

FOREWORD

INTRODUCTION

Calcium chloride
CAS N°:10043-52-4

SIDS Initial Assessment Report**For****SIAM 15**

Boston, USA 22-25th October 2002

1. Chemical Name: Calcium chloride

2. CAS Number: 10043-52-4

3. Sponsor Country: Japan

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4. Shared Partnership with:

5. Roles/Responsibilities of the Partners:

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- Process used

6. Sponsorship History

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

7. Review Process Prior to the SIAM:

The industry consortium collected new data and prepared the updated IUCLID, and draft versions of the SIAR and SIAP. Japanese government peer-reviewed the documents, audited selected studies.

8. Quality check process:

9. Date of Submission:

10. Date of last Update:

11. Comments:

No testing (X) Testing ()

The CaCl₂-HPV Consortium members:

(Japan)

Asahi Glass Co., Ltd.

Central Glass Co., Ltd.

Sanuki Kasei Co., Ltd.

Tokuyama Corporation [a global leader of the CaCl₂-HPV Consortium]

Tosoh Corporation

(Europe)

Brunner Mond (UK) Ltd.

Solvay S.A.

(North America)

The Dow Chemical Company

General Chemical Industrial Products Inc.

Tetra Technologies, Inc.

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

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	10043-52-4
Chemical Name	Calcium chloride
Structural Formula	CaCl ₂

SUMMARY CONCLUSIONS OF THE SIAR**Human Health**

Calcium chloride is easily dissociated into calcium and chloride ions in water. The absorption, the distribution and the excretion of the ions in animals are regulated separately. Both ions are essential constituents of the body of all animals. Calcium is essential for the formation of skeletons, neural transmission, muscle contraction, coagulation of the blood, and so on. Chloride is required for regulating intracellular osmotic pressure and buffering.

The acute oral toxicity is low: LD₅₀ in mice is 1940-2045 mg/kg bw, 3798-4179 mg/kg bw in rats, and 500-1000 mg/kg bw in rabbits. The acute oral toxicity is attributed to the severe irritating property of the original substance or its high-concentration solutions to the gastrointestinal tract. In humans, however, acute oral toxicity is rare because large single doses induce nausea and vomiting. The dermal acute toxicity is negligible: LD₅₀ in rabbits >5000 mg/kg bw. No significant change was found by gross necropsy examination except skin lesions at or near the site of administration. Hypercalcemia may occur only when there exists other factors that alter calcium homeostasis, such as renal inefficiency and primary hyperthyroidism.

Irritation/corrosiveness studies conducted under OECD test guidelines indicate that calcium chloride is not/slightly irritating to skin but severely irritating to eyes of rabbits. Prolonged exposure and application of moistened material or concentrated solutions resulted in considerable skin irritation, however. Irritating effect of the substance was observed in human skin injuries caused by incidental contact with the substance or its high-concentration solutions.

A limited oral repeated dose toxicity study shows no adverse effect of calcium chloride on rats fed on 1000-2000 mg/kg bw/day for 12 months. Calcium and chloride are both essential nutrients for humans and a daily intake of more than 1000 mg each of the ions is recommended. The establishment of the ADI for calcium chloride has not been deemed necessary by JECFA (Joint FAO/WHO Expert Committee on Food Additives). Considering further the well-established metabolism and mechanisms of action of calcium and chloride ions in the human body, no further study is considered necessary for this endpoint.

Genetic toxicity of calcium chloride was negative in the bacterial mutation tests and the mammalian chromosome aberration test.

No reproductive toxicity study has been reported. A developmental toxicity study equivalent to an OECD Guideline study, on the other hand, reveals no toxic effects on dams or fetuses at doses up to 189 mg/kg bw/day (mice), 176 mg/kg bw/day (rats) and 169 mg/kg bw/day (rabbits). In view of the nutritional aspects, the metabolism, and the mechanisms of action of calcium and chloride ions, no further study is considered necessary for these endpoints.

Environment

Calcium chloride's vapour pressure is negligible and its water solubility is 745 g/L at 20°C. Calcium chloride is readily dissociated into calcium and chloride ions in water. These physico-chemical properties indicate that calcium chloride released into the environment is distributed into the water compartment in the form of calcium and chloride ions.

Acute toxicity studies (lowest effect values) reveal a 72-hour EC₅₀ of 2900 mg/L for algae (*Selenastrum capricornutum*), a 48-hour EC₅₀ of 1062 mg/L for daphnids (*Daphnia magna*) and a 96-hour LC₅₀ of 4630 mg/L for fish (*Pimephales promelas*).

The chronic toxicity study with *Daphnia magna* shows that a 16% impairment of reproduction (EC₁₆) is caused at

the concentration of 320 mg/L. The 72-hour EC₂₀ for *Selenastrum capricornutum* determined by the OECD TG 201 study is 1000 mg/L. All the data compiled on the acute and chronic toxicity are greater than 100 mg/L.

Calcium is known as an essential nutrient for higher plants and one of the basic inorganic elements of algae. Calcium plays crucial roles in strengthening cell walls and plant tissues, reducing the toxicity of soluble organic acids, elongating roots, and so on. Chloride is also an essential micronutrient for plants and has important roles in the photosynthesis and osmoregulation.

Deicing agents used as road salts are usually chloride salts, mainly sodium chloride or calcium chloride with minor amounts of magnesium chloride and potassium chloride. The primary cause of the damage to roadside plants is considered to be the accumulation of chloride in plant tissues to a toxic level by excess loading of inorganic chloride salts.

Calcium chloride constituted 2% of the total composition (approx. 5 million tonnes) of deicing agents used in Canada in the 1997-1998 winter season, while sodium chloride constituted 95% of the total. In addition, there is a report that shows the uptake of chloride by plants is considerably inhibited in the presence of calcium chloride. The impact of calcium chloride on plants is expected to be minimal compared to other chloride-containing agents, given the factors discussed above as well as the difference of usage of calcium chloride as compared to sodium chloride.

Exposure

The production capacity of calcium chloride in North America was reported in 2002 to be approximately 1,687,000 tonnes per year. The estimated production volume in Japan was approximately 245,000 tonnes in 2000. The total amount used in Western Europe including Scandinavia is around 300,000 tonnes per year.

Calcium chloride is produced in the closed system by refining of natural brine, by ammonia soda process as a by-product or by neutralization reaction of limestone with hydrochloric acid. Commercial products are supplied as flakes, pebbles, pellets, powders and solutions with varying concentrations. Calcium chloride is used for deicing, road stabilization, dust control, accelerator in concrete, industrial processing, oil and gas well fluids, and for others such as food additives and medication.

Almost half of the volume of calcium chloride is consumed as deicing agents and road stabilizers, and directly released into the environment, where the substance is dissociated into calcium and chloride ions. In the 1997-1998 winter season, 5 million tonnes of road salts including sodium chloride (95%), calcium chloride (2%), magnesium chloride, potassium chloride and ferrocyanide salts were used in Canada. Based on the global water quality monitoring conducted by UNEP, the mean, 10th-percentile and 90th-percentile of calcium concentrations in 76 rivers were 37.4, 5.1 and 86.5 mg/L, respectively. In addition, the mean, 10th-percentile and 90th-percentile of chloride concentrations in 77 rivers were 41.1, 1.1 and 64.8 mg/L, respectively. It should be noted that both the concentrations of calcium and chloride ions are tightly related to various factors, such as geological parameters, weathering and human activities.

As for human exposure, oral intake is expected via foods that contain calcium chloride in the dissociated form as food additives or as residues of food processing agents. There is potential for exposure to workers and consumers via skin contact and dust inhalation at working places or elsewhere by versatile uses such as road stabilizers.

RECOMMENDATION

The chemical is currently of low priority for further work.

RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

The chemical is currently of low priority for further work based on a low hazard potential.

Because of the effects of calcium chloride on soil dwelling organisms and plants and the exposure associated with the use of calcium chloride as a deicing agent in some countries, these countries may decide to assess the environmental risk related to this exposure scenario.

FULL SIDS SUMMARY

CAS NO: 10043-52-4		SPECIES	PROTOCOL	RESULTS
PHYSICAL-CHEMICAL				
2.1	Melting Point		Unknown	772°C
2.2	Boiling Point		Unknown	>1600°C
2.3	Density		Unknown	2.16 g/cm ³ at 25°C
2.4	Vapour Pressure			Negligible
2.5	Partition Coefficient (Log Pow)			Not applicable
2.6 A.	Water Solubility		Unknown	745 g/L at 20°C
B.	pH			
	pKa			
2.12	Oxidation: Reduction Potential			
ENVIRONMENTAL FATE AND PATHWAY				
3.1.1	Photodegradation			Not applicable
3.1.2	Stability in Water			Dissociated into calcium and chloride ions
3.2	Monitoring Data			According to UNEP global monitoring, Calcium in 76 rivers: Mean: 37.4 mg/L 10th-percentile: 5.1 mg/L 90th-percentile: 86.5 mg/L Chloride in 77 rivers: Mean: 41.1 mg/L 10th-percentile: 1.1 mg/L 90th-percentile: 64.8 mg/L
3.3	Transport and Distribution			According to the physico-chemical properties of calcium chloride, low vapour pressure and high water solubility, the substance is likely to be distributed into the water compartment in the form of calcium and chloride ions.
3.5	Biodegradation			Not applicable

CAS NO: 10043-52-4		SPECIES	PROTOCOL	RESULTS
ECOTOXICOLOGY				
4.1	Acute/Prolonged Toxicity to Fish	<i>Pimephales promelas</i> <i>Lepomis macrochirus</i> <i>Gambusia affinis</i>	EPA/600/4-90/027, EPA/600/6-91/003	LC ₅₀ (96 hr) = 4630 mg/L LC ₅₀ (96 hr) = 9500-11300 mg/L LC ₅₀ (96 hr) = 10650 mg/L LC ₅₀ (96 hr) = 13400 mg/L
4.2	Acute Toxicity to Aquatic Invertebrates e.g. Daphnia	<i>Daphnia magna</i> <i>Daphnia magna</i> <i>Daphnia magna</i> <i>Daphnia hyaline</i> <i>Ceriodaphnia</i> sp. <i>Cyclops abyssorum prealiinus</i> <i>Eudiaptomus padanus padanus</i> <i>Nitocra spinipes</i> <i>Tubifex tubifex</i> <i>Caenorhabditis elegans</i>	OECD TG 202 EPA/600/4-90/027, EPA/600/6-91/003 EPA/600/4-90/027, EPA/600/6-91/003	EC ₅₀ (48 hr) = 2400 mg/L (immobilization) LC ₅₀ (48 hr) = 2770 mg/L EC ₅₀ (48 hr) = 1062 mg/L (immobilization) LC ₅₀ (48 hr) = 1285 mg/L LC ₅₀ (48 hr) = 8300 mg/L LC ₅₀ (48 hr) = 1830 mg/L LC ₅₀ (48 hr) = 19400 mg/L LC ₅₀ (48 hr) = 11100 mg/L LC ₅₀ (96 hr) = 1600 mg/L EC ₅₀ (96 hr) = 780 mg/L (immobilization) LC ₅₀ (24 hr) = 44400 mg/L
4.3	Toxicity to Aquatic Plants e.g. Algae	<i>Selenastrum capricornutum</i>	OECD TG 201	EC ₅₀ (72 hr) = 2900 mg/L (biomass) EC ₂₀ (72 hr) = 1000 mg/L (biomass) EC ₅₀ (72 hr) = >4000 mg/L (growth rate) EC ₂₀ (72 hr) = 2700 mg/L (growth rate)
4.5.2	Chronic Toxicity to Aquatic Invertebrates (Daphnia)	<i>Daphnia magna</i>		EC ₁₆ (21 d) = 320 mg/L (reproduction) EC ₅₀ (21 d) = 610 mg/L (reproduction) LC ₅₀ (21 d) = 920 mg/L
4.6.1	Toxicity to Soil Dwelling Organisms			No reliable data available
4.6.2	Toxicity to Terrestrial Plants			No reliable data available

CAS NO: 10043-52-4		SPECIES	PROTOCOL	RESULTS
(4.6.3)	Toxicity to Other Non-Mammalian Terrestrial Species (Including Birds)			No data available
TOXICOLOGY				
5.1.1	Acute Oral Toxicity	Mouse Rat Rabbit	Other Other Equivalent to OECD TG 401	LD ₅₀ = 2045 mg/kg (male), 1940 mg/kg (female) LD ₅₀ = 3798 mg/kg (male), 4179 mg/kg (female) LD ₅₀ = 500-1000 mg/kg
5.1.2	Acute Inhalation Toxicity			No reliable data available
5.1.3	Acute Dermal Toxicity	Rabbit	Other	LD ₅₀ > 5000 mg/kg
5.2.1	Skin Irritation	Rabbit Rabbit	OECD TG 404 Other	Not/slightly irritating Irritating
5.2.2	Eye Irritation	Rabbit Rabbit	OECD TG 405 Other	Irritating Irritating
5.3	Skin Sensitization			No reliable data available
5.4	Repeated Dose Toxicity			No reliable data available
5.5	Genetic Toxicity In Vitro			
A.	Bacterial Test (Gene mutation)	<i>S. typhimurium</i>	Other	Negative (With metabolic activation) Negative (Without metabolic activation)
B.	Non-Bacterial In Vitro Test (Chromosomal aberrations)	CHL cells	Other	Negative (Without metabolic activation)
5.6	Genetic Toxicity In Vivo			No data available
5.7	Carcinogenicity			No data available
5.8	Toxicity to Reproduction			No data available
5.9	Developmental Toxicity/ Teratogenicity	Mouse	Other	NOEL Maternal toxicity: > 189 mg/kg bw/day NOEL Teratogenicity: > 189 mg/kg bw/day
		Rat	Other	NOEL Maternal toxicity: > 176 mg/kg bw/day NOEL Teratogenicity: > 176 mg/kg bw/day

CAS NO: 10043-52-4		SPECIES	PROTOCOL	RESULTS
		Rabbit	Other	NOEL Maternal toxicity: > 169 mg/kg bw/day NOEL Teratogenicity: > 169 mg/kg bw/day
5.11	Experience with Human Exposure			Case reports available

SIDS Initial Assessment Report

1 IDENTITY

1.1 Identification of the Substance

CAS Number: 10043-52-4
IUPAC Name: Calcium chloride
Molecular Formula: CaCl_2
Molecular Weight: 110.99
Synonyms: Bovikalc
Calcium dichloride
Calcium (2+) chlorid
Calol
Calcosan
Calplus
Caltac
Calzina oral
Caso
Daraccel
Dowflake
EXPRESS
Liquidow
Peladow
Snomelt
Stopit
Superflake anhydrous
Uramine MC

1.2 Purity/Impurities/Additives

Purity: > 94%
Impurities: Sodium chloride
Calcium dihydroxide
Sulfates
Potassium chloride
Magnesium chloride
Additives: None

1.3 Physico-Chemical properties

Table 1-1. Relevant chemicals.

Name	CAS No.	Molecular Formula	Molecular Weight
Calcium chloride monohydrate	22691-02-7	CaCl ₂ .H ₂ O	129.00
Calcium chloride dihydrate	10035-04-8	CaCl ₂ .2H ₂ O	147.01
Calcium chloride tetrahydrate	25094-02-4	CaCl ₂ .4H ₂ O	183.04
Calcium chloride hexahydrate	7774-34-7	CaCl ₂ .6H ₂ O	219.08

Table 1-2. Physical and chemical properties of calcium chloride (Anhydrous).

Items	Protocols	Results	Reference
Melting Point	Unknown	772°C	[1, 2, 3]
Boiling Point	Unknown	>1600°C	[1]
Density	Unknown	2.16 g/cm ³ (25°C)	[2]
Vapour pressure		Negligible	
Water Solubility	Unknown	745 g/L (20°C)	[4]

Calcium chloride is a white and odourless inorganic salt that forms hydrates as described in *Table 1-1*. Calcium chloride has hygroscopic and deliquescent properties and is readily dissociated into calcium and chloride ions in water. Calcium chloride's vapour pressure is negligible because the substance is an inorganic solid with a high melting point.

2 GENERAL INFORMATION ON EXPOSURE

2.1 Production Volumes and Use Pattern

Estimated national production

The production capacity of calcium chloride in North America was reported in March, 2002, to be approximately 1,687,000 tonnes per year [5]. In Japan, the production volume was estimated to be 245,000 tonnes in 2000 [6]. The total amount used in Western Europe including Scandinavia is around 300,000 tonnes per year [7].

Calcium chloride is produced in a closed system by refining natural brine, by the ammonia soda process as a by-product or by the neutralization reaction of limestone with hydrochloric acid. Commercial products are supplied as flakes, pebbles, pellets, powders and solutions with varying concentrations [8].

Use categories and/or functions

The main uses of calcium chloride are as follows [5,8].

- as deicing agents (deicers)
- for road stabilization and dust control
- for industrial processing
- (additive in plastics, for calcium salt production, drainage aid for wastewater treatment etc.)

- as accelerator in concrete
- for oil and gas well fluids
- Miscellaneous
- (Tire ballast, additive in fire extinguishers, admixture with starch paste, additive to control scaffolding in blast furnaces, desiccant, brine, food processing agent (e.g. coagulating agent), food additives, medication, additives in herbicide, pH regulating agent and laboratory chemicals)

Percentages of the uses are different among member countries and may vary from year to year. The percentages of the uses in North America are reported to be 22% for deicing, 20% for road stabilization and dust control, 20% for industrial processing, 17% for oil and gas well fluids, and 12% for concrete [6]. In Japan, about 50% of the total production is used for deicing and 25% for road stabilization.

Source of exposure

Calcium chloride and its dissociated form (calcium and chloride ions) are ubiquitous in the environment. Calcium and chloride ions can also be found as constituents in organisms.

As for the human exposure, oral intake is expected via foods that contain calcium chloride in the dissociated form as food additives or as residues of food processing agents. Skin contact and dust inhalation may also occur at working places or elsewhere via versatile uses such as road stabilizers.

The release of calcium chloride into the environment is mainly attributed to the use as deicing agents and road stabilizers, which occupies almost half volume of total calcium chloride consumed. Canadian Assessment of Road Salts under the Canadian Environment Protection Act (CEPA) reported that approximately 5 million tonnes of road salts including sodium chloride (95%), calcium chloride (2%), magnesium chloride, potassium chloride and ferrocyanide salts were consumed in the 1997-1998 winter season and that the wide use of chloride salts as road salts could cause the increase in chloride concentration in the environment [9]. It should be pointed out, however, that the major source of chloride released into the environment is sodium chloride although calcium chloride is one of the sources.

2.2 Environmental Exposure and Fate

Calcium chloride is soluble in water and its vapour pressure is negligible. This fact indicates that calcium chloride released into the environment is distributed into the water compartment in the form of calcium and chloride ions. Calcium chloride is not expected to be absorbed in soil due to its dissociation properties and high water solubility but may rather behave as free ions or may form stable inorganic or organic salts with other counter ions, leading to different fates between calcium and chloride ions in soil and water compartments in the environment. As for the behaviour of calcium in soil, the calcium ion may bind to soil particulate or may form stable inorganic salts with sulphate and carbonate ions. The chloride ion is mobile in soil and eventually drains into surface water because it is readily dissolved in water.

Calcium chloride is not expected to undergo photolysis or biodegradation. The Fugacity model is not applied to estimate the distribution of this substance in the environment because the programs are designed for organic chemicals and not for inorganic salts. Considering its dissociation properties, calcium chloride *per se* is not expected to accumulate in living organisms.

Monitoring data

Calcium is the most common cation found in surface water. At the global scale, the levels of natural calcium ion have been reported in the ranges of 0.06-210 mg/L in streams (<100 km²) and of 2-50 mg/L in major rivers (>100,000 km²) [10]. However, there are several other important factors that influence the calcium levels in surface water, for example, geological parameters, weathering and human activities. UNEP reported in 1995 that the global water quality monitoring was conducted in North America, South-America, Asia, Africa, Europe and Oceania. The mean, 10th-percentile and 90th-percentile of calcium concentrations in 76 rivers were 37.4, 5.1 and 86.5 mg/L, respectively [10].

As for the concentrations of chloride, they are tightly related to the geological parameters, weathering and human activities as well as calcium. The global monitoring in the same report revealed that the mean, 10th-percentile and 90th-percentile of concentrations of chloride in 77 rivers were 41.1, 1.1 and 64.8 mg/L, respectively [10].

Summary

Calcium chloride has a low vapour pressure and is readily dissociated into calcium and chloride ions in water. Calcium chloride released into the environment is thus likely to be distributed into the water compartment in the form of calcium and chloride ions. Otherwise, calcium ions may remain in the soil compartment by binding to soil particulate or by forming stable salts with other counter ions. On the other hand, the chloride ion is mobile and eventually drains into surface water. Almost half of the volume of calcium chloride is consumed as deicing agents and road stabilizers in the environment, where the substance is dissociated into calcium and chloride ions. Both ions originally exist in nature, and thus their concentrations in surface water will depend on various factors, such as geological parameters, weathering and human activities.

2.3 Human Exposure

2.3.1 Occupational Exposure

Workers are exposed to calcium chloride via dust inhalation and dermal routes at the various sites.

Dust can be formed from powdery products of calcium chloride or by smashing the flakes, pebbles and pellets of the substance. Occupational exposure limit (OEL) for calcium chloride of 5 mg/m³ has been established by the Ministry of Labour, Ontario, Canada [11]. Assuming 100% absorption of calcium chloride in the respiratory tracts, the maximum intake of calcium chloride via dust inhalation under the OEL concentration is 50 mg/day (breathing rate at 1.25 m³/h, 8-hour work/day).

There would be a potential of skin contact at packing, unpacking and use. Although the absorption of calcium chloride is not expected based on its physico-chemical properties, the use of personal protection equipments (mask, safety glasses and gloves) is recommended because calcium chloride could irritate skin and mucosa, and cause dermatitis or burns in human (see 3.1.3 and 3.1.9.1).

2.3.2 Consumer Exposure

Consumers are orally exposed to calcium and chloride via foods and medications. Calcium chloride was evaluated to be a food substance of very low toxicity and thus the establishment of the acceptable daily intake (ADI) for calcium chloride has not been deemed necessary by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) [12, 13]. The substance has also been considered as generally recognized as safe (GRAS) substance by the U.S. Food and Drug

Administration (USFDA). The average intake of calcium chloride as food additives has been estimated to be 160-345 mg/day for individuals [14].

The substance is available to consumers for versatile uses as road stabilizers, deicing agents and condensation traps. Thus there is potential for consumer exposure via dust inhalation and skin contact.

2.3.3 Indirect Exposure via Environment

Calcium chloride or its dissociated forms (calcium and chloride ions) are commonly found in drinking water and foods. In addition, the substance is released into the environment as deicing agents, road salts, and so on. Thus, indirect exposure in man to the substance via the environment occurs through drinking surface water or food consumption.

3 HUMAN HEALTH HAZARDS

3.1 Effects on Human Health

3.1.1 Toxicokinetics, Metabolism and Distribution

Calcium chloride is easily dissociated into calcium and chloride ions in water. The absorption, the distribution and the excretion of the ions in animals are regulated separately. Calcium chloride exerts its irritating property to tissues directly in contact with the compound. Once calcium chloride is taken up, the effect of the substance on animals should be attributed to the effect of calcium ions, the effect of chloride ions, or both.

The homeostasis and mechanisms of action of calcium and chloride ions are well reviewed in standard textbooks on pharmacology, physiology, biochemistry and nutritional science.

Metabolism, biotransformation and kinetics

Calcium is the most abundant inorganic constituent of all animal species and has an important role in the nutrition of animals. In adult humans, the total calcium in the body is approx. 830-1100 g. Ninety-nine percent of the calcium is retained in skeletons. Hormonal systems maintain a relatively constant calcium concentration of about 100 ug/mL in the plasma by controlling the intestinal absorption of dietary calcium, the release of calcium from bones, and renal absorption/excretion. Excess calcium is excreted in the urine via glomerular filtration. The renal tubules are able to excrete as well as reabsorb calcium. Thus the tubules are able to produce efficiently a net excretion of calcium to achieve homeostasis when abnormally high levels of calcium are ingested. A significant increase in the calcium concentration in plasma will only occur after high calcium intake in conjunction with other disorders that alter calcium homeostasis, such as renal insufficiency and primary hyperthyroidism [15, 16, 17, 18].

Chloride is the most abundant anion in all animal species. In adult humans, the total chloride in the body is approx. 70-95 g. Eighty percent of the chloride is located extracellularly. The intracellular concentration of chloride is approx. 100-140 ug/mL. The chloride concentration in plasma is maintained around 3.55-3.90 mg/mL although chloride is absorbed efficiently from the intestine. Chloride is excreted from the renal tubular lumen by active transport systems, and also by passive diffusion [15, 16].

Mechanisms of action

Calcium is indispensable for the formation and maintenance of bones and teeth, and for the regulation of various physiological functions in all animal species. These include the regulation of neural transmission and muscle contraction, coagulation of the blood, cell membrane integrity, the activity of several enzymes, and the regulation of the acid-base balance [15, 16, 17].

Chloride is important in the regulation of osmotic and acid-base balances of the body fluids. Chloride maintains electrochemical neutrality by anion exchange with bicarbonate (the chloride shift) in the CO₂ transport in the blood red cells [15, 16].

Conclusion

Calcium chloride is easily dissociated into calcium and chloride ions in water. The absorption, the distribution and the excretion of the ions in animals are regulated separately. Calcium and chloride are essential constituents of the body of all animal species. Calcium is essential for the formation of skeletons and the regulation of neural transmission, muscle contraction and coagulation of the blood. Chloride is required for regulating intracellular osmotic pressure and buffering.

3.1.2 Acute Toxicity

There are several reliable studies on acute toxicity. The results of the studies are summarized in *Table 3-1*.

Table 3-1. Acute toxicity studies.

Species, strain	Route	Substance form	Vehicle	LD ₅₀ (mg/kg bw)	Reference
Mouse, ICR-SLC	Oral	Anhydride, powder	5% Arabic gum	2045 (male), 1940 (female)	[19]
Rat, Wistar	Oral	Anhydride, powder	5% Arabic gum	3798 (male), 4179 (female)	[19]
Rabbit, N. Z. white	Oral	Anhydride, powder	Gelatin capsule	500-1000 (male)	[20]
Rabbit, N. Z. white	Oral	33% solution	Water	1000 (male)	[21]
Rabbit, N. Z. white	Oral	Dihydrate, powder	Gelatin capsule	755 (male) ^{a)}	[22]
Rabbit, N. Z. white	Oral	Hexahydrate, powder	Gelatin capsule	507 (male) ^{a)}	[23]
Rabbit, N. Z. white	Dermal	Anhydride, powder	None	>5000 (male/female)	[24]
Mouse, ICR-SLC	s.c.	Anhydride, powder	5% Arabic gum	823 (male), 867 (female)	[19]
Rat, Wistar	s.c.	Anhydride, powder	5% Arabic gum	2630 (male), 3798 (female)	[19]
Mouse, ICR-SLC	i.p.	Anhydride, powder	5% Arabic gum	382 (male), 402 (female)	[19]
Rat, Wistar	i.p.	Anhydride, powder	5% Arabic gum	264 (male), 342 (female)	[19]

^{a)} Corrected to the content of anhydrous calcium chloride.

Oral

LD₅₀ values of calcium chloride for mice and rats were determined by administering the substance orally to groups of 15 animals [19]. The LD₅₀ values were determined by the up and down method after 3-day observation period. Although necropsy was not described, the oral LD₅₀ ranged from 3798 (male) and 4179 mg/kg bw (female) in rats to 2045 (male) and 1940 mg/kg bw (female) in mice.

The studies on acute oral toxicity in male rabbits were carried out by the method similar to OECD Test Guideline 401 under GLP. Several forms of calcium chloride were administered orally by gavage to groups of 1 to 5 rabbits at doses of 250 to 2000 mg/kg bw to determine LD₅₀ values [20-23]. Weight loss in the surviving animals was observed in the first two days after dosing, which was then recovered. Gross post-mortem examination revealed perforation and severe ulceration of the

stomach in the dead animals. Old ulcers were also detected in the stomach of some of the surviving animals.

Dermal

A study on acute dermal toxicity in male/female rabbits was conducted by a scientifically accepted method [24]. No animal death was observed at the dose of 5000 mg/kg bw, indicating that the dermal LD₅₀ value for male/female rabbits is over 5000 mg/kg bw. No adverse effects were observed following treatment. No significant change was either found by gross necropsy examination except skin lesions at or near the site of administration.

Other Routes of Exposure

As previously noted for oral studies in rats and mice, LD₅₀ values of calcium chloride for mice and rats were further determined. The substance was administered to groups of 15 animals via subcutaneous and intraperitoneal routes [19]. The LD₅₀ values were determined by the up and down method after 3-day observation period. Necropsy results were not described. The LD₅₀ values for subcutaneous administration ranged from 823 (male) and 867 mg/kg bw (female) in mice to 2630 (male) and 3798 mg/kg bw (female) in rats. The values for intraperitoneal administration ranged from 382 (male) and 402 mg/kg bw (female) in mice to 264 (male) and 342 (female) in rats. The values for subcutaneous administration were lower than those for oral gavage and the values for intraperitoneal administration were lower than those for subcutaneous administration probably because the toxicity was due to the irritating nature of the substance.

Inhalation

An acute inhalation toxicity study in rats has been reported [25]. The reliability of this study is insufficient, due to the lack of adequate information on the method used. In this study, the animals were exposed to 40 and 160 mg/m³ CaCl₂ for 4h. No animal death was caused by the exposure, while several signs of irritation of trachea were observed in the animals.

Conclusion

The toxicity data available are considered sufficient on this endpoint. The oral LD₅₀ values were 2045 (male) and 1940 mg/kg bw (female) in mice, 3798 (male) and 4179 mg/kg bw (female) in rats and 500-1000 mg/kg bw in rabbits. The dermal LD₅₀ value in rabbits was over 5000 mg/kg bw.

3.1.3 Irritation

There are several studies on irritation/corrosiveness of calcium chloride with sufficient reliability.

Skin Irritation

Irritation/corrosiveness of calcium chloride to skin of rabbits was tested under OECD Test Guideline 404 [26, 27, 28, 29] or under national guidelines [24, 30, 31]. No or slight irritation to skin of the animals was observed in the exposure for 4 h to either one of anhydride powder, 33% solution, dihydrate powder, or hexahydrate powder [27, 28, 29, 30]. On the other hand, exposure to anhydride powder, dihydrate powder and 38% solution for 24 h caused slight to moderate irritation on intact skin of rabbits [24, 30, 31]. In addition, application of these samples on abraded skin of the animals caused much severer irritation [30, 31].

Eye Irritation

Irritation of calcium chloride to eyes of rabbits was tested under OECD Test Guideline 405 [32, 33, 34, 35] or under a national guideline [30, 31]. Severe irritation to eyes of the animals was observed

in either form of calcium chloride (anhydride, dihydrate, tetrahydrate and hexahydrate powders, and 33% and 38% solutions).

According to the EU's list of dangerous substances (OJEC No L 355 30.12.98), calcium chloride requires a label, R36 (irritating to eyes), which is consistent to the data obtained.

Conclusion

The toxicity data available are considered sufficient on irritation/corrosiveness. Calcium chloride is not/slightly irritating to skin but severely irritating to eyes of rabbits under OECD test guidelines. Prolonged exposure and application of moistened material or concentrated solutions resulted in considerable skin irritation, however.

3.1.4 Sensitisation

There is no reliable data available for sensitization of calcium chloride.

3.1.5 Repeated Dose Toxicity

Studies in Animals

No study on repeated dose toxicity has been carried out according to national or international guideline under GLP. Several studies for oral repeated dose toxicity in rats and rabbits have been reported. One feed study in rats [36] was considered relevant to note for repeated dose toxicity although the results presented in the study were limited. The other studies, on the other hand, were considered irrelevant to note because of the inappropriate test conditions used (gavage at the doses near or over the oral LD₅₀ values) and/or the lack of autopsy examination.

A group of twenty 40-day-old rats were fed on 20 mg CaCl₂/g diet for 12 months [36]. No difference in mortality, weight gain, or daily food consumption was observed between the test and the control groups. In addition, no neoplastic lesions were observed in gastrointestinal tract, urinary tract, liver, heart, brain or spleen of the animals. From the food consumption (22 g diet/day), the daily intake of calcium chloride was estimated to be 440 mg. Considering that 1 mg/g diet is equivalent to 100 and 50 mg/kg bw/day for young and old rats, respectively [37], the dose used in this study (20 mg CaCl₂/g diet) corresponds to 1000 to 2000 mg/kg bw/day.

There is no reliable data available for the repeated dose toxicity of calcium chloride via inhalation or dermal route.

Studies in Humans

Calcium and chloride are both essential nutrients for humans as well as other animal species. As for healthy humans, the tolerable upper intake level for calcium is set at 2500 mg per day (equivalent to 6.9 g CaCl₂ per day) [18] and the reference nutrient intake for chloride at 2500 mg/day (equivalent to 3.9 g CaCl₂ per day) [38]. The estimated intake of calcium chloride as food additives (160-345 mg/day, see **Sect. 2.3.2**) is considerably smaller than these values. Consistent with this, the establishment of the ADI for calcium chloride has not been deemed necessary by JECFA [12, 13]. The substance has also been considered a GRAS substance by USFDA [14]. It is thus very unlikely that calcium chloride taken orally as food additives adversely affects human health.

Calcium chloride is a non-volatile and hydrophilic substance, indicating that potential for its absorption via inhalation and dermal routes is low. Even when the substance is absorbed, the plasma concentrations of calcium and chloride ions are efficiently regulated by the hormonal systems and excess ions are rapidly excreted in the urine via glomerular filtration. Based on an estimated worst-

case scenario for occupational exposure, the maximum intake of calcium chloride from the working atmosphere is 50 mg/day (see **Sect. 2.3.1**). This value is considerably smaller than the tolerable upper intake level for calcium and the dietary reference value for chloride. It is not predicted that occupational exposure to this substance causes an adverse effect on human health.

Collectively, the information available is sufficient and no further study is considered necessary for this endpoint.

Conclusion

There is one study for repeated dose oral toxicity in rats although the data presented in the study is not sufficient. The study shows no adverse effect of calcium chloride on rats fed 20 mg CaCl₂/g diet (comparable to 1000 mg/kg bw/day or more) for 12 months.

3.1.6 Mutagenicity

Data on genetic toxicity of calcium chloride has been obtained from *in vitro* studies, while no *in vivo* study has yet been available. The reliability of the *in vitro* studies reported and the results obtained from the studies are considered sufficient for this endpoint.

Bacterial mutation tests

Two studies were carried out by the method similar to OECD Test Guideline 471. In a *Salmonella* mutation test, using TA92, TA94, TA98, TA100, TA1535 and TA1537, doses of calcium chloride up to 5 mg/plate were examined with metabolic activation [39]. In another *Salmonella* mutation test, using TA97 and TA102, doses up to 10 mg/plate were examined with or without metabolic activation [40]. No significant increases in mutation frequencies were observed in either study.

Two genetic toxicity studies with bacteria have further been reported although the studies are not OECD guideline studies. In a *Bacillus subtilis* mutagenicity assay the potential of calcium chloride to damage cellular DNA was examined at concentrations up to 0.5 M [41]. The result of the test was negative. In an *Escherichia coli* test the potential to induce an SOS response was tested at doses up to 1 mM, also giving a negative result [42].

