), and 0.0065 Pa at 35 °C, respectively. That indicates that this substance released into the environment is distributed into the water compartment in the form of ammonium ion and chloride ion. This substance is not expected to be adsorbed in soil. It is subjected to ion exchange to form inorganic or organic salts with other counter ions in soil and water. It is known that ammonia (NH_3 or NH_4^+) is easily mineralized to nitrite (NO_2^-) by numerous species of bacteria. This substance is not expected to undergo photolysis. The fugacity model cannot be applied to estimate the distribution of this substance in the environment because this substance is beyond the application limit of the model. Based on its physical-chemical properties, it can be assumed that water is the preferred compartment of the substance. Considering its properties it is not likely to accumulate in living organisms.

This substance has been tested in aquatic species (algae, invertebrates and fish). An acute growth inhibition test for algae was performed using algae (*Chlorella vulgaris*). The EC50 (biomass; 0-5 d) was 1,300 mg/L. An acute toxicity test with daphnids (Daphnia magna) and bivalves (*Mulinia lateralis*) reported results of 101 mg/L (survival; 48-h LC50) and 42.0 mg/L (growth weight; 10-d EC50), respectively. The 96-h LC50s using various kinds of fish were in a range of 74.2 [the lowest; bluegill (*Lepomis macrochirus*)] to 218 mg/L. The lowest acute toxicity value of this substance was 42.0 mg/L (10-d EC50 for bivalves). A chronic test for algae was performed using *Navicula sp*. The NOEC (growth rate; 0-10 d) was 26.8 mg/L. A chronic reproduction toxicity test was performed using daphnids (*Daphnia magna*). The 21-d NOEC was 14.6 mg/L. And NOECs from 28-d and 44-d chronic tests for fish were in a range of 8.0 to 23.9 mg/L. The lowest chronic toxicity value of this substance was reported for a marine fish, inland silverside (*Menidia beryllina*) to be 8.0 mg/L for 28-d NOEC.

In soil organisms, a LC50 for earthworms (*Eisenia fetida*) was reported to be 163 mg/kg. As a conclusion of effect in the environmental organism, effects are rather mild and transient.

5 RECOMMENDATIONS

The chemical is currently of low priority for further work.

The chemical possesses properties indicating a hazard for human health (acute toxicity and irritation) and the environment. Although these hazards do not warrant further work (as they are related to transient or non-lasting effects or to acute toxicity which may become evident only at very high exposure level), they should nevertheless be noted by chemical safety professionals and users.

Although the substance has a low inherent hazard potential for the environment, it degrades in the environment to nitrite. It is recommended that the use of ammonium chloride as a fertilizer is taken into account when assessing the exposure of nitrite and nitrate to humans through drinking water.

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I U C L I D

Data Set

Existing Chemical	:	ID: 12125-02-9
CAS No.	:	12125-02-9
EINECS Name	:	ammonium chloride
EC No.	:	235-186-4
TSCA Name	:	Ammonium chloride ((NH4)Cl)
Molecular Formula	:	ClH4N

Producer related part

Company	:	MITSUBISHI CHEMICAL SAFETY INSTITUTE LTD.
Creation date	:	23.06.2003

Substance related part

Company	:	MITSUBISHI CHEMICAL SAFETY INSTITUTE LTD.
Creation date	:	23.06.2003
Status	:	
Memo	:	SIAM 17 ammonium chloride
Printing date	:	07.12.2004
Revision date	:	23.06.2003
Date of last update	:	07.12.2004
Number of pages	:	89
Chapter (profile)	:	Chapter: 1, 2, 3, 4, 5
Reliability (profile)	:	Reliability: without reliability, 1, 2, 3, 4
Flags (profile)	:	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 APPLICANT AND COMPANY INFORMATION

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Country : United Kingdom
Phone :
Telefax :
Telex :
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Homepage :

17.12.2003

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Contact person :
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Country : Netherlands
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Telefax : 31-172-432494
Telex :
Cedex :
Email :
Homepage :

17.12.2003

1.0.2 LOCATION OF PRODUCTION SITE, IMPORTER OR FORMULATOR

Type	:	
Name of plant	:	Ube Plant, Central Glass Co., Ltd
Street	:	
Town	:	755-0001 Yamaguchi prefecture
Country	:	Japan
Phone	:	
Telefax	:	
Telex	:	
Cedex	:	
Email	:	
Homepage	:	

Remark : Central Glass Co., Ltd. Tokyo
17.12.2003

1.0.3 IDENTITY OF RECIPIENTS

Name of recipient	:	Mr. Yasuhisa Kawamura, Ministry of Foreign Affairs, Economic Affairs Bureau, Second International Organization Div.
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Telex	:	
Cedex	:	
Email	:	
Homepage	:	

1.0.4 DETAILS ON CATEGORY/TEMPLATE

1.1.0 SUBSTANCE IDENTIFICATION

1.1.1 GENERAL SUBSTANCE INFORMATION

Purity type	:	
Substance type	:	Inorganic
Physical status	:	Solid
Purity	:	>= 99.5 % w/w
Colour	:	
Odour	:	

Remark : As commercial product for industrial use and food additives (satndard value)
analytical result: 99.52% (mean) min. 99.51- max. 99.56%
Flag : Critical study for SIDS endpoint
17.12.2003 (17)

Purity type :
Substance type : Inorganic
Physical status : Solid
Purity : >= 95.5 % w/w
Colour :
Odour :

Remark : As commercial product for fertilizer (satndard value)
17.12.2003 (17)

Purity type :
Substance type : Inorganic
Physical status : Solid
Purity : = 99.5 - 99.8 % w/w
Colour :
Odour :

17.12.2003 (15)

1.1.2 SPECTRA

Type of spectra : IR

1.2 SYNONYMS AND TRADENAMES

Acide ammonium chloride

Flag : Critical study for SIDS endpoint

Amchlor

Flag : Critical study for SIDS endpoint

Ammonchlorid

Flag : Critical study for SIDS endpoint

Ammoneric

ammonii chloridum

Ammonium chlorid

Ammonium muriate

Flag : Critical study for SIDS endpoint

Ammoniumchlorid

CHLORHYDRATE D' AMMONIUM

Flag : Critical study for SIDS endpoint
17.12.2003

CHLORHYDRATE D'AMMONIAQUE

Chlorid amonny

Flag : Critical study for SIDS endpoint

CHLORURE D' AMMONIUM

Flag : Critical study for SIDS endpoint

CLORURO DI AMMONIO,AMMONIO CLORURO.

Darammon

Flag : Critical study for SIDS endpoint

Dermalcare 1673

17.12.2003

E 510

hydrochloric acid, ammonium salt

NH4Cl

Sal ammonia

Flag : Critical study for SIDS endpoint

Sal ammoniac

Flag : Critical study for SIDS endpoint

Sal ammonite

Flag : Critical study for SIDS endpoint

Sal amoniaco, sal de armenia, cloruro de amoniaco

17.12.2003

Salammonite

Salmiac

Flag : Critical study for SIDS endpoint

Salmiak

Salmiaksalz

Schercotaine CAB-A

Schercotaine SCAB-A

Säureregulator E 510

1.3 IMPURITIES

Purity :
CAS-No : 7732-18-5
EC-No : 231-791-2
EINECS-Name : Water
Molecular formula :
Value : <= .2 % w/w

Remark : As commercial product for industrial use (standard value)
Flag : Critical study for SIDS endpoint
17.12.2003 (17)

Purity :
CAS-No :
EC-No :
EINECS-Name : residue on ignition
Molecular formula :
Value : <= .2 % w/w

Remark : As commercial product for industrial use (standard value)
Flag : Critical study for SIDS endpoint
17.12.2003 (17)

Purity :
CAS-No : 7439-89-6
EC-No : 231-096-4
EINECS-Name : Iron
Molecular formula :
Value : <= .0005 % w/w

Remark : As commercial product for industrial use (standard value)
Flag : Critical study for SIDS endpoint
17.12.2003 (17)

Purity :
CAS-No :
EC-No :
EINECS-Name : heavy metal (as Pb)
Molecular formula :

Value : <= .0006 % w/w

Remark : As commercial product for industrial use (standard value)
Flag : Critical study for SIDS endpoint
17.12.2003 (17)

Purity :
CAS-No :
EC-No :
EINECS-Name : sulfate salt
Molecular formula :
Value : <= .02 % w/w

Remark : As commercial product for industrial use (standard value)
Flag : Critical study for SIDS endpoint
17.12.2003 (17)

1.4 ADDITIVES

1.5 TOTAL QUANTITY

Quantity : - tonnes produced in

Country : Japan
Remark : produced; 85600 tonnes in 2001
Flag : Critical study for SIDS endpoint
17.12.2003 (16)

Quantity : - tonnes imported in

Country : Japan
Remark : imported; 14100 tonnes in 2001
Flag : Critical study for SIDS endpoint
17.12.2003 (16)

Quantity : 10000 - 50000 tonnes produced in

Country : United States
17.12.2003 (16)

1.6.1 LABELLING

Labelling : as in Directive 67/548/EEC
Specific limits : no data
Symbols : Xn, , ,
Nota : E, ,
R-Phrases : (22) Harmful if swallowed
(36) Irritating to eyes
S-Phrases : (2) Keep out of reach of children
(22) Do not breathe dust

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1.6.2 CLASSIFICATION

Classified : as in Directive 67/548/EEC
Class of danger : Corrosive
R-Phrases : (22) Harmful if swallowed
Specific limits :

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Classified : as in Directive 67/548/EEC
Class of danger : Irritating
R-Phrases : (36) Irritating to eyes
Specific limits :

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1.6.3 PACKAGING

1.7 USE PATTERN

Type of use : Type
Category : Non dispersive use

Type of use : Type
Category : Wide dispersive use

Type of use : Industrial
Category : Agricultural industry

Flag : Critical study for SIDS endpoint

Type of use : Industrial
Category : Basic industry: basic chemicals

Flag : Critical study for SIDS endpoint

Type of use : Industrial
Category : Chemical industry: used in synthesis

Type of use : Industrial
Category : Electrical/electronic engineering industry

Flag : Critical study for SIDS endpoint

Type of use : Industrial
Category : Leather processing industry

Type of use : Industrial

Category : Metal extraction, refining and processing of metals

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Type of use : Industrial
Category : Polymers industry

Type of use : Industrial
Category : Other

Type of use : Use
Category : Cleaning/washing agents and disinfectants

Type of use : Use
Category : Conductive agents

Type of use : Use
Category : Electroplating agents

Flag : Critical study for SIDS endpoint

Type of use : Use
Category : Explosives

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Type of use : Use
Category : Fertilizers

Flag : Critical study for SIDS endpoint
17.12.2003

Type of use : Use
Category : Flux agents for casting

Type of use : Use
Category : Food/foodstuff additives

Flag : Critical study for SIDS endpoint
17.12.2003

Type of use : Use
Category : Laboratory chemicals

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Type of use : Use
Category : Pharmaceuticals

Flag : Critical study for SIDS endpoint
17.12.2003

Type of use : Use

Category : Process regulators

Type of use : Use
Category : Tanning agents

Type of use : Use
Category : Welding and soldering agents

Type of use : Use
Category : other: Flux component for galvanizing of zinc

Flag : Critical study for SIDS endpoint

1.7.1 DETAILED USE PATTERN

1.7.2 METHODS OF MANUFACTURE

Origin of substance :
Type : Production

17.12.2003

1.8 REGULATORY MEASURES

1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES

Type of limit : TLV (US)
Limit value : 10 mg/m3
Short term exposure limit value
Limit value : 20 mg/m3
Time schedule : 15 minute(s)
Frequency : 4 times

Remark : TWA is 10 mg/m3.
STEL/C is 20 mg/m3.
(as dust)
Flag : Critical study for SIDS endpoint
17.12.2003 (3)

Type of limit : OES (UK)
Limit value : 10 mg/m3
Short term exposure limit value
Limit value : 20 mg/m3
Time schedule : 8 hour(s)
Frequency : Times

17.12.2003 (67)

Type of limit : MAC (NL)

Limit value : 10 mg/m3

17.12.2003 (67)

Type of limit : MAK (DE)
Limit value : 10 mg/m3

17.12.2003 (67)

Type of limit : other: TWA/Switzerland
Limit value : 6 mg/m3

1.8.2 ACCEPTABLE RESIDUES LEVELS

1.8.3 WATER POLLUTION

Classified by : KBwS (DE)
Labelled by : KBwS (DE)
Class of danger : 1 (weakly water polluting)

17.12.2003 (38)

1.8.4 MAJOR ACCIDENT HAZARDS

Legislation : Stoerfallverordnung (DE)
Substance listed : No
No. in Seveso directive :

17.12.2003 (76)

1.8.5 AIR POLLUTION

1.8.6 LISTINGS E.G. CHEMICAL INVENTORIES

1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS

1.9.2 COMPONENTS

1.10 SOURCE OF EXPOSURE

Remark : NATS NATURAL OCCURING SOURCES:
** Occurs naturally in crevices in the vicinity of volcanoes. (KIRK-OTHMER
ENCYCLOPEDIA OF CHEMICAL TECHNOLOGY. 3RD ED.,

VOLUMES
1-26. NEW YORK, NY:
JOHN WILEY AND SONS, 1978-1984.,P. 2(78) 520)
RTEX PROBABLE ROUTES OF HUMAN EXPOSURE:
** Routes of entry: Inhalation of fumes, ingestion, skin and eye contact.
(SITTIG, M. HANDBOOK OF TOXIC AND HAZARDOUS CHEMICALS AND CARCINOGENS,
1985. 2ND ED. PARK RIDGE, NJ: NOYES DATA CORPORATION, 1985. 74)
** AMMONIUM CHLORIDE IS NOT CONSIDERED A SERIOUS INDUSTRIAL HAZARD.
(AMERICAN CONFERENCE OF GOVERNMENTAL INDUSTRIAL HYGIENISTS. DOCUMENTATION
OF THE THRESHOLD LIMIT VALUES AND BIOLOGICAL EXPOSURE
INDICES. 5TH ED.
CINCINNATI, OH:AMERICAN CONFERENCE OF GOVERNMENTAL INDUSTRIAL HYGIENISTS,
1986. 28)
(Reference: HSDB du NLM).

