FOREWORD INTRODUCTION

POTASSIUM CHLORIDE

CAS N°: 7447-40-7

SIDS Initial Assessment Report for 13th SIAM

(Bern, 6-9 November 2001)

Chemical Name: Potassium chloride

CAS No: 7447-40-7

Sponsor Country: Norway

National SIDS Contact Point in Sponsor Country: Marit Kopangen

HISTORY: SIDS Dossier, SIAR and SIAP are reviewed by the National Institute of Public Health (Norway) and the Norwegian Institute for Water Research (Norway) (August 2001). All original studies reported in the SIDS dossier were submitted for peer review.

TESTING:
no testing (X)
testing ( )

COMMENTS:

Deadline for circulation: 14 September 2001

Date of Circulation: 14 September 2001

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	7447-40-7
Chemical Name	Potassium chloride
Structural Formula	K-Cl

RECOMMENDATIONS

The chemical is currently of low priority for further work.

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

Potassium chloride is an essential constituent of the body for intracellular osmotic pressure and buffering, cell permeability, acid-base balance, muscle contraction and nerve function.

Acute oral toxicity of KCl in mammals is low (LD50 = 3020 mg/kg bw). In humans, acute oral toxicity is rare because large single doses induce nausea and vomiting, and because KCl is rapidly excreted in the absence of any pre-existing kidney damage. Usual therapeutic doses of potassium for oral solution-adults are 1.5-3 g/day to prevent depletion, and 3-7.5 g/day for replacement. For repeated dose toxicity, a NOAEL at 1820 mg/kg bw/day in rats, and a NOAEL > 80 mmol KCl/day (approx. 85 mg/kg bw/day) in humans can be retained. A threshold concentration for skin irritancy of 60 % was seen when KCl in aqueous solution was in contact with skin of human volunteers. The threshold concentration when applied to broken skin was 5 %.

No gene mutations were reported in bacterial tests, with and without metabolic activation. However, high concentrations of KCl showed positive results in a range of genotoxic screening assays using mammalian cells in culture. The action of KCl in culture seems to be an indirect effect associated with an increased osmotic pressure and concentration. Therefore KCl, do not have any direct relevance in the intact body were such concentrations can not occur. Further studies using *in vivo* systems are not considered necessary under SIDS.

No evidence of treatment-related carcinogenicity was observed in rats administered up to 1820 mg KCl/kg body weight/day through the food in a 2 year study.

A developmental study revealed no foetotoxic or teratogenic effects of KCl in doses up to 235 mg/kg/day (mice) and 310 mg/kg/day (rats). No fertility study has been located. Based on the extensive amount of knowledge on KCl intake, regulation and effects in the human body, and on a worst case exposure estimate (see Exposure), no further testing of fertility is considered required under SIDS.

Gastro-intestinal irritant effects in humans caused by KCl administrated orally have been reported at doses from about 31 mg/kg bw/day. One epidemiological investigation among potash miners disclosed no evidence of predisposition of underground miners to any of the diseases evaluated, including lung cancer.

Environment

KCl as inorganic salt is not subjected to further degradation processes in the environment. In water, potassium chloride is highly water soluble, and readily undergoes dissociation. In soil, transport/leaching of potassium and chloride is affected by the clay minerals (type and content), pH, and organic matter.

In short-term acute toxicity tests with fish, daphnia and algae the following results were found (lowest test result values): *Ictalurus punctulus* 48h-LC50 = 720 mg/l; *Daphnia magna*: 48h-LC50 = 177 mg/l; *Nitzschia linearis:* 120 h-EC50 = 1337 mg/l. A chronic reproductive test with the invertebrate Daphnia magna gave a LOEC of 101 mg/l. All the studies compiled on the acute and chronic aquatic toxicity were > 100 mg/L. Thus it is concluded that KCl is not hazardous to freshwater organisms. Taking into considerations the background concentrations of KCl in

seawater (380 mg/l K^+ and 19,000 mg/l Cl^-), it is concluded that there is no reason for further investigations of KCl on marine species. The low concern for the environment is supported by the absence of a bioaccumulation potential for the substance.

In plants, potassium is one of the three major nutrients and chloride is an essential micronutrient. The potassium requirement for optimal plant growth is in the range 2-5 % of the plant dry weight of vegetative parts. In most plant species the Cl requirement for optimal growth is in the range of 0.2-0.4 mg/g dry matter.

Potassium in plants is important for the osmotic and ionic regulation, plays a key role in the water homeostasis, and is closely connected with processes involved in the protein synthesis. In higher plants, potassium affects photosynthesis at various levels. Cl is also essential for the photosynthesis in plants, and has important functions in the osmotic regulation. An adequate supply of potassium and chloride in plants tends to improve the plant's resistance towards several diseases.

Exposure

World-wide production figures for KCl exceed 1 million metric tons/year. Virtually all commercial KCl is extracted from natural sources of the substance. More than 90 % of the total KCl consumption is used for fertilizer production. Production of potassium hydroxide accounts for more than 90 % of the non-fertilizer or industrial uses of KCl. Other non-fertilizer uses of KCl include food/foodstuff additives, supplement of animal feed, pharmaceutical products, laboratory chemicals, deicing agents and photo chemicals.

KCl is ubiquitous in the environment, occurring in minerals, soil and sediments, and natural waters. KCl is also present as a major and essential constituent in animals and plants. The main human exposure to KCl is the normal dietary intake (2-4 g K and 3.5-9 g Cl), and indirect exposure via the environment (drinking water).

Specific occupational exposure limits (OELs) and actual exposure levels in the mining, refining, fertilizer and other industries have not been found. Assuming 100 % body retention breathing from a working atmosphere containing 10 mg/m^3 KCl (in accordance with the TWA value for "Particulates Not Otherwise Classified), a worker's daily inhalation dose for KCl was calculated to 140 mg (worst case).

NATURE OF FURTHER WORK RECOMMENDED

No recommendation.

FULL SIDS SUMMARY

CAS NO: 7447-40-7		SPECIES	PROTOCOL	RESULTS
PHYSICAL-CHEMICAL				
2.1	Melting Point			772 °C
2.2	Boiling Point			1407 °C
2.3	Density			1984 kg/m^3
2.4	Vapour Pressure			5.73 hPa at 906 °C
2.5	Partition Coefficient (Log Pow)		Calculated	-0.46
2.6 A.	Water Solubility			342000 mg/l at 20°C
ENVIRONMENTAL FATE AND PATHWAY				
3.1.1	Photodegradation			N.A.
3.1.2	Stability in Water			N.A.
3.2	Monitoring Data			In surface water 2.3 mg K^+/l In surface water 8.3 mg Cl^-/l In seawater 380 mg K^+/l In seawater 19000 mg Cl^-/l In topsoil 0.2-3.3 % K^+ In KCl principal minerals 25-99 % KCl In humans (ad.) 2 g K^+/ kg bw In humans (ad.) 1 g Cl^-/kg bw
3.3	Transport and Distribution		Calculated (Fugacity Level 1 type)	In Air 0.03 % In Water 99.7 % In Sediment 0.01 % In Soil 0.03 %
3.5	Biodegradation			N.A.
ECOTOXICOLOGY				
4.1	Acute/Prolonged Toxicity to Fish	*Pimephales promelas*	US-EPA, 1990	LC_{50} (24 hr) = 950 mg/l LC_{50} (48 hr) = 910 mg/l LC_{50} (96 hr) = 880 mg/l
		Ictalurus punctatus	Other	LC_{50} (48 hr) = 720 mg/l
4.2	Acute Toxicity to Aquatic Invertebrates	*Daphnia magna*	US-EPA, 1990	EC_{50} (24 hr) = 740 mg/l EC_{50} (48 hr) = 660 mg/l
		Ceriodaphnia dubia	US-EPA, 1990	EC_{50} (48 hr) = 630 mg/l
		Daphnia magna	Other	EC_{50} (48h)=177 mg/l
4.3	Toxicity to Aquatic Plants e.g. Algae	*Nitzschia linearis*	Other	EC_{50} (120 hr) = 1337 mg/l
4.5.2	Chronic toxicity to aquatic invertebrates	*Daphnia magna*	Other	EC_{50} (21d) = 130 mg/l LOEC (21d) = 101 mg/l (16 % reproduction impairment)
TOXICOLOGY				
5.1.1	Acute Oral Toxicity	Rat	Other	LD_{50} = 3020 mg/Kg
5.4	Repeated Dose Toxicity	Rat	Other	No adverse effects observed up to 1820 mg/Kg bw/day
5.5	Genetic Toxicity In Vitro			
A.	Bacterial Test (Gene mutation)	*S. typhimurium*	Other (NTP modified standard assay)	- (With metabolic activation) - (Without metabolic activation)
		E. coli	Other (SOS Chromotest)	- (Without metabolic activation)

CAS NO: 7447-40-7		SPECIES	PROTOCOL	RESULTS
			Chromotest)	
B.	Non-Bacterial In Vitro Test (Gene mutation)	Mouse lymphoma cells	OECD 476	+ (With metabolic activation) - (Without metabolic activation)
	(Chromosomal aberrations)	Hamster ovary cells (CHO)	Other	+ (Without metabolic activation)
	(Genmutation)	Chinese hamster V79 cells	OECD 476	+ (With metabolic activation) + (Without metabolic activation)
	(Chromosomal aberrations)	CHO cells	OECD 473	- (With metabolic activation) + (Without metabolic activation)
	(Unscheduled DNA synthesis)	HeLa cells	OECD 482	- (With metabolic activation) - (Without metabolic activation)
5.6	Genetic Toxicity In Vivo			No data
5.7	Carcinogenicity	Rat	Other	No tumours related to treatment
5.8	Toxicity to Reproduction			No data
5.9	Developmental Toxicity/ Teratogenicity	Mice	Other	No effects observed at the highest dose level 235 mg/kg/day
		Rat	Other	No effects observed at the highest dose level 310 mg/kg/day
5.11	Experience with Human Exposure		Work place exposure among potash miners	Negative
			Other	Gastro-intestinal irritant effects

SIDS INITIAL ASSESSMENT REPORT

1 CHEMICAL IDENTITY

Name (OECD): Potassium chloride

CAS No.: 7447-40-7

Molecular Formula: Cl-K

Molecular Weight: 74.55

Melting Point: 772 °C **[1] [2]**

Boiling Point: 1407 °C **[2]**

Vapour pressure: 5.73 hPa at 906 °C **[3]**

Partition Coefficient: -0.46 at 20 °C **[4]**

Water solubility: 342 g/l water at 20 °C **[5][6]**

Potassium chloride is a solid. Impurities are usually sodium chloride, magnesium chloride, bromide and alkaline earth sulphates, depending on the raw material and production process **[6]**. Potassium chloride is readily soluble in water to potassium and chloride ions, and has a low vapour pressure.

2 GENERAL INFORMATION ON EXPOSURE [7]

Potassium chloride (KCl), commonly referred to as muriate of potash, is the most common source of potash (K_2O), and accounts for about 95 % of world potash production. Virtually all (90 %) commercial potash is extracted from natural sources of potassium salt deposits occurring in thin beds in large salt basins formed by the evaporation of ancient seas. Present-day salt lakes and natural brines represent about 10 % of total recoverable potash. Extraction is followed by milling, washing, screening, flotation, crystallization, refining and drying.

The annual global production volume of potash was approximately 22.6 million metric tons in 1994. World potash production is confined to thirteen countries and is dominated by Canada, the former USSR and Germany, which together account for about 73 % of world production. The United States, Israel and France account for about 15 %, and Jordan, Spain and the United Kingdom for an additional 11 %.

More than 90 % of the total KCl consumption is used for fertilizer production. Production of potassium hydroxide accounts for more than 90 % of the non-fertilizer or industrial use of KCl. KOH is also used in the production of some agricultural-grade liquid fertilizers. Other non-fertilizer uses of KCl include:

- wide dispersive use:
- food/ foodstuff additives: KCl is used as a nutrient and/or dietary supplement food additive. KCl also serves as a potassium supplement of animal feed;
- pharmaceutical products: KCl is used for prophylaxis and treatment of hypokalemia, in electrolyte replenishment solutions for general medical use and kidney dialysis, and in digitalis intoxication;
- laboratory chemicals: KCl is used in electrode cells, buffer solutions, and spectroscopy;
- photochemicals;
- drilling mud for oil production industry: KCl is used as conditioner in oil drilling muds and as a shale stabilizer to prevent swelling;
- flame retardants and fire preventing agents: KCl is used as a component in dry chemical fire extinguisher.
- anti-freezing agents: KCl is used to melt ice on streets and driveways;
- water treatment;
- detergent builders;
- glass and ceramics;
- textiles;
- dyes;
- non-dispersive use:
- flux agents for casting: KCl serves as a flux in secondary aluminium processing,
- use resulting in inclusion into or into matrix:
- intermediates for basic chemicals industry.

2.1 ENVIRONMENTAL FATE

KCl is ubiquitous in the environment, occurring in minerals, soil and sediments, and natural waters (oceans, lakes, rivers). An overview of background concentrations of KCl is presented in Table 2-1.

Table 2-1. Background concentrations of potassium chloride.

Medium	Concentration	References
Minerals	sylvinite: > 99 % KCl carnallite: approx. 25 % KCl kainite: approx. 30 % KCl	**[7]**
Soil (topsoil)	0.2-3.3 % total potassium	**[7]**
Seawater	380 mg/l potassium (K^+) 19 000 mg/l chloride (Cl^-)	**[8]**
Freshwater (mean composition of river waters)	2.3 mg/l potassium (K^+) 8.3 mg/l chloride (Cl^-)	**[9]**

KCl as inorganic salt is not subjected to further degradation processes in the environment. In water, potassium chloride is highly water soluble, and readily undergoes dissociation. In soil, transport/leaching of potassium and chloride is affected by clay minerals (type and content), pH, and organic matter **[10-11]**. K is in general less mobile and less prone to leaching than anions in soil, such as chloride and nitrate (NO_3^-). Chloride binds only weakly to soil particles, and therefore follows water movement. Anions do not leach alone, but always together with a counter-ion (cation). Hence, chloride and nitrate leaching may deplete soils of nutrients such as K. Loss of potassium by erosion or leaching carries no environmental concern.

Agricultural soil productivity is dependent on establishing a balanced availability of potassium throughout the growing season, often resulting in the need of fertilizing with potassium. Inadequate maintenance of K in agricultural soils will lead to loss of soil productivity. K deficiencies may also restrict a crop's ability to utilize N, resulting in increased potential for nitrate leaching, and lack of K can enhance a crop's susceptibility to disease and increase the need for pesticide application.

Environmental distribution of potassium chloride using a Generic Level I Fugacity Model under three emission scenarios showed that KCl is mainly distributed to water (99.7 %), while other compartments make minor contributions (< 0.03 % to air, < 0.03 % to soil solids, < 0.01 % to sediment solids). This result applied under the three emissions scenarios 100 % release to water, 100 % release to air, or 100 % release to soil **[12]**. Fugacity estimations may not be reliable for KCl. The modelling programs used are designed for organic chemicals and the chemical is not expected to undergo photolysis or biodegradation.

Taking into consideration the physico-chemical properties of potassium chloride, and a calculated octanol/water partition coefficient of −0.46, no potential for bioaccumulation/ bioconcentration can be identified

2.2 HUMAN EXPOSURE

KCl is ubiquitous in the environment, occurring in minerals, soil and sediments, and natural waters (Table 2-1). KCl is also present as a natural and essential constituent in biota, plants and animals. Hence, the main human exposure to KCl is indirect exposure via the environment, and the normal dietary intake. The normal daily dietary intake of potassium and chloride in humans is 50-100 mmol (2-4 g), and 100-250 mmol (3.5-9 g) respectively **[13-14]**.

Worst-case estimate for exposure of workers to KCl dust by inhalation:
No data on actual exposure levels in the mining, refining, fertilizer and other industries have been found. However, assuming 100 % body retention breathing from a working atmosphere containing 10 mg/m^3 KCl, the daily intake through inhalation during an 8 hr working day will only amount to 140 mg (breathing rate 30 l/min., medium hard work) as compared to a dietary intake of 2-4 g.

No specific occupational exposure limits (OELs) for potassium chloride has been located. Norsk Hydro ASA recommend the substance to be treated as "nuisance dust" with an OEL of 10 mg/m3, in accordance with the TWA value for "Particulates Not Otherwise Classified" as proposed by ACGIH. In the worst-case estimate it is assumed that the air concentration of dust equals the OEL and that the dust consists solely of KCl.

3 HUMAN HEALTH HAZARDS

3.1 EFFECTS ON HUMAN HEALTH

3.1.1 TOXICOKINETICS, METABOLISM, MECHANISMS OF ACTION [15-16]

Potassium and chloride are essential constituents and two of the most abundant ions in all animal species. In adult humans, the total body potassium is approx. 3.5 mol (135 g). 98 % of this is located intracellular (150 mmol/l), the extracellular potassium concentration is approx. 4 mmol/l. Total body chloride in adult humans is approx. 2.1 mol (75 g). 80 % of this is located extracellularly (120 mmol/l); the intracellular concentration of chloride is approx. 3-4 mmol/l.