Chromosome aberration test

An *in vitro* chromosome aberration test in Chinese hamster lung cells (CHL) has been reported [39]. The test was scientifically acceptable. The CHL cells were exposed to calcium chloride at doses up to 4 mg/mL for 48 hr without metabolic activation. No significant increase in polyploid formation or structural chromosome aberration was observed. The highest dose in the study was determined by the dose needed for 50% cell-growth inhibition.

Conclusion

Genetic toxicity of calcium chloride was negative in the bacterial mutation tests and the mammalian chromosome aberration test.

3.1.7 Carcinogenicity

There is no data available for carcinogenicity of calcium chloride.

3.1.8 Toxicity for Reproduction and Developmental Toxicity

No study on toxicity to reproduction has yet been reported. Thus the potential of reproductive toxicity of calcium chloride has thereby not been addressed according to the OECD requirement.

However, calcium and chloride are both essential constituents for all animals and are ingested daily. As mentioned above (see 3.1.5), any toxic effect of calcium chloride on mammalian reproduction is not predicted as far as ordinary consumer and occupational exposures are concerned. No further study is considered necessary for this endpoint.

There is one study on developmental toxicity with sufficient reliability. The method used in the study was equivalent to OECD Test Guideline 414 although the study was conducted before the establishment of the guideline. The developmental toxicity study examined the effect of calcium chloride on embryo lethality and teratogenicity in mice, rats and rabbits [43]. The test conditions used in the experiments are summarized in *Table 3-2*.

Table 3-2. Test conditions of developmental toxicity tests in mice, rats and rabbits.

Species, strain	No. of animals per group	Vehicle	Doses (mg/kg/day)	Administration (days of gestation)	Caesarian section (day of gestation)
Mouse, CD-1	25	Water	1.89, 8.78, 40.8, 189	6-15	17
Rat, Wistar	25	Water	1.76, 8.18, 38.0, 176	6-15	20
Rabbit, Dutch	16-22	Water	1.69, 7.85, 35.6, 169	6-18	29

In each experiment, the number of animals, dose levels and exposure time conformed to the guideline requirement. In addition, positive and negative controls were both included in each experiment. All animals were observed daily for appearance, body weight and behaviour with particular attention to food consumption. The numbers of implantation sites, resorption sites, and live and dead fetuses were recorded when all dams were subjected to Caesarean section. All fetuses were examined grossly for the presence of external congenital abnormalities. One-third of the fetuses of each litter underwent detailed visceral examinations. The remaining two-thirds were examined for skeletal defects. The administration of calcium chloride had no clearly discernible effect on implantation or on maternal or fetal survival. The number of abnormalities seen in either soft or skeletal tissues of the test groups did not differ from the number occurring spontaneously in the sham-treated controls. These facts reveal no toxic effects on dams or fetuses at doses up to 189 mg/kg bw/day (mouse), 176 mg/kg bw/day (rat) and 169 mg/kg bw/day (rabbit).

Conclusion

No study on reproductive toxicity has been reported. On the other hand, developmental toxicity data with sufficient reliability have been obtained, showing no toxic effects on dams or fetuses at doses up to 189 mg/kg bw/day (mouse), 176 mg/kg bw/day (rat) and 169 mg/kg bw/day (rabbit).

3.1.9 Experience with Human Exposure

There are several human data based on accidents caused by clinical uses of calcium chloride or by incidental exposures to the substance.

Oral route

There are three cases of gastrointestinal lesions due to calcium chloride administered by gavage to newborn babies for the treatment of tetany [44] although the substance is no longer being used for the treatment. In two of the cases, single doses of 3-4 g of the substance in water (16-17%) caused severe ulceration and necrosis of the mucosa and submucosa of gastrointestinal tracts, resulting in death. In the other case, a baby given twice 2 g of the substance in water also showed signs of gastrointestinal lesion but later recovered. Overall, the lesions observed in the cases are consistent to those noted for the acute oral toxicity in rabbits (see 3.1.2).

Dermal route

There are a couple of reports on skin injuries as a result of incidental contact with calcium chloride: skin injuries of thighs of boys exposed to calcium chloride powder put into pockets of pants; and those of forearms of a man who carried bags of the substance [45, 46]. As occupational cases, there are reports on skin injuries of workers exposed to dripping water in a coal mine containing calcium chloride, skin injury of a worker exposed to 40% solution of the substance used for spraying the roadway of mines and skin injury of a worker of an oil plant spending a day loading the substance into containers [47, 48, 49]. In these cases, lesions such as necroses, ulceration and calcinosis of the contact area of the skin have been observed. It has been suggested that dehydration by high-concentration solutions of calcium chloride may be the mechanism of injury [49].

Other route

Calcium chloride has been used for medical treatment of hypocalcemic tetany, calcium deficit in citrated blood, serum sickness after injection of antitoxins and antisera, and allergic diseases such as hay fever, urticaria and asthma. As an electrolyte replenisher calcium chloride is a pharmaceutical necessity for Ringer's solutions [50]. There is a report that intravenous infusions of 1 g of CaCl_2 in 100mL of normal saline administered over 1 hr to a patient with hypoparathyroidism caused extravasation of calcium chloride into the surrounding tissue along the flexural aspect of the left forearm, resulting in edema, warmth, and tenderness [51].

Conclusion:

Severe irritating effect of calcium chloride on gastrointestinal tracts of human babies was observed at 3-4 g, which was administered by gavage for the treatment of tetany. Irritating effect of the substance was also observed in human skin injuries caused by the incidental contact with the substance or its high-concentration solutions.

3.2 Initial Assessment for Human Health

Calcium chloride is easily dissociated into calcium and chloride ions in water. The absorption, the distribution and the excretion of the ions in animals are regulated separately. Once calcium chloride is taken up, the effect of the substance on animals should be attributed to the effect of calcium, the effect of chloride, or both.

Calcium and chloride ions are essential constituents of all animals. Absorption, transport, distribution, excretion, and the homeostatic regulation of calcium and chloride ions in animals are well established, as are the mechanisms of action. Calcium is essential for the formation and maintenance of bones and teeth, and for the regulation of various physiological functions such as neural transmission and muscle contraction. Chloride is also essential for the regulation of acid-base balance of the body and intracellular osmotic pressure and acid-base buffering.

The toxicity data available are considered sufficient on acute toxicity. The oral LD_{50} values were 2045 (male) and 1940 mg/kg bw (female) in mice, 3798 (male) and 4179 mg/kg bw (female) in rats and 500-1000 mg/kg bw in male rabbits. Acute oral toxicity of the substance is attributed to the severe irritating property of the original compound or its high-concentration solutions to the gastrointestinal tract, causing perforation and ulceration of the contact area of the tract. Similar toxic effect of calcium chloride on human newborn babies was observed at 3-4 g administered by gavage for the treatment of tetany. In humans, however, acute oral toxicity is rare because large single doses induce nausea and vomiting. The dermal LD_{50} value in male/female rabbits was over 5000 mg/kg bw. No significant change was found by gross necropsy examination except skin lesions at or near the site of administration. Hypercalcemia may occur only when there exist other factors that alter calcium homeostasis, such as renal inefficiency and primary hyperthyroidism.

The toxicity data available are considered sufficient on irritation/corrosiveness. Calcium chloride is not/slightly irritating to skin but severely irritating to eyes of rabbits under OECD test guidelines. Prolonged exposure and application of moistened material or concentrated solutions resulted in considerable skin irritation, however. In addition, much severe effects were noticed on abraded skin. Irritating effect of the substance has also been observed in human skin injuries caused by the incidental contact with the substance or its high-concentration solutions.

The limited oral repeated dose study shows no adverse effect of calcium chloride on rats fed on 20 mg CaCl_2/g diet (comparable to 1000 to 2000 mg/kg bw/day) for 12 months. Calcium and chloride ions are both essential nutrients for humans and daily intake more than 1000 mg each of the ions is recommended. Considering the intake profile of calcium chloride as foods and food additives with no limitation for ADI established by JECFA and the well-established metabolism and mechanisms of action of the ions in the human body, no further study is considered necessary for this endpoint.

In vitro studies for genetic toxicity with sufficient reliability have been reported. Genetic toxicity of calcium chloride was negative in the bacterial mutation tests and the mammalian chromosome aberration test. Thus no further study is required for this endpoint.

No reproductive toxicity study has been reported. A developmental toxicity study equivalent to OECD guideline study, on the other hand, reveals no toxic effects on dams or fetuses at doses up to 189 mg/kg/day (mice), 176 mg/kg/day (rats) and 169 mg/kg/day (rabbits). In view of the nutritional aspects, the metabolism, the mechanisms of action of calcium and chloride, however, the information available is sufficient and no further study is considered necessary for these endpoints.

4 HAZARDS TO THE ENVIRONMENT

4.1 Aquatic Effects

The aquatic toxicity of calcium chloride is summarized in *Table 4-1*. Each toxicity value was shown as anhydrous calcium chloride concentration. For some of the tests, calcium chloride is included as part of the standard test media. The descriptions of the toxic concentrations refer to the effect of additional calcium chloride added to the system, not to the total concentration of calcium and chloride ions present.

4.1.1 Toxicity to Aquatic Plants / Algae

There is one study with fresh water algae, *Selenastrum capricornutum*, which was conducted according to OECD guideline 201. The 72-hour EC_{50} and EC_{20} obtained on the basis of biomass from the study were 2900 and 1000 mg/L, respectively [52].

4.1.2 Toxicity to Invertebrates

There are seven acute toxicity data available for Cladocera. Two of them were conducted according to international or national guidelines, giving the 48-hour EC_{50} of 2400 mg/L for *Daphnia magna* [53] and the 48-hour LC_{50} of 1830 mg/L for *Ceriodaphnia* sp. [54]. The lowest 48-hour EC_{50} was 1062 mg/L for *Daphnia magna* [56].

The acute toxicity studies with other invertebrates showed LC_{50} or EC_{50} values in the range of 780-44400 mg/L. These studies were not conducted according to standard guidelines, but the test conditions were fully described and these data are acceptable.

The chronic effect of 21-day exposure on reproduction of *Daphnia magna* has been investigated as a long-term study. The methods and test conditions used in the study are fully described, and appear to be scientifically acceptable, although the study was conducted prior to the acceptance of standard guidelines for this type of study.

The concentration required for 16% and 50% inhibition of reproduction (EC₁₆ and EC₅₀) was 320 and 610 mg/L, respectively [56].

4.1.3 Toxicity to Fish

Several studies on acute toxicity to fish have been reported. Among them the study with fathead minnow (*Pimephales promelas*) conducted under EPA guideline showed the lowest 96-hour LC₅₀ value of 4630 mg/L [54].

No chronic toxicity studies on fish conducted under standard guidelines have been reported.

4.1.4 Toxicity to Aquatic Microorganisms

No toxicity data on aquatic microorganisms are available.

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

Species	Age/Size	Stat/ Flow	Temp (°C)	Dissolved oxygen (mg/L)	Hardness (mg CaCO ₃ /L)	pH	Endpoint	Concentration (mg/L)	Test method	Reference
Algae /plants										
<i>Selenastrum capricornutum</i> *	1x10 ⁴ cells/mL	Static	22.2- 22.4			7.5-8.5	72h EC ₅₀ 72h EC ₂₀ biomass 72h EC ₅₀ 72h EC ₂₀ growth rate	2900 1000 >4000 2700	OECD 201 GLP	[52]
Invertebrates										
<i>Daphnia magna</i>	0-24 h old	Static	19.8- 20.0	8.4-8.7		7.6-8.3	48h EC ₅₀ , immobilization	2400	OECD 202 GLP	[53]
	< 24 h old	Static	20	>40% of saturation		7.5-9.0	48h LC ₅₀	2770	EPA/600/4- 90/027, EPA/600/6- 91/003	[54]
		Static	11.5- 14.5	5.2-6.5	235-260	7.2-7.8	48h EC ₅₀ , immobilization	1062		[55]
	< 24 h old	Static	18±1		44.0-53.0	7.4-8.2	48h LC ₅₀	1285		[56]
	< 24 h old	Semi- static	18±1		44.0-53.0	7.4-8.2	21d LC ₅₀ 21d EC ₅₀ 21d EC ₁₆ , reproduction	920 610 320		
<i>Daphnia hyalina</i>	Adult, 1.27mm	Static	9.5- 10.5				48h LC ₅₀	8300		[57]
<i>Ceriodaphnia</i> sp.	< 24 h old	Static	20	>40% of saturation		7.5-9.0	48h LC ₅₀	1830	EPA/600/4- 90/027, EPA/600/6- 91/003	[54]

*now *Pseudokirchneriella subcapitata*

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

Species	Age/Size	Stat/ Flow	Temp (°C)	Dissolved oxygen (mg/L)	Hardness (mg CaCO ₃ /L)	pH	Endpoint	Concentration (mg/L)	Test method	Reference
Other invertebrates										
<i>Cyclops abyssorum prealiinus</i>	Adult, 0.62mm	Static	9.5-10.5				48h LC ₅₀	19400		[57]
<i>Eudiaptomus padanus padanus</i>	Adult, 0.43mm	Static	9.5-10.5				48h LC ₅₀	11100		[57]
<i>Nitocra spinipes</i>	Adult 0.7-0.8 mm	Static	20±0.5		Salinity (‰); 7		96h LC ₅₀	1600		[58]
<i>Tubifex tubifex</i>		Semi-static	29.5-31	5.2-6.0	230-250	7.5-7.7	96h EC ₅₀ Immobilization	780		[59]
<i>Caenorhabditis elegans</i>	Wild type (N2)	Static	20				24h LC ₅₀	44400		[60]
Fish										
<i>Pimephales promelas</i> Fathead minnow	1-7 d old	Static	25	>40% of saturation		7.5-9.0	96 hr LC ₅₀	4630	EPA/600/4-90/027, EPA/600/6-91/003	[54]
<i>Lepomis macrochirus</i> Bruegill	Small (3.88 cm, 0.96g), Medium (6.09 cm, 2.80g), Large (14.24 cm, 54.26g)	Static	20±1	5-9ppm			96 hr LC ₅₀	9500 (small) 9500 (medium) 11300 (large)		[61]
	5-9cm, 1-9g	Static	19-21		6314-11900	7.19-7.80	96 hr LC ₅₀	10650		[62]
<i>Gambusia affinis</i> Mosquitofish	Adult female	Static	20-23	7		6.8-7.6	96 hr LC ₅₀	13400		[63]

4.2 Terrestrial Effects

The data on effects to terrestrial plants and animals seem to be the useful information to assess the impact of calcium chloride to the environment as well as the biological functions or roles of calcium and chloride.

4.2.1 Toxicity to Soil Dwelling Organism and Terrestrial Plants

The results of toxicity to soil dwelling organism and terrestrial plants are summarized in *Table 4-2*.

Table 4-2. Summary of toxicity to soil dwelling organism and terrestrial plants.

Species	Test methods	Results	Reference
Earthworm			
<i>Eisenia foetida</i>	Laboratory soil test, Application of 5 g/m ² CaCl ₂ every week for 6 weeks	Cumulative mortality; 20%	[64]
Plants			
Rice, Wheat, Beer wheat, Rapeseed, Japanese radish, Welsh onion	Seed germination and growth test, Temp; 28-30°C Exposure conc.; 1-5 g/L Test period; 3-5 days	Tolerance limit for germination and growth; 2-3 g/L	[65]
White birch, Acacia, Poplar, Todo fir	Four tree seedlings were treated in CaCl ₂ solutions (0.250-25 g/L) for 60-100 days.	Tolerance conc; 1 g/L for white birch 5 g/L for acacia 2.5 g/L for poplar 0.5 g/L for todo firs	[66]
<i>Trifolium repens</i> L.	Test in flowerpot; application for 35 days	Survival rate; 28.6% at total dose of 750 g/ m ² 85.7% at 187.5 g/m ²	[67]
<i>Taxus cuspidata</i> Pinus mugo <i>Trifolium repens</i> L.	Spraying CaCl ₂ (5-100 g/m ²) on seedlings at weekly intervals for 15 weeks in the winter season.	EC ₅₀ on damage to leaves; 5-25 g/m ² for <i>T.cuspidata</i> and <i>P. mugo</i> 50-100 g/m ² for <i>T. repens</i> L.	[64]
<i>Salix sachalinensis</i>	Scions were treated in CaCl ₂ solutions (5-100 g/m ²) for 11 days.	EC ₁₀₀ on damage to leaves and root; < 5 g/m ²	[64]
<i>Taxus cuspidata</i> <i>Trifolium repens</i> L.	Spraying CaCl ₂ (0.25-25.0 g/m ²) on seedlings at weekly intervals for 15 weeks in the winter season.	EC ₅₀ as accumulated application; 18.75-37.5 g/m ² with <i>T.</i> <i>cuspidata</i> 37.5-375 g/m ² with <i>T. repens</i> L.	[68]

There are some studies that examined effects of deicing agents to plants and earthworm using calcium chloride, sodium chloride, CMA (calcium/magnesium acetate), urea and so on. Although these studies were not conducted under the standard methods and were not necessarily providing

reliable outcomes, they revealed a tendency to less damage to plants and earthworm from exposure to calcium chloride than to other deicing agents [64, 67, 68].

Damage to roadside vegetation has been reported and is attributed largely to the absorption of salt splashed foliage. Sugar maples (*Acer saccharum*) were exposed to runoff of sodium chloride and calcium chloride for 6 winters (total treatment of 112 tones /ha per treatment and 15 treatments per winter at weekly intervals). Leaves of these maple trees contained 3 to 6 times the chloride concentration compared to a control stand. Damage to the maples varied but could be correlated with the chloride concentration in the leaf [69]. From two field experiments with spruce tree carried out for ten weeks during a winter season, and a total dose of 1.5 kg/m² NaCl, CaCl₂ or a 75/25 NaCl/CaCl₂ mixture, it was found that in the presence of calcium chloride the uptake of Cl⁻ in the root was inhibited [70].

4.2.2 Biology of Terrestrial Plants [63, 70, 71, 72]

Calcium is well known as an essential nutrient for higher plants and has important roles for cell wall formation, cell division and cell elongation. The substance is also known as one of the basic inorganic elements of algae.

Chloride is an essential micronutrient for plants and has an important role in regulating osmotic pressure of cells.

Demands for calcium and chloride in plants/crops

The calcium content of plants varies between 0.1 and > 0.5% of the dry weight depending on the growing conditions, plant species, and plant organ. In well-balanced growing nutrient solutions with controlled pH, maximal growth rates were obtained at calcium supply levels of 2.5-100 µM. Also, calcium can be supplied at higher concentrations and might reach more than 10% of the dry weight without symptoms of serious inhibition of plant growth, at least in calcicole plant species.

A typical symptom of calcium deficiency is the disintegration of cell walls and the collapse of the affected tissues, such as the petioles and upper parts of the stems. Lower calcium contents in fleshy fruits also increase the losses caused by enhanced senescence of the tissue and by fungal infections.

In plant species with relatively low chloride requirement (<1 mg Cl/g leaf dry wt) the demand for chloride can be covered by a concentration of 100 µM Cl⁻ in the nutrient solution. At the supply of 10 µM Cl⁻ the shoot dry weight drops to 50%, indicating that chloride uptake is not so efficient as phosphorus uptake, because the demand for phosphorus in the leaf, which is much higher than that for chloride, can be fulfilled by the supply at a phosphorus concentration lower than 10 µM. In most plant species the Cl⁻ requirement for optimal growth is in the range of 0.2-0.4 mg/g dry matter. The principal effect of chloride deficiency is a reduction in leaf surface area and thereby plant dry weight. With severe deficiency, curling of the young leaves followed by shrivelling and necrosis might occur.

Biological effects monitoring

High proportion of the total calcium in plant tissues is often found in the cell walls. This unique distribution is mainly due to an abundance of binding sites for calcium in the cell walls and the restricted transport of calcium into the cytoplasm.

The proportion of calcium pectate in the cell walls is of importance for the susceptibility of the tissue to fungal and bacterial infections and for the ripening of fruits. Calcium has a significant effect on reducing the toxicity of soluble organic acids in the protoplasm of many plants. A soluble organic acid such as oxalic acid combines with Ca to form the very insoluble salt, calcium oxalate,

which is not toxic to plants. Calcium has the role in counterbalancing the harmful effects of high concentrations of other cations at the plasma membrane. In the absence of an exogenous calcium supply, root extension quickly ceases. On the other hand, the reduction in plant growth under heavy salinisation is also suppressed by the supply of calcium.

Calcium competes with Na^+ for binding to the exchangeable sites in soil. Since soil clay has a higher affinity for Ca^{2+} than Na^+ , more Na^+ is likely to be leached out to lower soil layers where it will become less available for plants roots.

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

Biotransformation and kinetics

Calcium is always present in the external solution in order to fulfil its functions at the plasma membrane, where it regulates the selectivity of ion uptake and prevents solute leakage from the cytoplasm. In the apoplasm, a part of calcium ions are firmly bound to its structures. Another part of the ions are exchangeable at the cell walls and at the exterior surface of the plasma membrane. A high proportion of intracellular calcium might be sequestered in vacuoles whereas the concentration in the cytosol is extremely low. The same is true for the mobility of calcium in the symplasm from cell to cell and in the phloem. Most of the functions of calcium as a structural component of macromolecules are related to its capacity for coordination, by which it provides stable but reversible intermolecular linkages, predominantly in the cell walls and at the plasma membrane.

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

4.3 Initial Assessment for the Environment

Acute toxicity studies with algae, invertebrates including *Daphnia*, and fishes have been reported. The lowest results obtained from these studies are the 72-hour EC_{50} of 2900 mg/L for *Selenastrum capricornutum*, the 48-hour EC_{50} of 1062 mg/L for *Daphnia magna*, and the 96-hour LC_{50} of 4630 mg/L for *Pimephales promelas*.

A chronic toxicity test has been performed on *Daphnia magna*. In this test a 16% impairment of reproduction (EC_{16}) was observed at the concentration of 320 mg/L. The 72-hour EC_{20} (biomass) for *Selenastrum capricornutum* was 1000 mg/L. All the data compiled on the short-term and long-term aquatic toxicity were greater than 100 mg/L, although no chronic toxicity study with fish has been reported.

Calcium is known as an essential nutrient for higher plants and one of the basic inorganic elements of algae. Calcium plays crucial roles in strengthening cell walls and plant tissues, reducing the toxicity of soluble organic acids, elongating roots, and so on. Chloride is also an essential micronutrient for plants and has important roles in the photosynthesis and osmoregulation.

The information on the effect of calcium chloride on terrestrial plants and soil dwelling organisms would be very helpful to assess the environmental effects of this substance because the substance is widely used as deicing agents on motorways during winter season, and is released into the terrestrial environment.

Deicing agents used as road salts are usually chloride salts, mainly sodium chloride or calcium chloride with minor amounts of magnesium chloride and potassium chloride. Deicing salts have been observed to accumulate in roadside vegetation and induce visible symptoms such as tipburn, browning and chlorosis of foliage. Application of road salts may also cause deleterious effects on physico-chemical properties of soil such as soil dispersion, soil permeability, soil swelling and crusting and soil osmotic potential.

The Canadian assessment report, evaluating the impact of road salts to the environment for 5 years (1995-2000) under Canadian Environment Protection Act (CEPA), has concluded that excess amount of road salts consisting of inorganic chloride salts may be harmful to the environment in Canada, and the government has decided to control the use of inorganic chloride salts for road salts and minimize the risks road salts pose to the environment while maintaining the level of roadway safety [9].

The primary cause of the damage to roadside plants is considered to be the accumulation of chloride in plant tissues to a toxic level by excess loading of inorganic chloride salts. Calcium chloride constituted 2% of the total composition (approx. 5 million tons) used in Canada as deicing agents in the 1997-1998 winter season, while sodium chloride constituted 95% of the total. Although there are several areas where calcium chloride was used at higher percentage, most of the deicing agents used in the urban areas (Ontario and Quebec) with the highest loadings in Canada are occupied by sodium chloride. The terrestrial toxicity data for calcium chloride reveal that the substance is less toxic than other road salts. In addition, there is a report that shows the uptake of chloride by plants is considerably inhibited in the presence of calcium chloride. The impact of calcium chloride on plants is expected to be minimal compared to other chloride containing agents, given the factors discussed above as well as the difference of usage of calcium chloride as compared to sodium chloride.

5 RECOMMENDATIONS

The chemical is currently of low priority for further work on the human health hazard.

The chemical is currently of low priority for further work on the hazard to the environment. However, because of the effects of calcium chloride on soil dwelling organisms and plants and the exposure associated with the use of calcium chloride as a deicing agent in some countries, these countries may decide to assess the environmental risk related to this exposure scenario.

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I U C L I D

Data Set

Existing Chemical : ID: 10043-52-4
CAS No. : 10043-52-4
EINECS Name : calcium chloride
EINECS No. : 233-140-8
TSCA Name : Calcium chloride (CaCl₂)
Molecular Formula : CaCl₂

Producer Related Part
Company : Tokuyama Corporation
Creation date : 28.11.2000

Substance Related Part
Company : Tokuyama Corporation
Creation date : 28.11.2000

Memo :

Printing date : 15.11.2002
Revision date :
Date of last Update : 15.11.2002

Number of Pages : 2

Chapter (profile) : Chapter: 1, 2, 3, 4, 5, 7
Reliability (profile) : Reliability: without reliability, 1, 2, 3, 4
Flags (profile) : Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE),
Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 OECD AND COMPANY INFORMATION

Type : cooperating company
Name : Asahi Glass Co., Ltd.
Partner :
Date :
Street : 1-12-1 Yurakucho, Chiyoda-ku
Town : 100-8405 Tokyo
Country : Japan
Phone : +81-3-3218-5471
Telefax : +81-3-3218-7847
Telex :
Cedex :
14.12.2001

Type : cooperating company
Name : Brunner Mond (UK) Ltd.
Partner :
Date :
Street : Po Box 4, Mond Mouse, Winnington
Town : CW8 4DT Northwich
Country : United Kingdom
Phone : +44-1606-724392
Telefax : +44-1606-784764
Telex :
Cedex :
13.12.2001

Type : cooperating company
Name : Central Glass Co.,Ltd.
Partner :
Date :
Street : 7-1,Kanda-Nishikicho 3-chome, Chiyoda-ku
Town : 101-0054 Tokyo
Country : Japan
Phone : +81-3-3259-7374
Telefax : +81-3-3293-2145
Telex :
Cedex :
13.12.2001

Type : cooperating company
Name : General Chemical Industrial Products Inc.
Partner :
Date :
Street : 201 City Center Drive, Suite 1100, Mississauga
Town : L5B 3A3 Ontario
Country : Canada
Phone : +1-905-566-3883
Telefax : +1-905-276-6594
Telex :
Cedex :
13.12.2001

Type : cooperating company
Name : Sanuki Kasei Co., Ltd.
Partner :
Date :

1. GENERAL INFORMATION

ID: 10043-52-4

DATE: 15.11.2002

Street : 2-4 Hama Ichiban-cho, Udazu-Cho, Ayauta-Gun
Town : 769-0201 Kagawa
Country : Japan
Phone : +81-877-49-3332
Telefax : +81-877-49-2213
Telex :
Cedex :
 13.12.2001

Type : cooperating company
Name : Solvay S.A.
Partner :
Date :
Street : Rue du Prince Albert 33
Town : 1050 Bruxelles
Country : Belgium
Phone : +32 2 2643398
Telefax : +32 2 2642990
Telex :
Cedex :
 13.12.2001

Type : cooperating company
Name : Tetra Technologies, Inc.
Partner :
Date :
Street : 25025 I-45 North, The Woodlands
Town : 77380 Texas
Country : United States
Phone : +1-281-367-1983
Telefax : +1-281-367-6471
Telex :
Cedex :
 13.12.2001

Type : cooperating company
Name : The Dow Chemical Company
Partner :
Date :
Street : 2020 Dow Center, Midland
Town : 48674 Michigan
Country : United States
Phone : +1-517-636-6978
Telefax : +1-517-638-9615
Telex :
Cedex :
 17.12.2001

Type : lead organisation
Name : Tokuyama Corporation
Partner :
Date :
Street : 3-3-1 Shibuya, Shibuya-ku
Town : 150-8383 Tokyo
Country : Japan
Phone : +81-3-3499-8478
Telefax : +81-3-3499-8967
Telex :
Cedex :
 17.12.2001

1. GENERAL INFORMATION

ID: 10043-52-4

DATE: 15.11.2002

Type : cooperating company
Name : Tosoh Corporation
Partner :
Date :
Street : Shiba-koen First BLDG, 3-8-2 Shiba, Minato-ku
Town : 105-8623 Tokyo
Country : Japan
Phone : +81-3-5427-5127
Telefax : +81-3-5427-5203
Telex :
Cedex :
 13.12.2001

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 : > 94 % w/w
Remark : There are five forms of calcium chloride by the different numbers(n) of the crystal water: $\text{CaCl}_2 \cdot n\text{H}_2\text{O}$.

n	RN	Physical Status
0 (anhydrous)	[10043-52-4]	solid
1 (monohydrate)	[22691-02-7]	solid
2 (dihydrate)	[10035-04-8]	solid
4 (tetrahydrate)	[25094-02-4]	solid
6 (hexahydrate)	[7774-34-7]	solid

crystal water is not regarded as impurity.

Source : Tokuyama Corporation
 06.08.2002

1.1.0 DETAILS ON TEMPLATE

1.1.1 SPECTRA

1.2 SYNONYMS

BOVIKALC
08.03.2002

CALCIUM (2+) CHLORIDE
08.03.2002

CALCIUM DICHLORIDE
13.12.2001

1. GENERAL INFORMATION

ID: 10043-52-4

DATE: 15.11.2002

CALCOSAN
13.12.2001

CALOL
08.03.2002

CALPLUS
13.12.2001

CALTAC
13.12.2001

CALZINA ORAL
08.03.2002

Caso
25.04.2002

DARACCEL
08.03.2002

DOWFLAKE
13.12.2001

EXPRESS
25.04.2002

LIQUIDOW
13.12.2001

PELADOW
13.12.2001

SNOMELT
28.02.2002

STOPIT
28.02.2002

SUPERFLAKE ANHYDROUS
13.12.2001

URAMINE MC
13.12.2001

1.3 IMPURITIES

CAS-No : 7647-14-5
EINECS-No : 231-598-3
EINECS-Name : sodium chloride
Contents : % w/w
Remark : According to the Japanese Pharmacopeia
Source : Tokuyama Corporation
25.04.2002

CAS-No : 1305-62-0
EINECS-No : 215-137-3
EINECS-Name : calcium dihydroxide
Contents : % w/w

1. GENERAL INFORMATION

ID: 10043-52-4

DATE: 15.11.2002

Remark : According to the Japanese Pharmacopeia
Source : Tokuyama Corporation
 25.04.2002

CAS-No : 7786-30-3
EINECS-No : 232-094-6
EINECS-Name : magnesium chloride
Contents : % w/w
Source : Tokuyama Corporation
 10.06.2002

(75)

CAS-No : 7447-40-7
EINECS-No : 231-211-8
EINECS-Name : potassium chloride
Contents : % w/w
Source : Tokuyama Corporation
 25.04.2002

CAS-No :
EINECS-No :
EINECS-Name : sulphates
Contents : % w/w
 10.05.2002

1.4 ADDITIVES

1.5 QUANTITY

Production during the last 12 months :
Import during the last 12 months :
Quantity : more than 1 000 000 tonnes in 2000
Remark : The production capacity of calcium chloride in North America was reported in March, 2002 to be approximately 1,687,000 tonnes per year.
 In Japan, the production volume was estimated to be 245,000 tonnes in 2000.
 The total amount used in Western Europe including Scandinavia is around 300,000 tonnes per year.
Source : Tokuyama Corporation
 15.07.2002

(18)

1.6.1 LABELLING

Labelling : as in Directive 67/548/EEC
Symbols : Xi
Nota : E
Specific limits : no
R-Phrases : (36) Irritating to eyes
S-Phrases : (2) Keep out of reach of children
 (22) Do not breathe dust
 (24) Avoid contact with skin
Source : Tokuyama Corporation
 08.03.2002

1.6.2 CLASSIFICATION

Classification : as in Directive 67/548/EEC
Class of danger : irritating
R-Phrases : (36) Irritating to eyes
Source : Tokuyama Corporation
17.12.2001

1.7 USE PATTERN

Type : type
Category : Non dispersive use
14.12.2001

Type : type
Category : Wide dispersive use
10.02.2000

Type : industrial
Category : Agricultural industry
17.12.2001

Type : industrial
Category : Basic industry: basic chemicals
17.12.2001

Type : industrial
Category : Chemical industry: used in synthesis
10.02.2000

Type : industrial
Category : Fuel industry
10.02.2000

Type : industrial
Category : Paper, pulp and board industry
10.02.2000

Type : industrial
Category : Personal and domestic use
10.02.2000

Type : industrial
Category : other
17.12.2001

Type : use
Category : Absorbents and adsorbents
17.12.2001

Type : use
Category : Anti-freezing agents
10.02.2000

Type : use
Category : Construction materials additives
10.02.2000

1. GENERAL INFORMATION

ID: 10043-52-4

DATE: 15.11.2002

Type	:	use
Category	:	Dustbinding agents
17.12.2001		
Type	:	use
Category	:	Fertilizers
14.12.2001		
Type	:	use
Category	:	Fillers
24.08.2001		
Type	:	use
Category	:	Food/foodstuff additives
10.02.2000		
Type	:	use
Category	:	Heat transferring agents
17.12.2001		
Type	:	use
Category	:	Intermediates
10.02.2000		
Type	:	use
Category	:	Laboratory chemicals
10.02.2000		
Type	:	use
Category	:	pH-regulating agents
14.12.2001		
Type	:	use
Category	:	Pharmaceuticals
17.12.2001		
Type	:	use
Category	:	Viscosity adjustors
17.12.2001		
Type	:	use
Category	:	other
14.12.2001		

1.7.1 TECHNOLOGY PRODUCTION/USE

1.8 OCCUPATIONAL EXPOSURE LIMIT VALUES

Type of limit	:	other: OELs (Ontario, Canada)
Limit value	:	5 mg/m ³
Source	:	Tokuyama Corporation
15.07.2002		

(72)

1.9 SOURCE OF EXPOSURE

Memo	:	Production process
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Remark : There are three major production processes for calcium chloride as follows:
production by the ammonia soda process, the natural brine process and the neutralization process.
All of them are operated in the closed production system.

1) Production by the ammonia soda process:
Calcium chloride is made from the concentrated brine produced in the ammonia soda process as the by-product. The crude brine in the ammonia soda process is removed from sodium chloride, separated from the alkali chloridesands and concentrated up to ca.45% for the calcium chloride production.

2) Production by the natural brine process:
Calcium chloride is made from the brine removed from the naturally occurring formation known as the "Filer Formation, which consists of calcium, magnesium, sodium, and potassium chlorides. The brine is removed from bromine and magnesium hydroxide, separated from the alkali chloridesands and concentrated up to ca. 45% for the calcium chloride production.

3) Production by the neutralization process:
Calcium chloride is made by neutralizing the limestone with the hydrochloric acid.