Test substance : LE FONTI DI ESPOSIZIONE DELLA SOSTANZA IN CONDIZIONI NORMALI
SONO LE SEGUENTI:
-INALAZIONE DELLE POLVERI
-INGESTIONE DELLE POLVERI
-CONTATTO CON OCCHI,MUCOSE E PELLE.

GLI EFFETTI DELLESPOSIZIONE SONO I SEGUENTI:
-IRRITAZIONE DEGLI OCCHI E DELLE MUCOSE,
-POSSIBILE IRRITAZIONE DELLA PELLE.

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Remark : Conventional dry cell batteries contain Ammonium Chloride and the public may be exposed to this when batteries deteriorate and the casing is holed.

Remark : Potential human exposure: During bagging off and emptying bags, during spreading on land (fertiliser).
Environmental exposure: Use as a fertiliser and landfill disposal.
Production process: Produced in the reaction of titanium tetrachloride with alcohol + solvent + ammonia (gas) to produce alkyl titanate + solvent + ammonium chloride by product. There is only 1 site of manufacture.

Remark : In Japan, this chemical is produced in one company.

Remark : About 70,000t/Y of this chemical is widely dispersed as fertilizer.

Country : Japan
Remark : Potential human exposure : During bagging off and emptying bags, during spreading on land (fertilizer).

Remark : Environmental exposure : Use as a fertilizer and land fill disposal (dry cell batteries)

Remark : Production process : Inhalation of fumes, ingestion, skin and eye contact

Remark : Release from the production cite : To bay, about 100t/Y

1.11 ADDITIONAL REMARKS

Memo : CAS NUMBER: 12125-02-9

Flag : Critical study for SIDS endpoint
31.07.2003

Memo : EINECS NUMBER: 235-186-4

Flag : Critical study for SIDS endpoint
31.07.2003

Memo : NAME (IUPAC NAME): ammonium chloride

Flag : Critical study for SIDS endpoint
31.07.2003

Memo : NAME (OECD NAME): ammonium chloride

Flag : Critical study for SIDS endpoint
31.07.2003

Memo : MOLECULAR FORMULA & WEIGHT: ClH4N, 53.49

Flag : Critical study for SIDS endpoint
31.07.2003 (15)

Memo : STRUCTUAL FORMULA: NH4-Cl

Flag : Critical study for SIDS endpoint
31.07.2003

Memo : OTHER: Colorless, odorless crystals or cryst masses; or white, granular powder, cooling, saline taste; somewhat hygroscopic. Tendency to cake. Strongly endothermic.

Flag : Critical study for SIDS endpoint
31.07.2003 (15)

Memo : Other: Consumer Exposure

Remark : [Consumer exposure is possible by inhalation (as dust) and dermal routes because of use as fertilizer to water paddy. This substance has been ingested for a long time. This substance can be added directly to human food in U.S. as affirmed as Generally Recognized As Safe (GRAS) [US FDA]. Bottled water containing this substance not exceeding 250.0 mg(as chloride)/L is allowed as portablepotable [US Federal Food, Drug and Cosmetic Act]. This substance is approved as drug in several countries for electrolyte replenishment or expectorants and as food additive (fermentation and blowing agent) without usage restrictions in Japan. This substance is also used as food additive (flavors) in Germany. This substance has been available as a therapeutic agent in Canada since its introduction in 1925. It has been used as a mild diuretic, an expectorant, a weight-reducing agent and as in the case, a urine-acidifying agent [Levene D.L 1974]. Usually the dose is 4 to 12 g a day orally [Survice-drug Inform. 88]. In the case of 70 kg of body weight, these doses correspond to 57 mg/kg and 171 mg/kg, respectively.]

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Remark : Options for disposal: Landfill
Transport information: By lorry
Approx 20 bags (each containing 850 kg - 1TE) per load. Average 1 - 11/2 loads per week. Ammonium chloride is in sealed bags during transport.
One site of manufacture: Process not closed.

1.12 LAST LITERATURE SEARCH

Type of search : Internal and External
Chapters covered :
Date of search :

Remark : ACGIH
AQUIRE (CIS, STN)
BEILSTEIN (STN)
BIOSIS (STN, Dialog)
CHEMCATS (STN)
CHRIS (CIS, CHEM-BANK)
CSCHEM (STN)
ChemFinder
ECDIN
GMELIN (STN)
HODOC(STN)
HSDB (CIS, STN, DataStar, CHEM-BANK)
IARC
IRIS (CIS, CHEM-BANK)
IUCLIDMSDS-CCOHS (STN, Dialog)
MEDLINE (STN, Dialog, Datastar)
MSDS-OHS (STN)
NCI
NIOSHOHMTADS (CIS, CHEM-BANK)
NIOSHTIC(STN, Dialog)

PROMT(STN, Dialog)
REGISTRY (STN, Dialog)
RTECS(STN, CIS, Dialog, CHEM-BANK)
SPECINFO (STN)
SRC PhysPro Database(SRC: Syracuse Research Corporation)
TOXCENTER (STN)
TOXFILE (Dialog, Datastar)
TSCATS (CIS)

Date of the literature search: 15 July, 2003

17.12.2003

1.13 REVIEWS

2.1 MELTING POINT

Decomposition : yes, at = 338 °C

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
17.12.2003 (43) (75)

Decomposition : yes, at = 337.8 °C
Sublimation :
Method :
Year :
GLP :
Test substance : as prescribed by 1.1 - 1.4

Reliability : (2) valid with restrictions
17.12.2003 (18) (38) (56) (69)

Decomposition : yes, at = 340 °C

Reliability : (3) invalid
17.12.2003 (78)

Decomposition : yes, at >= 335 °C

Reliability : (3) invalid
17.12.2003 (12)

Value : = 337.8 °C
Sublimation : yes
Method :
Year :
GLP :
Test substance :

Reliability : (3) invalid
17.12.2003 (1)

2.2 BOILING POINT

Remark : Sublimation at 520 degree C
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
17.12.2003 (43) (88)

2.3 DENSITY

Type : relative density
Value : = 1.53 at 20 °C

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint

17.12.2003 (84)

Type : relative density
Value : = 1.5274 at 25 °C

Reliability : (2) valid with restrictions
17.12.2003 (15)

Type : relative density
Value : = 1.5275 at 25 °C

Reliability : (2) valid with restrictions
17.12.2003 (78)

Type : density
Value : = 1.527 g/cm³ at 20 °C

Reliability : (2) valid with restrictions
17.12.2003 (38)

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value : = .0065 hPa at 35 °C

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
27.06.2003 (85)

Value : = 1.3 hPa at 160 °C

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
31.07.2003 (43) (59)

Value : = 66 hPa at 250 °C

Reliability : (4) not assignable
17.12.2003 (84)

Value : = 65 hPa at 250 °C

Reliability : (4) not assignable
17.12.2003 (49)

Value : = 1010 hPa at 338 °C

Reliability : (4) not assignable
17.12.2003 (49)

Value : = 1010 hPa at 338 °C

Reliability : (4) not assignable
17.12.2003 (84)

Value : = 35000 hPa at 520 °C

Reliability : (4) not assignable
17.12.2003 (44)

2.5 PARTITION COEFFICIENT

Remark : log Kow for this substance is inaccessible experimentally, it would be a very low value.
Flag : Critical study for SIDS endpoint
17.12.2003

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in :
Value : = 283 g/l at 25 °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
31.07.2003 (15)

Solubility in :
Value : = 229 g/l at 0 °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :

Reliability : (2) valid with restrictions
17.12.2003 (15)

Solubility in :
Value : = 260 g/l at 15 °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :

Reliability : (2) valid with restrictions
17.12.2003 (15)

Solubility in :
Value : = 396 g/l at 80 °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :

Reliability : (2) valid with restrictions
17.12.2003 (15)

Solubility in :
Value : at °C
pH value : = 5.5
concentration : 10 g/l at 25 °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :

Reliability : (2) valid with restrictions
17.12.2003 (15)

Solubility in :
Value : at °C
pH value : = 5.1
concentration : 30 g/l at 25 °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :

Reliability : (2) valid with restrictions
17.12.2003 (15)

Solubility in :
Value : at °C
pH value : = 5
concentration : 100 mg/l at 25 °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :

Reliability : (2) valid with restrictions
17.12.2003 (15)

2.6.2 SURFACE TENSION

2.7 FLASH POINT

2.8 AUTO FLAMMABILITY

Remark : Non auto flammable
17.12.2003 (12)

Remark : Non inflammable.
17.12.2003

2.9 FLAMMABILITY

Result : non flammable

17.12.2003 (26)

2.10 EXPLOSIVE PROPERTIES

Result : not explosive

17.12.2003 (12)

Remark : Staubexplosionsfaehigkeit: Klasse ST = 0
17.12.2003 (38)

2.11 OXIDIZING PROPERTIES

2.12 DISSOCIATION CONSTANT

2.13 VISCOSITY

2.14 ADDITIONAL REMARKS

Memo : Henry's law constant

Result : 3.88 X 10E-13 atm-m3/mole
Method: Calculated
Calculated using HENRYWIN version 1.90 - 2000 U.S. Environmental Protection Agency, Syracuse Research Co.
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
08.07.2003

3.1.1 PHOTODEGRADATION

Remark : Ammonium chloride has no absorption band in the UV and VIS region.
AOPWIN version 1.90, Syracuse Research Co.
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
31.07.2003

3.1.2 STABILITY IN WATER

Remark : Ammonium chloride dissociates to NH4+ and Cl- ions in water, immediately.

This substance is highly soluble in water and is dissociated to the ions, NH4+ and Cl-.
These ions exist in the following equilibrium.
NH4+ + Cl- + H2O <-> H3O+ + Cl- + NH3 <-> HCl + NH4+ + OH-
This equilibrium is affected by temperature and pH of the solution.
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
17.12.2003

3.1.3 STABILITY IN SOIL

3.2.1 MONITORING DATA

Type of measurement : other
Media : air
Concentration :
Method :

Result : Ammonium Chloride in air samples can be determined using colorimetric analysis (HSDB, 1991).

(No additional details available)
17.12.2003

3.2.2 FIELD STUDIES

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

3.3.2 DISTRIBUTION

Remark : This substance is not applied to Fugacity model.
Chemicals Evaluation and Research Institution, Japan (2002): report on genetic fugacity model (Mackay level III)

The substance is not expected to be adsorbed in soil. However it is subjected to ion exchange to form inorganic or organic salts with other counter ions in soil and water. Based on its physical-chemical properties, it can be assumed that water is the preferred compartment of the substance.

