

FOREWORD

INTRODUCTION

HYDROGEN CHLORIDE

CAS N°: 7647-01-0

SIDS Initial Assessment Report

For

SIAM 15

Boston, USA, 22-25th, October, 2002

1. Chemical Name: Hydrogen chloride

2. CAS Number: 7647-01-0

3. Sponsor Country: Japan

National SIDS Contact Point in Sponsor Country:
Mr. Yasuhisa Kawamura
Director
Second Organisations Division
Ministry of Foreign Affairs, Japan
2-2-1 Kasumigaseki, Chiyoda-ku, Tokyo 100

4. Shared Partnership with:

5. Roles/Responsibilities of the Partners:

- Name of industry sponsor /consortium Mr. Katsuji Ito
ASAHI GLASS CO., LTD.
E-mail: katsuji-itoh@om.agc.co.jp
- Process used The industry consortium collected new data and prepared draft versions of the Dossier, Robust Study Summary, SIAR and SIAP. Japanese government peer-reviewed the documents, audited selected studies.

6. Sponsorship History

- How was the chemical or category brought into the OECD HPV Chemicals Programme ? This substance is sponsored by Japan under the ICCA Initiative and is submitted for first discussion at SIAM 15.

7. Review Process Prior to the SIAM:

8. Quality check process: No testing (X) Testing ()

9. Date of Submission: 13, August, 2002

10. Date of last Update:

11. Comments:

The industry contact point is Mr. Ito, ASAHI GLASS CO., LTD. acting on behalf of the consortium members (ASAHI KASEI CORP., CENTRAL GLASS CO., LTD., DAISO CO., LTD., HOKKAIDO SODA CO., LTD., KANEKA CORPORATION, KANTO DENKA KOGYOU CO., LTD., MITUBISHI CHEMICAL CORPORATION, MITUI CHEMICALS, INC., MITUI TAKEDA CHEMICAL CO.,LTD., MITUI DUPONT FLUORO CHEMICAL CO.,LTD., NANKAI CHEMICAL INDUSTRY CO., LTD., NIPPON SODA CO., LTD., SHIN-ETSU CHEMICAL CO., LTD., SUMITOMO CHEMICAL CO., LTD., TOAGOSEI CO., LTD., TOKUYAMA CORPORATION, TOSOH CORPORATION, TSURUMI SODA CO., LTD., V-Tech Corporation, Euro Chlor).

The SIDS Initial Assessment Documents were prepared by Chemicals Evaluation and Research Institute (CERI), Japan.

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	7647-01-0
Chemical Name	Hydrogen chloride
Structural Formula	H-Cl

SUMMARY CONCLUSIONS OF THE SIAR**Human Health**

Hydrogen chloride will rapidly dissociate and its effects are thought to be a result of pH change (local deposition of H⁺) rather than effects of hydrogen chloride/hydrochloric acid.

The acute oral LD₅₀ values were determined to be 238-277 mg/kg bw for female rats, and the inhalation LC₅₀ values were determined to be 23.7-60.9 mg/L/5min, 5.7-7.0 mg/L/30min and 4.2-4.7 mg/L/60min for rats, 20.9 mg/L/5min, 3.9 mg/L/30min and 1.7 mg/L/30min for mice. Hydrogen chloride is corrosive to the skin and severe effects can be expected from exposure to the eyes. No skin sensitisation has been reported.

There are few detailed studies reported for human exposure. The irritation of hydrogen chloride to mucous is so severe that workers evacuate from the work place shortly after detecting its odor. A relation between concentrations from accidental exposure and health effects have not been reported in detail.

For repeated dose toxicity, local irritation effects were observed in the groups of 10 ppm and above in a 90-day inhalation study in compliance with FDA-GLP. The NOAEL for systemic toxicity has been determined to be 20 ppm for rats and mice.

For genetic toxicity, a negative result has been shown in the Ames test. A positive result, which is considered to be an artifact due to the low pH, has been obtained in a chromosome aberration test using Hamster ovary cells. The effects of low pH in *in vitro* studies are not a problem *in vivo* as the proton level is regulated systemically.

For carcinogenicity, no pre-neoplastic or neoplastic nasal lesions were observed in a 128-week inhalation study with SD male rats at 10 ppm hydrogen chloride gas. No evidence of treatment related carcinogenicity was observed either in other animal studies performed by inhalation, oral or dermal administration. In humans, no association between hydrogen chloride exposure and tumor incidence was observed.

No reliable studies have been reported regarding toxicity to reproduction and development in animals after oral, dermal or inhalation exposure to hydrogen chloride/hydrochloric acid. Because protons and chloride ions are normal constituents in the body fluid of animal species, low concentrations of hydrogen chloride gas/mist or solution do not seem to cause adverse effects to animals. In fact, the cells of gastric glands secrete hydrochloric acid into the cavity of the stomach and orally administered sulfuric acid, which results in pH change as well, did not cause developmental toxicity to laboratory animals. These facts indicate that hydrogen chloride/hydrochloric acid is not expected to have developmental toxicity. In addition, no effects on the gonads were observed in a good quality 90-day inhalation study up to 50 ppm.

Environment

Hydrogen chloride is a colourless gas which has a pungent odor, and has a vapour pressure of 42,200 hPa at 20°C and a water solubility of 823 g/L at 0°C, 673 g/L at 30°C. Its aqueous solution (called hydrochloric acid) possesses strong acidity, and reacts with most metals producing explosive hydrogen gas. Hydrogen chloride is readily dissociated in water into hydrated protons and chloride ion.

The physico-chemical properties indicate that hydrogen chloride released into the environment is distributed into the air and water.

Hydrogen chloride can react with hydroxyl radicals to form chloride free radicals and water and its half-life time is calculated as 11 days. No accumulation of hydrogen chloride *per se* in living organisms is expected due to its high solubility and dissociation properties.

The toxicity values to *Selenastrum capriornutum* 72h-EC₅₀ is pH 5.1 (0.780 mg/L) for biomass, pH 5.3 (0.492 mg/L) for growth rate and the 72h-NOEC is pH 6.0 (0.097 mg/L) for biomass and growth rate. The 48h-EC₅₀ for *Daphnia magna* is pH 5.3 (0.492 mg/L) based on immobilization.

The hazard of hydrochloric acid for the environment is caused by the proton (pH effect). For this reason the effect of hydrochloric acid on the organisms depends on the buffer capacity of the aquatic ecosystem. Also the variation in acute toxicity for aquatic organisms can be explained for a significant extent by the variation in buffer capacity of the test medium. For example, LC₅₀ values of acute fish toxicity tests varied from 4.92 to 282 mg/L.

It is not considered useful to calculate a PNEC for hydrochloric acid because factors such as the buffer capacity, the natural pH and the fluctuation of the pH are very specific for a certain ecosystem.

There is a possibility that the emission of hydrochloric acid could locally decrease the pH in the aquatic environment. Normally, the pH of effluents is measured very frequently to maintain the water quality. In addition to that, water quality including the range of pH could be managed properly to prevent adverse effects on the aquatic environment based on the criteria of the pH in rivers and lakes. Therefore, a significant decrease of the pH of the receiving water is not expected. Generally the changes in pH of the receiving water should stay within the natural range of the pH, and for this reason, adverse effects on the aquatic environment are not expected due to anthropogenic or naturally occurring hydrochloric acid.

Exposure

The production volume of hydrogen chloride in 1999 was 1,155,259 tonnes (Production; 1,144,779 tonnes, import; 10,480 tonnes) in Japan and approximately 7,150,000 tonnes (6,500,000 metric tonnes) in the U.S.A. The production capacity in the U.S.A. in 1999 was approximately 2,242,000 tonnes excluding the capacity for by-product HCl that is generated and recycled in integrated systems such as ethylene dichloride/vinyl chloride monomer (EDC/VCM) production plants. The market of the aqueous solution occupies only about 20% of the total demand in the U.S.A.

Hydrogen chloride is produced by the direct reaction of hydrogen and chlorine, by reaction of metal chlorides and acids, and as a by-product from many chemical-manufacturing processes such as chlorinated hydrocarbons. A large quantity of hydrogen chloride is recycled in a same line for other material production processes such as ethylene dichloride production.

Hydrogen chloride/hydrochloric acid is commercially available in a gaseous form and solutions at various concentrations. The anhydrous hydrogen chloride is mainly used for ethylene dichloride and vinyl chloride monomer production etc. In aqueous form, there are various uses such as oil well acidising and steel pickling.

Hydrogen and chlorine, which is the source of formation for hydrogen chloride, are commonly found in the environment. Thus, hydrogen chloride occurs in nature through the reaction of sea salt aerosol and acidic sulphate in the ocean, and through atmospheric or aquatic (hydrolysis or biodegradation) degradation of organo-halogens etc. Volcano eruption injects hydrogen chloride of 400,000-11,000,000 tonnes into the atmosphere. Additionally mammalian constantly secretes the gastric juice, which contains H⁺ concentration equivalent to 0.17 N HCl (pHs as low as 0.87) into the stomach cavity.

Hydrogen chloride may be released into air from artificial source such as production and use sites. Unwanted hydrogen chloride is released into the environment from garbage incineration plants and by open burning or fire. Practically, the emission of hydrogen chloride into air is controlled, for instance, by the absorption in water and neutralisation before the emission into the environment if significant release is expected.

For workers, a maximal concentration of hydrogen chloride in the atmosphere at the working place of 5 ppm (7.5 mg/m³) is established by ACGIH (TLV-ceiling limit). Since hydrogen chloride/hydrochloric acid is irritating or corrosive depending on the concentrations, exposure control such as ventilation should be provided and acid resistant protective equipment for eyes and skin, respiratory protective equipment and face shield should be ready to use.

The products using hydrochloric acid as food-processing agents are neutralized or buffered in the products, and no effects of the pH are expected. Action to reduce consumer exposure has also been taken for products such as toilet

cleaners containing high-level hydrochloric acid which produce hydrogen chloride gas or cause irritancy.

Hydrogen chloride which occurs in nature and exists in the atmosphere could be inhaled by the general population. Also, indirect exposure to hydrated protons and chloride ions occur via drinking surface water or food consumption occurs since both ions are commonly found in the environment. The significant acidic effect as hydrochloric acid, however, is not expected due to the buffering capacity in the environment.

RECOMMENDATION

The chemical is currently of low priority for further work.

RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

The chemical possesses corrosive properties indicating a hazard for human health and the environment. No further work is recommended if sufficient control measures are in place to avoid significant human exposure and environmental impact, including prevention of accidental exposure. In situations where this is not the case, risk assessment and if necessary, risk reduction measures are recommended.

SIDS Initial Assessment Report

1 IDENTITY

1.1 Identification of the Substance

CAS Number:	Hydrogen chloride
IUPAC Name:	7647-01-0
Molecular Formula:	H-Cl
Molecular Weight:	36.46
Synonyms:	Anhydrous hydrochloric acid Chlorohydric acid Dilute hydrochloric acid Hydrochloric acid gas Hydrochloric acid (6Cl, 7Cl, 8Cl, 9Cl) Muriatic acid

1.2 Purity/Impurities/Additives

Purity:	> 99.7 % as anhydrous hydrogen chloride
Impurities:	Water < 0.02%
	Remarks: Standard quality criteria for anhydrous hydrogen chloride
Additives:	None

1.3 Physico-Chemical properties

Table 1 Physical and chemical properties of hydrogen chloride

Items	Protocols	Results	Reference
Melting Point	Unknown	-114.22°C	The Merck Index, 13th Ed. (2001)
Boiling Point	Unknown	-85.05°C (1,013 hPa)	The Merck Index, 13th Ed. (2001)
Vapour Pressure	Measured	42,200 hPa (20°C)	BASF AG (1994)
Water Solubility	Unknown	823 g/L (0°C) 673 g/L (30°C)	The Merck Index, 13th Ed. (2001)
Density	Calculated	1.491 mg/cm ³ (25°C, 1,013hPa)	CERI (2002)

Note: The log Pow is not applicable to inorganic compounds such as hydrogen chloride.

Hydrogen chloride is a colorless gas which has a pungent odor. The aqueous solution of hydrogen chloride is called hydrochloric acid. Hydrogen chloride is very soluble and completely dissociates into protons and chloride ions in water. It is a strong acid and reacts with most metals producing explosive hydrogen gas.

2 GENERAL INFORMATION ON EXPOSURE

2.1 Production Volumes and Use Pattern

Estimated national production: The production volume of hydrogen chloride in 1999 was 1,155,259 tonnes (Production; 1,144,779 tonnes, import; 10,480 tonnes) in Japan (METI, Japan, 1999, The Chemical Daily, 2000) and approximately 7,150,000 tonnes (6,500,000 metric tons) in the U.S.A (CMAI, 2000). In Japan, hydrogen chloride and hydrochloric acid are manufactured at 23 and 8 companies, respectively. The production capacity in the U.S.A. in 1999 was approximately 2,242,000 tonnes excluding the capacity for by-product HCl that is generated and recycled in integrated systems such as ethylene dichloride/vinyl chloride monomer (EDC/VCM) production plants (Chemical Market Reporter, 1999).

According to CMAI, the market of the aqueous solution of hydrogen chloride occupies only about 20% of total demand in the U.S.A (CMAI, 2000).

Hydrogen chloride is produced by direct reaction of hydrogen and chlorine, by reaction of metal chlorides and acids, and as a by-product from chlorine-using processes to manufacture chlorinated hydrocarbons and so on. In the U.S.A. more than 95% of hydrogen chloride/hydrochloric acid is produced as a by-product and a large quantity of hydrogen chloride is recycled for other material production processes such as ethylene dichloride (EDC) production (CMAI, 2000).

Commercially, hydrogen chloride is available in its gaseous form and as a solution at various concentrations.

Use categories and/or functions (HSDB, CMAI, 2000)

The main uses of hydrogen chloride or hydrochloric acid are as follows;

- In chemical industry

- Production of inorganic salts
- Production of vinyl chloride from acetylene, alkyl chlorides from olefins, dyes, artificial silk, pigment, pesticides, pharmaceutical hydrochloride
- As catalyst and solvent in organic syntheses
- Alcohol chlorination reagent
- Nitration reaction
- Manufacture of phosphoric acid and in the production of ammonium chloride
- Neutralization of basic systems
- Cleaning agents

- Manufacture of fertilizers

- Hydrolysing of starch and proteins in the preparation of various food products

- Pickling and cleaning of metal products
- Refining ore
- Leather deliming / tanning agents
- Oil- and gas-well treatment
- Textile scouring agents
- Removing scale from boilers and heat-exchange equipment
- In the brewing industry
- Water treatment (pH control etc.)
- As laboratory reagents
- etc.

The hydrogen chloride gas is mainly used for EDC and vinyl chloride monomer (VCM) production etc. In aqueous form, there are various uses such as oil well acidification and steel pickling.

2.2 Environmental Exposure and Fate

2.2.1 Sources of Environmental Exposure

Potential sources

Hydrogen and chlorine, which is the source of formation for hydrogen chloride, are commonly found in the environment. Thus, hydrogen chloride occurs in nature through the reaction of sea salt aerosol with acidic sulphate in the ocean surface and through the atmospheric or aquatic (hydrolysis or biodegradation) degradation of organo-halogens etc. (European Commission- European Chemical Bureau 2000, WHO 1982). Also, volcano eruption injects approximately 400,000-11,000,000 tonnes/year of hydrogen chloride into the atmosphere.

Hydrogen chloride may be released into air from artificial sources such as production and user sites. Unwanted hydrogen chloride generated at garbage incineration plants and by open burning or fire is released into the environment. In case of emissions from chemical plants or waste incinerators, the concentration of hydrogen chloride depends on the technology and control methods used in such plants. Under Air Pollution Control Law in Japan, the emission standard is established as 700 mg/m³ (0°C, 1 atm) for waste incinerator facilities and 80 mg/m³ (0°C, 1 atm) for hydrogen chloride gas absorption or chemical chlorination facilities (MOE, Japan). Practically, the emission of hydrogen chloride into air is controlled, for instance, by the absorption in water and neutralisation before the emission if significant release is expected. The pH of effluents is also established as within the range of 5.8-8.6 for the water quality standard under the Water Pollution Control Law in Japan (MOE, Japan).

Hydrogen chloride/hydrochloric acid will be released from the consumer products such as a cleaners containing hydrochloric acid.

Most animals constantly secrete gastric juice, which contains a H⁺ concentration equivalent to 0.17 N HCl (pHs as low as 0.87) into the stomach cavity (Ganong, 2001).

2.2.2 Other Information on Environmental Fate

Hydrogen chloride can exist in its gaseous form at normal temperature and pressure (vapour pressure: 42,200 hPa at 20°C), and is very soluble in water (water solubility: 823 g/L at 0°C) in the form of protons and chloride ions. These physico-chemical properties indicate that hydrogen chloride/hydrochloric acid released into the environment is distributed into the air and water. The Fugacity model cannot be applied for ionised substances like this chemical.

Hydrogen chloride can react with hydroxyl radicals to form free chloride radicals according to the following equation:



The half-life of hydrogen chloride in air through the reaction with 10⁶ molecule/cm³ of hydroxyl radicals is calculated to be 11 days (Solvay S.A., 2002). However, this reaction cannot occur in the presence of moisture since hydrogen chloride is dissolved into moisture and exists in its dissociated form. No accumulation of hydrogen chloride *per se* in living organisms is expected due to its high water solubility and dissociation properties.

Monitoring data

The UNEP (United Nations Environment Programme) reported the mean, the 10th-percentile and the 90th-percentile of chloride concentrations in 77 rivers were 41.1, 1.1 and 64.8 mg/L, respectively. This global water quality monitoring was conducted in North America, South-America, Asia, Africa, Europe and Oceania. (UNEP, 1995). The chloride concentration is tightly related to the geological parameters and human activities and chloride is also extensively distributed into the environment. Thus the chloride concentration is not only related to the release of hydrogen chloride/hydrochloric acid into the environment. Regarding the H⁺ concentration measured as pH, UNEP reported that the average annual pH values were between 6.5 and 8.3 (UNEP, 1995).

Buffer capacity in the aquatic ecosystem

The increase of the concentration of hydrochloric acid in water decreases the pH in the aquatic ecosystem. Generally, the buffer capacity to maintain the pH in the aquatic ecosystem is important and the equilibrium between CO₂, HCO₃⁻ and CO₃²⁻ in the aquatic ecosystem is mainly responsible for the buffer capacity of receiving water.



According to UNEP (1995), the mean, the 10th-percentile and the 90th-percentile of bicarbonate concentrations for 77 rivers in North-America, South-America, Asia, Africa, Europe and Oceania were 106, 20 and 195 mg/L, respectively (UNEP, 1995). The amount (expressed as a concentration) of hydrochloric acid, which has to be added to bicarbonate solutions to obtain pH values of 6.0 and 4.0, is given in Table 2-1. The data of Table 2-1 were based on calculations but they were confirmed by experiments, and found that the decrease of the pH depends on the buffer capacity (bicarbonate concentration) of the receiving water. The buffering capacity for neutralization of receiving water with bicarbonate concentration of 20, 106 and 195 mg/L is calculated to be 2.19, 11.60 and 21.3 mg/L, respectively.

Table 2-1 Buffer capacity to maintain the pH based on bicarbonate concentration from UNEP monitoring data (Groot de W.A. and Dijk van N.R.M. 2002)

Initial concentration of HCO ₃ ⁻	Final pH	Concentration of HCl required to obtain the final pH value
		Calculated [mg/L]
20 mg/L HCO ₃ ⁻ (10th percentile 77 rivers)	6.0	8.28
	4.0	11.9
106 mg/L HCO ₃ ⁻ (mean value of 77 rivers)	6.0	43.9
	4.0	63.2
195 mg/L HCO ₃ ⁻ (90th percentile 77 rivers)	6.0	80.7
	4.0	116.3

The pH of effluents is frequently measured to maintain the water quality because the pH is a key parameter in water quality (WHO 1998), and can be adapted easily to the aquatic ecosystem. Significant decrease of the pH of the receiving water, therefore, is not expected.

2.3 Human Exposure

2.3.1 Occupational Exposure

Table 2-2. Occupational exposure levels (OELs) in several countries

	Type*	Value	Reference
ACGIH	STEL (Ceiling)	5 ppm (7.5 mg/m ³)	ACGIH, 2001
EU	TLV	5 ppm (8 mg/m ³)	European Commission Directive 2000/39/EC, 2000
	STEL	10 ppm (15 mg/m ³)	
OEL-Japan	STEL	5 ppm (7.5 mg/m ³)	Japan Society for Occupational Health, 2001
OEL-German	MAK	5 ppm (7 mg/m ³)	European Commission- European Chemical Bureau, 2000
OEL-United Kingdom	TWA	1 ppm (2 mg/m ³)	
	STEL	5 ppm (7 mg/m ³)	

* STEL: Short-Term Exposure Limit, TLV: Threshold Limit Value,

TWA: Time-Weighted Average, MAK: = TWA.

Occupational exposure to hydrogen chloride which possesses irritating or corrosive properties depending on its concentration has long been controlled in each country by the establishment of standard concentrations at the working place. Although hydrogen chloride is produced in a closed system, attention should be paid to leakages. The workers at user sites such as steel industry may inhale the gas or mist of hydrogen chloride, and may come into contact with its aqueous solution. Although dermal absorption of hydrogen chloride is not expected, hydrochloric acid is irritating or corrosive depending on the concentrations.

In the worst case estimation of intake by inhalation exposure to hydrogen chloride, workers may inhale air that contains hydrogen chloride at 7.5 mg/m^3 (ACGIH TLV-ceiling limit), the daily intake through inhalation during an 8-hour working day will amount to 108 mg/day (breathing rate: 30 L/min.).

Generally, workers who are at indoor work are expected to use protective equipments (gas mask, gloves, safety glasses) and drivers who transport the chemical have to always have those equipments ready. For any situation where potential exposure is expected, the use of acid resistant protective equipments for eyes and skin, respiratory protective equipment and face shield is recommended because of its irritating or corrosive properties.

2.3.2 Consumer Exposure

Hydrochloric acid is widely used as a food processing agent and is dissociated into its ions. Its acidity is neutralised or buffered in the products. Thus, effects of hydrochloric acid via such products are not expected.

In Japan, a cleaning agent containing hydrochloric acid at 9.5% is available to consumers and exposure to hydrogen chloride or hydrochloric acid may occur. In order to avoid consumer exposure from the effect of hydrogen chloride gas and hydrochloric acid, the following cautions are mentioned on the label of the product as product information (DAINIHON JOCHUGIKU Corporation, 2002);

Danger of chloride gas if mixed with other chloride contained cleaner;

Don't use for other usage;

Use rubber gloves or handled brush for use;

Don't grasp the bottle to open;

Don't leave the liquid.

Thus, actions to reduce the potential of consumer exposure have been taken.

Indirect Exposure via Environment

Hydrogen chloride, which occurs in the environment or is released from anthropogenic sources, could be inhaled by the general population. Also, indirect exposure to hydrated protons and chloride ions occurs via drinking surface water or food consumption since both ions are ubiquitous in the

environment. The significant acidic effect of hydrochloric acid, however, is not expected due to the buffering capacity of the environment.

3 HUMAN HEALTH HAZARDS

3.1 Effects on Human Health

Hydrogen chloride has been used in a dispersive way for a long time, and therefore its exposure and effects on humans are well known. The major human health hazard and mode of action of hydrogen chloride is local irritation and/or corrosion. Irritation of the upper airways appears to be the most sensitive indicator of exposure.

3.1.1 Toxicokinetics, Metabolism and Distribution

Hydrogen chloride or its aqueous solution, hydrochloric acid is corrosive and irritating and causes direct local effects on the skin, eyes and gastro-intestinal tract after direct exposure to sufficiently high concentrations. Vapour of hydrogen chloride or small droplets (aerosol/mist) of hydrochloric acid can also be inhaled and cause direct local effects on the respiratory tract. Hydrogen chloride will rapidly dissociate and the anion will enter the body electrolyte pool. That is, hydrogen chloride *per se* is not expected to cause effects to the body. The local effects of the aqueous solution of hydrogen chloride are the effects of the H⁺ ion (local deposition of protons, pH change) rather than effects of the chloride ion. Inhaled hydrogen chloride is partially neutralized before it reaches the lower respiratory tract by naturally occurring ammonia gas in the respiratory system (Soskolne et al., 1989). Under normal handling and use conditions (non-irritating), an aqueous solution of hydrogen chloride is not expected to be systemically available in the body. Immediate defence against pH changes is provided by body buffers that can take up or release protons instantaneously in response to changes in acidity of body fluids. Regulation of pH ultimately depends on the lungs (carbon dioxide excretion) and kidneys (bicarbonate regeneration through proton secretion in urine).

Chloride is a normal constituent of the blood and the excess is expected to be excreted into the urine (Ganong, 2001). The uptake of sodium chloride via food is about 3.5-9 gram per person per day (Battarbee and Meneely, 1978; FASEB, 1979). It means 2.1-5.5 g chloride is taken into the body via food. The daily intake through inhalation during an 8-hour work shift is estimated to be only 108 mg/day under the worst case at the working place. The body pool of this anion (Cl⁻) is large, and the uptake of chloride via exposure to hydrogen chloride/ hydrochloric acid is much less than the uptake of chloride via food, it is therefore unlikely that occupational aerosol exposures significantly alter the normal body load.

The uptake of protons via exposure to hydrogen chloride/ hydrochloric acid is not expected to change the pH in the blood under normal handling and use conditions (non-irritating). The pH of the extracellular fluid is regulated within a narrow range to maintain homeostasis. Via urinary excretion and exhalation of carbon dioxide, the pH is maintained at the normal pH of 7.4 (Ganong, 2001).

3.1.2 Acute Toxicity

There are no studies that have been carried out recently, under national or international guidelines, and in compliance with GLP. However, available studies are presented in Table 3-1, despite their poor reliability. Although there are no valid studies for the acute inhalation route, the available studies provide reasonably consistent information on lethality.

Table 3-1.

Species	Route	Endpoint	Value	Reliability	References
Rat	Oral	LD ₅₀	238-277 mg/kg	2	Hoechst AG(1966)
			700 mg/kg	4	Monsanto (1976)
Rabbit	Oral	LD ₅₀	900 mg/kg	3	Loewy and Munzer (1923)
Rat	Inhalation (Gas)	LC ₅₀	23.7 mg/L·5min	3	Hartzell et al. (1987)
			60.9 mg/L·5 min	3	Darmer et al. (1974a)
Rat	Inhalation (Gas)	LC ₅₀	5.7 mg/L·30min	3	Hartzell et al. (1987)
			7.0 mg/L·30min	3	Darmer et al. (1974a)
Rat	Inhalation (Gas)	LC ₅₀	4.2 mg/L·60min	3	Hartzell et al. (1990)
			4.7 mg/L·60min	3	MacEwean et al. (1974)
Mouse	Inhalation (Gas)	LC ₅₀	20.9 mg/L·30min	3	Darmer et al. (1974b)
Mouse	Inhalation (Gas)	LC ₅₀	3.9 mg/L·30min	3	Darmer et al. (1974b)
Mouse	Inhalation (Gas)	LC ₅₀	1.7 mg/L·60min	3	MacEwean et al. (1974)
Rabbit	Dermal	LD ₅₀	>5,010 mg/kg	4	Monsanto (1976)

Studies in Animals

Inhalation

In the studies in which rats and mice were exposed to hydrogen chloride (gas) and observed for 14 days, LC50 values were determined depending on exposure period. The LC50 values are reported to be 23.7-60.9 mg/L/5min, 5.7-7.0 mg/L/30min and 4.2-4.7 mg/L/60min for rats, 20.9 mg/L/5min, 3.9 mg/L/30min and 1.7 mg/L/60min for mice (Darmer et al., 1974a; Hartzell et al., 1990; MacEwean et al., 1974). Clinical signs observed were irritation and corrosion to the eye (cloudiness and erosion of cornea) and skin (especially, ulceration of scrotum), and animals died from respiratory failure (alveolar emphysema, atelectasis, and oedema of the lungs) shortly after exposure. As for hydrochloric acid aerosol, because hydrogen chloride gas is thought to be rapidly dissolved into water in the air or on the tissue, lethal concentrations (LC50 value: 45 mg/L/5min., 8.3 mg/L/30min for rats, 16.5 mg/L/5min, 3.2 mg/L/30min for mice), clinical signs and the observations at necropsy did not differ from those observed at exposure to the gas (Darmer et al., 1974a).

Although there are several experiments with rabbits, guinea pigs, monkeys, cats and dogs, that show clinical signs caused by irritation and death from respiratory failure, the details of the experiments were not described.

Dermal

Although, the details of the experiment, such as the concentration of the solution applied, were not reported, the lethal dose was above 5,010 mg/kg for the rabbits (Monsanto, 1976).

Oral

In an oral administration test, the LD₅₀ value for hydrogen chloride has been determined to be 238-277 mg/kg bw for female rats (Hoechst AG, 1966). In this test, hydrogen chloride was given to four different dose groups as 3.3% aqueous solution to minimize the corrosive effect, other data such as clinical or pathological observation were not reported. Although, ulceration of stomach, acute inflammation of intestine, discoloration of the liver and hyperemia of the lung were observed in another acute oral study with rats, the details of the experiment including concentration of the solution administered were not reported (Monsanto, 1976). The oral LD₅₀ value was also reported to be 900 mg/kg bw for rabbits, but the details of the experiment were not reported (Loewy and Munzer, 1923).

Studies in Humans

Inhalation

There are few detailed studies reported for human exposure. The irritation of hydrogen chloride gas / hydrochloric acid mist to mucosa is so severe that workers evacuate from the work place shortly after detecting a smell. The relation between concentration during accidental exposure and health effects were not reported in detail.

It is reported that acute exposure of 1,300 ppm (1.95 mg/L) hydrogen chloride gas for 30 minutes or 3,000 ppm (4.5 mg/L) for 5 minutes did not cause any death in a human experiment (Marchi Industry, 2000), and short-term exposure to airborne concentration up to 1.8 ppm did not cause irritation to the respiratory tract of sensitive asthmatic volunteers (Stevens et al. 1992).

Oral

In a suicide case, it is reported that a woman died 29 hours after ingestion of 60 mL of 35% hydrochloric acid (Hashimura et al., 1996). In the three cases of hydrochloric acid ingestion patients admitted to an Indian Hospital, gastric scarring was observed (Subbarao, 1988). The volume and concentration of the solution intake was not reported. They received gastroectomy and recovered.

Conclusion

None of the available studies have been carried out recently or under national/international guidelines, and in compliance with GLP. Although few reliable studies are available, the studies presented here can explain the nature of the acute toxicity of this chemical.

The oral LD₅₀ value of hydrogen chloride is reported to be 238-277 mg/kg bw for female rats, and 900 mg/kg bw for rabbits and the LC₅₀ values of hydrogen chloride (gas) by inhalation exposure are

23.7-60.9 mg/L/5min, 5.7-7.0 mg/L/30min and 4.2-4.7 mg/L/60min for rats, 20.9 mg/L/5min, 3.9 mg/L/30min and 1.7 mg/L/60min for mice. The lethal dose by dermal exposure was above 5,010 mg/kg bw for rabbits.

3.1.3 Irritation

Skin Irritation

Studies in Animals

There are several studies with reliability 1 or 2 available (see table 3-2). Concentrations above 3.3% cause irritation and concentrations above 17% cause corrosion in animal studies.

According to Annex I of the Directive 67/548/EEC, hydrochloric acid is classified as C; R34: Corrosive; Causes severe burns for concentration $C \geq 25\%$ and Xi; R37: Irritation; Irritating to the respiratory system for concentration $10\% \leq C < 25\%$.

Table 3-2.

Species	Results	Remarks	Reliabilities	Reference
Rabbit	Corrosive	37% hydrochloric acid aq. (1h, 4h) caused severe damage.	2	Potokar et al. (1985)
Rabbit	Corrosive	0.5 mL of 17% hydrochloric acid aq. was applied for 4h.	3	Vernot et al. (1977)
Rabbit	Moderately irritating	0.5 mL of 3.3% hydrochloric acid aq. applications for 5 days was moderately irritating.	2	Hoechst AG (1966)
Rabbit	Not irritating	0.5 mL of 1% hydrochloric acid aq. applications for 5 days was not irritating.	2	Hoechst AG (1966)

Studies in Humans

An aqueous solution (4%) of hydrogen chloride was slightly irritating (Agner and Serup, 1988), and a 10% solution was determined to be 'Irritating to skin' for the EU Dangerous Preparations Directive, in human volunteer experiments (York et al., 1996).

Eye Irritation

There are several studies with reliability 1 or 2 available (see table 3-3). Concentrations above 3.3 % cause irritation, and higher concentrations or prolonged exposure cause damage of the tissue in the animal studies. Conflicting results may be observed in eye irritation studies depending on the protocol used. The severity of the effects is influenced by the exposure amount, concentration, duration and the treatment, because tears induce buffering and diluting effects.

Table 3-3.

Species	Results	Remarks	Reliabilities	Reference
Rabbit	Highly irritating (OECD 405)	0.1 mL of 10% hydrochloric acid aq. severe irritation with corneal injury which may result in permanent impairment of vision.	2	Jacobs (1992)
Rabbit	Corrosive	0.03 mL or more of 5% hydrochloric acid aq. was severely irritating or corrosive.	3	Griffith et al. (1980)
Rabbit	Slightly irritating	0.1 mL of 3.3% hydrochloric acid aq. was applied into the conjunctival sac; 48h observation period.	2	Hoechst AG (1966)
Rabbit	Not irritating	0.1 mL of 0.33% hydrochloric acid aq. was applied into the conjunctival sac; 48h observation period.	2	Hoechst AG (1966)

3.1.4 Sensitisation

Studies in Animals

There are no studies that have been performed recently or under national/international guidelines, and in compliance with GLP. However, both guinea pig maximization test (1% HCl in EtOH [undefined concentration] was used in both sensitization and challenge phase) and mouse ear swelling test (MEST; 1% HCl in 70% EtOH for sensitization phase, 5% HCl for challenge phase was used) showed negative results (Gad et al., 1986). The concentration levels used were expected to refer to “not irritating (1%)” and “slightly irritating (5%)”.

Studies in Humans

In a human study, fifty volunteers were given nine 24-hour covered applications of an aqueous solution of hydrogen chloride of unspecified concentration over 3 weeks. None gave positive reactions in a challenge application, 10–14 days after the final induction application (Gad et al., 1986).

3.1.5 Repeated Dose Toxicity

Studies in Animals

Inhalation

For repeated dose toxicity, 13 inhalation and 7 oral dose studies has been reported. Among those, only the inhalation studies reported by CIIT (1984) were reliable. They were performed in compliance with FDA-GLP, and they are considered to be the critical studies for assessment. Four groups of 10 males and 10 females (mice: B6C3F1; rats: SD and F344) individually housed were exposed to hydrogen chloride gas at concentrations of 0, 10, 20 and 50 ppm for 90 days (6 hours/day, 5 days/week). For male and female mice at 50 ppm, a decrease in body weight gain, food consumption and liver weight (male) was noted. For male SD rats at 50 ppm, a decrease in food consumption was observed. For F344 rats, a decrease in body weight gain was observed in males at 50 ppm and a decrease in food consumption was observed in both sexes at 20 and 50 ppm.

No biologically significant difference was observed in urinalysis, haematology and serum chemistry. Inflammatory histo-pathological changes in lips or nasal cavity were observed in B6C3F1 mice and F344 rats above 10 ppm or in SD rats above 20 ppm. In addition, the histopathological examination of reproductive organs (testis, epididymis, prostate, seminal vesicle; ovary, uterus, oviduct, mammary glands) could not find any exposure related effects. The NOAEL for repeated dose inhalation toxicity, except for the local effects of irritation, is considered to be 20 ppm for rats and mice. Other inhalation studies with rats, mice, rabbits, guinea pigs and monkeys are not appropriate for initial assessment, as the methods of the experiments had some defects.

Dermal

There are no repeated dose dermal studies with hydrogen chloride.

Oral

For oral effects, groups of rats were fed diets containing 280-1250 mmol/kg diet (10.2-45.6 mg/kg diet) for 7-12 weeks (Upotn and L'Estrange, 1977). In the groups fed diet containing 280 mmol/kg and above, an increase in water intake was observed. At higher doses, all animals fed diet containing 937 mmol/kg and above for 9 weeks, and half of the animals fed diet containing 900 mmol/kg for 12 weeks died, and decreased body weight, food consumption, blood pH, femur length, rate of ash in bone were also observed. In an experiment with rats, hydrochloric acid was administered via drinking water (pH 2-3). Decreased protein levels in urine and decreased urine volumes were observed in the treatment groups (Clausing and Gottschalk, 1989). Other oral studies with rats and rabbits are not appropriate for initial assessment, as the methods of the experiments had some defects or the details of the results were not reported (Burns, 1929).

Studies in Humans

In a personal exposure monitoring program at a zinc galvanizing plant in the Netherlands, using 15% hydrochloric acid solution for pickling process, atmospheric concentrations of 1.8-12.4 mg/m³ (geometric mean) were observed at 6 sites (ca. 50 samples for each site) (Remijn et al., 1982). It was calculated that workers were exposed to hydrochloric acid concentrations above 7 mg/m³ for 27% of their work shift (length of employment is not shown). Erosion in more than one incisor was observed in 90% of the 38 workers examined in the plant.

Conclusion

From the result of the inhalation study in compliance with FDA-GLP in which rats and mice were exposed to hydrogen chloride gas at concentrations of 0, 10, 20 and 50 ppm (0, 15, 30, 75 mg/m³) for 90 days (6 hours/day, 5 days/week), the NOAEL for systemic toxicity has been determined to be 20 ppm for B6C3F₁ mice.

As hydrogen chloride/hydrochloric acid is a direct acting irritant and adverse effects are caused at the site of contact, exposure by inhalation, dermal or oral route at high concentration is not appropriate. Lower concentration of gas or mist is neutralized before it reaches the lower respiratory tract by naturally occurring ammonia gas in the respiratory system (Soskolne et al., 1989). Solutions of lower concentration, that might not cause skin irritation, are not expected to be

absorbed from the skin and are not expected to be available systemically in the body. And as the cells of the gastric glands secrete hydrochloric acid (H^+ concentration is equivalent to 0.17 N HCl, with pH as low as 0.87) into the stomach cavity (Ganong, 2001), it is empirically known that small volumes or lower concentrations of ingested hydrochloric acid do not cause systemic effects.