The metabolism and mechanisms of action of potassium and chloride are well reviewed in standard textbooks on pharmacology and physiology.

Metabolism, biotransformation and kinetics:
About 90 % of the ingested dose of potassium is absorbed by passive diffusion in the membrane of the upper intestine. Potassium is distributed to all tissues where it is the principal intracellular cation. Insulin, acid-base status, aldosterone, and adrenergic activity regulate cellular uptake of potassium.

The majority of ingested potassium is excreted in the urine via glomelural filtration. The distal tubules are able to secrete as well as reabsorb potassium, so they are able to produce a net secretion of potassium to achieve homeostasis in the face of a potassium load due to abnormally high levels of ingested potassium. About 15 % of the total amount of potassium excreted is found in faeces. Cl leaves the tubular lumen by secondary active transport of sodium, and also passive diffusion.

Excretion and retention of potassium is mainly regulated by the main adrenal cortical hormones. Normal homeostatic mechanisms controlling the serum potassium levels allow a wide range of dietary intake. The renal excretory mechanism is designed for efficient removal of excess K, rather for its conservation during deficiency. Even with no intake of K, humans lose a minimum of 585-1170 mg K per day. However, the distribution of potassium between the intracellular and the extracellular fluids can markedly affect the serum potassium level without a change in total body potassium.

Mechanisms of action:
K^+ is the principal cation mediating the osmotic balance of the body fluids. In animals, the maintenance of normal cell volume and pressure depends on Na^+ and K^+ pumping. The K^+/Na^+ separation has allowed for evolution of reversible transmembrane electrical potentials essential for nerve and muscle action in animals, and both potassium and chloride are important in transmission of nerve impulses to the muscle fibers.

Potassium transport through the hydrofobic interior of a membrane can be facilitated by a number of natural compounds that form lipid-soluble alkali metal cation complexes. Potassium serves the critical role as counterion for various carboxylates, phosphates and sulphates, and stabilizes macromolecular structures.

Potassium and chloride is also important in the regulation of the acid-base balance of the body. Potassium is the principal base in tissues of blood cells, and Cl maintains electrochemical neutrality by anion exchange with bicarbonate (the chloride shift) in the CO_2 transport in the blood red cells.

3.1.2 ACUTE TOXICITY

None of the studies on acute toxicity have been carried out under national or international guidelines, and according to GLP. Collectively, however, these studies (summarized in Table 3-1) show effects in the similar range of doses for given animal species.

Table 3-1. Acute toxicity studies with potassium chloride.

Species, strain	Administration	Endpoint	Value (mg/kg body weight)	References
Rat, Wistar	Oral	LD50	3020	**[17]**
Rat, Wistar	Oral	LDL0	2430	**[18]**
Guinea pig	Oral	LDL0	2500	**[18]**
Rat, Wistar	i.p.	LD50	660	**[19]**
Rat, Wistar	i.p.	LDL0	825	**[18]**
Rat	i.v.	LD50	142	**[20]**
Mouse	i.v.	LD50	117	**[21]**
Guinea pig	i.p.	LDL0	900	**[18]**
Guinea pig	i.v.	LDL0	77	**[22]**
Guinea pig	i.a.	LDL0	130	**[23]**
Guinea pig	i.c	LDL0	40	**[24]**

By oral administration, LD50-values of KCl have been determined to 3020 mg/kg body weight for rats **[17]**. Clinical signs of intoxication in animals that died included convulsions followed by exhaustion and respiratory failure. Autopsy revealed signs of irritant gastro-enteritis, and necrosis appeared in the renal tubular epithelium. Animals surviving the LD50 dose had convulsive movements, diarrhoea or constipation, loss of appetite, increased thirst and urine excretion and fever. Measurements of clinical signs were within the normal range within 2-3 days and organ weights and water levels returned to normal limits in survivors at two weeks after administration of KCl.

No data is available on the acute inhalation or acute dermal toxicity for potassium chloride. Due to the low vapour pressure and the low octanol-water partition coefficient of the substance, the potential for inhalation and dermal absorption is considered low.

3.1.2.1 HUMAN DATA

Acute KCl intoxication by oral intake is rare because large single doses usually induce vomiting and because in the absence of pre-existing kidney damage, potassium is rapidly excreted. Cases of acute KCl overload in humans due to accidental or intentional oral intake have been reported, however: a 2 month-old 4.8 kg boy died 2 days after accidentally being fed 1.5 g KCl (LDL0 approx. 938 mg/kg body weight/2 days) **[23]**, and a 46 year-old woman died after ingesting 35 g KCl in the form of slow-release KCl tablets **[24]**.

KCl overdoses manifests in neuromuscular signs in the form of general muscular weakness and ascending paralysis, listlessness, vertigo, mental confusion, hypotension, acute cardiovascular changes with ECG abnormalities, and heart block. Gastrointestinal symptoms manifest as nausea, vomiting, paralytic ileus, and local mucosal necrosis, which may lead to perforation **[25-26]**.

Serum potassium level of 40 mg/100 ml is fatal in man **[27]**. Probable oral lethal dose for humans is estimated to 500-5000 mg/kg **[28]**. Judging from the animal data and reference **[24]** it seems fair to assume that the actual value is in the upper region of this estimate.
The skin irritancy of topically applied KCl in aqueous solution was measured in human volunteers [**54**]. A chamber-scarification test was used. In this test a forearm test site is criss-cross scarified by drawing a 30-gauge needle over the skin with just enough pressure to cleave the epidermis without drawing blood. The test agent was applied in an aluminium chamber sealed to the skin once daily

for three days. A threshold concentration for irritancy of 60 % was seen when KCl in aqueous solution was in contact with the intact skin of volunteers. The threshold concentration when applied to broken skin for the same amount of time was 5 %. The scarification indices were 12. No grading of the skin irritating potential was measured in this study. No more relevant information was available in the study report.

3.1.3 REPEATED DOSE TOXICITY

None of the repeated dose toxicity studies located have been carried out under national or international guidelines, and according to GLP. The robust summaries lack necessary details because limited details are reported in the original publication. In view of the experiences with human volunteers, and the well-established mechanisms of action of this substance, the information available is considered sufficient on this endpoint.

Groups of 50 male rats were fed KCl in the diet at levels of 110, 450 or 1820 mg/kg bw/day for 2 years. The only treatment related effects observed were gastritis (inflammation of the stomach linking), an irritant effect. The level of gastritis and ulcer were higher in the treated groups compared to the control groups; 18 % in the 110 and 450 mg/kg bw/day groups and 30 % in the 1820 mg/kg bw/day group, compared to 6 % in the control group. Absolute and relative organ weights were measured for the following organs; brain, pituitary, thymus, heart, lung, liver, spleen, pancreas, kidney, adrenal gland, testis, seminal vesicle and prostate. However, no statistically significant changes were reported in any organs at any dose levels. Among non-tumerous lesions, nephritis was predominant in all groups, including the control group. At the end of the 2 year experimental period, the survival rates were 64 % in 0.25 % KCl, 58 % in 1 % KCl, 84 % in 4 % KCl, and 48 % in control groups **[29]**. The weakness of this study relates to the fact that the results are not given in sufficient detail, and that the mortality in the control group is very high (over 50%). In addition, the possible effect of KCl on kidneys can not be evaluated because of limited reporting and the fact that all animals, including controls, had nefrotic lesions. The NOAEL from this study is set at 1820 mg/kg bw/day since nephritis was reported in all treatment groups as well as in the control group. As regard the gastritis, this is considered a local effect, and is not used for deriving a NOAEL value.

In a 15-week study on rats, about 5250 mg/kg body weight/day given in the drinking water caused a decrease in heart weight, an increase in kidney weight and enlargement of part of the adrenals (no other organs were examined) in 10 animals terminated. All changes were reversible within one month in the remaining 4 animals **[30]**.

3.1.3.1 HUMAN DATA

No overt adverse effects were seen in 43 women receiving 80 mmol KCl/day (approx. 85 mg/kg body weight/day) in a wax matrix formulation for 4 weeks. The volunteers were randomly allocated to one of two groups who took either 80 mmol/day of KCl, or matching placebo for the first two 4-week treatment periods. The treatments were reversed during the second 4-week period. Blood pressure, heart rate, urinary volume, electrolytes and creatinine, were measured weekly during a screening period and the two 4-weeks treatment periods **[31]**.

No overt adverse effects were seen on 32 females receiving 65 mmol KCl/day (about 69 mg/kg body weight/day) for 6 weeks. The women were randomly allocated to one of two groups who took either 65 mmol/day of KCl, or matching placebo for a 6 weeks treatment period. The treatments were reversed after the 6-week period. Blood pressure, and urinary electrolytes (sodium and potassium) and creatinine, were measured weekly during the treatment period. Plasma sodium and potassium and serum albumin, calcium and magnesium were measured at 6th week only. The study showed that the KCl intake induced a significant reduction in systolic and diastolic blood pressure, from 153/104 to 146/101, and a significant increase in serum and urine potassium. Changes in

blood pressure did not correlate with changes in serum or urine electrolytes. Analysis of the 95 % confidence intervals in this and five other studies suggests that KCl supplementation lower blood pressure, but that the change is small and within the confidence levels of all six trials **[32]**.

3.1.4 GENETIC TOXICITY [33-38]

The reliability of the studies cited on genetic toxicity is considered sufficient for this endpoint. Two of the studies on non-bacterial mammalian cell in vitro test were carried out in accordance with OECD guideline study.

Bacterial tests:
In a Salmonella test (using the TA100, TA 1535, TA 1537 and TA 98 strains) doses of KCl between 0 and 10.000 µg/plate were tested with and without metabolic activation. No significant increases in mutation frequencies were noted. The highest dose tested in this study is higher than the standard test requirements. In an E. Coli test a maximal dose of 100.000 nM/ml of KCl was tested for its ability to induce a SOS response. This test was also negative. The two in vitro bacterial tests reported does not indicate any direct-acting mutagenic mechanism of action.

Lymphoma cell mutation assays:
Two independent laboratories performed the same L51784 mouse lymphoma mutation tests on a range of substances including KCl. KCl was found to be weakly mutagenic at high concentrations (above 7000 µg/ml without metabolic activation and above 4000 µg/ml with metabolic activation). The concentration in the test without metabolic activation, causing mutagenicity, exceeded the concentration recommended in the test guidelines.

Chromosome aberration tests:
There are two reports on the effect of KCl on formation of chromosome aberrations in Chinese hamster ovary cells (CHO). In these studies KCl concentrations of 75 and 80 mM (approximately 5500 and 6000 µg/ml) resulted in 19 % and 28 % aberrant cells respectively. Increased number of chromosome aberrations was observed with KCl concentrations that reduced cell survival 40 % and more. It is reasonable to conclude that the increases in mutagenicity and chromosome aberrations observed in these studies are related to cytotoxicity resulting from the high KCl concentrations used. This argument is supported by the studies on the effect of increased osmolarity on genotoxicity in cultured mammalian cells.

The reported mutagenic effect of KCl most probably results from a disruption of osmotic balance of cells with a subsequent interference with chromosomal stability. This may result in the clastogenic effects (DNA breakage and chromosome structural instability) due to K^+ effects on sequestering of Mg^{2+} ions required for normal maintenance of chromatin integrity. Other chemicals may also exert such effect (e.g. NaCl, sucrose).

3.1.5 CARCINOGENICITY [29]

In a long-term study performed with KCl, no carcinogenic effects were observed in male rats. Groups of 50 male rats were fed KCl in the diet at levels of 110, 450 or 1820 mg/kg bw/day for 2 years. A comprehensive examination of the tissue revealed no evidence of treatment-related carcinogenicity. Among non-tumerous lesions, nephrotic lesion was predominant in all treatment groups as well as in the control group. In tumerous lesions, testicular tumour (interstitial cell tumour) developed with a high incident in all groups. However, the incidence and type of tumour in experimental and control groups were comparable to those of spontaneous tumours in the test organisms.

3.1.6 REPRODUCTIVE TOXICITY/DEVELOPMENTAL TOXICITY [39]

The two studies on developmental toxicity available were not carried out under national or international guidelines, and according to GLP. The robust summaries lack necessary details because limited details are reported in the original publication. In view of the quality of the studies available, and the well-established mechanisms of action of KCl, the information available is considered sufficient on this endpoint.

A developmental study has been performed that examined the effect of KCl exposure on foetotoxicity and teratogenicity in virgin adult female albino rats (Wistar) and virgin adult female albino CD-1 outbred mice. Female rats or mice were mated with young adult male rats and mice, respectively, and observation of the vaginal sperm plug was considered day 0 of gestation. KCl was administrated from day 5 to day 15 of gestation to groups of 21-24 experimental animals by single daily oral intubation. KCl was administered as a water solution, 10 ml per kg body weight. The controls were sham treated with the vehicle i.e. water. Doses for mice were 2.35-235.0 mg/kg body weight. Body weights were recorded on days 0, 6, 11, 15 and 17 of gestation. Post exposure observation period was 2 days. Doses for rats were 3.1- 310.0 mg/kg body weight. Body weights were recorded on days 0, 6, 11, 15 and 20 of gestation. The dams were subjected to Caesarean section on gestation day 17 for mice and 20 for rats. Post exposure observation period was 5 days. The urogenital tract of each dam was examined in detail for anatomical normality.

The administration of up to 235 mg/kg body weight of KCl to pregnant mice or up to 310 mg/kg body weight of KCl to pregnant rats, revealed no significant effects on survival, total number of corpora lutea, implant sites, resorptions, soft tissue observations (urogenital tract), or live offspring. In the offspring, no effects were seen in mice or rats with regard to survival, sex ratio, average offspring weight, external congenital abnormalities, soft tissue defects (cleft palate), or skeletal defects (sternebrae, ribs, vertebrae, skull and extremities). No further information about the test conditions were included in the study report.

No fertility study has been localised. Thus, the potential of reproductive toxicity of KCl has thereby not been addressed according to OECD requirements. However, in the 2-year study [**29**] no changes were reported in the absolute and relative organ weights of the testis, seminal vesicle, and prostate. Furthermore, the maximum plasma concentration of potassium is efficiently and tightly regulated by renal elimination. A significant increase in the potassium concentration in the extracellular fluid will only occur after high potassium intake or in patients with severely reduced kidney function. Based on an estimated worst-case scenario for exposure of workers for KCl (see Sect. 2.2), it is concluded that the maximum intake of 140 mg/day of KCl from the working atmosphere is small compared to a normal dietary intake of 2-4 g KCl/day. It is considered unlikely that exposure for KCl in the working environment or normal dietary intake will significantly alter the plasma concentration of potassium. No effects of KCl exposure on gonadal function can be expected if the plasma KCl concentrations are within the normal range, as neither potassium nor chloride accumulates in the body. Based on the extensive amount of knowledge on KCl intake, regulation and effects in the human body, and on the exposure estimate in Sect. 2.2, no further testing of fertility is considered required.

3.1.8 OTHER INFORMATION

3.1.8.1 HUMAN DATA

Study on work place exposure: **[40]**

One study related to work place exposure/potash mining has been located, in which eight companies from the potash and milling industry in USA co-operated in the investigation.

Comparison was made between the observed risk of dying among the study cohort, with that expected according to age, sex, race, calendar time, and cause specific mortality rates for the general population of the United States.

The field studies conducted failed to disclose any evidence of predisposition of underground miners to any of the diseases evaluated, including lung cancer. Secondly, the study concluded there is no reason to believe that the underground environment increases respiratory diseases when pneumoconiosis producing dust or radon decay products are absent or present in only minute amounts. Exposure to dust, i.e. sodium and potassium salts, commonly encountered in the potash industry did not influence mortality due to heart disease or cerebrovascular accidents. A deficit of death from cancers other than respiratory among the surface workers could not be explained.

Gastric irritation: **[41-45]**
Gastro-intestinal irritant effects caused by KCl administrated orally has been reported at doses from about 31 mg/kg body weight/day. Oral preparations may cause nausea, vomiting, epigastric distress, abdominal discomfort and diarrhoea. High, local concentrations in the gastrointestinal tract can lead to ulceration. Esophageal ulceration may occur of there is dysphagia and gastric ulceration, especially if gastric emptying is delayed. Enteric coating lessens the incident of such side effects, but favours the development of small bowel lesions. In a wax matrix it has been promoted as a safe form, but esophageal, gastric and small bowel ulcerations nevertheless occur occasionally. If such forms are used, they should be taken with water.

Therapeutic uses of KCl: **[25]**
Diarrhoea, emsis, diuresis, starvation, prolonged saline infusion, or dietary deficiency may lead to K deficiency, which is characterized by muscle weakness, cardiac arrhythmia, paralysis, bone fragility, sterility, adrenal hypertrophy, decreased growth rate, loss of weight and death.

Potassium chloride is of value for the relief of symptoms of hypokaliemic periodic paralysis, and the symptoms of Meniere's disease. Daily intake of potassium decreases the risk of stroke-associated mortality.