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
17.12.2003

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Deg. product :
Method : other: (calculated) BIOWin calculation
Year :
GLP :
Test substance :

Remark : This substance is not applied to this system.
BIOWIN version 4.00, Syracuse Research Co.
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
31.07.2003

Remark : It was found that out of 229 species of bacteria which were tested 104 produced nitrite from ammonium salts.
Reliability : (4) not assignable
17.12.2003 (22)

Remark : Five genera are listed by Bergey as being capable of forming nitrite from ammonia, namely, Nitrosomonas europaea and monocella, Nitrosococcus, Nitrosospira, Nitrosocystis, Nitrosogloea.
Reliability : (4) not assignable
17.12.2003 (62)

Method : BACTERIA: Gram negative short rods.
MEDIA: Soil extract;50ml, Mixed phosphate buffer;20ml, Distilled water;30ml, (NH4)2CO3;0.01g
CONDITION: Incubated at 30 degree C for 22 days
Result : 4 types of bacteria converted 32-43% of NH4+ to NO2-.
Reliability : (4) not assignable
17.12.2003 (27)

3.6 BOD5, COD OR BOD5/COD RATIO

3.7 BIOACCUMULATION

Remark	:	This substance is not applied to this system. BCFWIN version 2.14, Syracuse Research Co.
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

31.07.2003

3.8 ADDITIONAL REMARKS

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	flow through
Species	:	Pimephales promelas (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
LC50	:	= 96.2 measured/nominal
Limit test	:	
Analytical monitoring	:	yes
Method	:	other: ASTM E729-80
Year	:	1985
GLP	:	no data
Test substance	:	other TS: Baker analyzed reagent, purity:99.7%
Method	:	-Test Organisms: a)Mean size: weight;0.28g, length;25.6mm b)Supplier/Source: Mammalian and Environmental Toxicology Lab., The Dow Chemical co., Lot No. FMO32783LR c)Pretreatment: maintained in laboratory water for at least 10d at 22 plus or minus 1 degree C and then moved to Tittabawassee River water(22 plus or minus 1 degree C) for at least 2d prior to testing. -Test Conditions: a)Dilution Water Source:pumped from Tittabawassee River b)Dilution Water Chemistry: hardness;190-230mg/L as CaCO3, alkalinity; 154-180mg/L as CaCO3, pH;8.2-8.5, Conductivity;381-510 micromhos/cm c)Exposure Vessel: glass vessel with a test volume of 7 liters d)Nominal Concentrations (as mg/L): 0(control), six test concentrations e)Number of Replicates: 4 f)Individuals per Replicates: 20 g)Flow-through Rate: 2 cycles per hour h)Water Temperature: 21.4-22.6 degree C i)Light Condition: 16hr light, 8hr dark -Method of Analytical Monitoring: The concentration of total ammonia nitrogen was determined by ammonia-selective electrode method. -Statistical Method: Finney's method of probit analysis
Remark	:	-The results are adjusted to 100% ammonium chloride by using EPA-600/3-79-091(Aqueous Ammonia Equiribrium-Tabulation of Percent Un-ionized Ammonia)
Result	:	-Measured Concentrations: not described -Water Chemistry in test: Mean dissolved oxygen; 8.1mg/L, pH; 7.89-8.39(mean;8.14) -Cumulative mortality: Not shown -Statistical Result: 96h LC50/95% CI: 87.8-107.1 mg/L -Results on the other species at the same test conditions (no additonal details available). 1)Walleye(3.0g, 65.6mmL): LC50; 84.0(77.1-97.9) 2)Bluegill(0.38g, 26.3mmL): LC50; 74.2(66.5-82.6)
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

18.12.2003 (54)

Type	:	flow through
Species	:	Menidia beryllina (Fish, estuary, marine)
Exposure period	:	96 hour(s)
Unit	:	mg/l
LC50	:	= 174 measured/nominal
Limit test	:	
Analytical monitoring	:	yes
Method	:	other: ASTM E729-80
Year	:	1990
GLP	:	no data
Test substance	:	other TS: Reagent grade, purity:unknown
Method	:	-Test Organisms: a)Age: one to two weeks old b)Supplier/Source: obtained from natural spawnings in the laboratory (EPA Environmental Research Lab.,) using brood stock from the Pettaquamscutt River, Narragansett, RI. c)Pretreatment: cultured in circular tanks under flow-through conditions with ambient salinity (- 30g/kg) at 25 degree C. d)Feeding: fed rotifers for the first five days post-hatch, followed by a mixture of rotifers and Artemia nauplii for two days and Artemia alone thereafter. -Test Conditions: a)Dilution Water Source: sand-filtered (- 15 micro m) Narragansett Bay sea water b)Dilution Water Chemistry: salinity;31 plus or minus 2g/kg, pH;7.8 plus or minus 0.2, c)Exposure Vessel: glass exposure cup d)Nominal Concentrations (as mg/L): 0(control), five test concentrations e)Number of Replicates: 4 f)Individuals per Replicates: 20 g)Flow-through Rate: 20 to 40 ml/min h)Water Temperature: 25 plus or minus 1 degree C i)Light Condition: Not described -Method of Analytical Monitoring: The concentration of total ammonia nitrogen was determined by an automated indophenolblue method. -Statistical Method: Finney's probit and Thompson's moving average methods
Result	:	-Measured Concentrations: not described -Water Chemistry in test: Salinity; 30.5g/kg, pH; 7.9-8.1, Dissolved oxygen; Not shown -Cumulative mortality: Not shown -Statistical Result: 96h LC50/ 95% CI: 161.2-196.0 mg/L
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

18.12.2003 (58)

Type	:	semistatic
Species	:	Cyprinus carpio (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
LC50	:	= 209 measured/nominal
LC50 (24hr)	:	= 275 measured/nominal
LC50 (48hr)	:	= 240 measured/nominal
Limit test	:	
Analytical monitoring	:	yes
Method	:	other:APHA, AWWA & WPCF (1960)

Year	:	1975
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Groups of ten fishes were exposed to nine concentrations of ammonium chloride. Average pH: 7.4, Hardness : 105mg/l as CaCO3, Temp: 27.5 degree C -Test organisms: The test organism (4-5cm in length) were acclimatized in cement plastered tanks containing water (without any toxic substance) for one week to conditions similar to these under which tests were to be made. -Test containers: Earthen ware vats with a diameter of 40 at the bottom 80 cm at the top and 50 cm deep and 140 lit. Capacity were used as acclimatization tanks and starvation tanks. Glass aquaria of 75 cm X 38 cm X 30 cm (capacity 80 lit.) and operational depth of 25 cm of top. The water in each of acclimatization tanks was once in 3 days. -Experimental technique: During the experiments, observation were made for room temperature, pH, dissolved oxygen once in 24 hr.
Remark	:	The temperature condition (27.5 degree C) is above the OCDE Guidelines No.203 for Cyprinus carpio (20-24□‹C). However, each fish is survived at control group during the test periods, and there are almost same values of size, weight, and survival rate compared control with the lower soncentration group.
Result	:	Temperature variation during the test did not exceed 3 degree C and this variation was well below the permissible value. The values of dissolved oxygen were always above 5 mg/L in all cases. The pH values were noted to vary from 7.2 to 7.8.
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

18.12.2003 (64)

Type	:	flow through
Species	:	Salmo gairdneri (Fish, estuary, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
LC50	:	= 127 measured/nominal
Limit test	:	
Analytical monitoring	:	yes
Method	:	other
Year	:	1983
GLP	:	no
Test substance	:	other TS: Reagent grade, purity:unknown
Method	:	-Groups of ten trouts were exposed to five ammonia concentrations and one control -Two replicates per treatment
Result	:	The LC50 (96h) was determined to be 127mg/L with a 95 % confidence level of 115 to 138mg/L. These values are based on concentration adjusted to 100% ammonium chloride. -Tests were conducted at mean temperature of 13.8 degree C, pH of 7.84 and dissolved oxygen of 9.0 mg/L

Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint
18.12.2003		(81)
Type	:	flow through
Species	:	Pimephales promelas (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
LC50	:	= 163 measured/nominal
Limit test	:	
Analytical monitoring	:	yes
Method	:	other
Year	:	1983
GLP	:	no
Test substance	:	other TS:Reagent grade, purity:unknown
Method	:	-Groups of ten minnows were exposed to five ammonia concentrations and one control -Two replicates per treatment
Result	:	The LC50 (96h) was determined to be 163 mg/L with a 95 % confidence level of 151 to 176 mg/L. These values are based on concentration adjusted to 100% ammonium chloride. -Tests were conducted at mean temperature of 22.0 degree C, pH of 8.06 and dissolved oxygen of 7.6 mg/L.
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint
18.12.2003		(83)
Type	:	flow through
Species	:	Lepomis cyanellus (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
LC50	:	= 218 measured/nominal
LC50(24hr)	:	= 256 measured/nominal
LC50(48hr)	:	= 222 measured/nominal
LC50(72hr)	:	= 218 measured/nominal
Limit test	:	
Analytical monitoring	:	yes
Method	:	other
Year	:	1984
GLP	:	no
Test substance	:	other TS:Fischer certified ACS grade, purity:unknown
Method	:	-Groups of twenty fishes were exposed to six ammonia concentrations and one control -Two replicates per treatment -Tests condition mean temperature; 22.4 plus or minus 0.1 degree C pH; 7.7 total hardness; 43.1 plus or minus 0.4 mg/L (as CaCO3) dissolved oxygen; 8.1 plus or minus 0.1 mg/L
Result	:	The LC50 (96h) was determined to be 218 mg/L with a 95 % confidence level of 203 to 237 mg/L. These values are based on concentration adjusted to 100% ammonium chloride.
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint
18.12.2003		(55)
Type	:	flow through

Species	:	Salmo clarki (Fish, fresh water, marine)
Exposure period	:	96 hour(s)
Unit	:	mg/l
LC50	:	= 144 measured/nominal
Limit test	:	
Analytical monitoring	:	yes
Method	:	other
Year	:	1978
GLP	:	no
Test substance	:	other TS:Reagent grade, purity:unknown
Method	:	-Groups of twenty fishes were exposed to five ammonia concentrations and one control
Result	:	The LC50 (96h) was determined to be 144 mg/L with a 95% confidence level of 136 to 153 mg/L. These values are based on concentration adjusted to 100% ammonium chloride. -Tests were conducted at mean temperature of 12.8 degree C, pH of 7.80, and dissolved oxygen of 8.4 mg/L.
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

18.12.2003 (82)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type	:	static
Species	:	Daphnia magna (Crustacea)
Exposure period	:	48 hour(s)
Unit	:	mg/l
EC0	:	= 39.7 measured/nominal
LOEC	:	= 74 measured/nominal
LC50 (survival)	:	= 101 measured/nominal
Analytical monitoring	:	yes
Method	:	other: ASTM E729-80
Year	:	1986
GLP	:	no
Test substance	:	other TS: Baker analyzed reagent, purity: 99.7%
Method	:	-Test Organisms: a)Source: A brood stock of Daphnia magna acclimated to Tettabawassee River water for approx. 9 weeks. b)Feeding: During the acclimation daphnids were fed a diet of the green alga in the culture water (1.25mg dry wt/L). -Test Conditions a)Dilution Water Source: Pumped from the west side of the Tittabawassee River and passed through 250 or 500 micro-m filter. b)Dilution Water Chemistry: hardness;220-240mg/L as CaCO3, alkalinity; 175-185mg/L as CaCO3, pH; 8.3-8.6, conductivity; 380-440 micro-m hos/cm c)Exposure Vessel Type: 250mL glass beakers containing into which 200mL of test water d)Nominal Concentration: 0, several test concentrations e)Vehicle/Solvent and Concentrations: not used f)Number of Replicates: 3 g)Individuals per Replicates: 10 h)Water Temperature Range: 20 plus or minus 1 degree C i) Light Condition: 16hr-light (970-1250lux) and 8hr-dark

j) Feeding: During the test the daphids were not fed.
k) Concentration: 10.3 to 140.0 mg/L (appropriate dilution of stock solution (0.532 g of NH4Cl / 200 mL)

-Method of Analytical Monitoring: The concentration of total ammonia species was determined by ammonia-selective electrode method.
-Statistical Method: Finney's method of probit analysis

Remark : -The results are adjusted to 100% ammonium chloride by using EPA-600/3-79-091(Aqueous Ammonia Equiribrium-Tabulation of Percent Un-ionized Ammonia)

Result : -Measured Concentrations: not described
-Water Chemistry in Test: pH; 8.4 to 8.6, DO; all greater than 90% saturation), Temp; 19.5 to 20.5 degree C
-Statistical Result: 48hr LC50/ 95% CI; 92.4-110

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
18.12.2003 (31)

Type : semistatic
Species : other:Mulinia laterails (Bivalve)
Exposure period : 10 day(s)
Unit : mg/l
EC50 : = 42 measured/nominal
LC50 : = 82.9 measured/nominal
NOEC(survival) : = 31.3 measured/nominal
NOEC(growth:weight) : = 8.8 measured/nominal
Analytical monitoring : yes
Method : other
Year : 1997
GLP : no data
Test substance : other TS:Reagent grade, purity:unknown

Method : -Groups of ten clams were exposed to five ammonia concentrations and one control
-Three replicates per treatment

Result : The LC50(10d) was determined to be 82.9mg/L with a 95 % confidence level of 72.6 to 106 mg/L.These values are based on concentration adjusted to 100% ammonium chloride.
-Tests were conducted at mean temperature of 21.8 degree C and pH 7.79.other
Dissolved oxygen was measured brfore renewls four times, however the values were not shown.