Source : Tokuyama Corporation
25.04.2002

Memo Remark : Source of environmental exposure
: - Natural background
- Use as a deicing agent
- Use as a dust control and roadway base stabilization
- Wastewater from production and user sites
- Use as an additive in herbicide

Source : Tokuyama Corporation
09.06.2002

Memo Remark : Source of human exposure
: - Inhalation of dust by handling of calcium chloride
- Skin contact by handling of calcium chloride as dust or solution
- Intake as a food additive
- Indirect exposure via food and surface water

Source : Tokuyama Corporation
01.03.2002

1.10.1 RECOMMENDATIONS/PRECAUTIONARY MEASURES

1.10.2 EMERGENCY MEASURES

1.11 PACKAGING

1.12 POSSIB. OF RENDERING SUBST. HARMLESS

1.13 STATEMENTS CONCERNING WASTE

1.14.1 WATER POLLUTION

Classified by : KBWS (DE)
Labelled by :
Class of danger : 0 (generally not water polluting)
Source : Tokuyama Corporation
 10.06.2002 (14)

1.14.2 MAJOR ACCIDENT HAZARDS

Legislation : Stoerfallverordnung (DE)
Substance listed : no
No. in directive :
Source : Tokuyama Corporation
 11.06.2002 (94)

1.14.3 AIR POLLUTION**1.15 ADDITIONAL REMARKS**

Memo : deicing agents
Remark : About half volume of the produced calcium chloride goes into the environment by the use of deicing agents (also called as the anti-freezing agents) and the dust control agents both in Japan and North America. The calcium chloride for these uses will eventually dissolve with water to go into the soil and surface water, spreading around the environment.

The Canadian government assessed the impact of "Road Salts" to the environment for 5 years under CEPA (Canadian Environment Protection Act). Road Salts, a category name of the deicing agents, includes (1) sodium chloride, (2) calcium chloride, (3) magnesium chloride, (4) potassium chloride and (5) ferrocyanide salts.

According to the Canadian Assessment Report, approximately five million tonnes of road salts were used in the 1997-98 winter season in Canada. Ninety-five percent (4.75 million tonnes) of the road salts used was sodium chloride and only 2 percent (0.11 million tonnes) of the salt was calcium chloride.

Source : Tokuyama Corporation
 15.11.2002 (13) (27)

Memo : Use categories
Remark : Calcium chloride is used for deicing, road stabilization, dust control, accelerator in concrete, industrial processing, oil and gas well fluids, and for others such as food additives and medication.
 Percentages of the uses are different among member countries and may vary from year to year. The percentages of the uses in North America are reported to be 22% for deicing, 20% for road stabilization and dust control, 20% for industrial processing, 17% for oil and gas well fluids, 12% for concrete. In Japan, about 50% of the total production is used for deicing and 25% for road stabilization.

Source : Tokuyama Corporation
 15.11.2002 (18)

1.16 LAST LITERATURE SEARCH**1.17 REVIEWS****1.18 LISTINGS E.G. CHEMICAL INVENTORIES**

- Remark** : Calcium chloride is regarded as the substance which added directly to human food affirmed as generally recognized as safe (GRAS) by the U.S. Food and Drug Administration (FDA).
The average intake of calcium chloride based on the quantity of calcium chloride used annually in foods in 1970 was 160 mg/day for individuals in U.S.
The average intake of calcium chloride based on the mean frequency of eating foods by food category was 345 mg/day for individuals over 2 years.
- Source** : Tokuyama Corporation (87)
15.11.2002
- Remark** : Calcium chloride was evaluated to be a food substance of very low toxicity and thus the establishment of the ADI for calcium chloride has not been deemed necessary by the Joint FAO/WHO Expert Committee on Food Additives (JECFA).
- Source** : Tokuyama Corporation (45) (46)
18.07.2002

2.1 MELTING POINT

Value : 772 °C
Source : Tokuyama Corporation
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
 10.06.2002 (78)

Value : 772 °C
Remark : Melting Point of $\text{CaCl}_2 \cdot n\text{H}_2\text{O}$:

n	RN	m.p. (°C)
0	[10043-52-4]	772
1	[22691-02-7]	187
2	[10035-04-8]	176
4	[25094-02-4]	45.3
6	[7774-34-7]	29.9

Source : Tokuyama Corporation
Reliability : (2) valid with restrictions
 06.08.2002 (89)

Value : 772 °C
Remark : Melting Point of $\text{CaCl}_2 \cdot n\text{H}_2\text{O}$:

n	RN	m.p. (°C)
0	[10043-52-4]	772
1	[22691-02-7]	260
2	[10035-04-8]	176
4	[25094-02-4]	45
6	[7774-34-7]	30

Source : Tokuyama Corporation
Reliability : (2) valid with restrictions
 06.08.2002 (50)

Value : 782 °C
Source : Tokuyama Corporation
Reliability : (2) valid with restrictions
 11.06.2002 (68)

2.2 BOILING POINT

Value : > 1600 °C
Source : Tokuyama Corporation
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
 11.06.2002 (78)

Value : 1935 °C
Remark : Boiling Point of $\text{CaCl}_2 \cdot n\text{H}_2\text{O}$:

n	RN	m.p. (°C)
0	[10043-52-4]	1935

2. PHYSICO-CHEMICAL DATA

ID: 10043-52-4

DATE: 15.11.2002

	1	[22691-02-7]	181*
	2	[10035-04-8]	175*
	4	[25094-02-4]	-
	6	[7774-34-7]	-

	*; 101.3 kPa		
Source	:	Tokuyama Corporation	
Reliability	:	(2) valid with restrictions	
11.06.2002			(89)
Value	:	1670 °C	
Source	:	Tokuyama Corporation	
Reliability	:	(2) valid with restrictions	
11.06.2002			(50)
Value	:	> 1600 °C at 1013 hPa	
Source	:	Tokuyama Corporation	
Reliability	:	(2) valid with restrictions	
11.06.2002			(68)

2.3 DENSITY

Type	:	density	
Value	:	2.125 g/cm ³ at 15° C	
Source	:	Tokuyama Corporation	
Reliability	:	(2) valid with restrictions	
10.06.2002			(78)

Type	:	density
Value	:	2.16 g/cm ³ at 25° C
Remark	:	Density of CaCl ₂ •nH ₂ O:

n	RN	density (g/cm ³)
0	[10043-52-4]	2.16
1	[22691-02-7]	2.24
2	[10035-04-8]	1.85
4	[25094-02-4]	1.83
6	[7774-34-7]	1.71

	at 25 °C		
Source	:	Tokuyama Corporation	
Reliability	:	(2) valid with restrictions	
Flag	:	Critical study for SIDS endpoint	
06.08.2002			(89)

Type	:	density
Value	:	2.22 g/cm ³ at 25° C
Remark	:	Density of CaCl ₂ •nH ₂ O:

n	RN	density (g/cm ³)
0	[10043-52-4]	2.22
1	[22691-02-7]	2.24
2	[10035-04-8]	1.85
4	[25094-02-4]	1.83
6	[7774-34-7]	1.72

at 25 °C

2. PHYSICO-CHEMICAL DATA

ID: 10043-52-4

DATE: 15.11.2002

Source : Tokuyama Corporation
Reliability : (2) valid with restrictions
 06.08.2002 (50)

Type : density
Value : = 2.15 g/cm³ at 25° C
Source : Tokuyama Corporation
Reliability : (2) valid with restrictions
 11.06.2002 (68)

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Remark : Calcium chloride is inorganic solid compound and has a high melting point (> 700°C). So vapor pressure is negligible.
Source : Tokuyama Corporation
 15.11.2002

Value : 11 hPa at 20° C
Decomposition :
Method :
Year : 1974
GLP :
Test substance : other TS
Source : Tokuyama Corporation
Test substance : 35 % solution
Reliability : (2) valid with restrictions
 10.06.2002 (28)

Value : 3.7 hPa at 40° C
Decomposition :
Method :
Year : 1974
GLP :
Test substance : other TS
Source : Tokuyama Corporation
Test substance : CaCl₂·2H₂O (Dihydrate)
Reliability : (2) valid with restrictions
 10.06.2002 (28)

2.5 PARTITION COEFFICIENT

Remark : Log Pow is not applicable to calcium chloride due to its dissociation property in water.
Source : Tokuyama Corporation
 15.11.2002

2.6.1 WATER SOLUBILITY

Value : 745 g/l at 20 ° C
Qualitative :
Pka : at 25 ° C
PH : at and ° C

Method	:		
Year	:		
GLP	:		
Test substance	:	as prescribed by 1.1 - 1.4	
Source	:	Tokuyama Corporation	
Reliability	:	(2) valid with restrictions	
Flag	:	Critical study for SIDS endpoint	
11.06.2002			(68)
Value	:	1590 g/l at 100 ° C	
Qualitative	:		
Pka	:	at 25 ° C	
PH	:	at and ° C	
Method	:		
Year	:		
GLP	:		
Test substance	:	as prescribed by 1.1 - 1.4	
Source	:	Tokuyama Corporation	
Reliability	:	(2) valid with restrictions	
11.06.2002			(68)

2.6.2 SURFACE TENSION

2.7 FLASH POINT

Remark	:	Calcium chloride has no flash point.
Source	:	Tokuyama Corporation
18.12.2001		

2.8 AUTO FLAMMABILITY

Remark	:	This product is non flammable.
Source	:	Tokuyama Corporation
18.12.2001		

2.9 FLAMMABILITY

Result	:	non flammable
Source	:	Tokuyama Corporation
18.12.2001		

2.10 EXPLOSIVE PROPERTIES

Result	:	not explosive
Source	:	Tokuyama Corporation
18.12.2001		

2.11 OXIDIZING PROPERTIES

Result	:	no oxidizing properties
Source	:	Tokuyama Corporation

18.12.2001

2.12 ADDITIONAL REMARKS

- Remark** : Calcium chloride (flakes) have a whit-greyish colour and are odour free. The solution is mildly corrosive to many metals including stainless steel; it is to be kept in a plastic bin. Materials to avoid:
1. Boiling water, boric and calcium oxide may react violently, generating heat;
 2. Reactive metal (e.g. zinc): prolonged reaction with calcium chloride solution on galvanised iron caused slow evolution of flammable and explosive hydrogen gas;
 3. Methyl vinyl ether: may react to initiate self-polymerization generating heat and pressure.
- Source** : Tokuyama Corporation
15.07.2002

3.1.1 PHOTODEGRADATION

Remark : not applicable
02.03.2002

3.1.2 STABILITY IN WATER

Remark : not applicable
02.03.2002
Calcium chloride readily dissociates into calcium and chloride ions in water.

3.1.3 STABILITY IN SOIL

Remark : not applicable
02.03.2002

3.2 MONITORING DATA

Type of measurement : background concentration
Medium : surface water
Method :
Concentration :
Remark : [Calcium statistics]

In North America Rivers (N=12)
Mean: 70.8 mg/l
Min.: 4.5 mg/l, Max.: 335.6 mg/l
10th percentile: 14.3 mg/l, 90th percentile: 204.5 mg/l

In South America Rivers (N=6)
Mean: 7.23 mg/l
Min.: 2.6 mg/l, Max.: 15.0 mg/l
10th percentile: 0.9 mg/l, 90th percentile: 11.5 mg/l

In Asian Rivers (N=25)
Mean: 29.1 mg/l
Min.: 5.5 mg/l, Max.: 93.5 mg/l
10th percentile: 10.2 mg/l, 90th percentile: 50.0 mg/l

In African Rivers (N=7)
Mean: 9.9 mg/l
Min.: 2.7 mg/l, Max.: 2.0 mg/l
10th percentile: 3.4 mg/l, 90th percentile: 19.7 mg/l

In European Rivers (N=20)
Mean: 52.3 mg/l
Min.: 3.8 mg/l, Max.: 108.0 mg/l
10th percentile: 4.7 mg/l, 90th percentile: 105.2 mg/l

In Oceania Rivers (N=6)
Mean: 16.9 mg/l
Min.: 7.0 mg/l, Max.: 23.0 mg/l
10th percentile: 10.5 mg/l, 90th percentile: 22.2mg/l

	Total (N=76) Mean: 37.4 mg/L Min.: 2.6 mg/L, Max.: 335.6 mg/L 10th percentile: 5.1 mg/L, 90th percentile: 86.5 mg/L The continental differences are not caused by human activities but by geological influences.	
Source 15.11.2002	: Tokuyama Corporation	(104)
Type of measurement	: background concentration	
Medium	: surface water	
Method	:	
Concentration	:	
Remark	: [Chloride statistics]	
	In North America Rivers (N=12) Mean: 17.5 mg/l Min.: 0.1 mg/l, Max.: 82.0 mg/l 10th percentile: 1.1 mg/l, 90th percentile: 29.7 mg/l In South America Rivers (N=6) Mean: 6.1 mg/l Min.: 0.9 mg/l, Max.: 14.3 mg/l 10th percentile: 1.6 mg/l, 90th percentile: 13.9 mg/l In Asian Rivers (N=25) Mean: 19.7 mg/l Min.: 0.3 mg/l, Max.: 59.7 mg/l 10th percentile: 1.2 mg/l, 90th percentile: 48.2 mg/l In African Rivers (N=7) Mean: 4.3 mg/l Min.: 0.9 mg/l, Max.: 10.6 mg/l 10th percentile: 1.0 mg/l, 90th percentile: 8.1 mg/l In European Rivers (N=21) Mean: 102.7 mg/l Min.: 1.1 mg/l, Max.: 1233 mg/l 10th percentile: 2.1 mg/l, 90th percentile: 173 mg/l In Oceania Rivers (N=6) Mean: 39.2 mg/l Min.: 0.1 mg/l, Max.: 171 mg/l 10th percentile: 0.3 mg/l, 90th percentile: 102.5 mg/l Total (N=77) Mean: 41.1 mg/L Min.: 0.1 mg/L, Max.: 1233 mg/L 10th percentile: 1.1 mg/L, 90th percentile: 64.8 mg/L	
Source 15.11.2002	: The WHO drinking water guideline for chloride ion is 200 mg/l. Tokuyama Corporation	(104)
Type of measurement	: background concentration	
Medium	: surface water	
Method	:	
Concentration	:	
Result	: CALCIUM and CHLORIDE concentrations (mean value): -----	

3. ENVIRONMENTAL FATE AND PATHWAYS

ID: 10043-52-4

DATE: 15.11.2002

	Location	Calcium	Chloride
		concentration (mg/l)	
	Jambes	65.7	20.3
	Nameche	75.3	64.6
	Liege	74.1	59.1
	Grobbendonk	71.6	63.1
	Lier	70.6	62.7
	Broechem	69.6	62.6
Source	: Tokuyama Corporation		
Test condition	: Belgium, Meuse, Canal Albert, Kempische kanalen, various cities, 1993		
10.06.2002	(105)		
Type of measurement	: background concentration		
Medium	: surface water		
Method	:		
Concentration	:		
Result	: Measured CALCIUM concentrations in natural waters (information of the rock type being drained by the freshwater system is given):		
	Aqueous System (type of rock drained)	Calcium Concentration (mg/l)	
	- Seawater	412	
	- Groundwater (limestone)	80	
	- Stream (granite)	4	
	- River/unpolluted	13.4	
	- River/including contribution of human activities	14.7	
	- Public water Supply/100 U.S. cities	26 (median) 0-145 (range)	
Source	: Tokuyama Corporation		
11.06.2002	(23) (39) (73) (95) (101)		
Type of measurement	: background concentration		
Medium	: surface water		
Method	:		
Concentration	:		
Result	: Chloride concentration:		
	Location	Chloride concentration (mg/l) mean value (min. - max.)	
	Baden-Wuerttemberg, Oehningen	6 (5-8)	
	Baden-Wuerttemberg, Weisweil	127 (18-251)	
	Baden-Wuerttemberg, Mannheim	123 (28-204)	
	Rheinland-Pfalz, Mainz	103 (55-191)	
	Rheinland-Pfalz, Koblenz	104 (56-186)	
	Nordrhein-Westfalen, Bad-Honnef	113 (27-160)	
	Nordrhein-Westfalen, Kleve-Bimmen	165 (93-302)	
Source	: Tokuyama Corporation		
Test condition	: Germany, Rhine, 1989		
10.06.2002	(103)		

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Remark : Fugacity model is not applied to estimate the distribution in the environment for inorganic substance such as calcium chloride because the programs are designed for organic chemicals and not for inorganic salts. Calcium chloride is readily dissociated into calcium and chloride ions in water and is not expected to evaporate because its vapour pressure is negligible. Calcium chloride released into the environment is thus likely to be distributed into the water compartment in the form of calcium and chloride ions. Otherwise, calcium ion may remain in the soil compartment by binding to soil particulate or by forming stable salts with other counter ions. On the other hand, chloride ion is mobile and eventually drains into surface water.

Source : Tokuyama Corporation
15.11.2002

3.3.2 DISTRIBUTION**3.4 MODE OF DEGRADATION IN ACTUAL USE****3.5 BIODEGRADATION**

Remark : not applicable for an inorganic compound
Source : Tokuyama Corporation
02.03.2002

3.6 BOD5, COD OR BOD5/COD RATIO

Remark : not applicable for an inorganic compound
Source : Tokuyama Corporation
02.03.2002

3.7 BIOACCUMULATION

Remark : not bioaccumulative
Log Po/w is not applicable for an inorganic compound which dissociates.
Source : Tokuyama Corporation
07.08.2002

3.8 ADDITIONAL REMARKS

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type : static
Species : *Pimephales promelas* (Fish, fresh water)
Exposure period : 96 hour(s)
Unit : mg/l
Analytical monitoring : yes
LC₅₀ : 4630
Method : other: EPA/600/4-90/027, EPA/600/6-91/003
Year : 1997
GLP : no data
Test substance : as prescribed by 1.1 - 1.4
Method : - Test Organisms:
 a) Size: Not described
 b) Age: 1-7 days old
 c) Pretreatment: no data
 d) Supplier/Source: ENSR, Fort Collins, CO, USA
 - Test Conditions:
 a) Dilution Water Source: moderately hard reconstituted water (MHRW)
 b) Exposure Vessel Type: 30ml plastic beaker
 c) Nominal Concentrations: 10,000, 5,000, 2,500, 1,250 mg/l
 d) Stock Solutions Preparations and Stability: 10,000mg/l in MHRW
 e) Number of Replicates: 2-5
 f) Individuals per Replicates: 5
 g) Renewal Rate of Test Water: not renewed
 h) Water Temperature: 25 °C
 i) Light Condition: 16:8h(light:dark)
 j) Feeding: concentrated brine shrimp nauplii was added after 48h of exposure.
 - Method of Analytical Monitoring: using ICP according to USEPA method 200.7
 - Statistical Method:
 a) Data Analysis: Spearman-Kärber method
Remark : LC₅₀ expressed as anhydrous CaCl₂.
Result : Table: Mean LC₅₀ values

Exposure period	24h	48h	96h
Number of test	3	3	3
LC ₅₀ (mg/l)*	>6660	>6560	4630
Range (mg/l)**	4700->10000	4390->10000	3930-5360

* Values are arithmetic mean of 3 tests.

** Range of three LC₅₀s

Source : Tokuyama Corporation
Reliability : (2) valid with restrictions
 Guideline study
Flag : Critical study for SIDS endpoint
 15.07.2002

(74)

Type : static
Species : *Lepomis macrochirus* (Fish, fresh water)
Exposure period : 96 hour(s)
Unit : mg/l
Analytical monitoring : yes
LC₅₀ : 9500 - 11300
Method : other: Doudroff et al., (1951)

Year : 1959
GLP : no data
Test substance : as prescribed by 1.1 - 1.4
Method : - Test Organisms:
a) Average Size: small(3.88cm 0.96g), medium(6.09cm 2.80g), large(14.24cm 54.26g)
b) Age: Not described
c) Pretreatment: acclimated for 7 days with dilution water before use
d) Supplier/Source: a fish hatchery in Pennsylvania or Pennsylvania Fish Commission, USA
- Test Conditions:
a) Dilution Water Source: prepared from distilled water and analytical grade or reagent chemicals
b) Dilution Water Chemistry:
KCl 0.02 g/l
Na₂SiO₃ 0.02
NaHCO₃ 0.04
MgSO₄·7H₂O 0.04
Ca(NO₃)₂ 0.03
CaCO₃ 0.01
K₂HPO₄ 0.002
Fe+++ 0.004
c) Exposure Vessel Type: 5 gallon glass jar with cork stopper
d) Nominal Concentrations: not described
e) Number of Replicates: 1 or 2
f) Individuals per Replicates: 10
g) Renewal Rate of Test Water: not renewed, maintained the dissolved oxygen content at 5-9 ppm by bubbling compressed air
h) Water Temperature: 20±1 °C
i) Light Condition: not described
- Method of Analytical Monitoring: not described
- Statistical Method:
a) Data Analysis: Doudoroff method
Remark : LC₅₀ expressed as anhydrous CaCl₂.
Result : - 96 hours LC₅₀ for three size ranges of fish

size	(length, weight)	LC ₅₀
small	(3.88cm, 0.96g)	9500 mg/l
medium	(6.09cm, 2.80g)	9500 mg/l
large	(14.24cm, 54.26g)	11300 mg/l

Source : Tokuyama Corporation
Reliability : (2) valid with restrictions
Comparable to guideline study with acceptable restrictions

15.07.2002

(15)

Type : static
Species : *Lepomis macrochirus* (Fish, fresh water)
Exposure period : 96 hour(s)
Unit : mg/l
Analytical monitoring : no
LC₅₀ : 10650
Method : other
Year : 1954
GLP : no data
Test substance : as prescribed by 1.1 - 1.4
Method : - Test Organisms:
a) Size: 5-9 cm, 1-9 g
b) Age: not described
c) Pretreatment: acclimated for 7 days with dilution water before use

d) Supplier/Source: a fish hatchery in Maryland, USA
 - Test Conditions:
 a) Dilution Water Source: prepared from distilled water and analytical or reagent chemicals
 b) Dilution Water Chemistry:
 KCl 0.02 g/l
 Na₂SiO₃ 0.02
 NaHCO₃ 0.04
 MgSO₄·7H₂O 0.04
 Ca(NO₃)₂ 0.03
 CaCO₃ 0.01
 K₂HPO₄ 0.002
 Fe+++ 0.004
 c) Exposure Vessel Type: 5-gallon Pyrex jar with rubber stopper
 d) Nominal Concentrations (as mg/l): 6500, 8700, 10500, 10800, 12000, 12500
 e) Number of Replicates: 2
 f) Individuals per Replicates: 10
 g) Dosing Rate, Flow-through Rate: not renewed, maintained the dissolved oxygen content at 5-9 ppm by bubbling compressed air
 h) Renewal Rate of Test Water: not renewed, aeration
 i) Water Temperature: 20±1 °C
 j) Light Condition: not described
 - Method of Analytical Monitoring: using Beckman pH meter (pH) and Winkler method (dissolved oxygen)
 - Statistical Method:
 a) Data Analysis: Doudoroff method
Remark : LC₅₀ expressed as anhydrous CaCl₂.
Result : - Table: Results at 96 hours

CaCl ₂ (mg/l)	pH	Surv.(%)
6500	7.28	100
6500	7.44	100
8700	7.30	80
8700	7.39	80
10500	7.46	60
10500	7.42	60
10800	7.39	40
10800	7.33	40
12000	7.59	20
12000	7.60	10

- Water Chemistry in Test
 Hardness (mg/l CaCO₃): 6314 - 11900
 Alkalinity (mg/l CaCO₃): 32.6 - 49.6
 Dissolved O₂ (mg/l) : 7.2 - 8.7
 pH : 7.19 - 7.80
 Water Hardness Code : 4 -- Very hard (>300 mg/l CaCO₃)
Source : Tokuyama Corporation
Reliability : (2) valid with restrictions
 Comparable to guideline study with acceptable restrictions

15.07.2002

(102)

Type : static
Species : *Gambusia affinis* (Fish, fresh water)
Exposure period : 96 hour(s)
Unit : mg/l
Analytical monitoring : no data
LC₀ : 10000
LC₅₀ : 13400

Method	:	other: not mentioned
Year	:	1957
GLP	:	no data
Test substance	:	no data
Method	:	- Test Organisms: a) Size: not described b) Age: adult, female c) Pretreatment: acclimated for 2-3 weeks before use d) Supplier/Source: Stillwater Creek in Payne Country, Oklahoma, USA - Test Conditions: a) Dilution Water Source: pond water (two farm ponds) b) Exposure Vessel Type: cylindrical Pyrex jar 12 inch high and 12 inch in diameter, Each jar contained 15 l c) Nominal Concentrations: 10000, 18000, 24000 mg/l d) Stock Solutions Preparations and Stability: not described e) Number of Replicates: 1 f) Individuals per Replicates: 10 g) Renewal Rate of Test Water: not renewed, aeration h) Light Condition: not described - Method of Analytical Monitoring: not described - Statistical Method: a) Data Analysis: Doudoroff method
Remark	:	LC ₅₀ expressed as anhydrous CaCl ₂ .
Result	:	Table: Toxicity to Gambusia

	Temp.(°C)	20-23
	Turb.(ppm)	
	Init.	320
	Final	<25
	pH Range	6.8-7.6
	LC ₅₀ (mg/l)	
	24h	13400
	48h	13400
	96h	13400

Source	:	Tokuyama Corporation
Reliability	:	(2) valid with restrictions Comparable to guideline study with acceptable restrictions
15.07.2002		(107)
Type	:	static
Species	:	other: <i>Lucioperca lucioperca</i> L.
Exposure period	:	18 hour(s)
Unit	:	mg/l
Analytical monitoring	:	no data
LC₀	:	4160
Method	:	other: not mentioned
Year	:	1975
GLP	:	no data
Test substance	:	no data
Remark	:	No mortality at tested concentration
Source	:	Tokuyama Corporation
Test condition	:	Age/life stage: 11.5 - 16 mm Dilution water source: pond water
Reliability	:	(3) invalid Documentation insufficient for assessment
10.06.2002		(93)
Type	:	static
Species	:	<i>Lepomis macrochirus</i> (Fish, fresh water)

Exposure period : 96 hour(s)
Unit : mg/l
Analytical monitoring : no
LC₅₀ : 10650
Method : other: Cairns, Scheier, Hess (1964)
Year : 1968
GLP : no
Test substance : other TS
Source : Tokuyama Corporation
Test condition : a) Dilution Water Source: Synthetic dilution water
 b) Dilution Water Chemistry:
 KCl 0.02 g/l
 Na₂SiO₃ 0.02
 NaHCO₃ 0.04
 MgSO₄·7H₂O 0.04
 Ca(NO₃)₂ 0.03
 CaCO₃ 0.01
 K₂HPO₄ 0.002
 Fe+++ 0.004
 c) Water Temperature: 18±2
Reliability : (3) invalid
 Documentation insufficient for assessment

11.06.2002

(84)

Type : static
Species : *Lepomis macrochirus* (Fish, fresh water)
Exposure period : 24 hour(s)
Unit : mg/l
Analytical monitoring : no
LC₅₀ : 8350
Method : other: Freeman (1953)
Year : 1965
GLP : no
Test substance : no data
Source : Tokuyama Corporation
Test condition : Dilution water source: Standard Reference Water
Reliability : (3) invalid
 Documentation insufficient for assessment

10.06.2002

(22)

Type : static
Species : *Carassius auratus* (Fish, fresh water)
Exposure period : 96 hour(s)
Unit : mg/l
Analytical monitoring : no data
LC₀ : 3
Method : other: not mentioned
Year : 1937
GLP : no data
Test substance : no data
Remark :

Exposure period	LC ₀ (mg/l)
80 h	4
96 h	3

 All fishes survived at test concentration without apparent injury.

Source : Tokuyama Corporation
Test condition : Age/life stage: 60 - 90 mm, 3 - 5 g
 Temperature: 18 - 23 °C
 Dissolved oxygen: 6 - 7 mg/l

Reliability : pH: 6.7
: (3) invalid
Documentation insufficient for assessment
11.06.2002

(26)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type : Static
Species : *Daphnia magna* (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
Analytical monitoring : No
NOEC : 2000
EC₅₀ : 2400
Method : OECD Guide-line 202, part 1 "Daphnia sp., Acute Immobilisation Test"
Year : 1998
GLP : Yes
Test substance : as prescribed by 1.1 - 1.4
Method : - Test Organisms: *Daphnia magna*, Crustacea
a) Age: 0-24 hours
b) Pretreatment: not described
c) Supplier/Source: Daphtoxkit F. magna from Bio International, The Netherlands
- Test Conditions:
a) Dilution Water Source: Elendt M4 medium
b) Dilution Water Chemistry:

Table:Composition of Elendt M4 medium (prepared in ultrapure water)

Compound	Concentration (mg/l)
CaCl ₂ ·2H ₂ O	290
MgSO ₄ ·7H ₂ O	120
KCl	5.8
NaHCO ₃	65
Na ₂ SiO ₃ ·9H ₂ O	10
NaNO ₃	0.27
KH ₂ PO ₄	0.14
K ₂ HPO ₄	0.18
H ₃ BO ₃	2.8
MnCl ₂ ·4H ₂ O	0.36
LiCl	0.30
RbCl	0.072
SrCl ₂ ·6H ₂ O	0.020
Na ₂ MoO ₄ ·2H ₂ O	0.064
CuCl ₂ ·2H ₂ O	0.017
ZnCl ₂	0.013
CoCl ₂ ·6H ₂ O	0.010
KI	0.0033
Na ₂ SeO ₃	0.0023
NH ₄ VO ₃	0.00060
Na ₂ EDTA·2H ₂ O	2.5
FeSO ₄ ·7H ₂ O	1.0
Thiamine hydrochloride	0.075
Cyanocobalamine(B12)	0.001
Biotine	0.00075

c) Exposure Vessel Type: 250ml glass beaker

d) Nominal Concentrations (as mg/l): 0, 1000, 1400, 2000, 2800, 4000

e) Stock Solutions Preparations and Stability: dissolving 8.20g calcium

chloride in 2050 ml Elendt M4 medium

f) Number of Replicates: 3

g) Individuals per Replicates: 10

h) Light Condition: 16 hours(from 6 a.m. to 10 p.m.) light and 8 hours dark

- Statistical Method:

a) Data Analysis: Fisher's Exact Test for NOEC, Probit analysis for EC₅₀

Remark

: EC₅₀ and NOEC expressed as anhydrous CaCl₂. The toxic values are shown as added calcium chloride concentraion to the system, although calcium chloride is included as part of the test media.

Result

: - Table: Immobility of water fleas during the test

Nominal calcium chloride concentration (mg/l)	Number of mobile water fleas (hours)			Mean immobility at test termination (%)
	0	24	48	
0	10	10	10	0
	10	10	10	
	10	10	10	
1000	10	10	10	0
	10	10	10	
	10	10	10	
1400	10	10	10	0
	10	10	10	
	10	10	10	
2000	10	10	10	3.3
	10	10	10	
	10	9	9	
2800	10	0	0	93
	10	2	2	
	10	0	0	
4000	10	0	0	100
	9	0	0	
	10	0	0	

- Table: Water parameters of test solutions

Nominal calcium chloride concentration (mg/l)	Temperature (°C)	Oxygen content (mg/l)	pH
0	20.0	8.4	8.2
1000	19.9	8.7	8.3
1400	19.9	8.5	8.2
2000	19.9	8.5	7.9
2800	19.8	8.5	7.8
4000	19.9	8.6	7.6

Source

: Tokuyama Corporation

Reliability

: (1) valid without restriction
OECD Guideline study

Flag : Critical study for SIDS endpoint
15.11.2002 (20)

Type : Static
Species : *Daphnia magna* (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
Analytical monitoring : Yes
LC₅₀ : 2770
Method : other: EPA/600/4-90/027, EPA/600/6-91/003
Year : 1997
GLP : no data
Test substance : as prescribed by 1.1 - 1.4
Method : - Test Organisms:
a) Age: less than 24 hours old
b) Pretreatment: not described
c) Supplier/Source: ENSR, Fort Collins, CO, USA
- Test Conditions:
a) Dilution Water Source: moderately hard reconstituted water (MHRW)
b) Dilution Water Chemistry: not described
c) Exposure Vessel Type: 30ml plastic beaker
d) Nominal Concentrations (as mg/l): 10000, 5000, 2500, 1250
e) Stock Solutions Preparations and Stability: 10,000mg/l in MHRW
f) Number of Replicates: 2
g) Individuals per Replicates: 5
h) Water Temperature Range: 20 °C
i) Light Condition: 16:8h(light:dark)
j) Feeding: yeast/cerophyl/trout chow and algae suspension was added at test initiation.
- Method of Analytical Monitoring: using ICP according to USEPA method 200.7
- Statistical Method:

Remark : LC₅₀ expressed as anhydrous CaCl₂.

Result :

Exposure periode	LC ₅₀ * (mg/l)	Range** (mg/l)
24h	3250	2680-4010
48h	2770	2330-3230

* Values are arithmetic means of 4 tests.

** Range of four LC₅₀s

Source : Tokuyama Corporation
Reliability : (2) valid with restrictions
Guideline study

15.07.2002 (74)

Type : static
Species : *Ceriodaphnia* sp. (Crustacea)
Exposure period : 48 hour(s)
Unit : Mg/l
Analytical monitoring : Yes
LC₅₀ : 1830
Method : other: EPA/600/4-90/027, EPA/600/6-91/003
Year : 1997
GLP : no data
Test substance : as prescribed by 1.1 - 1.4
Method : - Test Organisms:
a) Age: less than 24 hours old
b) Pretreatment: not described
c) Supplier/Source: ENSR, Fort Collins, CO, USA

- Test Conditions:
a) Dilution Water Source: moderately hard reconstituted water (MHRW)
b) Dilution Water Chemistry: not described
c) Exposure Vessel Type: 30ml plastic beaker
d) Nominal Concentrations (as mg/l): 10000, 5000, 2500, 1250
e) Stock Solutions Preparations and Stability: 10,000mg/l in MHRW
f) Number of Replicates: 2
g) Individuals per Replicates: 5
h) Water Temperature Range: 20 °C
i) Light Condition: 16:8h(light:dark)
j) Feeding: yeast/cerophyl/trout chow and algae suspension was added at test initiation.
- Method of Analytical Monitoring: using ICP according to USEPA method 200.7
- Statistical Method:
a) Data Analysis: Spearman-Kärber method
Remark : LC₅₀ expressed as anhydrous CaCl₂.
Result :

Exposure periode	LC ₅₀ * (mg/l)	Range (mg/l)
24h	2260	1770-2680
48h	1830	1770-2030

* Values are arithmetic means of 4 or 3 tests.
Source : Tokuyama Corporation
Reliability : (2) valid with restrictions
Guideline study

11.06.2002

(74)

Type : static
Species : *Daphnia magna* (Crustacea)
Exposure period : 48 hour(s)
Unit : Mg/l
Analytical monitoring : no data
EC₅₀ : 1062
Method : other
Year : 1989
GLP : no data
Test substance : other TS: Dihydrate
Method :
- Test Organisms:
a) Age: Not described
b) Pretreatment: not described
c) Supplier/Source: a natural pond at Gheru Campus of the Industrial Toxicology Research Centre, Lucknow
- Test Conditions:
a) Dilution Water Source: filtered aerated tubewell hard water
b) Dilution Water Chemistry:
Initial Physicochemical Properties of Tubewell Water

Parameter	Unit	Mean	Range
Temperature	°C	13	11.5-14.5
pH		7.6	7.2-7.8
Dissolved oxygen	mg/l	5.6	5.2-6.5
Total hardness	mg/l as CaCO ₃	240	235-260
Total alkalinity	mg/l as CaCO ₃	400	390-415
Calcium	mg/l	152	145-165
Magnesium	mg/l	92	85-96
Chloride	mg/l	7	5-10

c) Exposure Vessel Type: 200ml beaker

d) Nominal Concentrations (as mg/l): not described
e) Stock Solutions Preparations and Stability: made in distilled water
f) Number of Replicates: 3
g) Individuals per Replicates: 10
h) Water Temperature Range: 11.5-14.5 °C
i) Light Condition: not described
- Method of Analytical Monitoring: not described
- Statistical Method:
a) Data Analysis: moving average-angle method
Remark : EC₅₀ expressed as anhydrous CaCl₂.
Result : - Table: EC₅₀ and 95% confidence limit

EC₅₀ and 95% confidence limits (mg/l)

24h	48h
1587 (1243-1936)	1062 (893-1230)

Source : Tokuyama Corporation
Reliability : (2) valid with restrictions
Comparable to guideline study with acceptable restrictions

11.06.2002

(52)

Type : semistatic
Species : other aquatic worm: *Tubifex tubifex*
Exposure period : 96 hour(s)
Unit : mg/l
Analytical monitoring : yes
EC₅₀ : 780
Method : other
Year : 1991
GLP : No data
Test substance : As prescribed by 1.1 - 1.4
Method : - Test Organisms:
a) Age: not described
b) Pretreatment: acclimated to laboratory conditions for 7days before use.
c) Supplier/Source: Gheru Campus of the Industrial Toxicology Research Centre, Lucknow
- Test Conditions:
a) Dilution Water Source: Tubewell water
b) Dilution Water Chemistry:
Initial Physicochemical Properties of Tubewell Water

Parameter	Unit	Mean	Range
Temperature	°C	30	29.5-31
pH		7.6	7.5-7.7
Dissolved oxygen	mg/l	5.8	5.2-6.0
Total hardness	mg/l as CaCO ₃	245	230-250
Total alkalinity	mg/l as CaCO ₃	400	390-410
Calcium	mg/l	160	151-167
Magnesium	mg/l	90	80-98
Chloride	mg/l	10	7-12

c) Exposure Vessel Type: 200ml beaker
d) Nominal Concentrations: not described
e) Stock Solutions Preparations and Stability: made in distilled water
f) Number of Replicates: 3
g) Individuals per Replicates: 10
h) Renewal Rate of Test Water: every 24 hrs
i) Water Temperature Range: 29.5-31 °C

	j) Light Condition: not described
	k) Feeding: no
	- Method of Analytical Monitoring: not described
	- Statistical Method:
	a) Data Analysis: Moving average-angle method
Remark	: Endpoint: immobilization
Result	: EC ₅₀ expressed as anhydrous CaCl ₂ .