The salt (KCl) is most frequently used when the action of potassium cation is desired. Usual therapeutic doses of potassium for oral solution-adults are 1.5-3 g/day to prevent depletion, and 3-7.5 g/day for replacement. Doses given by intravenous infusion (adults) are not to exceed a total dose of 200-400 mEq/day, depending on plasma potassium levels.

3.2 INITIAL ASSESSMENT OF HUMAN HEALTH

Potassium and chloride are essential constituents and two of the most abundant ions in all humans, as in all animal species. Uptake, transport, distribution, excretion, and the homeostatic regulation of KCl is well established, as are the mechanisms of action. KCl is essential for intracellular osmotic pressure and buffering, cell permeability, acid-base balance, muscle contraction and nerve function.

Acute oral toxicity of KCl in mammals is low. In humans, acute oral toxicity is rare because large single doses induce nausea and vomiting, and because KCl is rapidly excreted in the absence of any pre-existing kidney damage. Hyperkalemia will occur only in conjunction with other factors that alter potassium homeostasis, such as renal inefficiency, ingestion of excess K^+ and the use of drugs that promote potassium retention. KCl overdoses manifests in gastrointestinal and neuromuscular symptoms, cardiac arrythmia and heart block. In light of the given vapour pressure and partition coefficient it can be assumed that exposure towards KCl is exclusively given by oral intake.

All studies located on repeated dose toxicity indicate low toxicity of KCl by oral administration. A 2 years study on rats suggests NOAEL at 1820 mg/kg bw/day, although stomach irritating effect was reported. A 15 weeks study on rats showed reversible effects on heart and kidney weight by intake of 5250 mg KCl/kg bw/day. Two studies on human volunteers, indicated respectively NOEL > 80 mmol KCl/day (approx. 85 mg/kg body weight/day), and 65 mmol KCl/day (about 88 mg/kg body weight/day).

High concentrations of KCl showed positive results in a range of genotoxic screening assays using cells in culture, but the results have been attributed to the changed physical environment of the cells rather than to a direct genotoxic effect. The action of KCl in culture seems to be an indirect effect associated with an increased osmotic pressure and concentration, and may not, therefore, be of any direct relevance in the intact body were such concentrations can not occur. Further studies using in-vivo systems are not considered necessary.

No evidence of treatment-related carcinogenicity was observed in rats administered up to 1820 mg KCl/kg body weight/day through the food in a 2 year study.

A developmental study revealed no foetotoxic or teratogenic effects of KCl in doses up to 235 mg/kg/day (mice) and 310 mg/kg/day (rats). No fertility study has been localised. Based on the extensive amount of knowledge on KCl intake, regulation and effects in the human body, and on an exposure estimate (maximum intake of 140 mg/day of KCl from the working atmosphere compared to a normal dietary intake of 2-4 g KCl/day), no further testing of fertility is considered required.

Gastro-intestinal irritant effects in humans caused by KCl administrated orally have been reported at doses from about 31 mg/kg body weight/day.

4 HAZARDS TO THE ENVIRONMENT

4.1 AQUATIC EFFECTS

In one published study carried out under national guidelines and with reliable procedure description, the following results on acute aquatic toxicity were found: *Pimephales promelas*: 96 h-LC50 = 880 mg/l (± 15); *Daphnia magna*: 48h EC50 = 177 mg/l; *Ceriodaphnia dubia*: 48 h-EC50 = 630 mg/l (± 14) **[46]**.

Several studies on acute aquatic toxicity have been published, but none of them under national or international guidelines, and according to GLP. The results reported in these studies have to be interpreted with care because of deficiencies in test procedure description or because they do not conform to presently accepted standard guidelines. Some of these studies are reported below. For fish species, these studies show effects in the similar range of doses: two studies on *Lepomis macrochirus* **[47-48],** one study on *Oncorhyncus mykiss* and one study on *Ictalurus punctatus* showed 48 h-LC50 values in the range 720-2010 mg/l **[49]**. The toxicity of KCl has been investigated in one algae species (*Nitzschia linearis*), showing 120 h-EC50 (growth rate) of 1337 mg/l **[47]**.

In two separate studies on aquatic invertebrates, *Physa heterostropha* (snail) **[47]** and *Nitocra spinipes* (a marine Crustacea) **[50]**, the 96 h-LC50 values were respectively 940 and 854 mg/l. Two studies on *Dreissena polymorpha* (zebra mussel) showed 24 h-LC50 = 138 mg/l **[49]**, and 48 h-LC50 = 150 mg/l (20-25 mm adults) **[51].** An acute test on *Daphnia magna* was performed initially in the chronic study reported below, this test gave an 48h EC50 of 177 mg/l [53].

A long term (21 day) study has been performed on *Daphnia magna* **[53]** where effects on reproduction were investigated for several metals. A 16 % impairment of reproduction (LOEC) was observed at a concentration of 53 mg/l of K^+, equal to KCl concentration of 101 mg/l.

4.2 TERRESTRIAL EFFECTS

Toxicity to terrestrial plants: **[10-11][52]**
Potassium is one of the three major nutrients and chloride is an essential micronutrient for plants. Literature search has not revealed studies related to toxic effects on terrestrial organisms, therefore this section only describes levels of potassium necessary for good growth of plants and its role in plant physiology.

Demands for potassium and chloride in plants/crops:
The potassium requirement for optimal plant growth is in the range 2-5 % of the plant dry weight of vegetative parts. In crops, uptake of K in plants ranges from about 50 to 300 kg K ha^{-1} per crop, broadly similar to the uptake of nitrogen. Inadequate supply of potassium makes plants more susceptible to frost damage, fungal attack and drought.

In most plant species the Cl requirement for optimal growth is in the range of 0.2-0.4 mg/g dry matter. Excessive Cl is detrimental to chloride-sensitive crops, or if it is necessary to guard against excessive salinity, and in arid areas. Cl deficiency may occur in highly leached soils with a low Cl input from rain. The principal effect of Cl deficiency in plants is a reduction in leaf surface area and thereby plants dry weight. With severe deficiency, necrosis might occur.

Biotransformation and kinetics in plants:
Uptake of K in plants is highly selective and closely coupled to metabolic activity. It is characterized by high mobility in plants at all levels, within individual cells, within tissues, and in long-distance transport via the xylem and phloem. K is the most abundant cation in the cytoplasm and its accompanying anions make a major contribution to the osmotic potential of cells. K is not metabolized, and it forms only weak complexes in which it is readily exchangeable.

Chloride is readily taken up by plants and its mobility in short and long-distance transport is high. In plants, chloride occurs mainly as free anion or is loosely bound to exchange sites.

Biological effects in plants:
Potassium in plants is important for the osmotic and ionic regulation, and for a large number of enzymes related to carbohydrate and protein metabolism. In almost all cases, cytosolic potassium concentrations are maintained in the range 100-200 mM. Potassium activates the membrane-bound proton pumping ATPases. This activation facilitate the transport of K from the external solution across the plasma membrane into the root cells, and make potassium the most important mineral element in cell extension and osmoregulation. Potassium, as the most prominent inorganic solute, plays a key role in the water homeostasis. When K is deficient, the stomata can not function properly and water loss from the plant may reach damaging levels. In higher plants, potassium affects photosynthesis at various levels, playing a key role in CO_2 fixation, and by affecting photosynthesis in leaves via its stomatal regulation. Potassium is also closely connected with processes involved in the protein synthesis in plants.

Cl is essential for the photosynthetic O_2 evolution and the membrane-bound proton-pumping ATPases. Chloride has important functions in osmoregulation at different levels. At the usually high plant content it is a main osmoticum in the vacuoles of the bulk tissue (50-150 mM chloride). At low contents that are in the range of a micronutrient (approx. 1 mM chloride or below), these osmoregulatory functions of chloride are confined to specialized tissues or cells (e.g. extension zones of roots and shoots). Cl also plays an essential role in stomatal regulations trough mediating the opening and closure of the stomata

Effects of potassium and chloride on plant diseases:
An adequate K supply is of notable importance for plants to make protective chemicals and barriers that restrict the progress of an infection and compensate for any damage through new growth. Potassium tends to improve the plant's resistance towards bacterial leaf blight, sheat blight and stem rot in rice; black rust in wheat; sugary disease in sorghum; and bacterial leaf blight in cotton

Chloride may hinder the plant fungus disease take-all in wheat due to its apparent action as a nitrification inhibitor. Chloride also decreases the NO_3^- concentration in plants, which may result in fewer attacks of common root rot on barley.

4.3 INITIAL ASSESSMENT FOR THE ENVIRONMENT

In short-term acute toxicity tests with fish, daphnia and algae the following results were found (lowest test result values): *Ictalurus punctatus*: 48 h LC50 =720 mg/l, *Daphnia magna*: 48h-EC50 = 177 mg/l; *Nitzschia linearis:* 120 h-EC50 = 1337 mg/l. A chronic reproductive test with the invertebrate *Daphnia magna* gave a LOEC of 101 mg/l. All the studies compiled on the acute and chronic aquatic toxicity were > 100 mg/l. Thus, it is concluded that KCl is not hazardous to freshwater aquatic organisms. Taking into considerations the background concentrations of KCl in seawater (380 mg/l K^+ and 19,000 mg/l Cl^-), it is concluded that there is no need for further

investigations of KCl on marine species. The low concern for the environment is supported by the absence of a bioaccumulation potential for the substance.

Potassium is one of the three major nutrients and chloride is an essential micronutrient for plants. The potassium requirement for optimal plant growth is in the range 2-5 % of the plant dry weight of vegetative parts. In most plant species the Cl requirement for optimal growth is in the range of 0.2-0.4 mg/g dry matter. Concentrations of chloride in the external solution of more than 20 mM can lead to toxicity in sensitive plant species.

Uptake of K in plants is closely coupled to metabolic activity. K is the most abundant cation in the cytoplasm and its accompanying anions make a major contribution to the osmotic potential of cells. K is not metabolized, and it forms only weak complexes in which it is readily exchangeable. Chloride, which is readily taken up by plants, occurs mainly as free anion or is loosely bound to exchange sites.

Potassium in plants is important for the osmotic and ionic regulation, plays a key role in the water homeostasis, and is closely connected with processes involved in the protein synthesis. In higher plants, potassium affects photosynthesis at various levels. Cl is also essential for the photosynthesis in plants, and has important functions in osmoregulation at different levels. An adequate supply of potassium and chloride in plants tends to improve the plant's resistance towards several diseases.

5 CONCLUSIONS AND RECOMMENDATIONS

5.1 CONCLUSIONS

General Information on Exposure:
Worldwide production figures for KCl exceed 1,000,000 tons/year. Virtually all commercial KCl is extracted from natural sources of the substance. More than 90 % of the total KCl consumption is used for fertilizer production. Production of potassium hydroxide accounts for more than 90 % of the non-fertilizer or industrial uses of KCl. Other non-fertilizer uses of KCl include food/foodstuff additives, supplement of animal feed, pharmaceutical products, laboratory chemicals, deicing agents and photochemicals.

KCl is ubiquitous in the environment, occurring in minerals, soil and sediments, and natural waters. KCl is also present as a natural and essential constituent in animals. Potassium is one of the three major nutrients and chloride is an essential micronutrient for plants. The main human exposure to KCl is the normal dietary intake, and indirect exposure via the environment. One work place investigation among potash miners disclosed no evidence of predisposition of underground miners to any of the diseases evaluated, including lung cancer.

Human Health Hazards:
Potassium and chloride are essential constituents and two of the most abundant ions in humans. Uptake, transport, distribution, excretion, and the homeostatic regulation of KCl is well established, as are the mechanisms of action. KCl is essential for intracellular osmotic pressure and buffering, cell permeability, acid-base balance, muscle contraction and nerve function.

Acute oral toxicity of KCl in mammals is low (LD50 = 3020 mg/kg bw). In humans, acute oral toxicity is rare because large single doses induce nausea and vomiting, and because KCl is rapidly excreted in the absence of any pre-existing kidney damage. Usual therapeutic doses of potassium for oral solution-adults are 1.5-3 g/day to prevent depletion, and 3-7.5 g/day for replacement. For repeated dose toxicity, no adverse effects were observed up to 1820 mg/kg bw/day in rats, and 80 mmol KCl/day (approx. 85 mg/kg bw/day) in humans.

No genmutations were reported in Bacterial tests, with and without metabolic activation. However, high concentrations of KCl showed positive results in a range of genotoxic screening assays using cells in culture. The action of KCl in culture seems to be an indirect effect associated with an increased osmotic pressure and concentration. Therefore, KCl do not have any direct relevance in the intact body were such concentrations can not occur. Further studies using in-vivo systems are not considered necessary under SIDS

No evidence of treatment-related carcinogenicity was observed in rats administered up to 1820 mg KCl/kg body weight/day through the food in a 2 year study.

A developmental study revealed no foetotoxic or teratogenic effects of KCl in doses up to 235 mg/kg/day (mice) and 310 mg/kg/day (rats). No fertility study has been located. Based on the extensive amount of knowledge on KCl intake, regulation and effects in the human body, and on an exposure estimate (maximum intake of 140 mg/day of KCl from the working atmosphere compared to a normal dietary intake of 2-4 g KCl/day), no further testing of fertility is considered required under SIDS.

Gastro-intestinal irritant effects in humans caused by KCl administrated orally have been reported at doses from about 31 mg/kg body weight/day.

Hazards to the Environment:

Environmental fate:

KCl as inorganic salt is not subjected to further degradation processes in the environment. In water, potassium chloride is highly water soluble, and readily undergoes dissociation. In soil, transport/leaching of potassium and chloride is affected by the clay minerals (type and content), pH, and organic matter. No potential for bioaccumulation/bioconcentration can be identified.

Ecotoxicity:

In short-term acute toxicity tests with fish, daphnia and algae the following results were found (lowest test result values): *Ictalurus punctatus*: 48 h-LC50= 720 mg/l; *Daphnia magna*: 48h-EC50 = 177 mg/l; *Nitzschia linearis:* 120 h-EC50 = 1337 mg/l. A chronic reproductive test with the invertebrate *Daphnia magna* gave a LOEC of 101 mg/l.

All the studies compiled on the acute and chronic aquatic toxicity were > 100 mg/l. Thus, it is concluded that KCl is not hazardous to freshwater aquatic organisms. Taking into considerations the background concentrations of KCl in seawater (380 mg/l K^+ and 19,000 mg/l Cl^-), it is concluded that there is no reason for further investigations of KCl on marine species. The low concern for the environment is supported by the absence of a bioaccumulation potential for the substance.

In plants, potassium is one of the three major nutrients and chloride is an essential micronutrient. The potassium requirement for optimal plant growth is in the range 2-5 % of the plant dry weight of vegetative parts. In most plant species the Cl requirement for optimal growth is in the range of 0.2-0.4 mg/g dry matter.

Potassium in plants is important for the osmotic and ionic regulation, plays a key role in the water homeostasis, and is closely connected with processes involved in the protein synthesis. In higher plants, potassium affects photosynthesis at various levels. Cl is also essential for the photosynthesis in plants, and has important functions in osmoregulation at different levels. An adequate supply of potassium and chloride in plants tends to improve the plant's resistance towards several diseases.

5.2 RECOMMENDATIONS

No further testing and/or exposure analysis is recommended.

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- National Center for Biotechnology Information/National Library of Medicine (PubMed).
- Registry of Toxic Effects of Chemical Substances (RTECS).
- Umwelt Bundes Amt, Katalog wassergefährdender Stoffe.
- UNEP CHEMICALS Data Bank Legal File.

(3) Other
- Aquire Database.
- Kali & Salz GmbH (1993). IUCLID Data Set, Potassium chloride.
- Lægreid, M., Bøckman, O.C., Kaarstad, O. (1999). Agriculture, Fertilizers and the Environment. CABI Publishing, Cambridge.

Date of literature search: year 2000

Search criteria: Potassium chloride and/or CAS. No.

I U C L I D Data Set

Existing Chemical ID: 7447-40-7
CAS No. 7447-40-7
EINECS Name Potassium chloride
EINECS No. 231-211-8
Molecular Formula ClK

Producer Related Part
Company: Norsk Hydro ASA
Creation date: 15-MAR-2001

Substance Related Part
Company: Norsk Hydro ASA
Creation date: 15-MAR-2001

Printing date: 30-MAR-2003
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Chapter (profile): Chapter: 1, 2, 3, 4, 5, 6
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Flags (profile): Flags: without flag, confidential, non confidential, WGK(DE), TA-Luft (DE), Material Safety Dataset, Directive 67/548/EEC, Key study(s) for SIDS

1.0.1 OECD and Company Information

Type: sponsor country
Name: Norsk Hydro ASA, Oslo, Norway
Partner: **Date:** 14-MAR-2001
Street: Bygdøy Allè 2
Town: N-0032 Oslo
Country: Norway
Phone: +47 2243 2100
Telefax: +47 2243 2611

Reliability: (1) reliable without restrictions
01-MAR-2001

1.0.2 Location of Production Site

1.0.3 Identity of Recipients

1.1 General Substance Information

Substance type: inorganic
Physical status: solid
Purity: Fertilizer grades 95-99 % weight/weight.