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
18.12.2003 (42)

Type : semistatic
Species : other aquatic mollusc
Exposure period : 96 hour(s)
Unit : mg/l
EC50 : = 221 measured/nominal
Analytical monitoring : yes
Method : other:APHA(1980) "Standard methods for the examination of water and waste water"
Year : 1987
GLP : no
Test substance : other TS:Technical grade, purity:>99.0%

Method : -Groups of ten snails were exposed to four ammonia

concentrations and one control
-Two replicates per treatment
-Tests were conducted at mean temperature of 22 degree C and pH 7.9.

Species: Snail (Helicoma trivolvus) adult
Endpoint: Mortality

Result : The LC50(96h) was determined to be 221 mg/L with a 95 % confidence level of 198 to 248 mg/L. These values are based on concentration adjusted to 100% ammonium chloride.

(No addtional details available)

Reliability : (4) not assignable
18.12.2003 (7)

Type : static
Species : other aquatic crustacea
Exposure period : 8 day(s)
Unit : mg/l
EC50 : = 152 measured/nominal
Analytical monitoring : yes
Method : other
Year : 1977
GLP : no
Test substance : other TS:Reagent grade, purity:unknown

Method : Each sixteen larvae were exposed to five concentrations of NH4Cl diluted by sea water at mean temperature of 21.9 degree C. Salinity:33.4ppt, pH: 8.0 to 8.1.

Remark : Species: Larvae of the American lobster (Homarus americanus)
Endpont: Mortality, checked daily and dead lobsters were removed after observation.

Result : The LC50(8d) was determined to be 152 mg/L with a 95 % confidence level of 142 to 162 mg/L. These values are based on concentration adjusted to 100% ammonium chloride.

(No addtional details available)

Reliability : (4) not assignable
18.12.2003 (23)

Type : static
Species : Daphnia magna (Crustacea)
Exposure period : 96 hour(s)
Unit : mg/l
EC50 : = 139 measured/nominal
Analytical monitoring : no data
Method : other
Year : 1965
GLP : no
Test substance : other TS: GR grade, purity:unknown

Method : -Each ten nouplis were exposed to several concentrations of NH4Cl diluted by standard reference water.
-pH:7.9, Temp: 25 degree C

(No addtional details available)

Reliability : (4) not assignable
18.12.2003 (24)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species	:	Navicula sp. (Algae)
Endpoint	:	growth rate
Exposure period	:	10 day(s)
Unit	:	mg/l
NOEC	:	= 26.8 measured/nominal
LOEC	:	= 53.5 measured/nominal
EC50	:	= 90.4 measured/nominal
Limit test	:	
Analytical monitoring	:	yes
Method	:	other
Year	:	1977
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4

Method :

-Test Organisms:
a)Species: Navicula arenaria, Mean valve length;45 micro-m
b)Source: Isolated from field samples (at Eems-Dollard estuary) by agar-plating and micro-pipetting.
c)Test Medium: Artificial sea water (Provasoli et al,1957, code U, salinity; 33.7 ppt) with additives/ 0.2mg/L NaHCO3, 0.5g/L tris-buffer(pH 8.0), minor-elements(Provasoli et al, 1957, p414), 26mg/L HBO3.
d)Exposure Vessel: 100mL Erlenmeyer flasks with a thin layer of analytical clean sand (Merck) and with 40mL of culture medium
e) Nominal Concentrations (as mg/L): 5.35, 26,75, 53.50,133.75, 267.5
f)Number of Replicates: Not described
g)Water Temperature: 12 degree C
h)Light Condition: a quantum irradiance of 85 micro-E.m-2.sec-1 (4000lux) from extra cool-white fluorescent tubes. light period; 16hr per day
-Evaluation:
a)Estimate of algae growth: made on the basis of their chlorophyll a content measured according to Lorenzen (1967).
b)Sampling: The cultures were sampled twice between the third day and tenth day.

Result :

-Ammonium chloride concentration vs Relative growth (as % chlorophyll a) : 5.35mg/L--86%, 26.8mg/L--100%, 53.5mG/L--75%,134mg/L--21%, 268mg/L--0-5%.
Nominal concentration were calculated, because measured concentrations (data were not shown) were within at least 80% of nominal concentrations, except the lowest test concentration. Much lowered measured concentration demonstrated that it was sub-optimal.

-REMARK: For the other five species (Nitzschiac.f.dissipata, Nitzschia dubiformis, Nitzschia closterium, Amphiprora c.f.paludosa and Stauroneis constricta) NOECs were observed to be 26.8mg/L

Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

02.12.2004 (4)

Species	:	Chlorella vulgaris (Algae)
Endpoint	:	growth rate
Exposure period	:	5 day(s)
Unit	:	mg/l

EC50	:	= 1300 measured/nominal
LC50	:	= 5080 measured/nominal
Limit test	:	
Analytical monitoring	:	no data
Method	:	other
Year	:	1977
GLP	:	no
Test substance	:	other TS: Ammonium carbonate
Method	:	Strain: Chlorella vulgaris Beijerinck, coll. Greifswald A-23 Media: Modified Prat's mineral medium (KH2PO4-0.135g, MgSO4-7H2O-0.5g, FeSO4-7H2O-0.003g, sodium citrate-0.006g, micronutriens solution-1ml, H2O-1000ml Growth conditions: A 48hr culture in medium with ammonium at concentration 0.138g N/l. Test Condition: The culture was centrifuged, the harvested cells washed with distilled water and resuspended in medium without nitrogen. 200ml aliquots were distributed into culture vessels containing appropriate amounts of nitrogen source. The cultures were incubated for 5 days at 26 degree C with illumination of 6000 lux. The culture was aerated with air containing 3% CO2. The initial pH of the medium was 7.0. Assays: Number of cells, optical density, percentage of living cells, average cell size and pH. pH 8.0-8.5 (after 5 days) 26 degree C (after 5 days)
Remark	:	EC50=0.33g NH4-N/L corresponds, 1.26g/L of ammonium chloride
Test substance	:	Ammonium carbonate, commercial, purity: unknown
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

18.12.2003 (63)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

4.5.1 CHRONIC TOXICITY TO FISH

Species	:	Pimephales promelas (Fish, fresh water)
Endpoint	:	other: survival and percent normal larvae at hatch
Exposure period	:	28 day(s)
Unit	:	mg/l
NOEC	:	= 11.8 measured/nominal
LOEC	:	= 18.7 measured/nominal
Analytical monitoring	:	yes
Method	:	other
Year	:	1986
GLP	:	no data
Test substance	:	other TS: Baker analyzed reagent, purity: 99.7%
Method	:	-Groups of 30 embryos were exposed to six ammonia concentrations and one control -Four replicates per treatment-Larval exposure continued through 28d after day to mean hatch. -Tests were conducted at mean temperature of 24 degree C and pH 8.0. -Result values are based on concentration adjusted to 100%

ammonium chloride.

Result : Embryo survival showed no concentration-related effects, with hatching success ranging from 97.5 to 100 percent. There was a significant (alpha equal 0.05) decrease in the number of normal larvae at hatch at the 18.7 mg NH3Cl/L level and higher abnormalities such as small, poorly developed larvae and scoliosis were the most frequently observed effects.
Larval survival showed a concentration-related response, with a significant (alpha equal 0.05) decrease at 18.7 mg NH3Cl/L and higher. There was no significant (alpha equal 0.05) decrease in growth at any of the concentrations tested; however , there was a significant increase in weight at the 11.8 mg NH3Cl/L level and higher. The increase in weight may be attributed to smaller numbers of fish at the higher concentrations, which reduced crowing effects and also resulted in more food on individual fish.
The MATC, which was based on survival and percent normal larvae at hatch, was between 11.8 and 18.7 mg NH3Cl/L, and was 15.3 mg NH3Cl/L when expressed at the geometric mean of the high and low chronic values.
Ranges for dissolved oxygen concentrations, pH and room temperature recorded during the test were 5.0-8.5 mg/L, 7.75-8.42, 23.7-25.8 degree C, respectively.

Measured concentrations were used to clculate.

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
18.12.2003 (54)

Species : Lepomis cyanellus (Fish, fresh water)
Endpoint : weight of young fish
Exposure period : 44 day(s)
Unit : mg/l
NOEC : = 23.9 measured/nominal
LOEC : = 53.2 measured/nominal
Analytical monitoring : yes
Method : other
Year : 1984
GLP : no
Test substance : other TS:Fischer certified ACS grade, purity:unknown

Method : -Groups of 30 embryos were exposed to five ammonium chloride concentrations and one control
-Two replicates per treatment
-Larval exposure continued through 40d after 4days of incubation.
-Tests were conducted at mean temperature of 22.0 degree C and pH 7.9.
-Result values are based on concentration adjusted to 100% ammonium chloride.
-Tests condition
mean temperature; 22.0 plus or minus 0.1 degree C
pH; 7.9 plus or minus 0.1
total hardness; 42.8 plus or minus 0.4 mg/L (as CaCO3)
dissolved oxygen; 7.9 plus or minus 0.1 mg/L

Measured concentrations were used to calculate.

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint

18.12.2003 (55)

Species	:	Menidia beryllina (Fish, estuary, marine)
Endpoint	:	weight of young fish
Exposure period	:	28 day(s)
Unit	:	mg/l
NOEC	:	= 8 measured/nominal
LOEC	:	= 16 measured/nominal
Analytical monitoring	:	yes
Method	:	other
Year	:	1990
GLP	:	no
Test substance	:	other TS:Reagent grade, purity:unknown
Method	:	-Groups of 20 larvae were exposed to five ammonia concentrations and one control -Four replicates per treatment -Tests were conducted at 23.5 to 25 degree C and pH 7.36 to 7.86. -Result values are based on concentration adjusted to 100% ammonium chloride. -Water was sand-filtered Narragansett Bay sea water; deionized. Measured concentrations were used to calculate.
Result	:	Salinity; 31 g/kg, pH; between 7 and 8, Dissolved oxygen; not shown NOEC (survival) = 65.0 LOEC (survival) = 141 NOEC (growth weight) = 8.0 LOEC (growth weight) = 16.0
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

18.12.2003 (58)

Species	:	Salmo clarki (Fish, fresh water, marine)
Endpoint	:	other: mortality
Exposure period	:	36 day(s)
Unit	:	mg/l
LC50	:	= 123 measured/nominal
Analytical monitoring	:	yes
Method	:	other
Year	:	1978
GLP	:	no
Test substance	:	other TS:Reagent grade, purity:unknown
Method	:	-Groups of twenty fishes were exposed to five ammonia concentrations and one control
Result	:	The LC50(36d) was determined to be 123 mg/L with a 95% confidence level of 111 to 136 mg/L. The LC50(29d) was determined to be 123 mg/L with a 95% confidence level of 111 to 136 mg/L. These values are based on concentration adjusted to 100% ammonium chloride. pH: 7.8 Water temperature: 12.8 degree C Dissolved oxygen: 8.4 mg/L Measured concentrations were used to calculate.

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
18.12.2003 (82)

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

Species : Daphnia magna (Crustacea)
Endpoint : other: Mortality , reproduction
Exposure period : 21 day(s)
Unit : mg/l
NOEC : = 14.6 measured/nominal
LOEC : = 30.2 measured/nominal
Analytical monitoring : yes
Method : other
Year : 1986
GLP : no
Test substance : other TS: Baker analyzed reagent, purity: 99.7%

Method :
-Test Conditions
a)Type: semi-static
b)Dilution Water Source: Pumped from the west side of the Tittabawassee River and passed through 250 or 500 micro-m filter.
c)Dilution Water Chemistry: hardness;220-240mg/L as CaCO3, alkalinity; 175-185mg/L as CaCO3, pH; 8.3-8.6, conductivity; 380-440 micro-mhos/cm
d)Exposure Vessel Type: 600mL glass beakers
e)Nominal concentrations: 0, five test concentrations
f)Number of Replicates: 4
g)Individuals per Replicates: 20
h)Water Temperature Range: 19.5 to 20.0 degree C
i)pH : 8.3 to 8.6
j) Light Condition: 16hr-light (970-1250lux) and 8hr-dark
-Method of Analytical Monitoring: The concentration of total ammonia species was determined by ammonia-selective electrode method.
-Statistical Method: Finney's method of probit analysis
-Result values are based on concentration adjusted 100% ammonium chloride.

Result :

Mean analyzed concentration (as ammonium chloride mg/L)	Survival (%)	Mean total young/Daphnid	Mean total number of broods /Daphnid	Mean brood size/Daphnid
- 0	100	66.7	4.0	17.5
- 7.6	95	67.6	3.6	17.7
-14.6	100	62.7	3.6	17.4
-30.2	85	49.3	3.4	14.7
-65.2	35	28.3	2.6	9.1
-33.2	0	0	0	0

The mean analyzed concentrations were within 82 to 92 percent of the corresponding nominal values. The ranges of the temperature, pH and dissolved oxygen measurements for all renewal periods during the study were 19.5 to 20.0 degree C, 8.3 to 8.6 and 8.8 to 9.2 mg/L, respectively.