	Exposure EC ₅₀ 95% confidence
	periode (mg/l) limits (mg/l)

	24h 2260 2080-2530
	48h 1830 910-1240
	96h 780 690- 910

Source	: Tokuyama Corporation
Reliability	: (2) valid with restrictions
15.07.2002	Comparable to guideline study with acceptable restrictions
	(51)
Type	: static
Species	: other aquatic crustacea: <i>Cyclops abyssorum prealpinus</i>
Exposure period	: 48 hour(s)
Unit	: Mg/l
Analytical monitoring	: No data
LC₅₀	: 19400
Method	: other: not mentioned
Year	: 1974
GLP	: No data
Test substance	: No data
Method	: - Test Organisms:
	a) Age: Adult
	b) Average size: 0.62 mm
	c) Supplier/Source: Lake Monate
	- Test Conditions:
	a) Dilution Water Source: Lake Monate water
	b) Dilution Water Chemistry: pH 7.2, conductivity 75µs, alkalinity 0.58meq/l, Ca 0.46 meq/l, Mg 0.20meq/l, Na+K 0.16meq/l, sulphate 0.18meq/l, Cl 0.06meq/l
	c) Exposure Vessel Type: 20ml Carrel flask
	d) Nominal Concentrations (as mg/l): not described
	e) Stock Solutions Preparations and Stability: prepared in lake water
	f) Number of Replicates: not described
	g) Individuals per Replicates: 5-20
	h) Water Temperature Range: 9.5-10.5 °C
	i) Light Condition: 70 lux, 12 hr/day
	j) Feeding: no
	- Method of Analytical Monitoring: not described
	- Statistical Method:
	a) Data Analysis: Graphic method using log-probit paper
Remark	: LC ₅₀ expressed as anhydrous CaCl ₂ .
Result	: 48h-LC ₅₀ : 19400 mg/l
	95% Confidence limits: 25600-14700 mg/l
Source	: Tokuyama Corporation
Reliability	: (2) valid with restrictions
11.06.2002	Comparable to guideline study with acceptable restrictions
	(4)
Type	: static
Species	: other aquatic crustacea: <i>Eudiaptomus padanus padanus</i>
Exposure period	: 48 hour(s)

Unit	: Mg/l
Analytical monitoring	: No data
LC₅₀	: 11100
Method	: other: not mentioned
Year	: 1974
GLP	: No data
Test substance	: No data
Method	: - Test Organisms: a) Age: Adult b) Average size: 0.43mm c) Supplier/Source: Lake Monate - Test Conditions: a) Dilution Water Source: Lake Monate water b) Dilution Water Chemistry: pH 7.2, conductivity 75µs, alkalinity 0.58meq/l, Ca 0.46 meq/l, Mg 0.20meq/l, Na+K 0.16meq/l, sulphate 0.18meq/l, Cl 0.06meq/l c) Exposure Vessel Type: 20ml Carrel flask d) Nominal Concentrations (as mg/l): not described e) Stock Solutions Preparations and Stability: prepared in lake water f) Number of Replicates: not described g) Individuals per Replicates: 5-20 h) Water Temperature Range: 9.5-10.5 °C i) Light Condition: 70 lux, 12 hr/day j) Feeding: no - Method of Analytical Monitoring: not described - Statistical Method: a) Data Analysis: Graphic method using log-probit paper
Remark	: LC ₅₀ expressed as anhydrous CaCl ₂ .
Result	: 48h-LC ₅₀ : 11100 mg/l 95% Confidence limits: 15100-8100 mg/l
Source	: Tokuyama Corporation
Reliability	: (2) valid with restrictions Comparable to guideline study with acceptable restrictions

11.06.2002

(4)

Type	: static
Species	: other aquatic crustacea: <i>Daphnia hyalina</i>
Exposure period	: 48 hour(s)
Unit	: Mg/l
Analytical monitoring	: No data
LC₅₀	: 8300
Method	: other: not mentioned
Year	: 1974
GLP	: No data
Test substance	: No data
Method	: - Test Organisms: a) Age: Adult b) Average size: 1.27 mm c) Supplier/Source: Lake Monate - Test Conditions: a) Dilution Water Source: Lake Monate water b) Dilution Water Chemistry: pH 7.2, conductivity 75µs, alkalinity 0.58meq/l, Ca 0.46 meq/l, Mg 0.20meq/l, Na+K 0.16meq/l, sulphate 0.18meq/l, Cl 0.06meq/l c) Exposure Vessel Type: 300ml cylindrical glass tube d) Nominal Concentrations (as mg/l): not described e) Stock Solutions Preparations and Stability: prepared in lake water f) Number of Replicates: not described g) Individuals per Replicates: 15-20 h) Water Temperature Range: 9.5-10.5 °C i) Light Condition: 70 lux, 12 hr/day

j) Feeding: no
- Method of Analytical Monitoring: not described
- Statistical Method:
a) Data Analysis: Graphic method using log-probit paper
Remark : LC₅₀ expressed as anhydrous CaCl₂.
Result : 48h-LC₅₀: 8300 mg/l
95% Confidence limits: 11000-6300 mg/l
Source : Tokuyama Corporation
Reliability : (2) valid with restrictions
Comparable to guideline study with acceptable restrictions
11.06.2002 (4)

Type : static
Species : other aquatic worm: *Caenorhabditis elegans*
Exposure period : 24 hour(s)
Unit : Mg/l
Analytical monitoring : yes
LC₅₀ : 44400
Method : other
Year : 1997
GLP : No data
Test substance : No data
Method : - Test Organisms:
a) Strain: Wild type (N2)
b) Average size: not described
- Test Conditions:
a) Dilution Water Source: K-medium
b) Dilution Water Chemistry: 2.36g KCl+3.0g NaCl /l of deionized water
c) Exposure Vessel Type: 12-well tissue culture plate
d) Nominal Concentrations (as mg/l): 6 conc. and control
e) Stock Solutions Preparations and Stability: prepared with the CaCl₂ using K-medium as the diluent
f) Number of Replicates: 6
g) Individuals per Replicates: 9-11
h) Water Temperature Range: 20 °C
i) Light Condition: 70 lux, 12 hr/day
- Method of Analytical Monitoring: atomic absorption spectrophotometer
- Statistical Method:
a) Data Analysis: Probit procedure
Remark : This experiment was repeated three times.
LC₅₀ expressed as anhydrous CaCl₂.
Result : 24h-LC₅₀ (mean±SD): 44400±1000 mg/l (n=3)
Source : Tokuyama Corporation
Reliability : (2) valid with restrictions
Comparable to guideline study with acceptable restrictions
15.07.2002 (99)

Type : static
Species : other aquatic crustacea: *Nitocra spinipes*
Exposure period : 96 hour(s)
Unit : Mg/l
Analytical monitoring : No data
LC₅₀ : 1600
Method : other: not mentioned
Year : 1978
GLP : No data
Test substance : No data
Method : - Test Organisms:
a) Age: adult
b) Average size: 0.7-0.8 mm
- Test Conditions:

a) Dilution Water Source: brakish water
b) Dilution Water Chemistry: salinity; 0.7%, pH; 8.0, alkalinity; 1.5 meqv/l
c) Exposure Vessel Type: Test tube
d) Nominal Concentrations (as mg/l): 10 conc. and control
e) Stock Solutions Preparations and Stability: not described
f) Number of Replicates: 1
g) Individuals per Replicates: 10
h) Water Temperature Range: 20±0.5 °C
i) Light Condition: not described
j) Feeding: no
- Method of Analytical Monitoring: atomic absorption spectrophotometer
- Statistical Method:
a) Data Analysis: Litchfield & Wilcoxon (1949)
Remark : LC₅₀ expressed as anhydrous CaCl₂.
Result : 96h-LC₅₀: 1600 mg/l
95% Confidence limits: 1490-2140 mg/l
Source : Tokuyama Corporation
Test condition : Age/life stage: adult
Temperature: 20 °C
Alkalinity: 75 mg/l CaCO₃
pH: 8.0Salinity: 7 ppt
Unmeasured concentration
Reliability : (2) valid with restrictions
Comparable to guideline study with acceptable restrictions

15.07.2002

(5)

Type : static
Species : *Daphnia magna* (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
Analytical monitoring : yes
LC₅₀ : 1285
Method : other: not mentioned
Year : 1972
GLP : No data
Test substance : other TS: Dihydrate
Method : - Test Organisms:
a) Age: 12±12 hr
b) Pretreatment: not discribed
c) Supplier/Source: University of Michigan, USA
- Test Conditions:
a) Dilution Water Source: Lake Superior water
b) Dilution Water Chemistry:
Table (mg/l except for pH)

Item	Mean	Range
pH	7.74	7.4-8.2
Dissolved O ₂	9	-
Total hardness	45.3	44-53
Alkalinity	42.3	41-50
Cl	1.217	1.17-1.34
Na	1.13	1.09-1.19
Ca	13.695	13-14.7
Mg	3.123	2.94-3.59
K	0.534	0.48-0.59
Sr	0.016	0.012-0.027
Ba	0.014	0.008-0.022
Fe	0.023	0.002-0.083
Mn	-	0.0002-0.0115
Cr	-	0.002-0.02

	Al	-	0.001-0.026
	Zn	0.00078	0.001-0.0027
	Ni	<0.0005	-
	Pb	-	0.007-0.02
	Cu	0.00151	0.0003-0.0032
	Co	<0.0005	-
	Hg	<0.00001	-
	Cd	<0.0001	-
c) Exposure Vessel Type: 40ml conical centrifuge tube			
d) Nominal Concentrations (as mg/l): 0, 86.4, 173, 277, 385, 554, 692, 831, 1110, 1380			
e) Individuals per Replicates: 10			
f) Water Temperature Range: 18 °C			
g) Feeding: suspension of powdered dried grass and enriched trout-fry granules			
- Method of Analytical Monitoring: according to procedures outlined by the American Public Health Association et al.(1960)			
- Statistical Method:			
a) Data Analysis: Litchifield and Wilcoxon			
Remark	:	LC ₅₀ expressed as anhydrous CaCl ₂ .	
Result	:	48h-LC ₅₀ : 1285 mg/l	
Source	:	Tokuyama Corporation	
Reliability	:	(2) valid with restrictions	
Comparable to guideline study with acceptable restrictions			
15.07.2002			(8)
Type	:	static	
Species	:	<i>Daphnia magna</i> (Crustacea)	
Exposure period	:	48 hour(s)	
Unit	:	mg/l	
Analytical monitoring	:	no data	
LC ₅₀	:	3005	
Method	:	other: Anderson et al, (1948)	
Year	:	1965	
GLP	:	no data	
Test substance	:	no data	
Result	:		
		Exposure periode	LC ₅₀ (mg/l)
		24h	3526
		48h	3005
Source	:	Tokuyama Corporation	
Test condition	:	Dilution water source: Standard Reference Water	
Reliability	:	(3) invalid	
Documentation insufficient for assessment			
11.06.2002			(22)
Type	:	static	
Species	:	<i>Daphnia magna</i> (Crustacea)	
Exposure period	:	96 hour(s)	
Unit	:	mg/l	
Analytical monitoring	:	no data	
LC ₅₀	:	649	
Method	:	other: Anderson et al, (1948)	
Year	:	1965	
GLP	:	no data	
Test substance	:	no data	
Result	:		
		Exposure periode	LC ₅₀ (mg/l)

		24h	1838
		48h	759
		72h	759
		96h	649
Source	:	Tokuyama Corporation	
Test condition	:	Dilution water source: grass-wool filtered University Lake water	
Reliability	:	(3) invalid	
		Documentation insufficient for assessment	
11.06.2002			(22)

Type	:	static
Species	:	other aquatic mollusc: <i>Lymnaea</i> sp.
Exposure period	:	96 hour(s)
Unit	:	mg/l
Analytical monitoring	:	no data
LC₅₀	:	2573
Method	:	other: Anderson et al, (1948)
Year	:	1965
GLP	:	no data
Test substance	:	no data
Result	:	

Exposure period	LC ₅₀ (mg/l)
-----------------	-------------------------

24h	4485
48h	3094
72h	3308
96h	2573

Source	:	Tokuyama Corporation	
Test condition	:	Age/life stage: eggs	
		Dilution water source: grass-wool filtered University Lake water	
Reliability	:	(3) invalid	
		Documentation insufficient for assessment	
15.07.2002			(22)

Type	:	
Species	:	<i>Daphnia magna</i> (Crustacea)
Exposure period	:	64 hour(s)
Unit	:	mg/l
Analytical monitoring	:	no
Toxicity threshold	:	920
Method	:	other: Anderson (1944 and 1946)
Year	:	1948
GLP	:	no
Test substance	:	other TS: calculated as anhydrous CaCl ₂
Remark	:	This endpoint can be considered at EC ₅₀ (immobilisation).
Source	:	Tokuyama Corporation
Test condition	:	Dilution water source: Lake Erie water
Reliability	:	(3) invalid
		Documentation insufficient for assessment

10.06.2002 (3)

Type	:	static
Species	:	<i>Daphnia magna</i> (Crustacea)
Exposure period	:	15 minute(s)
Unit	:	mg/l
Analytical monitoring	:	no data
LOEC	:	1332
Method	:	other: not mentioned

Year : 1944
GLP : no data
Test substance : no data
Source : Tokuyama Corporation
Test condition : Age/life stage: 8 hour, young
 Temperature: 25 °C
 Effect endpoint: threshold value for immobilization
Reliability : (3) invalid
 Documentation insufficient for assessment

10.06.2002

(2)

Type :
Species : other: *Polycelis nigra*
Exposure period : 48 hour(s)
Unit : mg/l
Analytical monitoring :
LC₅₀ : 7200
Method : other
Year : 1940
GLP : no data
Test substance : no data
Source : Tokuyama Corporation
Reliability : (3) invalid
 Documentation insufficient for assessment

12.06.2002

(47)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species : *Selenastrum capricornutum* (Algae)
Endpoint : biomass
Exposure period : 72 hour(s)
Unit : mg/l
Analytical monitoring : no
EC₅₀ : 2900
EC₂₀ : 1000
Method : OECD Guide-line 201 "Algae, Growth Inhibition Test"
Year : 1998
GLP : yes
Test substance : as prescribed by 1.1 - 1.4
Method : - Test Organisms:
 a) Supplier/Source (Strain Number): ATCC 22662
 - Test Conditions:
 a) Preculture: was transferred into fresh algal medium 4 days prior to the start of the test
 b) Test Medium: OECD medium
 Table:Composition of algal medium (prepared in ultrapure water)

Compound	Concentration (mg/l)
NH ₄ Cl	15
MgCl ₂ _6H ₂ O	12
CaCl ₂ _2H ₂ O	18
MgSO ₄ _7H ₂ O	15
KH ₂ PO ₄	1.6
FeCl ₃	0.048
Na ₂ EDTA_2H ₂ O	0.10
H ₃ BO ₃	0.19
MnCl ₂ _4H ₂ O	0.42
ZnCl ₂	0.003

CoCl ₂ ·6H ₂ O	0.0015
CuCl ₂ ·2H ₂ O	0.00001
Na ₂ MoO ₄ ·2H ₂ O	0.007
NaHCO ₃	50

- c) Exposure Vessel Type: Erlenmeyer flask
d) Nominal Concentrations (as g/l): 0, 1.0, 1.4, 2.0, 2.8, 4.0
e) Stock Solutions Preparations and Stability: dissolving 4.01g calcium chloride in 1 litre algal medium
f) Number of Replicates: 3 (6 for control)
g) Initial Cell Density: 1.0×10^4 cells/ml
h) Light Condition: wavelength 400-700 nm, Intensity $80.2 \mu\text{E} \cdot \text{m}^{-2} \cdot \text{s}^{-1}$
- Statistical Method:
a) Data Analysis: cell density measurement and calculation according to the formula;

$$A_n = \frac{N_1 - N_0}{2} + \frac{n(n-1) + N_n - 2N_0}{n=2 \quad 2} + [\text{SUM}]$$

where

A_n = biomass integral on day n (area under the growth curve)

N_n = cell density on day n (cells/ml)

Remark : EC_{50} and EC_{20} expressed as anhydrous CaCl₂. The toxic values are shown as added calcium chloride concentration to the system, although calcium chloride is included as part of the test media.

Result : - Table: Measured algal cell densities

Nominal test concentration (mg/l)	Cell density x 10 ⁴ (cells/ml)		
	Day 1	Day 2	Day 3
0	2.494	15.24	77.62
0	2.324	13.05	61.49
0	2.282	14.10	68.88
0	2.409	15.44	74.73
0	2.536	16.15	81.91
0	2.367	13.62	63.51
1000	1.859	9.106	39.74
1000	2.240	13.43	70.85
1000	2.071	12.02	60.09
1400	1.902	10.99	48.54
1400	1.859	10.19	46.84
1400	1.817	10.86	48.29
2000	1.859	17.49	33.98
2000	2.113	15.82	43.79
2000	1.902	12.52	32.03
2800	1.986	12.52	44.04
2800	2.155	8.389	30.73
2800	1.732	9.645	26.78
4000	1.775	8.299	19.88
4000	1.563	6.336	19.26
4000	1.732	11.93	18.35

- Table: Percent biomass inhibition per concentration

Nominal test concentration (mg/l)	Percent growth inhibition
	Area under the growth curve
0	0
1000	21.2
1400	33.6
2000	35.6
2800	47.1
4000	64.9

- Table: Water parameters of test solutions

concentration CaCl ₂ (mg/l)	Temperature (°C)	pH
0	22.2	8.5
1000	22.2	7.5
1400	22.4	7.8
2000	22.2	7.9
2800	22.3	7.9
4000	22.3	7.8

- Table: EC₅₀ and EC₂₀

Hours of exposure	EC ₅₀ (mg/l)	EC ₂₀ (mg/l)
72	2900	1000

Source : Tokuyama Corporation
Reliability : (1) valid without restriction
 OECD Guideline study
Flag : Critical study for SIDS endpoint

15.11.2002

(19)

Species : *Selenastrum capricornutum* (Algae)
Endpoint : growth rate
Exposure period : 72 hour(s)
Unit : mg/l
Analytical monitoring : no
EC₅₀ : > 4000
EC₂₀ : 2700
Method : OECD Guide-line 201 "Algae, Growth Inhibition Test"
Year : 1998
GLP : yes
Test substance : as prescribed by 1.1 - 1.4
Method :
 - Test Organisms:
 a) Supplier/Source (Strain Number): ATCC 22662
 - Test Conditions:
 a) Preculture: was transferred into fresh algal medium 4 days prior to the start of the test
 b) Test Medium: OECD medium
 c) Exposure Vessel Type: Erlenmeyer flask
 d) Nominal Concentrations (as g/l): 0, 1.0, 1.4, 2.0, 2.8, 4.0
 e) Stock Solutions Preparations and Stability: dissolving 4.01g calcium chloride in 1 litre algal medium
 f) Number of Replicates: 3 (6 for control)
 g) Initial Cell Density: 1.0 x 10⁴ cells/ml

h) Light Condition: wavelength 400-700 nm, Intensity 80.2 $\mu\text{E} \cdot \text{m}^{-2} \cdot \text{s}^{-1}$

- Statistical Method:

a) Data Analysis: cell density measurement and calculation according to the formula;

$$\text{The growth rate} = \frac{\ln(N_3/N_0)}{3}$$

Remark : EC_{50} and EC_{20} expressed as anhydrous CaCl_2 . The toxic values are shown as added calcium chloride concentration to the system, although calcium chloride is included as part of the test media.

Result : - Table: Measured algal cell densities

Nominal test concentration (mg/l)	Cell density $\times 10^4$ (cells/ml)		
	Day 1	Day 2	Day 3

0	2.494	15.24	77.62
0	2.324	13.05	61.49
0	2.282	14.10	68.88
0	2.409	15.44	74.73
0	2.536	16.15	81.91
0	2.367	13.62	63.51

1000	1.859	9.106	39.74
1000	2.240	13.43	70.85
1000	2.071	12.02	60.09

1400	1.902	10.99	48.54
1400	1.859	10.19	46.84
1400	1.817	10.86	48.29

2000	1.859	17.49	33.98
2000	2.113	15.82	43.79
2000	1.902	12.52	32.03

2800	1.986	12.52	44.04
2800	2.155	8.389	30.73
2800	1.732	9.645	26.78

4000	1.775	8.299	19.88
4000	1.563	6.336	19.26
4000	1.732	11.93	18.35

- Table: Percent growth rate inhibition per concentration

Nominal test concentration (mg/l)	Percent growth inhibition
	Growth rate

0	0
1000	4.9
1400	9.9
2000	15.5
2800	17.6
4000	31.0

- Table: Water parameters of test solutions

concentration	Temperature	pH
---------------	-------------	----

CaCl ₂ (mg/l)	(°C)	
0	22.2	8.5
1000	22.2	7.5
1400	22.4	7.8
2000	22.2	7.9
2800	22.3	7.9
4000	22.3	7.8

- Table: EC₅₀ and EC₂₀

Hours of exposure	EC ₅₀ (mg/l)	EC ₂₀ (mg/l)
72	> 4000	2700

Source : Tokuyama Corporation
Reliability : (1) valid without restriction
 OECD Guideline study
Flag : Critical study for SIDS endpoint
 15.11.2002

(19)

Species : *Anabaena* sp. (Algae)
Endpoint : other: Increase glycogen and sporulation
Exposure period : 20 day
Unit : mg/l
Analytical monitoring : no data
EC : 110
Method : other: not mentioned
Year : 1980
GLP : no data
Test substance : as prescribed by 1.1 - 1.4
Source : Tokuyama Corporation
Test condition : Static test
 Temperature: 30 °C
 24 hour photoperiod
Reliability : (3) invalid
 Documentation insufficient for assessment
 10.06.2002

(49)

Species : other algae: *Nitzschia linearis*
Endpoint : growth rate
Exposure period : 120 hour(s)
Unit : mg/l
Analytical monitoring : no
LC₅₀ : 3130
Method : other: Cairns, Scheier, Hess (1964)
Year : 1968
GLP : no
Test substance : no data
Source : Tokuyama Corporation
Test condition : Test Medium: synthetic dilution water for diatom
Reliability : (3) invalid
 Documentation insufficient for assessment
 10.06.2002

(84)

Species : *Chlorella vulgaris* (Algae)
Endpoint : biomass
Exposure period : 120 day
Unit : mg/l

Analytical monitoring : no data
LOEC : ≥ 140
Method : other: not mentioned
Year : 1965
GLP : no data
Test substance : other TS: Hexahydrate
Remark : LOEC expressed as anhydrous CaCl_2
Source : Tokuyama Corporation
Test condition : Static test
Room temperature
pH < 7
Effect endpoint: lowest inhibitory concentration
Reliability : (3) invalid
Documentation insufficient for assessment

10.06.2002

(21)

Species : other aquatic plant: *Lemna minor* L.
Endpoint : other: frond number
Exposure period : 14 day
Unit : mg/l
Analytical monitoring :
NOEC : 7200
LOEC : 9600
Method : other
Year : 1998
GLP : no data
Test substance : no data
Result : Frond number of duckweeds exposed to different concentration of tested solution during 14 days.

Conc. (mg/l)	no. at 0day	Relative frond number* by growth periods					
		3day	5day	8day	10day	12day	14day
2400	2.0	0.44	1.69	3.31	7.13	11.56	18.19
Control	2.0	0.50	1.88	3.00	6.38	10.13	14.00
4800	3.25	0.78	1.18	2.34	4.19	6.26	7.24
Control	3.63	0.75	1.40	2.30	3.96	4.75	5.63
7200	3.0	0.42	1.33	1.54	3.17	4.46	6.33
Control	3.0	1.17	1.71	1.93	3.23	3.90	4.29
9600	2.38	0.52	1.10	2.06	3.231	5.10	6.73
Control	2.38	0.69	1.88	3.06	5.96	8.27	11.33

* Relative frond number = $([\text{no. at day } n] - [\text{no. at day } 0]) / [\text{no. at day } 0]$
n=3,5,8,12,14

Source : Tokuyama Corporation
Reliability : (3) invalid
Documentation insufficient for assessment

11.06.2002

(100)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

Type : aquatic
Species : activated sludge, industrial
Exposure period :
Unit : mg/l

Analytical monitoring : no data
NOAEL : = 20000
Method : other
Year : 1985
GLP : no data
Test substance : no data
Source : Tokuyama Corporation
Reliability : (4) not assignable
Only secondary literature

11.06.2002

(98)

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

Species : *Daphnia magna* (Crustacea)
Endpoint : mortality
Exposure period : 21 day
Unit : mg/l
Analytical monitoring : no data
LC₅₀ : 920
Method : other: not mentioned
Year : 1972
GLP : no data
Test substance : no data
Method : - Test Organisms:
a) Age: 12±12 hr
b) Pretreatment: not described
c) Supplier/Source: University of Michigan, USA
- Test Conditions:
a) Dilution Water Source: Lake Superior water
b) Dilution Water Chemistry:
Table (mg/l except for pH)

Item	Mean	Range
pH	7.74	7.4-8.2
Dissolved O ₂	9	-
Total hardness	45.3	44-53
Alkalinity	42.3	41-50
Cl	1.217	1.17-1.34
Na	1.13	1.09-1.19
Ca	13.695	13-14.7
Mg	3.123	2.94-3.59
K	0.534	0.48-0.59
Sr	0.016	0.012-0.027
Ba	0.014	0.008-0.022
Fe	0.023	0.002-0.083
Mn	-	0.0002-0.0115
Cr	-	0.002-0.02
Al	-	0.001-0.026
Zn	0.00078	0.001-0.0027
Ni	<0.0005	-
Pb	-	0.007-0.02
Cu	0.00151	0.0003-0.0032
Co	<0.0005	-
Hg	<0.00001	-
Cd	<0.0001	-

c) Exposure Vessel Type: 250 ml beaker
d) Nominal Concentrations (as mg/l): 0, 86.4, 173, 277, 385, 554, 692, 831, 1110, 1380
e) Number of Replicates: 4
f) Individuals per Replicates: 5
g) Water Temperature Range: 18 °C
h) Light Condition: 16:8h(light:dark)
i) Feeding: suspension of powdered dried grass and enriched trout-fry granules
- Method of Analytical Monitoring: according to procedures outlined by the American Public Health Association et al.(1960)
- Statistical Method:
a) Data Analysis: Litchifield and Wilcoxon(1949)

Remark : LC₅₀ expressed as anhydrous CaCl₂;
Other observations: reproductive impairments, body weight, protein and enzyme activities.

Source : Tokuyama Corporation
Reliability : (2) valid with restrictions
Comparable to guideline study with acceptable restrictions

11.06.2002 (8)

Species : *Daphnia magna* (Crustacea)
Endpoint : reproduction rate
Exposure period : 21 day
Unit : mg/l
Analytical monitoring : no data
EC₅₀ : 610
EC₁₆ : 320
Method : other: not mentioned
Year : 1972
GLP : no data
Test substance : no data
Method : - Test Organisms:
a) Age: 12±12 hr
b) Pretreatment: not discribed
c) Supplier/Source: University of Michigan, USA
- Test Conditions:
a) Dilution Water Source: Lake Superior water
b) Dilution Water Chemistry:
Table (mg/l except for pH)

Item	Mean	Range
pH	7.74	7.4-8.2
Dissolved O ₂	9	-
Total hardness	45.3	44-53
Alkalinity	42.3	41-50
Cl	1.217	1.17-1.34
Na	1.13	1.09-1.19
Ca	13.695	13-14.7
Mg	3.123	2.94-3.59
K	0.534	0.48-0.59
Sr	0.016	0.012-0.027
Ba	0.014	0.008-0.022
Fe	0.023	0.002-0.083
Mn	-	0.0002-0.0115
Cr	-	0.002-0.02
Al	-	0.001-0.026
Zn	0.00078	0.001-0.0027

	Ni	<0.0005	-
	Pb	-	0.007-0.02
	Cu	0.00151	0.0003-0.0032
	Co	<0.0005	-
	Hg	<0.00001	-
	Cd	<0.0001	-

	c) Exposure Vessel Type: 250 ml beaker		
	d) Nominal Concentrations (as mg/l): 0, 86.4, 173, 277, 385, 554, 692, 831, 1110, 1380		
	e) Number of Replicates: 4		
	f) Individuals per Replicates: 5		
	g) Water Temperature Range: 18 °C		
	h) Light Condition: 16:8h(light:dark)		
	i) Feeding: suspension of powdered dried grass and enriched trout-fry granules		
	- Method of Analytical Monitoring: according to procedures outlined by the American Public Health Association et al.(1960)		
	- Statistical Method:		
	a) Data Analysis: Litchifield and Wilcoxon(1949)		
Remark	:	Effect endpoint: 16 and 50 % reproductive impairment; EC ₅₀ expressed as CaCl ₂ ; Other observations: body weight, protein and enzyme activities.	
Source	:	Tokuyama Corporation	
Reliability	:	(2) valid with restrictions Comparable to guideline study with acceptable restrictions	
15.07.2002			(8)
Species	:	other aquatic arthropod: <i>Tropisternus lateralis</i>	
Endpoint	:	other: histological effect	
Exposure period	:	14 day	
Unit	:	mg/l	
Analytical monitoring	:	no data	
EC	:	110	
Method	:	other: not mentioned	
Year	:	1969	
GLP	:	no data	
Test substance	:	no data	
Remark	:	Effect endpoint: damage to gut; No visible damage to gut at tested concentration; EC ₅₀ expressed as anhydrous CaCl ₂ .	
Source	:	Tokuyama Corporation	
Test condition	:	Age/life stage: adult Flow-through test pH: 7 Deionized water	
Reliability	:	(3) invalid Documentation insufficient for assessment	
10.06.2002			(108)

4.6.1 TOXICITY TO SOIL DWELLING ORGANISMS

Type	:	other
Species	:	<i>Eisenia fetida</i> (Worm (Annelida), soil dwelling)
Endpoint	:	
Exposure period	:	42 day
Unit	:	other: g/m ²
LC₂₀	:	30
Method	:	other

Year : 1999
GLP : no
Test substance : no data
Method : -Test organisms:
a) Size(Length and Weight): 5.4-6.9 cm in length, 0.16-0.38 g in body weight
b) Age: not described
-Test conditions:
a) Exposure vessel type:
b) Test concentrations (as g/m²): 0 and 5 (at the starat)
c) Vehicle/Solvent and concentrations: Not used
d) Method of application: Five g per m² of the test substance were applied every week for 6 weeks.
e) Number of replicates: five vessels per treatment
f) Individuals per replicates: five earthworms per replicate
g) Temperature range: 25°C
-Analytical monitoring: not described
Result : Table. Cumulative mortality after application of CaCl₂

Treatment	Cumulative mortality (%)			
	1 week	3 weeks	5 weeks	6weeks
Control	0	0	0	5
5 g/m ² X 6	0	0	0	20

Extent of the damage
CaCl₂ < CMA* < NaCl < Urea
* Calcium/Magnesium acetate
Reliability : (3) invalid
Documentation insufficient for assessment

10.06.2002

(35)

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

Method :
Year : 1984
GLP :
Test substance :
Remark : High concentrations of calcium chloride in irrigation water will reduce plant growth. The chloride ion threshold limit for chronic plant toxicity is 100 ppm.
A number of studies have been conducted on the effects of calcium chloride and sodium chloride as a result of their use as road de-icers. Damage to roadside vegetation has been reported and is attributed largely to the absorption of salt splashed on foliage. In one study, sugar maples were exposed to runoff of NaCl and CaCl₂ for 6 winters (total treatment of 112 tonnes/ha per treatment and 15 treatments per winter at weekly intervals). Leaves of these maple trees contained 3 to 6 times the chloride (Cl⁻) concentration compared to a control stand. Damage to the maples varied but could be correlated with the chloride concentration in the leaf: 0.5 to 6 mg/g dry weight - little damage; 4 to 10 mg/g – slight damage; and >10 mg/g - severe damage. Conifers are probably more susceptible to salt spray than other vegetation.
Although they do not grow during winter, they remain photosynthetically active; salt splashed onto the needles would thus have damaging effects. Grasses are less susceptible than conifers to damage probably because of

their inactivity in winter. In a series of tests, Kentucky 31 Fescue was found to be the most resistant of grasses and could tolerate up to 5 g NaCl/kg of soil. Several studies have shown foliage damage where salt was employed and have correlated this to the high level of chloride (Cl⁻) in foliage and twigs. Some studies have noted a higher occurrence of damage on the downwind portion of roads, thus indicating that sprayed salt has a higher potential for damage than that transmitted through the soil.

A generally accepted index of crop response to salt (applicable to CaCl₂) is as follows:

g/l of soil	Effect on Yield
0-1.3	Salinity effects negligible
1.3-2.6	Yields of sensitive crops affected
2.6-5.1	Yields of many crops restricted
5.1-10.2	Only tolerant crops yield satisfactorily
>10.2	Only a few very tolerant crops yield satisfactorily

Source : Tokuyama Corporation
Reliability : (2) valid with restrictions
Documentation sufficient for assessment

11.06.2002 (28)

Method :
Year : 1989
GLP :
Test substance : no data
Remark : NaCl and CaCl₂ are frequently used as deicing agents during the winter season. This study compares the effect of these deicing salts on salt injury on spruce trees. From two field experiments carried out for ten weeks during winter period, and a total dose of 1.5 kg/m² NaCl, CaCl₂ or a 72/25 NaCl/CaCl₂ mixture, it was found that the presence of calcium clearly reduced the salt injury as was indicated by salt tolerance rating. These rating corresponded well to the Cl⁻ concentrations found in needles and twigs. Though an equal dose of Cl⁻ was given, in the presence of CaCl₂ the uptake of Cl⁻ was inhibited. Surely the role of calcium on ion permeability in salinized soil should have its effect, together with the regulatory role that calcium has on ion accumulation and transport. Furthermore it was found that the climatic conditions and the calcium status of the soil only have an effect on the time of appearance of the injury.