Industrial grades 99.0-99.5 % weight/weight.

Chemical grades 99.8-99.9 % weight/weight.
Source: Norsk Hydro ASA, Norway
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (19)

1.1.0 Details on Template

1.1.1 Spectra

1.2 Synonyms

Chlorid draselny
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (46)(62)

Chloride of potash
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (41)

Chloropotassuril
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (41)(46)(62)

Chlorovescent
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (41)

Chlorure de potassium
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (27)

Cloreto de potassio
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (27)

Cloruro de potassio
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (27)

Cloruro di potassio
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (27)

Dipotassium dichloride
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (41)(46)(62)

Enseal
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (41)(46)(62)

Enseal potassium chloride
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (41)

Kalcorid
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (41)

Kalitabs
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (41)(46)(62)

Kaliumchlorid
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (27)

Kaliumchloride
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (27)

Kaochlor
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (46)(62)

Kaon-Cl
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (41)(46)(62)

Kay ciel
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (46)(62)

K-contin
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (41)

K-Dur
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (62)

K-Lor
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (46)(62)

Klotrix
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (41)(46)(62)

K-prende-dome
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (46)(62)

Muriate of potash
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (41)(62)

Natural sylvite
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (41)

Peter-KAL
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (41)

Pfiklor
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (46)(62)

Potash
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (37)

Potassium monochloride
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (41)(46)(62)

Potassium muriate
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (41)

Potavescent
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (41)(46)(62)

Rekawan
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (41)(46)(62)

Repone K
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (41)

Slow K
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (41)(46)(62)

Span K
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (41)

Super K
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (62)

Tripotassium trichloride
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (41)(46)(62)

1.3 Impurities

Remarks: Impurities are usually sodium chloride, magnesium chloride, bromide and alkaline earth sulphates, depending on the raw material and production process.
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (41)

1.4 Additives

1.5 Quantity

Quantity: Global production more than 1,000,000 tons in 1999.

EU import figure was more than 1,000,000 tons in 1994. Much of this import volume involves intraregional trade between EU countries.

The substance was produced during the 12 months following adoption of the EU regulation on existing chemicals.
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (17)

1.6.1 Labelling

Labelling: KCl is not included in Annex I of EEC Directive 67/548/EEC.
Proposed labelling: none
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: Directive 67/548/EEC
01-MAR-2001

1.6.2 Classification

Classification: KCl is not included in Annex I of EEC Directive 67/548/EEC.
Proposed classification: none
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: Directive 67/548/EEC
01-MAR-2001

1.7 Use Pattern

Type: type
Category: wide dispersive use
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001

Type: type
Category: non dispersive use
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001

Type: industrial
Category: agricultural industry
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001

Type: industrial
Category: basic chemicals industry
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001

Type: industrial
Category: photographic industry
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001

Type: industrial
Category: metal extraction, refining and processing industry
Source: Norsk Hydro ASA

Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001

Type: industrial
Category: public domain
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001

Type: industrial
Category: personal and domestic
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001

Type: industrial
Category: other: food industry
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001

Type: industrial
Category: other: oil production industry
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001

Type: use
Category: fertilizers
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001

Type: use
Category: food/foodstuff additives
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001

Type: use
Category: pharmaceuticals
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001

Type: use
Category: photochemicals
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001

Type: use
Category: laboratory chemicals: electrode cells, buffer solutions, spectroscopy
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001

Type: use
Category: intermediates
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001

Type: use
Category: anti-freezing agents
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001

Type: use
Category: other: water treatment
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001

Type: use
Category: other: drilling mud
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001

Type: use
Category: flame retardants and fire preventing agents
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001

Type: use
Category: flux agents for casting
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions

Flag: non confidential
01-MAR-2001

1.7.1 Technology Production/Use

1.8 Occupational Exposure Limit Values

Remark: No specific occupational exposure limits (OELs) for potassium chloride have been located. Norsk Hydro ASA recommend the substance to be treated as "inert dust" with an OEL of 10

mg/m^3, in accordance with the TWA value for "Particulates Not Otherwise Classified (PNOC)" as proposed by ACGIH [].
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions

Flag: non confidential
01-MAR-2001 (1)

1.9 Source of Exposure

Remark: KCl is ubiquitous in the environment, occurring in minerals, soil and sediments, and all natural waters (oceans, lakes, rivers). KCl is also present as a natural constituent in plants and animals.

Virtual all commercial KCl is extracted from two main types of natural sources of the substance: 1) potassium salts deposits occurring in thin beds in large salt basins formed by the evaporation of ancient seas; 2) present-day salt lakes and natural brines.
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (18)

10.1 Recommendations/Precautionary Measures

Recommended by: USA, CFR21(184)
Recommendation: The substances is Generally Recognized As Safe (GRAS) as a direct human food ingredient when used in accordance with good manufacturing practice.
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (27)

1.10.2 Emergency Measures

1.11 Packaging

1.12 Possib. of Rendering Subst. Harmless

1.13 Statements Concerning Waste

Classified by: EEC Council Regulation No 259/93 of 1 February 1993 on the supervision and control of shipments of waste within, into and out of the European Community.
Class of danger: Waste containing potassium chloride is listed in green list of wastes.
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential

01-MAR-2001 (73)

Classified by: The merchant shipping regulations 1987, Schedule I (control of pollution by noxious liquid substances in bulk)
Class of danger: Discharge into the sea of solid potassium chloride is prohibited; discharge into the sea of potassium chloride solution is not prohibited.
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (73)

1.14.1 Water Pollution

Classified by: Administrative Rules concerning Substances Hazardous to Water (Verwaltungsvorschrift Wassergefâhrdende Stoffe).
Class of danger: 1 (weakly water polluting)
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (72)

1.14.2 Major Accident Hazards

1.14.3 Air Pollution

1.15 Additional Remarks

1.16 Last Literature Search

1.17 Reviews

1.18 Listings e.g. Chemical Inventories

2.1 Melting Point

Value: = 772 degree C
Decomposition: no
Sublimation: no
Method: not stated
Source: Norsk Hydro ASA
Reliability: (2) reliable with restrictions
Flag: Key study for SIDS
01-MAR-2001 (40)(82)

Value: = 770-776 degree C
Source: Norsk Hydro ASA
Reliability: (2) reliable with restrictions
Flag: non confidential
01-MAR-2001 (41)(46)(62)(79)

2.2 Boiling Point

Value: = 1407 degree C
Source: Norsk Hydro ASA
Reliability: (2) reliable with restrictions
Flag: Key study for SIDS
01-MAR-2001 (83)

Value: = 1411 degree C
Source: Norsk Hydro ASA
Reliability: (2) reliable with restrictions
Flag: non confidential
01-MAR-2001 (39)

2.3 Density

Type: density
Value: = 1.984 g/cm3 at 20 degree C
Source: Norsk Hydro ASA
Reliability: (2) reliable with restrictions
Flag: non confidential
01-MAR-2001 (27)(41)(79)

Type: density
Value: = 1.987 g/cm3 at 15 degree C
Source: Norsk Hydro ASA
Reliability: (2) reliable with restrictions
Flag: non confidential
01-MAR-2001 (46)

2.3.1 Granulometry

2.4 Vapour Pressure

Value: = 5.73 hPa at 906 degree C
Source: Norsk Hydro ASA
Reliability: (2) reliable with restrictions
Flag: Key study for SIDS
01-MAR-2001 (38)

2.5 Partition Coefficient

log Pow: = -0.46 at 20 degree C
Method: other (calculated): according to Environmental Science, Syracuse Research Corporation (SRC) database, USA.
Source: Norsk Hydro ASA
Reliability: (2) reliable with restrictions
Flag: Key study for SIDS
01-MAR-2001 (67)

2.6.1 Water Solubility

Value: = 342 g/l water at 20 degree C
Source: Norsk Hydro ASA
Reliability: (2) reliable with restrictions
Flag: Key study for SIDS
01-MAR-2001 (26)(41)

Value: = 347 g/l at at 20 degree C
Source: Norsk Hydro ASA
Reliability: (2) reliable with restrictions
Flag: non confidential
01-MAR-2001 (79)

2.6.2 Surface Tension

2.7 Flash Point

Remark: Not tested; substance is a solid.
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001

2.8 Auto Flammability

2.9 Flammability

Remark: Not flammable; KCl is used as a component in dry-chemical fire extinguishers to absorb some of the heat of combustion.
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (21)

2.10 Explosive Properties

Remark: No studies located; not expected from the structure to have explosive properties.
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001

2.11 Oxidizing Properties

Remark: No studies located, but not expected from the structure to have oxidising properties.
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001

2.12 Additional Remarks

3.1.1 Photodegradation

Remark: KCl as an inorganic salt is not subjected to further degradation processes.
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: Key study for SIDS
01-MAR-2001

3.1.2 Stability in Water

Remark: Potassium chloride is highly water-soluble. Dissociates in water to K^+ and Cl^-.
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: Key study for SIDS
01-MAR-2001 (26)(41)(79)

3.1.3 Stability in Soil

Remark: Potassium chloride is stable in soil.

Information on adsorption and desorption of potassium chloride in soil is reported under item 3.3.1 Transport.
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001

3.2 Monitoring Data (Environment)

Type of measurement: Background
Medium: Minerals and soils
Concentration: Sylvite is a naturally occurring mineral with more than 99 % KCl. Other KCl principal minerals are carnallite ($KCl \cdot MgCl_2 \cdot 6H_2O$) with approx. 25 % KCl, and kainite ($KCl \cdot MgSO_4 \cdot 3H_2O$) with approx. 30 % KCl.

Potassium is the seventh most common element, composing 2.4 % of the earth's crust by weight. The amount of K in the topsoil varies in the range of 0.2-3.3 %. Chloride is the eleventh most common element, composing approx. 1-2 % of the earth's crust by weight.
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: Key study for SIDS
01-MAR-2001 (20)(26)

Type of measurement: Background
Medium: Seawater
Concentration: 380 mg/l potassium (K^+) and 19,000 mg/l chloride (Cl^-).
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: Key study for SIDS

01-MAR-2001 (68)

Type of measurement: Background
Medium: Freshwater
Concentration: Mean composition of river waters of the world contain 2.3 mg/l potassium (K^+) and 8.3 mg/l chloride (Cl^-).
Remarks: The concentrations of potassium and chloride of the surface waters of the world is highly variable in relation to ionic influences of drainage and exchange from surrounding land, atmospheric sources derived from the land, ocean, and human activity. The spatial and temporal distribution of potassium and chloride in natural freshwater lakes is relatively uniform as their concentrations within a lake undergo minor changes from biotic utilization or biotically mediated changes.
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: Key study for SIDS

01-MAR-2001 (81)

Type of measurement: Background
Medium: Animals
Concentration: Potassium and chloride are essential constituents and two of the most abundant ions in all animal species. The concentrations of these ions as predominant extracellular and intracellular electrolytes will differ somewhat among different organisms and cell types.

In adult humans, the total body potassium is approx. 3.5 mol (135 g). 98 % of this is located intracellularly (mostly within muscle cells), at a concentration of 150 mmol/l. The extracellular potassium concentration is approx. 4 mmol/l.

Total body chloride in adult humans is approx. 2.1 mol (75 g) or 33 mmol/kg body weight. 80 % of this is located extracellularly, at a concentration of 120 mmol/l. The intracellular concentration of chloride is approx. 3-4 mmol/l.
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: Key study for SIDS

01-MAR-2001 (13)(32)

Type of measurement: Background
Medium: Plants
Concentration: Potassium is a primary nutrient, and chloride is a micronutrient for plants (Cl is a major element for some coastal plants, e.g. coconut). The uptake of K and Cl by plants will vary with crop species, climate and soil conditions. Examples on amount of K removed per ton of produce as harvested are 3 kg for wheat grain and 31 kg for rough rice/Philippines. Examples on amount of Cl removed

per ton of produce as harvested are 0.5 kg for potato tubers, and 10.7 kg

for rough rice/Philippines.

Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: Key study for SIDS
01-MAR-2001 (23)(29)(41)(49)

Type of measurement: Background
Medium: Foodstuff
Concentration: Potassium and chloride is present in all natural foods from plants and animal sources. Potassium content of some foodstuffs: Olives 55 mg/100 g edible portion; peas 380 mg/100 g edible portion; dried nonfat milk 1335 mg/100 g edible portion; bacon 225 mg/100 g edible portion. Average contents of Cl in plants/crops are in the range of 2-20 mg/g dry matter.

Normal daily dietary intake of potassium in humans is 50-100 mmol (2-4 g).

Normal daily dietary intake of chloride in humans is 100-250 mmol (3.5-9 g).

Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: Key study for SIDS
01-MAR-2001 (7)(30)

3.3.1 Transport between Environmental Compartments

Type: adsorption - desorption
Media: water - soil
Method: other
Results: Transport/leaching of potassium and chloride as major constituents in soil has been extensively reviewed:
Soil contains potassium in different forms: (1) Soil solution K, which is immediately available to plants, is present only in very small quantities. (2) Exchangeable K, which is the main source of replenishment, takes form of K ions attached to the solid soil material. As the solution K concentration falls, adsorbed K is released into the solution. (3) Other forms of K are more tightly held than the exchangeable K, i.e. chemically combined in the minerals of the rocks from which the soil is formed.

Clay minerals are the main source of K, but much of the soil K is present as part of insoluble mineral particles and is inaccessible to plants. Only the slow process of weathering can liberate this K. Outside a range of pH of approximately 5.0 to 7.0, the availability of K is reduced.

The pool of exchangeable K is particularly important for plants, and the main site of exchangeable K is the clay. Various types of clay binding K at different strengths, from weak surface binding that do not hold K against leaching (e.g. kaolinite clays), to a binding that restricts plant availability (e.g. illitic and smectite clays).

Most soils contain a mixture of the different clay minerals; the proportion in which they occur dictate the way the soil will behave as far as K is concerned. The larger the amount

of clay in a soil the higher will be its capacity to adsorb K and the better this will be able to replenish the K in the soil solution when this is depleted. Organic and light sandy soils have low capacity for binding K. If such soils should contain more K than the plant can take up, the K ions are easily washed out or leached beyond the range of crop roots. Heavier soil has an advantage in that the clay holds much K, and any temporary excess over the plant's immediate requirement is not easily leached.

The organic matter in soil (humus) also has exchangeable properties, somewhat similar to those of clays. While in most temperate mineral soils containing clay, the contribution of organic matter to the pool of exchangeable K is not very important, it is very important in sandy soils and in soils where the clay minerals are predominantly of the kaolinitic type, as in many tropical soils.

K is in general less mobile and less prone to leaching than anions in soil, such as chloride and nitrate (NO_3^-), but more so than phosphate. Chloride binds only weakly to soil particles, and therefore follows water movement. Anions do not leach alone, but always together with a counter-ion (cation). Hence, chloride and nitrate leaching may deplete soils of nutrients such as K. Leaching can be minimized by keeping the land covered by crops.

Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: Key study for SIDS
01-MAR-2001 (37)(49)

3.3.2 Distribution

Media: air, water, soil and sediment
Method: Fugacity Level I.
Generic Model of OECD (FUGMOD, 1992).
Result: Environmental distribution of potassium chloride using a Generic Level I Fugacity Model under three emission scenarios showed the same result

irrespective if the substance is released 100 % to water or 100 % air or 100 % to soil:
> 99.7 % will be distributed to water, < 0.03 % to air, < 0.03 % to soil solids, < 0.01 % to sediment solids.

Remark: The Global Reference model of OECD Existing Chemicals Programme was used for calculation.
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: Key study for SIDS
01-MAR-2001 (56)

3.5 Biodegradation

Remark: KCl as an inorganic salt is not subjected to further biodegradation processes.
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: Key study for SIDS
01-MAR-2001

3.7 Bioaccumulation

Species: other: calculated
BCF: = 0.47
Method: other: calculated based on using water solubility
Test substance: no data
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (47)

Species: other: calculated
BCF: = 0.26
Method: other: calculated based on using $\log P_{ow}$
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (48)

3.8 Additional Remarks

AQUATIC ORGANISMS

4.1 Acute/Prolonged Toxicity to Fish

Type of test: static
Species: Pimephales promelas (Fathead minnows)
Exposure period: 24, 48, 96 hours
Unit: mg/l **Analytical monitoring:** yes
LC50/24 hours: = 950
LC50/48 hours: = 910
LC50/96 hours: = 880
Method: other: EPA/600/4-90/027
Year: 1997 **GLP:** no
Test substance: as prescribed by 1.1-1.4; reagent grade
Remarks: All organisms, 1 to 7 days old, were obtained from in-house cultures. Brood stock were cultured at 20-25 degrees C in tap water pretreated with activated carbon. Larva were fed Artemia sp. twice daily until they were used in testing.