Survival mean total young per daphnid and mean brood size were equally sensitive and differed significantly from the controls at 30.2 mg NH4Cl/mL and higher.

Measured concentrations were used to calculate.

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
18.12.2003 (31)

Species : other aquatic crustacea
Endpoint : mortality
Exposure period : 56 day(s)
Unit : mg/l
LC50 : = 38.8 measured/nominal
Analytical monitoring : yes
Method : other: APHA (1985)
Year : 1992
GLP : no
Test substance : other TS:Reagent grade, purity:unknown

Method : -Groups of ten juveniles were exposed to four ammonia concentrations and one control
-Three replicates per treatment
-Tests were conducted at 19.2 to 24.2 degree C and pH 8.20 to 8.29.
-Result values are based on concentration adjusted to 100% ammonium chloride.

Measured concentrations were used to calculate.

(No addtional details available)

Remark : Species: Shrimp (penaeus penicillatus)
Reliability : (4) not assignable
18.12.2003 (19)

4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS

Type : artificial soil
Species : Eisenia fetida (Worm (Annelida), soil dwelling)
Endpoint : Mortality
Exposure period : 14 day(s)
Unit : mg/kg soil dw
LC50 : = 163 measured/nominal
Method : other: EPA/600/3-88/029 (1988)
Year :
GLP : no data
Test substance : other TS:Reagent grade, purity:unknown

Method : -Groups of ten worms were exposed to five ammonium chloride concentrations and one control
-Three replicates per treatment

-Tests were conducted at 22 plus or minus 2 degree C and pH 7.7.
-Analytical monitoring was not carried out.
-Soil type used for the test: Silica sand 70%, Clay 20%, Peat moss 10%,
-Soil pH: 5.3

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
03.07.2003 (89)

4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES

Species	:	other:Xenopus laevis (African clawed frog tadpoles)
Endpoint	:	
Exposure period	:	10 day(s)
Unit	:	other: mg/L
EC50	:	= 245 measured/nominal
Method	:	other: ASTM E729-96(1997)
Year	:	1999
GLP	:	no data
Test substance	:	other TS: Baker analyzed reagent, purity: 99.7%
Method	:	-Groups of fifteen tadpoles were exposed to seven ammonia concentrations and one control -Three replicates per treatment -Tests were conducted at mean temperature of 22 degree C and pH 7.15.
Remark	:	Type: semistatic Analytical monitoring: yes Endpoint: mortality, considered dead when the respiration and other movement were stopped and when there was no reaction to prodding with a glass rod.
Result	:	The LC50(10d) was determined to be 245 mg/L with a 95 % confidence level of 211 to 2838 mg/L. These values are based on concentration adjusted to 100% ammonium chloride.
Reliability	:	(4) not assignable

18.12.2003 (71)

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

Memo : ammonia toxicity

Remark : In most biological fluids ammonia exists in two forms and the toxicity is determined primarily by the pH of the solution. Since toxicity depends on the ammonia which enters the organism, and thence the cell, it is of particular importance that cell membranes are relatively impermeable to one form (ionized ammonia), whereas the other (un-ionized ammonia) passes tissue barriers with ease.

(86)

Memo : fertilizer use

Remark : It has been said that the paddy rice manured with ammonium chloride grows healthier, strong against diseases, hard to be lodged and good for ripening. Main reasons are considered as follows.
(1)Chlorine promotes the metabolism of carbohydrate, participating eventually in forming cellulose, lignin etc. to accelerate the development of tissues of stalk and leaf in the plant.
(2)The effect lasts longer while acting quickly; At the height of tillering, the nitrogen in ammonia sulphate and urea is taken by the plant in larger quantity at a time, resulting often in too many tillerings and soon going on the wane while that in ammonium chloride makes its appearance slower and longer in its effect to make the plant grow healthier.
*Effect of ammonium chloride on paddy rice (conducted at Hokuriku Agri. Experiment Station/NIigata,Japan in 1973):
NH_4Cl dose: 60-40kg/ha -- Brown rice yield: 5.77t/ha
(Control: 3.96t/ha)

08.07.2003 (29)

Memo : toxicity to algae

Remark : OECD Guide-line 201 recommends to use the Algal medium including 15 mg/l of ammonium chloride as a nutrient. NOEC is considered to be > 15mg/l.

24.06.2003 (60)

5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

5.1.1 ACUTE ORAL TOXICITY

Type	:	LD50
Value	:	= 1410 mg/kg bw
Species	:	Rat
Strain	:	Wistar
Sex	:	male/female
Number of animals	:	20
Vehicle	:	Water
Doses	:	
Method	:	other
Year	:	1983
GLP	:	No
Test substance	:	other TS
Method	:	-Test Organisms: a)Breeder: Dr.K.THOMAE GmbH, Biberach, Germany b)Acclimatization: for at least one week in the animal care unit c)Weight at study initiation: male;170-178g, female;171-187g d)No. of animals per dose: 10 males and 10 females e)Feeding: Diet;SSNIFF R, Ssniff Versuchstierdiaeten, Soest, Germany Water;Tap water f)Fasting period: The animals are given no feed for 16 hours before administration, but water is available ad libitum. -Test Conditions a)Temperature: 20-26 degree C in fully air-conditioned room b)Humidity: 30-70% c)Lightning: 12hr-light, 12hr-dark d)Form of administration: solution in bidistilled water e)Type of administration: single oral administration by gavage f)Dose: (mg/kg) 2150, 1780, 1470, 1000, 681, (ml/kg) g)Post dose observation period: 14 days -Examinations: a)Morality b)Body weight c)Clinical sings and symptoms d)Pathology: necropsy and gross-pathological examination (Heart, Stomach, Intestines)
Result	:	-Mortality: (out of 10 males and 10 females) a)Number of dead males at dose,2150/1780/1470/1000/681: (after 1h) 8/7/4/0/0, (after 1d) 8/7/4/0/0, (after 2-14d)8/7/4/0/0 b)Number of dead females at dose, 2150/1789/1470/1000/681: (after 1h) 10/9/7/0/0, (after 1d) 10/9/7/3/0, (after 2-14d)10/9/7/3/0 -Clinical Signs and Symptoms: at over dose 1000mg/kg, Dyspnea, Apathy, Abnormal position and Staggering were observed in 15min to 2hr. -Mean Weight: No significant difference among the survival animals -Necropsy Findings:(Heart) dilatation bilaterally; sporadically dilatation on the left side (Stomach) atonic

		several times; liquid contents; malacia of the mucosa in the glandular stomach (Intestines) atonic, diarrheal and mucous contents; malacia of the mucosa in several cases -Sex-specific Differences:(Male) LD50=1630mg/kg; slope factor=1.29 (Probit analysis) (Female) LD50=1220mg/kg; slope factor=1.31(M & F) LD50=1410mg/kg; slope factor=1.36
Test substance	:	BASF, Ammonium chloride fine white, No.83/44, purity: not described
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint
19.12.2003		(11)

Type	:	LD50
Value	:	= 1300 mg/kg bw
Species	:	Mouse
Strain	:	CD-1
Sex	:	Male
Number of animals	:	10
Vehicle	:	Water
Doses	:	
Method	:	other
Year	:	1990
GLP	:	No
Test substance	:	other TS
Method	:	Administered at 0, 800, 1000, 1200, 1400, 1700, 2100 mg/kg through stomach tube.
Result	:	-Clinical signs: Diarrhoea, cyanosis and ataxic gait were observed. -Necropsy: Swelling and whitening of kidney and hemorrhage in brain were observed. -Mortality Dose: 0, 800, 1000, 1200, 1400, 1700, 2100 mg/kg Mortality: 0, 0, 0, 4, 7, 10, 10 (/10) respectively
Test substance	:	Koizumi chemical reagent grade, purity:unknown
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint
04.08.2003		(77)

Type	:	LDLo
Value	:	= 1000 mg/kg bw
Species	:	other: albino rat, Guinea pig, rabbit
Strain	:	
Sex	:	no data
Number of animals	:	150
Vehicle	:	Water
Doses	:	
Method	:	other
Year	:	1946
GLP	:	No
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	The animals were given 50,250,1000 mg/kg of ammonium chloride dissolved in water through stomach tube.
Result	:	No untoward effects were observed from any of these doses in any species. (No additonal details available)

Reliability : (4) not assignable
19.12.2003 (14)

Type : LDLo
Value : = 1000 mg/kg bw
Species : Sheep
Strain :
Sex : Female
Number of animals :
Vehicle : Water
Doses :
Method : other
Year : 1971
GLP : No
Test substance : as prescribed by 1.1 - 1.4

Method : Ewes were given 1000 to 2500 mg/kg of ammonium chloride dissolved in water through stomach tube.

(No additonal details available)
Test substance : ACS analytical grade, purity:unknown
Reliability : (4) not assignable
19.12.2003 (74)

Type : LDLo
Value : = 600 mg/kg bw
Species : Dog
Strain : no data
Sex : no data
Number of animals :
Vehicle : no data
Doses :
Method : other
Year : 1935
GLP : No
Test substance : as prescribed by 1.1 - 1.4

Remark : (No additonal details available)
Reliability : (4) not assignable
19.12.2003 (2)

Type : LDLo
Value : = 1000 mg/kg bw
Species : Rabbit
Strain : no data
Sex : no data
Number of animals :
Vehicle : no data
Doses :
Method : other
Year :
GLP : No
Test substance : as prescribed by 1.1 - 1.4

Remark : (No additonal details available)
Reliability : (4) not assignable
19.12.2003 (2)

5.1.2 ACUTE INHALATION TOXICITY

5.1.3 ACUTE DERMAL TOXICITY

5.1.4 ACUTE TOXICITY, OTHER ROUTES

Type	:	LC50
Value	:	= 353 mg/kg bw
Species	:	Mouse
Strain	:	Swiss
Sex	:	no data
Number of animals	:	10
Vehicle	:	Water
Doses	:	
Route of admin.	:	i.v.
Exposure time	:	
Method	:	Other
Year	:	1957
GLP	:	No
Test substance	:	other TS
Method	:	Mice were injected one ml of isotonic saline containing the ammonium chloride (three to five concentration levels) into tail vain.
Test substance	:	Reagent grade, purity:unknown
Reliability	:	(3) invalid

19.12.2003 (87)

Type	:	LC50
Value	:	= 78 mg/kg bw
Species	:	Rabbit
Strain	:	no data
Sex	:	no data
Number of animals	:	
Vehicle	:	no data
Doses	:	
Route of admin.	:	i.v.
Exposure time	:	
Method	:	
Year	:	1935
GLP	:	No
Test substance	:	as prescribed by 1.1 - 1.4
Reliability	:	(3) invalid

24.06.2003 (2)

Type	:	LC50
Value	:	= 30 mg/kg bw
Species	:	Rat
Strain	:	no data
Sex	:	no data
Number of animals	:	10
Vehicle	:	Water
Doses	:	
Route of admin.	:	i.m.
Exposure time	:	

Method :
Year : 1946
GLP : No
Test substance : as prescribed by 1.1 - 1.4

Reliability : (3) invalid
24.06.2003 (14)

Type : LCLo
Value : = 72 mg/kg bw
Species : guinea pig
Strain : no data
Sex : no data
Number of animals :
Vehicle : no data
Doses :
Route of admin. : s.c.
Exposure time :
Method :
Year : 1935
GLP : No
Test substance : as prescribed by 1.1 - 1.4

Reliability : (3) invalid
24.06.2003 (2)

5.2.1 SKIN IRRITATION

Species : Rabbit
Concentration : Undiluted
Exposure : Occlusive
Exposure time : 24 hour(s)
Number of animals : 6
Vehicle :
PDII :
Result : moderately irritating
Classification : not irritating
Method : other: Federal Register, vol.43, no 163-Tuesday, Aug.22, 1978
Year : 1985
GLP : Yes
Test substance : other TS

Method : Six New Zealand White Albino Rabbits were randomly selected from a shipment of 12 rabbits received on September 16, 1985 from Rich-Glo-farms (U.S.D.A. 74-AA-29), El Campo, Texas. The animals were good health, being observed for 21 days prior to testing.
The animals were housed in galvanized steel cages placed over trays lined with aspen bedding. Purena Complete Rabbit Chow, Lot #197C and City of Houston Tap Water was available at all tomes. The rabbit quarters are air conditioned, temperature ranged from 72 - 76 dgree F, relative humidity from 40 to 60 %. The backs of 6 rabbits were clipped free of hair in an area of about 15 X 12 square cm. The backs of the animals were divided into quadrants. The animals were abraided in a 2 square mm cross-hatch pattern on the tatoo side by drawing a lancet across the skin, being careful not to penetrate the dermis. Two-one square inch areas on each

rabbit were tested. Two unabraided additional 1 squre inch sites on each rabbit were also tested.
0.5 gram of crystalline Ammonium chloride were placed in a double layered 1 square inch gauze pad and affixed to the four test sites on each animal with adhesive tape. The gauze was moistened with about 1 mL of distilled-deionized water and a polyethylene wrapper was placed over the bandages and wound around the trunk. The wrapper was secured with masking tape.
The animals were placed in a restraining box and replaced in their individual cages. Water was available to the animals during the test.
After 24 hours the animals were released from their restraints and the bandages were removed. All bandages were stuck to the skin by the test materials but peeled away with no skin removed. The remaining test materials was brushed of the skin but was not other wise removed.
The skin was sored according to the method of Draize.