Reliability : (2) valid with restrictions
Documentation sufficient for assessment

11.06.2002 (9)

Species : other terrestrial plant: several trees
Endpoint : other: damage to leaves
Exposure period : 60 - 100 day
Unit :
Method : other
Year : 1975
GLP : no
Test substance : no data
Result : Tolerance for trees as antifreezing agent
- White birch 1 g/l
- Acacia 5 g/l
- Poplar 2.5 g/l
- Todo fir 0.5 g/l

Source : Tokuyama Corporation
Reliability : (3) invalid
Documentation insufficient for assessment

11.06.2002 (44)

Species : other terrestrial plant: Crops
Endpoint : other: germination and growth
Exposure period : 3 - 6 day
Unit : g/l
LOAEL : 2 - 3
Method : other
Year : 1962
GLP : no
Test substance : no data
Result : Table: LOAEL (g/l)

Crops	Budding	Growth
Paddy-field rice	2	2
Wheat	3	2
Beer wheat	3	---
Rapeseed	2	---
Japanese radish	2	---
Welsh onion	2	2

Source : Tokuyama Corporation
Reliability : (3) invalid
Documentation insufficient for assessment

11.06.2002

(55)

Species : other terrestrial plant: *Trifolium repens* L.
Endpoint : other: leaves surface destroyed
Exposure period : 35 day
Unit : g/m²
EC₀ : < 93.9
Method : other
Year : 1997
GLP : no
Test substance : no data
Method : -Test conditions:
Test treatments (as total dose g/m²): < 93.9, 187.5 and 750
Number of replicates: Seven seedlings per treatment
-Analytical monitoring: atomic absorption spectrophotometer
Result : Table. Survival rate of *Trifolium repens* L.

Application concentration (ppm)	Total dose applied for experiment. (g/m ²)	Survival rate(%)
< 5000	< 93.9	100
100000	187.5	85.7
400000	750	28.6

Extent of the damage
CaCl₂ < NaCl < CMA*
* Calcium/Magnesium acetate

Reliability : (3) invalid
Documentation insufficient for assessment

11.06.2002

(37)

Species : other terrestrial plant
Endpoint : other: leaves surface destroyed
Exposure period : 105 day
Unit :

Method : other
Year : 1999
GLP : no
Test substance : no data
Method : -Test organisms:
a) Size(Length and Weight): *Taxus cuspidata* ;15.9 cm, *Pinus mugo*;45 cm
b) Age: *Taxus cuspidata*; 3 year, *Pinus mugo*; 7 year, *Trifolium respens* L.; 1 year
-Test conditions:
a) Exposure vessel type: plastic pot for *Trifolium respens* L.
b) Test treatments: 0, 5, 25, 50 and 100 g/m² per week
c) Method of application: The desired amount of the aqueous test substance was neblized with a spray pump every week for 15 weeks.
d) Number of replicates: five seedlings per treatment for *Pinus mugo*, 7 seedlings per treatment for *Taxus cuspidata* and *Trifolium respens* L.
-Analytical monitoring: not described
Result : Table. EC₅₀ of CaCl₂ to three plants

Species	EC ₅₀ (g/m ²)
<i>Taxus cuspidata</i>	5-25
<i>Pinus mugo</i>	5-25
<i>Trifolium respens</i> L	50-100

Extent of the damage
CaCl₂ < CMA40* < NaCl < Urea
* Calcium/Magnesium acetate: 40%, NaCl: 60%
Reliability : (3) invalid
Documentation insufficient for assessment

10.06.2002

(35)

Species : other terrestrial plant
Endpoint : other: leaves surface destroyed
Exposure period : 11 day
Unit : g/m²
EC₁₀₀ : 5
Method : other
Year : 1999
GLP : no
Test substance : no data
Method : -Test organisms:
a)Size(Length and Weight): *Salix sachalinensis*; 30 cm(scion)
b) Age: 2-3 year
-Test conditions:
a) Exposure vessel type: not described
b) Test treatments: 0, 5, 25, 50 and 100 g/m²
c) Method of application: The desired amount of the aqueous test solution was added into each treatment.
d) Number of replicates: seven scions per treatment
e) Temperture range: 25°C
-Analytical monitoring: not described
Result : Table. EC₅₀ of CaCl₂ to *Salix sachalinensis*

Species	EC ₅₀ (g/m ²)
<i>Salix sachalinensis</i> (scion)	=< 5

Reliability : Extent of the damage
CaCl₂ < NaCl < urea, CMA40*
* Calcium/Magnesium acetate: 40%, NaCl: 60%
(3) invalid
Documentation insufficient for assessment
10.06.2002 (35)

Species : other terrestrial plant
Endpoint : other: leaves surface destroyed
Exposure period : 105 day
Unit :
Method : other
Year : 2000
GLP : no
Test substance : no data
Method : -Test organisms:
a) Size(Length and Weight): not described
b) Age: *Taxus cuspidata*; 3 year, *Trifolium respens* L.; 1 year
-Test conditions:
a) Exposure vessel type: Plastic pot for *Trifolium respens* L.
b) Test treatments: 0, 0.25, 1.25, 2.5, 12.5 and 25 g/m² per week for *Taxus cuspidata*, 0, 0.25, 2.5 and 25 g/m² per week for *Trifolium respens* L.
c) Method of application: The desired amount of the aqueous test substance was neblized with a spray pump every week for 5-15 weeks.
d) Number of replicates: five seedlings per treatment for *Trifolium respens* L, 7 seedlings per treatment for *Taxus cuspidata*
-Analytical monitoring: not described
Result : Table. EC₅₀ of CaCl₂ to *Taxus cuspidata* and *Trifolium respens* L.

Species	EC ₅₀ as total dose applied (g/m ²)		
	Application times		
	5	10	15
<i>Taxus cuspidata</i>	>125	>250	8.75-37.5
<i>Trifolium respens</i> L	>125	>250	37.5-375

Reliability : Extent of the damage
CaCl₂, CMA* < NaCl, Urea, MgCl₂
* Calcium/Magnesium acetate
(3) invalid
Documentation insufficient for assessment
11.06.2002 (36)

4.6.3 TOXICITY TO OTHER NON-MAMM. TERRESTRIAL SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

Memo : Mineral Nutrition
Remark : The effect of calcium chloride is attributed by calcium and chloride ions because of its dissociation property in water phase. Both calcium and chloride are one of the nutrient elements for plant.

- Calcium -
The calcium content of plants varies between 0.1 and > 0.5% of dry weight depending on the growing conditions, plant species, and plant organ. In well-balanced growing nutrient solutions with controlled pH, maximal

growth rates were obtained at calcium supply levels of 2.5 - 100 µM. Also, calcium can be supplied at high concentration and might reach more than 10% of the dry weight without symptoms of toxicity or serious inhibition of plant growth, at least in calcicole plant species.

Typical symptom of calcium deficiency is the disintegration of cell walls and the collapse of the affected tissues, such as the petioles and upper parts of the stems. Low tissue contents of calcium in fleshy fruits also increase the losses caused by enhanced senescence of the tissue and by fungal infections.

The proportion of calcium pectate in the cell walls is also of importance for the susceptibility of the tissue to fungal and bacterial infections and for the ripening of fruits.

Calcium has the role in counterbalancing the harmful effects of high concentrations of other cations at the plasma membrane. In the absence of an exogenous calcium supply, root extension quickly ceases.

Transient increase in cytosolic free Ca^{2+} concentration which is activated by auxin stimulates the synthesis of cell wall precursors in the cytosol and its secretion into the apoplast. Also, calcium is required for the formation of secretory vesicles and their fusion with the plasma membrane leading to exocytosis. The secretion is triggered by a rise in cytosolic free Ca^{2+} concentration from about 0.1 to 1.0 µM or even higher.

In plant species which preferentially synthesize oxalate in response to nitrate reduction, the formation of calcium oxalate in the vacuoles is important for maintenance of a low cytosolic free Ca^{2+} concentration. The formation of sparingly soluble calcium oxalate is also important for the osmoregulation of cells and provides a means of salt accumulation in vacuoles of nitrate-fed plants without increasing the osmotic pressure in the vacuoles.

- Chloride -

In plant species with relatively low chloride requirement (<1 mg Cl/g) the demand can be covered by a concentration of 100 µM Cl^- in the nutrient solution; at 10 µM Cl^- supply the shoot dry weight drops to 50%, indicating that the selectivity of chlorine uptake is not very high as compared, for example, with phosphorus, where the much higher requirement in the leaf dry weight can be covered by supply of even less 10 µM. In most plant species the Cl^- requirement for optimal growth is in the range of 0.2-0.4 mg/g dry matter.

Chloride has a role on photosynthetic O_2 evolution.

Chloride has also important functions in osmoregulation at different levels. At the usually high plant contents it is a main osmoticum in the vacuoles of the bulk tissue (50-150 mM Cl^-), together with potassium. At low contents which are in the range of micronutrient (~1 mM Cl^- or below), these osmoregulatory.

Opening and closure of stomata is mediated by fluxes of potassium and accompanying anions such as malate and chloride. Thus, chlorine can play an essential role in stomatal regulation. Chloride can stimulate the proton-pumping ATPase.

Reliability

- : (2) valid with restrictions
- : Documentation sufficient for assessment

10.06.2002

(70)

Memo Remark

- : The Effects of Calcium on Growth and Morphogenesis
- : Calcium is an essential element which regulates both the development and growth of a alga. The literature offers many strong suggestions that this element is necessary for processes such as activation of several enzymes, cell division, cell wall formation, colony formation, nitrogen fixation in

	bacteria, reduction of the toxicity of other element, and reproduction. Some reports show that Calcium deficiency causes a general degeneration of cytoplasmic organelles which are important for vital processes such as cell wall formation, photosynthesis, protein synthesis and respiration.
Reliability	: (2) valid with restrictions Documentation sufficient for assessment
11.06.2002	(85)

4.8 BIOTRANSFORMATION AND KINETICS

Type	: plant
Remark	: - Calcium - In the apoplasm, part of the calcium is firmly bound in structures, another part is exchangeable at the cell walls and at the exterior surface of the plasma membrane. A high proportion of calcium might be sequestered in vacuoles whereas its concentration in the cytosol is extremely low. The same is true for the mobility of calcium in the symplasm from cell to cell and in the phloem. Most of the functions of calcium as a structural component of macromolecules are related to its capacity for coordination, by which it provides stable but reversible intermolecular linkages, predominantly in the cell walls and at the plasma membrane.
	- Chlorine - Chloride is readily taken up by plants and its mobility in short- and long-distance transport is high. In plants chlorine occurs mainly as a free anion of is loosely bound to exchange sites.
Reliability	: (2) valid with restrictions Documentation sufficient for assessment
10.06.2002	(70)

4.9 ADDITIONAL REMARKS

5.1.1 ACUTE ORAL TOXICITY

Type : LD₅₀
Species : rabbit
Strain : New Zealand white
Sex : male
Number of animals : 8
Vehicle : other: gelatin capsule
Value : 500 - 1000 mg/kg bw
Method : other
Year : 1986
GLP : yes
Test substance : other TS
Remark : [Test substance]

Anhydrous calcium chloride (CaCl₂), a white powder, prepared from calcium chloride dihydrate flakes (Batch No. Solvay Couillet 8/OCT/1985 FLAKES). The test material was solid at the application time. Upon analysis sample contained: 97.0% CaCl₂, 2.2% NaCl and 0.11% Ca(OH)₂.

[Method]

The method was in principle equivalent to OECD Guideline 401, except that only 2 doses were employed in this study.

[Test condition]

Single doses of anhydrous calcium chloride were given by a dosing-gun to fasted male rabbits. Three and five rabbits were used for the doses of 500 and 1000 mg/kg, respectively.

During the experiments the animals had free access to food, except from 16 hours prior to dosing until 6 hours after dosing. Water was available ad libitum. The animals were weighed one day before and at 2, 7 and 14 days after dosing.

The rabbits were observed frequently the first day of dosing and, thereafter on each day till the end of the experiment.

Any sign of intoxication of the animals during 14-day observation period was recorded. Gross post-mortem examination was made on all dead animals. The surviving animals were killed by Nembutal[®] injection in the ear vein and autopsied.

[Result]

- Table 1: Summary of the observed signs in the acute oral toxicity study with anhydrous calcium chloride in rabbits.

Dose levels (mg/kg)	no.dead/ no.treated M	Signs
1000	5/5	One rabbit died immediately after dosing by choking. One rabbit died about 45 minutes after dosing. The following signs were observed: respiratory difficulties, cyanosis and convulsions. One rabbit died within two hours after dosing. Two other rabbits were killed in moribund state,
one		about 30 minutes after dosing and one 6 days after dosing. This latter animal did not eat and drink after dosing.
500	1/3	One rabbit died immediately after dosing in

convulsion. The rabbit is probably choked. At autopsy capsules were found in the trachea. In the surviving animals, no signs were observed, but one rabbit did not eat and drink the first two days after dosing.

The surviving rabbits of the 500 mg/kg group lost weight in the first two days after dosing, thereafter the rabbits recovered.

- Table 2: Individual body weight of the rabbits (kg)

Dose (mg/kg)	Animal No.	Pre-Dosing	2 days after dosing	7 days after dosing	14days after dosing
1000	1	2.30	-(a)	-(a)	-(a)
	2	2.55	-(b)	-(b)	-(b)
	3	2.86	-(a)	-(a)	-(a)
	4	2.46	2.14	2.07(c)	-(b)
	5	2.70	-(a)	-(a)	-(a)
500	6	2.95	-(a)	-(a)	-(a)
	7	2.66	2.41	2.68	2.75
	8	2.93	2.90	3.11	3.07

(a) rabbit died

(b) rabbit killed in moribund state

(c) weight 6 days after dosing.

Rabbit was killed on that day in moribund state.

- Table 3: Mean body weight-gain of the rabbits (kg)

Dose (mg/kg)	0-2 days after dosing	2-7 days after dosing	7-14 days after dosing
1000	-0.32(a)	- (b)	- (b)
500	-0.14(c)	0.24(c)	0.01(c)

(a) n=5

(b) rabbits died or killed

(c) n=2

Autopsy of the rabbits that died as a result of treatment or the rabbits that were killed in moribund state, mainly revealed severe ulcers in the fundus of the stomach, haemorrhagic trachea and stomach, red areas on lungs, an irritated throat, and an oedematous oesophagus. In the two surviving rabbits of the 500 mg/kg group, no abnormalities were detected.

- Table 4: The autopsy findings of interim deaths

Autopsy findings	1000 mg/kg	500 mg/kg
Muzzle: wet	1	
blood staining, slight	3	1
Oesophagus, upper: capsules sticking on the wall	2	1
oedematous	2	
Throat: irritated by capsules, white	2	

Trachea:	haemorrhagic wall	3	
	mucoïd/foam	3	
Lungs:	red areas	1	
	not collapsed	4	1
Stomach:	fundus with severe ulcers	4	
	haemorrhagic areas/spots	2	
Interim deaths		5	1

Source : Tokuyama Corporation
Reliability : (1) valid without restriction
Comparable to OECD guideline study
Flag : Critical study for SIDS endpoint

10.06.2002

(56)

Type : LD₅₀
Species : rabbit
Strain : New Zealand white
Sex : male
Number of animals : 9
Vehicle : other: gelatin capsule
Value : 1000 mg/kg bw
Method : other
Year : 1986
GLP : yes
Test substance : other TS
Remark : [Test substance]
Calcium chloride dihydrate (CaCl₂·2H₂O), a white powder, prepared from calcium chloride dihydrate flakes (Batch No. Solvay Couillet 8/OCT/1985 FLAKES). The test sample was solid at the application time. Upon analysis sample contained: 76.7% CaCl₂, 1.8% NaCl and 0.08% Ca(OH)₂.

[Method]

The method was in principle equivalent to OECD Guideline 401, except that only 2 or 3 animals were used for each dose.

[Test condition]

Single doses of calcium chloride dihydrate were given with a dosing-gun to fasted male rabbits. Two rabbits were used for each dose group, except three for the 2000 mg/kg group.

During the experiments the animals had free access to food, except from 16 hours prior to dosing until 6 hours after dosing. Water was available ad libitum. The animals were weighed one day before and at 2, 7 and 14 days after dosing.

The rabbits were observed frequently the first day of dosing and, thereafter on each day till the end of the experiment.

Any sign of intoxication of the animals during 14-day observation period was recorded. Gross post-mortem examination was made on all animals that died during the observation period. The surviving animals were killed by Nembutal[®] injection in the ear vein and autopsied.

[Result]

- Table 1: Summary of the observed signs in the acute oral toxicity study with calcium chloride dihydrate in rabbits.

Dose levels (mg/kg)	no.dead/ no.treated M	Signs
2000	1/2*	One rabbit died 24 hours after dosing. The

following signs were observed: alternately increase and decrease in respiratory rate, diminished body tone, ptosis, miosis.

The surviving rabbit did not eat very well from two days after dosing, till 6 days after dosing. Time of onset of most signs was between 0-2 hours after dosing, and had disappeared 4 hours after dosing in the surviving rabbit.

1000	1/2	One rabbit died three days after dosing. The following signs were observed: diminished locomotor activity, diminished respiratory rate and, respiratory difficulties, diminished startle-response, salivation, ptosis. The rabbits didn't eat after dosing until death (one rabbit) or until 6 days after dosing. Signs in the surviving rabbit had disappeared 5 days after dosing. Time of onset of most signs was between 0-3 hours after dosing.
500	0/2	One rabbit did not eat well till three days after dosing. No other signs were observed.
250	0/2	No signs were observed.

* One rabbit (No.2) not included in this table because it broke its back during dosing (received dose 932 mg/kg), and was killed for humane reasons 6 hours after dosing.

All surviving rabbits lost weight in the first two days after dosing, except one out of two rabbits of the 250 mg/kg group. Thereafter the rabbits recovered, but weight gain was rather poor.

- Table 2: Individual body weight of the rabbits (kg)

Dose (mg/kg)	Animal No.	Pre- Dosing	2 days after dosing	7 days after dosing	14 days after dosing
2000	1	2.75	2.36	2.41	2.68
	2	3.02	-(a)	-(a)	-(a)
	3	2.87	-(b)	-(b)	-(b)
1000	4	3.20	2.90	2.96	3.09
	5	3.43	2.88	-(a)	-(a)
500	6	3.03	2.99	3.01	3.04
	7	3.23	3.00	3.14	3.23
250	8	3.17	3.20	3.24	3.32
	9	3.56	3.50	3.51	3.67

(a) rabbit broke his back during dosing (received dose 932 mg/kg) and was killed 6 hours after dosing for humane reasons

(b) rabbit died

- Table 3: Mean body weight-gain of the rabbits (kg)

Dose (mg/kg)	0-2 days after dosing	2-7 days after dosing	7-14 days after dosing
-----------------	-----------------------------	-----------------------------	------------------------------

2000	-0.39(a)	0.05(a)	0.27(a)
1000	-0.43(b)	0.06(a)	0.13(a)
500	-0.13(b)	0.08(b)	0.06(b)
250	-0.01(b)	0.03(b)	0.12(b)

(a) n=1

(b) n=2

Autopsy of the rabbits that died as a result of treatment, mainly revealed haemorrhagic trachea, severe ulcers in the stomach, dark areas on the lungs and an accentuated hepatic pattern and pale areas in the liver. The surviving animals of the 500, 1000, 2000 mg/kg group had old ulcers in the stomach 14 days after dosing.

- Table 4: The autopsy findings of interim deaths

Autopsy findings	2000 mg/kg	1000 mg/kg
Muzzle wet	1	
with blood		1
Throat and tongue with scar-tissue		1
Trachea partly haemorrhagic with white spots		1
Lung: emphysema and dark areas		1
Stomach: ulcers(s), severe	1	1
distended	1	
Liver: hepatic pattern and pale areas	1	
Autolysis	1	1
Interim deaths	1	1

Source : Tokuyama Corporation
Reliability : (1) valid without restriction
Comparable to OECD guideline study

10.06.2002

(58)

Type : LD₅₀
Species : rabbit
Strain : New Zealand white
Sex : male
Number of animals : 8
Vehicle : other: gelatin capsule
Value : 1000 mg/kg bw
Method : other
Year : 1986
GLP : yes
Test substance : other TS
Remark : [Test substance]
Calcium chloride hexahydrate (CaCl₂·6H₂O), a white powder, prepared from calcium chloride dihydrate (Batch No. Solvay Couillet 8/OCT/1985 FLAKES). The test material was solid at application time. Upon analysis sample contained: 50.2% CaCl₂, 1.2% NaCl and 0.05% Ca(OH)₂.

[Method]

The method was in principle equivalent to OECD Guideline 401, except that only 1 or 2 animals were used for each dose group.

[Test condition]

Single doses of calcium chloride hexahydrate were given in gelatin capsules with a dosing-gun. The doses were 100, 200, 500, 1000 and 2000 mg/kg. During the experiments the animals had free access to food, except

from 16 hours prior to dosing until 6 hours after dosing. Water was available ad libitum. The animals were weighed one day before and at 2, 7 and 14 days after dosing. The rabbits were observed frequently the first day of dosing and, thereafter on each day till the end of the experiment. Any sign of intoxication of the animals during 14-day observation period was recorded. Gross post-mortem examination was made on all dead animals. The surviving animals were killed by Nembutal® injection in the ear vein and autopsied.

[Result]

- Table 1: Summary of the observed signs in the acute oral toxicity study with calcium chloride hexahydrate in rabbits.

Dose levels (mg/kg)	no.dead/ no.treated M	Signs
2000	1/1	The rabbit died during dosing in convulsion, after it had received 1.43 g/kg.
1000	1/2	One rabbit died eight days after dosing. The following signs were observed: diminished locomotor activity, dark skin colour at the first day, thereafter pale skin colour salvation, diminished respiratory rate and, respiratory difficulties, diminished alertness and startle-response, abnormal body posture and gait, ptosis, hypothermia. The died rabbit did not eat and from day 4 onwards also, no water consumption was noted. The surviving rabbit recovered after one day. Signs had disappeared 2 days after dosing. Time of onset of most signs was within 1 hour after dosing.
500	0/2	No signs were observed.
200	0/1	No signs were observed.
100	0/2	No signs were observed.

Especially the surviving rabbit of the 1000 mg/kg group lost weight in the first week after dosing, thereafter the rabbits recovered. In the other dose groups the effects on weight gain were less

- Table 2: Individual body weight of the rabbits (kg)

Dose (mg/kg)	Animal No.	Pre-Dosing	2 days after dosing	7 days after dosing	14days after dosing
2000	1	2.45	-(a)	-(a)	-(a)
1000	2	2.47	2.13	1.74	-(a)
	3	2.45	2.23	2.30	2.48
500	4	2.46	2.41	2.40	2.50
	5	2.32	2.33	2.44	2.50
200	6	2.65	2.69	2.83	2.98

100	7	2.55	2.56	2.52	2.68
	8	2.16	2.23	2.20	2.47

(a) rabbit died

- Table 3: Mean body weight-gain of the rabbits (kg)

Dose (mg/kg)	0-2 days after dosing	2-7 days after dosing	7-14 days after dosing
2000	(a)	(a)	(a)
1000	-0.28(b)	-0.16(b)	0.18(c)
500	-0.02(b)	0.05(b)	0.08(b)
200	0.04(c)	0.14(c)	0.15(c)
100	0.04(b)	-0.04(b)	0.22(b)

(a) rabbit diet

(b) n=2

(c) n=1

Autopsy of the rabbits that died as a result of treatment or the rabbits, mainly revealed a haemorrhagic trachea and perforation and/or severe ulceration of the stomach. Two surviving rabbits, one in the 500, and another in the 1000 mg/kg group, had haemorrhagic tracheas, and the rabbit of the 200 mg/kg group had a white spot on the heart.

- Table 4: The autopsy findings of interim deaths

Autopsy findings	2000 mg/kg	1000 mg/kg
Muzzle with blood	1	
Trachea wall thickened, white precipitate haemorrhagic and foam	1	1
Lungs: tissue hardened	1	
not collapsed	1	1
partly gray staining and pale		1
dark	1	
Heart: right part with jelly, left is pale		1
Stomach: fundus with severe ulcers		1
haemorrhagic areas		1
brown mucus		1
perforated	1	
Spleen: small		1
Autolysis		1
Interim deaths	1	1

- Table 5: The autopsy findings of the surviving animals.

Autopsy findings	1000 mg/kg	500 mg/kg	200 mg/kg
Trachea: haemorrhagic	1	1	1
Heart: white spot			1
Interim deaths	1	1	1

Source : Tokuyama Corporation
Reliability : (1) valid without restriction
Comparable to OECD guideline study
10.06.2002 (59)

Type : LD₅₀
Species : rabbit
Strain : New Zealand white
Sex : male
Number of animals : 6
Vehicle : water
Value : 1000 mg/kg bw
Method : other
Year : 1986
GLP : yes
Test substance : other TS
Remark : [Test substance]
Calcium chloride 33%, a colorless, clear liquid (Batch No. Solvay Couillet RS1 21/FEB/1986). Upon analysis sample contained: 33.1% CaCl₂, 1.1% NaCl and 0.07% Ca(OH)₂.

[Method]

The method was in principle equivalent to OECD Guideline 401, except that only one or two animals were used for each dose.

[Test condition]

The test material was given by a gastric intubation via a cannula. The numbers of animals used were as follows: 1 rabbit each for 250 and 500 mg/kg groups; and 2 rabbits each for 1000 and 2000 mg/kg groups. During the experiments the animals had free access to food, except from 16 hours prior to dosing until 6 hours after dosing. Water was available ad libitum. The animals were weighed one day before and at 2, 7 and 14 days after dosing. The rabbits were observed frequently the first day of dosing and, thereafter on each day till the end of the experiment. Any sign of intoxication of the animals during 14-day observation period was recorded. Gross post-mortem examination was made on all dead animals. The surviving animals were killed by Nembutal[®] injection in the ear vein and autopsied.

[Result]

- Table 1: Summary of the observed signs in the acute oral toxicity study with calcium chloride 33 % in rabbits.

Dose levels (mg/kg)	no.dead/ no.treated M	Signs
2000	1/2	One rabbit was found dead 29 hours after dosing. The following signs were observed: positional passivity, diminished respiratory rate and respiratory difficulties, diminished locomotor activity, abnormal body posture and gait, diminished alertness and startle-response. The onset of signs was between 7 and 24 hours. These signs were moderate to severe in intensity. In the other rabbit no signs were observed.
1000	1/2	One rabbit was killed 5 days after dosing, because

of a broken back, this animal had less food-consumption.
No signs were observed in the other rabbit.

500	0/1	No signs were observed.
250	0/1	No signs were observed.

The rabbits of all dose groups lost weight the first two days after dosing, except the surviving rabbit of the 2000 mg/kg group. Thereafter the rabbits recovered with exception of the surviving rabbit in the 2000 mg/kg group, which recovered in the second week after dosing.

- Table 2: Individual body weight of the rabbits (kg)

Dose (mg/kg)	Animal No.	Pre-Dosing	2 days after dosing	7 days after dosing	14 days after dosing
2000	1	3.12	3.30	3.12	3.24
	2	2.98	-(a)	-(a)	-(a)
1000	3	3.68	3.24	-(b)	-(b)
	4	3.66	3.43	3.56	3.68
500	5	3.60	3.49	3.53	3.60
250	6	3.40	3.33	3.35	3.48

(a) rabbit died

(b) rabbit was killed, because of a broken back

- Table 3: Mean body weight-gain of the rabbits (kg)

Dose (mg/kg)	0-2 days after dosing	2-7 days after dosing	7-14 days after dosing
2000	0.18(a)	-0.18(a)	0.12(a)
1000	-0.33(b)	0.13(a)	0.12(a)
500	-0.11(a)	0.04(a)	0.07(a)
250	-0.07(a)	0.02(a)	0.13(a)

(a) n=1

(b) n=2

Autopsy of the rabbits of the 2000 and 1000 mg/kg group, that died as a result of treatment or that were killed, mainly revealed perforation and ulcers of the stomach, haemorrhagic intestine and a distended urine bladder. In the surviving rabbits no abnormalities were detected.

- Table 4: The autopsy findings of interim deaths

Autopsy findings	2000 mg/kg	1000 mg/kg
Hydrothorax, slight	1	
Stomach: perforation	1	
ulcers and haemorrhagic spots		1
Abdominal cavity: stomach contents	1	

		Intestine: visceral surfaces with petechial haemorrhages	1	
		Urine bladder severely distended	1	
		Broken back	1	1
		Interim deaths	1	1
Source	:	Tokuyama Corporation		
Reliability	:	(1) valid without restriction		
10.06.2002		Comparable to OECD guideline study		(57)
Type	:	LD ₅₀		
Species	:	mouse		
Strain	:	ICR		
Sex	:	male		
Number of animals	:	15		
Vehicle	:	other: 5 % Arabic gum in water		
Value	:	2045 mg/kg bw		
Method	:	other		
Year	:	1977		
GLP	:	no data		
Test substance	:	no data		
Remark	:	[Method] The method was in principle equivalent to OECD Guideline 401, except that mortality was determined by the up and down method after 3-day period observation. [Test condition] Three groups of 15 male mice were used. During the experiments the animals had free access to food, except for 5-6 hours prior to dosing. Water was available ad libitum. Single doses of calcium chloride dissolved in 5% Arabic gum in H ₂ O were given by stomach tube to the fasted animals. Any sign of intoxication of the animals was observed for 7 days. Mortality was determined after 3-day observation period, however. Gross post-mortem examination was made on all dead animals. The surviving animals were killed by ether and autopsied.		
Source	:	Tokuyama Corporation		
Reliability	:	(2) valid with restrictions		
10.06.2002		Comparable to guideline study with acceptable restrictions		(1)
Type	:	LD ₅₀		
Species	:	mouse		
Strain	:	ICR		
Sex	:	female		
Number of animals	:	15		
Vehicle	:	other: 5 % Arabic gum in water		
Value	:	1940 mg/kg bw		
Method	:	other		
Year	:	1977		
GLP	:	no data		
Test substance	:	no data		
Remark	:	[Method] The method was in principle equivalent to OECD Guideline 401, except that mortality was determined by the up and down method after 3-day period observation. [Test condition] Three groups of 15 female mice were used. During the experiments the		

animals had free access to food, except for 5-6 hours prior to dosing.
Water was available ad libitum.
Single doses of calcium chloride dissolved in 5% Arabic gum in H₂O were given by stomach tube to the fasted animals. Any sign of intoxication of the animals was observed for 7 days.
Mortality was determined after 3-day observation period, however. Gross post-mortem examination was made on all dead animals. The surviving animals were killed by ether and autopsied.

Source : Tokuyama Corporation
Reliability : (2) valid with restrictions
Comparable to guideline study with acceptable restrictions

10.06.2002 (1)

Type : LD₅₀
Species : rat
Strain : Wistar
Sex : male
Number of animals : 15
Vehicle : other: 5 % Arabic gum in water
Value : 3798 mg/kg bw
Method : other
Year : 1977
GLP : no data
Test substance : no data
Remark : [Method]
The method was in principle equivalent to OECD Guideline 401, except that mortality was determined by the up and down method after 3-day period observation.

[Test condition]
Three groups of 15 male rats were used. During the experiments the animals had free access to food, except for 5-6 hours prior to dosing.
Water was available ad libitum.
Single doses of calcium chloride dissolved in 5% Arabic gum in H₂O were given by stomach tube to the fasted animals. Any sign of intoxication of the animals was observed for 7 days.
Mortality was determined after 3-day observation period, however. Gross post-mortem examination was made on all dead animals. The surviving animals were killed by ether and autopsied.

Source : Tokuyama Corporation
Reliability : (2) valid with restrictions
Comparable to guideline study with acceptable restrictions

10.06.2002 (1)

Type : LD₅₀
Species : rat
Strain : Wistar
Sex : female
Number of animals : 15
Vehicle : other: 5 % Arabic gum in water
Value : 4179 mg/kg bw
Method : other
Year : 1977
GLP : no data
Test substance : no data
Remark : [Method]
The method was in principle equivalent to OECD Guideline 401, except that mortality was determined by the up and down method after 3-day period observation.

[Test condition]

	Three groups of 15 female rats were used. During the experiments the animals had free access to food, except for 5-6 hours prior to dosing. Water was available ad libitum. Single doses of calcium chloride dissolved in 5% Arabic gum in H ₂ O were given by stomach tube to the fasted animals. Any sign of intoxication of the animals was observed for 7 days. Mortality was determined after 3-day observation period, however. Gross post-mortem examination was made on all dead animals. The surviving animals were killed by ether and autopsied.
Source	: Tokuyama Corporation
Reliability	: (2) valid with restrictions Comparable to guideline study with acceptable restrictions
10.06.2002	(1)
Type	: other
Species	: rabbit
Strain	: no data
Sex	: no data
Number of animals	: 25
Vehicle	: water
Method	: other
Year	: 1946
GLP	: no data
Test substance	: no data
Remark	: [Test condition] Twenty-five rabbits, from two days to six weeks of age, were used. The animals were fasted for 48 hr before gavage and permitted to eat six hr after gavage. A soft rubber catheter (French No. 8) was employed and the animals were sacrificed 48 hr after treatment. Anhydrous calcium chloride was administered in 5, 7.5, 10, 15, and 20% aqueous solutions. Two rabbits were intubated and the catheter manipulated roughly to determine whether this procedure alone would cause trauma. Gross and microscopic study of the stomach and intestines was performed in all instances. [Result] Rough intubation caused no lesions. All animals, independent of weight and age, receiving 20% solution of calcium chloride (0.75 to 1.5 g/kg) had severe gastric damage, which consisted of mucosal necrosis and ulceration, submucosal edema, cellular infiltration and angionecrosis. Necrosis and exudation occasionally extended through all coats and fibrinous exudates was present on the serosal surface. Perforation of the stomach of one of the larger rabbits occurred. The lesions were most marked along the greater curvature of the stomach, especially in the region of the fundus. No lesions were produced in the small or larger intestine. With doses of 15% calcium chloride (0.68 to 1.5 g/kg), lesions were not found in the older rabbits but severe ulcers, similar to those described above, occurred in the unweaned animals receiving over 0.75 g/kg. Similar results were obtained with the 10 and 5% solutions (0.75 to 1.5 g/kg).
Source	: Tokuyama Corporation
Reliability	: (3) invalid Documentation insufficient for assessment
15.07.2002	(24)
Type	: LD ₅₀
Species	: rat
Strain	: no data
Sex	: no data
Number of animals	: 150
Vehicle	: water

Value	:	> 1000 mg/kg bw	
Method	:	other	
Year	:	1946	
GLP	:	no data	
Test substance	:	no data	
Source	:	Tokuyama Corporation	
Reliability	:	(3) invalid	
		Documentation insufficient for assessment	
10.06.2002			(11)

Type	:	LD ₅₀	
Species	:	guinea pig	
Strain	:	no data	
Sex	:	no data	
Number of animals	:	150	
Vehicle	:	water	
Value	:	> 1000 mg/kg bw	
Method	:	other	
Year	:	1946	
GLP	:	no data	
Test substance	:	no data	
Source	:	Tokuyama Corporation	
Reliability	:	(3) invalid	
		Documentation insufficient for assessment	
10.06.2002			(11)

Type	:	LD ₅₀	
Species	:	rabbit	
Strain	:	no data	
Sex	:	no data	
Number of animals	:	150	
Vehicle	:	water	
Value	:	> 1000 mg/kg bw	
Method	:	other	
Year	:	1946	
GLP	:	no data	
Test substance	:	no data	
Source	:	Tokuyama Corporation	
Reliability	:	(3) invalid	
		Documentation insufficient for assessment	
10.06.2002			(11)

Type	:	LD ₅₀	
Species	:	rat	
Strain	:	no data	
Sex	:	no data	
Number of animals	:		
Vehicle	:	water	
Value	:	1000 - 2000 mg/kg bw	
Method	:	other	
Year	:	1948	
GLP	:	no data	
Test substance	:	other TS: commercial grade	
Source	:	Tokuyama Corporation	
Reliability	:	(3) invalid	
		Documentation insufficient for assessment	
10.06.2002			(30)

Type	:	LD ₅₀
Species	:	rat
Strain	:	no data

Sex : no data
Number of animals :
Vehicle : no data
Value : 1000 mg/kg bw
Method : other
Year : 1988
GLP : no data
Test substance : no data
Source : Tokuyama Corporation
Reliability : (4) not assignable
Only secondary literature

10.06.2002

(41)

Type : LD₅₀
Species : rat
Strain : no data
Sex : no data
Number of animals :
Vehicle : no data
Value : > 2500 mg/kg bw
Method : other
Year : 1978
GLP : no data
Test substance : no data
Source : Tokuyama Corporation
Reliability : (4) not assignable
Only secondary literature

12.06.2002

(89)

5.1.2 ACUTE INHALATION TOXICITY

Type : LC₅₀
Species : rat
Strain : no data
Sex : no data
Number of animals :
Vehicle :
Exposure time : 4 hour(s)
Value : > 160 mg/m³
Method : other
Year : 1990
GLP : no data
Test substance : other TS: technical grade
Remark : [Test condition]
Rats were exposed to 40 and 160 mg/m³ CaCl₂ for 4h.