3.1.6 Mutagenicity

In vitro Studies

Bacterial test

There are results available from six bacterial studies. Among those, the Ames test reported by Isquith et al. (1988) and Litton Bionetics, Inc. (1978) was performed according to a good quality method, and is considered to be a critical study for the initial assessment. Negative results were reported. In the same report, negative results have been also reported from a Mitotic recombination test using *S. cerevisiae* (D4) and Rec assay using *E. coli* (W3110, P3078) (Isquith et al., 1988; Litton Bionetics, Inc., 1978). Negative results were also reported from an *E. coli* reverse mutation assay, in which the survival rate of the bacteria widely varied and the result is not reliable (Demerec et al, 1951).

In the other *in vitro* studies, Rec assay using *B. subtilis* or *E. coli*, though the method is not quantitative, the former shows negative results, and the latter shows positive results, but which were not relating to DNA damage (McCarroll et al., 1981a, b).

Non-bacterial test

There are results available from six non-Bacterial studies. Among those the chromosome aberration test using Chinese hamster ovary K1 (CHO-K1) cells (Morita et al., 1989) is a critical study for assessment, because the test method used met the OECD-TG and GLP except for a single dose level of pH 5.3 and 5.5 used with and without metabolic activation, respectively. Positive results were obtained in both systems (Morita et al., 1989). Positive results were also observed in the Chromosome aberration test (pH 5.25, with metabolic activation) using Chinese hamster ovary cells, but experimental details were missing (Brusick, 1986). In a mammalian cell gene mutation assay using Mouse lymphoma L5178Y cells, positive results at cytotoxic conditions (below pH 6.3) were also found (Cifone et al., 1987).

In the other *in vitro* studies, Chromosome aberration test, Sister chromatid exchange assay or Mammalian cell gene mutation assay using Fischer L5178Y mouse-lymphoma cells (Isquith et al., 1988; Litton Bionetics, Inc., 1978), negative results have been obtained at dose levels of 0.1-0.8 uL(36.5-38% hydrochloric acid)/mL, 0.1-0.8 uL/mL and 0.4-1.6 uL/mL, respectively.

Conclusion

While consistent negative results have been obtained in the bacterial systems, positive results have been obtained in the non-bacterial systems. The positive results were observed at high concentration, but they were considered to be artifacts due to low pH.

In vivo Studies

Mutagenic effects of hydrochloric acid were obtained in the sex linked recessive lethal study with *D. melanogaster* by inhalation of vapour or larval feeding of the solution (only one dose level tested) (Stumm-Tegethoff, 1969).

Conclusion

Positive results were obtained in a Sex Linked Recessive Lethal study with *D. melanogaster*. There are no mammalian studies on *in vivo* mutagenicity with hydrogen chloride

3.1.7 Carcinogenicity

Inhalation

In a 128-weeks inhalation study (6h/d, 5d/w) at 10 ppm hydrogen chloride gas with SD male rats, although hyperplasia of the larynx and trachea were observed in treated animals (22/99 and 26/99, respectively), no pre-neoplastic or neoplastic nasal lesion were observed in any group (Sellakumar et al., 1985). Because this test was performed along with the carcinogenicity study of formaldehyde, only one experimental group was set for hydrogen chloride. But, as the concentration (10 ppm) used was high enough (irritation effects were observed in a 90-day inhalation toxicity study (CIIT, 1984) and it is also the maximum tolerable dose for human exposure) and furthermore, as enough animals (100 animals/group) were used, the result is considered to be appropriate for assessment.

The following test supports the above-described result. In a study in which 20 male SD rats were exposed to hydrogen chloride gas for 588 days, there were no carcinogenic responses in exposed animals (Albert et al., 1982).

Dermal

For dermal administration, results are available from an experiment with mice administered 3-5% hydrochloric acid for 25-46 weeks (Narat, 1925). Though no malignant tumor was reported, it is not appropriate for the assessment of carcinogenicity. Because the methods (no negative control, shortage of administration period) used were not appropriate.

Oral

For oral administration, results are available from an experiment with mice administered hydrochloric acid for ten months (Dyer et al., 1946). Because the methods such as strain used, duration and dose of administration, presence of co-administration substance, were not appropriate, it cannot be used for the assessment of carcinogenicity of hydrogen chloride.

Studies in Humans

In some case-control studies, no association between hydrogen chloride exposure and preleukemia (Farrow et al., 1989), lung cancer (Bond et al., 1986, 1991), intracranial neoplasms (Bond, 1983), renal cancer (Bond, 1985) could be found. On the one hand, although there are some reports that hydrogen chloride exposure increases risk of respiratory cancers (ANON, 1987) or lung cancer

(Beaumont, 1987), the effect of exposure of other acids or smoking habit cannot be excluded. The International Agency for Research on Cancer (IARC) reviewed the epidemiology studies and reported in a Monograph, "There is an inadequate evidence for carcinogenicity in humans and in experimental animals of hydrochloric acid", and concluded to classify hydrochloric acid as Group 3 (The agent is not classifiable as to its carcinogenicity to humans) carcinogenic activity (IARC, 1992).

3.1.8 Toxicity for Reproduction

Studies in Animals

Effects on Fertility

No reliable studies were identified regarding reproductive toxicity in animals after oral, dermal or inhalation exposure to hydrogen chloride/hydrochloric acid.

The following data related to reproduction has been obtained, though it is not appropriate for assessment. The experiment was based on an assumption that target organs of a toxic chemical substance in pregnant dams would be the same as in offspring. Female rats were mated 12 days after a single exposure of hydrogen chloride vapour (302 ppm, 453 mg/m³) for 1 hour. Death from severe dyspnea and cyanosis occurred in one third of the dams, functional disorders of the lungs, the kidneys, the liver were observed in surviving dams and offspring, decreased bodyweight was observed in offspring (Pavlova, 1976).

Developmental Toxicity

No reliable studies were identified regarding developmental toxicity in animals after oral, dermal or inhalation exposure to hydrogen chloride/hydrochloric acid.

The following data related to developmental toxicity has been obtained, though it is not appropriate for assessment. The experiment was based on an assumption that target organs of a toxic chemical substance in pregnant dams would be the same as in offspring. Pregnant female rats (9th day of gestation) were exposed to hydrogen chloride vapour for 1 hour. Death from severe dyspnea and cyanosis occurred in one third of the dams, functional disorders of the lungs, the liver were observed in surviving dams and offspring, increased mortality was observed in offspring.

Conclusion

No reliable studies were identified regarding toxicity to reproduction and development in animals after oral, dermal or inhalation exposure to hydrogen chloride/hydrochloric acid.

3.2 Other data

Increased urinary excretion of the chloride ion were observed in rats and dogs intravenously injected 0.15 M hydrochloric acid solution (Kotchen et al., 1980).

3.3 Initial Assessment for Human Health

Hydrogen chloride will rapidly dissociate and its effects are thought to be a result of pH change (local deposition of H⁺) rather than effects of hydrogen chloride/hydrochloric acid.

The acute oral LD₅₀ values were determined to be 238-277 mg/kg bw for female rats, and the inhalation LC₅₀ values were determined to be 23.7-60.9 mg/L/5min, 5.7-7.0 mg/L/30min and 4.2-4.7 mg/L/60min for rats, 20.9 mg/L/5min, 3.9 mg/L/30min and 1.7 mg/L/60min for mice. Hydrogen chloride is corrosive to the skin and severe effects can be expected from exposure to the eyes. No skin sensitisation has been reported.

There are few detailed studies reported for human exposure. The irritation of hydrogen chloride to mucous is so severe that workers evacuate from the work place shortly after detecting its odor. A relation between concentrations from accidental exposure and health effects have not been reported in detail.

For repeated dose toxicity, local irritation effects were observed in the groups of 10 ppm and above in a 90-day inhalation study in compliance with FDA-GLP. The NOAEL for systemic toxicity has been determined to be 20 ppm for rats and mice.

For genetic toxicity, a negative result has been shown in the Ames test. A positive result, which is considered to be an artifact due to the low pH, has been obtained in a chromosome aberration test using Hamster ovary cells. The effects of low pH in *in vitro* studies are not a problem *in vivo* as the proton level is regulated systemically.

For carcinogenicity, no pre-neoplastic or neoplastic nasal lesions were observed in a 128-week inhalation study with SD male rats at 10 ppm hydrogen chloride gas. No evidence of treatment related carcinogenicity was observed either in other animal studies performed by inhalation, oral or dermal administration. In humans, no association between hydrogen chloride exposure and tumor incidence was observed.

No reliable studies have been reported regarding toxicity to reproduction and development in animals after oral, dermal or inhalation exposure to hydrogen chloride/hydrochloric acid. Because protons and chloride ions are normal constituents in the body fluid of animal species, low concentrations of hydrogen chloride gas/mist or solution do not seem to cause adverse effects to animals. In fact, the cells of gastric glands secrete hydrochloric acid into the cavity of the stomach and orally administered sulfuric acid, which results in pH change as well, did not cause developmental toxicity to laboratory animals. These facts indicate that hydrogen chloride/hydrochloric acid is not expected to have developmental toxicity. In addition, no effects on the gonads were observed in a good quality 90-day inhalation study up to 50 ppm.

4 HAZARDS TO THE ENVIRONMENT

4.1 Aquatic Effects

The toxicity of hydrochloric acid is summarized in Table 4-1. Each toxicity result is related to 12N HCl.

Toxicity to Aquatic Plants / Algae

There is only one study available on acute and chronic toxicity to unicellular green algae. For *Selenastrum capricornutum*, 72h EC₅₀ and NOEC based on growth rate are pH 5.3 (equivalent to a substance concentration of 0.492 mg/L) and pH 6.0 (0.097 mg/L), respectively (MLIT, Japan, 1999). This study was conducted according to OECD guideline 201.

Toxicity to Invertebrates

The results from studies conducted according to OECD guideline 202 are a 48h EC₅₀ of pH 5.3 (0.492 mg/L) for *Daphnia magna* (MLIT, Japan, 1999). No long-term or chronic toxicity data on invertebrates have been reported.

Toxicity to Fish

Several studies on acute toxicity to fish have been published. The lowest 96h LC₅₀ reported is pH 4.3 (4.92 mg/L) for *Cyprinus carpio*, which was conducted according to OECD guideline 203 (MLIT, Japan, 1999). The 96h LC₅₀ for *Oncorhynchus mykiss* is pH 4.12 (7.45 mg/L) for hard water and pH 3.98 (10.3 mg/L) for soft water (Graham and Wood, 1981). Ellgaard and Gilmore (1984) reported that 96h LC₅₀ on *Lepomis macrochirus* was pH 3.25 - 3.5 (55.1–30.9 mg/L) and low pH caused a reduction in the oxygen carrying capacity of haemoglobin and excessive secretion of mucus from the gills which in turn interfered with gas exchange.

Generally, the results of toxicity test with acid or base depend on the buffer capacity of the test medium. Dechlorinated tap water was used as a test medium in the three tests described above. Furthermore, a 96h LC₅₀ of pH 3.5-3.6 (30.9-24.6 mg/L) for *Lepomis macrochirus* using artificial water prepared from distilled water and analytical or reagent grade chemicals (Cairns and Scheier, 1959), and a 96h LC₅₀ of 282 mg/L for *Gambusia affinis* (Wallen et al., 1957) and a 16h LC₁₀₀ value of pH 5.3 (0.492 mg/L) for the pike perch fry, *Lucioperca lucioperca* (Stangenberg, 1975) conducted with pond water (pH 6.0-8.2) are reported. A 24h LC₅₀ value of 60-80 mg/L for *Semotilus atromaculatus* with river water (pH 8.3) is also reported (Gillette et al., 1952).

No long-term or chronic toxicity data on fish have been reported.

Table 4-1. Summary of toxicity test results to aquatic organisms

Species	Age/Size	Stat/ Flow	Temp (°C)	Dissolved oxygen (mg/L)	Test medium	pH	Endpoint	Result	Test method	Reference
Algae /plants										
<i>Selenastrum capricornutum*</i>	1x10 ⁴ cells/mL	Static	21.1- 22.0		OECD medium	3.5-8.8	72h EC ₅₀ biomass 72h NOEC biomass 72h EC ₅₀ growth rate 72h NOEC growth rate	pH 5.1 (0.780 mg/L) pH 6.0 (0.097 mg/L) pH 5.3 (0.492 mg/L) pH 6.0 (0.097 mg/L)	OECD 201	MLJT, Japan, 1999
Daphnids										
<i>Daphnia magna</i>	< 24h	Semi- static	20.1- 20.5	8.7-8.8	Dechlorinated tap water, (hardness; 52 mg CaCO ₃ /L)	3.7-7.8	48h EC ₅₀ immobilization	pH 5.3 (0.492 mg/L)	OECD 202	MLJT, Japan, 1999
Fish										
<i>Cyprinus carpio</i>	4.6 ± 0.3 cm 1.1 ± 0.1 g	Semi- static	23.0- 24.0	7.2-8.4	Dechlorinated tap water, (hardness; 52 mg CaCO ₃ /L)	4.0-7.3	96h LC ₅₀	pH 4.3 (4.92 mg/L)	OECD 203	MLJT, Japan, 1999
<i>Oncorhynchus mykiss</i>	7.6 ± 0.3 cm 3.5 ± 0.1 g	Recircu- lated	15 ± 2		Dechlorinated tap water, (hardness; 140 mg CaCO ₃ /L 14 mg CaCO ₃ /L)	3.0-8.0	96h LC ₅₀ hard water soft water	pH 4.12 (7.45 mg/L) pH 3.98 (10.3 mg/L)		Graham and Wood, 1981

*now *Pseudokirchneriella subcapitata*

The values in parentheses express converted 12N HCl (mg/L). Table 4-1. Summary of toxicity test results to aquatic organisms (continued)

Species	Age/Size	Stat/ Flow	Temp (°C)	Dissolved oxygen (mg/L)	Test medium	pH	Endpoint	Result	Test method	Reference
Fish										
<i>Lepomis macrochirus</i>	4 cm	Static	23 ± 2		Dechlorinated tap water	3.0-7.5	96h LC ₅₀	pH 3.25 - 3.5 (55-31 mg/L)		Ellgaard and Gilmore, 1984
	Small; (3.88 cm, 0.96g), Medium; (6.09 cm, 2.80g), Large; (14.24 cm, 54.26g)	Flow- through	20±1	5-9	Artificial water prepared from distilled water and analytical or reagent chemicals		96h LC ₅₀	Small; pH 3.6 (24.6 mg/L) Medium; pH 3.6 (24.6 mg/L) Large; pH 3.5 (30.9 mg/L)		Cairns and Scheier, 1959
		Static	21-23		Pond water (turbidity; 114 - < 25ppm)	6.0-8.2	96h LC ₅₀	282 mg/L		Wallen et al., 1957
<i>Lucioperca lucioperca</i>	Fry, 11.5 mm	Static			Pond water (hardness; 130 mg CaCO ₃ /L)		16h LC ₁₀₀	pH 5.3 (0.492 mg/L)		Stangenberg, 1975
<i>Semotilus astromaculatus</i>	7.6-10.2 cm	Static	15-21		River water (hardness; 98.0 mg CaCO ₃ /L)		24h LC ₅₀	60-80 mg/L		Gillrette et al., 1952

The values in parentheses express converted 12N HCl (mg/L).

Toxicity to Microorganisms

Results with aquatic microorganisms are not available. It is generally known that acids have biocidal properties. Acidification is also used in the preservation of food. However, information from standard guideline tests with hydrochloric acid has not been found.

4.2 Terrestrial Effects

Data on terrestrial organisms are not available.

4.3 Initial Assessment for the Environment

PNEC derivation

Short-term studies with algae, invertebrates including *Daphnia* and fishes have been reported. The lowest results obtained from OECD guideline studies are: 72h EC₅₀ of pH 5.3 (equivalent to a substance concentration of 0.492 mg/L) for *Selenastrum capricornutum*, 48h EC₅₀ of pH 5.3 (0.492 mg/L) for *Daphnia magna* and 96h LC₅₀ of pH 4.3 (4.92 mg/L) for *Cyprinus carpio*.

A long-term toxicity test has been performed on *Selenastrum capricornutum*. The 72h NOEC on biomass and growth rate was pH 6.0 (0.097 mg/L).

In these data algal medium and dechlorinated tap water were used as test medium and the values are very low. These data may be not representative for normal ecosystems. The amount (expressed as a concentration) of hydrochloric acid which has to be added to a bicarbonate solution of 20-195 mg/L in the environment to obtain a pH of 6.0 is 8.3-81 mg/L (see section see 2.1). Thus, the observed variation in L(E)C₅₀ values can be explained by the buffer capacity of the testing water that was used (see 4.1.1).

Aquatic ecosystems are characterized by a pH and the organisms of the ecosystem are adapted to these specific natural conditions. Based on the natural pH of waters, organisms will have different optimum pH conditions, ranging from poorly buffered waters with a pH of 6 to very hard waters with pH values up to 9. A lot of information is available about the relationship between pH and ecosystem structure and also natural variation in pH of aquatic ecosystems have been quantified and reported extensively in ecological publications and handbooks.

Based on the available data it is not considered useful to derive a PNEC for hydrochloric acid because the buffer capacity, pH and the fluctuation of the pH are very specific for a certain aquatic ecosystem.

Comparison on toxicity between HCl and H₂SO₄

The toxicity of hydrochloric acid probably results from the hydrogen ion (pH effect) because chloride toxicity values to aquatic organisms are much higher (most toxicity values are greater than 100 mg/L, which are derived from some chlorides such as sodium chloride, calcium chloride, potassium chloride.). Therefore, the hydrochloric acid hazard assessment seems to be the hazard assessment of acidity. All the observations and results would be the same for any other strong acid such as sulfuric acid and nitric acid.

A comparison of acute aquatic toxicity results between hydrochloric acid and sulfuric acid is shown in Table 4-2.

For a given species the toxicity results for both substances are similar. This means that the hazard of hydrochloric acid is caused by the pH effect. The long-term toxicity of hydrochloric acid seems to be the same as that of sulfuric acid, if it is assumed that the test medium used is the same.

Therefore, the data required (e.g. long-term toxicity) of hydrochloric acid with aquatic organisms might be estimated from the value of sulfuric acid or other acids.

Table 4-2. Comparison on toxicity between HCl and H₂SO₄

Species	Unit	HCl	H ₂ SO ₄	End point Test medium	Reference
<u>Fish</u>					
<i>Lepomis macrochirus</i>	pH	3.25-3.5	3.5	96h LC ₅₀	Ellgaard and Gilmore (1984)
	mg/L	(55-31)	(16)	Dechlorinated tap water	
<i>Oncorhynchus mykiss</i>	pH	4.12	3.98	96h LC ₅₀	Graham and Wood (1981)
	mg/L	(7.45)	(5.29)	Dechlorinated tap water	
<i>Lucioperca lucioperca</i> fry	pH	5.3	5.2	16h LC ₁₀₀ for HCl, 1h LC ₁₀₀ for H ₂ SO ₄	Stangenberg (1975)
	mg/L	(0.49)	(0.32)	Pond water	
<u>Daphnid</u>					
<i>Daphnia magna</i>	pH	(3.20)	(2.76)	32h EC ₁₀₀	Anderson (1944)
	mg/L	62	88	Lake Erie water	
<u>Other</u>					
<i>Ophryotrocha diadema</i>	pH	(3.0-3.5)	(2.7-3.2)	48h LC ₅₀	Parker (1984)
	mg/L	100-33	100-33	Sea water including metal ion	

The values in parentheses express converted 12N HCl (97% H₂SO₄) concentration or pH.

Effects on terrestrial organisms

The toxicity data on terrestrial organisms are not available. In general the results of terrestrial toxicity test will depend stronger on the buffer capacity of the soil than the surface water.

5 RECOMMENDATIONS

The chemical is currently of low priority for further work.

The chemical possesses corrosive properties indicating a hazard for human health and the environment. No further work is recommended if sufficient control measures are in place to avoid significant human exposure and environmental impact, including prevention of accidental exposure. In situations where this is not the case, risk assessment and if necessary, risk reduction measures are recommended.

6 REFERENCES

- ACGIH (2001) Documentation of the Threshold Limit Values and Biological Exposure Indices 7th ed.
- Agner, T. and Serup, J. (1988) Contact Thermography for assessment of Skin Damage Due to experimental irritants., *Acta. Dermatol. Venerol.*, 68, 192-195.
- Albert, R.E. et al. (1982) Gaseous formaldehyde and hydrogen chloride induction of nasal cancer in the rat. *J Natl Cancer Inst*, 68, 597-604.
- Anderson B.G. (1944) The Toxicity Thresholds of Various Substances Found in Industrial Wastes as Determined by the Use of *Daphnia magna*. *SEWAGE WORKS JOURNAL*, 16(6): 1156-1165.
- ANON, ed. (1987) *Pestic. Toxic. Chem. News.*, 15(43), 6.
- BASF AG (1994) cited in European Commission- European Chemical Bureau (2000)
- Battarbee, H.D., Meneely, G.T. (1978) The toxicity of salt. *CRC Crit. Rev. Toxicol.* 5(4):355-376.
- Beaumont, J. J. et al. (1987) Lung cancer mortality in workers exposed to sulfuric acid mist and other acid mists. *J. Natl. Cancer Inst.*, 79, 911-921.
- Bond G.G. et al. (1983) A case-control study of brain tumor mortality at a Texas chemical plant. *J. Occup. Med.*, 25, 377-386.
- Bond G.G. et al. (1985) A case-control study of renal cancer mortality at a Texas chemical plant. *Am. J. Ind. Med.*, 7, 123-139.
- Bond G.G. et al. (1986) Nested case-control study of lung cancer among chemical workers. *Am. J. Epidemiol.*, 124, 53-66.
- Bond G.G. et al. (1991) Lung cancer and hydrogen chloride exposure: Results from a nested case-control study of chemical workers. *J. Occup. Med.*, 33, 958-961.
- Brusick, D.(1986) Genotoxic effects in cultured mammalian cells produced by low pH treatment conditions and increased ion concentrations., *Environ. Mutagen.*, 8, 879-886.
- Burns, C. M. (1929) The effect of the continued ingestion of mineral acid on growth of body and bone and on the composition of bone and of the soft tissues. *Biochem. J.*, 23, 860-867.
- Cairns, J. and Scheier, A. (1959) The relationship of bluegill sunfish body size to tolerance for some common chemicals. *Proc. 13th Ind. Waste Conf., Purdue Univ. Eng. Bull.*, 96, 243-252.
- CERI (2002) Chemicals Evaluations & Research Institute, Japan, unpublished data.
- Chemical Market Reporter (1999) Chemical Profile 'Hydrochloric acid' November 22, 1999. (<http://63.236.84.14/news/newsframe.cfm?framebody=/news/profile.cfm>)
- Cifone, M.A., Myhr, B., Eiche, A. and Bolcsfoldi, G. (1987) Effect of pH shifts on the mutant frequency at the thymidine kinase locus in mouse lymphoma L5178Y TK+/- cells. *Mutat. Res.*, 189, 39-46.
- CIIT (1984) Ninety-day Inhalation Toxicity Study of Hydrogen chloride gas In B6C3F1 mice, Sprague-Dawley and Fischer-344 rats, *ToxiGenics* 420-1087.
- Cipollaro M. et al. (1986) Sublethal pH decrease may cause genetic damage to eukaryotic cell: a study on sea urchins and *Salmonella typhimurium*., *Terat. Carc. and Mutagen Teratog.*, 6, 275-287.

Clausing, P. and Gottschalk, M. Z. (1989) Effects of drinking water acidification, restriction of water supply and individual caging on parameter of toxicological studies in rats. *Versuchstierkd.*, 32, 129-134 .

CMAI (2000) World Petrochemical Conference, Fifteenth Annual, March 29&30.

DAINIHON JOCHUGIKU Corporation (2002) Product information.

Darmer, K.I. et al. (1974a) Acute toxicity in rats and mice exposed to hydrogen chloride gas and aerosol. *Am. Ind. Hyg. Assoc. J.*, 35, 623-631.

Darmer, K.I. et al. (1974b) Hygienic assessment of the hydrogen ion content in the atmosphere. *Giginea I Sanitariya*, 38(3), 6-9.

Demerec, M. et al. (1951) A survey of chemicals for mutagenic action on *E. coli*. *Am. Nat.*, 85, 119-136.

Dyer, H.M. et al. (1946) Effect of administration of hot water, acids, alkali, mecholyl chloride, or atropine sulfate upon the gastric mucosa of mice. *J Natl Cancer Inst*, 7, 67.

Ellgaard, E.G. and Gilmore, J. Y. III (1984) Effects of different acids on the bluegill sunfish, *Lepomis macrochirus* Rafinesque. *J. Fish Biol.*, 25(2): 133-137.

European Commission Directive 2000/39/EC (2000) Commission Directive 2000/39/EC of 8 June 2000 establishing a first list of indicative occupational exposure limit values in implementation of Council Directive 98/24/EC on the protection of the Health and safety of workers from the risks related to chemical agents at work, 2000 O.J. (L 142) 47, 16 June 2000.

European Commission- European Chemical Bureau (2000)

Farrow, A. et al. (1989) Myelodysplasia, chemical exposure, and other environmental factors. *Leukemia*, 3, 33-35.

FASEB (1979). Evaluation of the health aspects of sodium chloride and potassium chloride as food ingredients. Report No. FDA7BF-79/112. Federation of American Societies for Experimental Biology, Bethesda, Maryland.

Fujita, H. Sumi, C. and Sasaki, M.(1992) Mutagenicity test of food additives with *Salmonella typhimurium* T97 and TA102., Tokyo Metropolitan Research Laboratory of Public Health Annual Reports, 43, 219-227.

Gad, S.C., Dunn, B.J., Dobbs, D.W., Reilly, C., and Walsh, R.D. (1986) Development and validation of an alternative dermal sensitisation test: the mouse ear swelling test (MEST)., *Toxicol. Appl. Pharmacol.* 84, 93-114.

Ganong, W. F. (2001) Review of medical physiology. 20th ed. McGraw-Hill Professional Publishing, California.

Gillette, L. A., Miller, D. L. and Redman, H. E. (1952) Appraisal of a Chemical Waste Problem by Fish Toxicity Tests. *SEWAGE AND INDUSTRIAL WASTERS*, 24 (11): 1397-1401.

Groot de W.A. and Dijk van N.R.M. .(2002) Addition of hydrochloric acid to a solution with sodium bicarbonate to a fixed pH. *Solvay Pharmaceuticals; Study No. A SOL.S.027*

Graham, M. S. and Wood, C. M. (1981) Toxicity of environmental acid to the rainbow trout: interactions of water hardness, acid type, and exercise., *CAN.J. ZOOL.*, Vol. 59, 1518-1526.

- Griffith, J.F. et al. (1980) Dose-response studies with chemical irritants in the albino rabbit eye as a basis for selecting optimum testing conditions for predicting hazard to the human eye. *Toxicol. Appl. Pharmacol.*, 55, 501-513 .
- Hartzell, G.E. et al. (1987) Modeling of toxicological effects of fire gases: VI. Further studies on the toxicity of smoke containing hydrogen chloride. *J. Fire Sci.*, 5, 368-391.
- Hartzell, G.E. et al. (1990) Toxicity of smoke containing hydrogen chloride. *ACS Symp. Ser.*, 425, 12-20.
- Hashimura, Y. et al. (1996) *Japanese Journal of Toxicology*, 9, 353.
- Hoechst AG (1966) *Farbwerke Hoechst AG Report 150/66*.
- HSDB (2001) *Hazardous Substances Data Bank*; Updated on 08/09/2001
- IARC (1992) *Hydrochloric acid*, 54, 189-211.
- Isquith, A., Matheson, D., and Slesinski, R. (1988) Genotoxicity studies on selected organosilicon compounds: in vitro assays. *Fd. Chem. Toxic.* 26, 255-261.
- Jacobs, G. A. (1992) OECD eye irritation tests on two acids. *J. Am. Coll. Toxicol.* 11(6), 734.
- Japan Society for Occupational Health (2001)
- Kotchen, T.A. et al. (1980) Inhibition of rennin secretion by HCl is related to chloride in both dog and rat. *Amer. J. Physiol.*, 239, F44-F49.
- Loewy, A and Munzer, E. (1923) Beiträge zur von der experimentellen Säurevergiftung., *Bioch. Z.* 134, 437-441.
- Litton Bionetics, Inc. (1978) Mutagenicity evaluation of Hydrochloric acid, Final report. LBI Project No. 20893.
- MacEwean, J.D. et al. (1974) Toxic Hazard Research Unit, Annual Technical Report, NTIS AD-A011-559.
- Marchi Industry (2000) MSDS of Hydrochloric acid 32% solution.
- McCarroll, N.E., Keech, B.H., and Piper, C.E. (1981a) An E coli microsuspension assay for the detection of DNA damage induced by direct-acting agents and promutagens., *Environ. Mutagenesis*, 3, 429-444.
- McCarroll, N.E., Keech, B.H., and Piper, C.E. (1981b) A microsuspension adaptation of the *Bacillus subtilis* "rec" assay. *Environ., Mutagenesis*, 3, 607-616.
- METI, Japan (1999) Ministry of Economy, Trade and Industry (former MITI), unpublished data.
- MLIT (1999). Ministry of Land, Infrastructure and Transport, Japan
- MOE, Japan. Ministry of Environment, Japan
- Monsanto (1976), unpublished report YO-76-0404 of Monsanto cited in European Commission-European Chemical Bureau (2000)
- Morita, T., Watanabe, Y., Takeda, K. and Okumura, K. (1989) Effects of pH in the in vitro chromosomal aberration test. *Mutat. Res.*, 225, 55-60.

- Murray, F. J. (1979) Embryotoxicity of inhaled sulfuric acid aerosol in mice and rabbits. *J. Environ. Sci. Health*, C13(3), 251-266.
- Narat, J. K. (1925) Experimental production of malignant growths by simple chemicals. *J. Cancer. Res.*, 9, 135-147.
- Parker, J.G. (1984) The effects of Selected Chemicals and Water Quality on the Marine Polychaete *Ophryotrocha diadema*. *Water Res.*, 18(7): 865-868.
- Pavlova T.E. (1976) Disturbances in the development of the progeny of rats subjected to the influence of hydrogen chloride. *Byull. Eksp. Biol. Med.*, 82, 866-868.
- Potokar, M. et al. (1985) Studies on the design of animal tests for the corrosiveness of industrial chemicals. *Fd. Chem. Toxic.*, 23, 615.
- Remijn, B., Koster, P., Houthuijs, D., Boleij, J., Willems, H., Brunekreef, B., Biersteker, K. and vanLoveren, C. (1982) Zinc chloride, zinc oxide, hydrochloric acid exposure and dental erosion in a zinc galvanizing plant in the Netherlands. *Ann. Occup. Hyg.*, 25, 299-307.
- Sellakumar, A.R. et al. (1985) Carcinogenicity of formaldehyde and hydrogen chloride in rats. *Toxicol. Appl. Pharmacol.*, 81, 401-406.
- Soskolne, C.L. et al (1989) Epidemiologic and toxicologic evidence for chronic health effects and the underlying biologic mechanisms involved in sub-lethal exposures to acidic pollutants *Arch. Environ. Health*, 44, 180-191.
- Solvay S.A. (2002) ATOMOSPHERIC FATE OF HYDROGEN CHLORIDE. Unpublished report.
- Stangenberg, E. (1975) The influence of the chemical composition of water on the pike perch (*Lucioperca lucioperca L.*) fry from the lake Goplo. *Limnologica*, 9(3): 421-426.
- Stumm-Tegethoff, B.F.A. (1969) Formaldehyde-induced mutations in *Drosophila melanogaster* independence of the presence of acids. *Theor. Appl. Genet.*, 39, 330-334.
- Subbarao, K.S.V.K. (1988) Cicatricial gastric stenosis caused by corrosive ingestion. *Aust. N.Z. Surg.*, 58, 143-146.
- The Chemical Daily (2000) 13700 Chemical Products, p26-27, 276 (in Japanese).
- The Merck Index, 13th Ed. (2001)
- UNEP (1995) Water quality of world river basins, UNEP Environment Library No.14.
- Upotn, P. K. and L'Estrange, J. L. (1977) Effects of chronic hydrochloric and lactic acid balance and bone composition of the rat. *Quarterly Journal of Experimental Physiology*, 62, 223-235.
- Wallen, I. E., Greer, W. C. and Lasater, R. (1957) Toxicity to *Gambusia affinis* of Certain Pure Chemicals in Turbid Water. *SEWAGE AND INDUSTRIAL WASTERS*, 29 (6): 695-711.
- WHO (1982) World Health Organization Environmental Health Criteria 21 (Chlorine and Hydrogen chloride)
- WHO (1998) Guidelines for drinking-water quality, second edition, Vol.2
- York, M. H., Griffiths, A. E., Whittle, E. and Basketter, D. A. (1996) Evaluation of a human patch test for the identification and classification of skin irritation potential. *Contact Dermatitis*, 34(3), 204-212.

Zeiger, E., Anderson, B., Haworth, S., Lawlor, T. and Mortelmans, K. (1992) Salmonella mutagenicity tests: V. Results from the testing of 311 chemicals., *Environ. Mol. Mutagen.*, 19 Suppl. 21, 2-141.

SIDS DOSSIER
Including
Robust Study Summary

Hydrogen chloride

CAS No. 7647-01-0

Sponsor Country: Japan

DATE: August 9, 2002

1.01 SUBSTANCE INFORMATION

A.	CAS-number	7647-01-0
B.	Name (IUPAC name)	Hydrogen chloride
C.	Name (OECD name)	Hydrogen chloride
D.	CAS Descriptor	
E.	EINECS-Number	231-595-7
F.	Molecular Formula	HCl
G.	Structural Formula	H-Cl
H.	Substance Group	Not applicable
I.	Substance Remark	None
J.	Molecular Weight	36.46

1.02 OECD INFORMATION

A.	Sponsor Country:	Japan
B.	Lead Organisation:	
	Name of Lead Organisation:	ASAHI GLASS CO., LTD.
	Contact Person:	Katuji Ito
	Address:	
	Postal code:	100-8405
	Town:	1-12-1, Yurakucho, Chiyoda-ku, Tokyo
	Country:	Japan
C.	Name of responder	Katuji Ito (same as above contact person)
	Address:	
	Postal code:	290-8566
	Town:	10, Goikaigan, Ichihara-shi, CHIBA
	Country:	Japan
	Tel:	+81-436-23-3871
	Fax:	+81-436-22-5710
	E-mail:	katsuji-itoh@om.agc.co.jp

1.1 GENERAL SUBSTANCE INFORMATION**A. Type of Substance**

Element []; Inorganic [**X**]; Natural substance []; Organic [];
Organometallic []; Petroleum product []

B. Physical State

Gaseous [**X**]; Liquid [**X**]; Solid []

C. Purity

> 99.7 %

Remarks: Standard quality for anhydrous hydrogen chloride

1.2 SYNONYMS

Anhydrous hydrochloric acid,
Chlorohydric acid,
Hydrochloride, Hydrochloric acid,
Muriatic acid

1.3 IMPURITIES

Water < 0.02%

Remarks: Standard quality criteria for anhydrous hydrogen chloride

1.4 ADDITIVES

No additives

1.5 QUANTITY

(a)

1,155,259 tonnes (Production; 1,144,779 tonnes, import; 10,480 tonnes) in Japan in 1999

Remarks: There are twenty-three and eight companies manufacturing hydrochloric acid and anhydrous hydrochloric acid, respectively, in Japan.

Reference: METI, Japan (1999).
The Chemical Daily (2000)

(b)

Remarks: - HCl demand in U.S.
Demand growth for total HCl is forecast to average 1.7 percent per year through 2003 and hydrochloric acid demand is expected to remain at about 20 percent of total consumption.
- HCl supply in U.S.

More than 95% of HCl is produced as a by-product from chlorine related processes. Many HCl producers are also HCl consumers, therefore a large portion of the HCl produced in the U.S. never makes it to the merchant market. Vinyl chloride monomer (VCM) production accounts for 65% of total production but is not a source of hydrochloric acid because all of the HCl produced in this process is recycled in ethylene dichloride (EDC) production. Significant source of hydrochloric acid include isocyanate and fluorocarbon production, as well as on-purpose production from burner acid.

U.S. HCl Source in 1999 (production=6,500,000 metric tons)

	Sources	Percentage
Captive	HCl from VCM	65%
	Methyl Chloride HCl	6%
	Magnesium Chloride HCl	5%
	Isocyanate to EDC	6%
Merchant	Net Isocyanate to EDC	6%
	HCl form burner	5%
	Fluorocarbon HCl	5%
	By-product HCl	2%

U.S. HCl demand Sectors in 1999 (demand=6,500,00 metric tons)

	Demands	Percentage
Captive	EDC/VCM	66%
	*MDI-TDI to EDC	6%
	Methyl Chloride/Magnesium Chloride	10%
Merchant	Steel Pickling	3%
	Brine Treating	2%
	Oil Well Acidifying	1%
	Food Grade	4%
	Calcium Chloride	4%
	Other	4%

*MDI; Methylene diphenyl diisocyanate
 TDI; Toluene diisocyanate

Reference: CMAI (2000)

(c)

The production capacity 1999 was 2,471,000 short tons per year (=approx. 2,242,000 tonnes) excluding the data for by-product HCl which is generated and recycled in integrated systems such as ethylene dichloride/vinyl chloride monomer (EDC/VCM) plants.

Reference: Chemical Market Reporter (2002)

1.6 Use Pattern**A. General**

Type of Use:	Category:
(a)	
Main	Use in a closed system or Non dispersive use
Industrial	Basic industry: basic chemicals; Chemical industry: used in synthesis; Polymers industry; Other: pharmaceutical industry, food processing
Use	Intermediates; process regulators
Remarks:	Production of inorganic chlorides, vinyl chloride, alkyl chlorides, dyes, artificial silk, pigment, pesticides, pharmaceuticals, plasticizer, hydrochlorinated rubber etc. and processing in food processing of starch, corn syrup, gelatin, proteins, sodium glutamate etc.
(b)	
Main	Non dispersive use
Industrial	Electrical/electronic engineering industry; Leather processing industry; Textile processing industry; Paper, pulp and board industry; Other: water treatment (pH regulation and resins regeneration)
Use	Semiconductors; Other: etching tanning agents; bleaching agents pH-regulating agents; Other: regeneration of ion-exchange resin
(c)	
Main	Wide dispersive use
Industrial	Fuel industry; Metal extraction, refining and processing of metals
Use	Other: oil well acidifying; reducing agent; Other: pickling in steel manufacture; Other: stripping metals
Reference:	European Commission- European Chemical Bureau (2000) HSDB (2001) The Chemical Daily (2000)

B. Uses In Consumer Products

Function	Amount present	Physical state
Toilet-bowl cleaner	ca. 9.5%	solution

Remarks:

Reference: DAINIHON JOCHUGIKU Corporation.