Result : Redness/Edema/Eschar
Abraided(12tests) :Score(2)X7,(3)X5 /0 /0
Unabraided(12tests):Score(2)X7,(3)X5 /0 /0
after 24 hours
These changes were not observed after 48, 72, 96 hours.
Test substance : Reagent Chemical, Lot #50820
Conclusion : Ammonium chloride is moderately irritant to skin.
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
19.12.2003 (57)

Species : Rabbit
Concentration : Undiluted
Exposure : Occlusive
Exposure time : 20 hour(s)
Number of animals :
Vehicle :
PDII :
Result : slightly irritating
Classification : not irritating
Method : other: patch test
Year : 1968
GLP : No
Test substance : other TS

Method : 1)Test patchs coated with ammonium chloride was attached to the dorsal skins of the rabbit for 20 hr.
2)Test cotton swab coated with ammonium chloride was attached to the skin of rabbit's ear for 20 hr.
Result : 1)Dorsal skin: After application, the signs of inflammation were slighter, there were no skin hemorrhages and there was only an indication of scaling.
2)Ear: It caused very slight erythema after application which subsided without any signs of degeneration.
Test substance : Merck analytical grade, purity:unknown
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
25.06.2003 (13)

5.2.2 EYE IRRITATION

Species	:	Rabbit
Concentration	:	Undiluted
Dose	:	50 other: mg
Exposure time	:	
Comment	:	not rinsed
Number of animals	:	
Vehicle	:	
Result	:	moderately irritating
Classification	:	Irritating
Method	:	other
Year	:	1968
GLP	:	No
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	About 50mg of the powdery product was applied to the conjunctival sac of the rabbit's eye.
Result	:	-After 10min, 1 and 24hrs, clear signs of inflammation with redness, swelling and cloudy corneal opacity were observed. -The changes were reversible within 8 days without leaving any residues. There were no differences in the irritation between the powder and aqueous solution.
Test substance	:	Merck analytical grade, purity:unknown
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

19.12.2003 (13)

Species	:	Rabbit
Concentration	:	1 %
Dose	:	
Exposure time	:	
Comment	:	Other
Number of animals	:	2
Vehicle	:	
Result	:	slightly irritating
Classification	:	Irritating
Method	:	other
Year	:	1950
GLP	:	No
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Replace of the aqueous humor with ammonium chloride 1% solution
Result	:	Caused considerable hypermia of the iris but by the next day the eyes appeared almost normal.
Reliability	:	(3) invalid

19.12.2003 (33)

5.3 SENSITIZATION

Type	:	Guinea pig maximization test
Species	:	guinea pig
Concentration	:	1^{st}: Induction 5 % intracutaneous 2^{nd}: Induction 25 % occlusive epicutaneous 3^{rd}: Challenge 10 % occlusive epicutaneous
Number of animals	:	20

Vehicle	:	other: 0.9% NaCl Solution
Result	:	not sensitizing
Classification	:	not sensitizing
Method	:	other:EPA 540/9-82-025
Year	:	1986
GLP	:	Yes
Test substance	:	as prescribed by 1.1 - 1.4

Method :

Animal: Pribright-White guinea pigs (Female)
About 8 weeks age, Mean weight; 240g
Day 1 : Intradermal induction exposure (Injection)
The injection sites were not covered.
1-7: The application area was investigated.
9 : Dermal induction exposure
0.5ml of the test substance preparation were applied to a cellulose patch of 2x4 cm. This patch covered the area of the intradermal injection sites.
An occlusive dressing with impermeable foil and an elastic bandage sealed the application site for 48 hours.
11 : Removal of the occlusive dressing
Recording of the irritation
22 : Dermal challenge exposure
0.5ml of test substance preparation were applied to a cellulose patch and placed onto the clipped skin of the flank. An occlusive dressing with impermeable foil and an elastic bandage sealed the application site for 24 hours.
23 : Removal of the occlusive dressing
24-25: Assessment of the skin

Result : 1)The treated animals did not show any signs of toxicity throughout the study period.
2)Induction: Very slight to slight edema were observed in the treatment group.
3)Challenge: 24 and 48 hours after removal of the occlusive dressing, a total of 2 animals (in 20) of the treatment group showed very slight, hardly perceptible erythema.

Ten percent of the animal s of treatment group demonstrated a positive reaction after the challenge exposure (the criteria: the limit value of 30 percent).

Test substance	:	Hoechst:white,crystalline, purity:99.1%
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

04.08.2003 (40)

5.4 REPEATED DOSE TOXICITY

Type	:	
Species	:	Rat
Sex	:	Male
Strain	:	Sprague-Dawley
Route of admin.	:	oral feed
Exposure period	:	70 days
Frequency of treatm.	:	7 days per week7
Post exposure period	:	7 days
Doses	:	12300ppm in the diet (equivalent to 684 mg/kg bw/day)
Control group	:	yes, concurrent no treatment

NOAEL	:	= 684 mg/kg bw
Method	:	other
Year	:	1997
GLP	:	No
Test substance	:	other TS: Sigma Chemical, purity:>98.7%
Method	:	-Test Organisms: a)Age: 4-5 weeks old b)Source: Charles River Breeding Laboratories Inc. (Kingston, NY) c)Weight at study initiation: mean;175g d)No. of animals per dose: 10 males e)Feeding: Food (Purina Mills Certified Rodent Lab Chow) and water were available ad libitum throughout the study. f)Quarantine: The animals were quarantined for 12 days before initiation of treatment. -Test Conditions: a)Temperature: 22 plus or minus 4 degree C b)Humidity: 55 plus or minus 15% c)Lightning: 12hr-light(07:00 to 19:00), 12hr-dark d)Dose: 12300ppm in the diet e)Positive Control: 3000ppm of Tributyl phosphate(TBP) -Examinations: a)Food consumption b)Body weight c)Urine analysis; pH, osmolality, Magnesium, Calcium, Creatinine, Phosphate, Protein d)Pathology: necropsy and bladder examination; bladder weight, bladder histology (hyperplasia), Labeling index
Remark	:	NOEL is calculated by using average food consumption and final body weight
Result	:	-Food Consumption: No significant difference among any of the groups (ammonium chloride, TBP and control); mean 110g/kg b.w./day (initial) to 55.6g/kg b.w./day (final) -Body weight: No significant difference between ammonium chloride treatment and control. Significantly decreased in the TBP treatment group. -Urinary Chemistries: a)pH: ammonium chloride treatment reduced urinary pH to 6.04 (control:7.56) b)Calcium: significantly increased in the ammonium chloride treatment. However the crystals from urine were not found. -Histopathologic Examinations: a)Bladder weight(mean, g/kg bw): NH4Cl/0.260, Control/0.227, TBP/0.446 b)Bladder histology: (No.of Normal / Simple hyperplasia /Papillary or Nodular hyperplasia) NH4Cl; 10 / 0 / 0, Control; 10 / 0 / 0, TBP; 0 / 10 / 6 c)Labeling index(mean) : NH4Cl/0.17, Control/0.20, TBP/1.81
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

19.12.2003 (6)

Type :
Species : Cattle
Sex : male/female
Strain :
Route of admin. : oral feed
Exposure period : 112 days
Frequency of treatm. : 7 days a week
Post exposure period :
Doses : 21.3, 85.1 g/head/day
Control group : yes, concurrent no treatment
NOAEL : = 206 mg/kg bw
Method : other
Year : 1973
GLP : No
Test substance : as prescribed by 1.1 - 1.4

Method : -Test Organisms:
1)Source: commercial feedlot cattle of mixed breeds
2)Weight at study initiation: 278-283kg
3)No. of animals per dose: 91-93
4)Ration: The primary components were milo grain, alfalfa and fat to which was added a supplement containing cottonseed meal, urea, salt, calcium carbonate, rock phosphate, vitamins A, D, and E, choline chloride and trace minerals. All rations were calculated to contain the same level of crude protein (11.4%), digestible protein (8.62%) and NPN (1.64%).
5)Water: available at all times
-Test Conditions:
1)Cite: The test was conducted at a West Texas feed yard. The cattle were handled in accordance with the standard practices of the feed yard.
2)Dose: (initial) 91.2mg/kg/day, 325mg/kg/day, (final) 58.1mg/kg/day, 206.4mg/kg/day
-Examinations:
1)Food consumption
2)Body weight: weighed by lot every 28 days
3)Clinical sign
4)Carcasses inspection: At the end of 112 days on test, the animals were marketed through commercial channels. At the time of slaughter, the carcasses were inspected by the U.S.D.A. and the number of condemned livers recorded. The hot carcass weight was recorded and a chilled carcass weight calculated, allowing a 2% shrink. Dressing percent was calculated, using average final live lot weights with a 4% shrink. Carcass grades were determined by a grader from the C & MS, U.S.D.A.

Remark : NOEL is calculated based on the feed consumption and final body weight.

Result :

	Control	low-NH4Cl	High-NH4Cl
No.animals	92	91	93
Days on test	112	112	112
Final weight(kg)	442	444	438
Initial weight(kg)	276	283	278
Ave. daily gain(kg)	1.48	1.43	1.43
Feed consumption(kg)	10.75	10.97	9.63

Feed conversion(%)	7.26	7.67	6.73
Dressing %			
Hot	63.9	63.4	62.6
Chilled	62.6	62.1	61.4
Carcass grades %			
Prime	-	1.2	-
Choice	61.0	65.9	67.5
Good	39.0	32.9	32.5
Condemned livers %	25.6	24.4	26.5

*No clinical signs of ammonia t

Reliability : (2) valid with restrictions
19.12.2003 (20)

Type :
Species : rat
Sex : male
Strain : Fischer 344
Route of admin. : oral feed
Exposure period : 56 days
Frequency of treatm. : 7 days a week
Post exposure period :
Doses : 1% in the diet
Control group : yes, concurrent no treatment
NOAEL : = 580 mg/kg bw
Method : other
Year : 1989
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Method : 11 rats (6 weeks old, mean weight; 121g) were given ammonium chloride for eight weeks.
Remark : NOEL is calculated by average food consumption and final body weight.
Result : -No clinical signs were observed and only weight gain was significantly decreased in comparison with control
-No deaths occurred during the treatment period
-No significant difference in morphological investigation on urinary bladders and DNA synthesis in them
Test substance : Wako Pure Chemical, reagent grade, purity: unknown
Reliability : (2) valid with restrictions
03.12.2004 (73)

Type :
Species : rat
Sex : male
Strain : Fischer 344
Route of admin. : oral feed
Exposure period : 224 days
Frequency of treatm. : 7 days a week
Post exposure period : 7 days
Doses : 1% in the diet
Control group : yes, concurrent no treatment
NOAEL : = 493 mg/kg bw
Method : other
Year : 1986
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Method	:	In the first 4 weeks 20 rats are given drinking water with BBN(N-butyl-N-(4 hydroxybutyl) nitrosamine) as a strong initiator of urinary bladder carcinogenesis, and then for 32 weeks they were given powdered basal diet containig 1% of ammonium chloride or no added chemical.
Remark	:	NOEC is calculated by using final weight and food consumption.
Result	:	-Rats showed no toxic symptoms. -The final body weight was significantly lower than control, while food and water consumption were not so different. -In comparison with control, urine pH was significantly decreased. -The urinary bladder weight and the incidence of hyperplasia, papilloma and carcinoma was not significantly different from that in control.
Test substance	:	Wako Pure Chemical, purity:unknown
Reliability	:	(2) valid with restrictions
19.12.2003		(30)

Type	:	
Species	:	rat
Sex	:	
Strain	:	Sprague-Dawley
Route of admin.	:	drinking water
Exposure period	:	5 days
Frequency of treatm.	:	
Post exposure period	:	
Doses	:	
Control group	:	
Remark	:	Groups of 6 Sprague-Dawley rats, 225-275 g (sex unspecified) were administered 0 or 1.28 g/kg/day of ammonium chloride for 5 days either via drinking-water or by gavage. Treatment-related renal hypertrophy was observed, but no increase occurred in uptake of radioactive thymidine by the kidney, implying that no increase in DNA synthesis or cell division occurred during renal enlargement. No other treatment-related effects were observed. (No additional datails available)
Reliability	:	(4) not assignable
22.12.2003		(48)

Type	:	
Species	:	rat
Sex	:	female
Strain	:	
Route of admin.	:	drinking water
Exposure period	:	7 days (Lotspeich, 1965), 6 days (Thompson and Halliburton,1966)
Frequency of treatm.	:	
Post exposure period	:	
Doses	:	
Control group	:	
Remark	:	Groups of 6 female Holtzman rats, 200-250 g, were administered 0 or 1.5% ammonium chloride in the drinking-water for 7 days. Renal hypertrophy was observed, along with increases in total DNA and total RNA of kidney. No other treatment-related effects were reported. Similar effects were observed in another study in which rats were

fed ammonium chloride in the diet at 0 or 3% for a period of 6 days.