The toxicity tests followed the general guidance of the U.S. Environmental Protection Agency. All tests were conducted in 30-ml plastic beakers containing 10 ml test solution and five organisms per chamber. Tests were conducted under a 16-h:8-h light-dark photoperiod at 25 degrees C. Dilution/control water for all tests was moderately hard reconstituted water (MHRW). Exposure period was 96 hours, with daily observations of mortality. The criteria for death were no visible movement and no response to prodding. 100 µl of concentrated brine shrimp nauplii was added after 48 hours of exposure.

Test solutions were prepared by dissolving 10,000 mg/l KCl salt in MHRW, and diluting with MHRW to a series of 5 test concentrations spaced on 0.5 dilution factor. As testing proceeded, test concentrations were spaced much more closely to better define responses near the effect threshold.

All ion concentrations measured in stock solutions were compared to nominal values. If measured concentration differed from the nominal value by more than 20 %, the actual measured concentrations were substituted for the nominal concentrations. Background KCl content in the dilution water MHRW were added to the calculated contributions from the stock solutions.

Dissolved oxygen (DO) and pH were measured in selected test solutions during actual toxicity testing: Measured DO concentrations were always > 40 % saturation; measured pH was between 7.5-9.0.

3 replicate tests were conducted, and average LC50 values were calculated as the arithmetic mean of the values; SD = 15, range 1.4-62.

Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: Key study for SIDS
04-MAR-2001 (54)

Type of test: static
Species: Lepomis macrochirus (Bluegill)
Exposure period: 96 hours
Unit: mg/l **Analytical monitoring:** yes
LC50: = 2010
Method: other: acute toxicity
Year: 1968 **GLP:** no data
Test substance: as prescribed by 1.1-1.4; A.C.S.-grade chemicals
Remarks: Bluegills were exposed to a graded series of KCl and synthetic soft dilution water and controls. Eighteen series of bioassays were done. Fish tests were made in 18 litres of solution at 18 degrees C. Dissolved oxygen concentrations were maintained between 5 and 9 ppm. No food was given during the test period or during the 36 hours before the tests began. Fish were acclimatized to the dilution water and other test conditions for 2 weeks before being used as experimental organisms. The nominal concentrations of KCl were not measured.
Source: Norsk Hydro ASA
Reliability: (2) reliable with restrictions
Flag: non confidential
04-MAR-2001 (58)

Type of test: static
Species: Lepomis macrochirus (Bluegill)
Exposure period: 96 hours
Unit: mg/l **Analytical monitoring:** yes
LC50: = 2010
Method: other: acute toxicity
Year: 1954 **GLP:** no data
Test substance: as prescribed by 1.1-1.4
Remarks: Groups of ten Bluegills were exposed to analyzed treatment levels of 1661, 1911, 2054 and 2200 mg/l active ingredient and synthetic soft dilution water controls.
Source: Norsk Hydro ASA
Reliability: (2) reliable with restrictions
Flag: non confidential
04-MAR-2001 (70)

Type of test: static
Species: Oncorhynchus mykiss (rainbow trout)
Exposure period: 48 hours
Unit: mg/l **Analytical monitoring:** yes
LC50: = 1610
Method: other: acute toxicity
Year: 1993 **GLP:** no data
Test substance: as prescribed by 1.1-1.4; 99 % active ingredient
Remarks: Fish (0.8-1.2 g) were obtained form the National Fisheries Research Centre and maintained in 5000 l fiberglass tanks supplied with flowing well water and fed as libitum daily. Fish were taken off feed 4 days before tests.

Static tests were conducted following procedures of the Committee on Methods for Acute Toxicity Testing with Aquatic Organisms (1975). Test water was reconstituted soft water of pH 7.7, alkalinity $6x10^{-4}$ m/L (30 mg/l as $CaCO_3$), and total hardness 40 mg/l as $CaCO_3$. Tests were conducted at 17 degrees C. Dissolved oxygen, pH and temperature were measured daily. Treatment of 10 animals per vessel were duplicated.

Source: Norsk Hydro ASA
Reliability: (2) reliable with restrictions
Flag: non confidential
Date: 04-MAR-2001

Type of test: static
Species: Ictalurus punctatus (channel catfish)
Exposure period: 48 hours
Unit: mg/l **Analytical monitoring:** yes
LC50: = 720
Method: other: acute toxicity
Year: 1993 **GLP:** no data
Test substance: as prescribed by 1.1-1.4; 99 % active ingredient
Remarks: Fish (0.8-1.2 g) were obtained from the National Fisheries Research Centre and maintained in 5000 l fiberglass tanks supplied with flowing well water and fed as libitum daily. Fish were taken off feed 4 days before tests. Static tests were conducted following procedures of the Committee on Methods for Acute Toxicity Testing with Aquatic Organisms (1975). Test water was reconstituted soft water of pH 7.7, alkalinity $6x10^{-4}$ m/L (30 mg/l as $CaCO_3$), and total hardness 40 mg/l as $CaCO_3$. Tests were conducted at 17 °C. Dissolved oxygen, pH and temperature were measured daily. Oxygen saturation was above 60 % in all tested vessels throughout the test. Two vessels each with 10 animals were tested at each concentration.
Source: Norsk Hydro ASA
Reliability: (2) reliable with restrictions
Flag: non confidential
04-MAR-2001 (76)

Type of test: static
Species: Gambusia affinis (mosquitofish)
Exposure period: 24, 48, 96 hours
Unit: mg/l **Analytical monitoring:** yes
LC50/24 hours: = 10000
LC50/48 hours: = 4200
LC50/96 hours: = 920
Method: other: acute toxicity
Year: 1957 **GLP:** no data
Test substance: as prescribed by 1.1-1.4
Remarks: Groups of ten fish were exposed to analyzed treatment levels of 560, 1000, 1800, 3200, 5600, 10000 and 18000 mg/l active ingredient. Water used for experimental dilutions and controls was turbid pond water. Initial turbidity was 250 ppm.
Source: Norsk Hydro ASA
Reliability: (3) not reliable
Flag: non confidential

04-MAR-2001 (77)

Type of test: static
Species: Lepomis macrochirus (Bluegill)
Exposure period: 24 hours
Unit: mg/l **Analytical monitoring:** no data
LC50: = 5500
Method: other: acute toxicity
Year: 1965 **GLP:** no data
Test substance: as prescribed by 1.1-1.4
Remarks: Water used for experimental dilutions and controls was Standard Reference Water free from organics.
Source: Norsk Hydro ASA
Reliability: (3) not reliable
Flag: non confidential

02-MAR-2001 (25)

Type of test: static
Species: Leuciscus idus
Exposure period: 48 hours
Unit: mg/l **Analytical monitoring:** yes
LC0: = 2000
LC50: = 2300
LC100: = 2600
Method: other: DIN 38412 part 31
Year: 1989 **GLP:** no data
Test substance: as prescribed by 1.1-1.4
Source: Norsk Hydro ASA
Reliability: (4) not assignable
Original reference could not be checked
Flag: Material Safety Dataset

02-MAR-2001 (22)

4.2 Acute Toxicity to Aquatic Invertebrates

Type of test: static
Species: Daphnia magna
Exposure period: 24, 48 hours
Unit: mg/l **Analytical monitoring:** yes
LC50/24 hours: = 740
LC50/48 hours: = 660
Method: other: EPA/600/4-90/027
Year: 1997 **GLP:** no
Test substance: as prescribed by 1.1-1.4; reagent grade
Remarks: All organisms were obtained from in-house cultures. D. magna were cultured in hard reconstituted water at 20 degrees C. Test organisms were less than 24 hours old at test initiation.
The toxicity tests followed the general guidance of the U.S. Environmental Protection Agency. All tests were conducted in 30-ml plastic beakers containing 10 ml test solution and five organisms per chamber. Tests were conducted under a 16-h:8-h light-dark photoperiod at 20 degrees C.
Dilution/control water for all tests was moderately hard reconstituted water (MHRW).

Exposure period was 48 hours, with daily observations of mortality. 100 µl of a 1:1 mix of YCT and algal suspension was added to the test chambers at test initiation. The criteria for death were no visible movement and no response to prodding.
Test solutions were prepared by dissolving 10,000 mg/l KCl salt in MHRW, and diluting with MHRW to a series of 5 test concentrations spaced on 0.5 dilution factor. As testing proceeded, test concentrations were spaced much more closely to better define responses near the effect threshold. All ion concentrations measured in stock solutions were compared to nominal values. If measured concentration differed from the nominal value by more than 20 %, the actual measured concentrations were substituted for the nominal concentrations. Background KCl content in the dilution water MHRW were added to the calculated contributions from the stock solutions.
Dissolved oxygen (DO) and pH were measured in selected test solutions during actual toxicity testing: Measured DO concentrations were always > 40 % saturation; measured pH was between 7.5-9.0. 5 replicate tests were conducted, and average LC50 values were calculated as the arithmetic mean of the values; SD = 7.5,
range 4.8-31.

Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: Key study for SIDS
04-MAR-2001 (54)

Type of test: static
Species: Ceriodaphnia dubia
Exposure period: 24, 48 hours
Unit: mg/l **Analytical monitoring:** yes
LC50/24 hours: = 630
LC50/48 hours: = 630
Method: other: EPA/600/4-90/027
Year: 1997 **GLP:** no
Test substance: as prescribed by 1.1-1.4; reagent grade
Remarks: All organisms were obtained from in-house cultures. C. dubia were cultured in either moderately hard reconstituted water (MHRW) or 20 % mineral water at 25 degrees C. Test organisms were less than 24 hours old at test initiation.

The toxicity tests followed the general guidance of the U.S. Environmental Protection Agency. All tests were conducted in 30-ml plastic beakers containing 10 ml test solution and five organisms per chamber. Tests were conducted under a 16-h:8-h light-dark photoperiod at 20 degrees C.
Dilution/control water for all tests was MHRW.
Exposure period was 48 hours, with daily observations of mortality. 100 µl of a 1:1 mix of YCT and algal suspension was added to the test

chambers at test initiation. The criteria for death were no visible movement and no response to prodding.

Test solutions were prepared by dissolving 10,000 mg/l KCl salt in MHRW, and diluting with MHRW to a series of 5 test concentrations spaced on 0.5 dilution factor. As testing proceeded, test concentrations were spaced much more closely to better define responses near the effect threshold.

All ion concentrations measured in stock solutions were compared to nominal values. If measured concentration differed from the nominal value by more than 20 %, the actual measured concentrations were substituted for the nominal concentrations. Background KCl content in the dilution water MHRW were added to the calculated contributions from the stock solutions.

Dissolved oxygen (DO) and pH were measured in selected test solutions during actual toxicity testing: Measured DO concentrations were always > 40 % saturation; measured pH was between 7.5-9.0.

53 replicate tests were conducted, and average LC50 values were calculated as the arithmetic mean of the values; SD = 14, range 0.0-61.

Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: Key study for SIDS
04-MAR-2001 (54)

Type of test: no data
Species: Daphnia magna
Exposure period: 100 hours
Unit: mg/l **Analytical monitoring:** no data

EC50: = 679
Method: other: acute toxicity
Year: 1965 **GLP:** no data
Test substance: as prescribed by 1.1-1.4
Remarks: Water used for experimental dilutions and controls was Standard Reference Water.
Source: Norsk Hydro ASA
Reliability: (3) not reliable
Flag: non confidential
02-MAR-2001 (25)

Type of test: no data
Species: Daphnia magna
Exposure period: 24 hours
Unit: mg/l **Analytical monitoring:** no data
EC50: = 343
Method: other: acute toxicity
Year: 1961 **GLP:** no data
Test substance: as prescribed by 1.1-1.4
Remarks: Groups of ten daphnids were exposed to 9 treatment levels. Maximum treatment level was 10,000 mg/l active ingredient.

All tests were conducted at 23 +/- 1 degree C. Water used for experimental dilutions and controls was Standard Reference Water. Observations were made at 12 hour intervals.
Source: Norsk Hydro ASA
Reliability: (3) not reliable
Flag: non confidential
02-MAR-2001 (24)

Type of test: no data
Species: Daphnia magna
Exposure period: 24 hours
Unit: mg/l **Analytical monitoring:** yes
EC0: = 587
EC100: = 1010
Method: other: DIN 38412 part 11
Year: 1982 **GLP:** no data
Test substance: no data
Source: Norsk Hydro ASA
Reliability: (4) not assignable
Original reference could not be checked
Flag: Material Safety Dataset
02-MAR-2001 (22)

Type of test: no data
Species: Daphnia magna
Exposure period: 48 hours
Unit: mg/l **Analytical monitoring:** yes
EC0: = 587
EC50: = 825
EC100: = 1010
Method: other: DIN 38412 part 11
Year: 1982 **GLP:** no data
Test substance: no data
Source: Norsk Hydro ASA
Reliability: (4) not assignable
Original reference could not be checked
Flag: Material Safety Dataset
02-MAR-2001 (22)

Type of test: no data
Species: Daphnia magna
Exposure period: 48 hours
Unit: mg/l **Analytical monitoring:** yes
EC50: = 177 (calculated from 93 mg/l as potassium)
Method: other:
Year: 1972 **GLP:** no data
Test substance: KCL reagent grade according to AMCS
Source: Norsk Hydro ASA
Reliability: (2)published article, reliable with restrictions
Remark: Potassium was added in a geometric series of concentrations, from 5 to 12 concentration levels were used. Test medium was natural Lake Superior water. The test was run with and without food addition. Two parallel beakers were used at each concentration. There was 10 daphnids less than 24h old in each beaker at the start of the test. Test temperature was 18 ± 1 °C. A 16 h photoperiod was used during testing. Only the result of test without food is referred.

Flag: non confidential
6-Des-2001 (11)

Type of test: static
Species: Physa heterostropha (fresh water snail)
Exposure period: 96 hours
Unit: mg/l **Analytical monitoring:** yes
LC50 = 940
Method: other
Year: 1968 **GLP:** no data
Test substance: as prescribed by 1.1-1.4, purity: A.C.S.-grade chemicals
Remarks: Snails were exposed to a graded series of KCl and synthetic dilution water and controls. Eighteen series of bioassays were done. Tests were made in 1 litre of solution at 20 degrees C. Dissolved oxygen concentrations were maintained between 5 and 9 ppm. No food was given during the test period or during the 36 hours before the tests began. Snails were acclimatized to the dilution water and other test conditions for 2 weeks before being used as experimental organisms. The nominal concentrations of KCl were not measured.
Source: Norsk Hydro ASA
Reliability: (2) reliable with restrictions
Flag: non confidential
02-MAR-2001 (58)

Type of test: static
Species: Dreissena polymorpha (zebra mussel)
Exposure period: 48 hours
Unit: mg/l **Analytical monitoring:** yes
LC50: = 150 (20-25 mm ad.)
LC50: = 147 (5-8 mm ad.)
Method: other: acute toxicity
Year: 1993 **GLP:** no data
Test substance: as prescribed by 1.1-1.4; 99 % active ingredient
Remarks: Mussels (20-25 mm and 5-8 mm) were obtained from Lake Eire, Ohio, and maintained in 2000 l aquaria containing dechlorinated municipal water. Before exposures, two size classes of adult mussels from the stock culture were placed in glass petri dishes and allowed to attach. The mussels were exposed in 3.8 l glass jars containing 2.5 l test water without aeration. Test water was reconstituted soft water of pH 7.7, alkalinity $6x10^{-4}$ m/L (30 mg/l as $CaCO_3$), and total hardness 40 mg/l as $CaCO_3$. Tests were conducted at 17 degrees C. Dissolved oxygen, pH and temperature were measured daily. Treatment of 10 animals per vessel were triplicated.
Source: Norsk Hydro ASA
Reliability: (2) reliable with restrictions
Flag: non confidential
04-MAR-2001 (76)

Type of test: static
Species: Dreissena polymorpha (zebra mussel)
Exposure period: 24 hours

Unit: mg/l **Analytical monitoring:** yes
LC50: = 138
Method: other: acute toxicity
Year: 1991 **GLP:** no data
Test substance: as prescribed by 1.1-1.4; 99 % active ingredient
Remarks: Mussels (15-20 mm) were obtained from Lake Eire, Ohio. Before exposures, two size classes of adult mussels from the stock culture were placed in glass petri dishes and allowed to attach. The mussels were exposed to 5 concentrations and 3 replicates of each concentration.
Source: Norsk Hydro ASA
Reliability: (2) reliable with restrictions
Flag: non confidential
04-MAR-2001 (33)

Type of test: static
Species: Nitocra spinipes (Crustacea)
Exposure period: 96 hours
Unit: mg/l **Analytical monitoring:** yes
LC50 = 854
Method: not stated
Year: 1978 **GLP:** no data
Test substance: as prescribed by 1.1-1.4, purity: reagent grade
Remarks: Groups of ten crustaceans were exposed to ten analyzed treatment levels of the active ingredient. Water used for experimental dilutions and controls was brackish water (filtered and heated to 80°C) (salinity 0.007 %). The 96 hour LC50 was determined to be 854 mg/l with a 95 % confidence level of 562-1298 mg/l.
Source: Norsk Hydro ASA
Reliability: (2) reliable with restrictions
Flag: non confidential
02-MAR-2001 (8)