1.7 Sources of Exposure

(a)

Media of release: Media of release: Air or water from natural sources

Quantities per media:

Remarks:

- The most important source of atmospheric hydrogen chloride is the ocean surface, which through the actions of wind, waves and bubbles, injects sea salt particles. An amount of 2 to 20 % of the chlorine in sea salt aerosol is probably released as hydrogen chloride by reaction with acidic sulfate.
- Volcanoes eruptions inject 0.4-11 Tg (400,000-11,000,000 tonnes) hydrogen chloride per year into the atmosphere; 10 % of this is injected into the stratosphere in large explosive eruptions.
- Hydrogen chloride is the ultimate product from the atmospheric or aquatic (hydrolysis or biodegradation) degradation of organo-halogens.

Reference: European Commission- European Chemical Bureau (2000)

(b)

Media of release: Air or water from combustion

Quantities per media:

Remarks:

- Combustion of fuels (organic chlorides and gasoline) produce hydrogen chloride.
- Hydrochloric acid is produced from refuse incineration and the secondary metals industry (smelting of scrap, not of ore).
- Hydrochloric acid is produced from thermo-decomposition of gases: from pyrolysis of some wire insulation materials such as polyvinyl chloride, also chlorinated acrylics and retardant treated materials.
- The emissions from municipal incinerators depend on the technology and the control methods used.

Reference: European Commission- European Chemical Bureau (2000)
World Health Organization (1982)

(c)

Media of release: Air or water from consumer product

Quantities per media:

Remarks: Consumer products containing hydrochloric acid may be released into the effluent. Hydrogen chloride may, also, be released from the product by evaporation.

(d)

Remarks: Most of the mammalian constantly secrete the gastric juice, which contains

H⁺ concentration equivalent to 0.17 N HCl (pHs as low as 0.87) into the cavity of stomach.

1.8 ADDITIONAL INFORMATION

A. Classification and Labelling

(a) Hydrogen chloride Classification

Type: Directive67/548/EEC
 Category of danger: Toxic, corrosive
 R-phrases: 23-35
 Remarks: Text of R-phrase, toxic by inhalation, causes severe burns

Labelling

Type: Directive67/548/EEC
 Specific limits: Table of Limit Concentrations for Hydrogen Chloride

C >= 5%	T; C; R23-35
1% <= C < 5%	C; R20-35
0.5% <= C < 1% %	C; R20-34
0.2% <= C < 0.5%	C; R34
0.02% <= C < 0.2%	Xi; R36/37/38

Symbols: T, C
 Nota:
 R-phrases: 23-35
 S-phrases: 1/2-9-26-36/37/39-45
 Text of S-phrases: Keep locked up and out of the reach of children.
 Keep container in a well-ventilated place.
 In case of contact with eyes, rinse immediately with plenty of water and seek medical advice.
 Wear suitable protective clothing, gloves and eye/face protection.
 In case of accident or if you feel unwell, seek medical advice immediately.
 (Show the label where possible.)
 Remarks: Note 5 is applied
 Note 5; the concentration limits for gaseous preparation are expressed as volume percentage.

(b) Hydrochloric acid Classification

Type: Directive67/548/EEC
 Category of danger: Corrosive, Irritant
 R-phrases: 34-37
 Remarks: Text of R-phrase, Cause burns, Irritant to respiratory system

Labelling

Type: Directive 67/548/EEC

Specific limits: Table of Limit Concentrations for Hydrochloric Acid

C >= 25%	C; R34-37
10% <= C < 25%	Xi; R36/37/38

Symbols: C, Xi

Nota:

R-phrases: 34-37

S-phrases: 1/2-9-26-45

Text of S-phrases: Keep locked up and out of the reach of children.

In case of contact with eyes, rinse immediately with plenty of water and seek medical advice.

In case of accident or if you feel unwell, seek medical advice immediately.
(Show the label where possible.)

Remarks: Note B is applied

Note B; Some substances (acids, bases, etc.) are placed on the market in aqueous solutions at various concentrations and therefore require different labelling since the hazards vary at different concentrations.

Reference: European Commission- European Chemical Bureau (2000)

B. Occupational Exposure Limits

(a)

Exposure Limit Value

Type: MAC (NL)

Value: 7 mg/m³

Remarks: Ceiling value

References: European Commission- European Chemical Bureau (2000)

(b)

Exposure limit value

Type: MAK (DE)

Value: 7 mg/m³Short term exposure limit valueValue: 14 mg/m³

Length of exposure period: 5 minutes

Frequency: 8 times

Remarks:

References: European Commission- European Chemical Bureau (2000)

(c)

Exposure limit value

Type: OES (UK)

Value: 1 ppm (2 mg/m³)Short term exposure limit value

Value: 5 ppm (7 mg/m³)
Length of exposure period: 15 minutes
Frequency: 1 time
Remarks: as gas or aerosol mist
United Kingdom
References: European Commission- European Chemical Bureau (2000)

(d)

Exposure limit value

Type: TLV
Value: 5 ppm (7.5 mg/m³)
Remarks: Ceiling value. Critical effects are irritation and corrosion.
References: ACGIH (2001)

(e)

Exposure limit value

Type: OEL
Value: 5 ppm (7.5 mg/m³)
Remarks: Ceiling value
References: Japan Society for Occupational Health (2001)

(f)

Exposure limit value

Type: OEL (EU)
Value: 5 ppm (8 mg/m³)
Short term exposure limit value
Value: 10 ppm (15 mg/m³)
Length of exposure period: 15 minutes
Frequency: 1 time
Remarks: United Kingdom
References: European Commission Directive 2000/39/EC (2000)

C. OPTIONS FOR DISPOSAL

D. Other Remarks

None

2.1 MELTING POINT

(a)

Value: -114.22 °C
Decomposition: Yes No Ambiguous
Sublimation: Yes No Ambiguous
Method: Unknown
GLP: Yes No ?
Remarks:
Reliabilities: (2) Reliable with restrictions
Flag: Critical study for SIDS
Reference: The Merck Index, 13th Ed. (2001)

(b)

Value: -114.4 °C
Decomposition: Yes No Ambiguous
Sublimation: Yes No Ambiguous
Method: Other
GLP: Yes No ?
Remarks:
Reliabilities: (2) Reliable with restrictions
Reference: Elvers et al. (1989)

(c)

Value: ca. -30 °C
Decomposition: Yes No Ambiguous
Sublimation: Yes No Ambiguous
Method: Other
GLP: Yes No ?
Remarks: Hydrochloric acid, 37%
Reliabilities: (2) Reliable with restrictions
Reference: Hoechst AG (1994)

(d)

Value: -42 °C
Decomposition: Yes No Ambiguous
Sublimation: Yes No Ambiguous
Method: Other
GLP: Yes No ?
Remarks: Hydrochloric acid, 32%
Reliabilities: (2) Reliable with restrictions
Reference: Dow Europe S.A. (1993)

2.2 BOILING POINT

(a)
Value: -85.05 °C
Pressure: at 1,013 hPa
Decomposition: Yes [] No [X] Ambiguous []
Method: Unknown
GLP: Yes [] No [] ? [X]
Remarks:
Reliabilities: (2) Reliable with restrictions
Flag: Critical study for SIDS
Reference: The Merck Index, 13th Ed. (2001)

(b)
Value: -85 °C
Pressure: at 1,013 hPa
Decomposition: Yes [] No [X] Ambiguous []
Method: other
GLP: Yes [] No [] ? [X]
Remarks:
Reliabilities: (2) Reliable with restrictions
Reference: Elvers et al. (1989)

(c)
Value: 108.5 °C
Pressure: at 1,013 hPa
Decomposition: Yes [] No [X] Ambiguous []
Method: other
GLP: Yes [] No [] ? [X]
Remarks: Hydrochloric acid, ca. 37%
Reliabilities: (2) Reliable with restrictions
Reference: Hoechst AG (1993)

2.3 †DENSITY (relative density)

(a)
Type: Bulk density []; Density [X]; Relative Density []
Value: 1.491 mg/cm³
Temperature: 25 °C
Method: Calculation
GLP: Yes [] No [] ? [X]
Remarks: Type: gas density Pressure: 1,013 hPa
Reliabilities: (2) Reliable with restrictions
Reference: CERI (2002)

(b)

Type: Bulk density []; Density [X]; Relative Density []
 Value: 0.42 g/cm³
 Temperature: 51.4 °C
 Method: Unknown
 GLP: Yes [] No [] ? [X]
 Remarks: Type: liquid density Pressure: 81.6 atm Critical density
 Reliabilities: (2) Reliable with restrictions
 Reference: The Merck Index, 13th Ed. (2001)

(c)

Type: Bulk density []; Density [X]; Relative Density []
 Value: 1.187 g/cm³
 Temperature: -85 °C
 Method: other
 GLP: Yes [] No [] ? [X]
 Remarks: Type: liquid density
 Reliabilities: (2) Reliable with restrictions
 Reference: Elvers et al. (1989)

(d)

Type: Bulk density []; Density [X]; Relative Density []
 Value: 1.183 - 1.187 g/cm³
 Temperature: 20 °C
 Method: other
 GLP: Yes [] No [] ? [X]
 Remarks: Hydrochloric acid, ca. 37%
 Reliabilities: (2) Reliable with restrictions
 Reference: Hoechst AG (1993)

2.4 VAPOUR PRESSURE

(a)

Value: 42,200 hPa
 Temperature: 20 °C
 Method: calculated []; measured [X]
 Other (measured)
 GLP: Yes [] No [] ? [X]
 Remarks: Vapour pressure at 40 °C is 65,400 hPa.
 The vapour pressure at 25 °C of 47,350 hPa was estimated by using the linear regression equation between logarithm of vapour pressure and reciprocal of temperature (Clausius-Clapeyron equation), drawn from two vapour pressure values at 20 and 40 °C.
 Reliabilities: (2) Reliable with restrictions
 Flag: Critical study for SIDS
 Reference: BASF AG (1994)

(b)

Value: 31.33 hPa
Temperature: 20 °C
Method: calculated [**X**]; measured []
Other
GLP: Yes [] No [] ? [**X**]
Remarks: Hydrochloric acid, 32% HCl
Reliabilities: (2) Reliable with restrictions
Reference: Dow Europe S.A. (1993)

2.5 PARTITION COEFFICIENT $\log_{10}P_{ow}$

Not applicable

2.6 WATER SOLUBILITY

A. SOLUBILITY

(a)
Value: 823 g/L
Temperature: 0 °C
Description: Miscible []; Of very high solubility [**X**];
Of high solubility []; Soluble []; Slightly soluble [];
Of low solubility []; Of very low solubility []; Not soluble []
Method: unknown
GLP: Yes [] No [] ? [**X**]
Remarks: Solubility in water:
at 30 °C = 673 g/L
at 60 °C = 561 g/L
Reliabilities: (2) Reliable with restrictions
Flag: Critical study for SIDS
Reference: The Merck Index, 13th Ed. (2001)

B. pH VALUE, pKa VALUE

(a)
pH Value: 0.10
Concentration: 0.1N
Temperature: unknown
Method: unknown
GLP: Yes [] No [] ? [**X**]
pKa value: at 25°C
Remarks: Hydrogen chloride is completely ionised in water
Reliabilities: (2) Reliable with restrictions
Reference: The Merck Index (1996)

2.7 FLASH POINT

No data available

2.8 AUTO FLAMMABILITY

No data available

2.9 FLAMMABILITY

(a)

Results: Extremely flammable []; Extremely flammable - liquified gas [];
Highly Flammable []; Flammable []; Non flammable [X];
Spontaneously flammable in air []; Contact with water liberates highly
flammable gases []; Other []
Method: other: DIN 51 584
GLP: Yes [] No [] ? [X]
Remarks: Hydrochloric acid, ca. 37%
Reliabilities: (2) Reliable with restrictions
Reference: Hoechst AG (1993)

2.10 EXPLOSIVE PROPERTIES

No data available

2.11 OXIDISING PROPERTIES

No data available

2.12 OXIDATION: REDUCTION POTENTIAL

No data available.

2.13 ADDITIONAL DATA

A. Partition co-efficient between soil/sediment and water (Kd)

No data available

B. Other data

No data available

3.1 STABILITY**3.1.1 PHOTODEGRADATION**

(a)

Type: Air [**X**]; Water []; Soil []; Other []

Indirect Photolysis:

Type of sensitizer: OH radical

Concentration of sensitizer: 1,000,000 molecules/cm³Method: calculated [**X**]; measured[]GLP: Yes [] No [**X**] ? []

Test substance: . hydrogen chloride

Remarks: Hydrogen chloride reacts with OH-radical to form chloride free radical according to the following reaction;
 $\text{HCl} + \text{OH}\cdot \rightarrow \text{H}_2\text{O} + \text{Cl}\cdot$ (Rate constant=7 x 10⁻¹³ cm³/molecule/s)
 Half-life of tropospheric gaseous HCl calculated from a mean concentration of OH-radicals of 1,000,000 molecules/cm³ is 11 days.

Reliabilities: (2) Reliable with restrictions

Reference: Solvay S.A. (2002)

3.1.2 STABILITY IN WATER

(a)

Remarks: In water, hydrogen chloride is ionised and neutralisation is depending on the buffer capacity of the receiving water.

Reliabilities: (2) Reliable with restrictions

Reference: European Commission- European Chemical Bureau (2000)

3.1.3 STABILITY IN SOIL

Remarks: In water hydrogen chloride is ionised and neutralisation is depending on the buffer capacity of the soil/water. The high water solubility indicates a high mobility in soil.

Reliabilities: (2) Reliable with restrictions

Reference: European Commission- European Chemical Bureau (2000)

3.2 MONITORING DATA (ENVIRONMENTAL)

(a)

Type of Measurement: Background [**X**]; At contaminated site []; Other []

Media: Surface water

Results: [Chloride statistics]

In North America Rivers (N=12)

Mean: 17.5 mg/L

Min.: 0.1 mg/L, Max.: 82.0 mg/L

10th percentile: 1.1 mg/L, 90th percentile: 29.7 mg/L

In South America Rivers (N=6)

Mean: 6.1 mg/L

Min.: 0.9 mg/L, Max.: 14.3 mg/L

10th percentile: 1.6 mg/L, 90th percentile: 13.9 mg/L

In Asian Rivers (N=25)

Mean: 19.7 mg/L

Min.: 0.3 mg/L, Max.: 59.7 mg/L

10th percentile: 1.2 mg/L, 90th percentile: 48.2 mg/L

In African Rivers (N=7)

Mean: 4.3 mg/L

Min.: 0.9 mg/L, Max.: 10.6 mg/L

10th percentile: 1.0 mg/L, 90th percentile: 8.1 mg/L

In European Rivers (N=21)

Mean: 102.7 mg/L

Min.: 1.1 mg/L, Max.: 1233 mg/L

10th percentile: 2.1 mg/L, 90th percentile: 173 mg/L

In Oceania Rivers (N=6)

Mean: 39.2 mg/L

Min.: 0.1 mg/L, Max.: 171 mg/L

10th percentile: 0.3 mg/L, 90th percentile: 102.5 mg/L

The WHO drinking water guideline for chloride ion is 200 mg/L.

Remarks:

Reliabilities:

Reference:

(1) Reliable without restrictions

UNEP (1995) Water quality of world river basins, UNEP Environment Library No.14.

(b)

Type of Measurement: Background []; At contaminated site []; Other []

Media: Air

Results: Continental: 0.0 - 22.9 ppb

Maritime: 12.6 – 1,780 ppb

Remarks: Concentration of Cl – in precipitation

Reliabilities:

Reference:

(2) Reliable with restrictions

Galloway et al. (1982)

3.3 TRANSPORT AND DISTRIBUTION BETWEEN ENVIRONMENTAL COMPARTMENTS INCLUDING ESTIMATED ENVIRONMENTAL CONCENTRATIONS AND DISTRIBUTION

3.3.1 TRANSPORT

- Type: Adsorption []; Desorption []; Volatility [X]; Other []
- Media: water - air.
- Method: other: Calculation for K_H (thermodynamic equilibrium constant) [$\text{mol}^2 \cdot \text{kg}^{-2} \cdot \text{atm}^{-1}$]
- When the partitioning of a strong acid HX between aqueous and gas phases is most simply represented as an equilibrium between gaseous HX and its dissociation forms into ions
- $$\text{HX}_g = \text{H}^+_{\text{aq}} + \text{X}^-_{\text{aq}}$$
- The thermodynamic equilibrium constant K_H is given by
- $$K_H = m\text{H}^+ \cdot m\text{X}^- \cdot \gamma^2_{\text{HX}} / p\text{HX};$$
- where m is total concentration (mol kg^{-1})
- γ^2_{HX} is the mean activity coefficient of H+ and X- ion in solution and $p\text{HX}$ is the equilibrium partial pressure of HX.
- γ can be $\text{callog}(\gamma) = -0.5108 m^{1/2} / (1 + 1.525 m^{1/2}) + 1.0494 \times 10^{-1} m + 6.5360 \times 10^{-3} m^2 - 4.2058 \times 10^{-4} m^3 - 4.070 \times 10^{-6} m^4 + 5.258 \times 10^{-7} m^5$
($m=0 - 16$)
- Results: K_H was calculated from available partial pressure and other thermodynamic parameters, over the temperature range 0 to 40 °C.

T (°C)	K_H ($\text{mol}^2 \cdot \text{kg}^{-2} \cdot \text{atm}^{-1}$)
0	2.95×10^7
5	1.68×10^7
10	9.71×10^6
15	5.68×10^6
20	3.37×10^6
25	2.04×10^6
30	1.23×10^6
35	7.54×10^5
40	4.66×10^5

- Reliabilities: (2) Reliable with restrictions
- Reference: Brimblecombe P and Clegg SL (1988)

3.3.2 THEORETICAL DISTRIBUTION (FUGACITY CALCULATION)

- Remarks: Fugacity calculation is not applicable for ionised substance.
Based on its physicochemical properties (water solubility: 823 g/L at 0°C, vapour pressure: 42,200 hPa at 20°C), the chemical is mainly distributed into air and water compartments. In water, the hydrogen chloride is present as ionised forms.
- Reliabilities: (2) Reliable with restrictions

3.4 IDENTIFICATION OF MAIN MODE OF DEGRADABILITY IN ACTUAL USE

No data available.

3.5 BIODEGRADATION

Not applicable

3.6 BOD₅, COD OR RATIO BOD₅/COD

No data available

3.7 BIOACCUMULATION

No data available

3.8 ADDITIONAL REMARKS**A. Sewage treatment**

Remarks: Under Water Pollution Control Law in Japan, the effluent standard is established as within the range of pH 5.8-8.6

References: MOE, Japan

B. Other information

Remarks: Under Air Pollution Control Law in Japan, the emission standard of hydrogen chloride is established as 700 mg/m³ (0°C, 1 atm) to waste incinerator facilities and 80 mg/m³ (0°C, 1 atm) to hydrogen chloride gas absorption or chemical chlorination facilities

References: MOE, Japan

4. ECOTOXICOLOGICAL DATA

4.1 ACUTE/PROLONGED TOXICITY TO FISH

(a)

- Type of test: static []; semi-static [**X**]; flow-through []; other (*e.g. field test*) [] open-system [**X**]; closed-system []
- Species: *Cyprinus carpio* (Common carp)
- Exposure period: 96 hour(s)
- Unit: pH
- Analytical monitoring: Yes [**X**] No [] ? []
- LC₅₀: 4.3
- Year: 1999
- Method: OECD TG 203 (1992)
- GLP: Yes [] No [**X**] ? []
- Test substance: 12N (37.2%) hydrochloric acid
- Method: -Test Organisms:
- a) Average Size: 4.6±0.3 cm in body length, 1.1±0.1 g in body weight
 - b) Pretreatment: acclimated for 7days before testing; any groups showing >5% mortality during this period were not used for testing, fish were selected at random.
 - c) Supplier/Source: Sugishima fish hatchery in Kumamoto prefecture, Japan
- Test Conditions:
- a) Dilution Water Source: Dechlorinated tap water
 - b) Dilution Water Chemistry: Hardness: 52.0 mg/L as CaCO₃; alkalinity: 33.0 mg/L as CaCO₃, pH: 7.5, DO: 8.4
 - c) Exposure Vessel Type: 50-L glass tank (60 x 29.5 x 36 cm)
 - d) Nominal Concentrations: Five pH series (4.0, 4.5, 5.0, 5.5 and 6.0) and a dilution water control were tested.
 - e) Stock and Test solutions: The dilution water was added into the test vessel and the test solutions were prepared by adjusting to desired pH with hydrochloric acid.
 - f) Number of Replicates, fish per replicate: 1, 10 fish per replicate
 - g) Renewal Rate of Test Water: Renewed once per day
 - h) Water Temperature Range: 23.0±2°C (Containers used for testing were placed in a incubator)
 - i) Light Condition: 16h:8h light-darkness cycle
- Statistical Method:
- a) Data Analysis: Graphical method using logarithmic probability paper
- Results: - Measured concentrations (as mg/L): Not described
- Water chemistry in Test: DO= 7.2-8.4 mg/l; Temp. = 23.0-24.2°C

Table 1 Measured pH of test solutions

Nominal pH	Measured pH							
	0-24h		24-48h		48-72h		72-96h	
	new	old	new	old	new	old	new	old
Control	7.3	7.2	7.3	7.3	7.3	7.1	7.3	7.3
6.0	6.0	6.1	6.0	6.2	6.0	6.3	6.0	6.1
5.5	5.5	5.7	5.5	5.6	5.5	5.7	5.5	5.6
5.0	5.0	5.2	5.0	5.1	5.0	5.2	5.0	4.8
4.5	4.5	4.7	4.5	4.7	4.5	4.7	4.5	4.7
4.0	4.0	4.1	*	*	*	*	*	*

*All fish died in this treatment

new: freshly prepared test solutions

old: test solutions after 24h exposure

- Unit [results expressed in what unit]: % survival after 24, 48, 72, 96h

-LC₅₀:

Table 2. LC₅₀ of hydrochloric acid with Common carp

Hours of exposure	LC ₅₀ (pH)*	LC ₅₀ (mg/L)**
24	4.3	4.92
48	4.3	4.92
72	4.3	4.92
96	4.3	4.92

*Values based on nominal pH

**Converted values as 12N HCl

- Cumulative mortality:

Table 3. Cumulative mortality

pH	Cumulative mortality (%)			
	24h	48h	72h	96h
Control	0	0	0	0
6.0	0	0	0	0
5.5	0	0	0	0
5.0	0	0	0	0
4.5	0	0	0	0
4.0	100	100	100	100

Reliability:

(2) valid with restrictions

Test procedure according to national standards

Flag:

Critical study for SIDS endpoint

Reference:

Ministry of Land, Infrastructure and Transport, Japan (1999).

Test was conducted by Chemicals Evaluation and Research Institute, Japan.

(b)
 Type of test: static []; semi-static []; flow-through []; other (*e.g. field test*) [X] open-system [X]; closed-system []
 Species: *Oncorhynchus mykiss* (Rainbow trout)
 Exposure period: 7 day
 Unit: pH
 Analytical monitoring: Yes [] No [X] ? []
 LC₅₀: 4.46 (hard water)
 4.06 (soft water)
 Method: Not described
 Year: 1981
 GLP: Yes [] No [X] ? []
 Test substance: Hydrochloric acid
 Method: -Test Organisms:
 a) Average Size: Weight 3.50±0.09 g, Length 7.59±0.30 cm
 b) Pretreatment: Acclimated to the experimental temperature and water type for at least 7days
 c) Supplier/Source: Spring Valley Trout Farm, Canada
 - Test Conditions:
 a) Dilution Water Source: Dechlorinated tap water
 b) Dilution Water Chemistry:
 Hard water (hardness; 140mg/L as CaCO₃)
 Ca⁺ 2.0-4.0 meq/L
 Na⁺ 0.8-2.0
 Cl⁻ 0.8-2.0
 K⁺ < 0.1
 Soft water (hardness; 14mg/L as CaCO₃)
 Ca⁺ 0.2-0.4 meq/L
 Na⁺ 0.2-0.8
 Cl⁻ 0.2-1.2
 K⁺ < 0.1
 c) Exposure Vessel Type: 60-L system recirculated at 10 mL/min
 d) Nominal Concentrations: pH 3.0-4.8 in 0.2 increments
 e) Number of Replicates: 1
 f) Individuals per Replicates: 10
 g) Water Temperature Range: 15±2 °C
 h) Light Condition: Not described
 - Statistical Method:
 a) Data Analysis: Graphical method using log/probit paper for LC₅₀, nomographic method of Litchfield for 95% confidence limit
 Results: -LC₅₀:

Table The LC₅₀ for two hardness water

Day	Hard water LC ₅₀ [*]	Soft water LC ₅₀ [*]
4	4.12±0.08 (7.45 mg/L)**	3.98±0.16 (10.3 mg/L)**

7 4.46±0.04 (3.39 mg/L)** 4.06±0.08 (8.55 mg/L)**

* pH ± 95% confidence limits

** Converted values as 12N HCl

Reliability: (2) valid with restrictions
Well documented study
Reference: Graham, M. S. and Wood, C. M. (1981)

(c)
Type of test: static [**X**]; semi-static []; flow-through []; other (*e.g. field test*) [] open-system [**X**]; closed-system []
Species: *Lepomis macrochirus* (Bluegill)
Exposure period: 96 hour(s)
Unit: pH
Analytical monitoring: Yes [] No [**X**] ? []
LC₅₀: 3.25-3.5
Method: Not described
Year: 1984
GLP: Yes [] No [**X**] ? []
Test substance: Hydrochloric acid
Method: -Test Organisms:

- a) Average Size: Approximately 4cm
- b) Pretreatment: Maintained at pH7.5 for 7days
- c) Supplier/Source: A fish hatchery in Louisiana, USA

- Test Conditions:

- a) Dilution Water Source: Dechlorinated tap water
- b) Exposure Vessel Type: 38-L tank (51 x 32 x 27 cm)
- c) Nominal Concentrations: pH 3.0, 3.25, 3.5, 4.0, 4.5, 5.0 and 7.5(control)
- d) Number of Replicates: 1
- e) Individuals per Replicates: 8
- f) Renewal Rate of Test Water: Not renewed
- g) Water Temperature Range: 23±2 °C
- h) Light Condition: Not described

Results: -LC₅₀:

Table 1. LC₅₀ of hydrochloric acid with Bluegill

Hours of exposure	LC ₅₀ (pH)	LC ₅₀ (mg/L)*
24	3.25-3.5	55.1-30.9
48	3.25-3.5	55.1-30.9
96	3.25-3.5	55.1-30.9

*Converted values as 12N HCl

- Cumulative mortality:

Table 2. Cumulative mortality

pH	Cumulative mortality (%)		
	24h	48h	96h
Control	0	0	0
5.0	0	0	0
4.5	0	0	0
4.0	0	0	0
3.5	0	0	0
3.25	75	75	80
3.0	100	100	100

- Water chemistry in Test: Maintained a constant pH value throughout the test period

Reliability: (2) Valid with restrictions

Basic data given

Reference: Ellgaard, E. G. and Gilmore III J. Y. (1984)

(d)

Type of test: static []; semi-static []; flow-through [**X**]; other (*e.g. field test*) [] open-system [**X**]; closed-system []

Species: *Lepomis macrochirus* (Bluegill)

Exposure period: 96 hour(s)

Unit: pH

Analytical monitoring: Yes [] No [**X**] ? []

LC₅₀: 3.5-3.6

Method: Not described

Year: 1959

GLP: Yes [] No [**X**] ? []

Test substance: Hydrochloric acid

Method: -Test Organisms:

a) Average Size: Small (3.88cm 0.96g), medium (6.09cm 2.80g), large (14.24cm 54.26g)

b) Pretreatment: Acclimated for 7days with dilution water before use

c) Supplier/Source: A fish hatchery in Pennsylvania or Pennsylvania Fish Commission, USA

- Test Conditions:

a) Dilution Water Source: Prepared from distilled water and analytical or reagent chemicals

b) Dilution Water Chemistry:

KCl 0.02 g/L

Na₂SiO₃ 0.02

NaHCO₃ 0.04

MgSO₄·7H₂O 0.04

Ca(NO₃)₂ 0.03

CaCO₃ 0.01

K₂HPO₄ 0.002

Fe⁺⁺⁺ 0.004

- c) Exposure Vessel Type: 5 gallon glass jar with cork stopper
 - d) Nominal Concentrations: not described
 - e) Number of Replicates: 1 or 2
 - f) Individuals per Replicates: 10
 - g) Renewal Rate of Test Water: The rate of flow was 30.6 L per 24h.
 - h) Water Temperature Range: 20±1 °C
 - i) Light Condition: Not described
- Statistical Method:
a) Data Analysis: Doudoroff method

Results:

-LC₅₀:

The 96 h LC₅₀s for three size ranges of fish

Size	(Length, Weight)	96h LC ₅₀ (pH)
small	(3.88cm, 0.96g)	3.6 (24.6 mg/L)*
medium	(6.09cm, 2.80g)	3.6 (24.6 mg/L)*
large	(14.24cm, 54.26g)	3.5 (30.9 mg/L)*

* Converted values as 12N HCl

Reliability: (2) Valid with restrictions

Basic data given

Reference: Cairns, J. Jr. and Scheier, A. (1959)

(e)

Type of test: static [**X**]; semi-static []; flow-through []; other (*e.g. field test*) [] open-system [**X**]; closed-system []

Species: *Gambusia affinis* (Mosquitofish)

Exposure period: 96 hour(s)

Results: LC₅₀ (24h) = 282 mg/L

LC₅₀ (48h) = 282 mg/L

LC₅₀ (96h) = 282 mg/L

Analytical monitoring: Yes [] No [**X**] ? []

Method: Not described

GLP: Yes [] No [**X**] ? []

Test substance: Hydrochloric acid

Remarks: Lethal concentrations for hydrochloric acid were determined on groups of 10 fish at 23±2 °C. The fish (4 cm TL) were exposed to 100, 180, 320, 560 and 1000 mg/L of hydrochloric acid. Pond water with turbidity was used as dilution water and pH was 6.0-8.2. Artificial aeration from compressor served to maintain the oxygen level and to disperse the turbidity-producing soil as long as possible in the mixture.

The LC₅₀ (24h, 48h, 96h) for hydrochloric acid was 282 mg/L.

Reliability: (4) not assignable

Documentation insufficient for assessment

Reference:	Wallen, I. E. et al. (1957)	
(f)		
Type of test:	static [X]; semi-static []; flow-through []; other (<i>e.g. field test</i>) [] open-system [X]; closed-system []	
Species:	<i>Lucioperca lucioperca</i> (Pike perch)	
Exposure period:	16 hour(s)	
Results:	LC ₁₀₀ (16h) = pH 5.3	
Analytical monitoring:	Yes [] No [X] ? []	
Method:	Not described	
GLP:	Yes [] No [X] ? []	
Test substance:	Hydrochloric acid	
Remarks:	Fish with the total length 11.5-16 mm were used for the experiment. Pond water was used as dilution water. Dilution water chemistry;	
	Color	55.0 mg/l Pt
	Total hardness	130.0 mg/l as CaCO ₃
	Carbonate hardness	110.0 mg/l as CaCO ₃
	Noncarbonate hardness	20.0 mg/l as CaCO ₃
	Ammonium	0.04 mg/l N (NH ₃)
	Nitrates	0.030 mg/l N (NO ₃)
	Iron	0.20 mg/l Fe
	Chlorides	9.0 mg/l
	Phosphates	0.30 mg/l PO ₄
	Oxydability	11.8 mg/l O ₂
	Total residue	204.0mg/l
	Loss on ignition	34.0 mg/l
	Rest on ignition	170.0 mg/l
	Solutions of hydrochloric acid in pond water killed the fry in 20% after 16 h at the pH 6.4, in 60% at pH 6.0 and total at pH 5.3.	
	The LC ₁₀₀ (16h) was equivalent to 0.492 mg/L as 12N HCl concentration.	
Reliability:	(4) not assignable Documentation insufficient for assessment	
Reference:	Stangenberg, E. (1975)	
(g)		
Type of test:	static [X]; semi-static []; flow-through []; other (<i>e.g. field test</i>) [] open-system [X]; closed-system []	
Species:	<i>Semotilus atromaculatus</i> (Creek chub)	
Exposure period:	24 hour(s)	
Results:	LC ₅₀ (24h) = 60-80 mg/L	
Analytical monitoring:	Yes [] No [X] ? []	
Method:	Not described	
GLP:	Yes [] No [X] ? []	
Test substance:	Hydrochloric acid	
Remarks:	Lethal concentrations for hydrochloric acid were determined on groups of 4 fish (3 to 4 in.). The fish were exposed to 20, 40, 60, 80 and 100 mg/L of test	

solution at 15-21°C. River water was used as dilution water. Dilution water chemistry;

SiO ₂	2.9 ppm
Fe	0.02
Ca	27.0
Mg	7.3
Na	6.7
K	2.2
Mn	0.0
CO ₃	6.0
HCO ₃	88.0
SO ₄	14.0
Cl	9.0
F	0.10
NO ₃	0.60
Dissolved solids	120.0
Total hardness	98.0
Color	3.0
pH	8.3
Specific conductance at 25°C	218

The LC₅₀ (24h) was 60-80 mg/L.

Reliability: (4) not assignable
Documentation insufficient for assessment
Reference: Gillette, L. A. et al. (1952)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

A. *Daphnia*

(a)

Type of test: static []; semi-static [**X**]; flow-through []; other (*e.g. field test*) []; open-system [**X**]; closed-system [**X**]

Species: *Daphnia magna* Straus

Exposure period: 48 hour(s)

Unit: pH

Analytical monitoring: Yes [**X**] No [] ? []

EC₅₀: 5.3

Year: 1999

Method: OECD TG 202 (1984)

GLP: Yes [] No [**X**] ? []

Test substance: 12N (37.2%) hydrochloric acid

Method: -Test Organisms:

a) Age at study initiation: neonates (<24h old)

b) Supplier/Source: Laboratory bred daphnids which was basically supplied by the University of Sheffield (Sheffield S10 2UQ, UK) were used.

- Test Conditions:

a) Dilution Water Source: Dechlorinated tap water

- b) Dilution Water Chemistry: Hardness: 52.0 mg/L as CaCO₃; alkalinity: 33.0 mg/L as CaCO₃, pH: 7.5, DO: 8.4
 - c) Exposure Vessel Type: 200 mL test solution in a 250 mL glass beaker; 4 beakers per treatment
 - d) Nominal Concentrations: Five pH series (4.0, 4.5, 5.0, 5.5 and 6.0) and a dilution water control were tested.
 - e) Stock and Test solutions: The dilution water was added into the test vessel and the test solutions were prepared by adjusting to desired pH with hydrochloric acid.
 - f) Number of Replicates: 4 replicates
 - g) Individuals per Replicates: 5 daphnids per replicate
 - h) Renewal Rate of Test Water: Renewed once a day
 - i) Water Temperature Range: 20.0±1°C (Containers used for testing were placed in a incubator)
 - j) Light Condition: <1,200 lx, 16h:8h light-darkness cycle
- Statistical Method:
- a) Data Analysis: Graphical method using logarithmic probability paper
 - Water chemistry in Test: DO= 8.7-8.8 mg/l; Temp.= 20.1-20.5°C

Results:

Table 1 Measured pH of test solutions

Nominal pH	Measured pH			
	0h(new)	24h(old)	24h(new)	48h(old)
Control	7.8	7.8	7.5	7.5
6.0	6.0	6.0	5.8	6.1
5.5	5.5	5.3	5.3	5.8
5.0	4.9	5.2	4.9	5.2
4.5	4.3	4.5	4.3	4.6
4.0	3.8	3.7	*	*

*All daphnids died in this treatment
new: freshly prepared test solutions
old: test solutions after 24h exposure

- Unit [results expressed in what unit]: % immobilization after 24, 48h
- EC₅₀:

Table 2. EC₅₀ of hydrochloric acid with *Daphnia magna*

Hours of exposure	EC ₅₀ (pH)*	EC ₅₀ (mg/L)**
24	5.3	0.492
48	5.3	0.492

*Values based on nominal pH

**Converted values as 12N HCl

- Cumulative immobilization:

Table 3. Cumulative immobilization

	pH	Cumulative numbers of immobilized <i>Daphnia</i> (Percent immobility)		
		3h	24h	48h
	Control	0(0)	0(0)	0(0)
	6.0	0(0)	0(0)	0(0)
	5.5	0(0)	0(0)	0(0)
	5.0	0(0)	11(55)	20(100)
	4.5	4(20)	20(100)	20(100)
	4.0	20(100)	20(100)	20(100)

Reliability: (2) valid with restrictions
Test procedure according to national standards

Flag: Critical study for SIDS endpoint

Reference: Ministry of Land, Infrastructure and Transport, Japan (1999).
Test was conducted by Chemicals Evaluation and Research Institute, Japan.

(b)

Type of test: static []; semi-static [**X**]; flow-through []; other (*e.g. field test*) []; open-system [**X**]; closed-system [**X**]

Species: *Daphnia magna*

Exposure period: 32 hour(s)

Results: EC₁₀₀ (32h) = 62 mg/L

Analytical monitoring: Yes [] No [**X**] ? []

Method: Not described

GLP: Yes [] No [**X**] ? []

Test substance: Hydrochloric acid

Remarks: Immobility for hydrochloric acid was determined on groups of 10 daphnids at 25°C. Dilution water source was grass-wool filtered University Lake water.
The EC₁₀₀ (32h) was 62 mg/L.