(No additional details available)

Reliability : (4) not assignable
22.12.2003 (52) (80)

Type :
Species : rat
Sex : male
Strain : Sprague-Dawley
Route of admin. : drinking water
Exposure period : 330 days
Frequency of treatm. :
Post exposure period :
Doses :
Control group :

Remark : Groups of 7-12 adult male Sprague-Dawley rats were administered 0 or 1.5% ammonium chloride in their drinking-water for 330 days. In a concurrent study by the same laboratory, similar animals in groups of 5-9 were administered 0 or 2% ammonium chloride in their drinking-water for 6 months. Test animals developed osteoporosis due to a loss of organic bone substance and bone minerals. Growth depression also occurred in treated animals. The ammonium chloride-induced osteoporosis was reversible with supplements of bicarbonate, but not by calcium supplementation of the diet.

(No additional details available)

Reliability : (4) not assignable
22.12.2003 (9) (10)

Type :
Species : rabbit
Sex :
Strain :
Route of admin. :
Exposure period : from 11 days to 11 months
Frequency of treatm. :
Post exposure period :
Doses :
Control group :

Remark : A group of 9 rabbits averaging 2 kg in weight were given ammonium chloride by stomach tube in doses ranging from 16.6 to 166 g for periods from 11 days to 11 months; 6 controls were used. Severe acidosis was observed, with casts and albumen in the urine. Histological studies of the kidneys showed acute degeneration of the convoluted tubules and marked pyknosis of nuclei. These effects were reversible upon discontinuance of the acidotic diet.

(No additonal details available)

Reliability : (4) not assignable
22.12.2003 (72)

5.5 GENETIC TOXICITY 'IN VITRO'

Type	:	Bacterial reverse mutation assay
System of testing	:	Salmonella tryphimurium TA98,TA100,TA1535,TA1537,TA1538, Escherichia coli WP2uvrA
Test concentration	:	0, 4, 20, 100, 500, 2500, 5000 micro gram/plate
Cycotoxic concentr.	:	Toxicity was not observed up to 5000 micro gram/plate in six strains with or without S9 mix
Metabolic activation	:	with and without
Result	:	negative
Method	:	OECD Guide-line 471
Year	:	1987
GLP	:	yes
Test substance	:	other TS
Remark	:	-Sterility checks and control plates Sterility of S9 mix and the test compound was indicated by the absence of contamination on the test material and S9 mix sterility check plates. Control plates (background control and positive controls) gave the expected number of colonies.
Test condition	:	a)Number of replicates : 2 b)Plates/test : 3 c)Procedure: Pre-incubation at 37 degree C for 2-3 days d)Solvent: Water e)Positive controls:-S9mix ; Sodium-azide(TA100,TA1535),9-Aminoacridine(TA1537), 2-Nitrofluorene (TA98, TA1538), MNNG(WP2uvrA) +S9mix; 2-Aminoanthracen (six strains), Benzo(a)pyrene (six strains)
Test substance	:	Hoechst AG, Hoe 0922978, purity: 99.1%, Kept at 4 degree C until use
Conclusion	:	Bacterial gene mutation is negative with and without metabolic acivation
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

19.12.2003 (39)

Type	:	Bacterial reverse mutation assay
System of testing	:	Salmonella trphimurium TA92, TA94, TA98, TA100, TA1535, TA1537
Test concentration	:	Six different concentrations. Maximum concentration was 10mg/plate.
Cycotoxic concentr.	:	Toxicity was not observed up to 10mg/plate in six strains with of without S9 mix.
Metabolic activation	:	with and without
Result	:	negative
Method	:	other: Ames test
Year	:	1984
GLP	:	no data
Test substance	:	other TS
Test condition	:	a)Number of replicates : 2 b)Procedure: Pre-incubation at 37 degree C for 2 days. c)Solvent: Water (phosphate buffered) d)Activation system: Liver S-9 fraction from Fisher rats (Charles River Japan Co.) pretreated 5 days before with polychlorinated biphenyls.
Test substance	:	Japan Food Additives Association, purity: 99.7%
Conclusion	:	Bacterial gene mutation is negative with and without metabolic activation

Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint
24.06.2003		(45)

Type	:	Cytogenetic assay
System of testing	:	CHL/IU cell
Test concentration	:	0 - 0.4mg/ml
Cycotoxic concentr.	:	
Metabolic activation	:	without
Result	:	positive
Method	:	other: Chromosomal aberration test
Year	:	1984
GLP	:	no data
Test substance	:	other TS
Remark	:	The pH was not measured, however, this result is ascribable to the acidity of this substance with considering the physico-chemical properties of this substance.
Result	:	-The incidence of polyploid cells for 48hr after treatment was 0.0%. -The incidence of cells with structural chromosomal aberrations at 0.4mg/ml for 48hr after treatment was 47.0%. -Also positive at 0.3 mg/ml at 24hr (11.0 %) and at 48hr (30.0%). -D20 was 0.25 mg/ml (the dose at which structural aberrations were detected in 20 % of the metaphasesobserved). -TR value (the frequency of cells with exchange-type aberrations per unit dose(mg/ml)) was 0.35.
Test condition	:	The cells were exposed to NH4Cl at three different doses for 24 and 48 hr. The maximum dose was selected by a preliminary test. The solvent was physiological saline. Untreated cells and solvent-treated cells served as negative controls.
Test substance	:	Japan Food Additives Association, purity: 99.7%
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint
19.12.2003		(45)

5.6 GENETIC TOXICITY 'IN VIVO'

Type	:	Micronucleus assay
Species	:	mouse
Sex	:	male
Strain	:	other:ddY
Route of admin.	:	i.p.
Exposure period	:	24 hours after injection
Doses	:	(1)Single injection: 0, 62.5, 125, 250,500mg/kg (2)Four injections with 24hr intervals: 0, 31.3, 62.5, 125, 250mg/kg
Result	:	negative
Method	:	other
Year	:	1988
GLP	:	no
Test substance	:	other TS
Result	:	Single injection (i.p.)

Test substance	MNPCE(%)	PCE(%)	Mortality
Saline	0.18+/-0.18	56.8+/-4.7	0/6
Ammonium chloride			
62.5(mg/kg)	0.12+/-0.12	60.9+/-4.2	0/6
125(mg/kg)	0.15+/-0.14	61.7+/-3.8	0/6
250(mg/kg)	0.13+/-0.05	64.3+/-2.5	0/6
500(mg/kg)	0.12+/-0.08	56.9+/-6.1	0/6
Mitomycin C 2.0(mg/kg)	4.18+/-1.30*	52.3+/-4.6	0/6

Four times injection every 24 hours (i.p.)

Test substance	MNPCE(%)	PCE(%)	Mortality
Saline	0.20+/-0.09	59.9+/-8.3	0/6
Ammonium chloride			
31.3(mg/kg)	0.25+/-0.19	67.2+/-13.5	0/6
62.5(mg/kg)	0.17+/-0.10	63.7+/-4.5	0/6
125(mg/kg)	0.20+/-0.18	64.0+/-9.2	0/6
250(mg/kg)	0.17+/-0.08	61.6+/-6.9	0/6
Mitomycin C 2.0(mg/kg)	7.15+/-3.92*	32.2+/-11.0	0/6

*:p<0.01

Test condition : -The maximum dose of NH4Cl was determined by pilot experiments using the multisampling at multi-dose levels method.
Dose up to MTD (maximum tokerance dose)
-6 male/group
-Single injection: 0, 62.5, 125, 250, 500, mitocycin C 2.0 (mg/kg)
-Fgour times injection: 0, 31.3, 62.5, 125, 250, mitocycin C 2.0 (mg/kg)
-Bone marrow cells were used.
-Mice was killed 24hr after an administration.
-Femoural marrow cells were flushed out with foetal bovine serum and fixed with methanol and stained with Giemsa.
-One thousand polychromatic erythrocytes per mouse were scored using a light microscope and the number of micronucleated erythrocytes (MNPCE) was recorded.

Positive control: mitomycin C 2.0 mg/kg

Test substance : Japan Food Additives Association, purity: 99.7%
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
19.12.2003 (37)

5.7 CARCINOGENICITY

Species : rat
Sex : male
Strain : Fischer 344/DuCrj
Route of admin. : oral feed
Exposure period : 32 weeks
Frequency of treatm. : 7 days a week
Post exposure period :
Doses : 1% in the diet
Result : negative

Control group : yes, concurrent no treatment
Method : other: Initiation-promotion study
Year : 1994
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Method : Urinary bladder carcinogenesis in rats was initiated with BBN (N-butyl-N-(4-hydroxybutyl) nitrosamine.
Rats were given 0.05% BBN for 4 weeks and then treated ammonium chloride from weeks 5 to 36 (15 rats per treatment).
Observed and measured abnormalities, body weight, urine pH and electrolyte concentrations, organ weight, and histopathological findings - kidney and urinary bladder.

Result : -Ammonium chloride reduced the incidence of papillomas

Test compound	No of animals	PN hyperplasia/Papillomas/Carcinomas
BBN to NH4Cl	15	6/0/0
BBN only	15	9/5/0

Test substance : Wako Pure Chemical, purity:unknown
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
19.12.2003 (35)

Species : mouse
Sex : female
Strain : other: (1F X C57)F1
Route of admin. : drinking water
Exposure period : 652 days
Frequency of treatm. : 7 days a week
Post exposure period :
Doses : 1% in the drinking water
Result : negative
Control group : yes, concurrent no treatment
Method : other
Year : 1975
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Method : 50 mice were given 1.0% of ammonium chloride in the drinking water.
Result : -The average survival time was 492 days . (Control : 485days)
-Control animals and those given ammonium chloride were free from bladder tumours, epithelial hyperplasia and calculi.
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
25.06.2003 (28)

Species : rat
Sex : male/female
Strain : Fischer 344
Route of admin. : oral feed
Exposure period : 8 weeks
Frequency of treatm. : 7 days a week
Post exposure period :

Doses	:	1% in the diet
Result	:	negative
Control group	:	yes, concurrent no treatment
Method	:	other
Year	:	1991
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	6 male and 5 female rats were treated with 1% of NH4Cl in the diet for 8 weeks. Evaluation after 8 weeks Body weight, urinary volume, urinary pH, urinary electrolytes, Hyperplastic changes in the urinary bladders.
Result	:	1)Body weight: significantly lower than control, especially in male rats. 2)Urine volume: increased in male 3)Urine pH: decreased in both sexes 4)Urinary bladder analysis: No hyperplasia (Positive control: 1.25% o-phenyphenol(OPP) plus 3% NaHCO3)
Test substance	:	Wako Pure Chemical, purity:unknown
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

25.06.2003 (36)

5.8.1 TOXICITY TO FERTILITY

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species	:	rat
Sex	:	female
Strain	:	Sprague-Dawley
Route of admin.	:	drinking water
Exposure period	:	From seven to tenth day of gestation (4 days)
Frequency of treatm.	:	once a day
Duration of test	:	20 days
Doses	:	1/6M, 1 mL/kg b.w. (equivalent to 8.9 mg/kg bw/day)
Control group	:	yes, concurrent vehicle
Method	:	other
Year	:	1964
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Ammonium chloride was administered orally dissolved in saline. Number of animals: 10 The fetuses were examined grossly after delivery by cesarean section on day 20.
Result	:	Control /NH4Cl /Na salicylate(500mg/kg) 1)Maternal death(%): 0 /0 /0 2)Resorption-early(%): 6 /15 /15 3)Resorption-late(%) : 0 /1 /11 4)No.of conceptions : 136 /122 /288 5)Anomalous live young(%): 0 /0 /14 6)Growth weight(g): 3.2 /2.0 /2.0 7)Growth height(mm):38 /27 /27 Maternal death, resorptions (early, late), number of conceptions, anomalous live young, growth-weight and height

was inspected.

Conclusion : The authors regards decrements in fetuses length and weight as meaning full, but they also write that there were obvious maternal effect saying "The amount of ammonium chloride consumed by pregnant rat is found to be about 2.5 mEq/24 hours, which in a rat weighing between 250 and 300 gm is sufficient to produce a metabolic acidosis"..
The author referred that as "the inhibition of growth by a metabolic acidosis". Although, no statistical and/or baackground data were not shown, it is agreeable.