[Result]

No animal death was observed at 40 or 160 mg/m³ CaCl₂ during 8-day observation period. Many signs of irritation of respiratory tract were observed at both doses. The signs observed were decreased respiration, deep respiration, decrease in peroxidase activity, increases in the number of leukocytes, catalase activity and calcium levels in blood, and so on. The animals exposed to 40 mg/m³ CaCl₂ recovered 2 days after exposure, while the animals exposed to 160 mg/m³ CaCl₂ still showed a couple of the signs, deep respiration, the increase in the number of leukocytes and the decrease in peroxidase activity, 8 days after exposure.

Source : Tokuyama Corporation
Reliability : (3) invalid
Documentation insufficient for assessment

10.06.2002

(96)

5.1.3 ACUTE DERMAL TOXICITY

Type : LD₅₀
Species : rabbit
Strain : New Zealand white
Sex : male/female
Number of animals : 4
Vehicle : water
Value : > 5000 mg/kg bw
Method : other
Year : 1981
GLP : no
Test substance : as prescribed by 1.1 - 1.4
Remark : [Method]

Twenty four hours prior to application of the test material, the entire trunk of 2 male and 2 female rabbits/dose level was clipped free of hair with electric clippers. Rabbits were treated with 5000 mg/kg of undiluted test material which was applied under a heavy-gauge SARAN* film sleeve held in place with rubber bands. Five ml distilled water was applied along with the test material to simulate moistened skin and enhance skin contact. The plastic sleeve was covered by a cloth bandage taped securely to the marginal hair. All rabbits on test were placed in individual holding cages with free access to food and water.

After 24 hours, the sleeves were removed, and the skin was washed with a mild soap and water, rinsed thoroughly and dried with a soft disposable towel. The topical response at the site of application was evaluated after removal of the plastic sleeve. The animals were observed frequently during exposure and for the following 2 weeks for signs of toxicity. Body weights were recorded before and after the 24 hours exposure period and at 1 and 2 weeks post-treatment. All surviving rabbits were submitted for a gross pathological examination 2 weeks post-treatment.

* Trademark of The Dow Chemical Company.

[Result]

The dermal LD₅₀ was >5000 mg/kg. All four rabbits topically treated with the test material survived. No adverse effects were observed following treatment. Topical responses observed on the application sites of test rabbits 24 hours post-treatment included slight (1/4) or moderate (3/4) redness, moderate (3/4) or marked (1/4) swelling and moderate (2/4) or marked (2/4) necrosis. Gross necropsy examination of rabbits 2 weeks post-treatment revealed skin lesions at or near the site of administration, characterized by scab formation, skin thickening and subchronic inflammation. Internal observations were not considered to be the result of compound exposure and/or absorption.

Source : Tokuyama Corporation
Reliability : (2) valid with restrictions
Study report that meets generally accepted scientific principles
Flag : Critical study for SIDS endpoint

11.06.2002

(16)

5.1.4 ACUTE TOXICITY, OTHER ROUTES

Type : LD₅₀
Species : mouse
Strain : ICR

Sex	:	male	
Number of animals	:	15	
Vehicle	:	other: 5 % Arabic gum in water	
Route of admin.	:	s.c.	
Exposure time	:		
Value	:	823 mg/kg bw	
Method	:	other	
Year	:	1977	
GLP	:	no data	
Test substance	:	no data	
Remark	:	[Method] Study conducted in accordance with generally accepted scientific principles.	
		[Test condition] Three dose groups of 15 male mice were used. Single doses of calcium chloride dissolved in 5% Arabic gum in water were administered by subcutaneous injection in the neck area. Any sign of intoxication of the animals was observed for 7 days. Mortality was determined by the up and down method after 3-day observation period, however. Gross post-mortem examination was made on all dead animals. The surviving animals were killed by ether and autopsied.	
Source	:	Tokuyama Corporation	
Reliability	:	(2) valid with restrictions Study report that meets basic scientific principles	
10.06.2002			(1)
Type	:	LD ₅₀	
Species	:	mouse	
Strain	:	ICR	
Sex	:	female	
Number of animals	:	15	
Vehicle	:	other: 5 % Arabic gum in water	
Route of admin.	:	s.c.	
Exposure time	:		
Value	:	867 mg/kg bw	
Method	:	other	
Year	:	1977	
GLP	:	no data	
Test substance	:	no data	
Remark	:	[Method] Study conducted in accordance with generally accepted scientific principles.	
		[Test condition] Three dose groups of 15 female mice were used. Single doses of calcium chloride dissolved in 5% Arabic gum in water were administered by subcutaneous injection in the neck area. Any sign of intoxication of the animals was observed for 7 days. Mortality was determined by the up and down method after 3-day observation period, however. Gross post-mortem examination was made on all dead animals. The surviving animals were killed by ether and autopsied.	
Source	:	Tokuyama Corporation	
Reliability	:	(2) valid with restrictions Study report that meets basic scientific principles	
10.06.2002			(1)
Type	:	LD ₅₀	
Species	:	rat	

Strain	:	Wistar	
Sex	:	male	
Number of animals	:	15	
Vehicle	:	other: 5 % Arabic gum in water	
Route of admin.	:	s.c.	
Exposure time	:		
Value	:	2630 mg/kg bw	
Method	:	other	
Year	:	1977	
GLP	:	no data	
Test substance	:	no data	
Remark	:	[Method] Study conducted in accordance with generally accepted scientific principles.	
		[Test condition] Three dose groups of 15 male rats were used. Single doses of calcium chloride dissolved in 5% Arabic gum in water were administered by subcutaneous injection in the neck area. Any sign of intoxication of the animals was observed for 7 days. Mortality was determined by the up and down method after 3-day observation period, however. Gross post-mortem examination was made on all dead animals. The surviving animals were killed by ether and autopsied.	
Source	:	Tokuyama Corporation	
Reliability	:	(2) valid with restrictions Study report that meets basic scientific principles	
10.06.2002			(1)
Type	:	LD ₅₀	
Species	:	rat	
Strain	:	Wistar	
Sex	:	female	
Number of animals	:	15	
Vehicle	:	other: 5 % Arabic gum in water	
Route of admin.	:	s.c.	
Exposure time	:		
Value	:	3798 mg/kg bw	
Method	:	other	
Year	:	1977	
GLP	:	no data	
Test substance	:	no data	
Remark	:	[Method] Study conducted in accordance with generally accepted scientific principles.	
		[Test condition] Three dose groups of 15 female rats were used. Single doses of calcium chloride dissolved in 5% Arabic gum in water were administered by subcutaneous injection in the neck area. Any sign of intoxication of the animals was observed for 7 days. Mortality was determined by the up and down method after 3-day observation period, however. Gross post-mortem examination was made on all dead animals. The surviving animals were killed by ether and autopsied.	
Source	:	Tokuyama Corporation	
Reliability	:	(2) valid with restrictions Study report that meets basic scientific principles	
10.06.2002			(1)
Type	:	LD ₅₀	

Species	:	mouse	
Strain	:	ICR	
Sex	:	male	
Number of animals	:	15	
Vehicle	:	other: 5 % Arabic gum in water	
Route of admin.	:	i.p.	
Exposure time	:		
Value	:	382 mg/kg bw	
Method	:	other	
Year	:	1977	
GLP	:	no data	
Test substance	:	no data	
Remark	:	[Method] Study conducted in accordance with generally accepted scientific principles.	
		[Test condition] Three dose groups of 15 male mice were used. Single doses of calcium chloride dissolved in 5% Arabic gum in water were administered by intraperitoneal injection. Any sign of intoxication of the animals was observed for 7 days. Mortality was determined by the up and down method after 3-day observation period, however. Gross post-mortem examination was made on all dead animals. The surviving animals were killed by ether and autopsied.	
Source	:	Tokuyama Corporation	
Reliability	:	(2) valid with restrictions Study report that meets basic scientific principles	
10.06.2002			(1)
Type	:	LD ₅₀	
Species	:	mouse	
Strain	:	ICR	
Sex	:	female	
Number of animals	:	15	
Vehicle	:	other: 5 % Arabic gum in water	
Route of admin.	:	i.p.	
Exposure time	:		
Value	:	402 mg/kg bw	
Method	:	other	
Year	:	1977	
GLP	:	no data	
Test substance	:	no data	
Remark	:	[Method] Study conducted in accordance with generally accepted scientific principles.	
		[Test condition] Three dose groups of 15 female mice were used. Single doses of calcium chloride dissolved in 5% Arabic gum in water were administered by intraperitoneal injection. Any sign of intoxication of the animals was observed for 7 days. Mortality was determined by the up and down method after 3-day observation period, however. Gross post-mortem examination was made on all dead animals. The surviving animals were killed by ether and autopsied.	
Source	:	Tokuyama Corporation	
Reliability	:	(2) valid with restrictions Study report that meets basic scientific principles	
10.06.2002			(1)

Type : LD₅₀
Species : rat
Strain : Wistar
Sex : male
Number of animals : 15
Vehicle : other: 5 % Arabic gum in water
Route of admin. : i.p.
Exposure time :
Value : 264 mg/kg bw
Method : other
Year : 1977
GLP : no data
Test substance : no data
Remark : [Method]
 Study conducted in accordance with generally accepted scientific principles.

 [Test condition]
 Three dose groups of 15 male rats were used. Single doses of calcium chloride dissolved in 5% Arabic gum in water were administered by intraperitoneal injection. Any sign of intoxication of the animals was observed for 7 days.
 Mortality was determined by the up and down method after 3-day observation period, however. Gross post-mortem examination was made on all dead animals. The surviving animals were killed by ether and autopsied.
Source : Tokuyama Corporation
Reliability : (2) valid with restrictions
 Study report that meets basic scientific principles

10.06.2002

(1)

Type : LD₅₀
Species : rat
Strain : Wistar
Sex : female
Number of animals : 15
Vehicle : other: 5 % Arabic gum in water
Route of admin. : i.p.
Exposure time :
Value : 342 mg/kg bw
Method : other
Year : 1977
GLP : no data
Test substance : no data
Remark : [Method]
 Study conducted in accordance with generally accepted scientific principles.

 [Test condition]
 Three dose groups of 15 male mice were used. Single doses of calcium chloride dissolved in 5% Arabic gum in water were administered by intraperitoneal injection. Any sign of intoxication of the animals was observed for 7 days.
 Mortality was determined by the up and down method after 3-day observation period, however. Gross post-mortem examination was made on all dead animals. The surviving animals were killed by ether and autopsied.
Source : Tokuyama Corporation
Reliability : (2) valid with restrictions
 Study report that meets basic scientific principles

10.06.2002

(1)

Type : LD₅₀
Species : rat
Strain : no data
Sex : no data
Number of animals : 112
Vehicle : water
Route of admin. : i.m.
Exposure time :
Value : 25 mg/kg bw
Method : other
Year : 1946
GLP : no data
Test substance : no data
Source : Tokuyama Corporation
Reliability : (3) invalid
Documentation insufficient for assessment

10.06.2002

(11)

Type : LDLo
Species : guinea pig
Strain : no data
Sex : no data
Number of animals :
Vehicle : water
Route of admin. : i.v.
Exposure time :
Value : 150 - 160 mg/kg bw
Method : other
Year : 1928
GLP : no data
Test substance : other TS
Source : Tokuyama Corporation
Reliability : (3) invalid
Does not meet important criteria of today's standard method

10.06.2002

(25)

Type : LDLo
Species : guinea pig
Strain : no data
Sex : no data
Number of animals :
Vehicle : water
Route of admin. : other: intraarterial
Exposure time :
Value : 300 - 350 mg/kg bw
Method : other
Year : 1928
GLP : no data
Test substance : no data
Source : Tokuyama Corporation
Reliability : (3) invalid
Does not meet important criteria of today's standard method

10.06.2002

(25)

Type : LD₅₀
Species : mouse
Strain : no data
Sex : no data
Number of animals :
Vehicle : water

Route of admin. : i.p.
Exposure time :
Value : 210 mg/kg bw
Method : other
Year : 1990
GLP : no data
Test substance : other TS: technical grade
Source : Tokuyama Corporation
Reliability : (3) invalid
Documentation insufficient for assessment

10.06.2002

(96)

Type : LD₅₀
Species : mouse
Strain : other: AGNES-BLUHM-Stamm
Sex : female
Number of animals : 56
Vehicle : water
Route of admin. : i.p.
Exposure time : 48 hour(s)
Value : 245 mg/kg bw
Method : other
Year : 1961
GLP : no data
Test substance : other TS: 10 % solution from VEB Pharm. Werk Johannisthal
Source : Tokuyama Corporation
Reliability : (3) invalid
Documentation insufficient for assessment

10.06.2002

(54)

Type : LDLo
Species : rat
Strain : no data
Sex : no data
Number of animals : 22
Vehicle : water
Route of admin. : i.v.
Exposure time :
Value : 161 mg/kg bw
Method : other
Year : 1929
GLP : no data
Test substance : no data
Source : Tokuyama Corporation
Reliability : (3) invalid
Does not meet important criteria of today's standard method

10.06.2002

(69)

Type : LD₅₀
Species : mouse
Strain : ICR
Sex : no data
Number of animals : 10
Vehicle : water
Route of admin. : i.v.
Exposure time : 720 hour(s)
Value : 42.4 mg/kg bw
Method : other
Year : 1972
GLP : no data
Test substance : no data

Source	:	Tokuyama Corporation	
Reliability	:	(3) invalid Documentation insufficient for assessment	
10.06.2002			(97)
Type	:	LCLo	
Species	:	rat	
Strain	:	no data	
Sex	:	no data	
Number of animals	:		
Vehicle	:	no data	
Route of admin.	:	i.p.	
Exposure time	:		
Value	:	500 mg/kg bw	
Method	:	no data	
Year	:	1988	
GLP	:	no data	
Test substance	:	no data	
Source	:	Tokuyama Corporation	
Reliability	:	(4) not assignable Only secondary literature	
10.06.2002			(41)
Type	:	LDLo	
Species	:	rat	
Strain	:	no data	
Sex	:	no data	
Number of animals	:		
Vehicle	:	no data	
Route of admin.	:	i.v.	
Exposure time	:		
Value	:	161 mg/kg bw	
Method	:	other	
Year	:	1988	
GLP	:	no data	
Test substance	:	no data	
Source	:	Tokuyama Corporation	
Reliability	:	(4) not assignable Only secondary literature	
10.06.2002			(41)
Type	:	LD ₅₀	
Species	:	mouse	
Strain	:	no data	
Sex	:	no data	
Number of animals	:		
Vehicle	:	no data	
Route of admin.	:	i.p.	
Exposure time	:		
Value	:	280 mg/kg bw	
Method	:	no data	
Year	:	1988	
GLP	:	no data	
Test substance	:	no data	
Source	:	Tokuyama Corporation	
Reliability	:	(4) not assignable Only secondary literature	
10.06.2002			(41)
Type	:	LD ₅₀	
Species	:	mouse	

Strain : no data
Sex : no data
Number of animals :
Vehicle : no data
Route of admin. : i.v.
Exposure time :
Value : 42 mg/kg bw
Method : no data
Year : 1988
GLP : no data
Test substance : no data
Source : Tokuyama Corporation
Reliability : (4) not assignable
Only secondary literature

10.06.2002

(41)

5.2.1 SKIN IRRITATION

Species : rabbit
Concentration : undiluted
Exposure : Occlusive
Exposure time : 4 hour(s)
Number of animals : 3
PDII :
Result : not irritating
EC classification : not irritating
Method : OECD Guide-line 404 "Acute Dermal Irritation/Corrosion"
Year : 1986
GLP : yes
Test substance : other TS
Remark : [Test substance]
Anhydrous calcium chloride (CaCl_2), a white powder, prepared from calcium chloride dihydrate flakes (Batch No. Couillet 8/OCT/1985 FLAKES). The test material was solid at the application time. Upon analysis sample contained: 97.0% CaCl_2 , 2.2% NaCl and 0.11% Ca(OH)_2 .

[Result]

- Table 1: Scores of the skin reaction of the rabbit after application of anhydrous calcium chloride at different times after patch removal.

Animal No.	Symptom	score after			
		30-60 minutes	24 hours	48 hours	72 hours
1	erythema	0	0	0	0
	oedema	0	0	0	0
2	erythema	0	0	0	0
	oedema	0	0	0	0
3	erythema	0	0	0	0
	oedema	0	0	0	0

Source : Tokuyama Corporation
Reliability : (1) valid without restriction
OECD Guideline study
Flag : Critical study for SIDS endpoint
11.06.2002

(61)

Species : rabbit
Concentration : undiluted
Exposure : Occlusive
Exposure time : 4 hour(s)
Number of animals : 3
PDII :
Result : not irritating
EC classification : not irritating
Method : OECD Guide-line 404 "Acute Dermal Irritation/Corrosion"
Year : 1986
GLP : yes
Test substance : other TS
Remark : [Test substance]
Calcium chloride dihydrate ($\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$), a white powder, prepared from calcium chloride dihydrate flakes (Batch No. Solvay Couillet 8/OCT/1985 FLAKES). The test sample was solid at the application time. Upon analysis sample contained: 76.7% CaCl_2 , 1.8% NaCl and 0.08% $\text{Ca}(\text{OH})_2$.

[Result]

- Table 1: Scores of the skin reaction of the rabbit after application of calcium chloride dihydrate at different times after patch removal.

Animal No.	Symptom	score after			
		30-60 minutes	24 hours	48 hours	72 hours
1	erythema	0	0	0	0
	oedema	0	0	0	0
2	erythema	0	0	0	0
	oedema	0	0	0	0
3	erythema	0	-(a)	-	-
	oedema	0	-(a)	-	-

(a) rabbit was killed one hour after application because of a broken back.

Source : Tokuyama Corporation
Reliability : (1) valid without restriction
OECD Guideline study

10.06.2002

(65)

Species : rabbit
Concentration : undiluted
Exposure : Occlusive
Exposure time : 4 hour(s)
Number of animals : 3
PDII :
Result : slightly irritating
EC classification : not irritating
Method : OECD Guide-line 404 "Acute Dermal Irritation/Corrosion"
Year : 1986
GLP : yes
Test substance : other TS
Remark : [Test substance]
Calcium chloride hexahydrate ($\text{CaCl}_2 \cdot 6\text{H}_2\text{O}$), a white powder, prepared from calcium chloride dihydrate (Batch No. Solvay Couillet 8/OCT/1985 FLAKES). The test material was solid at application time. Upon analysis sample contained: 50.2% CaCl_2 , 1.2% NaCl and 0.05% $\text{Ca}(\text{OH})_2$.

[Result]

A well-defined erythema and a slight oedema were noted at 1 and 24 hours after application in one rabbit. Thereafter the skin reactions diminished and at 72 hours there was only a slight erythema, which had disappeared seven days after treatment. Neither erythema nor oedema was observed in the other two rabbit.

- Table 1: Scores of the skin reaction of the rabbit after application of calcium chloride hexahydrate at different times after patch removal.

Animal No.	Symptom	score after					
		30-60 minutes	24 hours	48 hours	72 hours	7 days	14 days
1	erythema	2	2	1	1	0(a)	0(a)
	oedema	2	2	1	0	0	0
2	erythema	0	0	0	0		
	oedema	0	0	0	0		
3	erythema	0	0	0	0		
	oedema	0	0	0	0		

(a) slight scaling of the skin.

Source
Reliability

: Tokuyama Corporation
: (1) valid without restriction
OECD Guideline study

11.06.2002

(67)

Species
Concentration
Exposure
Exposure time
Number of animals
PDII
Result
EC classification
Method
Year
GLP
Test substance
Remark

: rabbit
: 33 %
: Occlusive
: 4 hour(s)
: 3
:
: not irritating
: not irritating
: OECD Guide-line 404 "Acute Dermal Irritation/Corrosion"
: 1986
: yes
: other TS
: [Test substance]

Calcium chloride 33%, a colorless, clear liquid (Batch No. Solvay Couillet RS1 21/FEB/1986). Upon analysis sample contained: 33.1% CaCl₂, 1.1% NaCl and 0.07% Ca(OH)₂.

[Result]

- Table 1: Scores of the skin reaction of the rabbit after application of calcium chloride 33 % at different times after patch removal.

Animal No.	Symptom	score after			
		30-60 minutes	24 hours	48 hours	72 hours
1	erythema	0	0	0	0

		oedema	0	0	0	0
	2	erythema	0	0	0	0
		oedema	0	0	0	0
	3	erythema	0	0	0	0
		oedema	0	0	0	0
Source	:	Tokuyama Corporation				
Reliability	:	(1) valid without restriction				
		OECD Guideline study				
11.06.2002						(63)
Species	:	rabbit				
Concentration	:	undiluted				
Exposure	:	Occlusive				
Exposure time	:	24 hour(s)				
Number of animals	:	6				
PDII	:					
Result	:	moderately irritating				
EC classification	:					
Method	:	other: US Federal Register 38: 187, Part 1500, Section 41, 1973.				
Year	:	1981				
GLP	:	no				
Test substance	:	as prescribed by 1.1 - 1.4				
Remark	:	[Test substance]				
		PELADOW: calcium chloride (anhydrous, 94-97%)				
		[Method]				
		The backs of 6 rabbits were clipped free of hair with electric clippers 24 hours prior to use. Under a surgical gauze patch held in place with adhesive tape, 0.5 ml of the test material was applied to an intact and an abraded site on each animal. The patches were loosely covered with a piece of SARAN* Film to retard evaporation. The rabbits were fitted with a plastic collar to prevent them from ingesting any material. After 24 hours, the patches were removed and each site was assessed: the severity of the reaction was recorded then and at 72 hours from the beginning of the test.				
		* Trademark of The Dow Chemical Company.				
		[Result]				
		Application of the undiluted test material to intact and freshly abraded skin on the backs of 6 rabbits resulted in slight (3/6) or moderate (3/6) redness and slight (5/6) swelling. The primary irritation score was calculated to be 1.4 out of a possible 8.0.				
		Comment:				
		This report states that 0.5 ml of the test material was applied to the skin. The report also states that the material was undiluted, suggesting that the material applied to the skin was a solid. It is most likely that 0.5 g of test material was applied.				
Source	:	Tokuyama Corporation				
Reliability	:	(2) valid with restrictions				
		Study report that meets generally accepted scientific principles				
06.08.2002						(16)
Species	:	rabbit				
Concentration	:	undiluted				
Exposure	:	Occlusive				
Exposure time	:	24 hour(s)				
Number of animals	:	6				
PDII	:					

Result : moderately irritating
EC classification :
Method : other: US Federal Hazardous Labeling Act. procedures recommended by the FDA CFR, Part 191, Chapter 1, Title 21, January 1, 1970.
Year : 1971
GLP : no
Test substance : as prescribed by 1.1 - 1.4
Remark : [Test substance]
DOWFLAKE*: calcium chloride (dihydrate)

[Method]

Twenty-four hours prior to application of the test material, the skin on the backs of 6 albino rabbits was carefully clipped free of hair using electric clippers. The animals were caged individually and were allowed to eat and drink ad libitum. During the exposure period, the rabbits were restrained in stocks. Test material, 0.5 grams, was introduced under a square gauze patch (1 inch square) to intact and abraded skin. The patches were secured in place by adhesive tape. The entire trunk of the animals was wrapped in an impervious plastic cuff for the 24 hour exposure period. After the 24 hours of exposure, the patches were removed and the reactions evaluated according to the rating system recommended in the Federal Hazardous Labeling Act.

[Result]

Application of DOWFLAKE* to intact skin of six rabbits produced very slight or slight erythema and edema in 5 of the animals and moderate erythema and edema in one animal. The abraded skin response was slight erythema in three animals and moderate to severe erythema in three animals. The edematous response was very slight or slight in three animals and moderate in three animals.

* Trademark of The Dow Chemical Company.

Source : Tokuyama Corporation
Reliability : (2) valid with restrictions
Study report that meets generally accepted scientific principles
Flag : Critical study for SIDS endpoint

06.08.2002

(76)

Species : rabbit
Concentration : undiluted
Exposure : Occlusive
Exposure time : 6 hour(s)
Number of animals : 2
PDII :
Result : moderately irritating
EC classification :
Method : other
Year : 1971
GLP : no
Test substance : as prescribed by 1.1 - 1.4
Remark : [Test substance]
DOWFLAKE*: calcium chloride (dihydrate)

[Method]

The abdominal skin of two albino rabbits was shaved free of hair. The animals were rested for several days to allow any abrasions to heal completely. During the 6 hour exposure period, the animals were placed in a stock ventral side up. Test material, 0.5 grams, was placed under a moist cotton pad, on two intact skin areas per rabbit. Skin reactions were observed periodically during the six hour exposure period.

	[Result]
	Application of DOWFLAKE* under a moistened pad to the intact skin resulted in, at the most, slight or moderate erythema, edema and slight necrosis (eschar) in four hours. At the termination of the test, two skin areas displayed necrosis. The two remaining skin areas were unchanged.
	* Trademark of The Dow Chemical Company.
Source	: Tokuyama Corporation
Reliability	: (2) valid with restrictions
	Study report that meets generally accepted scientific principles
06.08.2002	(76)
Species	: rabbit
Concentration	: 38 %
Exposure	: Occlusive
Exposure time	: 24 hour(s)
Number of animals	: 6
PDII	:
Result	: moderately irritating
EC classification	:
Method	: other: US Federal Hazardous Labeling Act. procedures recommended by the FDA CFR, Part 191, Chapter 1, Title 21, January 1, 1970.
Year	: 1971
GLP	: no
Test substance	: as prescribed by 1.1 - 1.4
Remark	: [Test substance] LIQUIDOW*: liquid calcium chloride (38% CaCl ₂ and 62% water)

[Method]

Twenty-four hours prior to application of the test material, the skin on the backs of 6 albino rabbits was carefully clipped free of hair using electric clippers. The animals were caged individually and were allowed to eat and drink ad libitum. During the exposure period, the rabbits were restrained in stocks. Test material, 0.5 grams, was introduced under a square gauze patch (1 inch square) to intact and abraded skin. The patches were secured in place by adhesive tape. The entire trunk of the animals was wrapped in an impervious plastic cuff for the 24 hour exposure period. After the 24 hours of exposure, the patches were removed and the reactions evaluated according to the rating system recommended in the Federal Hazardous Labeling Act.

[Result]

Very slight or slight erythema was observed on the intact skin of 5 of 6 rabbits with the remaining rabbit displaying moderate necrosis, no edema by 2 rabbits, very slight to slight edema by 3 rabbits and moderate edema by the remaining rabbit. The abraded skin responded at 24 hours with severe erythema in 2 rabbits, moderate necrosis in 3 rabbits and moderate erythema in 1 rabbit. The edematous response was moderate in 5 of the 6 rabbits with the remaining animal displaying very slight edema. At the 72nd hour observations all inflammatory reactions had subsided and the necrotized skin areas were in the process of healing.

	* Trademark of The Dow Chemical Company.
Source	: Tokuyama Corporation
Reliability	: (2) valid with restrictions
	Study report that meets generally accepted scientific principles
06.08.2002	(77)

5.2.2 EYE IRRITATION

Species : rabbit
Concentration : undiluted
Dose : 100 mg
Exposure Time :
Comment : not rinsed
Number of animals : 3
Result : highly irritating
EC classification :
Method : OECD Guide-line 405 "Acute Eye Irritation/Corrosion"
Year : 1986
GLP : yes
Test substance : other TS
Remark : [Test substance]
Anhydrous calcium chloride (CaCl_2), a white powder, prepared from calcium chloride dihydrate flakes (Batch No.Solvay Couillet 8/OCT/1985 FLAKES). The test material was solid at the application time. Upon analysis sample contained: 97.0% CaCl_2 , 2.2% NaCl and 0.11% $\text{Ca}(\text{OH})_2$.

[Test condition]

Grading and scoring of irritation were performed in accordance with the following table:

- Table 1

CORNEA

A. Opacity-degree of density(area taken for reading)	Grade
- No ulceration or opacity	0
- Scattered or diffuse areas; details of iris clearly visible	1
- Easily discernible translucent areas, details of iris slightly obscured	2
- Opalescent areas of opacity, no details of iris visible, size of pupil barely discernible	3
- Opaque, iris invisible	4

B. Area of cornea involved	Grade
- No damaged cornea	0
- One quarter (or less) but not zero	1
- Greater than one quarter less than one half	2
- Greater than one half less than three quarters	3
- Greater than three quarters up to whole area	4

IRIS

A. Values	Grade
- Normal	0
- Folds above normal, congestion, swelling, circumcorneal injection (any one or all of these or combination of any thereof), iris still reacting to light (sluggish reaction is positive)	1
- No reaction to light, hemorrhage, gross destruction (any one or all of these)	2

CONJUNCTIVA

A. Redness (refers to palpebral cconjunctiva only)	Grade
- Vessels normal	0
- Vessels definitely injected above normal	1
- More diffuse, deeper crimson red, individual vessels not easily discernible	2
- Diffuse beefy red	3
B. Chemosis	Grade
- No swelling	0
- Any swelling above normal (includes nictitating membrane)	1
- Obvious swelling with partial eversion of the lids	2
- Swelling with lids about half closed	3
- Swelling with lids about half closed to completely closed	4
C. Discharq	Grade
- Normal	0
- Any amount different from normal (does not include small amount observed in inner canthus of normal animals)	1
- Discharge with moistening of the lids and hairs just adjacent to the lids	2
- Discharge with moistening of the lids and considerable area around the eye	3

[Result]

The cornea and conjunctiva were moderately to severely irritated all rabbits from one hour till 14 days after treatment. Thereafter the eye of one rabbit recovered, but there was still a slight haze on the cornea, 21 days after treatment. In the two other rabbits the cornea and conjunctiva were still moderately irritated 21 days after treatment.

- Table 2: Numerical grades awarded to the ocular reactions elicited by anhydrous calcium chloride.

Rabbit No.	Region of eye	hours(h)/days(d) after application							
		0h	1h	24h	48h	72h	7d	14d	21d
1	Cornea Opacity	0	2	2	2	2	1	1	2
		0	4	4	4	4	4	4	3
	Area involved								
	Iris								
	0 2 1 1 1 1 0 0								
	Conjunctiva	0	1	2*	2#	2#	2#	1#	1#
		0	3	3	2	2	2	2	1
		0	0\$	0	2	2\$	0\$	1	1
	Discharge								
	0 2 2 2 2 2 2 2								
2	Cornea Opacity	0	2	2	2#	2#	2#	4	2
		0	4	4	4	4	4	4	4
	Area involved								
	Iris								
	0 1 1 1 1 1 2 1								
	Conjunctiva	0	1	1	2	3	3	2	2*
		0	2	2	2	2	2	3	2
	Redness								
	Chemosis								
	0 2 2 2 2 2 3 2								
	Discharge								

	Discharge	0	0\$	0	3	3	3	3	2
3	Cornea Opacity	0	2	2	2	2#	2#	2	0@
	Area involved	0	4	4	4	4	4	3	0
	Iris	0	1	1	1	1	1	1	0
Conjunctiva	Redness	0	1	1	2	2	2	1	0
	Chemosis	0	3	3	2	2	2	2	0
	Discharge	0	0\$	0\$	3	3	3	2	0\$

* - conjunctiva was damaged.

- the eye was difficult to observe due to discharge.

\$ - lacrimation

@ - slight haze on cornea

Source : Tokuyama Corporation
Reliability : (1) valid without restriction
 OECD Guideline study
Flag : Critical study for SIDS endpoint
 11.06.2002

(60)

Species : rabbit
Concentration : undiluted
Dose : 100 mg
Exposure Time :
Comment : not rinsed
Number of animals : 3
Result : irritating
EC classification :
Method : OECD Guide-line 405 "Acute Eye Irritation/Corrosion"
Year : 1986
GLP : yes
Test substance : other TS
Remark : [Test substance]
 Calcium chloride dihydrate ($\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$), a white powder, prepared from calcium chloride dihydrate flakes (Batch No. Solvay Couillet 8/OCT/1985 FLAKES). The test sample was solid at the application time. Upon analysis sample contained: 76.7% CaCl_2 , 1.8% NaCl and 0.08% $\text{Ca}(\text{OH})_2$.

[Result]

The conjunctiva of the eye of one rabbit (No. 1) was moderately to severely irritated from one till 24 hours after treatment. Thereafter the irritation diminished and had disappeared at 14 days after treatment, although a slight lacrimation was still noted. The cornea of this rabbit was slightly opaque up to and including 72 hours. The conjunctiva of the eye of the second rabbit (No. 2), was moderately irritated at the one hour reading. Thereafter the irritation diminished, although the conjunctiva was still slightly damaged at the end of the observation period. In the third rabbit (No. 3), the cornea was moderately irritated from 24 till 72 hours. Thereafter the irritation diminished, but was still slight at the end of the experiment. The conjunctiva was moderately irritated from one till 72 hours. Thereafter the eye recovered, but the irritation was still present 21 days after application. The iris was slightly irritated from one hour up to 14 days after treatment.

- Table 1: Numerical grades awarded to the ocular reactions elicited by calcium chloride dihydrate.