Reliability: (4) not assignable
Documentation insufficient for assessment

Reference: Anderson, B. G. (1944)

B. OTHER AQUATIC ORGANISMS

Type of test: static [**X**]; semi-static []; flow-through []; other (*e.g. field test*) [**X**]; open-system []; closed-system []

Species: *Ophryotrocha diadema* (polychaete)

Exposure period: 48 hour(s)

Results: LC₅₀ (48h) = 33-100 mg/L

Analytical monitoring: Yes [] No [**X**] ? []

Method: Not described

GLP: Yes [] No [**X**] ? []

Test substance: Hydrochloric acid

Remarks: The 48h LC₅₀ test was carried out using 10 organisms at each concentration

in duplicated trials. The test medium was filtered sea water (3.2%). For this experiment, a batch of sea water made up with the following added concentrations of metal:
 Hg²⁺ (as mercuric chloride) 0.001 mg/L
 Cu²⁺ (as cupric chloride) 0.1 mg/L
 Zn²⁺ (as zinc chloride) 0.001 mg/L
 The test temperature was 21°C. The LC₅₀ (48h) was 33-100 mg/L.

Reliability: (4) not assignable
 Documentation insufficient for assessment

Reference: Parker, J. G (1984)

4.3 TOXICITY TO AQUATIC PLANTS e.g. Algae

Species: *Selenastrum capricornutum*
 End-point: Biomass [X]; Growth rate [X]; Other []
 Exposure period: 72 hour(s)
 Unit: pH
 Analytical monitoring: Yes [X] No [] ? []
 EC₅₀ Biomass: 5.1
 Growth rate: 5.3
 NOEC Biomass: 6.0
 Growth rate: 6.0
 Year: 1999
 Method: OECD TG 201 (1984)
 open-system [X]; closed-system []
 GLP: Yes [] No [X] ? []
 Test substance: 12N (37.2%) hydrochloric acid
 Method: -Test Organisms:
 a) Supplier/Source: *Selenastrum capricornutum* ATCC 22662
 - Test Conditions
 a) Test Temperature Range: 21.1-22.0°C
 b) Growth/Test medium: OECD medium
 c) Shaking: 100 rpm
 d) Dilution water source: OECD medium
 H₃BO₃ 0.185 mg/L
 MnCl₂·4H₂O 0.415 mg/L
 ZnCl₂ 0.003 mg/L
 FeCl₃·6H₂O 0.08 mg/L
 Na₂EDTA·2H₂O 0.1 mg/L
 CoCl₂·6H₂O 0.0015 mg/L
 Na₂MoO₄·2H₂O 0.007 mg/L
 CuCl₂·2H₂O 0.00001 mg/L
 CaCl₂·2H₂O 18 mg/L
 NH₄Cl 15 mg/L
 KH₂PO₄ 1.6 mg/L
 NaHCO₃ 50 mg/L
 MgCl₂·6H₂O 12 mg/L

MgSO₄·7H₂O 15 mg/L

- e) Exposure Vessel Type: 100 mL medium in a 300 mL conical flask with a cap that allow ventilation
- f) Water Chemistry in Test (pH) in one replicate of each concentration (at start and end of the test): 8.0 at start and 8.8 at end of the test (72 h) in the control
- g) Stock and Test Solution: Stock solution was not prepared. Each test medium was adjusted to pH with hydrochloric acid and filter-sterilized with 0.45µm membrane filter.
- h) Light Levels and Quality during Exposure: 4300-4400 lx, continuous
- Test design:
- a) Number of replicates: Triplicate
- b) Concentrations: Five pH series (3.5, 4.0, 4.5, 5.0 and 6.0) and a control were tested.
- c) Initial cell number in cells/mL: 1×10^4
- Statistical Method:
- a) Data Analysis: Graphical method using logarithmic probability paper for EC₅₀, one-way analysis of variance for NOEC
- Measured pH: pH in one replicate of each concentration (at start and end of the test):

Results:

Nominal pH	Measured pH	
	0h	72h
Control	8.0	8.8
6.0	6.0	7.9
5.0	5.0	5.1
4.5	4.5	4.8
4.0	4.0	4.3
3.5	3.5	3.7

- Unit [results expressed in what unit]: % growth inhibition after 24, 48, 72h
- Cell density at each flask at each measuring point:

pH	Cell density for each exposure (x 10 ⁴ cells/mL)			
	0h	24h	48h	72h
Control	1.00	2.96	15.5	70.6
6.0	1.00	2.81	15.7	67.7
5.0	1.00	2.42	10.1	16.7
4.5	1.00	0.986	1.07	1.24
4.0	1.00	0.827	0.925	0.926
3.5	1.00	0.634	0.551	0.508

- Percent biomass/growth rate inhibition per concentration:

pH	Percent growth inhibition		
	Area under the growth curve	Growth rate (24-48h)	Growth rate (0-72h)
6.0	2.72	-3.87	0.992
5.0	64.2	13.7	34.8
4.5	99.6	94.6	95.0
4.0	101	93.3	102
3.5	102	110	118

- EC₅₀:

Hours of exposure	EC ₅₀ (pH)*		
	Area under the growth curve (Biomass)	Growth rate	
		24-48h	0-72h
72	5.1(0.780 mg/L)	4.8(1.55 mg/L)	5.3(0.492 mg/L)

*Values based on nominal pH

The values in parentheses express converted values as 12N HCl.

- NOEC:

Hours of exposure	NOEC (pH)*		
	Area under the growth curve (Biomass)	Growth rate	
		24-48h	0-72h
72	6.0(0.097 mg/L)	6.0(0.097 mg/L)	6.0(0.097 mg/L)

*Values based on nominal pH

The values in parentheses express converted values as 12N HCl.

Reliability: (2) valid with restrictions
Test procedure according to national standards

Flag: Critical study for SIDS endpoint

Reference: Ministry of Land, Infrastructure and Transport, Japan (1999).
Test was conducted by Chemicals Evaluation and Research Institute, Japan.

5.1 ACUTE TOXICITY

5.1.1 ACUTE ORAL TOXICITY

(1)

Test Substance Hydrochloric acid, CAS No. 7647-01-0
Identity (purity): 15% (w/w) hydrochloric acid of normal laboratory quality
Remarks:

Method

Method/guideline followed): According to internal guidelines of Hoechst AG
Type: Acute oral toxicity study
GLP: Yes [] No [X]
Year: 1966
Species/Strain: rat/ mixed strain albino
Sex: female
No. of animals per sex per dose: Ten rats were used per dose.
Vehicle: not described
Route of administration: oral

Remarks:

- **Age:** not described
- **Volume administered or concentration:**
0.40, 0.63, 1.00 and 1.60 mL of 3.3 % HCl per 100 g body weight.
The rats received no more feed 12 hours before application.
- **Post dose observation period:**
The post-application observation period was 6-7 days.

Results

Value ([LD50] with confidence limits if calculated):
7.2-8.4 mL/kg b.w. (238 – 277 mg/kg)

Number of deaths at each dose level:

4.0 mL/kg b.w.	0/10 rats died
6.3 mL/kg b.w.	3/10 rats died
10.0 mL/kg b.w.	8/10 rats died
16.0 mL/kg b.w.	10/10 rats died

Remarks:

- **Time of death:** N/A
- **Description, severity, time of onset and duration of clinical signs at each dose level:** N/A
- **Necropsy findings, included doses affected, severity and number of animals affected:** N/A
- **Potential target organs:** N/A
- **If both sexes tested, results should be compared:** N/A

Conclusions

Remarks:

Data Quality

Reliabilities:

(2) Reliable with restrictions

Remarks:

Quality Check

Study with an internal guideline of a company.

References (*Free Text*)

Hoechst AG, (1966) Report 150/66

Other

Last changed:

Order number for sorting:

Remarks

(2)

Type: LD₀ []; LD₁₀₀ []; LD₅₀ [X]; LDL₀ []; Other []

Species/strain: Rabbit

Value: 900 mg/kg b.w.

Method: Other: No data

GLP: Yes [] No [X] ? []

Test substance: Grade and purity not stated

Remarks: Oral administration

Reliability : (3) Not reliable

Reference: Loewy, A. and Munzer, E. (1923)

(3)

Type: LD₀ []; LD₁₀₀ []; LD₅₀ []; LDL₀ []; Other [X]

Species/strain: Rat/CFY

Value: No data

Method: Other: No data

GLP: Yes [] No [X] ? []

Test substance: Grade and purity not stated

Remarks: Method: 22 mg HCl/animal (1 mL; 0.6M HCl) was applied to rats starved for 24 or 48 h, and to unstarved rats receiving 5 or 20% glucose solution; the number and severity of gastric mucosal lesions were significantly higher in the rats starved for 24 or 48 h and in those fed 5% glucose than in those receiving 20% glucose; the tissue levels of ATP, ADP, AMP, adenylyate pool, and cAMP were significantly decreased in 24 and 48 h starved rats in contrast with the unstarved animals; the energy charges in 24 and 48 h starved rats were significantly higher than those in the unstarved rats; the animals fed 20% glucose showed significantly highest levels of different biochemical compounds, while the number of gastric lesions were the lowest; the increased energy turnover in the gastric mucosa may produce a better metabolic adaptation against the necrotizing effect of hydrochloric acid.

Reliability : (3) Not reliable

Reference: Moron, F. et al. (1984)

- (4)
- Type: LD₀ []; LD₁₀₀ []; LD₅₀ []; LDL₀ []; Other [X]
- Species/strain: Rat/Wistar
- Value: No data
- Method: Other: No data
- GLP: Yes [] No [X] ? []
- Test substance: Grade and purity not stated
- Remarks: Oral administration of 0.35 N HCl protected the gastric mucosa of rats against 0.6 N HCl-induced gastric lesions for 2 h. The pretreatment significantly increased prostaglandin concentrations in the gastric fundic mucosa.
- Reliability : (3) Not reliable
- Reference: Orihara, M. et al. (1989)
- (5)
- Type: LD₀ []; LD₁₀₀ []; LD₅₀ []; LDL₀ []; Other [X]
- Species/strain: Rat/Wistar
- Value: No data
- Method: Other: No data
- GLP: Yes [] No [X] ? []
- Test substance: Grade and purity not stated
- Remarks: The concentrations of nonprotein sulfhydryls (NP-SH) were significantly decreased in the gastric mucosa following the oral administration of 1 mL of 2% hydrochloric acid.
- Reliability : (3) Not reliable
- Reference: Parmer, N.S. et al. (1988)
- (6)
- Type: LD₀ []; LD₁₀₀ []; LD₅₀ [X]; LDL₀ []; Other []
- Species/strain: Rat
- Value: 700 mg/kg b.w.
- Method: Other: No data
- GLP: Yes [] No [X] ? []
- Test substance: 31.5% hydrochloric acid
- Remarks: Lung: hyperemia
Liver: discoloration
Gut: acute inflammation
Stomach: ulceration
- Reliability : (4) Not assignable
- Reference: Monsanto (1976) cited in European Commission- European Chemical Bureau (2000)

5.1.2 ACUTE INHALATION TOXICITY

- (1)
- Type: LC₀ []; LC₁₀₀ []; LC₅₀ [X]; LCL₀ []; Other []
- Species/strain: Rat/Wistar

Exposure time: 5 minutes
 Value: 61 mg/L/5 min (40,989 ppm)
 Method: Other: No data
 GLP: Yes [] No [] ? [X]
 Test substance: Grade and purity not stated.
 Remarks: Observation period: 7 days
 At 30,000 ppm 0/10 rats died
 At 32,000 ppm 1/10 rats died
 At 39,850 ppm 6/10 rats died
 At 45,200 ppm 7/10 rats died
 At 57,290 ppm 9/10 rats died
 Reliability : (3) Not reliable
 Reference: Higgins, E.A. et al. (1972)

(2)
 Type: LC₀ []; LC₁₀₀ []; LC₅₀ [X]; LCL₀ []; Other []
 Species/strain: Rat
 Exposure time: 5, 10, 15, 22.5, 30, or 60 minutes
 Value: 23.7 mg/L/5 min
 12.5mg/L/10 min
 10.3mg/L/15 min
 8.8mg/L/22.5 min
 5.7mg/L/30 min
 4.2mg/L/60 min
 Method: Other: No data
 GLP: Yes [] No [] ? [X]
 Test substance: Grade and purity not stated.
 Remarks: Observation period: 14 days
 Reliability : (3) Not reliable
 Reference: Hartzell, G.E. et al. (1987); (1990)

(3)
 Type: LC₀ []; LC₁₀₀ []; LC₅₀ [X]; LCL₀ []; Other []
 Species/strain: Rat/SD
 Exposure time: 5 or 30 minutes
 Value: Gas: 60.9 mg/L/5 min, 7.0 mg/L/30 min
 Aerosol: 45.6 mg/L/5 min, 8.3 mg/L/30 min
 Method: Other: No data
 GLP: Yes [] No [] ? [X]
 Test substance: Grade and purity not stated.
 Remarks: Single-exposure, acute toxicity studies were conducted in rats with both HCl gas and HCl aerosol. Hydrochloric acid was extremely irritating to the eyes, mucous membranes, and exposed areas of the skin, such as the scrotum. Corneal erosion and cloudiness occurred, and pathological examination of animals that died during or shortly following exposure showed that respiratory tract was the primary target for the Hydrochloric acid. Alveolar emphysema, atelectasis, and oedema of the lungs were observed; there was also severe injury to the epithelial lining of the nasotracheal passages.

Necropsy examination of the animals surviving for 14 days after exposure revealed residual injury in the respiratory tract. The death patterns observed were similar for both the gas and the aerosol, with delayed deaths in both cases.

Reliability : (3) Not reliable
Reference: Darmer, K.I. et al. (1974a)

(4)
Type: LC₀ []; LC₁₀₀ []; LC₅₀ [X]; LCL₀ []; Other []
Species/strain: Rat/SD
Exposure time: 60 minutes
Value: 4.7 mg/L/60 min
Method: Other: No data
GLP: Yes [] No [] ? [X]
Test substance: Grade and purity not stated.
Remarks: Gross pathological examination of animals dying from exposure showed pulmonary congestion and intestinal hemorrhages with exhibiting thymic hemorrhages. Surviving animals sacrificed after 14-day observation period demonstrated multifocal areas of red hepatisation in lungs of rats and occasional engorged or pale livers.

Reliability : (3) Not reliable
Reference: MacEwean, J.D. et al. (1974); Wohlslagel, J. et al. (1976); Vernot, E.H. et al. (1977)

(5)
Type: LC₀ []; LC₁₀₀ []; LC₅₀ [X]; LCL₀ []; Other []
Species/strain: Rat
Exposure time: 60 minutes
Value: Aerosol: 1.68 mg/L/60 min
Method: Other: No data
GLP: Yes [] No [] ? [X]
Test substance: Grade and purity not stated.

Remarks:
Reliability : (3) Not reliable
Reference: Vernot, E.H. et al. (1977)

(6)
Type: LC₀ []; LC₁₀₀ []; LC₅₀ [X]; LCL₀ []; Other []
Species/strain: Mouse/ICR
Exposure time: 5 minutes
Value: 20.5 mg/L/5 min (13,745 ppm)
Method: Other: No data
GLP: Yes [] No [] ? [X]
Test substance: Grade and purity not stated.
Remarks: Observation period: 5 days
At 3,200 ppm 0/15 rats died
At 5,060 ppm 1/15 rats died
At 6,145 ppm 2/15 rats died

	At 6,410 ppm	0/15 rats died
	At 7,525 ppm	6/15 rats died
	At 8,065 ppm	2/15 rats died
	At 9,276 ppm	5/15 rats died
	At 26,485 ppm	13/15 rats died
	At 30,000 ppm	13/15 rats died
Reliability	:	(3) Not reliable
Reference:		Higgins, E.A. et al. (1972)
 (7)		
Type:	LC ₀ [] ; LC ₁₀₀ [] ; LC ₅₀ [X] ; LCL ₀ [] ; Other []	
Species/strain:		Mouse/ICR
Exposure time:		5 or 30 minutes
Value:	Gas:	20.9 mg/L/5 min, 3.9 mg/L/30 min
	Aerosol:	16.5 mg/L/5 min, 3.2 mg/L/30 min
Method:		Other: No data
GLP:		Yes [] No [] ? [X]
Test substance:		Grade and purity not stated.
Remarks:		Single-exposure, acute toxicity studies were conducted in mice with both HCl gas and HCl aerosol. HCl was extremely irritating to the eyes, mucous membranes, and exposed areas of the skin, such as the scrotum. Corneal erosion and cloudiness occurred, and pathological examination of animals that died during or shortly following exposure showed that respiratory tract was the primary target for the Hydrochloric acid. Alveolar emphysema, atelectasis, and oedema of the lungs were observed; there was also severe injury to the epithelial lining of the nasotracheal passages. Necropsy examination of the animals surviving for 14 days after exposure revealed residual injury in the respiratory tract. The death patterns observed were similar for both the gas and the aerosol, with delayed deaths in both cases.
Reliability	:	(3) Not reliable
Reference:		Darmer, K.I. et al. (1974a)
 (8)		
Type:	LC ₀ [] ; LC ₁₀₀ [] ; LC ₅₀ [X] ; LCL ₀ [] ; Other []	
Species/strain:		Mouse/ICR
Exposure time:		60 minutes
Value:		1.7 mg/L/60 min
Method:		Other
GLP:		Yes [] No [] ? [X]
Test substance:		Grade and purity not stated.
Remarks:		Gross pathological examination of animals dying from exposure showed pulmonary congestion and intestinal hemorrhages. Surviving animals sacrificed after 14-day observation period demonstrated no gross lesions.
Reliability	:	(3) Not reliable
Reference:		MacEwean, J.D. et al (1974); Wohlslagel, J. et al. (1976)
 (9)		
Type:	LC ₀ [] ; LC ₁₀₀ [] ; LC ₅₀ [] ; LCL ₀ [] ; Other [X]	

Species/strain: Mouse/SwissWebster
 Exposure time: 10 minutes
 Value: 0.46 mg/L
 Method: Other: No data
 GLP: Yes [] No [] ? [X]
 Test substance: Grade and purity not stated.
 Remarks: Mice were exposed for 10 minutes to concentrations ranging from 0.06 to 1.4 mg/L, and dose-response curves were plotted, using the percentage decrease in respiratory rate for each exposure as the reaction reflecting sensory irritation of the upper respiratory tract. RD₅₀ value (concentration that caused a 50 % decrease in respiratory rate) was 0.46 mg/L.
 Reliability : (3) Not reliable
 Reference: Barrow, C.S. et al. (1977)

(10)
 Type: LC₀ []; LC₁₀₀ []; LC₅₀ []; LCL₀ []; Other [X]
 Species/strain: Mouse/Swiss-Webster
 Exposure time: 10 minutes
 Value: Not stated
 Method: Other: No data
 GLP: Yes [] No [] ? [X]
 Test substance: Grade and purity not stated.
 Remarks: 0.025 mg/L: minimal superficial ulceration in the respiratory epithelium and its junction with the squamous epithelium of the external nares
 0.19-0.41 mg/L: mucosal ulceration of the adjacent respiratory epithelium
 0.73 mg/L: mucosal ulceration of the respiratory epithelium and the squamous epithelium of the external nares
 2.90 mg/L and more: mucosal damage of the squamous respiratory and olfactory epithelium of the upper respiratory tract, followed by damage of the under-lying supportive tissues
 Reliability : (3) Not reliable
 Reference: Lucia, H.L. et al. (1977)

(11)
 Type: LC₀ []; LC₁₀₀ []; LC₅₀ []; LCL₀ []; Other [X]
 Species/strain: Mouse/Swiss-Webstar
 Exposure time: 10 minutes
 Value: > 12.0 mg/L
 Method: Other: No data
 GLP: Yes [] No [] ? [X]
 Test substance: Grade and purity not stated.
 Remarks: Mice were exposed to concentrations ranging from 0.03 to 29.0 mg/L with deaths occurring above 12.0 mg/L. Histopathological changes noted in mice, killed 24 hours after the exposure, revealed that the target organs included the upper respiratory tract and the eyes, with secondary changes and passive congestion in the lungs, intestine, liver, and kidneys.
 Reliability : (3) Not reliable
 Reference: Barrow, C.S. et al. (1979)

- (12)
- Type: LC₀ []; LC₁₀₀ []; LC₅₀ []; LCL₀ []; Other [X]
- Species/strain: Rabbit
- Exposure time: 5 -360 minutes
- Value: Not stated
- Method: Other: No data
- GLP: Yes [] No [] ? [X]
- Test substance: Grade and purity not stated.
- Remarks: 5.5 mg/L (5 min): no deaths
6.4 mg/L (30 min): 100% deaths
1.0 mg/L (120, 360 min): 100% deaths
Groups of 3 rabbits were exposed to hydrogen chloride gas of various concentration. Definite gross pathological acute changes in the lung and liver were noted in the animals died within a week. But relation to doses were not clarified.
- Reliability : (3) Not reliable
- Reference: Machle, M. et al. (1942)
- (13)
- Type: LC₀ []; LC₁₀₀ []; LC₅₀ []; LCL₀ []; Other [X]
- Species/strain: Rabbit
- Exposure time: 90 or 360 minutes
- Value: not stated
- Method: Other: No data
- GLP: Yes [] No [] ? [X]
- Test substance: Grade and purity not stated.
- Remarks: 5 mg/L/90 min : Death occurred after 2-6 days
0.15 mg/L/360 min: Symptoms of toxicity: irritation of the nasal mucosa, salivation (symptoms were reversible)
0.45 mg/L/360 min: Symptoms of toxicity: irritation of the cornea, catarrhs
- Reliability : (4) Not assignable
- Reference: Lehmann (1886) cited in European Commission- European Chemical Bureau (2000)
- (14)
- Type: LC₀ []; LC₁₀₀ []; LC₅₀ [X]; LCL₀ []; Other []
- Species/strain: Guinea pig
- Exposure time: 15 or 30 minutes
- Value: 4.3 mg/L/15 min
2.0 mg/L/30 min
- Method: Other: No data
- GLP: Yes [] No [] ? [X]
- Test substance: Grade and purity not stated.
- Remarks: The guinea pig was considerably mor sensitive to hydrogen chloride, presumably due to its tendency for bronchoconstriction.
- Reliability : (3) Not reliable

Reference:	Hartzell, G.E. et al. (1988)
(15)	
Type:	LC ₀ []; LC ₁₀₀ []; LC ₅₀ [X]; LCL ₀ []; Other []
Species/strain:	Guinea pig
Exposure time:	30 minutes
Value:	3.8 mg/L
Method:	Other: No data
GLP:	Yes [] No [] ? [X]
Test substance:	Grade and purity not stated.
Remarks:	Observation period: 7 days Symptoms of toxicity: high frequency of respiration, cough, foam-forming in the nasal area, retardation of movements, irritation of the eyes, opacity of the cornea, reduced weight, reduced food consumption; autopsy: changes of the respiratory tract, crusts in the noses, edema and emphysema of the lungs
Reliability :	(3) Not reliable
Reference:	Kirsch, V. and Drabke, P. (1982)
(16)	
Type:	LC ₀ []; LC ₁₀₀ []; LC ₅₀ []; LCL ₀ []; Other [X]
Species/strain:	Guinea pig
Exposure time:	5 -360 minutes
Value:	No data
Method:	Other: No data
GLP:	Yes [] No [] ? [X]
Test substance:	Grade and purity not stated.
Remarks:	5.5 mg/L (5 min): No deaths. 6.4 mg/L (30 min): 100% deaths. 1.0 mg/L (120, 360 min): 100% deaths Groups of 3 guinea pigs were exposed to hydrogen chloride gas of various concentration. Definite gross pathological acute changes in the lung and liver were noted in the animals died within a week. But relation to doses were not clarified.
Reliability :	(3) Not reliable
Reference:	Machle, W. et al. (1942)
(17)	
Type:	LC ₀ []; LC ₁₀₀ []; LC ₅₀ []; LCL ₀ []; Other [X]
Species/strain:	Guinea pig
Exposure time:	30 minutes (head-only)
Value:	No data
Method:	Other: No data
GLP:	Yes [] No [] ? [X]
Test substance:	Grade and purity not stated.
Remarks:	Pulmonary effects of HCl-inhalation were determined in guinea-pigs during and following exposure; HCl inhalation resulted in sensory and pulmonary irritation; onset of sensory irritation: 6 minutes at 0.5 mg/L, < 1 minute at

	1.0, 1.5 and 2.0 mg/L; the onset of pulmonary irritation showed a concentration-response relationship; HCl exposure also affected baseline respiratory rate and tidal volume of the animals after exposure; impairments of respiratory function were supported by evidence of morphological injury in the airways and the alveolar region; clinical observations: 2 deaths in the highest dose group during exposure, 2 animals died following exposure to 1.5 mg/L and 1 died following exposure to 2.0 mg/L (observation period: 16 days), corneal opacities, reduction of body weight.
Reliability :	(3) Not reliable
Reference:	Burleigh-Flayer, H. et al. (1985)
 (18)	
Type:	LC ₀ []; LC ₁₀₀ []; LC ₅₀ []; LCL ₀ []; Other [X]
Species/strain:	Baboon/Papio cynocephalus
Exposure time:	15 minutes
Value:	No data
Method:	Other: The guidelines provided in the National Research Council's Guide for the Care and Use of Laboratory Animals
GLP:	Yes [] No [] ? [X]
Test substance:	Grade and purity not stated.
Remarks:	Each of 4 groups of three anesthetized animals was exposed I ahead only mode for 15 minutes to air or one of three hydrogen chloride concentrations (0.75, 7.5, 14.9 mg/L). The acute respiratory response considered of a concentration-related increase in frequency and minute volume, with a marked decrease in blood PaO ₂ at the two highest concentrations. The exposure did not cause significant alterations in any of the pulmonary function parameters measured at 3 days and 3 months postexposure.
Reliability :	(3) Not reliable
Reference:	Kaplan, H.L. et al. (1988)
 (19)	
Type:	LC ₀ []; LC ₁₀₀ []; LC ₅₀ []; LCL ₀ []; Other [X]
Species/strain:	Dog
Exposure time:	10 minutes
Value:	No data
Method:	Other: No data
GLP:	Yes [] No [] ? [X]
Test substance:	Grade and purity not stated.
Remarks:	HCl was added to synthetic smoke composed of carbon particles; anesthetized dogs were intubated and ventilated. Dose-related pathological changes in the lungs; 0.1-1N HCl: focal mucosal degeneration, desquamation, acute inflammation on the trachea, carina, and large bronchi; 6N HCl: transmural necrosis of the trachea and carina, mucosal slough, inflammation, vascular thromboses.
Reliability :	(3) Not reliable
Reference:	Hales, C.A. et al. (1988)

(20)

Type: LC₀ []; LC₁₀₀ []; LC₅₀ []; LCL₀ [X]; Other []
 Species/strain: Rat
 Exposure time: 5 minutes
 Value: 130.61 mg/L/5 min
 Method: Other: No data
 GLP: Yes [] No [] ? [X]
 Test substance: Grade and purity not stated.
 Remarks:
 Reliability : (4) Not assignable
 Reference: Kaplan, K.L. et al. (1989)

(21)

Type: LC₀ []; LC₁₀₀ []; LC₅₀ [X]; LCL₀ []; Other []
 Species/strain: Rat
 Exposure time: 30 or 60 minutes
 Value: 213 mg/L/30 min
 283 mg/L/60 min
 Method: Other
 GLP: Yes [] No [] ? [X]
 Test substance: Grade and purity not stated.
 Remarks:
 Reliability : (4) Not assignable
 Reference: Cohen M. (1981) cited in European Commission- European Chemical Bureau (2000)

(22)

Type: LC₀ []; LC₁₀₀ []; LC₅₀ []; LCL₀ [X]; Other []
 Species/strain: Mouse
 Exposure time: 5 minutes
 Value: 17.11 mg/L/5 min
 Method: Other: No data
 GLP: Yes [] No [] ? [X]
 Test substance: Grade and purity not stated.
 Remarks:
 Reliability : (4) Not assignable
 Reference: Kaplan .H.L.et al. (1989)

(23)

Type: LC₀ []; LC₁₀₀ []; LC₅₀ [X]; LCL₀ []; Other []
 Species/strain: Mouse
 Exposure time: 5, 30 or 60 minutes
 Value: 103 mg/L/5 min
 96 mg/L/30 min
 99 mg/L/60 min
 Method: Other: No data
 GLP: Yes [] No [] ? [X]

Test substance:	Grade and purity not stated.
Remarks:	
Reliability :	(4) Not assignable
Reference:	Cohen M. (1981) cited in European Commission- European Chemical Bureau (2000)
(24)	
Type:	LC ₀ []; LC ₁₀₀ []; LC ₅₀ [X]; LCL ₀ []; Other []
Species/strain:	Mouse
Exposure time:	10 minutes
Value:	15.1 mg/L/10 min
Method:	Other: No data
GLP:	Yes [] No [] ? [X]
Test substance:	Grade and purity not stated.
Remarks:	Method: observation period: 3 h
Reliability :	(4) Not assignable
Reference:	Hartzell et al. (1990)
(25)	
Type:	LC ₀ []; LC ₁₀₀ []; LC ₅₀ []; LCL ₀ [X]; Other []
Species/strain:	Rabbit
Exposure time:	30 minutes
Value:	6.7 mg/L/30 min
Method:	Other: No data
GLP:	Yes [] No [] ? [X]
Test substance:	Grade and purity not stated.
Remarks:	
Reliability :	(4) Not assignable
Reference:	European Commission- European Chemical Bureau (2000)
(26)	
Type:	LC ₀ []; LC ₁₀₀ []; LC ₅₀ []; LCL ₀ []; Other [X]
Species/strain:	Rabbit
Exposure time:	90 or 360 minutes
Value:	Not stated
Method:	Other: No data
GLP:	Yes [] No [] ? [X]
Test substance:	Grade and purity not stated.
Remarks:	0.149-0.209 mg/L (up to 6 h): slight nasal irritation, salivation 0.447 mg/L (6 h): slight corneal erosion, respiratory, irritation 2.012 mg/L (90 min): severe irritation, shortness of breath 5.066 mg/L (90 min): death within 2-6 days Histopathology: pulmonary edema, hyperemia and occasionally haematemesis
Reliability :	(4) Not assignable
Reference:	Flury and Zernik (1931) cited in European Commission- European Chemical Bureau (2000) and BIBRA (1990)

(27)	
Type:	LC ₀ []; LC ₁₀₀ []; LC ₅₀ []; LCL ₀ []; Other [X]
Species/strain:	Guinea pig
Exposure time:	75 or 360 minutes
Value:	2 mg/L/75 min 0.45 mg/L/360 min
Method:	Other: No data
GLP:	Yes [] No [] ? [X]
Test substance:	Grade and purity not stated.
Remarks:	Symptoms of toxicity 2 mg/L/75 min:: severe irritation, shortness of breath, opacity of the cornea 0.45 mg/L/360 min: irritation of the cornea, catarrhs
Reliability :	(4) Not assignable
Reference:	Lehmann (1886) cited in European Commission- European Chemical Bureau (2000)
(28)	
Type:	LC ₀ []; LC ₁₀₀ []; LC ₅₀ [X]; LCL ₀ []; Other []
Species/strain:	Guinea pig
Exposure time:	90 or 360 minutes
Value:	2.012 mg/L (90 min) 5.066 mg/L (90 min) 0.447 mg/L (6 h)
Method:	Other: No data
GLP:	Yes [] No [] ? [X]
Test substance:	Grade and purity not stated.
Remarks:	2.012 mg/L (90 min): slight corneal erosion, respiratory irritation 5.066 mg/L (90 min): severe irritation, shortness of breath 0.447 mg/L (6 h): death within 2-6 days Histopathology: pulmonary edema, hyperemia, and occasionally haematemesis
Reliability :	(4) Not assignable
Reference:	Flury and Zernik (1931) cited in European Commission- European Chemical Bureau (2000) and BIBRA (1990)
(29)	
Type:	LC ₀ []; LC ₁₀₀ []; LC ₅₀ []; LCL ₀ [X]; Other []
Species/strain:	Baboon
Exposure time:	5, 10, or 15 minutes
Value:	44.7 mg/L/5 min 22.35 mg/L/10 min 14.9 mg/L/15 min
Method:	Other: No data
GLP:	Yes [] No [] ? [X]
Test substance:	Grade and purity not stated.
Remarks:	
Reliability :	(4) Not assignable
Reference:	Kaplan H.L. et al. (1989)

(30)
 Type: LC₀ []; LC₁₀₀ []; LC₅₀ []; LCL₀ []; Other [X]
 Species/strain: Cat
 Exposure time: 360 minutes
 Value: 0.12 mg/L/360 min
 Method: Other: No data
 GLP: Yes [] No [] ? [X]
 Test substance: Grade and purity not stated.
 Remarks: Symptoms of toxicity: irritation of the nasal mucosa, salivation (symptoms were reversible)
 Reliability : (4) Not assignable
 Reference: Lehmann (1886) cited in European Commission- European Chemical Bureau (2000)

(31)
 Type: LC₀ []; LC₁₀₀ []; LC₅₀ []; LCL₀ []; Other [X]
 Species/strain: Cat
 Exposure time: up to 360 minutes
 Value: No data
 Method: Other: No data
 GLP: Yes [] No [] ? [X]
 Test substance: Grade and purity not stated.
 Remarks: Only slight reaction (nasal irritation, salivation); no adverse effects
 Reliability : (4) Not assignable
 Reference: Flury and Zernik (1931) cited in European Commission- European Chemical Bureau (2000) and BIBRA (1990)

5.1.3 ACUTE DERMAL TOXICITY

(1)
 Type: LD₀ []; LD₁₀₀ []; LD₅₀ [X]; LDL₀ []; Other []
 Species/strain: Rabbit
 Value: > 5,010 mg/kg
 Method: Other: No data
 GLP: Yes [] No [] ? [X]
 Test substance: 31.5% hydrochloric acid
 Remarks: Exposure time: 24 hours
 Lung : hyperemia
 Liver : hyperemia
 Gall bladder : slight enlargement
 Spleen : darkened
 Kidney : darkened
 Reliability : (4) Not assignable
 Reference: Monsanto (1976) cited in European Commission- European Chemical Bureau (2000)

(2)

Type: LD₀ []; LD₁₀₀ []; LD₅₀ [**X**]; LDL₀ []; Other []
 Species/strain: Mouse
 Value: 1,449 mg/kg
 Method: Other: No data
 GLP: Yes [] No [] ? [**X**]
 Test substance: Grade and purity not stated.
 Remarks: This value is deleted from the latest database.
 Reliability : (4) Not assignable
 Reference: RTECS 86 (NIOSH) COREAF 256, 1043, 63 Comptes Rendus Hebdomadaires des Seances, Academie des Sciences (Paris – France) V.1-261, 1835-1965 cited in European Commission- European Chemical Bureau (2000)

5.1.4 ACUTE TOXICITY, OTHER ROUTES OF ADMINISTRATION

(1)
 Type: LD₀ [**X**]; LD₁₀₀ []; LD₅₀ []; LDL₀ []; Other []
 Species/strain: Mouse (strain, sex and number not given)
 Route of Administration: i.m. []; i.p. []; i.v. [**X**]; infusion []; s.c. []; other []
 Exposure time: No data
 Value: LD₀ > 0.7 mg/kg
 Method: Other: No data
 GLP: Yes [] No [] ? [**X**]
 Test substance: Grade and purity not stated.

Remarks:

Reliability : (3) Not reliable

Reference: Cosgrove, G.E. et al. (1965)

(2)
 Type: LC₀ []; LC₁₀₀ []; LC₅₀ []; LCL₀ []; Other [**X**]
 Species/strain: Rat /F344
 Route of Administration: i.m. []; i.p. []; i.v. []; infusion []; s.c. []; other [**X**]
 Exposure time: 30 minutes
 Value: No data
 Method: Other: No data
 GLP: Yes [] No [] ? [**X**]
 Test substance: Grade and purity not stated.

Remarks: **Pseudo-mouth-breathing (MB)**: tracheal tubes connected to mouth pieces were inserted into temporarily anesthetized rats.
Nose-breathers (NB): similarly pretreated rats were exposed without the mouth piece. The rats were exposed to 1.94 mg/L hydrochloric acid for 30 minutes.
NB-exposure: tissue injury confined to the nasal region: epithelial and submucosal necrosis, accumulations of inflammatory cells,

exudate, extravasation of erythrocytes.

MB-exposure: higher mortality rates (in comparison to NB), major tissue disruption in the trachea including epithelial, submucosal, glandular and cartilage necrosis, accumulations of inflammatory cells and exudates; more peripheral lung damage was manifested by lung gravimetric increases and histopathologic changes primarily in the larger conducting airways; the authors suggest that the injuries response profile of HCl markedly differs as a function of the route by which they are inhaled.

Reliability: (3) Not reliable

Reference: Starvert, D.M. et al. (1991)

(3)

Type: LC₀ []; LC₁₀₀ []; LC₅₀ []; LCL₀ []; Other [X]

Species/strain: Rat (strain and sex not given)

Route of Administration: i.m. []; i.p. []; i.v. []; infusion []; s.c. []; other [X]

Exposure time: No data

Value: No data

Method: Other: No data

GLP: Yes [] No [] ? [X]

Test substance: Grade and purity not stated.

Remarks: Hydrochloric acid of different pH (1, 1.5, 2) was instilled into the trachea of 23 rats; 5 minutes after treatment a marked increase in tracheo-bronchial Evans blue content was observed compared to controls; an acute, pH-dependent protein extravasation in the lower airways could be demonstrated upon local instillation of acidic solutions, no increased extravasation was present 24 h after intratracheal injections; Evans blue, when injected into systemic circulation, rapidly binds to macromolecules, i.e. serum albumin; therefore an increased tissue content of Evans blue is considered to reflect increased extravasation of plasma proteins through postcapillary venules, subsequently leading to edema formation.

Reliability: (3) Not reliable

Reference: Martling, C.R. and Lundberg, J.M. (1988)

(4)

Type: LC₀ []; LC₁₀₀ []; LC₅₀ []; LCL₀ []; Other [X]

Species/strain: Dog

Route of Administration: i.m. []; i.p. []; i.v. []; infusion []; s.c. []; other [X]

Exposure time: 30 minutes

Value: No data

Method: Other: No data

GLP: Yes [] No [] ? [X]

Test substance: Grade and purity not stated.

Remarks: Effect on oesophagus. 0.1% hydrochloric acid (pH 1.6) in contact with the oesophagus of dogs for 30 minutes caused local proliferation of epithelial cells but no inflammation or damage.