Conclusion :
Maternal effect was supposely to be acidosis, no teratogenic toxicity was found. The effects of this substance on fetal survival and growth noted were considered a consequence of maternal acidosis. No fetus with malformations was observed in this substance-treated group. This substance has no teratogenicity at this dose level.

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
07.12.2004 (32)

5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

5.9 SPECIFIC INVESTIGATIONS

5.10 EXPOSURE EXPERIENCE

Remark : Ammonium chloride has been available as a therapeutic agent in Canada since its introduction in 1925. It has been used as a mild diuretic, an expectorant, a weight-reducing agent and a urine-acidifying agent. As little as 100mg/kg of ammonium chloride as a single dose may cause a fall of urine pH to less than 5.2, a level that is bacteriostatic for many organisms. Some commonly used agents suchas methenamine and nitrofurantoin seem more effective in an acid environment.
The use of ammonium chloride clearly requires caution of renal disease.
Therapeutic agent use
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
19.12.2003 (51)

Remark : Ammonium chloride not only provides the bulk of the fertilizer supply, but are useful therapeutic agents for a variety of human ills. When the LD50 of ammonium chloride is compared, on an m.equiv./kg basis, to that of many other common drugs it appears to be relatively non-toxic. When administered of absorbed at a slow rate, vast quantities of ammonia may be tolerated by most living organisums because of their highly efficient detoxifying mechanisms in which urea, glutamine or asparagine is formed.
Human toxicity
Reliability : (3) invalid
24.06.2003 (86)

Remark : Absorption and Fate
Ammonium chloride is effectively absorbed from the gastro-intestical tract. The ammonium ions converted into urea in the liver; the anion thus liberated into the blood stream and extracellular fluid causes a metabolic acidosis and decreases the pH of the urine. In healthy persons, absorption of ammonium chloride given by mouth was practically complete. Only 1 to 3% of the dose was recovered in the faeces.
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
25.06.2003 (66)

Remark : Drug information / Use
[USES]
*A systemic acidifier in patients with metabolic alkalosis resulting from chloride loss following vomiting, gastric suction, gastric fistula drainage, and pyloric stenosis.
*Useful in the treatment of diuretic -induced chloride depletion.
*In a variety of conditions to induce incipient acidosis for the purpose of promoting diuresis, particularly in edematous conditions associated with hypochloremia.
*Used to increase the solubility of calcium and phosphate ions in the management of patients with phosphatic calculi in the urinary tract and to increase calcium ionization in alkalotic tetany.
*Used as an adjunct in the treatment of urinary tract infections when a low urinary pH is desired.
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
25.06.2003 (5)

Remark : A diuretic and expectorant. It is also used as a systemic acidifier. Ammonium chloride is a combination of a labile cation and a fixed anion. When the ammonium ion is converted to urea, the liberated hydrogen ion reacts with bicarbonate and other body buffers. The end result is that chloride ion displaces bicarbonate ion; the latter is converted to CO2. Thus, the chloride load to the kidneys is increased and an appreciable amount escapes reabsorption along with an equivalent amount of cation (predominantly sodium) and an isoosmotic quantity of water. This is the basic mechanism by which ammonium chloride brings about a net loss of extracellular fluid and promotes the mobilization of edema fluid. Ammonium chloride is sometimes employed alone for its diuretic action but usually it is given in conjunction with mercurial diuretics, the action of which it potentiates. The fact that ammonium chloride causes systemic acidosis makes the salt of some value in the treatment of alkalosis. It also renders the urine acid and is prescribed for this purpose in conjunction with methenamine.
Drug information / Use
Reliability : (3) invalid
24.06.2003 (41)

Remark : Drug information / Use
Oral: 4 to 12g daily (usual,oral, 1 to 2g, 4 times a day) intravenous: 100 to 1000ml of 2% solution(usual, intravenous, 500ml of a 2% solution infused over a 3-hour period. The drug is usually taken with or after meals to avoid gastric irritation.
*Veterinary dose: Horses, 4 to 15g; Cattle, 15 to 30g; sheep and swine, 1 to 2g; dogs, 200 to 500g
Reliability : (3) invalid
24.06.2003 (41)

Remark : Drug information / Use
The usual adult oral dosage of ammonium chloride is 4-12g daily administered in divided doses every 4-6hours. The usual oral acidifying dose for children is 75mg/kg daily given in 4 divided doses. The drug is most effective as a diuretic when given for 3 or 4 days followed by a rest period of a few days after which therapy is resumed. For the treatment of Meniere's syndrome, the oral dosage of ammonium chloride is 3 g given 3 times daily with meals for 3 days. The drug is then omitted for 2 days and the cycle is repeated indefinitely. For use in the treatment of premenstrual edema, 3 g of ammonium chloride may be given daily in divided doses for 4-5 days prior to menstruation.
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
25.06.2003 (5)

Remark : As an acidifying agent, ammonium chloride is administered orally or by slow i.v.infusion. It is administered orally as a diuretic. Solutions of the drug should not be administered subcutaneously, intraperitoneally, or rectally. The 26.75% concentrate for injection must be diluted in 0.9% sodium chloride injection prior to administration. For i.v. infusion, the dilute solution should be administered at a rate not exceeding 5mL/min in adults.
Drug information / Administration
Reliability : (3) invalid
24.06.2003 (5)

Remark : Drug information / Adverse effect
Large doses of ammonium chloride may cause nausea, vomiting, thirst, headache, hyperventilation, and progressive drowsiness, and lead to profound acidosis and hypokalaemia.
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
25.06.2003 (66)

Remark : Drug information / Adverse effect
Following oral administration, ammonium chloride, especially in large doses, is irritating to the gastric mucosa and may cause gastric distress, anorexia, nausea, vomiting, and thirst.

Large dose of ammonium chloride may cause metabolic acidosis secondary to hyperchloremia, especially in patients with impaired renal function. Acidosis or electrolyte loss resulting from ammonium chloride therapy may be treated with i.v. sodium bicarbonate or sodium lactate. Potassium depletion has been reported during ammonium chloride therapy and potassium gluconate may be administered orally if hypokalemia results.

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
25.06.2003 (5)

Remark : *Active Ingredient : Ammonium chloride
*Route: Injectable/Injection
*Proprietary Name: Ammonium Chloride in Plastic Container
*Applicant: ABBOTT
*Strength: 5Meq/ml
*Application Number: 088366
*Approval Date: June 13, 1984
FDA information

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
31.07.2003 (5)

Remark : A 58-year-old woman with a long history of renal stone disease and urinary tract infection presented to the emergency room with exhaustion and air hunger. Laboratory data confirmed profound metabolic acidosis. Unduly large quantities of bicarbonate and potassium were required for correction of the deficits. She had been taking 6 g daily of ammonium chloride as a urine-acidifying agent for a period of six months in addition to agents directed against urinary tract infection. The combination of impaired renal function and effective hydrogen ion loading resulted in profound systemic acidosis. The metabolic derangement associated with the administration of ammonium chloride and its use as a therapeutic agent are discussed.
Human experience / Case 1

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
19.12.2003 (51)

Remark : An 18-year-old photographer's model, who had always been in good health, was taken to the hospital by her parents because of hyperventilation and confusion of 1 day's duration. It was learned that for the past 6 months, in an effort to stay slim and photogenic, she had been taking up to 15 1-gm. enteric-coated ammonium chloride tablets daily for short periods. No ill-effects had been noted except on 1 occasion, 4weeks earlier, when she became nauseated and weak, with transient hyperventilation. During a period of 48hours, ending 2 days before admission, she took 82 gm. of ammonium chloride. Thereafter, although she took no more medication, headache and nausea developed; she vomited once or twice and was noted to become progressively drowsy and confused. Soon after admission the patient lapsed into a

comatose state. --- Large amounts of sodium bicarbonate solution were administrated intravenously. There was a steady rise in serum carbon dioxide content, which reached normal levels in 20 hours and then became higher than normal thereafter.
Human experience / Case 2

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
19.12.2003 (65)

Remark : For human, the restriction to medication to a pregnant woman is not indicated by the appending document of the medical supplies using this substance in Japan. Moreover, it is also used as medical supplies and classified into Category A in Australia. Category A means that it is the medicine which has been used for many pregnant women and the woman of the conceivable age, and any proof that increase in the frequency of deformation and the frequency of the direct and indirect detrimental action to an embryo is not observed.
Human experience

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
19.12.2003

Remark : A number of clinical studies of duration less than 1 week have been carried out with ammonium chloride. In one report, a man was given 62 g of ammonium chloride in the diet over a 3-day period. No effects were reported except for increased red cell count, increased BUN and decreased plasma pH (Guest and Rapoport, 1940).

In another study, 3 young men were given ammonium chloride in drinking-water at doses ranging from 52 to 105 g over 3-5 days. Headache, insomnia, nausea and diarrhoea occurred along with increased urinary acidity and ammonia. A reduction in glucose tolerance was also noted, consisting of hyperglycaemia and a slow return of blood sugar to fasting levels following glucose ingestion (Thompson et al., 1933).

Pregnant women (6 normal, 8 toxaemic, 3 hypertensive) were given 15 g/day of ammonium chloride in their beverage for a period of 3 days. Treated women experienced hyperventilation, anorexia, diminished thirst, nausea, and loss in weight. Urinary chloride, potassium, acidity and volume all increased, blood pH and CO2 decreased while haematocrit increased (Assali et al., 1955).

Eleven men, 21-38 years of age, given daily oral doses of 6-8 g ammonium chloride for 6-9 days, showed a mild metabolic acidosis (Owen and Robinson, 1963). A similar dosage of ammonium chloride was employed in a study with 5 women of unspecified age suffering from rheumatoid arthritis, who were administered the test compound for 23-33 days. Some fluid loss was noted, but no other adverse effects were reported (Owen and Robinson, 1963; Jacobson et al., 1942).

Three women and 3 men, aged 23-37, were given daily an oral

dose of 8 g of ammonium chloride for 5 days. The treatment group experienced increased urinary excretion of magnesium, calcium and phosphate and decreased urinary pH. No other effects were attributed to ammonium chloride (Martin and Jones, 1961). These results were corroborated in a 24-hour study in which 18 men and 6 women, age unspecified, were given 0.1 kg of ammonium chloride by capsule (Lavan, 1969).

No adverse effects were reported in a 3-day study in which 4-5 patients, middle aged and older, were given a daily oral dose of 8 g of ammonium chloride (Jailer et al., 1947).

Thirteen women and 2 men, aged 22-60, were given an oral dose of ammonium chloride, 3 g/day, for 20 consecutive days a month for a period of 3 months. Increased appetite and fat deposition were noted which were attributed by the author to treatment-related acidosis and resulting stimulation of adrenal cortical function. No other effects due to ammonium chloride administration were reported (Fazekas, 1955).

(No additonal details available)
Clinical Studies

Reliability : (4) not assignable
22.12.2003 (8) (25) (34) (46) (47) (50) (53) (61) (79)

5.11 ADDITIONAL REMARKS

Type : other: veterinary use

Remark : Ammonium chloride has been used in cattle feedlot finishing rations as a source of non-protein nitrogen and to help control urinary calculi.

Reliability : (3) invalid
25.06.2003 (20)

Type : other: veterinary use

Remark : Ammonium chloride produced no noticeable toxicosis when administered orally to calves at a dosage level of 1 to 1.5 oz daily and to wethers at a dosage level of 0.25 oz daily. The animals had an increased water intake, indicating ammonium chloride would be of value in preventing urinary calculi.

Reliability : (3) invalid
24.06.2003 (70)

Type : other: veterinary use

Method : ANIMAL: commercial fine wool wether lambs, initial average
- Initial average weight: 26.0 and 24.5 kg(two experiments)
- No. of animals: 20 per treatment
DOSE: 0.5% of the mixed diet
CONTROL DIET: 40% each of ground sorghum grain and cottonseed hulls and 10% each of cottonseed meal and molasses. Three thousand IU of stabilized vitamine A were added per kilo mixed diet.
TEST PERIOD: 112 days
EVALUATION: Any lamb which exhibited clinical symptoms of

calculi was slaughtered immediately, and the urinary tract examined for the presence of uroliths. All other lambs were slaughtered at the completion of the test period, and the bladder and one kidney examined for the presence of uroliths. The animals were individually weighed every 28 days and feed consumption recorded.

Test substance : Ammonium chloride, purity: 99%

Conclusion : Ammonium chloride is the preferred compound to control calculi.

Reliability : (3) invalid

24.06.2003 (21)

Type : other: veterinary use

Remark : Most materials and practices offering some degee of protection against phosphatic urinary calculi appear to result in at least one of the following: (1) a lowering of urinary phosphorus levels, (2) acidification of the urine, (3) an increase in urine volume. Acidification of the urine may be achieved by the feeding of acid forming salts. It is recommended to supplement ammonium chloride daily at a rate of 0.25 oz. to sheep, or 1.0 to 1.5 oz. to finishing cattle.

Reliability : (3) invalid

08.07.2003 (68)

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