Species: Austropotamobius pallipes pallipes (Crustacea)
Exposure period: 96 hours
Unit: mg/l **Analytical monitoring:** yes
LC50 = 740
Method: not stated
Year: 1973 **GLP:** no data
Test substance: as prescribed by 1.1-1.4
Source: Norsk Hydro ASA
Reliability: (3) not reliable
Flag: non confidential
02-MAR-2001 (12)

Species: Orconectus limosus (Crustacea)
Exposure period: 96 hours
Unit: mg/l **Analytical monitoring:** yes
LC50 = 1214
Method: not stated
Year: 1973 **GLP:** no data
Test substance: as prescribed by 1.1-1.4
Source: Norsk Hydro ASA
Reliability: (3) not reliable
Flag: non confidential
02-MAR-2001 (12)

4.3 Toxicity to Aquatic Plants e.g. Algae

Species: Nitzschia linearis (diatom)
Endpoint: growth rate
Exposure period: 120 hours
Unit: mg/l **Analytical monitoring:** yes
EC50 = 1337
Method: other
Year: 1968 **GLP:** no data
Test substance: as prescribed by 1.1-1.4, purity: A.C.S.-grade chemicals
Remarks: Diatoms were cultured in synthetic dilution water under controlled conditions. Tests were made by putting standard inoculum of cells in each of the 150 ml Erlenmeyer flasks, and comparing the number of cells produced at the end of a 5-day period. A graded series of test concentrations were used.
Reliability: (2) reliable with restrictions
Source: Norsk Hydro ASA
Flag: Key study for SIDS
02-MAR-2001 (58)

Species: Skeletonema costatum
Endpoint: biomass
Exposure period: 72 hours
Unit: mg/l **Analytical monitoring:** no data
EC10: 850
EC20: 1250
EC50: 2500
Method: other: DIN 38412 part 33
Year: 1991 **GLP:** no data
Test substance: not stated
Remark: German standard methods for the examination of water, waste water and sludge, bio-assays (group L); determination of the non-poisonous effect of waste water to green algae (Scenedesmus chlrophyll fluorescnece test) by dilution limits (L 33).
Source: Norsk Hydro ASA
Reliability: (4) not assignable
Original reference could not be checked
Flag: Material Safety Dataset
02-MAR-2001 (22)

4.4 Toxicity to Microorganisms e.g. Bacteria

4.5 Chronic Toxicity to Aquatic Organisms

4.5.1 Chronic Toxicity to Fish

4.5.2 Chronic Toxicity to Aquatic Invertebrates

Species: Austropotamobius pallipes pallipes (Crustacea)
Exposure period: 30 days
Unit: mg/l **Analytical monitoring:** yes
LC50 = 398 - 531
Method: not stated
Year: 1973 **GLP:** no data

Test substance: as prescribed by 1.1-1.4
Remark: Lower LC50 - animals were not fed during the exposure period; higher LC50 – animals were fed during exposure period.
Source: Norsk Hydro ASA
Reliability: (3) not reliable
Flag: non confidential
03-MAR-2001 (12)

Species: Orconectus limosus (Crustacea)
Exposure period: 30 days
Unit: mg/l **Analytical monitoring:** yes
LC50 = 626 - 854
Method: not stated
Year: 1973 **GLP:** no data
Test substance: as prescribed by 1.1-1.4
Remark: Lower LC50 - animals were not fed during the exposure period; higher LC50 – animals were fed during exposure period.
Source: Norsk Hydro ASA
Reliability: (3) not reliable
Flag: non confidential
03-MAR-2001 (12)

Type: semi-static
Species: Daphnia magna
Endpoint: reproductive impairment
Exposure period: 21 days
Unit: mg potassium /l **Analytical monitoring:** yes
Results: 16 % reproductive impairment = 101 (calculated from 53 mg/l as potassium
50 % reproductive impairment = 130 (calculated from 68 mg/l as potassium)
Method: other: not stated
Year: 1972 **GLP:** no
Test substance: as prescribed by 1.1-1.4
Remark: Potassium was added a geometric series of concentrations for obtaining approximation of toxicity. After determination of test concentration, 8 groups of animals were tested at the mean nominal concentrations 54,8 and 102.8 mg potassium /l added to Lake Superior water with 1.2 mg chloride /l. Test concentrations were renewed each week. Test temperature was 18 ±1 °C and photoperiod 18 hours. Reproduction was assessed each week by counting juveniles produced. Three to seven tests were performed and the results of all tests were pooled and statistically analysed.
Source: Norsk Hydro ASA
Reliability: (2) reliable with restriction
Flag: non confidential
03-MAR-2001 (11)

TERRESTRIAL ORGANISMS

4.6.1 Toxicity to Soil Dwelling Organisms

4.6.2 Toxicity to Terrestrial Plants

Type: As potassium is one of the three major nutrients and chloride is an essential micronutrient for plants, the demands for these nutrients in plants/crops are reported. Background concentrations of K and Cl in plants are reported under item 3.2.; information about the essential functions of potassium and chloride in plants is reported under item 4.7; biotransformation and kinetics in plants is reported under item 4.8.

Remark: Crops have a high K demand, and uptake of K in plants ranges from about 50 to 300 kg K ha^{-1} per crop, broadly similar to the uptake of nitrogen (N). The potassium requirement for optimal plant growth is in the range 2-5 % of the plant dry weight of vegetative parts. The distribution of K within the plant differs from that of N; for most crops, the produce contains less K than the crop residues, whereas for cereals more than 70 % is contained in the straw. A rice crop of 8 t ha^{-1} removes 250 kg K ha^{-1} if straw is removed, and 24 kg K ha^{-} if straw remains in the field. Similar amounts are found for other cereals. For a 40 t ha^{-1} sugarbeet crop, the numbers are 250 and 110 kg K ha^{-}, respectively, if crop residues are removed or left in the field.

Crop utilization of K depends not only on the availability of K in soil, but also in that of other nutrients; excessive amounts of NH_4^+ or Mg hamper K uptake, and excessive K can reduce the uptake of Ca and Mg.

The appearance of visual symptoms due to K deficiency, generally resulting in yellowing and than death of the marginal leaf tissue, signals a very severe deficiency. Growth is restricted with resultant loss of crop yield long before symptoms become obvious. Earlier and less obvious symptoms of K deficiency are a general decrease in vigour and turgor. A further general effect is weakening of the structural tissues, with consequent susceptibility to lodging. Inadequate supply of potassium makes plants more susceptible to frost damage, and to fungal attack.

In most plant species the Cl requirement for optimal growth is in the range of 0.2-0.4 mg/g dry matter.

Excessive Cl is detrimental to chloride-sensitive crops (e.g. most fruit trees, bean and cotton), or if it is necessary to guard against excessive salinity (e.g. in intensive cropping under glass,

intensive fertilizer use on vegetables), and in arid areas. In hot, dry areas a high rate of evaporation from the surface causes soil water to move upwards and with it the salts it contains which may reach toxic levels to plants when accumulated in the surface layers of the soil. On average, concentrations of chloride in the external solution of more than 20 mM can lead to toxicity in sensitive plant species, whereas in tolerant species (e.g. barley, spinach, lettuce and sugar beet), the external concentration can be four to five times higher without reducing growth.

The principal effect of Cl deficiency in plants is a reduction in leaf surface area and thereby plants dry weight. With severe deficiency, necrosis might occur. In leaves and roots, besides cell division, cell extension is particularly impaired. Cl deficiency may occur in highly leached soils with a low Cl input from rain in areas far distant from oceans.

Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (37)(49)

4.6.3 Toxicity to other Non-Mamm. Terrestrial Species

Type: LDL0
Species/strain: frog
Route of Administration: s.c.
Exposure time:
Value: 2120 mg/kg body weight
Method: other: acute toxicity
Year: 1935 **GLP:** no data
Source: Norsk Hydro ASA
Reliability: (4) not assignable
Original reference could not be checked
Flag: without flag
01-MAR-2001 (2)

Type: LDL0
Species/strain: pigeon
Route of Administration: s.c.
Exposure time:
Value: 2210 mg/kg body weight
Method: other: acute toxicity
Year: 1935 **GLP:** no data
Source: Norsk Hydro ASA
Reliability: (4) not assignable
Original reference could not be checked
Flag: without flag
01-MAR-2001 (2)

4.7 Biological Effects Monitoring

Type: Animals
Remark: Potassium and chloride are essential constituents and two of the most abundant ions in all animal species. The biological effects of action of these ions are well reviewed :
K^+ is the principal cation mediating the osmotic balance of the body fluids. In animals, the maintenance of normal cell volume and pressure depends on Na^+ and K^+ pumping. Metabolic energy is expended in maintaining the gradient. In the absence of such pumping, chloride and sodium would enter the cells down their concentration gradients, and water would follow along the osmotic gradient thus created, causing the cells to swell until the pressure inside them balance the influx. Because sodium and potassium are actively transported, the osmolality of the cells remains the same as that of the interstitial fluid. The membrane potential is maintained, and the chloride concentration inside the cells remains low.

The K^+/Na^+ separation has allowed for evolution of reversible transmembrane electrical potentials essential for nerve and muscle action in animals.

Potassium transport through the hydrofobic interior of a membrane can be facilitated by a number of natural compounds that form lipid-soluble alkali metal cation complexes. Potassium serves the critical role as counterion for various carboxylates, phosphates and sulphates, and stabilizes macromolecular structures.
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (35)(61)

Type: Plants
Remark: Biological effects of potassium as one of the three major plant nutrients, and chloride as an essential micronutrient for plants, is well reviewed :
An adequate K supply is necessary to ensure crop resistance to lodging, disease and drought. K is an important quality agent both through a direct effect on crops and because it strengthens resistance to diseases, and sufficient K is important for vitamin and mineral content, for texture, firmness and resistance to damage during transport.

Potassium in plants is important for the osmotic and ionic regulation, and for a large number of enzymes related to carbohydrate and protein metabolism. In almost all cases, cytosolic potassium concentrations are maintained in the range 100-200 mM. Due to its high concentration

in the cytosol and chloroplasts it neutralizes the soluble and insoluble inorganic anions and stabilizes the pH between 7 and 8 in these compartments, the optimum for most enzyme reactions.

Potassium activates the membrane-bound proton pumping ATPases. This activation facilitate the transport of K from the external solution across the plasma membrane into the root cells, and make potassium the most important mineral element in cell extension and osmoregulation. A high osmotic pressure in the stele of roots is prerequisite for turgor-pressure-driven solute transport in the xylem and for the water balance of plants. In principle the same mechanism is responsible for cell extension and various types of movement at the level of individual cells or in certain tissues.

Potassium, as the most prominent inorganic solute, plays a key role in the control of water in plants. When K is deficient, the stomata can not function properly and water loss from the plant may reach damaging levels. In addition to the effect of the opening and closing of stomata on conserving water within the plant, the plant's potassium status also affects the ease with which it can extract water from the soil.

In higher plants, potassium affects photosynthesis at various levels, playing a key role in CO_2 fixation. Potassium nutritional status also affect photosynthesis in leaves via its stomatal regulation. Inefficient operation of the stomata means that the supplies of the raw materials essential for the formation of sugars are restricted and photosynthesis declines. The soluble products of photosynthesis are moved from the leaves in the phloem and this transport is speeded up in the presence of adequate potassium.

Potassium is closely connected with processes involved in the protein synthesis in plants. When nitrate is taken up from the soil, the negative charge on this ion is neutralized by the positive charge on the K ion and the N is then taken up in the transpiration stream to the leaves where it is manufactured into protein. At the top the K ion combines with organic acids and, in this form, flows down to the root again to take part in the next cycle. The role of K in protein synthesis is not only reflected in the accumulation of soluble nitrogen compounds (e.g. amino acids, amides, and nitrate), but is also directly required for incorporation of inorganic nitrogen into the protein fraction. It is probable that potassium is involved in several steps of the translation process. Because K is concerned in nitrogen metabolism in the plant, a consequence of low K supply to plants receiving

large amounts of N fertilizer is that intermediate products of protein synthesis accumulate. Increasing the K supply improves the conversion of these low molecular weight N compounds into protein.

Cl is essential for the photosynthetic O_2 evolution and the membrane-bound proton-pumping ATPases. Cl also plays an essential role in stomatal regulations trough mediating the opening and closure of the stomata.

Chloride has important functions in osmoregulation at different levels. At the usually high plant content it is a main osmoticum in the vacuoles of the bulk tissue (50-150 mM chloride). At low contents which are in the range of a micronutrient (approx. 1 mM chloride or below), these osmoregulatory functions of chloride are confined to specialized tissues or cells (e.g. extension zones of roots and shoots).

Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (37)(49)

4.8 Biotransformation and Kinetics

Type: Plants
Remark: Biotransformation and kinetics of potassium as one of the three major plant nutrients, and chloride as an essential micronutrient for plants, is well reviewed:
Uptake of K in plants is highly selective and closely coupled to metabolic activity. It is characterized by high mobility in plants at all levels, within individual cells, within tissues, and in long-distance transport via the xylem and phloem. K is the most abundant cation in the cytoplasm and its accompanying anions make a major contribution to the osmotic potential of cells. K is not metabolized and it forms only weak complexes in which it is readily exchangeable.
Chloride is readily taken up by plants and its mobility in short- and long-distance transport is high. In plants, chloride occurs mainly as free anion or is loosely bound to exchange sites. In higher plants, more than 130 chlorinated organic compounds have been found. However, the importance of these compounds in terms of functional requirement of Cl for higher plants is not known.

Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (37)(49)

4.9 Additional Remarks

Type: Effects of potassium and chloride on plant diseases
Remark: Generally, potassium tends to improve the plant's resistance towards several diseases, and the potassium effect appears to be related to soil K status. An adequate K supply is of notable importance for plants to make protective chemicals and barriers that restrict the progress of an infection and compensate for any damage through new growth. Application of K is shown to reduce the damage from bacterial leaf blight, sheat blight and stem rot in rice; black rust in wheat; sugary disease in sorghum; and bacterial leaf blight in cotton. The ability to resist bacterial and fungal diseases often depends on the N:K ratio.

Chloride may hinder the plant disease take-all in wheat due to its apparent action as a nitrification inhibitor: Cl forces the plant to take up more N as NH_4^+ with exchange of hydrogen ions; this makes the soil at the root surface more acidic, and some microbes that thrive under acidic conditions inhibit the development of take-all. Chloride also decreases the NO_3^- concentration in plants. Reduced NO_3^- may result in fewer attacks of common root rot on barley.
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (37)(60)

Remark: Biological effects, and biotransformation and kinetics of potassium and chloride in humans is reported under item 5.10.
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001

5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

Type: LD50
Species: rat
Strain: Wistar
Sex: female
Number of Animals: 109
Vehicle: other: none
Value: 3020 mg/kg body weight
Method: other; acute toxicity
Year: 1961 **GLP:** no data
Test substance: as prescribed by 1.1-1.4, purity: not stated
Remark: The animals weighed 200-300 g and were fed ad libitum. They were placed in metabolism cages, one animal per cage, and given water for 16 hours before administration. KCl was given by stomach tube in doses of 2.1, 2.4, 2.7, 3.3, 3.6 and 3.9 g/kg body weight. Each dose was dissolved in distilled water and given in a volume of 20 ml/kg body weight.

Clinical signs were recorded at hourly or other intervals.
Body weight, food and water intake, urine volume and urinanalysis, and colonic temperature were recorded upon survivors at intervals of 24 hours after drug administration. Autopsies were performed upon nonsurvivors. Clinical and pathological parameters were also recorded on 13 survivors and controls over a period of two weeks following the treatment period.

The acute oral LD50 +/- SE was determined to be 3020 +/- 0.14 mg/kg body weight. The mean +/- SD interval to death was 2.2 +/- 3.2 hours. Clinical signs of intoxication in animals that died included convulsions followed by exhaustion and respiratory failure. Autopsy revealed signs of irritant gastro-enteritis, and necrosis appeared in the renal tubular epithelium. The heart was dilated with blood at death, and the lung alveoli were frequently collapsed. Compared to control animals the organ weight changes in nonsurvivors were; pyloric stomach – 19.0 % change compared to controls, kidney – 16.8 % change compared to controls, lungs – 14.7 % change compared to controls, jejunum – 14 % change compared to controls, ileum - 14 % change compared to controls, colon –9.5 % change from controls, and hearth + 11.3 % change from controls. Survivors recovered quickly from the toxic effects of KCl.

Animals surviving the LD50 dose had convulsive movements, diarrhoea or constipation, loss of appetite, increased thirst and urine excretion and fever. Measurements of clinical signs were within

the normal range within 2-3 days. Organ weights and water levels returned to normal limits in survivors at two weeks after administration of KCl. KCl had no effect on the amount of urinary acetone, albumin, occult blood, bilirubin or glucose.