Reliability: (3) Not reliable

Reference:	De Backer, A. et al. (1985)
(5)	
Type:	LC ₀ []; LC ₁₀₀ []; LC ₅₀ []; LCL ₀ []; Other [X]
Species/strain:	Dog(strain, sex and number not given)
Route of Administration:	i.m. []; i.p. []; i.v. []; infusion []; s.c. []; other [X]
Exposure time:	No data
Value:	No data
Method:	Other: No data
GLP:	Yes [] No [] ? [X]
Test substance:	Grade and purity not stated.
Remarks:	Endpoint: lung damage and death Lung damage and death occurred in dogs following insyillation into the lungs of 2-3 mL of approximately 0.4% hydrochloric acid solution.
Reliability:	(3) Not reliable
Reference:	Greenfield, L.J. et al. (1969)
(6)	
Type:	LD ₀ []; LD ₁₀₀ []; LD ₅₀ [X]; LDL ₀ []; Other []
Species/strain:	Mouse (strain, sex and number not given)
Route of Administration:	i.m. []; i.p. [X]; i.v. []; infusion []; s.c. []; other []
Exposure time:	No data
Value:	1,449 mg/kg
Method:	Other: No data
GLP:	Yes [] No [] ? [X]
Test substance:	Grade and purity not stated.
Remarks:	
Reliability:	(4) Not assignable
Reference:	Anon (1963) cited in European Commission- European Chemical Bureau (2000)
(7)	
Type:	LD ₀ []; LD ₁₀₀ []; LD ₅₀ [X]; LDL ₀ []; Other []
Species/strain:	Mouse (strain, sex and number not given)
Route of Administration:	i.m. []; i.p. [X]; i.v. []; infusion []; s.c. []; other []
Exposure time:	30 minutes
Value:	40.1 mg/kg
Method:	Other: No data
GLP:	Yes [] No [] ? [X]
Test substance:	Grade and purity not stated.
Remarks:	
Reliability:	(4) Not assignable
Reference:	European Commission- European Chemical Bureau (2000)

5.2.1 SKIN IRRITATION/CORROSION

(a)

Test substance: Hydrochloric acid, CAS No. 7647-01-0

Test Substance Remarks: The test solutions of 1 and 3.3 wt% were prepared by the dilution 1:14.5 and 1:4.5 of 15 wt% of hydrochloric acid (normal laboratory quality)

pH: Not described. The calculated value of pH does not correspond to the definition of pH.

Method: Other: according to internal guidelines of Hoechst AG.

Test type: *In vivo*

GLP: Yes [] No [X] ? []

Year: 1966

Species: Rabbit

Strain: Not described

Sex: Not described

Number of animals per sex per dose: Three animals

Total dose: 0.5 mL of 1 wt% of hydrochloric acid x 5 applications
0.5 mL of 3.3 wt% of hydrochloric acid x 5 applications

Vehicle: 0.9% of NaCl solution

Exposure time period: Five applications in 5 days

Grading scale: Not described

Method remarks:

- Test animals: Three yellow/silver strain animals were used for each test and kept in single cages during the test under constant observation. The animals received standard ALTROMIN K of the Altrogge Company in Lage/Lippe and effluent as feed.
- Applications: Five applications of 0.5 mL of test solution in 5 days were given to the depilated and intact flank skin of animals in each test.

Results: One-third of animals were responded to 3.3% of hydrochloric acid treatment. While, no findings were observed in the group treated with 1 wt% of hydrochloric acid.

Primary irritation index: Not described

Results remarks: Slight to marked reddening, isolated small necrosis, and flank skin slightly cracked and slightly bloody in 1/3 animal were observed in 3.3% of hydrochloric acid treatment group.

Remarks: This experiment for HCl was conducted as a positive control for other test substances.

The concentration of test solution could be calculated as follows;
 1.075 g/cm^3 (density of 15 wt%) x 1000 (L) x 0.15/36.5
= 4.42 mol/L
1 wt% of hydrochloric acid = $4.42 \text{ mol/L} / 14.5 = 0.31 \text{ mol/L}$
3.3 wt% of hydrochloric acid = $4.42 \text{ mol/L} / 4.5 = 0.98 \text{ mol/L}$

Conclusions: Application of 3.3 wt% hydrochloric acid solution caused moderate skin irritation to the rabbit skin, while no skin damage by the 1 wt% hydrochloric acid solution.

Data Quality: (2) Reliable with restrictions

Quality Check: Comparable to guideline study with acceptable restrictions

Reference: Hoechst AG, (1966) Report 150/66

General Remarks: None

- (b)
- Test substance:** Hydrochloric acid, CAS No. 7647-01-0
 Test Substance Remarks: 37% of hydrochloric acid
 pH: Not described. The calculated value of pH does not correspond to the definition of pH.
- Method:** Based on the OECD TG 404 (1981)
 Test type: *In vivo*
 GLP: Yes [] No [] ? [X]
 Year: Not described
 Species: Rabbit
 Strain: New Zealand White
 Sex: Male/female
 Number of animals per sex per dose: Six animals
 Total dose: 0.5 mL of 37% HCl
 Vehicle: No
 Exposure time period: 1, 4 hours
 Grading scale: The criteria used to define irritation and corrosion were those given in the EEC directive (EEC, 1983).
- Method remarks:**
- Test animals: Animals with healthy and intact skin were used.
 - Test conditions: the dorsal and lateral parts of the trunk were shorn 15-24h before treatment. The results were assessed 1, 24, 48 and 72 hr and 7 days after removal of the patch.
 - Applications: Four samples were attached dorsally (laterally) to each animal. The local reactions were determined after both 1 and 4 hr exposure both under occlusive and semi-occlusive conditions. 0.5 mL/patch were applied to gauze pads 3 cm x 3 cm. The patches were fixed on the prepared skin areas of the flanks and covered by wrapping an air-permeable circular bandage (semi-occlusive method) or airtight plastic foil (occlusive method) around the animals. After removal of the bandages and patches the treated skin areas were rinsed with water and dried.
- Results:** The test substance was corrosive after both 1 hr and 4 hr application of occlusive or semi-occlusive exposure. However, the cumulative total and percent responders were not described in the report.
- Primary irritation index: Not described
 Results remarks: Classified as the material which causes burns according to EEC(1967).
Remarks: The concentration of test solution could be calculated as follows;
 1.185g/cm^3 (density of 37 wt%) x 1000 (L) x 0.37/36.5 = 12 mol/L
Conclusions: Hydrochloric acid at 37% is corrosive to skin.
Reliability: (2) Reliable with restrictions
Quality Check: Guideline study without detailed documentation.
 Reference: Potokar, M. (1985) Studies on the Design of Animal Tests for the Corrosiveness of Industrial Chemicals. *Fd. Chem. Toxic.*, 23, 615-617.
- (c)
- Species/strain: Rabbit/New Zealand
 Sex: Female
 Results: Highly corrosive []; Corrosive [X]; Highly irritating []; Irritating [];

Classification:	Moderate irritating []; Slightly irritating []; Not irritating [] Highly corrosive (causes severe burns) []; Corrosive (caused burns) []; Irritating []; Not irritating []
Method:	Other - Test animals: Six rabbits that had been clipped hair on backs and flanks 24 hr prior to exposure. - Applications: The 0.5 mL of hydrochloric acid solution at 15 and 17 wt% was applied for 4 h. The material was applied to the designated patch areas and covered by a 1-in. square of surgical gauze two single layers thick. Test areas were evaluated for visible tissue destruction.
GLP:	Yes [] No [] ? [X]
Test substance:	Hydrochloric acid
Remarks:	Result: 17 wt% of hydrochloric acid was corrosive. Solution of hydrochloric acid in water at 15 wt % was not corrosive under the test conditions. No further details. - Criterion: When the skin damage causing visible tissue destruction was observed in at least two of six rabbits, the material applied was classified as corrosive.
Reliability :	(3) Not reliable
Reference:	Vernot et al. (1977)
 (d)	
Species/strain:	Pig /Yorkshire
Results:	Highly corrosive []; Corrosive []; Highly irritating []; Irritating [X]; Moderate irritating []; Slightly irritating []; Not irritating []
Classification:	Highly corrosive (causes severe burns) []; Corrosive (caused burns) []; Irritating []; Not irritating []
Method:	Other
GLP:	Yes [] No [] ? [X]
Test substance:	Hydrochloric acid, Fisher Scientific.
Remarks:	Method: - Test animals: The groups of 4 pig were used for each concentration applied. - Application: The application of 200 uL of 2N, 4N or 6N hydrochloric acid to a 5 cm ² area on the lower abdominal region were conducted as a pilot study. Macroscopic observations were recorded for 30 minutes, and 6 mm biopsy samples were taken for light microscopy (LM). Results: The 2 N hydrochloric acid had no visual effects in 3/4 pigs. One pig showed a slight erythema after 15 minutes of application, which then disappeared by 30 minutes. LM observation showed normal histology except for slight intracellular edema in the stratum basale, stratum spinosum, and stratum granulosum layers of the epidermis. The 4 N hydrochloric acid treated skin showed mild erythema after 5-10 minutes and intracellular edema was seen by LM in 2/4 pigs. All pigs tested with 6N hydrochloric acid showed considerable erythema within 5-10 minutes with a slight increase in epidermal intracellular edema.
Reliability :	(3) Not reliable
Reference:	Srikrishna V. and Monteiro-Riviere N.A. (1991)

- (e)
- Species/strain: Mouse/CF-1 (ICR derived)
- Sex: Male
- Results: Highly corrosive []; Corrosive []; Highly irritating []; Irritating [**X**]; Moderate irritating []; Slightly irritating []; Not irritating []
- Classification: Highly corrosive (causes severe burns) []; Corrosive (caused burns) []; Irritating []; Not irritating []
- Method: Other
Hydrogen chloride gas was mixed with a saturated water droplet mist in Longley exposure chamber to obtain hydrochloric acid aerosol atmospheres and the tested concentration was analysed by a chloride ion specific electrode analysis. The groups of 10 mice were exposed to hydrochloric acid aerosol at 13.3 - 27.6 mg/L (9,058 – 18, 773 ppm) for 5 minutes and 1.8 - 6.5 mg/L (1,204 - 4,432 ppm) for 30 minutes.
- GLP: Yes [] No [] ? [**X**]
- Test substance: Hydrochloric acid as aerosol, Matheson company
- Remarks: Results: The exposures caused skin irritation and ulceration with fur discoloration to greenish hue.
- Reliability : (3) Not reliable
- Reference: Darmer et al. (1974a)
- (f)
- Species/strain: Mouse/CF-1 (ICR derived)
- Results: Highly corrosive []; Corrosive []; Highly irritating []; Irritating [**X**]; Moderate irritating []; Slightly irritating []; Not irritating []
- Classification: Highly corrosive (causes severe burns) []; Corrosive (caused burns) []; Irritating []; Not irritating []
- Method: Other
Desired concentrations of hydrogen chloride were prepared by hydrogen chloride and pre-dried air. The groups of 15 mice were exposed to hydrochloric acid gas at 3,200 - 30,000 ppm for 5 minutes and 410 - 5,363 ppm for 30 minutes.
- GLP: Yes [] No [] ? [**X**]
- Test substance: Hydrogen chloride, Matheson company
- Remarks: Results: Skin irritation and ulceration with fur discoloration to greenish hue were occurred.
- Reliability : (3) Not reliable
- Reference: Darmer et al. (1974a)
- (g)
- Species/strain: Rat / CFE (Sprague-Dawley derived)
- Results: Highly corrosive []; Corrosive []; Highly irritating []; Irritating [**X**]; Moderate irritating []; Slightly irritating []; Not irritating []
- Classification: Highly corrosive (causes severe burns) []; Corrosive (caused burns) []; Irritating []; Not irritating []
- Method: Other: aerosol application
Hydrogen chloride gas was mixed with a saturated water droplet mist in

	Longley exposure chamber to obtain hydrochloric aerosol atmospheres. The groups of 10 rats were exposed to hydrochloric acid as aerosol at 9.7 - 91.3 mg/L (6,571 - 62,042 ppm) for 5 minutes and of 4.3 - 9.8 mg/L (2,910 - 6,640 ppm) for 30 minutes.
GLP:	Yes <input type="checkbox"/> No <input type="checkbox"/> ? <input checked="" type="checkbox"/>
Test substance:	Hydrochloric acid as aerosol, Matheson company
Remarks:	Results: The exposure caused skin irritation and ulceration with fur discoloration to greenish hue.
Reliability :	(3) Not reliable
Reference:	Darmer et al. (1974a)
 (h)	
Species/strain:	Rat / CFE (Sprague-Dawley derived)
Results:	Highly corrosive <input type="checkbox"/> ; Corrosive <input type="checkbox"/> ; Highly irritating <input type="checkbox"/> ; Irritating <input checked="" type="checkbox"/> ; Moderate irritating <input type="checkbox"/> ; Slightly irritating <input type="checkbox"/> ; Not irritating <input type="checkbox"/>
Classification:	Highly corrosive (causes severe burns) <input type="checkbox"/> ; Corrosive (caused burns) <input type="checkbox"/> ; Irritating <input type="checkbox"/> ; Not irritating <input type="checkbox"/>
Method:	Other Desired concentrations of hydrogen chloride were prepared by hydrogen chloride and pre-dried air. The groups of 10 rats were exposed to hydrochloric acid gas at 30,000 - 57,290 ppm for 5 minutes and 2,078 - 6,681 for 30 minutes.
GLP:	Yes <input type="checkbox"/> No <input type="checkbox"/> ? <input checked="" type="checkbox"/>
Test substance:	Hydrogen chloride, Matheson company
Remarks:	Results: Skin irritation and ulceration with fur discoloration to greenish hue were observed.
Reliability :	(3) Not reliable
Reference:	Darmer et al. (1974a)
 (i)	
Species/strain:	Pig/ Danish Landrace
Results:	Highly corrosive <input type="checkbox"/> ; Corrosive <input type="checkbox"/> ; Highly irritating <input type="checkbox"/> ; Irritating <input checked="" type="checkbox"/> ; Moderate irritating <input type="checkbox"/> ; Slightly irritating <input type="checkbox"/> ; Not irritating <input type="checkbox"/>
Classification:	Highly corrosive (causes severe burns) <input type="checkbox"/> ; Corrosive (caused burns) <input type="checkbox"/> ; Irritating <input type="checkbox"/> ; Not irritating <input type="checkbox"/>
Method:	Other - Test animals: Seven young and fully anaesthetized pigs were used. Five pigs were exposed to the test material and two pigs were treated with alkaline solution (pH 9.1). - Test conditions: Abdominal skin of the pigs was exposed to 0.5N and 1N hydrochloric acid. Biopsies were made and examined. - Examination: punch biopsies were obtained immediately after exposure, at day1 and day 7 from one pig, while knife biopsies of the entire exposed area were obtained immediately after the exposure, at day 4, day 6 and day7.
GLP:	Yes <input type="checkbox"/> No <input type="checkbox"/> ? <input checked="" type="checkbox"/>
Test substance:	Hydrochloric acid
Remarks:	Results: 0.5 N hydrochloric acid showed no dermal changes immediately

	or after day 4 - day 7 but slight alteration was seen at biopsy on day 1. 1N hydrochloric acid presented that collagen fibers just beneath the epidermis were tightly packed and appeared slightly shrunken with increased affinity to eosin immediately and on day 1. No dermal changes were observed on day 4 - day 7 as well as by the application of 0.5 N HCl.
Reliability :	(3) Not reliable
Reference:	Karlsmark T. et al. (1988)
 (j)	
Species/strain:	Pig /Yorkshire
Results:	Highly corrosive []; Corrosive []; Highly irritating []; Irritating [X]; Moderate irritating []; Slightly irritating []; Not irritating []
Classification:	Highly corrosive (causes severe burns) []; Corrosive (caused burns) []; Irritating []; Not irritating []
Method:	Other
Test type:	<i>In vitro</i>
GLP:	Yes [] No [] ? [X]
Test substance:	Hydrochloric acid, Fisher Scientific.
Remarks:	Method: The steady perfusion with hydrochloric acid (4N or 6N) for 8 h were given to the isolated perfused porcine skin flap (n=4/dose), which was raised from a pig from the ventral abdominal region. Results: The skin wrinkled during the course of perfusion treated with 4 and 6 N hydrochloric acid. The light microscopy revealed a homogenous intercellular edema, with some intracellular epidermal edema in the stratum corneum with normal desmosomes. The stratum spinosum showed typical nucleolar pleomorphism, seen with perfused skin. Mitochondrial swelling in the stratum spinosum and stratum basale layers were occasionally present. The basement membrane and the dermis appeared normal. Flaps treated with 6 N hydrochloric acid reacted similar to the 4 N hydrochloric acid. However, there was a slight increase in the occurrence of intercellular epidermal edema and vacuoles.
Reliability :	(3) Not reliable
Reference:	Srikrishna V. and Monteiro-Riviere N.A., (1991)
 (k)	
Species/strain:	Rabbit/(strain not described)
Results:	Highly corrosive []; Corrosive [X]; Highly irritating []; Irritating []; Moderate irritating []; Slightly irritating []; Not irritating []
Classification:	Highly corrosive (causes severe burns) []; Corrosive (caused burns) []; Irritating []; Not irritating []
Method:	Other
	Occlusive exposure for 24 hours was given to three rabbits with 0.5 mL of 31.5% hydrochloric acid.
GLP:	Yes [] No [] ? [X]
Test substance:	Hydrochloric acid
Remarks:	Loosening about edges of scab in 10-14 days showing injury in depth was observed.

Reliability : (4) Not assignable
Reference: Monsanto (1976) cited in European Commission- European Chemical
Bureau (2000) cited in IUCLID

5.2.2 EYE IRRITATION/CORROSION

(a)

Test substance: Hydrochloric acid, CAS No. 7647-01-0
pH: Not described.
Method: OECD 405
Test type: *In vivo*
GLP: Yes [] No [] ? [**X**]
Year: 1988 (when the study completed)
Method remarks: - Application: 100 uL of 10% hydrochloric acid in water was applied into the lower conjunctival sac.
Species: Rabbit
Strain: New Zealand
Sex: Not described
Number of animals per sex per dose: Six animals
Dose used: 10% in water (100uL)
Observation period: 96 h
Scoring method used: Draize scoring criteria
Corrosive: yes/no
Irritation score: Cornea/Iris 0-4 / 0-2
Irritation score: Conjunctivae (redness / Chemosis) 0-3 / 0-4
Overall irritation score: Not described

Classification according to EC (EEC (1983) Annex VI, Part IID of Council Directive 79/831/EEC (19 September 1983))

Tool used to assess score: Application of one drop of 2% sodium fluorescein was given before visual scoring of percentage corneal damage.

Description of lesions (if seen): Not described

Results remarks: Table Results of the application to eyes by 10% HCl in water

Time after end of application (h)	4	24	48	72	96
Mean score of Conjunctivitis (3 maximum)	1.9	2.8	3.0	3.0	2.9
Mean score of Chemosis (4 maximum)	1.0	1.7	2.3	2.3	2.0
Mean score of Iritis (2 maximum)	1.0	1.3	1.7	1.7	1.7
Mean score of Corneal Opacity: (4 maximum)	1.3	2.0	2.7	3.3	3.0
Mean surface of Corneal Damage (100% maximum)	15	59	49	42	28

Conclusions: In this report, hydrochloric acid was classified as 'Risk of serious damage to eyes' according to the EC Criteria (mean over 24/48/72 Hrs of iritis>1.5). Hydrochloric acid may cause severe irritation with corneal injury that may result in permanent impairment of vision.

Data Quality: (2) Reliable with restrictions

Quality Check: Guideline study without detailed documentation.

Reference: Jacobs, G. A., OECD Eye Irritation Tests on Two Strong Acids, J. Am. Coll. Toxicol., 11, 6 (1992)

General Remarks: The calculated value of pH does not correspond to the definition of pH due to high-concentration solution.

(b)

Test substance: Hydrochloric acid, CAS No. 7647-01-0

pH: pH 0 at 5.0 % (w/v) (1.39 mol/L), pH 1.28 at 0.3 % (w/v) (0.08 mol/L)

Test substance remarks: Reagent grade from Fisher Scientific Company, Fair Lawn, NJ

The pH of all solutions was measured with Corning Model 110 pH meter by using the Beckman 4049 standard calomel reference glass electrode with ceramic pin.

Method: Other, modified Draize test

Test type: *In vivo*

GLP: Yes [] No [] ? [X]

Year: 1973 and 1974 (when the study conducted)

Method remarks: Modified Draize testing: The rights eye was used for testing. The lids of the eye were held apart and 0.1 mL of hydrochloric acid solution was instilled onto the central portion of the cornea at 5.0 % (w/v) of pH 0 to 2 groups of 9 animals and 0.3 % (w/v) of pH 1.28 to 2 groups of 6 animals. The lids were then gently brought together for approximately 1 sec. and released. The eyes of each concentration of one group were washed with tap water 30 seconds after treatment. The left eye served as an untreated control.

- Examination: Each test and control eye was examined prior to instillation of the test material and graded at 1h and Days 1, 2, 3 and 7 after instillation. Exposed eyes of the washed group were stained with 1 drop of a 2% fluorescein solution 1h after the initial instillation; exposed eyes of both groups were stained at 24h and at 3 days. The stain was allowed to remain in the eye for 15-20s and then was flushed out with approximately 5-10 mL of sterile isotonic saline.

The eyes were examined grossly and the grades of damage and irritation to the cornea, iris and conjunctiva were recorded at all observation times.

Species: Rabbit

Strain: New Zealand White

Sex: Not described (Unselected as to sex)

Number of animals per sex per dose: 9 animals at 5.0 % (w/v) for unwashed or washed
6 animals at 0.3% (w/v) for unwashed or washed

Dose used: 0.1 mL of 0.3% (w/v) and 5.0 % (w/v)

Observation period: 7 days

Scoring method used: Draize method

Corrosive: yes/no

Irritation score; Cornea/ Iris: 0-4 / 0-2

A cornea opacity of grade 1 or more, iritis of grade 1 or more are considered as positive.

Irritation score; Conjunctivae: (redness / Chemosis) 0-3 / 0-4

Conjunctival redness and chemosis each of grade 2 or more are considered as positive.

Overall irritation score: The following categories used.

Severe: Corneal opacity, iritis and conjunctivitis-positive at 24 h, one or more of the treated eyes still exhibit opacity, iritis, and conjunctivitis at 7th day.

Moderate: Corneal opacity and/or iritis and conjunctivitis- positive at 24 - 72 h, conjunctivitis and iritis remaining at 7th day.

Irritant: Iritis and/or conjunctivitis- positive at 24 h, eyes normal at 3rd day.

Non-irritant: No positive responses in any of the test animals at 24h.

Tool used to assess score: 2% fluorescein solution

Description of lesions (if seen): The area of corneal damage, pannus and keratoconus were not included in the scoring system but were recorded separately. Each portion of the eye was considered independently without reference to the total score.

Results

Table. Number of animals with corneal opacities.

	pH	Unwashed ^{a)}	Washed ^{a)}
0.3% (w/v)	1.28	0/6	0/6
5.0 % (w/v)	0.0	4/9	5/9

a) No. of positive response / No. animals used

Table. Corneal opacities and iritis scores (mean Draize intensity scores \pm S.E.) produced in eyes treated with 5.0 % (w/v) of HCl

		1 h	Day 1	Day 2	Day 3
Corneal opacities	Unwashed	0.3 \pm 0.2	0.3 \pm 0.3	0.8 \pm 0.5	0.2 \pm 0.2
	Washed	0.2 \pm 0.2	0.2 \pm 0.2	0.7 \pm 0.3	0.7 \pm 0.5
Iritis	Unwashed	0.0 \pm 0.0	0.5 \pm 0.3	0.6 \pm 0.3	0.0 \pm 0.0
	Washed	1.3 \pm 0.4	0.7 \pm 0.4	1.0 \pm 0.5	0.5 \pm 0.3

Results remarks: Conjunctivitis was present in all animals tested and lasted through day 7. One-half the animals treated with 5 % (w/v) hydrochloric acid were fluorescein-positive at 24h in both unwashed and washed groups. In unwashed group, 5% hydrochloric acid generated corneal opacities in less than 24h.

Conclusion: Mild to moderate eye irritation occurred by 5% (w/v) hydrochloric acid instillation, while mild irritation by 0.3% solution.

Data Quality: (2) Reliable with restrictions

Quality Check: Comparable to the guideline study with acceptable restrictions

Reference: Murphy, J. C., Osterberg, R.E., Seabaugh, V.M. and Bierbower, G.W., Toxicology, 23, 281-291 (1982)
General Remarks: The authors did not give any categorized result to the tested solutions

(c)

Test substance: Hydrochloric acid, CAS No. 7647-01-0
Test Substance Remarks: The test solution of 0.33 wt% and 3.3 wt% were prepared by dilution 1:45 and 1:4.5 of 15 wt % of hydrochloric acid (normal laboratory quality)
pH: Not described. The calculated value of pH does not correspond to the definition of pH due to high-concentration solution.
Method: Other: according to internal guidelines of Hoechst AG
Test type: *In vivo*
GLP: Yes [] No [**X**] ? []
Year: 1966
Method remarks: - Test animals: Three yellow/silver strain animals were used for each test and kept in single cages during the test under constant observation. The animals received standard ALTROMIN K of the Altrogge Company in Lage/Lippe and effluent as feed. The animals were controlled for any irritation phenomena occurring 1, 3, 7, 24 and 48 hours after application.
- Application: A single application of 0.1 mL of test solution was given into the conjunctival sac of the rabbit eye.
Species/strain: Rabbit
Strain: Not described
Sex: Not described
Number of animals per sex per dose: Three animals
Dose used: 0.1 mL of 0.33 and 3.3 wt% of hydrochloric acid
Observation period: 48 h
Scoring method used: Not conducted
Corrosive: Not described
Irritation score: Cornea/Iris: Not conducted
Irritation score: Conjunctivae: Not conducted
Overall irritation score: Not conducted
Tool used to assess score: No
Description of lesions (if seen): See Results Remarks
Results Remarks: No findings were observed in the eyes treated with 0.33 wt% of hydrochloric acid solution. In 3.3 wt% treatment group, very slight to slight reddening, and a slight glassy to more marked, somewhat opaque swelling of the conjunctiva, and a slight corneal opacity were observed.
Conclusions: No eye irritation was caused by the application of 0.33 wt% hydrochloric acid solution as reported. Mild irritation occurred at 3.3 wt% hydrochloric acid solution.
Remarks: This experiment for HCl was conducted as a positive control for other test substances.
The concentration of test solution could be calculated as follows;
 1.075 g/cm^3 (density of 15 wt%) x 1000 (L) x 0.15/36.5
= 4.42 mol/L
0.33 wt% of hydrochloric acid = 4.42 mol/L /45 = 0.1 mol/L

3.3 wt% of hydrochloric acid = 4.42 mol/L /4.5 = 0.98 mol/L

Data Quality: (2) Reliable with restrictions

Quality Check: Comparable to the guideline study with acceptable restrictions

Reference: Hoechst AG, (1966) Report 150/66

(d)

Species/strain: Rabbit/New Zealand Albino

Sex: Male/Female

Dose used: 0.003, 0.01, 0.03 and 0.10 mL of 5% of hydrochloric acid

Observation period: 21 days

Scoring method used: Draize score

Results: Highly corrosive []; Corrosive []; Highly irritating [**X**]; Irritating []; Moderate irritating []; Slightly irritating []; Not irritating []

Classification: Irritating []; Not irritating []; Risk of serious damage to eyes []

Method: Other, modified Draize Test

Three young adult rabbit were used for the treatment. The test material placed directly on the cornea. Only one eye of each animal was used in a test; the other eye being untreated served as a control. Eyes were examined and scored according to the scale of Draize 1, 3, 7, 14 and 21 days after dosing.

Maximum score was not specified in the report.

GLP: Yes [] No [**X**] ? []

Results:

Table Average maximum Draize score

Dose (mL)	0.003	0.01	0.03	0.10
Average maximum Draize score	1 ± 1	0 ± 0	90 ± 0	- ^a
Number of days to return to normal	Animal 1	1	1	>21
	Animal 2	1	1	>21
	Animal 3	2	1	>21

^a: Animals sacrificed on Day2 or Day3 due to extent of injuries which prevented scoring

Results remarks: The application of 0.01 mL of 5% hydrochloric acid caused only slight irritation that cleared within a few days.

Conclusions: 0.03 and 0.10 mL of 5% hydrochloric acid causes severe irritation or corrosion.

Remarks: In this experiment, the irritation of several substances was examined.

Reliability : (3) Not reliable

Reference: Griffith et al. (1980)

(e)

Species/strain: Rabbit

Results: Highly corrosive []; Corrosive [**X**]; Highly irritating []; Irritating []; Moderate irritating []; Slightly irritating []; Not irritating []

Classification: Irritating []; Not irritating []; Risk of serious damage to eyes []

Method: Other

Twenty-eight adult animals were used for experiment. The applications of 10 uL of 0.000001 - 1 N hydrochloric acid were given to the upper limbus corneae. Five or thirty minutes after application, the animals were killed and the corneas fixed were examined with Stereoscan.

GLP: Yes [] No [**X**] ? []

Test substance: Hydrochloric acid

Results: Concentration of 0.001-1 N HCl result in cell desquamation with destruction of all microstructure on the cell surface and even cause the dissolution of the cytoplasm.

Reaction with hydrochloric acid for 5 minutes:

0.1 - 1N (3,646 - 36,460 mg/L) :
severe damage with the change to the lower lying cell.

0.001- 0.01N (36.46 - 364.6 mg/L):
desquamation of the surface epithelial cells.

0.0001 N: did not produce signs of desquamation, massive cell damage
The morphological alterations in the corneal epithelium 30 min after application of hydrochloric acid were not essentially different from those after a reaction of 5 min.

Reliability : (3) Not reliable

Reference: Brewitt & Honegger (1979)

(f)

Species/strain: Rabbit

Results: Highly corrosive []; Corrosive [**X**]; Highly irritating []; Irritating []; Moderate irritating []; Slightly irritating []; Not irritating []

Classification: Irritating []; Not irritating []; Risk of serious damage to eyes []

Method: Other

GLP: Yes [] No [] ? [**X**]

Test substance: Hydrochloric acid

Remarks: Contact with 0.5 mL of an approx. 1% (38 mg/L) solution for 5 minutes caused corneal scarring.

Reliability : (3) Not reliable

Reference: Harley R.D. (1952)

(g)

Species/strain: Rabbit, guinea pig

Results: Highly corrosive []; Corrosive []; Highly irritating []; Irritating [**X**]; Moderate irritating []; Slightly irritating []; Not irritating []

Classification: Irritating []; Not irritating []; Risk of serious damage to eyes []

Method: Other

GLP: Yes [] No [**X**] ? []

Test substance: Hydrogen chloride, generated by mixing commercial C.P. hydrochloric acid with 10-15 times its volume of concentrated sulfuric acid.

Remarks: The exposure to hydrogen chloride in concentrations ranging from 0.05-20.5 mg/L for periods ranging form 5-7200 minutes caused irritation to eyes of animals.

Reliability : (3) Not reliable

Reference:	Machle, W. et al. (1942)
 (h)	
Species/strain:	Mouse/CF-1 (ICR derived)
Results:	Highly corrosive []; Corrosive []; Highly irritating []; Irritating [X]; Moderate irritating []; Slightly irritating []; Not irritating []
Classification:	Irritating []; Not irritating []; Risk of serious damage to eyes []
Method:	Other Hydrogen chloride gas was mixed with a saturated water droplet mist in Longley exposure chamber to obtain hydrochloric acid aerosol atmospheres and the tested concentration was analysed by a chloride ion specific electrode analysis. The groups of 10 mice were exposed to hydrochloric acid aerosol at 13.3 - 27.6 mg/L (9,058 – 18, 773 ppm) for 5 minutes and 1.8 - 6.5 mg/L (1,204 - 4,432 ppm) for 30 minutes.
GLP:	Yes [] No [] ? [X]
Test substance:	Hydrochloric acid as aerosol
Remarks:	Results: There was evidence of corneal erosion and clouding in animals.
Reliability :	(3) Not reliable
Reference:	Darmer et al. (1974a)
 (i)	
Species/strain:	Mouse/CF-1 (ICR derived)
Results:	Highly corrosive []; Corrosive []; Highly irritating []; Irritating [X]; Moderate irritating []; Slightly irritating []; Not irritating []
Classification:	Irritating []; Not irritating []; Risk of serious damage to eyes []
Method:	Other Desired concentrations of hydrogen chloride were prepared by hydrogen chloride and pre-dried air. The groups of 15 mice were exposed to hydrochloric acid gas at 3,200 - 30,000 ppm for 5 minutes and 410 - 5,363 ppm for 30 minutes.
GLP:	Yes [] No [] ? [X]
Test substance:	Hydrochloric acid gas
Remarks:	Results: There was evidence of corneal erosion and clouding in animals.
Reliability :	(3) Not reliable
Reference:	Darmer et al. (1974a)
 (j)	
Species/strain:	Rat/ CFE (Sprague-Dawley derived)
Results:	Highly corrosive []; Corrosive []; Highly irritating []; Irritating [X]; Moderate irritating []; Slightly irritating []; Not irritating []
Classification:	Irritating []; Not irritating []; Risk of serious damage to eyes []
Method:	Other Hydrogen chloride gas was mixed with a saturated water droplet mist in Longley exposure chamber to obtain hydrochloric aerosol atmospheres. The groups of 10 rats were exposed to hydrochloric acid as aerosol at 9.7 - 91.3 mg/L (6,571 - 62,042 ppm) for 5 minutes and of 4.3 - 9.8 mg/L (2,910 - 6,640 ppm) for 30 minutes.

GLP:	Yes [] No [] ? [X]
Test substance:	Hydrochloric acid as aerosol
Remarks:	Results: There was evidence of corneal erosion and clouding in animals.
Reliability :	(3) Not reliable
Reference:	Darmer et al. (1974a)
 (k)	
Species/strain:	Rat/ CFE (Sprague-Dawley derived)
Results:	Highly corrosive []; Corrosive []; Highly irritating []; Irritating [X]; Moderate irritating []; Slightly irritating []; Not irritating []
Classification:	Irritating []; Not irritating []; Risk of serious damage to eyes []
Method:	Other Desired concentrations of hydrogen chloride were prepared by hydrogen chloride and pre-dried air. The groups of 10 rats were exposed to hydrochloric acid gas at 30,000 - 57,290 ppm for 5 minutes and 2,078 - 6,681 for 30 minutes.
GLP:	Yes [] No [] ? [X]
Test substance:	Hydrochloric acid gas
Remarks:	Results: There was evidence of corneal erosion and clouding in animals.
Reliability :	(3) Not reliable
Reference:	Darmer et al. (1974a)
 (l)	
Species/strain:	Rabbit
Results:	Highly corrosive []; Corrosive [X]; Highly irritating []; Irritating []; Moderate irritating []; Slightly irritating []; Not irritating []
Classification:	Irritating []; Not irritating []; Risk of serious damage to eyes []
Method:	other
GLP:	Yes [] No [] ? [X]
Year:	1976
Test substance:	Hydrochloric acid, 31.5% in water (20 degree Baume)
Remarks:	Method: Three animals were used and 0.1 mL of undiluted 31.5% of hydrochloric acid was instilled. Result: 31.5% of hydrochloric acid was corrosive in 15 sec.
Reliability :	(4) Not assignable
Reference:	Monsanto (1976) cited in European Commission- European Chemical Bureau (2000)
 (m)	
Species/strain:	Rabbit
Results:	Highly corrosive []; Corrosive []; Highly irritating []; Irritating [X]; Moderate irritating []; Slightly irritating []; Not irritating []
Classification:	Irritating []; Not irritating []; Risk of serious damage to eyes []
Method:	no data
GLP:	Yes [] No [X] ? []
Test substance:	Hydrochloric acid
Remarks:	Eye damage occurred following contact with solutions of pH < 3 [> 0.004%].
Reliability :	(4) Not Assignable

Reference: BIBRA (1990)

(n)

Species/strain: Rabbit

Results: Highly corrosive []; Corrosive []; Highly irritating []; Irritating []; Moderate irritating [**X**]; Slightly irritating []; Not irritating []

Classification: Irritating [**X**]; Not irritating []; Risk of serious damage to eyes []

Method: no data

GLP: Yes [] No [] ? [**X**]

Test substance: No data

Remarks: 5 mg/30 secondi su coniglio danno irritazione moderata

Reliability : (4) Not assignable

Reference: European Commission- European Chemical Bureau (2000)

5.3 SKIN SENSITISATION

(a)

Type: Mouse ear swelling test

Species/strain: Mouse

Results: Sensitising []; Not sensitising [**X**]; ambiguous []

Classification: Sensitising []; Not sensitising []

Method: other

GLP: Yes [] No [] ? [**X**]

Test substance: 1% hydrochloric acid in 70% ethanol.

Remarks: Four consecutive daily-uncovered applications of 1% HCl solution in 70% ethanol to the abdominal skin were followed 7 days later by a challenge with a 5% uncovered application to the ear. No evidence of sensitisation was seen.

No. of animals with skin reaction at challenge:
Treated: Not stated Control group: Not stated

Reliability : (3) Not reliable

Reference: Gad et al., (1986)

(b)

Type: Guinea pig maximization test

Species/strain: guinea pig

Results: Sensitising []; Not sensitising [**X**]; ambiguous []

Classification: Sensitising []; Not sensitising []

Method: other

GLP: Yes [] No [] ? [**X**]

Test substance: 1% hydrochloric acid in ethanol.

Remarks: Sensitisation was not induced in 15 guinea pigs that were given two intradermal injections and a covered application (48-hr) of 1% HCl (in ethanol of undefined concentration) and challenged 2 weeks later by a similar 24-hr covered.