Rabbit	Region of eye	hours(h)/days(d) after application
--------	---------------	------------------------------------

No.										
			0h	1h	24h	48h	72h	7d	14d	21d
1	Cornea	Opacity	0	0	1	1	1	0	0	
		Area involved	0	0	1	1	1	0	0	
	Iris		0	0	0	0	0	0	0	
	Conjunctiva	Redness	0	1	3*	2	2	1	0	
		Chemosis	0	2	3	2	2	1	0	
		Discharge	0	0\$	0\$	1\$	1\$	0\$	0\$	
	Cornea	Opacity	0	0	0	0	0	0	0	0
		Area involved	0	0	0	0	0	0	0	0
	Iris		0	0	0	0	0	0	0	0
	Conjunctiva	Redness	0	2	1*	0*	0*	0*	0*	0*
Chemosis		0	2	1	1	1	1	0	0	
Discharge		0	0\$	0\$	0\$	0	0	0	0	
3	Cornea	Opacity	0	0	2	2	2	1	1	1
		Area involved	0	0	4	4	1	1	2	2
	Iris		0	2	1	1	1	1	0	0
	Conjunctiva	Redness	0	2	2*	2*	2*	1*	2*	2
		Chemosis	0	2	2	2	1	0	0	0
		Discharge	0	0\$	0\$	1\$	1\$	0\$	0\$	0\$

* - conjunctiva was damaged.

\$ - lacrimation

Source : Tokuyama Corporation
Reliability : (1) valid without restriction
 OECD Guideline study

06.02.2002

(64)

Species : rabbit
Concentration : undiluted
Dose : 100 mg
Exposure Time :
Comment : not rinsed
Number of animals : 3
Result : moderately irritating
EC classification :
Method : OECD Guide-line 405 "Acute Eye Irritation/Corrosion"
Year : 1986
GLP : yes
Test substance : other TS
Remark : [Test substance]
 Calcium chloride hexahydrate (CaCl₂·6H₂O), a white powder, prepared from calcium chloride dihydrate (Batch No. Solvay Couillet 8/OCT/1985 FLAKES). The test material was solid at application time. Upon analysis sample contained: 50.2% CaCl₂, 1.2% NaCl and 0.05% Ca(OH)₂.

[Result]

The conjunctiva was slightly irritated in one rabbit (No. 2), till 48 hours; the irritation had disappeared at 72 hours. The cornea was slightly irritated at

24 hours after treatment. In a second rabbit (No. 1), the conjunctiva was moderately irritated from one till 48 hours after treatment, thereafter the conjunctiva recovered. The cornea was slightly irritated from one till 72 hours. The irritation of cornea and conjunctiva had disappeared at 7 days after treatment. In the third rabbit (No. 3), the cornea was slightly irritated from 24 hours till 72 hours after treatment. The conjunctiva was slightly irritated from 1 hour till 14 days. At day 21 only some lacrimation was noted in this rabbit.

- Table 1: Numerical grades awarded to the ocular reactions elicited by calcium chloride hexahydrate.

Rabbit application No.	Region of eye		hours(h)/days(d) after							
			0h	1h	24h	48h	72h	7d	14d	21d
1	Cornea	Opacity	0	0	1	1	1	0		
		Area involved	0	0	1	1	1	0		
	Iris		0	0	0	0	0	0		
	Conjunctiva	Redness	0	1	2*	1*	0*	0		
		Chemosis	0	2	2	1	1	0		
		Discharge	0	0\$	0\$	0\$	0\$	0		
	Cornea	Opacity	0	0	1	0	0			
		Area involved	0	0	2	0	0			
	Iris		0	0	0	0	0			
	Conjunctiva	Redness	0	1	1	0	0			
Chemosis		0	2	1	0	0				
Discharge		0	0\$	0\$	0\$	0				
3	Cornea	Opacity	0	0	2	1	1	0	0	0
		Area involved	0	0	1	1	0	0	0	0
	Iris		0	0	0	0	0	0	0	0
	Conjunctiva	Redness	0	1	1	0	1	0	1	0
		Chemosis	0	2	1	0	1	0	0	0
		Discharge	0	0\$	0\$	1\$	1\$	0\$	0\$	0\$

* - conjunctiva was damaged.

\$ - lacrimation

Source : Tokuyama Corporation
Reliability : (1) valid without restriction
OECD Guideline study

11.06.2002

(66)

Species : rabbit
Concentration : 33 %
Dose : .1 ml
Exposure Time :
Comment : not rinsed
Number of animals : 3
Result : moderately irritating

EC classification :
Method : OECD Guide-line 405 "Acute Eye Irritation/Corrosion"
Year : 1986
GLP : yes
Test substance : other TS
Remark : [Test substance]
Calcium chloride 33%, a colorless, clear liquid (Batch No. Solvay Couillet RS1 21/FEB/1986). Upon analysis sample contained: 33.1% CaCl₂, 1.1% NaCl and 0.07% Ca(OH)₂.

[Result]

The conjunctiva was slightly irritated in one rabbit (No. 3), from 1 till 48 hours after treatment. The irritation had disappeared at 48 hours, although some lacrimation was still noted. In a second rabbit (No. 2), the cornea and conjunctiva were moderately irritated till 48 hours. Thereafter the eye recovered and the irritation had disappeared 14 days after treatment. In the third rabbit (No. 1), the cornea and conjunctiva were moderately irritated till 72 hours. Thereafter, the cornea and conjunctiva recovered, but 21 days after treatment, the cornea was still slightly irritated.

- Table 1: Numerical grades awarded to the ocular reactions elicited by calcium chloride 33 %.

Rabbit No.	Region of eye		hours(h)/days(d) after							
			0h	1h	24h	48h	72h	7d	14d	21d
1	Cornea	Opacity	0	2	2	2	2	1	1	1
		Area involved	0	4	4	2	2	1	1	1
	Iris		0	1	0	0	0	0	0	0
	Conjunctiva	Redness	0	1	2*	1*	1*	1	1	0
		Chemosis	0	2	2	2	2	1	1	0
		Discharge	0	0\$	0\$	0\$	0\$	0\$	1\$	0\$
2	Cornea	Opacity	0	2	2	2	2	1	0	
		Area involved	0	4	4	4	1	0	0	
	Iris		0	1	0	1	0	0	0	
	Conjunctiva	Redness	0	2	1*	2*	1*	1	0	
		Chemosis	0	2	2	1	1	0	0	
		Discharge	0	0\$	0\$	0\$	0	0	0	
3	Cornea	Opacity	0	0	0	0	0			
		Area involved	0	0	0	0	0			
	Iris		0	0	0	0	0			
	Conjunctiva	Redness	0	1	1*	0	0			
		Chemosis	0	2	1	0	0			
		Discharge	0	0\$	0\$	0\$	0			

* - conjunctiva was damaged.

\$ - lacrimation

Source : Tokuyama Corporation

Reliability : (1) valid without restriction
OECD Guideline study
11.06.2002 (62)

Species : rabbit
Concentration : undiluted
Dose : .1 other: g
Exposure Time :
Comment : not rinsed
Number of animals : 6
Result : moderately irritating
EC classification :
Method : other: US Federal Hazardous Labeling Act. procedures recommended by the FDA CFR, Part 191, Chapter 1, Title 21, January 1, 1970.
Year : 1971
GLP : no
Test substance : as prescribed by 1.1 - 1.4
Remark : [Test substance]
DOWFLAKE*: calcium chloride (dihydrate)

[Method]

Test material, 0.1 grams, was instilled in the conjunctival sac of the right eye of 6 albino rabbits. The left eye of each animal served as an untreated control. Both eyes of each rabbit were considered to be without defects or irritation prior to the study. The eyes were examined 24, 48, 72 hours, and 7 days post-installation. Ocular reaction was graded in accordance with the rating system recommended under the Federal Hazardous Labeling Act.

[Result]

Instillation of DOWFLAKE* into the eyes of 6 rabbits produced corneal opacity with details of the iris slightly obscured, congestion and circumcorneal injection of the iris, diffuse conjunctival redness and conjunctival chemosis causing the eye lids to be half or more closed.

* Trademark of The Dow Chemical Company.

Source : Tokuyama Corporation
Reliability : (2) valid with restrictions
Study report that meets generally accepted scientific principles
06.08.2002 (76)

Species : rabbit
Concentration : 38 %
Dose : .1 other: g
Exposure Time :
Comment : not rinsed
Number of animals : 6
Result : moderately irritating
EC classification :
Method : other: US Federal Hazardous Labeling Act. procedures recommended by the FDA CFR, Part 191, Chapter 1, Title 21, January 1, 1970.
Year : 1971
GLP : no
Test substance : as prescribed by 1.1 - 1.4
Remark : [Test substance]
LIQUIDOW*: liquid calcium chloride (38% CaCl₂ and 62% water)

[Method]

Test material, 0.1 grams, was instilled in the conjunctival sac of the right eye of 6 albino rabbits. The left eye of each animal served as an untreated control. Both eyes of each rabbit were considered to be without defects or

irritation prior to the study.. The eyes were examined 24, 48, 72 hours, and 7 days post-installation. Ocular reaction was graded in accordance with the rating system recommended under the Federal Hazardous Labeling Act.

[Result]

Instillation of LIQUIDOW* into the eyes of 6 rabbits produced diffuse corneal opacities in 5 of the 6 eyes with no discernible corneal effect in the remaining eye, slight iritis in 4 of the 6 eyes with no discernible effect in the remaining 2 eyes, slight conjunctival redness in 3 eyes and moderate conjunctival redness in the remaining 3 eyes, and no chemosis in one eye, slight chemosis causing inversions of the lids in 2 eyes and moderate chemosis causing the lids to be half closed in 3 eyes. The ocular reactions at 48 hours were essentially the same as at 24 hours. The reactions at 72 hours were the same as or less than those reactions observed at 24 hours except in the case of 2 eyes which displayed marked chemosis causing the eye lids to be more than half closed.

* Trademark of The Dow Chemical Company.

Source : Tokuyama Corporation
Reliability : (2) valid with restrictions
Study report that meets generally accepted scientific principles

06.08.2002

(77)

5.3 SENSITIZATION

Type : Skin painting test
Species : guinea pig
Number of animals :
Vehicle : no data
Result : not sensitizing
Classification :
Method : other
Year : 1990
GLP : no data
Test substance : other TS: technical grade
Source : Tokuyama Corporation
Reliability : (3) invalid
Documentation insufficient for assessment

10.06.2002

(96)

5.4 REPEATED DOSE TOXICITY

Species : rat
Sex : no data
Strain :
Route of admin. : oral feed
Exposure period : 12 months
Frequency of treatment : daily
Post obs. period :
Doses : 20000 ppm
Control group : yes
NOAEL : >= 20000 ppm
Method : other
Year : 1977
GLP : no data
Test substance : other TS

Remark : [Test substance]
Obtained from Sigma Chemical Company, St. Louis, MO.

[Test condition]

Twenty 40-day-old rats received diet containing 20 mg CaCl₂ per g diet for the experimental period of 12 months. The rats were weighed biweekly for the first 3 months and monthly thereafter. Rats that died or were killed at the termination of the experiment were necropsied. Representative histological sections of gastrointestinal tract, urinary tract, liver, heart, brain and spleen were prepared and studied from all available animals.

[Result]

No differences in daily food consumption were detected between the control and the test groups. Each rat consumed about 22 g basic diet with supplements, which corresponded to 440 mg of CaCl₂ as the daily intake. The average weights and survivals of both groups were comparable throughout the experimental period. No neoplastic lesions were observed in the organs studied histologically.

- Table. Effect of CaCl₂ on the survival of rats

Group	No. of rats used	No. of rats died or killed (month)		
		6-8	8-10	10-12
Control	20	2	0	18
CaCl ₂	20	1	1	18

Source : Tokuyama Corporation
Reliability : (3) invalid
Documentation insufficient for assessment

10.06.2002

(81)

Species : rat
Sex : male/female
Strain :
Route of admin. : oral feed
Exposure period : 12 weeks
Frequency of treatment : daily
Post obs. period :
Doses : 20000 ppm in basal diet or 10000 ppm in drinking water
Control group : yes
NOAEL : >= 20000 ppm
Method : other
Year : 1940
GLP : no data
Test substance : other TS
Remark : [Test substance]
Calcium chloride was prepared from calcium oxide and hydrochloric acid.

[Test condition]

Both male and female rats, 4 to 5 weeks old, were used. The sexes were kept separate and two or three animals were placed in each cage. Littermates were distributed through the diets as much as possible. Two per cent calcium chloride was added to the basal diet. In the experiment with the water, 1% calcium chloride was added to the drinking water. Seventy-one and twenty-four rats were used for the basal diet group and the drinking water group, respectively, while 212 rats were used for the control group.

	[Result] Calcium salts added to the basal diet or drinking water did not affect growth and survival of rats. The thyroid weight, iodine content and concentration for rats fed the different calcium salts were recorded. None of the calcium salts produced a real enlargement of the thyroid. The iodine concentration on the dry weight basis was almost identical for all diets. Examination of some glands from each group showed no real differences in the microscopic structure. The results demonstrate that a high calcium intake does not affect the size of the thyroid. However, along with vitamin D calcium chloride produced an increase in thyroid weight.	
Source	: Tokuyama Corporation	
Reliability	: (3) invalid Documentation insufficient for assessment	
10.06.2002		(88)
Species	: rat	
Sex	: no data	
Strain	: no data	
Route of admin.	: gavage	
Exposure period	: 70 days	
Frequency of treatment	: 6 days/week	
Post obs. period	:	
Doses	: 1.1, 2.8, 5.6 g/kg-bw	
Control group	: no	
Method	: other	
Year	: 1942	
GLP	: no data	
Test substance	: no data	
Remark	: [Test condition] Calcium chloride in solution was administered by stomach tube to rats six days weekly throughout the experiment. Ten animals comprised each group. The animals were weighed at least once a week. Certain tissues from animals dying during the experiments, as well as those surviving for its duration, were examined histologically.	
	[Result] All the animals of the 5.6 g/kg group died after a single dose. Administration of calcium chloride at 2.8 g/kg also produced death after one or two doses. In the 1.1 g/kg group, 5 of the original 10 rats survived the entire period (70 days). No apparent histological change was observed in the heart, kidney or liver of the surviving rats.	
Source	: Tokuyama Corporation	
Reliability	: (3) invalid Documentation insufficient for assessment	
10.06.2002		(90)
Species	: rat	
Sex	: no data	
Strain	: no data	
Route of admin.	: inhalation	
Exposure period	: 4 months, 4 hours/day	
Frequency of treatment	: 5 days/week	
Post obs. period	:	
Doses	: 8.5, 14.9, 43.1 mg/m ³	
Control group	: no data specified	
LOAEL	: 8.5 mg/m ³	
Method	: other	
Year	: 1990	
GLP	: no data	

Test substance	: other TS: technical grade
Remark	: [Result] Marked toxic symptoms were observed in rats administered at 43.1 mg/m ³ , most of which were not recovered during the post observation period. Those included decreases in the number of leukocytes, phagocytic activity in blood, lysozyme level in serum, and catalase activity, plasma recalcification, shortening of clotting, clot retraction, an increase in peroxidase activity, and so on. Similar symptoms were also observed in the rats of the 14.9 mg/m ³ group, although the symptoms were considerably weaker than those at 43.1 mg/m ³ and disappeared during the post observation period. At 8.5 mg/m ³ , only a few parameters of physiological and biochemical functions of rats were changed.
Source	: Tokuyama Corporation
Reliability	: (3) invalid Documentation insufficient for assessment
10.06.2002	(96)
Species	: rabbit
Sex	: no data
Strain	: no data
Route of admin.	: gavage
Exposure period	: 4 days
Frequency of treatment	: daily
Post obs. period	:
Doses	: 1.5, 1.8, 2.2, 2.5 g/kg/day
Control group	: no
Method	: other
Year	: 1949
GLP	: no data
Test substance	: no data
Remark	: [Test condition] Twelve rabbits were used in the experiment. These were housed in urine cages. Calcium chloride in a 10% solution was administered daily by stomach-tube. Two animals received 1.5 g/kg, two received 1.8 g/kg, two received 2.2 g/kg, and six received 2.5 g/kg. Urines were collected daily for the estimation of urea, chlorides, phosphates, ammonia and pH. Routine tests for albumen were carried out. Blood was withdrawn every second day for analysis. For histological analysis, formol saline was used as a routine fixative for paraffin and frozen sections. [Result] Group 1: All of the animals receiving 1.5 or 1.8 g/kg and one animal receiving 2.2 g/kg showed no signs of toxemia, ate their food and appeared to be healthy in every way. Histological analysis showed minor abnormalities in lung and kidney of these animals. Group 2: Five animals receiving 2.5 g/kg died on the 5th day. The remaining two animals, one receiving 2.5 g/kg and another receiving 2.2 g/kg were comatose on the 5th day. All of the animals in this group showed gross abnormalities in lung, myocardium, liver, and kidney at autopsy. Because no irritation was observed, it is probable that older rabbits were used in this study.
Source	: Tokuyama Corporation
Reliability	: (3) invalid Does not meet important criteria of today's standard method
10.06.2002	(33)

5.5 GENETIC TOXICITY 'IN VITRO'

Type : Ames test
System of testing : *Salmonella typhimurium* strains TA92, TA1535, TA100, TA1537, TA94, TA98
Concentration : max 5.0 mg/plate
Cycotoxic conc. :
Metabolic activation : with
Result : negative
Method : other
Year : 1984
GLP : no data
Test substance : other TS
Remark : [Test substance]
 Supplied from the Japan Food Additives Association, Tokyo, at the request of the Ministry of Health and Welfare of Japan, where the purity and quality of the sample was checked. The purity of CaCl₂ used was 74.5%.

[Method]

The method was in principle equivalent to OECD Guideline 471, except that the test was carried out only with metabolic activation.

[Test condition]

Duplicate plates were used for each of six different concentrations of the sample. The liver microsome fraction (S9) was prepared from the liver of Fischer rats pretreated 5 days before with polychlorinated biphenyls (500 mg/kg body weight of Kanechlor KC-400 in olive oil, ip). The result was considered positive if the number of colonies found was twice the number of colonies of the control, which was exposed to phosphate buffer, the solvent for CaCl₂.

[Result]

A negative result indicates that no significant increases in the number of revertant colonies were detected in any *S. Typhimurium* strains at the maximum dose.

Source : Tokuyama Corporation
Reliability : (2) valid with restrictions
 Comparable to guideline study with acceptable restrictions
Flag : Critical study for SIDS endpoint

11.06.2002

(42)

Type : Ames test
System of testing : *Salmonella typhimurium* TA97, TA102
Concentration : 0.1 - 10 mg/plate
Cycotoxic conc. :
Metabolic activation : with and without
Result : negative
Method : other
Year : 1987
GLP : no data
Test substance : other TS
Remark : [Test substance]
 Obtained from Wako Pure Chemicals Co., Japan (lot No. DCG 7053).

[Method]

The method was in principle equivalent to OECD Guideline 471, except that some of the recommended test strains were not included.

[Test condition]

Triplicate plates were used for each of five different concentrations of the

sample. The liver microsome fraction (S9) was prepared from the liver of male SD rats pretreated with Aroclor 1254.

[Result]

Table. Mutation test with CaCl_2

Dose* (mg/plate)	No. of Revertants			
	TA97		TA102	
	-S9	+S9	-S9	+S9
10	140	173	168	287
5	141	170	230	340
1	132	206	291	376
0.5	140	213	286	424
0.1	149	225	313	437
0	146	212	325	447
PC**	205	2292	4930	1428

* CaCl_2 was dissolved in water and 0.1 ml solution containing the indicated amount of CaCl_2 was used for each plate.

** Positive controls used: 9-aminoacridine (20 $\mu\text{g}/\text{plate}$) for TA97 without S9; 2-aminoanthracene (5 $\mu\text{g}/\text{plate}$) for TA97 with S9; mytomycin C (0.5 $\mu\text{g}/\text{plate}$) for TA102 without S9; and 2-aminoanthracene (5 $\mu\text{g}/\text{plate}$) for TA102 with S9.

Source : Tokuyama Corporation
Reliability : (2) valid with restrictions
Basic data given: comparable to guideline study
Flag : Critical study for SIDS endpoint
10.06.2002

(31)

Type : *Bacillus subtilis* recombination assay
System of testing : *Bacillus subtilis* H17 (rec+), H45 (rec-)
Concentration : 0.005-0.5 M
Cycotoxic conc. :
Metabolic activation : without
Result : negative
Method : other
Year : 1980
GLP : no data
Test substance : other TS
Remark : [Test substance]
 CaCl_2 of highest purity commercially available

[Test condition]

CaCl_2 was dissolved in distilled water. On the day of the experiments, each bacterial stock was melted and streaked radially from small pipettes onto B-2 agar. A 0.05-ml portion of each metal solution (0.005-0.5 M) was dropped on to a filter paper disk (diameter 10 mm), and the disk was placed on the starting point of the streak. The plates were kept at 4°C for 24h and then incubated at 37°C overnight. When a chemical inhibits the growth of recombination-deficient cells (H45 cells) much stronger than that of wild-type cells (H17 cells), the chemical is considered positive for mutagenicity.

Source : Tokuyama Corporation
Reliability : (3) invalid
Documentation insufficient for assessment
11.06.2002

(48)

Type : other: SOS Chromotest
System of testing : *Escherichia coli* PQ37
Concentration : 1 - 1000 µmol/l (0.1-111 mg/l)
Cycotoxic conc. :
Metabolic activation : without
Result : negative
Method : other
Year : 1987
GLP : no data
Test substance : other TS
Remark : [Test substance]
Obtained from Merck

[Test condition]

The SOS Chromotest is a simple colorimetric assay of the induction of the bacterial gene *sfiA* in *E. coli*. The *sfiA* expression is induced after DNA damage as part of the SOS system. In the Chromotest the *sfiA* expression is monitored by assaying β-galactosidase activity in a tester strain as PQ37, which has a *sfiA-lacZ* gene fusion. An exponentially growing culture of PQ37 was incubated for 2h with 100 µl of a CaCl₂ solution in L medium. After the incubation, β-galactosidase activity was determined as the *sfiA* expression and alkaline phosphatase as a bacterial survival. The mutagenic activity at a concentration, C, is expressed by the ratio, $R(C) = \beta/p$, where β represents the β-galactosidase activity and p the alkaline phosphatase activity. The induction factor for a compound at the concentration, C, was defined as $I(C) = R(C)/R(O)$ in which R(O) is the mutagenic activity measured in the absence of CaCl₂. At least 3 experiments were carried out to determine the mutagenic activity of CaCl₂.

Source : Tokuyama Corporation
Reliability : (3) invalid
Documentation insufficient for assessment

11.06.2002

(79)

Type : Chromosomal aberration test
System of testing : Chinese hamster fibroblast cell line CHL
Concentration : max. 4 mg/plate
Cycotoxic conc. :
Metabolic activation : without
Result : negative
Method : other
Year : 1984
GLP : no data
Test substance : other TS
Remark : [Test substance]

Supplied from the Japan Food Additives Association, Tokyo, at the request of the Ministry of Health and Welfare of Japan, where the purity and quality of the sample was checked. The purity of CaCl₂ used was 74.5%.

[Method]

The method was in principle equivalent to OECD Guideline 473, except that no test was carried out with metabolic activation.

[Test condition]

The doubling time of CHL cells was approximately 15 hr. The cells were exposed to CaCl₂ at three different doses for 24 and 48 h. The maximum dose was selected by a preliminary test, in which the dose needed for 50% cell-growth inhibition was estimated using a cell densitometer. Colcemid (final concn 0.2 mg/ml) was added to the culture 2hr before cell harvesting and chromosome preparations were made. A hundred well-spread metaphases were observed under the microscope. The incidence of polyploid cells as well as of cells with structural chromosomal aberrations

such as chromatid or chromosome gaps, breaks, exchanges, ring formations, fragmentations and others, was recorded. Untreated cells and solvent (physiological saline)-treated cells served as negative controls, in which the incidence of aberrations was usually less than 3.0%. The results were considered to be negative if the incidence was less than 4.9%.

[Result]

Table: Mutagenicity of CaCl_2 in chromosomal aberration test *in vitro*

Max dose	4.0 mg/ml
Solvent	Physiological saline
Polyploid	0 %
Structural aberration	1.0 % (48 hr)
Result	Negative

Source : Tokuyama Corporation
Reliability : (2) valid with restrictions
Comparable to guideline study with acceptable restrictions
Flag : Critical study for SIDS endpoint
11.06.2002

(42)

Type : other: anchorage independence assay
System of testing : Cultured primary human diploid foreskin cells
Concentration : 1.00 μM (0.1mg/l)
Cytotoxic conc. :
Metabolic activation : without
Result : negative
Method : other
Year : 1987
GLP : no data
Test substance : no data
Remark : [Test condition]
Primary-cultured human foreskin cells (HFC) were treated for 48 h with 0.1 mg/l CaCl_2 . At the optimal expression time, 1×10^5 cells were suspended in 3 ml of 0.3% agar supplemented with growth medium and solidified on top of 5 ml of a 0.5% agar base layer containing growth medium in a 60-mm dish. Cells were fed every 6 days with 0.5 ml of H-MEM containing 15% fetal calf serum. Four weeks later, cells were stained with 1mg/ml iodinitrotetrazolium violet in PBS, and colonies greater than 0.1 mm in diameter were scored as anchorage-independent (AI) colonies by microscopic examination.

[Result]

Table. Induction of AI in primarily cultured human diploid foreskin fibroblasts.

Treatment	None	CaCl_2
Cytotoxicity: relative plating efficiency (%)	100	95
Absolute no. of AI colonies per dish*	4 $\pm$ 2	6 $\pm$ 2
Frequency of AI per 10^5 survivors**	19	24

* 10^5 cells were seeded per dish into soft agar.

** Total number of AI colonies/(10^5 cells seeded x plating efficiency of reseeded cells on plastic).

Source : Tokuyama Corporation
Reliability : (3) invalid
Documentation insufficient for assessment

12.06.2002

(7)

Type : other: viral transformation assay
System of testing : Cultured Primary Syrian hamster embryo cells
Concentration : max. 6.8 mmol/l (0.75 g/l)
Cycotoxic conc. :
Metabolic activation : without
Result : negative
Method : other
Year : 1979
GLP : no data
Test substance : no data
Remark : [Test condition]
Two plates of primary-cultured Syrian hamster embryo cells (HEC) were treated with metal salts for 18 hr prior to inoculation of simian adenovirus SA7. After the treatment, HEC were rinsed with complete medium and inoculated with SA7. Three hours later, the cells were harvested, plated into 60-mm dishes at 2×10^5 cells /dish, and incubated for 6 days. Then the plates were overlaid with the medium containing Bacto-agar 6 days. At intervals of 4, 5, and 6 days, additional agar medium were added. Final focus counts were made 25 to 30 days from the beginning of the experiment. Enhancement was expressed as the ratio between the transformation frequency of treated, surviving cells and that of control cells.

Source : Tokuyama Corporation
Reliability : (3) invalid
Documentation insufficient for assessment

12.06.2002

(17)

Type : other: recombination and production of disomic and/or diploid spores during meiosis
System of testing : *Saccharomyces cerevisiae* DIS13
Concentration : 10 - 300 mM (1-33 g/l)
Cycotoxic conc. :
Metabolic activation :
Result : positive
Method : other
Year : 1986
GLP : no data
Test substance : no data
Remark : [Test substance]
Substance of the analytical reagent grade obtained from Farmitalia-Carlo Erba, Milan, Italy.

[Test condition]
The experimental procedure used involves the selection of meiotic products carrying two copies of chromosome V and which are consequently prototrophic for the nutritional requirements specified by markers located in alternate trans positions along the right arm of chromosome V. Such clones can be both diploid or disomic. The analysis of the segregation of the markers *leu1* (chromosome VII), *ade2* (chromosome XV) and MAT (chromosome III) allows us to attribute the selected clones to one or other class, to confirm their meiotic origin and whether they are the product of the Meiosis 1 or Meiosis 2. The phenotypes of 96 colonies per dose were actually analysed. The recombination frequency was also determined from the frequency of prototrophs for the markers *hom3* and *his1* present in the trans position on chromosome V. CaCl_2 was dissolved in the sporulation medium and added at the time of cell transfer from the vegetative to the sporulation medium.

[Result]
Chromosomal segregation was seriously disturbed by calcium chloride,

Source : which caused a clear increase in diploid spore occurrence. Calcium
Reliability : Tokuyama Corporation
: (3) invalid
: Relevant methodological deficiencies

11.06.2002

(92)

5.6 GENETIC TOXICITY 'IN VIVO'**5.7 CARCINOGENITY****5.8 TOXICITY TO REPRODUCTION****5.9 DEVELOPMENTAL TOXICITY/TERATOGENICITY**

Species : rat
Sex : female
Strain : Wistar
Route of admin. : gavage
Exposure period : 6th to 15th day of pregnancy
Frequency of treatment : daily
Duration of test : up to the last day of pregnancy
Doses : 1.76, 8.18, 38.0, 176 mg/kg/day
Control group : other: sham-treated
NOAEL Maternal. : > 176 mg/kg bw/day
NOAEL Teratogen : > 176 mg/kg bw/day
Method : other
Year : 1974
GLP : no data
Test substance : other TS
Remark : [Test substance]
Fine white granular material marked with FDA 71-87

[Method]

The method was in principle equivalent to OECD Guideline 414.

[Test condition]

Virgin adult female albino rats were mated with young adult males and observation of the vaginal sperm plug was considered Day 0 of gestation. Beginning on Day 6 and continuing daily through Day 15 of gestation, the females were dosed with the indicated dosages by oral intubations. The controls were sham treated with the vehicle at a level equivalent to the group receiving the highest test dose. The test material prepared and doses calculated according to the following table:

Dosage (mg/kg)	Dose (ml/kg)	Concentration (mg/ml)
<= 250	1	<= 250
251-500	2	125-250
501-750	3	133-250
751-1000	4	187-250
1001-1250	5	200-250

1251-1500	6	208-250
1501-1600	6.4	235-250

Body weights were recorded on Day 0, 6, 11, 15, and 20 of gestation. All animals were observed daily for appearance and behavior with particular attention to food consumption and weight, in order to rule out any abnormalities that may have occurred as a result of anorexic effects in the pregnant female animal. On Day 20 all dams were subjected to Caesarean section under surgical anesthesia, and the numbers of implantation sites, resorption sites, and live and dead fetuses were recorded. The body weights of the live pups were also recorded. The urogenital tract of each dam was examined in detail for anatomical normality.

All fetuses were examined grossly for the presence of external congenital abnormalities. One-third of the fetuses of each litter underwent detailed visceral examinations employing the Wilson technique. The remaining two-thirds were cleared in potassium hydroxide (KOH), stained with alizarin red S dye and examined for skeletal defects.

[Result]

- Table 1: Fate Summary

Group	Material	Dose*** mg/kg	Total		Surviving at Term	
			Mated	Pregnant	Total	Pregnant*
341	Sham	0.0	25	25	25	25
342	Aspirin**	250.0	25	23	25	23
347	CaCl ₂	1.76	25	22	25	22
348	CaCl ₂	8.18	25	24	25	24
349	CaCl ₂	38.0	25	22	25	22
350	CaCl ₂	176.0	25	24	24	23

* Includes all dams examined at term

** Positive Control: 250.0 mg/kg

*** Administered as a water solution

- Table 2: Reproduction Data

Group	341	342	347	348	349	350
Dose (mg/kg)	Sham	Aspirin*	1.76	8.18	38.0	176.0
-----Pregnancies-----						
Total No.	25	23	22	24	22	24
Died or Aborted (before Day 20)	0	0	0	0	0	1
To term (on Day 20)	25	23	22	24	22	23
-----Live Litters-----						
Total No.**	25	18	22	24	22	23
-----Implant Sites-----						
Total No.	279	231	234	261	254	246
Average/dam**	11.2	10.0	10.6	10.9	11.6	10.7
-----Resorptions-----						
Total No.**	4	62	3	1	1	2
Dams with 1 or more sites resorbed	3	11	2	1	1	2
Dams with all sites resorbed	-	4	-	-	-	-
% partial resorptions	12.0	47.8	9.09	4.17	4.55	8.70
% complete resorptions	-	17.4	-	-	-	-
-----Live Fetuses-----						
Total No.	275	168	231	260	253	244
Average/dam**	11.0	7.30	10.5	10.8	11.5	10.6

Sex ratio (M/F)	1.07	1.06	1.10	0.95	0.90	0.89
-----Dead Fetuses-----						
Total* *	-	1	-	-	-	-
Dams with 1 or more dead	-	1	-	-	-	-
Dams with all dead	-	1	-	-	-	-
% partial dead	-	4.35	-	-	-	-
% all dead	-	4.35	-	-	-	-
-----Average Fetus Weight (g)-----						
	3.68	2.39	4.13	3.80	3.84	3.72

* Positive Control: Aspirin 250.0 mg/kg

** Includes only those dams examined at term.

- Table 3: Summary of Skeletal Findings**

Group No.	341	342	347	348	349	350
Dose (mg/kg)	Sham	Aspirin*	1.76	8.18	38.0	176.0
Live Fetuses Examined (at term)	191/25	120/18	161/22	180/24	176/22	173/23
-----Sternebrae-----						
Incomplete oss.	86/22	44/15	34/13	53/14	51/16	47/17
Scrambled						
Bipartite	1/1	2/2	-	1/1	-	1/1
Fused						
Extra						
Missing	34/17	103/18	15/9	19/10	18/9	12/7
Other						
-----Ribs-----						
Incomplete oss.	-	15/9	1/1	3/2	-	1/1
Fused/split						
Wavy	22/10	41/16	13/9	11/6	34/17	19/10
Less than 12	-	1/1	-	3/1	-	-
More than 13	-	95/17	-	4/3	1/1	2/2
Other						
-----Vertebrae-----						
Incomplete oss.	24/14	76/18	23/10	12/7	34/13	20/9
Scrambled						
Fused						
Extra ctrs. oss.						
Scoliosis	-	1/1	-	-	-	-
Tail defects						
Other; spina bifida	-	1/1	-	-	-	-
-----Skull-----						
Incomplete closure	36/13	54/17	25/11	54/19	40/17	31/13
Missing	-	2/2	-	-	-	-
Craniostosis						
Other						
-----Extremities-----						
Incomplete oss.	-	3/3	-	-	-	-
Missing						
Extra						
-----Miscellaneous-----						
Hyoid; missing	26/14	57/17	14/9	9/7	25/9	15/9
Hyoid; reduced	17/12	8/4	18/7	33/17	23/12	16/10

* Positive Control: 250.0 mg/kg

** Numerator = Number of fetuses affected;

Denominator = Number of litters affected.

- Table 4: Summary of Soft Tissue Abnormalities

Group	Material	Dose Level (mg/kg)	Dam	Number of Pups	Description
342	Aspirin*	250.0	A7088 A7093	1	Meningoencephalocele
				3	Encephalomyelocele; umbilical hernia
			A7107	1	Hydrocephalus; exophthalmos; gastroschisis
				1	Meningoencephalocele; umbilical hernia
347	CaCl ₂	1.76	N6016	1	Gastroschisis

* Positive Control: 250.0 mg/kg

- Table 5: Average Body Weights*** (g)

Group	Material	Dose Level (mg/kg)	Day0	Day6	Day11	Day15	Day20**
341	Sham	0.0	232	252	268	295	353 (25)
342	Aspirin*	250.0	226	247	253	268	311 (23)
347	CaCl ₂	1.76	229	248	265	286	353 (22)
348	CaCl ₂	8.18	226	246	261	279	345 (24)
349	CaCl ₂	38.0	226	247	264	285	357 (22)
350	CaCl ₂	176.0	231	251	262	280	346 (23)

* Positive Control: 250.0 mg/kg

** Number of surviving dams in parentheses (c.f. Table 1)

*** Of pregnant dams

[Conclusion]

The administration of up to 176 mg/kg (body weight) of the test material to pregnant rats for 10 consecutive days had no clearly discernible effect on nidation or on maternal or fetal survival. The number of abnormalities seen in either soft or skeletal tissues of the test groups did not differ from the number occurring spontaneously in the sham-treated controls.