Source: Norsk Hydro ASA
Reliability: (2) reliable with restrictions
Flag: Key study for SIDS
28-FEB-2001 (14)

Type: LDL0
Species: rat
Strain: Wistar
Sex: not stated
Number of Animals: 12
Vehicle: other: none
Value: 2430 mg/kg body weight
Method: other: acute toxicity
Year: 1929 **GLP:** no data
Test substance: as prescribed by 1.1-1.4, purity: chemical grade
Remarks: A M/2 solution of KCl was administrated to the animals. Clinical signs of acute poisoning in animals included increased respiration and heart action, and occasionally asphyxial convulsions. Sub-acute poisoning produced convulsions. The animals showed wide variation in the effects produced by KCl, and survival from an average lethal dose took place.
Source: Norsk Hydro ASA
Reliability: (2) reliable with restrictions
Flag: non confidential
28-FEB-2001 (71)

Type: LDL0
Species: guinea pigs
Strain:
Sex: not stated
Number of Animals: 14
Vehicle: other: none
Value: 2500 mg/kg body weight
Method: other: acute toxicity
Year: 1929 **GLP:** no data
Test substance: as prescribed by 1.1-1.4, purity: chemical grade
Remarks: A M/2 solution of KCl was administrated to the animals. Clinical signs of acute poisoning in animals included increased respiration and heart action, and occasionally asphyxial convulsions. Sub-acute poisoning produced convulsions. The animals showed wide variation in the effects produced by KCl, and survival from an average lethal dose took place.
Source: Norsk Hydro ASA
Reliability: (2) reliable with restrictions
Flag: non confidential
28-FEB-2001 (71)

Type: LDL0
Species: sheep

Strain:
Sex: not stated
Number of Animals: 6
Vehicle: other: none
Value: 4000 mg/kg body weight
Method: other: acute toxicity
Year: 1955 **GLP:** no data
Test substance: as prescribed by 1.1-1.4, purity: chemical grade
Remarks: KCl was administered orally to six sheep maintained on a normal ration, in single doses of 2, 3, and 4 g/kg body weight, and observed for toxic signs. The Minimum Lethal Dose (MLD) in nonfasted animals was 4 g/kg body weight. Two sheep receiving this dose has a time to death of 40 to 85 minutes. Salivation, vomiting, heart throbbing, accelerated breathing, mydriasis, staggering walk, spasms, and finally coma preceded death. Sublethal doses of KCl caused depression, refusion to eat, polyuria, increased respiration rate, and rapid pulse for a period of 4 to 6 hours, but the animals recovered without any further signs of toxicity.
Reliability: (3) not reliable
Flag: non confidential
28-FEB-2001 (69)

Type: LDL0
Species: goat
Strain:
Sex: not stated
Number of Animals: not stated
Vehicle: other: none
Value: 4000 mg/kg body weight
Method: other: acute toxicity
Year: 1955 **GLP:** no data
Test substance: as prescribed by 1.1-1.4, purity: chemical grade
Remarks: Acute oral toxicity of KCl was studied for goats on salt-poor diet (no added NaCl for 1.5 months) as compared with animals on a normal ration. A single oral dose of 4 g/kg body weight caused death within 35 to 85 minutes in the salt-deficient animals, whereas those on a normal feed ration survived. Clinical signs of toxicity in animals given lethal doses: Vomiting, polyuria, tetanic spasms of muscles of extremities, accelerated respiration and pulse. At autopsy, the kidneys were swollen, the heart muscle was flabby, and the rumen, reticulum, abomasum and duodenum mucosae were hyperemic.
Reliability: (3) not reliable
Flag: non confidential
28-FEB-2001 (69)

Type: LD50
Species: rat
Exposure time:
Value: 2600 mg/kg
Method: other: acute toxicity

Year: 1972 **GLP:** no data
Source: Norsk Hydro ASA
Reliability: (4) not assignable
Original reference could not be checked.
Flag: without flag
28-FEB-2001 (3)

5.1.2 Acute Inhalation Toxicity

Remark: No studies located.
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001

5.1.3 Acute Dermal Toxicity

Remark: Not relevant; potassium chloride is not likely to be absorbed through the skin because of the low octanol-water partition coefficient of the substance.
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001

5.1.4 Acute Toxicity, other Routes

Type: LD50
Species/strain: rat / Food and Drug strain, Wistar stock
Route of Administration: i.p.
Exposure time: 24 hours
Value: 660 mg/kg
Method: other: acute toxicity
Year: 1965 **GLP:** no data
Test substance: as prescribed by 1.1-1.4, purity: not stated.
Remarks: KCl was administrated as a single dose by the intraperitoneal route to groups of 10 rats.
Source: Norsk Hydro ASA
Reliability: (2) reliable with restrictions
Flag: non confidential
01-MAR-2001 (82)

Type: LD50
Species/strain: rat
Route of Administration: i.v.
Exposure time: 6 hr
Value: 142 mg/kg
Method: other: acute toxicity
Year: 1964 **GLP:** no data
Test substance: as prescribed by 1.1-1.4, purity: not stated.
Remarks: KCl was administrated as a single dose by the intravenous route.
Source: Norsk Hydro ASA
Reliability: (2) reliable with restrictions
Flag: non confidential
01-MAR-2001 (75)

Type: LD50
Species/strain: mouse/Cobs Charles River

Route of Administration: i.v.
Exposure time: 24 hr
Value: 117 mg/kg
Method: other: acute toxicity
Year: 1975 **GLP:** no data
Test substance: as prescribed by 1.1-1.4, purity: not stated.
Remarks: Groups of ten animals were injected 0.5 ml KCl solution/20 g body weight.

Source: Norsk Hydro ASA
Reliability: (2) reliable with restrictions
Flag: non confidential
01-MAR-2001 (9)

Type: LDL0
Species/strain: rat/Wistar
Route of Administration: i.p.
Exposure time:
Value: 825 mg/kg body weight
Method: other: acute toxicity
Year: 1929 **GLP:** no data
Test substance: as prescribed by 1.1-1.4, purity: chemical grade.
Remarks: A M/2 solution of KCl was administrated to 12 animals by means of a catheter. Clinical signs of acute poisoning in animals included increased respiration and heart action, and occasionally asphyxial convulsions. Sub-acute poisoning produced convulsions. The animals showed wide variation in the effects produced by KCl, and survival from an average lethal dose took place.
Source: Norsk Hydro ASA
Reliability: (2) reliable with restrictions
Flag: non confidential
01-MAR-2001 (71)

Type: LDL0
Species/strain: guinea pig
Route of Administration: i.p.
Exposure time:
Value: 900 mg/kg body weight
Method: other: acute toxicity
Year: 1929 **GLP:** no data
Test substance: as prescribed by 1.1-1.4, purity: chemical grade.
Remarks: A M/2 solution of KCl was administrated to 14 animals by means of a hypodermic syringe. Clinical signs of acute poisoning in animals included increased respiration and heart action, and occasionally asphyxial convulsions. Sub-acute poisoning produced convulsions. The animals showed wide variation in the effects produced by KCl, and survival from an average lethal dose took place.
Source: Norsk Hydro ASA
Reliability: (2) reliable with restrictions
Flag: non confidential

01-MAR-2001 (71)

Type: LDL0
Species/strain: guinea pig
Route of Administration: i.a., i.v., i.c.
Exposure time:
Value: intraarterial: 130 mg/kg
intravenous: 77 mg/kg
intracardial: 40 mg/kg
Method: other: acute toxicity
Year: 1928 **GLP:** no data
Test substance: as prescribed by 1.1-1.4, purity: not stated.
Remarks: Animals were injected 5 % KCl solution (maximum volume 0.6 ccm).
Source: Norsk Hydro ASA
Reliability: (2) reliable with restrictions
Flag: non confidential
01-MAR-2001 (28)

Type: LD50
Species/strain: mouse
Route of Administration: i.p.
Exposure time:
Value: 620 mg/kg
Method: other: acute toxicity
Year: 1963 **GLP:** no data
Source: Norsk Hydro ASA
Reliability: (4) not assignable
Original reference could not be checked.
Flag: without flag
01-MAR-2001 (4)

Type: LDL0
Species/strain: guinea pig
Route of Administration: s.c.
Exposure time:
Value: 2550 mg/kg body weight
Method: other: acute toxicity
Year: 1935 **GLP:** no data
Source: Norsk Hydro ASA
Reliability: (4) not assignable
Original reference could not be checked.
Flag: without flag
01-MAR-2001 (2)

5.2 Corrosiveness and Irritation

5.2.1 Skin Irritation

Species: humans
Result: A threshold concentration for irritancy of 60 % was seen when KCl in aqueous solution was in contact with the skin of volunteers. The threshold concentration when applied to broken skin for the same amount of time was 5 %. No grading of the

skin irritating potential was measured in this study.
Method: Chamber scarification test
Year: 1976 **GLP:** no data
Test substance: no data
Remark: A forearm test site was criss-crossed scarified by drawing a needle over the skin with enough pressure to cleave epidermis without bleeding. The test agent was applied in an aluminium chamber sealed to the skin once daily for 3 days.
Source: Norsk Hydro ASA
Reliability: (3) not reliable
Flag: non confidential
28-FEB-2001 (34)

5.2.2 Eye Irritation

Species: rabbit
Result: Instillation of 500 mg KCl produced a mild reaction in the rabbit eye at 24 hours.
Method: other: eye Irritation
Year: 1976 **GLP:** no data
Test substance: no data

Source: Norsk Hydro ASA
Reliability: (4) not assignable
Original reference could not be checked.
Flag: without flag
28-FEB-2001 (3)

5.3 Sensitization

5.4 Repeated Dose Toxicity

Species: rat **Sex:** male
Strain: F344/Scl
Route of admin.: oral feed
Exposure period: 2 years
Frequency of treatment: daily
Post. obs. period: none
Doses: 0.25, 1 % and 4 % KCl; 0.11, 0.45 and 1.82 g/kg body weight/day
Control Group: yes, concurrent no treatment
Results: NOAEL > 1.82 g/kg body weight/day. The only treatment related effects seen in rats fed about 0.11-1.82 g/kg body weight/day were gastritis (inflammation of the stomach linking), an irritant effect. The percentages of gastritis were 18 % in the 0.11 and 0.45 g/kg bw/day groups, and 30 % in the 1.82 g/kg bw/day group, compared to 6 % in the control group. At the end of the 2 year experimental period, the survival rates were 64 % in 0.25 % KCl, 58 % in 1 % KCl, 84 % in 4 % KCl, and 48 % in control groups. Absolute and relative organ weights were measured for the following organs; brain, pituitary, thymus, heart, lung,

liver, spleen, pancreas, kidney, adrenal gland, testis, seminal vesicle and prostate. However, no statistically significant changes were reported in any organs at any dose levels.
Nephrotic lesion was predominant in all groups, including controls. Pathological non-tumerous and tumors lesions did not indicate any carcinogenic effects of KCl.

Method: other: Repeated Dose Toxicity
Year: 1961 **GLP:** no data
Test substance: as prescribed by 1.1-1.4, purity: commercial grade
Remark: Groups of 50 rats (male) were exposed to KCl administered through the food.
Source: Norsk Hydro ASA
Reliability: (2) reliable with restrictions
Flag: Key study for SIDS
01-MAR-2001 (44)

Species: rat **Sex:** female
Strain: Wistar
Route of admin: oral feed
Exposure period: 105 days
Frequency of treatment: daily
Post. obs. period: 1 month
Doses: 5.25 g/kg body weight per day administrated as 2.5 % aqueous solution of KCl
Control Group: yes, concurrent no treatment
Result: Mean heart weight was significantly less (270±34 mg/100 g) and mean kidney weight was significantly higher (845±112 mg/100 g) than that of control animals (respectively 324±19 and 731±31 mg/100 g). Histological studies of the adrenals indicated

hypertrophy in the glomerular zone. All changes seen were reversible in the control animals.

Method: other: Repeated Dose Toxicity
Year: 1951 **GLP:** no data
Test substance: as prescribed by 1.1-1.4, purity: unknown
Remarks: 14 experimental animals and 6 control rats were fed ad libitum on a diet (Purina laboratory chow) and a 2.5 % aqueous solution of KCl as the sole source of fluid. At the end of the exposure period, 10 animals were terminated, the remaining 4 animals were supplied with tap water in place of KCl for one further month. At termination of the study, the heart and kidneys were weighed. The adrenals and kidneys were prepared for histological studies which included detection of ascorbic acid, cholesterol and other lipids.
Source: Norsk Hydro ASA
Reliability: (2) reliable with restrictions
Flag: non-confidential
01-MAR-2001 (5)

Species: humans **Sex:** female
Route of admin: oral feed
Exposure period: 4 week placebo controlled crossover study

Frequency of treatment: daily
Post. obs. period: 1 month
Doses: 80 mmol KCl/day (approx. 85 mg/kg body weight/day)

Control group: yes, concurrent no treatment
Result: NOAEL > 85 mg/kg body weight.
No significant changes in blood pressure or heart rate. Significant increases in potassium urinary excretion (P<0.001) and plasma potassium level (equivalent to 0.2 mmol/l; P<0.007).
Method: other: Repeated Dose Toxicity
Year: 1985 **GLP:** no data
Test substance: as prescribed by 1.1-1.4, purity: unknown
Remarks: 44 females aged 18-55 years were selected for the study on the basis of lower prevailing potassium intake. They were randomly allocated to one of two groups who took either 80 mmol/day of KCl (Slow-K, Ciba Geigy), or matching placebo for the first two 4-week treatment periods. The treatments were reversed during the second 4-week period. Blood pressure, heart rate, urinary volume, electrolytes and creatinine, were measured weekly during a screening period and the two 4-weeks treatment periods.
Source: Norsk Hydro ASA
Reliability: (2) reliable with restrictions
Flag: non-confidential
01-MAR-2001 (6)

Species: humans **Sex:** female
Route of admin: oral feed
Exposure period: 6 week placebo controlled crossover study
Frequency of treatment: daily
Post. obs. period: 1 month
Doses: 65 mmol KCl/day (approx. 69 mg/kg body weight/day)

Control group: yes, concurrent no treatment
Results: NOAEL > 69 mg/kg body weight/day

Significant reduction in systolic and diastolic blood pressure, from 153±3.1/104±1.7 to 146±3.1/101±1.6. Significant increase in serum potassium (from 51±3 to 112±8) and urine potassium (from 3.88±0.10 to 4.36±0.11). Changes in blood pressure did not correlate with changes in serum or urine electrolytes. Analysis of the 95 % confidence intervals in this and five other studies suggests that KCl supplementation lower blood pressure, but that the change is small and within the confidence levels of all six trials.

Method: other: Repeated Dose Toxicity
Year: 1986 **GLP:** no data
Remarks: 32 hypertensive females aged 34-62 years were selected for the study. They were randomly allocated to one of two groups who took either 65 mmol/day of KCl, or matching placebo for a 6 weeks treatment period. The treatments were reversed

after the 6-week period. Blood pressure, and urinary electrolytes (sodium and potassium) and creatinine, were measured weekly during the treatment period. Plasma sodium and potassium and serum albumin, calcium and magnesium were measured at 6th week only.

Source: Norsk Hydro ASA
Reliability: (2) reliable with restrictions
Flag: non-confidential
01-MAR-2001 (50)

5.5 Genetic Toxicity 'in Vitro'

Type: Bacterial reverse mutation assay (Salmonella preincubation assay)
System of testing: S. typhimurium TA 100, TA 1535, TA 1537, TA 9
Concentration: 0, 100, 333, 1000, 3333, 10000 µg/plate
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other, Salmonella preincubation assay (NTP modified standard plate incorporation assay)
Year: 1986 **GLP:** no data
Test substance: as prescribed by 1.1-1.4, purity: commercial grade
Remark: Procedure: Pre-incubation. Activation system: S-9 fraction from the liver of Arochlor 254-induced male SD rats with a NADPH-generating system. No. replicates: 3 plates per dose level
Source: Norsk Hydro ASA
Reliability: (2) reliable with restriction
Flag: Key study for SIDS
01-MAR-2001 (53)

Type: bacterial colorimetric assay (SOS Chromotest)
System of testing: E. coli PQ37
Concentration: 1 - 100 000 nM/ml
Metabolic activation: without
Results: negative
Method: other, SOS Chromotest
Year: 1987 **GLP:** no data
Test substance: as prescribed by 1.1-1.4, purity: commercial grade
Remarks: No. replicates: 3 plates per dose level.
Source: Norsk Hydro ASA
Reliability: (2) reliable with restriction

Flag: non-confidential
01-MAR-2001 (57)

Type: mammalian cell gene mutation test
System of testing: mouse lymphoma cell (L5178Y), $TK^{+/-}$ heterozygote
Concentration: 0-5000 µg/ml
Metabolic

activation: With Aroclor 1254 induced Fisher rat liver S9 homogenate or with noninduced Fisher 344 rat liver S9, without activation
Results: With metabolic activation (Aroclor 1254 induced): positive at 5000 µg/ml. With metabolic activation (noninduced): positive at 4000 and 5000 µg/ml. Without metabolic activation: negative up to 5000 µg/ml, however, higher, concentrations up to 8000 µg/ml, appeared to be toxic and mutagenic.
Method: OECD 476
Year: 1988 **GLP:** no data
Test substance: as prescribed by 1.1-1.4, purity: commercial grade
Remarks: Media: Fischer's liquid medium for leucemic cells supplemented with 10 % horse serum. Positive control was Ethyl methanesulfonate or 3-methylcholantrene and was positive under all test conditions. Negative control was 10 % water and solvent for the test chemical, and was negative under all test conditions. Treatment up to 5000 µg/ml was not toxic, and did not reduce the relative total growth below 50-65 %.
Source: Norsk Hydro ASA
Reliability: (1) reliable without restriction
Flag: Key study for SIDS
01-MAR-2001 (55)

Type: mammalian cell gene mutation test
System of testing: mouse lymphoma cell (L5178Y), $TK^{+/-}$ heterozygote
Concentration: 0-5000 µg/ml
Metabolic activation: With Aroclor 1254 induced male Fisher 344 rats S9 liver homogenate. Without activation
Results: With metabolic activation: In the first trial the relative total growth decreased with increased concentrations up to 4000 µg/ml, and no mutagenicity was reported. The second trial yielded a positive mutagenic response with a twofold increase at 4000 µg/ml and a 2.5 fold increase at 5000 µg/ml. The third trial yielded a concentration-dependent increase in mutations of about twofold at 3645 µg/ml, and threefold at 4050 µg/ml. Overall the test with S9 activation was evaluated as positive.
Without metabolic activation: negative up to 5000 µg/ml in the first trial. In the second trial mutations was increased 2.5 fold from 1049 to 3200 µg/ml, however, the increase was not dose-related. In the third trial cytotoxicity with no mutagenicity was reported. Overall the results without S9 activation were evaluated as negative.
Method: OECD 476
Year: 1988 **GLP:** no data
Test substance: as prescribed by 1.1-1.4, purity: commercial grade
Remarks: Media: Fischer's liquid medium for leucemic cells supplemented with 10 % horse serum. Positive control was Ethyl methanesulfonate or 3-methylcholantrene and was positive under all test conditions. Negative control was 10 % water and

solvent for the test chemical, and was negative under all test conditions.