No. of animals with skin reaction at challenge:
Treated: 0/15 Control group: 0/6

Reliability : (3) Not reliable

Reference: Gad et al.(1986)

5.4 REPEATED DOSE TOXICITY

(1)

Test Substance

Identity (purity): Hydrogen chloride (>99.99%), CAS No. 7647-01-0

Remarks:

Source: Matheson Gas Company (Code Number 9/82-426)

Method

Method/guideline followed:

Test type: 90-day repeated inhalation study

GLP: Yes [X] No []

Year: 1983

Species: Mouse

Strain: B₆C₃F₁/CrI Br

Route of administration: inhalation (aerosol)

Duration of test: 91 days

Doses/concentration levels: 10, 20, 50 ppm (nominal)

Sex: male and female

Exposure period: 90 days

Frequency of treatment: 6 hours/day, 5 days/week

Control group and treatment: yes, concurrent vehicle: air

Post exposure observation period: one day

Statistical methods:

Parametric data: ANOVA and Turkey's (equal populations) or Scheffe's (unequal populations) Test of multiple comparison

non-Parametric data: Kruskal-Wallis ANOVA and test of multiple comparison

Discontinuous data: CHI-square or Fischer's Exact Probability test

Remarks: This experiment was performed in compliance with FDA-GLP (21CFR58).

- *Test Subjects*

- ◆ *Age at study initiation:* 6 - 7 weeks of age

- ◆ *No. of animals per sex per dose:* 10 males and 10 females per dose

- *Study Design*

- ◆ *Vehicle:* air

- ◆ *Satellite groups and reasons they were added:*

Ten males and 10 females of each dose group were sacrificed on the following day of the fourth exposure and microscopically examined for the damage of respiratory tract.

Five males of each dose were sacrificed on the following day of the fourth (five males) and the 90th (five males) exposure and the fixed cranial specimen were shipped to the sponsor.

◆ *Clinical observations performed and frequency:*

Each animal was observed at least twice daily for incidence of mortality and clinical signs.

Body weight and food consumption were individually measured once a week.

Urine samples collected from 10 male and 10 female animals were analyzed and the following parameters were determined [volume, appearance, occult blood, specific gravity, protein, pH, ketone, glucose].

Blood samples collected from orbital sinus were measured for the following parameters for hematology [erythrocyte count, hemoglobin, hematocrit, total and differential leukocyte counts, platelet and thrombocyte counts, mean corpuscular volume, mean corpuscular hemoglobin, and mean corpuscular hemoglobin concentration].

Serum samples collected from abdominal aorta were measured for the following parameters for blood chemistry [glutamic pyruvic transaminase, urea nitrogen, total bilirubin, glucose, inorganic phosphorus, calcium, and alkaline phosphatase].

◆ *Organs examined at necropsy:*

Each animal was pathologically examined at necropsy and following organs were weighed [brain, heart, kidney, liver, and ovary/testis].

And the following tissues of the control and the highest dose group and [nasal turbinates, trachea, lung] of the low and the mid dose group were examined microscopically [nasal turbinates, trachea, lung, brain, heart, kidney, liver, testis, adrenal, duodenum, eyes and optic nerve, mesenteric lymph nodes, aorta, sternum bone, ear canal, bone marrow, colon, epididymis, jejunum, mandibular lymph nodes, oviducts, ovaries, prostate, skin, pituitary glands, spinal cord, sciatic nerve, peripheral nerve, salivary gland, spleen, thyroid glands, urinary bladder, uterus, thymus, fore and glandular stomach, pancreas, parathyroid, skeletal muscle, seminal vesicle, tongue, femur bone, cecum, esophagus, ileum, lacrimal gland, mammary glands, larynx].

Results

NOAEL (NOEL): 20 ppm

LOAEL (LOEL): 50 ppm

Actual dose received by dose level by sex (if known):

Time weighted average of analytical concentration for low, middle and high dose group were 9.8, 19.1 and 46.7 ppm, respectively. Each test chamber was sampled approximately once per hour.

Toxic response/effects by dose level:

One male of the highest dose group and one male of the low dose group found dead on the 12th and 20th day of the study, respectively. One female sacrificed on the 92nd day in extremis in the highest dose group.

On the 90th days, significant decrease in body weight was observed in 50 ppm, and decrease in food consumption was observed in 50ppm. Cheilitis with accumulating of hemosiderin-laden macrophages at 50 ppm and

eosinophilic globules in epithelium of nasal turbinates in treated mice were observed. Decrease in liver weight was noted in 50ppm male mice. No biologically significant difference was observed in urinalysis, hematology and serum chemistry.

Remarks:

Body weight:

Summary of Body weight data (B₆C₃F₁ mouse)

week	Mean Body weight (g)							
	male				female			
	cont.	10ppm	20ppm	50ppm	cont.	10ppm	20ppm	50ppm
ini.	21.9	21.9	21.7	21.9	18.5	18.5	18.9	18.7
1	23.3	23.5	23.1	22.1	19.7	19.8	19.8	18.7
2	23.5	23.5	23.0	20.7**	19.4	19.4	19.6	17.2**
3	25.8	26.3	25.5	24.1*	22.2	22.6	21.8	20.6
4	26.7	26.9	26.5	24.4**	22.9	23.4	22.7	21.0*
5	27.7	28.1	27.0	24.7**	23.8	23.8	23.2	21.2**
6	28.5	28.4	27.5	25.5**	24.7	24.1	23.5	21.8**
7	28.7	28.4	27.8	26.0**	25.0	25.2	24.1	22.3**
8	28.2	28.4	28.2	27.0	25.0	24.9	24.6	23.1*
9	29.0	29.1	28.6	27.5*	25.5	25.8	25.2	23.3*
10	29.6	29.9	29.0	26.8**	25.9	26.3	26.1	22.6**
11	30.3	30.1	29.1	27.6**	26.2	26.5	26.0	24.5
12	30.3	29.9	29.5	27.8**	27.0	26.7	26.3	24.0**
13	31.2	31.2	30.3	28.5**	26.9	26.4	26.5	25.0
fin. ^{a)}	26.4	26.7	25.7	23.5**	23.4	22.0	22.1	20.5**
gain	9.3	9.3	8.6	6.5**	8.4	7.8	7.6	6.5*

*: Statistically significant difference from the control at the 95% level of confidence (p<0.05).

** : Statistically significant difference from the control at the 99% level of confidence (p<0.01).

a): Fasted animal.

Food consumption:

Summary of food consumption data (B₆C₃F₁)

week	Mean food consumption (g)							
	male				female			
	cont.	10ppm	20ppm	50ppm	cont.	10ppm	20ppm	50ppm
1	38.9	40.0	41.6	36.4	38.5	44.3	40.2	34.3
2	50.1	49.1	49.1	41.6*	49.5	56.6	45.6	37.8
3	29.4	29.3	32.8	24.5	35.5	37.5	32.8	23.8*
4	45.6	49.8	50.3	42.8	57.7	56.8	49.6	38.6**
5	45.6	51.6	55.7*	43.1	55.2	57.8	50.0	43.0
6	53.4	54.9	54.8	42.3**	57.2	53.0	55.8	42.9*
7	50.1	48.4	46.1	38.3**	50.4	54.1	48.4	36.4**
8	51.9	51.6	50.3	38.9**	53.9	55.5	55.5	38.2**
9	46.6	51.0	52.0	36.9**	54.8	53.2	50.3	35.6**
10	49.3	54.4	51.6	39.1**	56.0	53.0	53.5	39.3**
11	47.4	53.2	50.6	36.6*	55.0	55.2	50.0	34.4**
12	52.3	52.2	49.9	36.6**	53.7	57.1	48.4	35.1**
13	48.8	50.8	53.4	41.2	51.0	58.1	51.6	38.4*

*: Statistically significant difference from the control at the 95% level of confidence (p<0.05).

** : Statistically significant difference from the control at the 99% level of confidence (p<0.01).

Organ weight changes:

Summary of Organ weight data(B₆C₃F₁ mouse)

Organ	Mean Organ weight (g)							
	male				female			
	cont.	10ppm	20ppm	50ppm	cont.	10ppm	20ppm	50ppm
Brain	0.48	0.50	0.48	0.46	0.50	0.50	0.49	0.48
Heart	0.18	0.20	0.17	0.17	0.14	0.14	0.14	0.14
Kidney	0.53	0.53	0.50	0.48	0.36	0.34	0.34	0.35
Liver	1.35	1.30	1.21	1.15*	1.13	1.02	1.01	1.00
Testis	0.24	0.24	0.23	0.21	-	-	-	-
Ovary	-	-	-	-	0.02	0.02	0.02	0.02

*: Statistically significant difference from the control at the 95% level of confidence (p<0.05).

Histopathology incidence and severity :

Summary of Histopathology data(B₆C₃F₁ mouse)

Organ	Incidence							
	male				female			
	cont.	10ppm	20ppm	50ppm	cont.	10ppm	20ppm	50ppm
Eosinophilic Globules of Nasal Turbinate	0/10	4/10	0/10	3/10	0/10	4/10	6/10	7/10
Ulcerative cheilitis of Lip	-	-	-	4/7	-	-	-	1/10
Pigmented macrophages of Lip	-	-	-	7/7	-	-	-	1/10

Conclusions

As histopathologically inflammatory changes were observed in the lowest dose, NOAEL could not be determined. LOAEL is determined to be 10 ppm. NOAEL except for the effects of irritation have been determined to be 10ppm for B6C3F1 mice.

Remarks: No exposure related change were observed in the reproductive organs examined histo-pathologically.

Data Quality

Reliability : (2) Reliable with restrictions

Flag: Critical study for SIDS

Quality Check: Comparable to the guideline study with acceptable restrictions

References :

CIIT (1984), Ninety-day Inhalation Toxicity Study of Hydrogen chloride gas In B6C3F₁ mice, Sprague-Dawley and Fischer-344 rats., ToxiGenics, 420-1087.

Other

Last changed:

Order number for sorting:

Remarks

(2)

Test Substance

Identity (purity): Hydrogen chloride (>99.99%), CAS No. 7647-01-0

Remarks: *(Use for any pertinent, test substance-specific remarks.)*

Source: Matheson Gas Company (Code Number 9/82-426)

Method

Method/guideline followed:

Test type: 90-day repeated inhalation study

GLP: Yes [X] No []

Year (*study performed*): 1983

Species: Rat

Strain: Crl:CD(SD)Br

Route of administration: inhalation (aerosol)
Duration of test: 91 days
Doses/concentration levels: 10, 20, 50 ppm (nominal)
Sex: male and female
Exposure period: 90 days
Frequency of treatment: 6 hours/day, 5 days/week
Control group and treatment: yes, concurrent vehicle: air
Post exposure observation period: one day
Statistical methods:
Parametric data: ANOVA and Turkey's (equal populations) or Scheffe's (unequal populations) Test of multiple comparison
non-Parametric data: Kruskal-Wallis ANOVA and test of multiple comparison
Discontinuous data: CHI-square or Fischer's Exact Probability test
Remarks: This experiment was performed in compliance with FDA-GLP (21CFR58).

● *Test Subjects*

- ◆ *Age at study initiation:* 6 - 7 weeks of age
- ◆ *No. of animals per sex per dose:* 10 males and 10 females per dose

◆ *Study Design*

◆ *Vehicle:* air

◆ *Satellite groups and reasons they were added:*

Ten males and 10 females of each dose group were sacrificed on the following day of the fourth exposure and microscopically examined for the damage of respiratory tract.

Five males of each dose were sacrificed on the following day of the fourth (five males) and the 90th (five males) exposure and the fixed cranial specimen were shipped to the sponsor.

◆ *Clinical observations performed and:*

Each animal was observed at least twice daily for incidence of mortality and clinical signs.

Body weight and food consumption were individually measured once a week.

Urine samples collected from 10 male and 10 female animals were analyzed and the following parameters were determined [volume, appearance, occult blood, specific gravity, protein, pH, ketone, glucose].

Blood samples collected from orbital sinus were measured for the following parameters for hematology [erythrocyte count, hemoglobin, hematocrit, total and differential leukocyte counts, platelet and thrombocyte counts, mean corpuscular volume, mean corpuscular hemoglobin, and mean corpuscular hemoglobin concentration].

Serum samples collected from abdominal aorta were measured for the following parameters for blood chemistry [glutamic pyruvic transaminase, urea nitrogen, total bilirubin, glucose, inorganic phosphorus, calcium, and alkaline phosphatase].

◆ *Organs examined at necropsy:*

Each animal was pathologically examined at necropsy and following organs were weighed [brain, heart, kidney, liver, and ovary/testis].

And the following tissues of the control and the highest dose group and [nasal turbinates, trachea, lung] of the low and the mid dose group were examined microscopically [nasal turbinates, trachea, lung, brain, heart, kidney, liver, testis, adrenal, duodenum, eyes and optic nerve, mesenteric lymph nodes, aorta, sternum bone, ear canal, bone marrow, colon, epididymis, jejunum, mandibular lymph nodes, oviducts, ovaries, prostate, skin, pituitary glands, spinal cord, sciatic nerve, peripheral nerve, salivary gland, spleen, thyroid glands, urinary bladder, uterus, thymus, fore and glandular stomach, pancreas, parathyroid, skeletal muscle, seminal vesicle, tongue, femur bone, cecum, esophagus, ileum, lacrimal gland, mammary glands, larynx].

Results

NOAEL (NOEL): 20 ppm

LOAEL (LOEL): 50 ppm

◆ Actual dose received by dose level by sex (if known):

Time weighted average of analytical concentration for low, middle and high dose group were 9.8, 19.0 and 46.7 ppm (SD rat), respectively. Each test chamber was sampled approximately once per hour.

◆ Toxic response/effects by dose level:

One female of the highest dose group found dead on the 4th day of the treatment. Slight and transient decrease in food consumption was observed in 10 ppm female, which was not considered to be dose related, and 50ppm male. Minimal to mild rhinitis was observed in the anterior portion of the nasal cavity at the histopathological observation above 20 ppm. No biologically significant difference was observed in urinalysis, hematology and serum chemistry.

◆ Statistical results

Remarks:

Food/water consumption:

Summary of food consumption data (SD rat)

week	Mean food consumption (g)							
	male				female			
	cont.	10ppm	20ppm	50ppm	cont.	10ppm	20ppm	50ppm
1	119	132	128	119	98	89	100	93
2	160	158	159	144*	115	102	114	112
3	167	165	165	152	118	93**	119	119
4	126	123	125	110	88	84	82	90
5	170	194	176	162	121	115	127	124
6	181	176	179	172	133	127	136	144
7	175	173	181	167	124	107	128	128
8	168	172	177	159	118	108	123	123
9	172	167	178	161	115	109	124	122
10	171	162	178	163	117	109	120	125
11	173	165	176	159	116	102	116	116
12	169	157	171	173	109	106	115	116
13	169	164	166	153	109	99	118	112

*: Statistically significant difference from the control at the 95% level of confidence (p<0.05).

** : Statistically significant difference from the control at the 99% level of confidence (p<0.01).

Histopathology incidence and severity :

Summary of Histopathology data((SD rat)

Organ	Incidence							
	male				female			
	cont.	10ppm	20ppm	50ppm	cont.	10ppm	20ppm	50ppm
Rhinitis in the nasal cavity	0/10	0/10	3/10	5/10	0/10	0/10	1/10	4/10

Conclusions

As histopathologically inflammatory changes were observed above 20 ppm, NOAEL was determined to be 10 ppm.

Remarks: No exposure related change were observed in the reproductive organs examined histo-pathologically.

Data Quality

Reliability : (2) Reliable with restrictions

Flag: Critical study for SIDS

Quality Check: Comparable to the guideline study with acceptable restrictions

References

CIIT (1984), Ninety-day Inhalation Toxicity Study of Hydrogen chloride gas In B6C3F₁ mice, Sprague-Dawley and Fischer-344 rats., ToxiGenics, 420-1087.

Other

Last changed:
Order number for sorting:
Remarks

(3)

Test Substance

Identity (purity): Hydrogen chloride (>99.99%), CAS No. 7647-01-0

Remarks:

Source: Matheson Gas Company (Code Number 9/82-426)

Method

Method/guideline followed:

Test type: 90-day repeated inhalation study

GLP: Yes [X] No []

Year: 1983

Species: Rat

Strain: F-344/Crl Br

Route of administration: inhalation (aerosol)

Duration of test: 91 days

Doses/concentration levels: 10, 20, 50 ppm (nominal)

Sex: male and female

Exposure period: 90 days

Frequency of treatment: 6 hours/day, 5 days/week

Control group and treatment: yes, concurrent vehicle: air

Post exposure observation period: one day

Statistical methods:

Parametric data: ANOVA and Turkey's (equal populations) or Scheffe's (unequal populations) Test of multiple comparison

non-Parametric data: Kruskal-Wallis ANOVA and test of multiple comparison

Discontinuous data: CHI-square or Fischer's Exact Probability test

Remarks: This experiment was performed in compliance with FDA-GLP (21CFR58).

● *Test Subjects*

◆ *Age at study initiation:* 6 - 7 weeks of age

◆ *No. of animals per sex per dose:* 10 males and 10 females per dose

● *Study Design*

◆ *Vehicle:* air

◆ *Satellite groups and reasons they were added:*

Ten males and 10 females of each dose group were sacrificed on the following day of the fourth exposure and microscopically examined for the damage of respiratory tract.

Five males of each dose were sacrificed on the following day of the fourth (five males) and the 90th (five males) exposure and the fixed cranial specimen were shipped to the sponsor.

◆ *Clinical observations performed and frequency:*

Each animal was observed at least twice daily for incidence of mortality and clinical signs.

Body weight and food consumption were individually measured once a week.

Urine samples collected from 10 male and 10 female animals were analyzed and the following parameters were determined [volume, appearance, occult blood, specific gravity, protein, pH, ketone, glucose].

Blood samples collected from orbital sinus were measured for the following parameters for hematology [erythrocyte count, hemoglobin, hematocrit, total and differential leukocyte counts, platelet and thrombocyte counts, mean corpuscular volume, mean corpuscular hemoglobin, and mean corpuscular hemoglobin concentration].

Serum samples collected from abdominal aorta were measured for the following parameters for blood chemistry [glutamic pyruvic transaminase, urea nitrogen, total bilirubin, glucose, inorganic phosphorus, calcium, and alkaline phosphatase].

◆ *Organs examined at necropsy:*

Each animal was pathologically examined at necropsy and following organs were weighed [brain, heart, kidney, liver, and ovary/testis].

And the following tissues of the control and the highest dose group and [nasal turbinates, trachea, lung] of the low and the mid dose group were examined microscopically [nasal turbinates, trachea, lung, brain, heart, kidney, liver, testis, adrenal, duodenum, eyes and optic nerve, mesenteric lymph nodes, aorta, sternum bone, ear canal, bone marrow, colon, epididymis, jejunum, mandibular lymph nodes, oviducts, ovaries, prostate, skin, pituitary glands, spinal cord, sciatic nerve, peripheral nerve, salivary gland, spleen, thyroid glands, urinary bladder, uterus, thymus, fore and glandular stomach, pancreas, parathyroid, skeletal muscle, seminal vesicle, tongue, femur bone, cecum, esophagus, ileum, lacrimal gland, mammary glands, larynx].

Results

NOAEL (NOEL): 20 ppm

LOAEL (LOEL): 50 ppm

◆ Actual dose received by dose level by sex (if known):

Time weighted average of analytical concentration for low, middle and high dose group were 9.8, 19.1 and 46.8 ppm, respectively. Each test chamber was sampled approximately once per hour.

◆ Toxic response/effects by dose level:

NO death observed during the test period.

Significant decrease in body weight was observed in 50 ppm male on the 90th days, and decrease in food consumption was observed in 20 and 50ppm. No biologically significant difference was observed in urinalysis, haematology and serum chemistry. Minimal to mild rhinitis were observed in the anterior portion of the nasal cavity at the histopathological observation in all treatment groups.

Remarks:

Body weight:

Summary of Body weight data (F344 rat)

week	Mean Body weight (g)							
	male				female			
	cont.	10ppm	20ppm	50ppm	cont.	10ppm	20ppm	50ppm
ini.	111	111	111	112	95	95	96	96
1	140	137	139	134	113	112	113	110
2	168	165	166	158*	125	122	124	119
3	192	189	191	181*	133	132	133	129
4	212	208	208	201	142	142	139	139
5	225	219	220	213*	147	148	145	142
6	240	233	233	224**	153	154	150	148
7	252	244	246	234**	158	159	155	152
8	254	254	253	244	161	165	160	156
9	264	263	264	256	165	168	164	162
10	273	271	271	264	168	172	166	165
11	279	277	278	270	171	174	169	165
12	287	266**	285	275	175	178	174	169
13	291	287	287	280	176	179	174	169
fin. ^{a)}	279	275	273	264	166	167	162	159
gain	179	176	176	168	81	84	78	73*

*: Statistically significant difference from the control at the 95% level of confidence (p<0.05).

** : Statistically significant difference from the control at the 99% level of confidence (p<0.01).

a): Fasted animal.

Food/water consumption:

Summary of food consumption data (F344 rat)

week	Mean food consumption (g)							
	male				female			
	cont.	10ppm	20ppm	50ppm	cont.	10ppm	20ppm	50ppm
1	91	87	84*	76**	72	68	66**	58**
2	108	105	106	100*	78	77	80	76
3	78	78	73	67**	56	59	56	54
4	114	113	112	112	79	80	75	82
5	119	117	114	114	83	84	84	85
6	110	110	111	109	76	80	77	82
7	113	108	111	109	79	78	73	80
8	112	109	108	104	80	79	77	79
9	105	109	109	114**	91	81	81	82
10	105	107	107	108	75	78	75	81
11	102	108	105	107	71	75	72	75
12	102	109	106	104	73	79	75	76
13	99	107	103	104	73	75	73	78

*: Statistically significant difference from the control at the 95% level of confidence (p<0.05).

**: Statistically significant difference from the control at the 99% level of confidence (p<0.01).

Histopathology incidence and severity :

Summary of Histopathology data((F344 rat)

Organ	Incidence							
	male				female			
	cont.	10ppm	20ppm	50ppm	cont.	10ppm	20ppm	50ppm
Rhinitis in the nasal cavity	0/10	3/10	7/10	9/10	0/10	3/10	5/10	6/10

Conclusions

As histopathologically inflammatory changes were observed in the lowest dose, NOAEL could not be determined. LOAEL is determined to be 10 ppm. . NOAEL except for the effects of irritation have been determined to be 10ppm for F344 rat.

Remarks: No exposure related change were observed in the reproductive organs examined histo-pathologically.

Data Quality

Reliability : (2) Reliable with restrictions

Quality Check: Comparable to the guideline study with acceptable restrictions

References

CIIT (1984) Ninety-day Inhalation Toxicity Study of Hydrogen chloride gas In B6C3F₁ mice, Sprague-Dawley and Fischer-344 rats., ToxiGenics, 420-1087.

Other

Last changed:

Order number for sorting:

Remarks

(4)

Species/strain: Gunia pig

Sex: Female []; Male []; Male/Female []; No data []

Route of Administration: nose only inhalation

Exposure period: 28 days

Frequency of treatment: 2 h/day, 5 days/week

Post exposure observation period: No

Dose: 0.15 mg/m³

Control group: Yes []; No []; No data [];
Concurrent no treatment []; Concurrent vehicle []; Historical []

NO(A)EL: N/A

LO(A)EL: N/A

Results: No abnormal clinical sign observed. No abnormality found at gross necropsy compared to the control.

Method: Other

A group of 8 animals were used for the experiment.

GLP: Yes [] No [] ? []

Test substance: Hydrogen chloride, generated by adding concentrated sulfuric acid to sodium chloride

Reliability : (3) Not reliable

Reference: Kirsch, V. H. and Drabke, P. (1982)

(5)

Species/strain: Rat / Wistar (Weanling)

Sex: Female []; Male []; Male/Female []; No data []

Route of Administration: Oral feed

Exposure period: 7 weeks

Frequency of treatment: Daily

Post exposure observation period: No

Dose: 280, 420, 560 mmol HCl/kg diet

Control group: Yes []; No []; No data [];
Concurrent no treatment []; Concurrent vehicle []; Historical []

NOAEL: 560 mmol HCl/kg diet

LOAEL: N/A

Results:

Table

mmol HCl/kg diet	Control (0)	280	420	560
pH of diets ^{#1}	5.90	4.60	4.10	3.50
Food intake (g/day)	14.6	14.2	14.6	14.4
Dose (mg/animal/day) ^{#2}	0	145	224	294
Water intake (mL/day)	28.9	33.6*	36.5*	36.3*
^{#1} : HCl was diluted (1:5 (v/v)) with distilled water, then added to the diet. ^{#2} : Calculated from food intake *: P<0.001				

Water intake was significantly increased by hydrochloric acid supplementation compared to the control. There was no significant treatment effect on food intake, bodyweight gain, haematocrit levels and haemoglobin concentration in blood, and blood acid-base status as measured by blood pH, plasma CO₂ and Base Excess (BE). No significant effects were observed on femur length, fat free solid (FFS), or the % ash in the FFS or Ca, Mg, Na, or K in the FFS.

Method:

Other

Groups of weanling rats of 4 males and 4 females were given a commercial diet supplemented with 280, 420 or 560 mmol HCl/kg diet, respectively. The diet for control was prepared by the addition of a similar amount of distilled water to the basal diet. Residues of food were collected weekly and intake was calculated for weekly period. At the end of experiment blood samples for acid-base and mineral analysis were taken. After exsanguination, the removed right femur from slaughtered rat was cleansed of adherent soft tissue to be dried and subjected to the procedure for obtaining FFS. Thus obtained FFS was analysed.

GLP: Yes [] No [**X**] ? []
 Test substance: Hydrochloric acid, no data
 Reliability : (3) Not reliable
 Reference: Upotn, P. K. and L'Estrange, J. L. (1977)

(6)
 Species/strain: Rat / Wistar (adult)
 Sex: Female []; Male []; Male/Female [**X**]; No data []
 Route of Administration: Oral feed
 Exposure period: 9 weeks
 Frequency of treatment: Daily
 Post exposure observation period: No
 Dose: 312, 625, 937, 1250 mmol HCl/kg diet
 Control group: Yes [**X**]; No []; No data [];
 Concurrent no treatment []; Concurrent vehicle [**X**]; Historical []
 NOAEL: 625 mmol HCl/kg diet
 LOAEL: 937 mmol HCl/kg diet

Results:

Table

mmol HCl/kg diet	Control(0)	312	625	937	1250
pH of diets ^{#1}	5.80	4.17	2.84	2.23	1.82
Food intake (g/kg)	14.8	15.8	15.3	10.7 ^{#3}	9.56 ^{#3}
Dose (mg HCl/animal/day) ^{#2}	0	180	349	366	436
Water intake (mL/day)	33.9	35.7	44.8	44.2 ^{#3}	25.9 ^{#3}
Live weight change (g/day)	-0.31	-0.22	-0.47	-2.40 ^{#3}	-1.72 ^{#3}

^{#1}: HCl was diluted (1:5 (v/v)) with distilled water, then added to the diet.

^{#2}: Calculated from food intake

^{#3}: Values refer to means obtained during the period the animals survived.

The treatments with 937 and 1,250 mmol/kg diet resulted in 100% mortality of the rats and the average survival time being 51.2 and 19.1 days, respectively. Food intake and live-weight gain of the rats were significantly reduced by these treatment. Water intake was significantly increased by hydrochloric acid supplementation except on the high dose level, where the animals survived for a short period. The blood samples were not taken from the rats which died before the end of experiment. Plasma CO₂ concentration was reduced by the HCl supplementation compared to the control but the effect was not significant. Femur length, % fat free solid (FFS) in bone or the % ash, Ca or P in the FFS were not affected.

Method:

Other

Groups of adult rats (approx. 1 year-old) consisted of 4 males and 4 females were given a commercial diet supplemented with 312, 625, 937, 1250 mmol HCl/kg diet. Residues of the diet were collected weekly and intake calculated for weekly period. At the end of experiment blood samples for acid-base and mineral analysis were taken only on the rats which survived through the experiments. After exsanguination, the removed right femur from slaughtered rat was cleansed of adherent soft tissue to be dried and subjected to the procedure for obtaining FFS. Thus obtained FFS was analysed. Where treatment effects were statistically significant the means were compared with each other using Duncan's multiple range tests.

GLP: Yes [] No [] ? [**X**]
 Test substance: Hydrochloric acid, no data
 Reliability : (3) Not reliable
 Reference: Upotn, P. K. and L'Estrange, J. L. (1977)

(7)
 Species/strain: Rat / Wistar (Weanling)
 Sex: Female []; Male []; Male/Female [**X**]; No data []
 Route of Administration: Oral feed
 Exposure period: 12 weeks
 Frequency of treatment: Daily
 Post exposure observation period: No
 Dose: 300, 600, 900 mmol HCl/kg diet

Control group: Yes [**X**]; No []; No data [];
 Concurrent no treatment []; Concurrent vehicle [**X**]; Historical []
 NO(A)EL: 600 mmol HCl/kg diet
 LO(A)EL: 900 mmol HCl/kg diet
 Results:

Table

mmol HCl/kg diet	Control(0)	300	600	900
pH of diets* ¹	5.81	4.27	3.09	2.54
Food intake (g/day)	15.4	15.0	14.0	7.2
Dose (mg/animal/day)* ²	0	164	307	237
Water intake (mL/day)	39.2	41.3	44.9	33.2
Live weight change (g/day)	2.57	2.52	2.21	0.84
Blood pH	7.36	7.35	7.37	7.24
Plasma CO ₂ (mmol/L)	22.0	22.7	19.4	15.3
BE (mmol/L)	-3.20	-3.89	-5.69	-12.97
FFS in femur (mg)	495	490	428	248
% Ash in FFS	69.4	67.1	68.8	62.1

^{#1}: HCl was diluted (1:5 (v/v)) with distilled water, then added to the diet.

^{#2}: Calculated from food intake.

*¹: Diluted 1:5 (v/v) with distilled water, *²: Calculated from daily intake

At 900 mmol/kg diet where 3 animals died, both food intake and bodyweight gain were significantly decreased. Blood pH was not significantly affected at 300 and 600 mmol/kg diet, though it was considerably lower in 900 mmol/kg diet fed group than in control. However, plasma CO₂ values were significantly reduced by the HCl supplementation at 600 and 900 mmol/kg diet. Thus, mild degree of metabolic acidosis was indicative at 900 mmol/kg diet. Also, base Excess (BE) values was significantly reduced by the HCl supplementation at 900 mmol/kg diet. As for the bone measurements, femur length, % fat free solid (FFS) in the femur and % ash in the FFS was all significantly reduced by the HCl supplementation at 900 mmol/kg diet.

Method:

Other

Groups of the weanling rats consisted of 6 males and 4 females were given a commercial diet supplemented with 300, 600 and 900 mmol HCl /kg diet. Residues were collected weekly and intake calculated for weekly period. At the end of experiment blood samples for acid-base and mineral analysis were taken on the rats which survived through the experiments. After exsanguination, the removed right femur from slaughtered rat was cleansed of adherent soft tissue to be dried and subjected to the procedure for obtaining FFS. Thus obtained FFS was analysed. Treatment effects were statistically significant the means were compared with each other using Duncan's multiple range tests.

GLP: Yes [] No [] ? [X]
 Test substance: Hydrochloric acid, no data
 Reliability : (3) Not reliable
 Reference: Upotn, P. K. and L'Estrange, J. L. (1977)

(8)

Species/strain: Rat / Wistar
 Sex: Female []; Male [X]; Male/Female []; No data []
 Route of Administration: Drinking water
 Exposure period: 21 weeks
 Frequency of treatment: Daily
 Post exposure observation period: No
 Dose: Acidification of drinking water to pH 2 or 3
 Control group: Yes [X]; No []; No data [];
 Concurrent no treatment []; Concurrent vehicle [X]; Historical []
 NO(A)EL: N/A
 LO(A)EL: N/A
 Results: Acidification to pH 2 and 3 resulted in a slightly but significantly reduced excretion of phenol red, urine volume. Lowered proteinuria was also observed at pH 2. No effects were observed on body weight development, food and water consumption, organ weights, hematological parameters, liver-specific serum enzymes, serum protein and serum creatinine.

Method: Other
 Eight animals for pH 2 *ad lib.* and ten animals for pH 3 *ad lib.* were individually caged. At week 2, 13 and 21, urine was sampled overnight (16h), and its volume and phenol red excretion (for 2 h after tail vein injection) were measured. Also, hematology and serum analysis were conducted.

GLP: Yes [] No [] ? [X]
 Test substance: Hydrochloric acid
 Remarks: The experiment was subject to a variety of environmental influences and the effect of drinking water acidification was the one of the factors the author investigated.
 Reliability : (3) Not reliable
 Reference: Clausing, P. and Gottschalk, M. Z. (1989)

(9)

Species/strain: Mouse / Swiss-Webster [CrI:COBS CRW (SW) BR]
 Sex: Female []; Male [X]; Male/Female []; No data []
 Route of Administration: Inhalation
 Exposure period: 3 days
 Frequency of treatment: 6 hours/day
 Post exposure observation period: 0 or 72h
 Dose: 304 ppm (447 mg/ m³)
 Control group: Yes [X]; No []; No data [];
 Concurrent no treatment [X]; Concurrent vehicle []; Historical []
 NO(A)EL: N/A
 LO(A)EL: N/A

Results: Body weights were decreased compared to controls but, in most cases, returned to normal levels by 3 days post-exposure. The exposure to hydrogen chloride resulted in exudate in the nasal passage. Haircoats of the exposed mice turned a yellowish-green color during exposure. Respiratory epithelial exfoliation, erosion, ulceration, necrosis and less pronounced lesions in the olfactory epithelium were observed in respiratory tract.

Method: Other
Groups of 16-24 mice were exposed. Half of each group of exposed mice were necropsied immediately after the last exposure. The remaining mice were necropsied about 72 hr after the last exposure.
Fixed sections of mouse nasal passages were examined and the severity of the lesions was scored by light microscopy.

GLP: Yes No ?

Test substance: Hydrogen chloride, purity > 95%, impurity: nitrogen chloride
Source: Matheson Gas (Morrow, Ga.)
Analytical monitoring: The mixture gas of hydrogen chloride and nitrogen at the concentration that reduces the respiratory rate by 50% was metered directly into the chamber inlet and the time-weighted average exposure concentration measured by infrared spectrometry was 304 ppm.

Remarks: The objectives of this study were to determine if pathologic changes occur in the respiratory tract of groups of mice after inhalation exposure to various sensory irritants (10 chemicals including hydrogen chloride) at their respective RD50 concentrations (that concentration which elicits a respiratory rate decrease of 50%) and to compare any changes with respect to type, distribution, and severity.

Reliability : (3) Not reliable

Reference: Buckley, L.A. et al. (1984)

(10)

Species/strain: Rabbit /(strain was not described)

Sex: Female ; Male ; Male/Female ; No data

Route of Administration: Inhalation

Exposure period: 12, 30, 120 h

Frequency of treatment: 12 h exposure group; 6 hours/day, 2 days
30 h exposure group; 6 h/day, 5 days
120 h exposure group; 6 h/day, 5 days/week, 4 weeks

Post exposure observation period: 2 months

Dose: ca. 0.4, 1.2 and 3.0 mg/L for 12h exposure
ca. 0.09 and 0.19 mg/L for 30 h
ca. 0.05 mg/L for 120 h
These concentrations were read from the figure in the report since the concentrations tested were not clearly described.

Control group: Yes ; No ; No data ;
Concurrent no treatment ; Concurrent vehicle ; Historical ;
Remarks: The control group consisted of seven rabbits.

NO(A)EL: N/A

LO(A)EL: N/A

Results: All concentrations used had some extent of irritation to the eyes and

mucous membranes of the animals. No death was observed by the exposure to 0.09 mg/L hydrochloric acid for 30 h. The animals exposed to hydrogen chloride at 0.05 mg/L for 120 h showed no immediate toxic effects and no pathological changes which could be attributed to the exposure when killed several months later. Fatality of 100% was found over at 1.2 and 3.0 mg/L exposure for 12 h.

Severe hepatic lesions were found in 16 of the 51 rabbits died in 12 or 30 h exposure group.

Method: Other
Groups of 3 rabbits were exposed to hydrogen chloride gas of various concentrations and administration schedule.

GLP: Yes No ?

Test substance: The hydrogen chloride gas was generated by mixing commercial C.P. hydrochloric acid with 10-15 times its volume of concentrated sulfuric acid.

Remarks: The author reported that the upper limit of safety in atmospheres containing hydrogen chloride must be 0.05 mg/L (about 30 ppm), though it is possible that even this concentration would be harmful if daily exposures were continued over periods longer than a month.

A loss of weight was evident in every instance and in general paralleled the severity of exposure. However, it was rapidly regained after about two weeks.

Reliability : (3) Not reliable

Reference: Machle, W. et al. (1942)

(11)

Species/strain: Guinea pig

Sex: Female ; Male ; Male/Female ; No data

Route of Administration: Inhalation

Exposure period: 12, 30, 120 h

Frequency of treatment: 12 h exposure group; 6 h/day, 2 days
30 h exposure group; 6 h/day, 5 days
120 h exposure group; 6 h/day, 5 days/week, 4 weeks

Post exposure observation period: 2 months

Dose: ca. 0.4, 1.2 and 3.0 mg/L for 12h exposure
ca. 0.09 and 0.19 mg/L for 30 h
ca. 0.05 mg/L for 120 h

These concentrations were read from the figure in the report since the concentrations tested were not clearly described.

Control group: Yes ; No ; No data ;
Concurrent no treatment ; Concurrent vehicle ; Historical

Remarks: The control group consisted of six guinea pigs.

NO(A)EL: N/A

LO(A)EL: N/A

Results: All concentrations used had some extent of irritation to the eyes and mucous membranes of the animals. No death was observed by the exposure to 0.09 mg/L hydrochloric acid for 30 h. Also, the author reported that the animals exposed to hydrogen chloride at 0.05 mg/L for 120 h showed no immediate toxic effects and no pathological changes which could be attributed to the

exposure when killed several months later. Fatality of 100% was found at 1.2 and 3.0 mg/L exposure for 12 h.

Definite gross pathological changes in the liver were noted in 45 of 57 guinea pigs died in 12 or 30 h exposure group.

Method: Other
Groups of 3 guinea pigs were exposed to hydrogen chloride gas of various concentrations and administration schedule.

GLP: Yes [] No [**X**] ? []

Test substance: The hydrogen chloride gas was generated by mixing commercial C.P. hydrochloric acid with 10-15 times its volume of concentrated sulfuric acid.

Remarks: The author reported that the upper limit of safety in atmospheres containing hydrogen chloride must be 0.05 mg/L (about 30 ppm), though it is possible that even this concentration would be harmful if daily exposures were continued over periods longer than a month.