Source Reliability

- : Tokuyama Corporation
- : (1) valid without restriction
- : Comparable to OECD guideline study

Flag

15.11.2002

- : Critical study for SIDS endpoint

(29)

Species Sex Strain Route of admin. Exposure period Frequency of treatment Duration of test Doses Control group NOAEL Maternalt. NOAEL Teratogen Method Year GLP Test substance

- : mouse
- : female
- : CD-1
- : gavage
- : 6th to 15th day of pregnancy
- : daily
- : up to the last day of pregnancy
- : 1.89, 8.78, 40.8, 189 mg/kg/day
- : other: sham-treated
- : > 189 mg/kg bw/day
- : > 189 mg/kg bw/day
- : other
- : 1974
- : no data
- : other TS

Remark : [Test substance]
Fine white granular material marked with FDA 71-87

[Method]
The method was in principle equivalent to OECD Guideline 414.

[Test condition]
Virgin adult female albino outbred mice were mated with young adult males, and observation of the vaginal sperm plug was considered Day 0 of gestation. Beginning on Day 6 and continuing daily through Day 15 of gestation, the females were dosed with the indicated dosages by oral intubations. The controls were sham treated with the vehicle (water) at a level equivalent to the group receiving the highest test dose. Body weights were recorded on Day 0, 6, 11, 15, and 17 of gestation. All animals were observed daily for appearance and behavior with particular attention to food consumption and weight, in order to rule out any abnormalities that may have occurred as a result of anorexic effects in the pregnant female animal. On Day 17 all dams were subjected to Caesarean section under surgical anesthesia, and the numbers of implantation sites, resorption sites, and live and dead fetuses were recorded. The body weights of the live pups were also recorded. The urogenital tract of each dam was examined in detail for anatomical normality. All fetuses were examined grossly for the presence of external congenital abnormalities. One-third of the fetuses of each litter underwent detailed visceral examinations employing the Wilson technique. The remaining two-thirds were cleared in potassium hydroxide (KOH), stained with alizarin red S dye and examined for skeletal defects.

[Result]
- Table 1: Fate Summary

Group	Material	Dose*** mg/kg	Total		Surviving at Term	
			Mated	Pregnant	Total	Pregnant*
341	Sham	0.0	25	22	25	22
342	Aspirin**	150.0	25	19	25	19
347	CaCl ₂	1.89	25	22	25	22
348	CaCl ₂	8.78	25	21	24	20
349	CaCl ₂	40.8	25	21	25	21
350	CaCl ₂	189.0	25	23	25	23

* Includes all dams examined at term

** Positive Control: 150.0 mg/kg

*** Administered as a water solution (10 ml/kg-bw)

- Table 2 : Reproduction Data

Group	341	342	347	348	349	350
Dose (mg/kg)	Sham	Aspirin*	1.89	8.78	40.8	189.0
-----Pregnancies-----						
Total No.	22	19	22	21	21	23
Died or Aborted (before Day 17)	0	0	0	1	0	0
To term (on Day 17)	22	19	22	20	21	23
-----Live Litters-----						
Total No.**	21	29	21	20	21	21
-----Implant Sites-----						
Total No.	251	240	244	248	235	272

Average/dam**	11.4	12.6	11.6	12.4	11.2	11.8
-----Resorptions-----						
Total No.**	19	8	12	7	5	35
Dams with 1 or more sites resorbed	6	5	8	6	4	13
Dams with all sites resorbed	1	-	1	-	-	2
% partial resorptions	27.3	26.3	36.4	30.0	19.1	56.5
% complete resorptions	4.55	-	4.55	-	-	8.70
-----Live Fetuses-----						
Total No.	229	224	229	238	227	234
Average/dam**	10.4	11.8	10.4	11.9	10.8	10.2
Sex ratio (M/F)	1.16	1.07	0.80	0.84	0.89	0.93
-----Dead Fetuses-----						
Total* *	3	8	3	3	3	3
Dams with 1 or more dead	2	6	3	3	3	3
Dams with all dead	-	-	-	-	-	-
Per cent partial dead	9.09	31.6	13.6	15.0	14.3	13.0
Per cent all dead	-	-	-	-	-	-
-----Average Fetus Weight (g)-----						
	0.89	0.87	0.90	0.93	0.91	0.90

* Positive Control: 150.0 mg/kg

** Includes only those dams examined at term.

- Table 3: Summary of Skeletal Findings**

Group No.	341	342	347	348	349	350
Dose (mg/kg)	Sham	Aspirin*	1.89	8.78	40.8	189.0
Live Fetuses Examined (at term)	158/21	160/19	160/21	162/20	159/21	161/21
-----Sternebrae-----						
Incomplete oss.	25/10	28/10	21/11	15/6	24/10	12/5
Scrambled						
Bipartite	11/9	9/7	3/3	12/8	13/10	7/6
Fused						
Extra						
Missing	9/7	11/5	16/10	12/5	10/6	12/5
Other						
-----Ribs-----						
Incomplete oss.						
Fused/split						
Wavy	-	-	-	-	1/1	-
Less than 12						
More than 13	41/14	30/12	28/12	42/14	35/14	20/12
Other						
-----Vertebrae-----						
Incomplete oss.	3/3	1/1	2/2	-	-	2/2
Scrambled						
Fused						
Extra ctrs. oss.						
Scoliosis						
Tail defects						
Other						
-----Skull-----						
Incomplete closure						
Missing						
Craniostosis						
Other;facial bones,inc	1/1	-	-	-	-	-
-----Extremities-----						
Incomplete oss.	1/1	1/1	1/1	-	-	2/2

Missing
Extra
-----Miscellaneous-----
Hyoid; missing 23/14 23/11 33/14 26/11 20/10 30/13
Hyoid; reduced 23/13 4/4 22/14 12/9 23/12 12/9

* Positive Control: 150.0 mg/kg
** Numerator = Number of fetuses affected
Denominator = Number of litters affected

- Table 4: Summary of Soft Tissue Abnormalities

Group	Material	Dose Level (mg/kg)	Dam	Number of Pups	Description
342	Aspirin*	150.0	A6102	1	Gastroschisis
349	CaCl ₂	40.8	N5070	1	Umbilical hernia
350	CaCl ₂	189.0	N5112	1	Cleft palate

* Positive Control: 150.0 mg/kg

- Table 5: Average body Weights*** (g)

Group	Material	Dose Level (mg/kg)	Day0	Day6	Day11	Day15	Day17**
341	Sham	0.0	27.7	30.6	34.5	41.1	46.8 (22)
342	Aspirin*	150.0	28.7	31.9	35.0	43.4	50.2 (19)
347	CaCl ₂	1.89	29.3	31.3	35.4	43.6	49.2 (22)
348	CaCl ₂	8.78	28.7	30.7	35.2	45.2	51.5 (20)
349	CaCl ₂	40.8	29.0	30.9	35.8	44.1	50.2 (21)
350	CaCl ₂	189.0	30.9	33.6	37.4	45.4	50.4 (23)

* Positive Control: 150.0 mg/kg

** Number of surviving dams in parentheses (c.f. Table 1)

*** Of pregnant dams

[Conclusion]

The administration of up to 189 mg/kg (body weight) of the test material to pregnant mice for 10 consecutive days had no clearly discernible effect on nidation or on maternal or fetal survival. The number of abnormalities seen in either soft or skeletal tissues of the test groups did not differ from the number occurring spontaneously in the sham-treated controls.

Source : Tokuyama Corporation
Reliability : (1) valid without restriction
Comparable to OECD guideline study
Flag : Critical study for SIDS endpoint

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(29)

Species : rabbit
Sex : female
Strain : Dutch
Route of admin. : gavage
Exposure period : 6th to 18th day of pregnancy
Frequency of treatment : daily
Duration of test : up to the last day of pregnancy
Doses : 1.69, 7.85, 35.6, 169 mg/kg/day
Control group : other: sham-treated
NOAEL Maternalt. : > 169 mg/kg bw/day

NOAEL Teratogen : > 169 mg/kg bw/day
Method : other
Year : 1974
GLP : no data
Test substance : other TS
Remark : [Test substance]
 Fine white granular material marked with FDA 71-87

[Method]

The method was in principle equivalent to OECD Guideline 414.

[Test condition]

On Day 0, each virgin, adult, female rabbits was given an injection of 0.4 ml of human chorionic gonadotropin (400 IU) via the marginal ear vein. Three hours later, each doe was inseminated artificially with 0.3 ml of diluted semen from a proven donor buck using approximately 20 x 10⁶ motile sperm according to the procedure described by Vogin et al.

(Pharmacologist 11, 282 (1969)). Beginning on Day 6 and continuing daily through Day 18 the females were dosed with the indicated dosages by oral intubations. The controls were sham treated with the vehicle at a level equivalent to the group receiving the highest test dose.

Body weights were recorded on Day 0, 6, 12, 18, and 29 of gestation. All animals were observed daily for appearance and behavior with particular attention to food consumption and weight, in order to rule out any abnormalities that may have occurred as a result of anorexic effects in the pregnant female animal.

On Day 29 all does were subjected to Caesarean section under surgical anesthesia, and the numbers of corpora lutea, implantation sites, resorption sites, and live and dead fetuses were recorded. Body weights of the live pups were also recorded. The urogenital tract of each animal was examined in detail for normality.

All fetuses underwent a detailed gross examination for the presence of external congenital abnormalities. The live fetuses of each litter were then placed in an incubator for 24 hours for the evaluation of neonatal survival. All surviving pups were sacrificed, and all pups examined for visceral abnormalities (by dissection). All fetuses were then cleared in potassium hydroxide (KOH), stained with alizarin red S dye and examined for skeletal defects.

[Result]

- Table 1: Fate Summary

Group	Material	Dose*** mg/kg	Total		Surviving at Term	
			Mated	Pregnant	Total	Pregnant*
341	Sham	0.0	18	13	18	13
342	6-AN**	2.5	20	10	19	10
347	CaCl ₂	1.69	22	13	18	12
348	CaCl ₂	7.85	22	14	16	11
349	CaCl ₂	35.6	17	14	14	12
350	CaCl ₂	169.0	16	16	14	14

* Includes all dams examined at term

** Positive Control: 2.5 mg/kg of 6-aminonicotinamide dosed on Day 9

*** Administered as a water solution

- Table 2: Reproduction Data

Group	341	342	347	348	349	350
-------	-----	-----	-----	-----	-----	-----

Dose (mg/kg)	Sham	6-AN*	1.69	7.85	35.6	169.0
-----Pregnancies-----						
Total No.	13	10	13	14	14	16
Died or Aborted (before Day 29)	0	1	1	3	2	2
To term (on Day 29)	13	10	12	11	12	14
-----Corpora Lutea-----						
Total No.	174	122	148	129	138	146
Average/dam mated	9.67	6.42	7.40	7.17	8.63	10.4
-----Live Litters-----						
Total No. **	12	10	12	9	11	12
-----Implant Sites-----						
Total No.	69	56	86	63	69	72
Average/dam**	5.31	5.60	7.17	5.73	5.75	5.14
-----Resorptions-----						
Total No. **	4	2	12	8	8	4
Dams with 1 or more sites resorbed	3	1	4	4	6	3
Dams with all sites resorbed	1	-	-	2	1	-
Per cent partial resorptions	23.1	10.0	33.3	36.4	50.0	21.4
Per cent complete resorptions	7.69	-	-	18.2	8.33	-
-----Live Fetuses-----						
Total No.	65	54	74	55	61	58
Average/dam**	5.00	5.40	6.17	5.00	5.55	4.83
Sex ratio (M/F)	0.86	0.74	1.47	1.04	1.16	1.24
-----Dead Fetuses-----						
Total* *	-	-	-	-	-	10
Dams with 1 or more dead	-	-	-	-	-	2
Dams with all dead	-	-	-	-	-	1
Per cent partial dead	-	-	-	-	-	14.3
Per cent all dead	-	-	-	-	-	7.14
-----Average Fetus Weight (g)-----						
	38.2	33.8	37.3	38.0	36.8	39.2

* Positive Control: 2.5 mg/kg of 6-aminonicotinamide dosed on Day 9

** Includes only those dams examined at term.

- Table 3: Summary of Skeletal Findings***

Group No.	341	342	347	348	349	350
Dose (mg/kg)	Sham	6-AN**	1.69	7.85	35.6	169.0
Live Fetuses Examined						
(at term)	65/12	53/10*	74/12	54/9*	61/11	58/12
-----Sternebrae-----						
Incomplete oss.	-	-	2/1	-	1/1	-
Scrambled	-	-	1/1	-	-	-
Bipartite	-	-	-	-	-	-
Fused	-	1/1	-	-	-	-
Extra	-	-	-	-	-	-
Missing	-	-	-	-	-	-
Other	-	-	-	-	-	-
-----Ribs-----						
Incomplete oss.	-	2/1	-	-	-	-
Fused/split	-	-	-	-	-	-
Wavy	-	-	-	-	-	-
Less than 12	-	-	-	-	-	-
More than 13	-	-	-	-	-	-
Other	-	-	-	-	-	-

-----Vertebrae-----						
Incomplete oss.						
Scrambled	-	5/1	-	-	-	-
Fused						
Extra ctrs. oss.						
Scoliosis	-	1/1	-	-	-	-
Tail defects	-	10/3	-	-	-	-
Other; spina bifida						
-----Skull-----						
Incomplete closure	1/1	-	-	-	-	-
Missing						
Craniosclerosis	-	-	2/1	-	-	-
Other						
-----Extremities-----						
Incomplete oss.						
Missing						
Extra						
-----Miscellaneous-----						

* One pup lost in processing
 ** Positive Control: 2.5 mg/kg of 6-aminonicotinamide dosed on Day 9
 *** Numerator = Number of fetuses affected

- Table 4: Summary of Soft Tissue Abnormalities

Group	Material	Dose Level (mg/kg)	Dam	Number of Pups	Description
342	6-AN*	2.5	Z7640	2	Medial rotation of hind limbs

* Positive Control: 2.5 mg/kg of 6-aminonicotinamide dosed on Day 9

- Table 5: Average body Weights*** (g)

Group	Material	Dose Level (mg/kg)	Day0	Day6	Day12	Day18	Day29**
341	Sham 0.0	2.23	2.32	2.40	2.48	2.59	(13)
342	6-AN* 2.5	1.86	1.94	2.03	2.08	2.18	(10)
347	CaCl ₂ 1.69	2.20	2.31	2.43	2.51	2.64	(12)
348	CaCl ₂ 7.85	2.12	2.16	2.16	2.25	2.33	(11)
349	CaCl ₂ 35.6	2.22	2.31	2.34	2.40	2.50	(12)
350	CaCl ₂ 169.0	2.27	2.39	2.41	2.46	2.50	(14)

* Positive Control: 2.5 mg/kg of 6-aminonicotinamide dosed on Day 9

** Number of surviving dams in parentheses (c.f. Table 1)

*** Of pregnant dams

[Conclusion]

The administration of up to 169 mg/kg (body weight) of the test material to pregnant rats for 13 consecutive days had no clearly discernible effect on nidation or on maternal or fetal survival. The number of abnormalities seen in either soft or skeletal tissues of the test groups did not differ from the number occurring spontaneously in the sham-treated controls.

Source : Tokuyama Corporation
Reliability : (1) valid without restriction
 Comparable to OECD guideline study
Flag : Critical study for SIDS endpoint

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5.10 OTHER RELEVANT INFORMATION

Type : other: cytotoxicity to testicular cells *in vitro*
Remark : Toxicity of six metal salts, including calcium chloride, to testicular cells was investigated using four assay systems:
 1) inhibition of cellular respiration, as indicated by the reduction of a tetrazolium dye MTT; 2) uptake of neutral red, a supravital dye; 3) lactate production; and 4) germ cell release from Sertoli cell-germ cell co-cultures. For this purpose, two primary cell culture systems were prepared from rat testes. One was the Sertoli cell culture system, which was used for the assays 1 to 3 and another the Sertoli-germ cell co-culture system, used for the assay 4. By these assays, calcium chloride was shown to be non-toxic to rat spermatogenic cells when added at concentrations up to 10 mM, while the assays indicated that cadmium chloride was the most toxic, effective at concentrations lower than 10 µM.

Source : Tokuyama Corporation

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(12)

Type : other: cytotoxicity to tumor cells transplanted in rats
Remark : Twenty-three kinds of inorganic compounds including CaCl₂ were examined for their inhibitory effect on the MTK-sarcoma III, a rat ascites tumor. The tumor cells were transplanted in Wistar, Long-Evans and Gifu-agouti rats of both sexes. All the animals with the tumor cells died within 9 days after transfer. The test compounds were administered intraperitoneally to rats, starting on the 3rd or 4th day of tumor transfer, at dosages determined after several trials. Rats of control groups received intraperitoneal injection of physiological saline. Cytological preparations were made at appropriate intervals following application of the chemicals. Autopsy was made in some cases to examine any accompanying effect of the chemicals. Single administration of CaCl₂ (3.5 g/kg) exerted a marked damaging effect on the cytoplasm and nuclei of the tumor cells. Most cells generally underwent metaphase block by the effect of the compound. Daily administration of the chemical at one-fifth to one-half of the single dosage for 7 consecutive days caused a marked decrease in the number of dividing cells in the ascites of the tumor-bearing animals and resulted in slight prolongation of the life span of the animals.

Source : Tokuyama Corporation

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(53)

Type : other: ultrastructural changes of parathyroid gland
Remark : Ultrastructural changes of the parathyroid glands of 18-day-old mouse fetuses after administration of calcium chloride or ethylenediaminetetraacetic acid (EDTA) were examined. Pregnant mice at 18 days of gestation were anesthetized and their uteri were surgically opened, thereby exposing fetuses. The operation was performed in such a way as to enable the fetuses to remain alive as well as to keep the umbilical cords and placenta intact. Mouse fetuses were divided into three groups of 6 animals each. One group was given 10 µl of distilled water intraperitoneally as a control. The remaining groups were given intraperitoneally either 10 µl of 5% CaCl₂ solution or 10 µl of 5% EDTA solution. The parathyroid glands of each group were removed 10 min after injection, fixed, and examined with an electron microscope. The morphology of the parathyroid gland of control mouse fetuses resembled that of 1-day-old mice. Many chief cells in the parathyroid glands of the CaCl₂-treated mouse fetuses contained poorly developed Golgi complexes and cisternae of the granular endoplasmic reticulum and many prosecretory granules as compared with those of the control fetuses.

Source : Tokuyama Corporation
10.06.2002 (43)

Type : other: meiotic chromosome aberrations in grasshoppers
Remark : The effect of CaCl₂ on the spermatocyte chromosomes of grasshoppers was studied. Adult males of *Spathosternum prasiniferum* were injected individually with 0.05 ml of 1% calcium chloride solution and their testes fixed at 4, 8 and 12 hours. As no single individual of the series survived beyond 12 hours, the pertinent tissues could not be fixed at 16, 20 or 24 hours. As a control, distilled water was injected to the grasshoppers. No casualty was observed in the control series at 24 hours after injection. Chromosomal aberrations of any type were not seen in the control series. In the CaCl₂-treated series, on the other hand, the manifestation of general stickiness was readily seen, reflected in clumping of chromosomes in all divisional stages. Interbivalent connections were also observed in the diakinesis stage. No chromosome or chromatid type breaks were observed in the divisional stages. Very thin chromatin bridges were encountered, however, in most anaphase I cells. The frequency of aberrations, as seen at 12-hour treatment, is more than at 4- or 8-hour treatment.

Source : Tokuyama Corporation
10.06.2002 (82)

Type : other: meiotic chromosome aberrations in sandhoppers
Remark : The effect of CaCl₂ on the spermatocyte chromosomes of sandhoppers was studied. Adult males of *Chrotogonus trachypterus* were injected individually with CaCl₂ or with distilled water as a control. They were sacrificed 24 hours after injection and the testes were dissected and fixed. Hundreds of cells examined in the control series did not reveal any true gap or break type aberration. In the treated cells aberrations like chromatid type gap and break, chromosome type gap and break, constrictions etc. were observed. The frequency of aberration has been found to be 5.2% (18/388 cells). Regarding stage sensitivity anaphase I and anaphase II divisional stages were more affected. No exchange type of aberration was observed.

Source : Tokuyama Corporation
10.06.2002 (6)

Type : other: goiter production
Remark : Goiter was experimentally produced in one year old rats by feeding on 2% calcium chloride added to the basal diet with or without potassium iodide for 140 days. The estimated daily intake of calcium chloride was about 0.2 g per animal. The animals received a calcium-rich and iodine-poor diet presented a marked enlargement of the thyroid. Two large adenomas were found in this group. The thyroids in the animals received a calcium-rich and iodine-rich diet were also definitely enlarged. The glands in this group presented the microscopic picture of colloid goiter, however.

Source : Tokuyama Corporation
10.06.2002 (38)

Type : other: tumor promotion
Remark : The effect of some chemicals on promotion of chemical tumorigenesis was studied. Tumor initiation was carried out by painting right cheek pouches of Syrian golden hamsters with dimethylbenzanthracene (DMBA) solution (0.2% in dimethylsulfoxide (DMSO)) 3 times per week for 2-4 weeks. A test substance for promotion was then painted for another 4-6 weeks. Control animals were also initiated with DMBA but painted with DMSO alone during the promotion period. The animals were sacrificed and cheek pouches were excised, fixed and examined. Calcium chloride (0.2 M), calcium ionophore 23187 (20 µM) and the membrane labilizing agents such as triton X-100 (0.2%), trypsin (1 mg/ml) and phospholipase C (1 mg/ml) promoted benign hyperplastic lesions (BHLs) but rarely advanced tumors in hamster

	cheek pouch mucosa initiated with DMBA. On the other hand, retinyl acetate (50 mM) and croton oil markedly promoted both BHLs and advanced tumors. These results suggest that pathways modulated by intracellular calcium cause the promotion of BHLs, while additional mechanisms are required for the progression of BHLs to more advanced tumors.	
Source 10.06.2002	: Tokuyama Corporation	(71)
Type Remark	: other: embryotoxicity (chicken eggs) : The toxicity of 80 chemicals which have food additive use has been investigated by their administration to developing chicken embryos. Four test conditions were used: injection via the air cell and via the yolk; and two times, preincubation (0 hr) and 96 hr. For each condition, at least 100 embryos per dose level were treated at a minimum of five dose levels. Appropriate groups of vehicle controls and untreated controls were included in all experiments. All compounds were administered in a volume of 100 µl or less, and solvent controls were treated with the same volume of the solvent only. LD ₅₀ values were determined for each test condition. All embryos and hatched chicks were examined grossly for any abnormalities in development, both functional and structural. All abnormalities were tabulated and compared with values for the vehicle controls to determine teratogenicity. Calcium chloride showed no teratogenic effects on the developing embryo under the four conditions even at 10 mg/egg, the highest concentration tested.	
Source 10.06.2002	: Tokuyama Corporation	(106)
Type Remark	: other: embryotoxicity (chicken eggs) : Teratogenic effect of calcium salts on chick embryos were studied. In embryos 2 and 3 days of age, 0.01-0.04 ml of 0.01 M calcium chloride (pH 6.0) was injected into the subgerminal fluid of the yolk sac, immediately underneath the embryo. Otherwise, at 4 and 5 days, the fluid was injected into the allantois. The windows were then sealed with paraffin and the egg returned to the incubator. The eggs were checked daily and the embryos examined as soon as death was detected or, in survivors, 7 days after injection. It became apparent that very small quantities of calcium chloride solution injected into either the subgerminal area of the yolk sac or the allantois produced pronounced abnormalities. No explanation of this bizarre phenomenon could be offered.	
Source 10.06.2002	: Tokuyama Corporation	(34)

5.11 EXPERIENCE WITH HUMAN EXPOSURE

Memo Remark	: Direct observations (clinical cases) : Three cases of gastro-intestinal lesions due to calcium chloride administered by gavage to infants for the treatment of tetany are described.
	[Case 1] A female baby weighing 2,900 g was given 4 g of calcium chloride by gavage. Blood-stained vomitus appeared two hours later. Shock occurred in 4.5 hours, and peritonitis was suspected. The child vomited repeatedly and died on the 36th day of life. Microscopic examination revealed ulceration and necrosis of the mucosa and submucosa of stomach and small intestines.
	[Case 2] A male baby weighing 3,060 g was given 3 g of the substance followed by 1 g at each four-hour feeding thereafter. On the following day the infant vomited the feedings and respiratory difficulty was observed. This

was attributed to aspiration. Signs of collapse ensued, and despite transfusions and other supportive measures, death occurred on the 7th day of life. Microscopically, sections of the damaged portion of the stomach showed necrosis and disappearance of the mucosa with edema, polymorphonuclear cellular infiltration, and necrosis of the blood vessel walls in the submucosa and muscularis.

[Case 3] A female baby was given 2 g of calcium chloride in water before the 10 a.m. and 2 p.m. feedings. Both feedings were promptly vomited, and the vomitus was blood streaked. She took and retained one-half of the 6 p.m. feeding, which contained 2 g of calcium chloride. Saline clysis, transfusion, and hykinone were given because of the hematemesis. The baby did well on the regular formula without added calcium, and saline clyses for the next 2 days. No convulsions occurred. On the 11th day of life, 0.5 ml of 50% calcium chloride were added to each feeding, and continued for 2 days without incident. Discharge diagnosis was hypocalcemic tetany. The infant gained weight since discharge and showed no subsequent gastro-intestinal symptomatology.

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(24)

**Memo
Remark**

- : Direct observation (occupational exposure)
- : A 30-year-old oil worker spent a day loading calcium chloride powder into containers. Although he was wearing protective clothing some powder had come into contact with his skin. He had experienced no discomfort and had therefore taken no action. The same evening he presented to hospital with severely painful areas over both thighs. Examination revealed many small erythematous patches scattered over both thighs and patches that were larger and appeared to be of deep partial or full thickness skin loss affecting both thighs and the right arm. The patient was treated with copious prolonged irrigation in a shower and dressed on a regular basis for 14 days. During this time the wounds failed to show any signs of healing and seven larger areas were surgically removed. Four areas were small enough to allow excision to underlying fascia and direct closure. These areas healed slowly but uneventfully. The remaining three larger areas were tangentially shaved to apparently healthy tissue and meshed split-thickness skin grafts applied. Healing was completed by secondary intention. Finally, the scattered smallest wounds which were not excised, developed into punctate areas of full thickness skin loss which took a total of 5 months to heal.

The authors suggest that the desiccating effect of calcium chloride at high concentrations is the mechanism of injury. They recommend that the affected area should be washed immediately with soap and copious water and all contaminated clothing be removed.

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(86)

**Memo
Remark**

- : Direct observations (occupational exposure)
- : [Case 1] A 29-year-old coal-miner had developed a most unusual looking but symptomless eruption on his back, which had been abraded by a slight fall of roof three weeks before. He had had no treatment for the abrasions, which were no worse than he had sustained on many previous occasions, and he had continued working as a filler at the coal face. The eruption covered a large area of his back and consisted of many fine white firm papules 2-3 mm in diameter, some in ring formation and others linear, the majority of the papules having an erythematous flare around them. The epidermis appeared to be intact over the papules. There was no itching or pain. Most of the lesions were on the exact area where his skin had been abraded, but a few had developed on the posterior axillary fold where he was sure there had been no abrasions. The rest of his skin was normal. He felt in good health and there was nothing else relevant in his history.

[Case 2] A 21-year-old miner had two groups of lesions on his left elbow. The eruption had been present for several weeks. Here again, a series of whitish papules 2 mm in diameter were arranged in a line 1.5 cm long. He could not remember any particular injury to the elbow but it was reasonable to suppose that he had abraded it. The histology in this case was not identical with the first since there was a break in the epidermis and the gap was filled with metachromatic staining structureless material that did not stain completely with Von Kossa reagent. However, the two cases were so similar it was concluded that they must be variants of the same pathology.

It was then discovered that these men worked at the same colliery and were at the same part of the coal face, where there was a lot of water dripping from the roof but the conditions were not unusual. Samples of the roof water were analyzed and contained approximately 3.5% calcium chloride, 1% magnesium chloride and 10% sodium chloride.

The skin of the forearm of a doctor was experimentally scarified with a cutting needle as deeply as pain would allow and gauze dressing soaked in a solution of the same mineral content as the roof water was applied. This was kept moist with fresh lotion for 72 hours. As that time obvious calcium deposits appeared in the scratch marks with a considerable inflammatory reaction around them. The calcium deposits remained clinically visible for six weeks, being gradually extruded. This was a speedier recovery than the coal-miners had, presumably because the abrasions were not so deep. The miners recovered in four months.

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(91)

Memo

Remark

- : Direct observations (occupational exposure)
- : A man, while engaged in spraying in a coal mine, allowed some of 40% calcium chloride solution to contaminate his skin. Immediately after exposure, which lasted 8 hours, he experienced burning pain accompanied by the formation of wheals on the upper eyelids, forearms, and thighs. Similar effects were noticed on his hands and legs, where abrasions occurred during the work, those on the legs being due to friction from the tops of his rubber boots. Eleven days later the lesions on the legs and hands broke down. When first examined 16 days after exposure there were large sloughing ulcers with raised, dark red edges running transversely across the upper parts of both legs and smaller round ones on the backs of both hands, with crusts which, when removed, left deep pits. The lesions on the eyelids, forearms, and thighs were not ulcerated but consisted of pearly yellow, raised spots measuring 1-2 mm, some of them round and others shaped like splashes. These lesions have been observed for over 5 months. The ulcers were indolent, and epithelialization was not completed until after 13 weeks. From the seventh week onwards, the lesions on the legs were outlined by narrow zones of yellow discolouration in the deeper tissues. The appearance of the non-ulcerated lesions did not change for the first 4 months, but they finally disappeared.

Another man who was engaged in the same work noticed burning and redness at the sites of contact immediately after exposure. He alleged that he then washed very thoroughly with soap and that the effects disappeared in about a week.

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(40)

Memo

Remark

- : Direct observation (accidental exposure)
- : A white boy of four and a half years had a painless black patch on the anterior surface of the left thigh when he was undressed at about 10:30 p.m. His mother examined the boy's clothing to determine the cause and found wet slag in the left pocket of his blue jeans. The mother had helped him dress at about 11:00 a.m. with clean and recently laundered cloths and then the boy had played with his friends in or near a slag road treated with

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calcium chloride flakes to reduce the dust. The mother was unaware of a previous injury or abrasion of the skin in the involved area. When the boy was seen by a doctor on the next day, the area of dry gangrene was more than 2.5 cm in diameter on the anterior surface adjacent to the area where the pocket came in contact with the skin. Thirty-two days later, with separation at the edges, most of the necrotic area was excised. After excision, a greenish-grey base with several aggregations of brownish-black punctae was noted. The necrosis obviously extended into the subcutaneous fat. Six days later all of the necrotic tissue had sloughed out. Healing occurred by secondary intention.

(10)

**Memo
Remark**

- : Direct observations (accidental exposure)
- : Two cases of necrosis of the skin due to contact with calcium chloride powder are described.

[Case 1] A middle-aged white man visited a doctor, presenting popular lesions on both forearms. He stated that he had carried bags of calcium chloride on his bare forearms a few weeks before, and that there had been subsequent development of the lesions. Examination revealed peculiar firm pink-red papules up to pea size, single or in groups and streaks on both forearms, mainly the flexor surfaces. There were obtuse large horny plugs in some. Others showed whitish material under the surface. Two weeks after the first visit many of the lesions had disappeared, though there was still some pus and whitish necrotic material in the remaining lesions. Biopsy revealed epithelial proliferation and fibroblastic response. The lesion was apparently in the stage of repair.

[Case 2] A white boy, aged 7 years, was seen by a doctor, presenting an elevated plaque on the anterior left thigh. Three weeks before, he had put in his left pants pocket some calcium chloride powder obtained from a 25 lb. bag of the substance kept in the basement as dehumidifier. The mother noticed reddening of the anterior thigh that evening when the child took a bath. The lesion began as a red area about 3 inches in diameter, with a gray-green center about 1 inch wide. Raised papules were noted in this area about two weeks later. Examination showed a moderately elevated erythematous plaque about 2.5 by 1.5 cm in diameter. The lesion was studded throughout with small discrete and confluent white papules just under the skin surface. There was no noticeable surrounding inflammatory reaction. A month later, a gradual flattening of the lesion without ulceration was observed. Four months later, there remained only a smooth, slightly pink atrophic scar without infiltration. The lesion had been asymptomatic throughout. Sections of the biopsy specimen showed incrustation of large parts of superficial corium with lime salts which stained blue with hematoxylin, while the orcein-Giemsa stain showed that in corresponding areas the structure of collagenous and elastic fibers, but relatively few cells, were presented. There was reactive hypertrophy of the epidermis, and some of the calcified material was in the process of being extruded through the epidermis. There was some chronic inflammatory reaction in the upper corium.

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(109)

**Memo
Remark**

- : Direct observation (clinical case)
- : A 27-year-old woman with hypoparathyroidism developed multiple firm white-yellow papules along the path of an infiltrated calcium chloride intravenous infusion. A biopsy specimen obtained ten days after the extravasation revealed an ulcerarial reaction. A subsequent biopsy specimen, obtained 25 days after the extravasation, showed diffuse dermal calcification, confirmed by roentgenographic analysis, with incipient transepidermal elimination. A biopsy specimen obtained 40 days after the extravasation was consistent with an elimination reaction. An increase in

11.06.2002	mast cells was not noted. Electron microscopy showed mineral deposits along collagen fibrils without significant collagenous degeneration. There was no history of collagen or renal disease, hypervitaminosis D, or neoplasm. This episode was not associated with an elevated serum calcium or phosphate level. The patient's serum bicarbonate level was normal. She was afebrile, without lymphadenopathy or leukocytosis. The skin lesions were treated with warm soaks, with gradual improvement over four months as whitish material was eliminated from their centers.	(32)
Memo Remark	: Brief summary of occupational exposure : Calcium chloride has a powerful irritant action on the skin and mucous membranes and cases have been reported, amongst workers packing dry calcium chloride, of irritation accompanied by erythema and peeling of facial skin, lacrimation, eye discharge, burning sensation and pain in the nasal cavities, occasional nose bleeding and tickling in the throat. Cases of perforation of the nasal septum have also been reported.	(83)
10.06.2002		
Memo Remark	: Brief summary of health effects : Calcium chloride is a nonvolatile substance under normal conditions, thus limiting routes of exposure. Consequently, no data have been accumulated on the health effects of inhalation of calcium chloride in man or in animals. Published literature indicates that exposure to calcium chloride dust causes irritation to the eyes and throat while solutions can cause burns and eye damages when tissue contact is made. Prolonged exposure can cause serious burns, especially on previously injured tissue.	(28)
10.06.2002		
Memo Remark	: Brief summary of side effects : Calcium chloride has been used for medical treatment of hypocalcemic tetany, calcium deficit in citrated blood, serum sickness after injection of antitoxins and antisera, and allergic diseases such as hay fever, urticaria and asthma. As an electrolyte replenisher calcium chloride is a pharmaceutical necessity for Ringer's solutions. Side effects result from too rapid injection; these include vasodilation and a burning sensation in the skin. Overdosage can cause hypercalcemia. Because of the danger of overdosage, calcium chloride is contraindicated in renal insufficiency even if hypocalcemia exists. It should be given cautiously to the digitalized patient and the electrocardiogram should be monitored. Extravasation can cause tissue necrosis.	(80)
11.06.2002		

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