Source: Norsk Hydro ASA
Reliability: (1) reliable without restriction
Flag: Key study for SIDS
01-MAR-2001 (52)

Type: chromosome aberration
System of testing: Chinese Hamster Ovary cells (CHO)
Concentration: 0, 70, 80, 90 mM
Metabolic activation: without
Results: Cytotoxicity conc: Without metabolic activation: 90 mM
without metabolic activation: positive
Method: other
Year: 1988 **GLP:** no data
Test substance: as prescribed by 1.1-1.4, purity: commercial grade
Remarks: 50 cells were scored for each dose. The osmotic pressure of the media was 300, 430, 445 and 465 mOsm/kg H_2O for 0, 70, 80 and 90 mM KCl, respectively. The survival in % was 100, 60, 45 and 25 for 0, 70, 80 and 90 mM KCl, respectively. After 24 hours the % aberrant cells were 4, 10, 28 and 30 for 0, 70, 80 and 90 mM KCl, respectively. After 42 hours the % aberrant cells were 2, 6, 4 and 23 for 0, 70, 80 and 90 mM KCl, respectively. In the OECD guidelines the recommended limit concentration is 10 mM, and in this chromosomal aberration test positive results were reported around 80 mM KCl.
Source: Norsk Hydro ASA
Reliability: (2) reliable with restriction
Flag: Key study for SIDS
01-MAR-2001 (16)

Type: mammalian cell gene mutation (V79 cells), chromosome aberration tests (CHO cells), and Unscheduled DNA synthesis (HeLa cells)
System of testing: Chinese Hamster V79 cells (V79), Chinese hamster Ovary cells (CHO), HeLa S3 cells (HeLa)
Concentration: 0-300 mM
Metabolic activation: with S9 liver homogenate, and without
Results: Cytotoxicity conc:
With metabolic activation: 37.5 mM (V79), 150 mM (CHO)
Without metabolic activation: 100 mM (V79), 75 mM (CHO)
Genotoxic effects:
With metabolic activation: Genmutation; 3 to 7 fold increase in the mutation frequency. The increase was observed at toxic and nontoxic doses of KCl. Chromosomal aberration; at 200 mM 6.9 % of the cells had aberrations in the presence of slight toxicity. Unscheduled DNA Synthesis; No increase in

the incorporation of tritiated thymidine, rather a reduction was observed.
Without metabolic activation: Genmutations; Increases in gene mutations were observed in a very narrow dose range, reaching three-fold the negative control value at 75 mM KCl. Chromosomal aberrations; Up to 100 mM no significant increase in chromosomal aberrations compared to the control values, and at 150 mM KCl, the treatment was very toxic. Unscheduled DNA synthesis; No increase in the incorporation of tritiated thymidine, rather a reduction was observed.

Method: Other: Resembling OECD 473 (CHO), OECD 476 (V79) and OECD 482 (HeLa)
Year: 1988 **GLP:** no data

Test substance: as prescribed by 1.1-1.4, purity: commercial grade 99.5 %
Remarks: No. replicates: at least 2 replicates per experiment.
Source: Norsk Hydro ASA
Reliability: (2) reliable with restriction
Flag: Key study for SIDS
01-MAR-2001 (66)

5.6 Genetic Toxicity 'in Vivo'

5.7 Carcinogenicity

Species: rat, male **Sex:** male
Strain: F344/Scl
Route of admin.: oral feed
Exposure period: 2 years
Frequency of treatment: daily
Post. obs. period: none
Doses: 0.25, 1 and 4 % KCl, and 2 % KCl + 2 % NaCl, (110, 450, 1820 mg/kg body weight/day) administrated through the food
Result: negative
Control Group: yes, concurrent no treatment
Method: other
Year: 1961 **GLP:** no data
Test substance: as prescribed by 1.1-1.4, purity: commercial grade
Remark: Groups of 50 male rats were exposed to KCl administered through the food. At the end of the 2 year experimental period, the survival rates were 64 % in 0.25 % KCl, 58 % in 1 % KCl, 84 % in 4 % KCl, and 48 % in control groups.
Pathological non-tumerous and tumors lesions did not indicate any carcinogenic effects of KCl. Among non-tumerous lesions, nephrotic lesion was predominant in all groups. In tumerous lesions, testicular tumor (interstitial cell tumor) developed with a high incident in all groups. However, the incidence and type of tumor in experimental and control groups were comparable to

those of spontaneous tumors in F344/Scl rats. The only treatment related effect was gastritis, 18 % in the 0.25%and 1.0% KCl group, and 30% in the 4% KCl group compared to 6% in the control group.
Source: Norsk Hydro ASA
Reliability: (2) reliable with restriction
Flag: non-confidential
01-MAR-2001 (44)

5.8 Toxicity to Reproduction

Remarks: no studies located
Source: Norsk Hydro ASA
Reliability: (2) valid with restrictions
Flag: non confidential
01-MAR-2001

5.9 Developmental Toxicity/Teratogenicity

Type: Developmental toxicity study
Species: mice **Sex:** female
Strain: virgin adult albino CD-l outbred
Route of admin.: oral intubation
Exposure Period: ten days (day 6 to 15 of gestation)
Frequency of treatment: single daily administration by oral intubation
Premating Exposure Period
male: none
female: none
Duration of test: sacrifice on the 17th day
Doses: 2.35, 10.9, 50.6, 235.0 mg/kg body weight
Control Group: yes
NOAEL Parental: > 235 mg/kg
NOAEL F1 Offspr.: > 235 mg/kg
Method: other
Year: 1975 **GLP:** no data
Test substance: as prescribed by 1.1-1.4, purity: not stated. Vehicle was water.
Remark: Groups of 21-24 experimental animals were used. Female mice were mated with young adult male mice, and observation of vaginal sperm plug was considered day 0 of gestation. Body weights were recorded on days 0, 6, 11, 15 and 17 of gestation. The dams were subjected to Caesarean section on gestation day 17. Post exposure observation period: 2 days. The urogenital tract of each dam was examined in detail for anatomical normality.

The administration of up to 235 mg/kg body weight of KCl to pregnant mice for 10 consecutive days had no effect on nidation or on maternal or offspring survival. The number of abnormalities seen in either soft or skeletal tissues of the test group did not differ from the controls.

General parental/maternal toxicity:
No effects seen in survival, total number of corpora lutea, implant sites, resorptions, soft tissue observations (urogenital tract), or live offspring.

Toxicity to offspring:
No effects seen in survival, sex ratio, average offspring weight, external congenital abnormalities, soft tissue defects (cleft palate), or skeletal defects (sternebrae, ribs, vertebrae, skull and extremities).
No further information was included in the study report.

Source: Norsk Hydro ASA
Reliability: (2) reliable with restrictions
Flag: Key study for SIDS
01-MAR-2001 (31)

Type: Developmental toxicity study
Species: rat **Sex:** female
Strain: Virgin adult Wistar
Route of admin.: oral intubation
Exposure Period: ten days (day 6 to 15 of gestation)
Frequency of treatment: single daily administration by oral intubation
Premating Exposure Period
male: none
female: none
Duration of test: sacrifice on the 20^{th} day
Doses: 3.1, 14.4, 66.8, 310.0 mg/kg body weight
Control Group: yes
NOAEL Parental: > 310 mg/kg

NOAEL F1 Offspr.: > 310 mg/kg
Method: other
Year: 1975 **GLP:** no data
Test substance: as prescribed by 1.1-1.4, purity: not stated. Vehicle was water.
Remark: Groups of 21-24 experimental animals were used. Female rats were mated with young adult male rats, and observation of vaginal plug was considered day 0 of gestation. Body weights were recorded on days 0, 6, 11, 15 and 20 of gestation. The dams were subjected to Caesarean section on gestation day 20. Post exposure observation period: 5 days. The urogenital tract of each dam was examined in detail for anatomical normality.

The administration of up to 310 mg/kg body weight of KCl to pregnant rats for 10 consecutive days had no clear discernible effects on nidation or on maternal or offspring survival. The number of abnormalities seen in either soft or skeletal tissues of the test group did not differ from the controls.

General parental toxicity:
No effects seen in survival, total number of corpora lutea, implant sites, resorptions, soft tissue observations (urogenital tract), or live offspring.

Toxicity to offspring:
No effects seen in survival, sex ratio, average offspring weight, external congenital abnormalities, soft tissue defects (cleft palate), or skeletal defects (sternebrae, ribs, vertebrae, skull and extremities).
No further information was included in the study report.

Source: Norsk Hydro ASA
Reliability: (2) reliable with restrictions
Flag: Key study for SIDS
01-MAR-2001 (31)

5.10 Other Relevant Information

Species: humans
Type: reported case on acute oral toxicity (LDL0)
Remarks: A 2 month-old 4.8 kg boy died 2 days after accidentally being fed 1,500 mg KCl (approx. 938 mg/kg body weight/2 days).
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (80)

Species: humans
Type: reported case on acute oral toxicity (LDL0)
Remarks: A 46 year-old women died after ingesting 35 g KCl in the form of slow-release KCl tablets.
Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (64)

Type: Gastric irritating effects in humans.
Results: In a group of 25 volunteers receiving 80 mEq (about 90 mg/kg body weight), in either a liquid or micro-encapsulated formulation, one case of flatulence and two cases of mild stomach ache were the only adverse effects reported.
Remarks: No gastro-intestinal examinations were carried out.
Source: Norsk Hydro ASA
Reliability: (2) reliable with restrictions
Flag: non confidential
01-MAR-2001 (10)

Type: Gastric irritating effects in humans.
Results: KCl administrated orally to groups of 48 to 110 volunteers in doses ranging from about 31-124 mg/kg body weight/day in either a wax or micro-encapsuled formulation for 7 days produced irritant effects in the stomach or small intestine.
Remarks: More severe effects, inflammatory lesions and gastric ulcers were seen particularly in volunteers receiving the wax formulations. 60 to 70 % of the volunteers treated with the wax-matrix KCl developed some type of gastric lesions. The lesions were graded from 0 (no mucosal damage) to 5 (severe

mucosal damage. The mean score for the control group was 0.267, and for the group receiving wax-matrix KCl 2.267.

Source: Norsk Hydro ASA
Reliability: (2) reliable with restrictions
Flag: non confidential
01-MAR-2001 (42)(51)(59)(63)

Type: Biological effects
Remark: K determines in large part the osmolality of the body fluids (see item 4.7). Potassium and chloride is also important in the regulation of the acid-base balance of the body. Potassium is the principal base in tissues and blood cells, and Cl maintains electrochemical neutrality by anion exchange with bicarbonate (the chloride shift) in the CO_2 transport in the blood red cells.

Both potassium and chloride are important in transmission of nerve impulses to the muscle fibers. Potassium is a choline esterase antagonist and affects the contractility of the muscle.

Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-20 (30)(32)(35)(45)

Type: Biotransformation and kinetics
Remark: Potassium is readily and rapidly absorbed by passive diffusion in the high-conductance membrane of the upper intestine. There is some secretion of potassium into the intestinal lumen. In the ileum and the colon, chloride is actively reabsorbed in exchange for bicarbonate. The concentration of potassium in the ileum is about 20 meq per liter, and in the colon the concentration is 40-50 meq per liter. About 90 % of the ingested dose of potassium is absorbed.

Potassium is distributed to all tissues where it is the principal intracellular cation. Cellular uptake of potassium is regulated by insulin, acid-base status, aldosterone, and adrenergic activity.

The majority of ingested potassium is excreted in the urine via glomelural filtration. Much of the filtered potassium is removed from the tubular fluids by active reabsorption. The distal tubules are able to secrete as well as reabsorb potassium, so they are able to produce a net secretion of potassium to achieve homeostatis in the face of a potassium load due to abnormally high levels of ingested potassium.

About 15 % of the total amount of potassium excreted is found in feces. Traces are excreted in sweat and tears. Cl leaves the tubular lumen by

secondary active transport of sodium, and also passive diffusion.

Excretion and retention of potassium is regulated by the main adrenal cortical hormones, although the pituary also influences electrolyte balance in the body. Adrenal mineralocorticoids such as aldosterone increase tubular reabsorption of sodium in association with secretion of potassium and H^+, and also reabsorption with chloride. Chloride reabsorption is increased when bicarbonate reabsorption is decreased, and vice versa.

Normal homeostatic mechanisms controlling the serum potassium levels allow a wide range of dietary intake. The renal excretory mechanism is designed for efficient removal of excess K, rather for its conservation during deficiency. Even with no intake of K, man loses a minimum of 585-1170 mg K per day. However, the distribution of potassium between the intracellular and the extracellular fluids can markedly affect the serum potassium level without a change in total body potassium.

In the parietal cells in the gastric mucosa, H^+ and Cl^- are transported actively across the apical membrane into the lumen of the stomach. This secretion of HCl is regulated by the hormone gastrin in response to intragastric protein and stomach distention.

Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions
Flag: non confidential
01-MAR-2001 (30)(32)(35)(45)(65)(74)

Type: Therapeutic uses
Remark: Diarrhea, emsis, diuresis, starvation, prolonged saline infusion, renal filaure, or dietary deficiency, may lead to K deficiency. Hypokalemia is characterized by muscle weakness, cardiac arrythmia, paralysis, bone fragility, sterility, adrenal hypertrophy, decreased growth rate, loss of weight and death.

Potassium chloride is of value for the relief of symptoms of hypokaliemic periodic paralysis, and the symptoms of Meniere's disease. Daily intake of potassium decreases the risk of stroke-associated mortality.

Usual therapeutic doses for oral solution-adults are 1.5-3 g/day to prevent depletion, and 3-7.5 g/day for replacement. Doses given by intravenous infusion (adults) is not to exceed a total dose of 200-400 mEq/day, depending on plasma potassium levels.

Source: Norsk Hydro ASA
Reliability: (1) reliable without restrictions

Flag: non confidential
01-MAR-2001 (15)(36)

5.11 Experience with Human Exposure

Type: Work place exposure - potash mining
Method: Eight companies from the potash and milling industry located near Carlsbad/USA cooperated in the investigation. Job classification was assessed as to whether it involved surface or underground activity, or both, and the men were divided into two categories after excluding men with less than one year experience in the potash industry or with more than one year in both surface and underground work (1058 men); 1) men with one year or more of underground potash work, and less than one year of surface potash work between 1940-1967 (2743 men), and 2) men who had one year or more of surface potash work, and less than one year underground potash work between 1940-1967 (1143 men).

Comparison was made between the observed risk of dying among the study cohort, with that expected according to age, sex, race, calendar time, and cause specific mortality rates for the general population of the United States.
Results: The field studies conducted failed to disclose any evidence of predisposition of underground miners to any of the diseases evaluated, including lung cancer. Secondly, the study concluded there is no reason to believe that the underground environment increases respiratory diseases when pneumoconiosis producing dust or radon decay products are absent or present in only minute amounts.

Exposure to dust, i.e. sodium and potassium salts, commonly encountered in the potash industry did not influence mortality due to heart disease or cerebrovascular accidents. A deficit of death from cancers other than respiratory among the surface workers could not be explained.
Source: Norsk Hydro ASA
Reliability: (2) reliable with restrictions
Flag: non confidential
28-FEB-2001 (78)

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