A loss of weight was evident in every instance and in general paralleled the severity of exposure. However, it was rapidly regained after one month.

Reliability : (3) Not reliable

Reference: Machle, W. et al. (1942)

(12)

Species/strain: Monkey

Sex: Female [**X**]; Male []; Male/Female []; No data []

Route of Administration: Inhalation

Exposure period: 4 weeks (120 hours)

Frequency of treatment: 6 hours/day, 5 days/week

Post exposure observation period: 2 months

Dose: 0.5 mg/L for 120 h

Control group: Yes [**X**]; No []; No data [];
Concurrent no treatment [**X**]; Concurrent vehicle []; Historical []

NO(A)EL: N/A

LO(A)EL: N/A

Results: Irritation of the eyes and the mucous membranes was observed. No immediate toxic effects and no pathological changes which could be attributed to the exposure were observed when killed several months later.

Method: Other
An adult female monkey was exposed to 0.05 mg/L hydrochloric acid for 120 h (6 h/day, 5 days/week, 4 weeks).

GLP: Yes [] No [**X**] ? []

Test substance: Hydrogen chloride, the hydrogen chloride gas was generated by mixing commercial C.P. hydrochloric acid with 10-15 times its volume of concentrated sulphuric acid.

Remarks: The author reported that the upper limit of safety in atmospheres containing hydrogen chloride must be 0.05 mg/L (about 30 ppm), though it is possible that even this concentration would be harmful if daily exposures were continued over periods longer than a month.

Reliability : (3) Not reliable

Reference: Machle, W. et al. (1942)

(13)

Species/strain: Rat

Sex: Female []; Male []; Male/Female [X]; No data []

Route of Administration: Oral feed

Exposure period: 9 weeks

Frequency of treatment: Daily

Post exposure observation period: No

Dose: At beginning of the experiment (6 weeks of age), each rat received about 12 mL of 0.1N HCl per day. This was gradually increased until at the end of 7 weeks when they were given 50 mL of 0.1N HCl daily.
For the last 2 weeks, animals were given 50 mL of 0.2 N HCl each per day.

Control group: Yes [X]; No []; No data [];
Concurrent no treatment [X]; Concurrent vehicle []; Historical []

NO(A)EL: N/A

LO(A)EL: N/A

Results: After the dose of acid reached at 25 mL of 0.1 N per day, the appetites of the treatment group was decreased. Both bone and body growth were slightly retarded in animals consuming the acid, but there were no appreciable changes in the chemical composition of the bones. The base content of the soft tissues was increased slightly. Death was preceded by a marked loss in weight.

Method: Other
Groups of eight rats were used. The acid was administered by mixing it with the maize mixture to 8 rats and the other 8 rats were used as controls.

Remarks: The animals were derived from 2 litters. Treatment group was compared to the litter mate control.
The experiment was carried out to determine whether acid ingestion exerted any influence on the storage of base in the tissues of young growing rats.

GLP: Yes [] No [X] ? []

Test substance: 0.1 N hydrochloric acid

Reliability : (3) Not reliable

Reference: Burns, C. M. (1929)

(14)

Species/strain: Rabbit

Sex: Female []; Male []; Male/Female []; No data [X]

Route of Administration: Oral

Exposure period: See details in results (17 - 35 days)

Frequency of treatment: Daily

Post exposure observation period: No

Dose: 120 mL to 200mL of 0.1 N HCl daily

Control group: Yes [X]; No []; No data [];
Concurrent no treatment [X]; Concurrent vehicle []; Historical []

NO(A)EL: N/A

LO(A)EL: N/A

Results: The treated animals showed retarded growth or weight loss and a reduction in the base content of their muscles. There was a marked reduction in fat content of the bones, but no reduction in percentage of ash.

Method: Other
Rabbits from three litters were given diet containing 0.1 N HCl. The amount of 0.1 N HCl consumed was expected to be 120-200 mL/day. Treatment group was compared to the litter mate control.

GLP: Yes [] No [**X**] ? []

Test substance: Hydrochloric acid, no data

Reliability : (3) Not reliable

Reference: Burns, C. M. (1929)

(15)

Species/strain: Chick/Indian River broiler

Sex: Female []; Male []; Male/Female []; No data [**X**]

Route of Administration: Oral feed

Exposure period: 27 days

Frequency of treatment: No data

Post exposure observation period: No

Dose: 0.21, 0.42, 0.84 % in the diet

Control group: Yes [**X**]; No []; No data [];
Concurrent no treatment []; Concurrent vehicle []; Historical []

NOAEL: N/A

LOAEL: N/A

Results: No significant effects were noted on the body weight gain, food consumption and mortality. However concentration of 0.84% in the diet resulted in a lower body weight gain and feed efficiency compared to control, but no mortality.

Method: Other
Each treatment was presented to one day of age of 30 unsexed chicks. On the 1st, 3rd, 10th, 17th and 24th day of age, group weights were measured and feed conversions were calculated.

GLP: Yes [] No [**X**] ? []

Test substance: Hydrochloric acid, U. S. P. (37.9%), J. T. Baker

Reliability : (3) Not reliable

Reference: Pritzl, M.C. and Kienholz, E.W. (1973)

(16)

Species/strain: Rabbit

Sex: Female []; Male []; Male/Female []; No data [**X**]

Route of Administration: Inhalation

Exposure period: 5 days

Frequency of treatment: 6 hours/day

Post exposure observation period: Daily

Dose: 149 mg/m³ (100 ppm)

Control group: Yes []; No []; No data [**X**];
Concurrent no treatment []; Concurrent vehicle []; Historical []

NO(A)EL: N/A

LO(A)EL: N/A

Results: Animals exhibited slight respiratory difficulties and eye and nasal irritation, and slightly decreased haemoglobin levels.

Method: Other

GLP: Yes [] No [] ? [**X**]
 Test substance: Hydrogen chloride, no data
 Reliability : (4) Not assignable
 Reference: Flury, F. and Zernik, F. (1931) cited European Commission- European Chemical Bureau (2000) and BIBRA (1990)

(17)

Species/strain: Guinea pig
 Sex: Female []; Male []; Male/Female []; No data [**X**]
 Route of Administration: Inhalation
 Exposure period: 5 days
 Frequency of treatment: 6 hours/day
 Post exposure observation period: Daily
 Dose: 149 mg/m³ (100 ppm)
 Control group: Yes []; No []; No data [**X**];
 Concurrent no treatment []; Concurrent vehicle []; Historical []
 NO(A)EL: N/A
 LO(A)EL: N/A
 Results: Animals exhibited slight respiratory difficulties and eye and nasal irritation, and slightly decreased haemoglobin levels.

Method: Other
 GLP: Yes [] No [] ? [**X**]
 Test substance: Hydrogen chloride, no data
 Reliability : (4) Not assignable
 Reference: Flury F. and Zernik F., (1931) cited European Commission- European Chemical Bureau (2000) and BIBRA (1990)

(18)

Species/strain: Pigeon
 Sex: Female []; Male []; Male/Female []; No data [**X**]
 Route of Administration: Inhalation
 Exposure period: 5 days
 Frequency of treatment: 6 hours/day
 Post exposure observation period: Daily
 Dose: 149 mg/m³ (100 ppm)
 Control group: Yes []; No []; No data [**X**];
 Concurrent no treatment []; Concurrent vehicle []; Historical []
 NO(A)EL: N/A
 LO(A)EL: N/A
 Results: Animals exhibited slight respiratory difficulties and eye and nasal irritation, and slightly decreased haemoglobin levels.

Method: Other
 GLP: Yes [] No [] ? [**X**]
 Test substance: Hydrogen chloride, no data
 Reliability : (4) Not assignable
 Reference: Flury, F. and Zernik, F. (1931) cited European Commission- European Chemical Bureau (2000)

(19)
 Species/strain: Rat
 Sex: Female []; Male []; Male/Female []; No data [X]
 Route of Administration: Inhalation
 Exposure period: ca. 2 weeks
 Frequency of treatment: 6 hours / day on 6 alternate days
 Post exposure observation period: 1 - 2 years
 Dose: 5-22 mg/m³
 Control group: Yes []; No []; No data [X];
 Concurrent no treatment []; Concurrent vehicle []; Historical []
 NOAEL: 22 mg/m³
 LOAEL: > 22 mg/m³
 Results: The exposure to HCl had no effect upon the body weight of 50 rats. 1 or 2 years later, unspecified examinations of a range of tissues which apparently included lung and bone, revealed no abnormalities.
 Method: Other
 GLP: Yes [] No [X] ? []
 Test substance: Hydrogen chloride, no data
 Reliability : (4) Not assignable
 Reference: European Commission- European Chemical Bureau (2000) and BIBRA (1990)

(20)
 Species/strain: Guinea pig
 Sex: Female []; Male [X]; Male/Female []; No data []
 Route of Administration: Inhalation
 Exposure period: 7 weeks
 Frequency of treatment: 2 hours/day, 5 days/ week
 Post exposure observation period: 5 days
 Dose: 0.015 mg/L
 Control group: Yes [X]; No []; No data []; not specified.
 Concurrent no treatment []; Concurrent vehicle []; Historical []
 NOAEL: N/A
 LOAEL: N/A
 Results: The measurements of the lung function parameters showed no differences between exposed animals and controls; histological examination of the lungs revealed no changes attributable to HCl-exposure
 Method: Other, not specified
 Twenty-three animals were exposed; 15 animals served as controls; from the 5th day post exposure several lung function parameters were evaluated
 GLP: Yes [] No [] ? [X]
 Test substance: No data
 Reliability : (4) Not assignable
 Reference: European Commission- European Chemical Bureau (2000)

5.5 GENETIC TOXICITY IN VITRO

A. BACTERIAL TEST

(a)

Test Substance

Identity (*purity*): Hydrogen chloride (7647-01-0) 36.5-38 %
Remarks: Not described

Method

Method/guideline followed Not described
Type: bacterial reverse mutation assay (plate incorporation assay)
GLP: Yes [] No [] Not described
Year 1978
Cell type and or cell line:
Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1537, TA 1538
Metabolic activation:
◆ Species and cell type: rat liver S-9 fraction
◆ Quantity: 0.1 mL/ mL of reaction mixture
◆ Induced or not induced: Induced by Aroclor 1254.
Concentrations tested: 0.001, 0.01, 0.1, 1.0, 5.0 uL/plate
(0.012-60 ug/plate)
Statistical methods: not used
Remarks: According to the method of Ames, B.N. et al. (Mutat. Res., 31, 347-364 (1975)).

• *Test Design*

- ◆ *Number of replicates:* one
- *Positive and negative control groups and treatment:*
Negative control: solvent
Positive control:

Without activation :	TA 98	NF	10 uL/mL
	TA 100	Ethylmethanesulfonate	10 uL/mL
	TA 1535	Ethylmethanesulfonate	10 uL/mL
	TA 1537	QM	10 uL/mL
	TA 1538	NF	10 uL/mL
With activation :	TA 98	2-Aminoanthracene	2.5 uL/mL
	TA 100	2-Aminoanthracene	2.5 uL/mL
	TA 1535	2-Aminoanthracene	2.5 uL/mL
	TA 1537	2-Aminoanthracene	2.5 uL/mL
	TA 1538	2-Aminoanthracene	2.5 uL/mL

NF, QM: not specified

- *Solvent:* deionized water
- *Media:* Selective agar plate and agar supplemented with biotine and a trace of histidine.
- *Description of follow up repeat study:* none

• *Criteria for evaluating results :*

TA 1535, TA 1537, TA 1538:

Positive dose-response over three concentrations with the lowest increase equal to twice the solvent control value.

TA 100:

Positive dose-response over three concentrations with the highest increase equal to twice the solvent control value.

TA 98:

Positive dose-response over three concentrations with the highest increase equal to 2-3 times the solvent control value.

Results

Cytotoxic concentration:

- *With metabolic activation:* 5.0 uL/plate
- *Without metabolic activation:* 5.0 uL/plate

Genotoxic effects (positive, negative, unconfirmed, dose-response, equivocal)

- *With metabolic activation:* negative
- *Without metabolic activation:* negative

Statistical results, as appropriate: N/A

Remarks:

Conclusions

Negative result was obtained in the systems.

Data Quality

Reliabilities: (2) Reliable with restrictions

Flag: Critical study for SIDS

Remarks

Quality Check Comparable to the guideline study with acceptable restrictions.

References

Litton Bionetics, Inc. (1978) Mutagenicity evaluation of Hydrochloric acid, Final report. LBI Project No. 20893.

Isquith, A., Matheson, D., and Slesinski, R. (1988) Genotoxicity studies on selected organosilicon compounds: in vitro assays. *Fd. Chem. Toxic.* 26, 255-261.

Other

Last changed:

Order number for sorting:

Remarks:

(b)

Type: Mitotic recombination in *Saccharomyces cerevisiae*

System of testing: *Saccharomyces cerevisiae* strain D4

Concentration: 0.001, 0.01, 0.1, 1.0, 5.0 uL/plate
(0.012-60 ug/plate)

Metabolic activation: With ; Without ; With and Without ; No data

Results:

Cytotoxicity conc: With metabolic activation: 5.0 uL/plate
Without metabolic activation: 5.0 uL/plate

Precipitation conc: N/A

Genotoxic effects: + ? -
With metabolic activation:
Without metabolic activation:

Method: other

GLP: Yes No ?

Test substance: Hydrogen chloride 36.5-38 %
Commercial

Remarks: Method: according to Brusick, D. and Andrews, H., Mutat. Res., 26, 491-500 (1974)

Procedure: Plate.
Plates/test: Not stated
Activation system: Liver S-9 fraction from Aroclor 1254 pretreated rats with NADPH-generating system
Media: tryptophan selective
No. replicates: Not stated

Reliability : (3) Not reliable

Reference: Isquith et al. (1988); Litton Bionetics, Inc. (1978)

(c)

Type: DNA damage and repair assay , 'rec' assay

System of testing: *Escherichia coli* W3110 (*pol A*⁺), P3078 (*pol A*⁻)

Concentration: 0.001, 0.01, 0.1, 1.0, 5.0 uL/plate
(0.012-60 ug/plate)

Metabolic activation: With ; Without ; With and Without ; No data

Results:

Cytotoxicity conc: With metabolic activation: 5.0 uL/plate
Without metabolic activation: 5.0 uL/plate

Precipitation conc: N/A

Genotoxic effects: + ? -
With metabolic activation:
Without metabolic activation:

Method: other

GLP: Yes No ?

Test substance: Hydrogen chloride 36.5-38 %

Remarks: Method: according to Slater E.E. et al., Cancer Res., 31, 970-973 (1971)
Plates/test: Not stated

Activation system: Liver S-9 fraction from Aroclor 1254 pretreated rats with NADPH-generating system
No. replicates: Not stated
Reliability : (3) Not reliable
Reference: Isquith et al. (1988); Litton Bionetics, Inc. (1978)

(d)

Type: Bacterial reverse mutation assay
System of testing: *Escherichia coli* B/Sd-4
Concentration: 0.00075- 0.00375 %
Metabolic activation: With []; Without [X]; With and Without []; No data []
Results:
Cytotoxicity conc: With metabolic activation: Not stated
Without metabolic activation: Not stated
Precipitation conc: Not stated
Genotoxic effects: + ? -
With metabolic activation: [] [] [X]
Without metabolic activation: [] [] []
Remarks: Because survival rate varied from 0.2 to 100 % under the same condition (concentration of hydrochloric acid 0.0015 %), the negative result is questionable.

Method: other
GLP: Yes [] No [] ? [X]
Test substance: hydrochloric acid (purity or concentration is not specified)
Remarks: Method: according to Bertani, G. et al., Genetics, (1951).
Procedure: preincubation
Plates/test: 2 - 10 plates
Activation system: Not tested
Media: streptomycin selective
No. replicates: Not stated
Reliability : (3) Not reliable
Reference: Demerec, M. et al. (1951)

(e)

Type: DNA damage and repair assay, 'rec' assay
System of testing: *Escherichia coli* WP2, WP2uvrA, WP67, CM611, W3110 (*pol A*⁺), P3478 (*pol A*⁻)
Concentration: Not stated
Metabolic activation: With []; Without []; With and Without [X]; No data []
Results:
Cytotoxicity conc: With metabolic activation: Not stated
Without metabolic activation: Not stated
Precipitation conc: Not stated
Genotoxic effects: + ? -
With metabolic activation: [] [X] [] ambiguous
Without metabolic activation: [] [X] [] ambiguous

Method: other
 GLP: Yes No ?
 Test substance: hydrochloric acid
 highest technical grade available
 Remarks: HCl showed inhibitory activity in the WP2uvrA stain; while this response was reproducible, it was not considered adequate evidence of DNA-damaging activity since the remaining WP2 deficient strains which also carried the uvrA mutation gave no indication of preferential kill at all.
 Plates/test: Not stated
 Activation system: Liver S-9 fraction from Aroclor 1254 pretreated rats with NADPH-generating system
 No. replicates: 1
 Reliability : (3) Not reliable
 Reference: McCarroll et al. (1981a)

(f)
 Type: DNA damage and repair assay, 'rec' assay
 System of testing: *B. subtilis* H17 arg⁻ try⁻ rec⁺ and M45 arg⁻ try⁻ rec⁻
 Concentration: not stated
 Metabolic activation: With ; Without ; With and Without ; No data
 Results:
 Cytotoxicity conc: With metabolic activation: Not stated
 Without metabolic activation: Not stated
 Precipitation conc: Not stated
 Genotoxic effects: + ? -
 With metabolic activation:
 Without metabolic activation:

Method: Other
 GLP: Yes No ?
 Test substance: hydrochloric acid
 Remarks: Plates/test: Not stated
 Activation system: Liver S-9 fraction from Aroclor 1254 pretreated male SD rats with NADPH-generating system
 No. replicates: Not stated
 Reliability : (3) Not reliable
 Reference: McCarroll et al. (1981b)

B. NON-BACTERIAL IN VITRO TEST

(a)

Test Substance

Identity: Hydrogen chloride (7647-01-0)

Remarks: Not described

Method

Method/guideline followed

Not described

Type: Chromosome aberration test

GLP: Yes [] No [X]

Year: 1988

Species/Strain or cell type and or cell line (bacterial or non-bacterial):

Chinese hamster ovary K1 (CHO-K1) cells

Metabolic activation:

◆ Species and cell type: rat liver S-9 fraction

◆ Quantity: Not described

◆ Induced or not induced: Phenobarbital and 5, 6-benzoflavone-induced

Statistical methods: No statistic analysis

Remarks:

• *Test Design*

◆ Concentrations tested: Cells were treated for 24 hours without S9. With S9 treatment, cells were treated for 6 hours and cultivated with fresh media for additional 18 hours.

-S9: 0, 8, 10, 12, 14, 16 mM
(pH 7.4, 6.1, 5.9, 5.7, 5.5, 5.3 respectively)

+S9: 0, 6, 8, 10, 12 mM
(pH 7.4, 6.3, 6.0, 5.8, 5.5 respectively)

◆ Number of replicates: 2 - 4

◆ Solvent: Ham's F12 medium supplemented with 10% foetal calf serum, sodium bicarbonate (16.7 mM) and Kanamycin (60 ug/mL)

◆ Positive and negative control groups and treatment: none

◆ Number of metaphases analyzed: 100/plate

• Description of follow up repeat study: none

• Criteria for evaluating results: not described

Results

Cytotoxic concentration:

● With metabolic activation: 12 mM (pH 5.5)

● Without metabolic activation: 16 mM (pH 5.3)

Genotoxic effects (positive, negative, unconfirmed, dose-response, equivocal)

● With metabolic activation: (positive) 8-10 mM (pH 5.8-6.0)

● Without metabolic activation: (positive) 14 mM (pH 5.5)

Statistical results, as appropriate:

Remarks:

● *Frequency of reversions/mutations/aberrations, polyploidy as appropriate:*

Dose (mM)	S9 mix	pH after treatment			cells scored	Type and number of aberrations							Aberrant cells ^a (%)
		Initial	6 h	24 h		ctg	csg	ctb	csb	cte	cse	f	
16	-	5.3	-	5.4	toxic								toxic
14	-	5.5	-	6.7	400	21	0	82	4	11	0	0	16.5
12	-	5.7	-	6.9	400	0	2	3	1	1	0	0	1.5
10	-	5.9	-	6.9	200	0	0	2	0	0	0	0	1.0
8	-	6.1	-	7.2	200	0	0	1	0	0	0	0	0.5
0	-	7.4	-	7.4	400	2	0	1	0	0	0	0	0.3
12	+	5.5	6.3	-	toxic								toxic
10	+	5.8	6.7	-	300	12	1	33	1	33	0	0	15.7
8	+	6.0	6.8	-	200	9	1	21	1	18	1	0	14.0
6	+	6.3	6.9	-	200	5	0	4	0	0	0	0	2.0
0	+	7.4	7.6	-	300	2	0	1	0	0	0	0	0.3

a: All structural aberrations except gaps.

Abbreviations: ctg, gaps; csg, chromosome gaps; ctb, chromatid breaks; csb, chromosome breaks; cte, chromatid exchange; cse, chromosome exchange; f, fragmentations.

- *Precipitation concentration if applicable:* none
- *Mitotic index:* not described

Conclusions

Weakly acidic media is clastogenic to CHO-K1 cells with and without metabolic activation.

Remarks:

Induced aberrations were almost all chromatid breaks.

Data Quality

Reliabilities: (2) Reliable with restrictions

Flag: Critical study for SIDS

Remarks:

Quality Check: Comparable to the guideline study with acceptable restrictions

References

Morita, T., Watanabe, Y., Takeda, K. and Okumura, K (1989) Effects of pH in the in vitro chromosomal aberration test., *Mutat. Res.*, **225**, 55-60.

Other

Last changed:

Order number for sorting:

Remarks

(b)

Test Substance

Identity (*purity*): Hydrogen chloride (7647-01-0) 36.5-38 %
Remarks: Not described

Method

Method/guideline followed Not described
Type: Chromosome aberration test
GLP: Yes [] No [] Not described
Year 1978
Species/Strain or cell type and or cell line (bacterial or non-bacterial):
Mouse lymphoma cell line L5178Y TK^{+/+}

Metabolic activation:

- ◆ Species and cell type: Male CD-1 mice.
- ◆ Quantity: 200 uL/mL
- ◆ Induced or not induced: Not induced

Statistical methods: Student *t*-test

Remarks:

The procedure by Clive and Spector (*Mutat. Res.*, 31, 17-29, 1975) was modified.

Fischer's medium for Leukemic cells of mice with 10% horse serum and sodium pyruvate and those with 20% horse serum, sodium pyruvate and 0.37% agar were used for maintaining and cloning, respectively.

● *Test Design*

Concentrations tested:

Without activation : 0.1, 0.2, 0.4 uL/mL (1.2, 2.4, 4.8 mM)
With activation : 0.2, 0.4, 0.8 uL/mL (2.4, 4.8, 9.6 mM)

● *Test Design*

Cells were treated with the test compound for 4 hours either with or without mouse-liver S9, followed by cultivation in growth medium with BrdU for approximately 20 hours. These cells were stained by the Giemsa method of Korenberg and Freedlander (*Chromosomes*, 48, 355, 1974).

- ◆ *Number of replicates:* one
- ◆ *Positive and negative control groups and treatment:*
 - Negative control:* Growth medium
 - Positive control:*
 - Without activation : Ethylmetanesulfonate 0.5 uL/mL
 - With activation : Dimethylnitrosoamine 0.3 uL/mL

- *Solvent:* Water
- *Description of follow up repeat study:* none

- *Criteria for evaluating results:*
Statistical significance is analyzed using a student *t*-test.

Results

Cytotoxic concentration:

- With metabolic activation: 0.8 uL/mL (100% growth inhibition)
- Without metabolic activation: ca 1.0 uL/mL (12.5% growth inhibition at 0.8 uL/mL)

Genotoxic effects (positive, negative, unconfirmed, dose-response, equivocal)

- With metabolic activation: Negative
- Without metabolic activation: Negative

Statistical results, as appropriate: N/A

Remarks:.

Conclusions

Negative result was obtained in the systems.

Remarks:

Data Quality

Reliabilities: (2) Reliable with restrictions

Flag:

Remarks

Quality Check Comparable to the guideline study with acceptable restrictions.

References

Litton Bionetics, Inc. (1978) Mutagenicity evaluation of Hydrochloric acid, Final report. LBI Project No. 20893.

Isquith, A., Matheson, D., and Slesinski, R. (1988) Genotoxicity studies on selected organosilicon compounds: in vitro assays. *Fd. Chem. Toxic.* 26, 255-261.

Other

Last changed:

Order number for sorting:

Remarks:

(c)

Test Substance

Identity (*purity*): Hydrogen chloride (7647-01-0) 36.5-38 %
Remarks: Not described

Method

Method/guideline followed not described
Type: Mammalian cell gene mutation assay
GLP: Yes [] No [] Not described
Year 1978
Species/Strain or cell type and or cell line (bacterial or non-bacterial):
Mouse lymphoma cell line L5178Y TK^{+/-}
Metabolic activation:
♦ Species and cell type: Male CD-1 mice
♦ Quantity: 200 uL/mL
♦ Induced or not induced: Not induced
Concentrations tested:
Without activation: 0.4, 0.5, 0.6, 0.7, 0.8 uL/mL (4.8-9.6 mM)
With activation: 0.8, 1.0, 1.2, 1.4, 1.6 uL/mL (9.6-23.0 mM)
Statistical methods: No statistic analysis
Remarks:

The procedure by Clive and Spector (*Mutat. Res.*, 31, 17-29, 1975) was modified.

Fischer's medium for Leukemic cells of mice with 10% horse serum and sodium pyruvate and those with 20% horse serum, sodium pyruvate and 0.37% agar were used for maintaining and cloning, respectively. For selection, 5.0 mg of BrdU was added to 100 ml of cloning medium.

• *Test Design*

Cells were treated with the test compound for 4 hours either with or without mouse-liver S9, followed by cultivation in growth medium for 3 days. The cells were cultured for additional 10 days in the selection and non-selection medium to determine mutation frequencies.

- ♦ *Number of replicates:* one
- ♦ *Positive and negative control groups and treatment:*
 - Negative control:* Growth medium
 - Positive control:*
 - Without activation: Ethylmetanesulfonate 0.5 uL/mL
 - With activation: Dimethylnitrosoamine 0.3 uL/mL

- *Solvent t:* Water
- *Description of follow up repeat study:* None
- *Criteria for evaluating results:*

A dose-response relationship over three concentrations of the four dose levels employed is observed, or an increase in the mutation frequencies at the highest dose is at least 2.5 times greater than the solvent control value.

Results

Cytotoxic concentration:

- With metabolic activation: 0.8 uL/mL (100% growth inhibition)
- Without metabolic activation: Ca 1.0 uL/mL (12.5% growth inhibition at 0.8 uL/mL)

Genotoxic effects (positive, negative, unconfirmed, dose-response, equivocal)

- With metabolic activation: Negative
- Without metabolic activation: Negative

Statistical results, as appropriate: No.

Remarks:

Conclusions

Negative result was obtained in the systems.

Remarks:

Data Quality

Reliabilities: (2) Reliable with restrictions

Flag:

Remarks

Quality Check Comparable to the guideline study with acceptable restrictions.

References

Litton Bionetics, Inc. (1978) Mutagenicity evaluation of Hydrochloric acid, Final report. LBI Project No. 20893.

Isquith, A., Matheson, D., and Slesinski, R. (1988) Genotoxicity studies on selected organosilicon compounds: in vitro assays. *Fd. Chem. Toxic.* 26, 255-261.

Other

Last changed:

Order number for sorting:

Remarks:

- (d)
- Type: Mammalian cell gene mutation assay
 - System of testing: Mouse lymphoma L5178Y cells, tk locus
 - Concentration: With metabolic activation: pH 6.3, 6.6, 6.9, 7.2, 7.5
Without metabolic activation: pH 6.0, 6.2, 6.5, 6.7, 6.9, 7.0
 - Metabolic activation: With []; Without []; With and Without [X]; No data []

Results:

Cytotoxicity conc.: With metabolic activation: pH 6.9>
Without metabolic activation: pH 6.6>=

Precipitation conc.: not stated

Genotoxic effects: + ? -
With metabolic activation: [X] [] []
Without metabolic activation: [] [] [X] []

Method: other

GLP: Yes [] No [] ? [X]

Test substance: 1N hydrochloric acid

Remarks: Positive result at the cytotoxic condition (pH 6.2>) with metabolic activation and weak positive result at the cytotoxic condition (pH 6.3) without metabolic activation were found.
Mouse lymphoma cultured *in vitro* was used.
Fixation time: not stated
Dose levels: not stated
Plates/test: 3
Activation system: S-9 fraction from the liver of Aroclor 1254-induced Fisher 344 derived rats with NADPH-generating system
Media: RPMI 1640 medium *plus* 10% heat-inactivated donor horse serum
No. replicates: not stated

Reliability : (3) Not reliable

Reference: Cifone et al. (1987)

(e)

Test Substance

Identity (*purity*): Hydrogen chloride (7647-01-0) 36.5-38 %
Remarks: Not described

Method

Method/guideline followed Not described
Type: sister chromatid exchange assay
GLP: Yes [] No [] Not described
Year 1978
Species/Strain or cell type and or cell line (bacterial or non-bacterial):
Mouse lymphoma cell line, L5178Y TK^{+/-}

Metabolic activation:

- ◆ Species and cell type: Male CD-1 mice.
- ◆ Quantity: 200 uL/mL
- ◆ Induced or not induced: not induced

Statistical methods: Student *t*-test

Remarks:

The procedure by Clive and Spector (*Mutat. Res.*, 31, 17-29, 1975) was modified.

Fischer's medium for Leukemic cells of mice with 10% horse serum and sodium pyruvate and those with 20% horse serum, sodium pyruvate and 0.37% agar were used for maintaining and cloning, respectively.

● *Test Design*

Concentrations tested:

Without activation: 0.1, 0.2, 0.4 uL/mL (1.2, 2.4, 4.8 mM)
With activation: 0.2, 0.4, 0.8 uL/mL (2.4, 4.8, 9.6 mM)

● *Test Design*

Cells were treated with the test compound for 4 hours either with or without mouse-liver S9, followed by cultivation in growth medium with BrdU for approximately 20 hours. These cells were stained by a modification of the Giemsa method of Korenberg and Freedlander (*Chromosomes*, 48, 355, 1974).

- ◆ *Number of replicates:* one
- ◆ *Positive and negative control groups and treatment:*
 - Negative control:* Growth medium
 - Positive control:*
 - Without activation : Ethylmetanesulfonate 0.5 uL/mL
 - With activation : Dimethylnitrosoamine 0.3 uL/mL

- *Solvent:* Water
- *Description of follow up repeat study:* none
- *Criteria for evaluating results:*

Statistical significance is analyzed using a student *t*-test.

Results

Cytotoxic concentration:

- With metabolic activation: 0.8 uL/mL (100% growth inhibition)
- Without metabolic activation: ca 1.0 uL/mL (12.5% growth inhibition at 0.8 uL/mL)

Genotoxic effects (positive, negative, unconfirmed, dose-response, equivocal)

- With metabolic activation: Negative
- Without metabolic activation: Negative

Statistical results, as appropriate: N/A

Remarks:.

Conclusions

Negative result was obtained in the systems.

Remarks:

Data Quality

Reliabilities: (2) Reliable with restrictions

Flag:

Remarks

Quality Check Comparable to the guideline study with acceptable restrictions.

References

- Litton Bionetics, Inc. (1978) Mutagenicity evaluation of Hydrochloric acid, Final report. LBI Project No. 20893.
- Isquith, A., Matheson, D., and Slesinski, R. (1988) Genotoxicity studies on selected organosilicon compounds: in vitro assays. *Fd. Chem. Toxic.* 26, 255-261.

Other

Last changed:

Order number for sorting:

Remarks:

(f)

Type: Chromosome aberration test

System of testing: Chinese hamster ovary cells

Concentration: 2.0 – 3.2 uL/mL (pH 5.00- 5.75) and control (pH 7.08)

Metabolic activation: With ; Without ; With and Without ; No data]

Results:

Cytotoxicity conc.: With metabolic activation: 3.2 uL/mL (pH 5.00)
Without metabolic activation: not stated

Precipitation conc.: not stated

Genotoxic effects: + ? -
With metabolic activation:
Without metabolic activation:

Hydrochloric acid induced significant increases in chromosome aberrations at pH 5.25 (2.8 uL/mL).

Method: other

GLP: Yes No ?

Test substance: hydrochloric acid

Remarks: The study was represented by Dr. A.K. Thilager of Sitek Research Laboratories at the 16th Annual Meeting of the Environmental Mutagen Society in Las Vegas, Nevada, 1985.

Method:
Plates/test: not stated
Activation system: S-9 fraction from unspecified source
Media: McCoy's 5a medium supplemented with 10% fetal calf serum, penicillin, streptomycin and L-glutamine.
No. replicates: not stated

Reliability : (3) Not reliable

Reference: Brusick (1986)

5.7 CARCINOGENICITY

(a)
 Species/strain: Rat / SD
 Sex: Female [] ; Male [X] ; Male/Female [] ; No data []
 Route of Administration: Inhalation
 Exposure period: Maximum, 128 weeks (for life)
 Frequency of treatment: 6 hours/day, 5 days/week.
 Post exposure observation period: Not described
 Doses: 10.0 ppm (9.7 mg/m³)
 Control group: Yes [X] ; No [] ; No data [] ;
 Concurrent no treatment [] ; Concurrent vehicle [X] ; Historical []
 Results: There were no statistical differences between the mortality of the hydrogen chloride and air control groups. No preneoplastic or neoplastic nasal lesion was observed in any group, but hyperplasia of the larynx and trachea was observed in treated animals (22/99 and 26/99, respectively). Tumour responses were similar in the treated and control groups, the total incidences of tumours at various sites being 19/99, 25/99 and 24/99 in treated, air control and colony control animals, respectively.

Observation		HCl	Air	Colony
No. animals examined		99	99	99
Larynx	Hyperplasia	22	2	2
	Squamous metaplasia	0	0	0
Trachea	Hyperplasia	26	6	2
	Squamous metaplasia	0	0	0
Nasal mucosa	Rhinitis	81	72	70
	Epithelial or squamous hyperplasia	62	51	45
	Squamous metaplasia	9	5	6
	Polyps or papillomas	0	0	0
	Squamous cell carcinoma	0	0	0
	Adenocarcinoma	0	0	0
	Mixed carcinoma	0	0	0
	Fibrosarcoma	0	0	0
Esthesioneuro-epithelioma	0	0	0	
Total no. of tumors		19	25	24

Method: Other
 GLP: Yes [] No [] ? [X]
 Test substance: Hydrogen chloride, purity: 99.0% grade, Matheson Gas Products, East Rutherford, N.J.)
 Remarks: Method: Three groups of 100 male rats, nine weeks old, were unexposed

	(colony controls), exposed by inhalation to air (air control) or exposed to 10 ppm of hydrogen chloride. Complete necropsy was performed on each animal and particular attention was give to the respiratory tract.
	The experiment was conducted on the aim to investigate the carcinogenic response to the combined and separate exposures to formaldehyde and hydrochloric acid.
Reliabilities:	(2) Reliable with restrictions
Remarks:	Comparable to the guideline study with acceptable restriction
Reference:	Sellakumar, A.R. et al., (1985)
 (b)	
Species/strain:	Rat / SD
Sex:	Female []; Male [X]; Male/Female []; No data []
Route of Administration:	Inhalation
Exposure period:	588 days (19.4 months)
Frequency of treatment:	6 hours/ day, 4.7 days/ week or two-thirds of each week
Postexposure observation period:	No
Doses:	Average concentration; 10.2 ppm
Control group:	Yes [X]; No []; No data []; Concurrent no treatment []; Concurrent vehicle [X]; Historical []
Results:	No carcinogenic response was observed. Mortality after 588 days (19.4months) was 29% in treated rats and 28% in airsham-exposed rats; at necropsy no nasal cancers were observed. There was no significant weight loss in treated group.
Method:	Other
GLP:	Yes [] No [] ? [X]
Test substance:	Hydrogen chloride, purity; 99.0% grade, Matheson Gas Product
Remarks:	Method: Twenty rats of 9-week-old were treated with hydrogen chloride gas or air sham-exposed as control. Complete necropsy was performed on each animals and particular attention was given to the respiratory tract. The experiment was conducted on the aim to investigate the carcinogenic response to the combined and separate exposures to formaldehyde and hydrochloric acid.
Reliability:	(3) Not reliable
Reference:	Albert, R.E. et al. (1982)
 (c)	
Species/strain:	Mouse / (Strain not described.)
Sex:	Female []; Male []; Male/Female [X]; No data []
Route of Administration:	dermal
Exposure period:	25 - 46 weeks
Frequency of treatment:	The applications were repeated at intervals of 1 to 2 days till the first appearance of macroscopic lesions, and renewed on the average twice weekly later on.
Post exposure observation period:	Not described
Doses:	Average concentration of 3 - 5% Hydrochloric acid (the volume used was not specified)
Control group:	Yes []; No [X]; No data [];

Concurrent no treatment []; Concurrent vehicle []; Historical []

Results: Hydrochloric acid treatment failed to produce malignant tumor growth. Repeated applications resulted in production of papillomatous lesion in 15 animals (7 males and 8 females).

Method: Other
Method: Fifty-two male and forty-seven female mice including 4 different strains were treated and the skin on the dorsum in the sacral region was painted without any previous epilation. The applications were repeated for about 4 to 6 weeks from the time of the first appearance of papillary growths and then discontinued. The total period of applications ranged from 25 to 46 weeks.

GLP: Yes [] No [] ? []

Test substance: Hydrochloric acid, no data

Remarks: This experiment was conducted on the basis of the assumption that any chemical substance able to cause irritation of the skin can lead to the formation of cancer after prolonged and repeated applications. Crude coal tar (*Ol. Lithanthracis*) was used as tumor producing or carcinogenic agents.

Reliability : (3) Not reliable

Reference: Narat, J. K. (1925).

5.8 TOXICITY TO REPRODUCTION

Type: Fertility []; One generation study [**X**]; Two generation study []; Other []
 Species/strain: Rat/Wistar
 Sex: Female [**X**]; Male []; Male/Female []; No data []
 Route of Administration: Inhalation
 Exposure period: Once, 12 days prior to mating period.
 Frequency of treatment: 1 h/day
 Postexposure observation period: not specified, but after weaning.
 Premating exposure period: male: no exposure, female: Once, 12 days prior to mating period.
 Duration of the test: From 12 days prior to mating period until three month after parturition (offspring).
 Doses: 450 mg/m³ (0.45 mg/L)
 Control group: Yes [**X**]; No []; No data []; but, not specified
 Concurrent no treatment [**X**]; Concurrent vehicle []; Historical []
 NOEL Parental: N/A
 NOEL F1 Offspring: N/A
 Results: **General parental toxicity:** Hemorrhagic oedema of the lungs; one third of the animals died of severe dyspnea and cyanosis; the surviving animals showed functional disorders of the lungs, the kidneys and the liver.
Repro. toxicity (parental): not stated.
Repro. toxicity (offspring) (weights of litter, postnatal growth, viability, etc.): Mainly the male offsprings suffered from functional disorders of the lungs, the kidneys and the liver. Mortality of offspring was not increased but body weight gain was decreased until the 4th week.
 Method: Other
 GLP: Yes [] No [] ? [**X**]
 Test substance: Hydrogen chloride in air.
 Remarks: Treatment was performed to non-pregnant rats. Number of maternal rats used was not specified.
 Maternal body weight change, fertility index, any parameters during gestation, delivery and lactation were not shown.
 Reliability : (4) Not assignable
 Reference: Pavlova, T.E. (1976)

5.9 DEVELOPMENTAL TOXICITY/TERATOGENICITY

(a)

Species/strain: Rat/Wistar
 Sex: Female [**X**]; Male []; Male/Female []; No data []
 Route of Administration: Inhalation
 Duration of the test: not exactly specified, but until three month after parturition (offspring).
 Exposure period: Once, on the 9th day of gestation
 Frequency of treatment: 1 h/day
 Doses: 450 mg/m³ (0.45 mg/L)
 Control group: Yes [**X**]; No []; No data []
 Concurrent no treatment [**X**]; Concurrent vehicle []; Historical []
 not specified

NOEL Maternal Toxicity: N/A
 NOEL teratogenicity: N/A
 Results: **maternal toxicity:** Hemorrhagic oedema of the lungs; one third of the animals died of severe dyspnea and cyanosis; the surviving animals showed functional disorders of the lungs, the kidneys and the liver.
embryotoxicity: Mainly the male offspring suffered from functional disorders of the lungs, the kidneys and the liver. Mortality of offspring was significantly higher compared to controls.
 Method: Other
 GLP: Yes [] No [] ? [X]
 Test substance: Hydrogen chloride in air.
 Remarks: Pregnant rats were treated. Number of maternal rats used was not specified. Maternal body weight change, fertility index, any parameters during gestation and delivery were not shown.
 Reliability : (4) Not assignable
 Reference: Pavlova T.E. (1976)

(b)
 Species/strain: Mice, strain not stated
 Sex: Female [X]; Male []; Male/Female []; No data []
 Route of Administration: Drinking water
 Duration of the test: not specified
 Exposure period: not specified, but during pregnancy
 Frequency of treatment: not specified
 Doses: pH 2.5 (c.a. 14.3 mg/kg)
 Control group: Yes []; No []; No data [X];
 Concurrent no treatment []; Concurrent vehicle []; Historical []
 NOEL Maternal Toxicity: N/A
 NOEL teratogenicity: N/A
 Results: No adverse effect was apparently seen.
 Method: Other
 GLP: Yes [] No [] ? [X]
 Test substance: no data
 Remarks: Number of mice used was not specified.
 Reliability : (4) Not assignable
 References: BIBRA (1990)

(c)
 Species/strain: Mice (random bred, H-Velaz)
 Sex: Female [X]; Male []; Male/Female []; No data []
 Route of Administration: intra-amniotic injection to the fetus of right side uterus
 Duration of the test: up to 16th day of gestation
 Exposure period: on the 13th day of gestation
 Frequency of treatment: once
 Doses: Five females were administered of 2 uL of 0.1M hydrogen chloride.
 Control group: Yes [X]; No []; No data [];
 Concurrent no treatment []; Concurrent vehicle []; Historical []

0.9% NaCl injection
NOEL Maternal Toxicity: N/A
NOEL teratogenicity: N/A
Results: A slight increase in foetal mortality (5/17) was occurred. Fetus with cleft palate was observed in one fetus (1/12) of the treated side. While, there were two (2/19) of the left side and no fetus (0/17) of the saline treated uterine.
Method: Other
GLP: Yes [] No [] ? [X]
Test substance: no data
Remarks: Number of mice used was not specified.
Reliability : (4) Not assignable
Reference: Dostal, M. (1973)

5.10 OTHER RELEVANT INFORMATION

Toxicodynamics, toxicokinetics

(a)
Type: Excretion
Results: Groups of seven male SD rats fed a low sodium chloride diet for 2 weeks were used for treatment. Following intravenous infusion of 0.15 M hydrochloric acid for 60 minutes to rats (ca.50 mL/kg bw per hour), urinary excretion of the chloride ion was increased.
Remarks: The study was performed to see the effects of Cl⁻ to the plasma renin activity.
Reliability : (3) Not reliable
References: Kotchen et al. (1980)

(b)
Type: Excretion
Results: Groups of ten female mongrel dogs fed a low sodium chloride (0.01%) diet for at least 1 week were used for treatment. Following intravenous infusion of 0.15 M hydrochloric acid for 60 minutes to dogs (20 mL/kg bw per hour), urinary excretion of the chloride ion was increased in five dogs.
Remarks: The study was performed to see the effects of Cl⁻ to the plasma renin activity.
Reliability : (3) Not reliable
References: Kotchen, T.A. et al. (1980)

5.11 EXPERIENCE WITH HUMAN EXPOSURE

(1)
Results: ACUTE TOXICITY, SUICIDE
Thirty eight year-old woman
Ingestion of c.a. 60 mL of 35% hydrochloric acid to kill herself.
After 1 hour: metabolic acidosis, Hypoxemia
After 2 hours: thrombocytopenia, DIC (Disseminated Intravascular Coagulation),
After 29 hours: multiple organ failure, death.
Remarks:

Reliability	:	(3) Not reliable
Reference:		Hashimura et al. (1996)
(2)		ACUTE TOXICITY, HUMAN EXPERIMENT
Results:		No deaths occurred in human following the inhalation of hydrogen chloride for 5 minutes. LCL ₀ = 4.53 mg/L/5 min (3000 ppm/ 5 min)
Remarks:		
Reliability	:	(3) Not reliable
Reference:		European Commission- European Chemical Bureau (2000)
(3)		ACUTE TOXICITY, HUMAN EXPERIMENT
Results:		No deaths occurred in human following the inhalation of hydrogen chloride for 30 minutes. LCL ₀ = 1.96 mg/L/30 min (1300 ppm/ 30 min)
Remarks:		
Reliability	:	(3) Not reliable
Reference:		European Commission- European Chemical Bureau (2000)
(4)		ACUTE TOXICITY, HUMAN EXPERIMENT
Results:		Short-term exposure to airborne concentration up to 1.8 ppm did not cause irritation to the respiratory tract of sensitive asthmatic volunteers.
Remarks:		Five male and five female young adult asthmatics were exposed to hydrogen chloride at concentrations of 0 (filtered air), 0.8 or 1.8 ppm via facemasks for 45 minutes. The facemasks were designed to prevent exposure of the eyes. The concentration of hydrogen chlorine in the test atmospheres was monitored by conductivity cell/ion chromatography analysis. Each exposure session consisted of two 15-minute periods of moderate exercise on a treadmill, interspersed by a 15-minute rest period. There were no increases in the reporting of symptoms of respiratory tract irritancy or effects on pulmonary function during or after the hydrogen chloride exposure sessions.
Reliability	:	(2) Reliable with restrictions
Reference:		Stevens et al. (1992)
(5)		SKIN IRRITATION/CORROSION
Species/strain:		Human
Results:		Highly corrosive []; Corrosive []; Highly irritating []; Irritating []; Moderate irritating []; Slightly irritating [X]; Not irritating []
Classification:		Highly corrosive (causes severe burns) []; Corrosive (caused burns) []; Irritating [X]; Not irritating []
Method:		Other
GLP:		Yes [X] No [] ? []
Test substance:		Hydrochloric acid
Remarks:		Method: Since 9 and 18% of HCl were determined as non-corrosive <i>in vitro</i> testing as screening test using discs of human tissue, patch test using Hill Top chambers of HCl (10%) on 30 volunteers at upper outer arm was proceeded for up to 4h. Sodium dodecyl sulphate (SDS, 20%) was used as the positive control.

	Results: Though six of 30 volunteers showed positive reaction to HCl (10%) within 4 hours, the degree of reaction was milder than positive control (SDS, 20%).
Reliability :	(2) Reliable with restrictions
Reference:	York, M.H. et al. (1996)
(6)	SKIN IRRITATION/CORROSION
Species/strain:	Human
Results:	Highly corrosive []; Corrosive []; Highly irritating []; Irritating []; Moderate irritating []; Slightly irritating [X]; Not irritating []
Classification:	Highly corrosive (causes severe burns) []; Corrosive (caused burns) []; Irritating []; Not irritating []
Method:	Other
GLP:	Yes [] No [] ? [X]
Test substance:	Hydrochloric acid, Danish Pharmacopea quality.
Remarks:	Method: Closed patch test were applied to the flexor side of both upper arms of 20 healthy volunteers (12 males and 8 females) for 24 hours. Propanol, sterile water and an empty chamber were served as controls and evaluation of the reaction was performed after, 48 and 96. Results: After 24 hours of application, 14 out of 20 clinically responded positively (very weak to weak erythema) to the test substance (4% HCl in water). Among the positive responders, 1 severe reaction was seen with ulceration after 48 hours. Remarks: Informed consent was obtained from all volunteers and the study was approved by the local ethcal committee.
Reliability :	(3) Not reliable
Reference:	Agner, T and Serup, J. (1989)
(7)	SKIN IRRITATION/CORROSION
Species/strain:	Human
Results:	Highly corrosive []; Corrosive []; Highly irritating []; Irritating []; Moderate irritating []; Slightly irritating [X]; Not irritating []
Classification:	Highly corrosive (causes severe burns) []; Corrosive (caused burns) []; Irritating []; Not irritating []
Method:	Other
GLP:	Yes [] No [] ? [X]
Test substance:	Hydrochloric acid
Remarks:	Method: Closed patch test with 4% of Hydrochloric acid was applied to both arms (anterolateral surface of the upper arm) of 16 healthy Caucasian volunteers for 24 hours. Distilled water was used as control. The degree of inflammation was scored visually according to a modified method described by Fregert S. (1974, Manual of contact dermatitis) 24 or 96 hours after application. Results: Median visual score at 24 and 96 hours after application showed weak positive reaction (erythema, possibly slight infiltration) and no reaction, respectively.
Reliability :	(3) Not reliable
Reference:	Agner, T. and Serup, J. (1988)

- (8) SKIN IRRITATION/CORROSION
Results: Brief contact with concentrated hydrochloric acid has caused ulceration and severe burns to human skin.
Remarks:
Reliability : (3) Not reliable
Reference: BIBRA (1990)
- (9) SKIN IRRITATION/CORROSION
Results: Contact with solutions to human skin described as dilute (where defined, 4-10%) for 2 hours or longer, sometimes repeatedly, has produced irritation.
Remarks:
Reliability : (3) Not reliable
References: BIBRA (1990)
- (10) SKIN IRRITATION/CORROSION
Results: When used in 24- or 48-hr covered patch tests to human to detect the sensitized state, 1% hydrochloric acid has been described as irritant.
Remarks: No data have been produced to support this statement.
Reliability : (3) Not reliable
References: BIBRA (1990)
- (11) SKIN IRRITATION/CORROSION
Results: Uncovered contact to human skin with solutions of around 1% caused stinging.
Remarks: The stinging response apparently occurs only in susceptible individuals and is not directly related to irritation.
Reliability : (3) Not reliable
References: BIBRA (1990)
- (12) EYE IRRITATION/CORROSION
Results: Dilute solutions produce mild irritation to human eyes, while concentrated solutions can cause permanent damage and loss of sight.
Remarks: concentration was not specified.
Reliability : (3) Not reliable
References: BIBRA (1990)
- (13) EYE IRRITATION/CORROSION
Results: According to a standard text, brief contact with acids of pH in excess of 2 (<0.04% for hydrochloric acid) can produce stinging but no damage to human eyes.
Remarks: The basis for this statement is not clear.
Reliability : (3) Not reliable
References: BIBRA (1990)

- (14) EYE IRRITATION/CORROSION
 Results: Exposure to high concentrations of mist or vapour is immediately irritating and may cause damage or blindness.
 Remarks: No further details
 Reliability : (3) Not reliable
 References: BIBRA (1990)
- (15) SKIN SENSITIZATION
 Type: Patch Test
 Species/strain: Human
 Results: Sensitizing []; Not sensitizing [X]; ambiguous []
 Classification: Sensitizing []; Not sensitizing []
 Method: other
 GLP: Yes [] No [] ? [X]
 Test substance: hydrochloric acid
 Remarks: Fifty subjects were given nine 24-hr covered application of HCl (at unspecified concentrations) over 3 weeks. None of the subjects gave positive reactions in a subsequent 24-hr covered patch test 10-14 days after final induction application.
 Reliability : (3) Not reliable
 Reference: Gad et al. (1986)
- (16) REPEATED EXPOSURE, HUMAN
 Results: Ingestion by 4 healthy volunteers of HCl at 50 mM/day for 4 days resulted in a fall in blood urea and urinary urea, with a concomitant rise in urinary excretion of ammonia (NH₄⁺).
 Remarks:
 Reliability : (3) Not reliable
 Reference: Fine, A. et al. (1977)
- (17) REPEATED EXPOSURE, HUMAN
 Results: Erosion in more than one incisor was observed in the workers of zinc galvanizing plant in the Netherlands.
 Remarks: In the plant, 15% hydrochloric acid solution was used in the pickling process, and the atmospheric concentration of 1.8-12.4 mg/m³ (geometric mean) were observed at 6 sites (ca. 50 samples for each site) of the plant. The workers were exposed to hydrochloric acid concentration above 7 mg/m³ for 27% of their work (length of employment is not shown) in a personal exposure monitoring program. Erosion in more than one incisor were observed in the 34 workers out of 38 workers examined.
 Reliability : (3) Not reliable
 Reference: Remijn et al. (1982)
- (18) CASE CONTROL STUDY
 Results: A pilot case control study comprised 39 male and 24 female preleukemia (myelodysplasia) patients. Questionnaires in outpatients and home interviews were used to estimate the exposure to specific chemicals and radiation.

- Hospital patients were compared with outpatient controls matched for age and sex. No association was established for exposure to hydrochloric acid with preleukemia.
- Remarks: Pilot study to confirm the effectiveness of methodology.
Reliability : (3) Not reliable
Reference: Farrow A. et al. (1989)
- (19) CASE CONTROL STUDY
Results: In a case control study the possible relationship between exposure to Hydrogen chloride (none, low, middle, high exposure) and lung cancer (trachea, bronchus, lungs) was investigated. 308 lung cancer deaths (death certificates) occurring from 1940 through 1980 among a cohort of 12,606 male employees of a chemical plant were compared to two matched (race, year of birth, year of hire) control groups. Adjusted lung cancer risks for duration of exposure, cumulative exposure and highest average exposure did not show increased relative risks or a dose-related trend.
- Remarks:
Reliability : (3) Not reliable
Reference: Bond et al. (1986) and Bond et al. (1991)
- (20) CASE CONTROL STUDY
Results: A case controlled study of primary intracranial neoplasms conducted at a US chemical plant, found no association with any exposure to Hydrogen chloride (Odds ratio, 1.40 ; 90%CI, 0.70 – 2.80 for first control group, odds ratio, 1.02 ; 90%CI, 0.81 – 1.29 for second control group).
- Although the odds ratio for exposure to Hydrogen chloride for people who had been employed for 1-4 years was 2.02 (90%CI, 0.50 – 8.1), no association was seen for individuals who had been employed for longer than 20 years (Odds ratio, 1.02 ; 90%CI, 0.81 – 1.29).
- Remarks:
Reliability : (3) Not reliable
Reference: Bond, G.G et al. (1983)
- (21) CASE CONTROL STUDY
Results: A case controlled study of renal cancer conducted at a US chemical plant, found no association with any exposure to hydrogen chloride (Odds ratio, 0.90 ; 90%CI, 0.44 – 1.83 for first control group, odds ratio, 0.86 ; 90%CI, 0.40 – 1.86 for second control group).
- Remarks:
Reliability : (3) Not reliable
Reference: Bond et al. (1985)
- (22) CASE CONTROL STUDY
Results: In a population based case controlled study of lung cancer (3,730 cancer patients), no association was found between all cancers of the lung and

- exposure to hydrogen chloride.
Remarks: Exposure was not limited to Hydrochloric acid. A case control study in Canada
- Reliability : (3) Not reliable
Reference: Siemiatycki, J., ed. (1991)
- (23) CASE CONTROL STUDY
Results: American Cyanamid noted an apparent excess of respiratory cancers among former employees who worked with Hydrochloric acid. The company said a Standard Mortality Ratio of 1.31 was found for respiratory cancer among male hired between 1925 and 1973 at Lindane facility (138.8 expected and 182 observed). The number of employee was 7,153.
Remarks: All cases of respiratory cancer were documented to be smokers.
Reliability : (3) Not reliable
Reference: ANON, ed. (1987)
- (24) COHORT STUDY
Results: In the study of 1,165 male workers employed in 1940-64 in the three US steel-pickling operations for at least six months, a subset of 189 workers had been exposed to mists of acids other than sulfuric, which were primarily of hydrochloric acid. An excess risk for lung cancer was seen (standardized mortality ratio [SMR], 2.24 [95%CI, 1.02-2.46]; 9 deaths). The excess persisted for workers who had been employed in 1950-54 when other steelworkers were used as a control for socio-economic and life-style factors such as smoking (SMR, 2.00; 95%CI,1.06-3.78).
Remarks: The other acid s used at the steel plants included hydrochloric, nitric, hydrofluoric, and hydrocyanoic acid with hydrochloric acid being most commonly used.
Reliability : (3) Not reliable
Reference: Beaumont, J.J. et al. (1987)

6. REFERENCES

ACGIH (2001) Documentation of the Threshold Limit Values and Biological Exposure Indices 7th ed.

Agner, T and Serup, J. (1989) Skin reactions to irritants assessed by non-invasive bioengineering methods. *Contact Dermatitis*, 20, 352-359.

Agner, T. and Serup, J. (1988) Contact Thermography for assessment of Skin Damage Due to experimental irritants., *Acta. Dermatol.Venerol.*, 68, 192-195.

Albert, R.E. et al. (1982) Gaseous formaldehyde and hydrogen chloride induction of nasal cancer in the rat. *J Natl Cancer Inst*, 68, 597-604.

Anderson B.G. (1944) The Toxicity Thresholds of Various Substances Found in Industrial Wastes as Determined by the Use of *Daphnia magna*. *SEWAGE WORKS JOURNAL*, 16(6): 1156-1165.

Anon (1963) C.r. Seanc. Soc. Biol, 256, 1043. cited in European Commission- European Chemical Bureau (2000).

Anon, ed. (1987) *Pestic. Toxic. Chem. News.*, 15(43), 6.

Barrow, C.S. et al. (1977) Comparison of the sensory irritation response in mice to chlorine and hydrogen chloride. *Arch. Environ. Health*, 31, 68-76.

Barrow, C.S. et al. (1979) A comparison of the acute inhalation toxicity of hydrogen chloride versus the thermal decomposition products of polyvinylchloride. *J. Comb. Tox.*, 6, 3-12.

BASF AG (1994) cited in European Commission- European Chemical Bureau (2000).

Beaumont, J. J. et al. (1987) Lung cancer mortality in workers exposed to sulfuric acid mist and other acid mists. *J. Natl. Cancer Inst.*, 79, 911-921.

BIBRA (1990) Toxicity Profile of Hydrochloric acid.

Bond G.G. et al. (1983) A case-control study of brain tumor mortality at a Texas chemical plant. *J. Occup. Med.*, 25, 377-386.

Bond G.G. et al. (1985) A case-control study of renal cancer mortality at a Texas chemical plant. *Am. J. Ind. Med.*, 7, 123-139.

Bond G.G. et al. (1986) Nested case-control study of lung cancer among chemical workers. *Am. J. Epidemiol.*, 124, 53-66.

Bond G.G. et al. (1991) Lung cancer and hydrogen chloride exposure: Results from a nested case-control study of chemical workers. *J. Occup. Med.*, 33, 958-961.

Brewitt, H and Honegger, H. (1979) Early Morphological Changes of the Corneal Epithelium after Burning with Hydrochloric Acid. *Ophthalmologica*, Basel 178, 327-336.

Brimblecombe, P. and Clegg, S.L. (1988) The solubility and behavior of acid gases in the marine aerosol. *J. Atmosph. Chem.* 7, 1-18.

Brusick, D (1986) Genotoxic Effects in cultured mammalian cells produced by low pH treatment conditions and increased ion concentration. *Environ., Mutagen.*, 8, 879-886.

Buckley, L.A. et al. (1984) Respiratory Tract lesions induced by sensory Irritants at the RD50 Concentration. *Toxicol. Appl. Pharmacol.*, 74, 417-429.

Burleigh-Flayer, H. et al. (1985) Evaluation of the pulmonary effects of hydrochloric-acid using CO₂ challenging in guinea pigs. *Fundam. Appl. Toxicol.*, 5, 978-985.

Burns, C. M. (1929) The effect of the continued ingestion of mineral acid on growth of body and bone and on the composition of bone and of the soft tissues. *Biochem. J.*, 23, 860-867.

Cairns, J. and Scheier, A. (1959) The relationship of bluegill sunfish body size to tolerance for some common chemicals. *Proc. 13th Ind. Waste Conf., Purdue Univ. Eng. Bull.*, 96, 243-252.

CERI (2002) Chemicals Evaluation & Research Institute, Japan. unpublished data.

Chemical Market Reporter (1999) Chemical Profile 'Hydrochloric acid' November 22, 1999. (<http://63.236.84.14/news/newsframe.cfm?framebody=/news/profile.cfm>)

Cifone, M.A., Myhr, B., Eiche, A. and Bolcsfoldi, G. (1987) Effect of pH shifts on the mutant frequency at the thymidine kinase locus in mouse lymphoma L5178Y TK+/- cells. *Mutat. Res.*, 189, 39-46.

CIIT (1984) Ninety-day Inhalation Toxicity Study of Hydrogen chloride gas In B6C3F₁ mice, Sprague-Dawley and Fischer-344 rats., *ToxiGenics*, 420-1087.

Clausing, P. and Gottschalk, M. Z. (1989) Effects of drinking water acidification, restriction of water supply and individual caging on parameter of toxicological studies in rats. *Versuchstierkd.*, 32, 129-134 .

CMAI (2000) World Petrochemical Conference, Fifteenth Annual, March 29&30.

Cosgrove, G.E. et al. (1965) Oncogenic effects of 4-(p-Dimethylaminostyryl)quinoline (4M20) in mice. *Cancer Res.*, 25, 938.

Cohen et al. (1981) Short term intermittent exposure to hydrochloric acid (Draft final report). cited in European Commission- European Chemical Bureau (2000).

DAINIHON JOCHUGIKU Corporation (2002) Product information.

Darmer, K.I. et al. (1974a) Acute toxicity in rats and mice exposed to hydrogen chloride gas and aerosol. *Am. Ind. Hyg. Assoc. J.*, 35, 623-631.

Darmer, K.I. et al. (1974b) Hygienic assessment of the hydrogen ion content in the atmosphere. *Giginea I Sanitariya*, 38(3), 6-9.

De Backer, A. et al. (1985) Hydrochloric acid. A trigger of cell proliferation in the esophagus of dogs. *Digist. Dis. Sci.*, 30, 884.

Demerec, M. et al. (1951) A survey of chemicals for mutagenic action on *E. coli*. *Am. Nat.*, 85, 119-136.

Dostal, M. (1973) Effect of some nonspecific factors accompanying intraamniotic injection in mouse foetus. *Folia morph. (Prague)*, 21, 97-101.

Dow Europe S.A (1993) Safety Data Sheet, Dow Europe S.A. cited European Commission-European Chemical Bureau (2000)

Dyer, H.M. et al. (1946) Effect of administration of hot water, acids, alkali, mecholyl chloride, or atropine sulfate upon the gastric mucosa of mice. *J Natl Cancer Inst*, 7, 67.

Ellgaard, E.G. and Gilmore, III, J.Y. (1984) Effects of different acids on the bluegill sunfish, *Lepomis macrochirus* Rafinesque. *J. Fish Biol.* 25(2), 133-137.

Elvers et al. (1989) Ullmann's Encyclopaedia of Industry Chemistry, Elvers et al. (eds), 5th edition, Vol. 13, p. 283-284, VCH, Weinheim, Germany.

European Commission Directive 2000/39/EC (2000) Commission Directive 2000/39/EC of 8 June 2000 establishing a first list of indicative occupational exposure limit values in implementation of Council Directive 98/24/EC on the protection of the Health and safety of workers from the risks related to chemical agents at work, 2000 O.J. (L 142) 47, 16 June 2000.

European Commission- European Chemical Bureau (2000) IUCLID Dataset.

Farmer, C.B. et al. (1976) Spectroscopic detection and vertical distribution of HCl in the troposphere and stratosphere. *Geophys. Res. Lett.*, 3, 13-16.

Farrow, A. et al. (1989) Myelodysplasia, chemical exposure, and other environmental factors. *Leukemia*, 3, 33-35.

Fine, A. et al. (1977) The effects of administrations of HCl, NH₄Cl and NH₄HCO₃ on the excretion of urea and ammonium in man. *Europ. J. Clin. Invest.*, 7, 587-589.

Flury and Zernik (1931) Harmful Gases, Vapors, Fog, Smoke and Dust Varieties, J. Springer Publishing House, Berlin, 125/128 cited European Commission- European Chemical Bureau (2000) and BIBRA (1990)

Gad, S.C., Dunn, B.J., Dobbs, D.W., Reilly, C., and Walsh, R.D. (1986) Development and validation of an alternative dermal sensitisation test: the mouse ear swelling test (MEST)., *Toxicol. Appl. Pharmacol.* 84, 93-114.

Galloway, J.N. et al. (1982) The composition of precipitation in remote areas of the world. *J. Geophy Res*, 87, 8771 - 8786.

Gillette, L. A., Miller, D. L. and Redman, H. E. (1952) Appraisal of a Chemical Waste Problem by Fish Toxicity Tests. *SEWAGE AND INDUSTRIAL WASTERS*, 24 (11): 1397-1401.

Graham, M. S. and Wood, C. M. (1981) Toxicity of environmental acid to the rainbow trout: interactions of water hardness, acid type, and exercise., *CAN.J. ZOOL.*, Vol. 59, 1518-1526.

Greenfield, L.J. et al. (1969) Pulmonary effects of experimental graded aspiration of hydrochloric acid. *Ann surg*, 170, 74.

Griffith, J.F. et al. (1980) Dose-response studies with chemical irritants in the albino rabbit eye as a basis for selecting optimum testing conditions for predicting hazard to the human eye. *Toxicol. Appl. Pharmacol.*, 55, 501-513 .

Hales, C.A. et al. (1988) Synthetic smoke with acrolein but not HCl produces pulmonary edema., *J. Appl. Physiol.*, 64, 1121-1133.

Harley, R.D. (1952) An experimental study on the evaluation of hydrosulphosol in the treatment of ocular injuries due to chemical burns. *Am. J. Ophthal.*, 35, 1653-1675.

- Hartzell, G.E. et al. (1987) Modeling of toxicological effects of fire gases: VI. Further studies on the toxicity of smoke containing hydrogen chloride. *J. Fire Sci.*, 5, 368-391.
- Hartzell, G.E. et al. (1988) Modeling of toxicological effects of fire gases: VII. Studies on evaluation of animal models in combustion toxicology. *J. Fire Sci.*, 6, 411-431.
- Hartzell, G.E. et al. (1990) Toxicity of smoke containing hydrogen chloride. *ACS Symp. Ser.*, 425, 12-20.
- Hashimura, Y. et al. (1996) *Japanese Journal of Toxicology*, 9, 353.
- Higgins, E.A. et al. (1972) Acute toxicity of brief exposures to HF, HCl, NO₂ and HCN with and without CO. *Fire Technol.*, 8, 120-130.
- Hoechst AG (1966) Report 150/66
- Hoechst AG (1993) Sicherheitsdatenblatt Salzsäure chemisch rein, 37% cited in European Commission- European Chemical Bureau (2000).
- Hoechst AG (1994) Sicherheitsdatenblatt Salzsäure chemisch rein, 37% cited in European Commission- European Chemical Bureau (2000).
- HSDB (2001) Hazardous Substance Data Bank, U.S. National Library of Medicine.
- IARC (1992) Hydrochloric acid, In: IARC Monographs on the evaluation of carcinogenic risks to humans., Occupational exposures to mists and vapours from strong inorganic acids; and other industrial chemicals. 54, 189-211.
- Isquith, A., Matheson, D., and Slesinski, R. (1988) Genotoxicity studies on selected organosilicon compounds: in vitro assays. *Fd. Chem. Toxic.* 26, 255-261.
- Jacobs, G. A. (1992) OECD eye irritation tests on two acids. *J. Am. Coll. Toxicol.* 11(6), 734.
- Japan Society for Occupational Health (2001) *J. Occupational Health*, **43**, 97.
- Kaplan, K.L. et al. (1988) Effects of hydrogen chloride on respiratory response and pulmonary function of the baboon. *J. Toxicol. Environ. Health*, 23, 473-493.
- Kaplan, K.L. et al. (1989) Evaluation of smoke toxic potency test methods: Comparison of the NBS Cup Furnace, the Radiant Furnace and the UPITT Tests. *J. Fire Sci.*, 7, 194- 213.
- Kaplan, K.L. et al. (1993) Acute and long-term effects of polyvinylchloride (PVC) smoke on the respiratory system of the baboon and comparison with the effects of hydrogen chloride. *J. Fire Sci.*, 11 (6), 485-511.
- Karlsmark, T. et al. (1988) The effect of sodium hydroxide and hydrochloric acid on pig dermis. A light microscopic study. *Forensic Sci. Int.*, 39, 227-233 and 235-243.
- Kirsch, V. and Drabke, P. (1982) Zur Beurteilung biologischer Wirkungen von Chlorwasserstoff. *Gesamte Hygiene*, 28, 107-109.
- Kotchen, T.A. et al. (1980) Inhibition of rennin secretion by HCl is related to chloride in both dog and rat. *Amer. J. Physiol.*, 239, F44-F49.

Lehman, K.B. (1886) Experimentelle Studien über den Einfluss technisch und hygienisch wichtiger Gase und Dämpfe auf Organismus. Arch. Hyg., 5, 1-126

Lehman, K.B. (1908) Neue Untersuchungen über die quantitative Absorption einiger giftiger Gase von Tier und Mensch durch den Respirationstraktus und seine Teile., Arch. Hyg., 67, 57-99.

Lehman, K.B. and Burch, A. (1910) Über die Absorption von Salzsäuredämpfen durch das in länger dauernden Versuchen., Arch. Hyg., 72, 343-357.

Litton Bionetics, Inc. (1978) Mutagenicity evaluation of Hydrochloric acid, Final report. LBI Project No. 20893.

Loewy, A and Munzer, E. (1923) Beiträge zur von der experimentellen Säurevergiftung., Bioch. Z. 134, 437-441.

Lucia, H.L. et al. (1977) A semi-quantitative method for assessing anatomic damage sustained by the upper respiratory tract of the laboratory mouse, *Mus Musculus*. J. Comb. Tox., 4, 472-486.

MacEwean, J.D. et al. (1974) Toxic Hazards Research Unit Annual Technical Report, NTIS AD-A011-559.

Machle, W. et al. (1942) The effect of the inhalation of hydrogen chloride. J. Ind. Hyg. Toxicol., 24, 222-225.

Martling, C.R. and Lundberg, J.M. (1988) Capsaicin sensitive afferents contribute to acute airway edema following tracheal instillation of hydrochloric acid or gastric juice in the rat. *Anesthesiology*, 68, 350-356.

McCarroll, N.E., Keech, B.H., and Piper, C.E. (1981a) An *E coli* microsuspension assay for the detection of DNA damage induced by direct-acting agents and promutagens., *Environ. Mutagenesis*, 3, 429-444.

McCarroll, N.E., Keech, B.H., and Piper, C.E. (1981b) A microsuspension adaptation of the *Bacillus subtilis* "rec" assay. *Environ., Mutagenesis*, 3, 607-616.

METI, Japan (1999) Ministry of Economy, Trade and Industry (former MITI), unpublished data.

Ministry of Environment, Japan (MOE), Japan

Ministry of Land, Infrastructure and Transport, Japan (1999), unpublished data. Test was conducted by Chemicals Evaluation and Research Institute, Japan.

Monsanto (1976) unpublished report YO-76-0404 of Monsanto cited in European Commission-European Chemical Bureau (2000)

Morita, T., Watanabe, Y., Takeda, K. and Okumura, K. (1989) Effects of pH in the in vitro chromosomal aberration test. *Mutat. Res.*, 225, 55-60.

Moron, F. et al. (1984) The gastric fundic mucosal energy systems and the HCl-induced lesions in rats in dependence on starvation. *Acta Med. Hung.*, 41, 253-258.

Murphy et al. (1982) Ocular irritancy responses to various pHs of acids and bases with and without irrigation. *Toxicology*, 23, 281-291.

- Narat, J. K. (1925) Experimental production of malignant growths by simple chemicals. *J. Cancer Res.*, 9, 135-147.
- Orihata, M. et al. (1989) The relationship between adaptive cytoprotection and prostaglandin contents in the rat stomachs after oral administration of 0.35 N HCl. *Scand. J. Gastroenterol*, 24(Suppl. 162) 79-82.
- Parker, J.G. (1984) The effects of Selected Chemicals and Water Quality on the Marine Polychaete *Ophryotrocha diadema*. *Water Res.*, 18(7): 865-868.
- Parmar, N.S. et al. (1988) Gastric anti-ulcer and cytoprotective effect of selenium in rats. *Toxicol Appl Pharmacol*, 92, 122-130.
- Pavlova T.E. (1976) Disturbances in the development of the progeny of rats subjected to the influence of hydrogen chloride. *Byull. Eksp. Biol. Med.*, 82, 866-868.
- Potokar, M. et al. (1985) Studies on the design of animal tests for the corrosiveness of industrial chemicals. *Fd. Chem. Toxic.*, 23, 615.
- Pritzl, M.C. and Kienholz, E.W. (1973) The effect of hydrochloric, sulfuric, phosphoric, and nitric acids in diets for broiler chicks. *Poult. Sci.*, 52, 1979-1981.
- Remijn, B., Koster, P., Houthuijs, D., Boleij, J., Willems, H., Brunekreef, B., Biersteker, K. and vanLoveren, C. (1982) Zinc chloride, zinc oxide, hydrochloric acid exposure and dental erosion in a zinc galvanizing plant in the Netherlands. *Ann. Occup. Hyg.*, 25, 299-307.
- Ronzani, E. (1909) Über den Einfluss der Einatmungen von reizenden Gasen der Industrien auf die Schutzkrankkräfte des Organismus gegenüber den infektiösen Krankheiten., *Arch. Hyg.* 70, 217-269.
- Sellakumar, A.R. et al. (1985) Carcinogenicity of formaldehyde and hydrogen chloride in rats. *Toxicol. Appl. Pharmacol.*, 81, 401-406.
- Siemiatycki, J., ed. (1991) Risk factors for cancer in the workplace, BocaRaton, FL, CRC Press. Cited in IARC Monograph 54.
- Solvay S.A.(2002) ATOMOSPHERIC FATE OF HYDROGEN CHLORIDE. Unpublished report
- Srikrishna, V. and Monteiro-Riviere, N.A. (1991) The effects of sodium hydroxide and hydrochloric acid on isolated perfused skin. *In Vitro Toxicol.*, 4, 207-215.
- Stangenberg, E. (1975) The influence of the chemical composition of water on the pike perch (*Lucioperca lucioperca L.*) fry from the lake Goplo. *Limnologica*, 9(3): 421-426.
- Stavert, D.M. et al. (1991) Relative acute toxicities of hydrogen fluoride, hydrogen chloride, and hydrogen bromide in nose- and pseudo-mouth-breathing rats. *Fundam. Appl. Toxicol.*, 16, 636-655.
- Stevens B, Koenig JQ, Rebolledo V, Hanley QS, Covert DS (1992) Respiratory effects from the inhalation of hydrogen chloride in young adult asthmatics. *JOM* 34, 923-929.
- Stumm-Tegethoff, B.F.A. (1969) Formaldehyde-induced mutations in *Drosophila melanogaster* independence of the presence of acids. *Theor. Appl. Genet.*, 39, 330-334.
- The Chemical Daily (2000) 13700 Chemical Products, p26-27, 276 (in Japanese).

The Merck Index, 13th Ed. (2001)

UNEP (1995) Water quality of world river basins, UNEP Environment Library No.14.

Upotn, P. K. and L'Estrange, J. L. (1977) Effects of chronic hydrochloric and lactic acid balance and bone composition of the rat. Quarterly Journal of Experimental Physiology, 62, 223-235.

Vernot, E.H. et al. (1977) Acute Toxicity and Skin Corrosion Data for Some Organic and Inorganic Compounds and aqueous Solutions. Toxicol. Appl. Pharmacol., 42, 417- 423.

Wallen, I. E., Greer, W. C. and Lasater, R. (1957) Toxicity to *Gambusia affinis* of Certain Pure Chemicals in Turbid Water. SEWAGE AND INDUSTRIAL WASTERS, 29 (6): 695-711.

Wohlslagel, J.et al. (1976) Toxicity of solid rocket motor exhaust: Effects of hydrogen chloride, hydrogen fluoride, and alumina on rodents. J. Comb. Tox., 3, 61-70.

World Health Organization (1982) Environmental Health Criteria 21 (Chlorine and Hydrogen chloride)

York, M. H., Griffiths, A. E., Whittle, E. and Basketter, D. A. (1996) Evaluation of a human patch test for the identification and classification of skin irritation potential. Contact Dermatitis, 34(3), 204-212.