FOREWORD INTRODUCTION

SODIUM BICARBONATE

CAS N°: 144-55-8

SIDS Initial Assessment Report
For
SIAM 15
(Boston, USA, 22-25 October 2002)

Chemical Name: Sodium bicarbonate

CAS No: 144-55-8

Sponsor country: Belgium

National SIDS Contact Point:

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Process:

The draft dossier was prepared by a consultant (TNO Chemistry, Zeist, The Netherlands). After a quality check of the IUCLID, SIAR, SIAP and Summary Table by the industry, the dossier was submitted in June 2002 to the sponsor country. On behalf of the sponsor country 2 experts (human health, environment) reviewed the dossier. The sponsor country and the industry consortium leader had been working together already for another ICCA HPV chemical (KOH), which facilitated the process.

History:

The substance is an ICCA HPV chemical. Industry did the literature search and collected all references. The consultant received the literature and prepared the draft dossier. The dossier of sodium carbonate (CAS number 497-19-8) was developed in parallel using a similar procedure.

No new SIDS testing conducted (X)

New SIDS Testing conducted ( )

Comments:

Date of first Submission: 6 August 2002

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	144-55-8
Chemical Name	Sodium bicarbonate
Structural Formula	$NaHCO_3$

SUMMARY CONCLUSIONS OF THE SIAR

Sodium bicarbonate is a white, odourless, crystalline powder. It decomposes when heated over 50°C and therefore a melting and boiling point can not be determined. Sodium bicarbonate is an inorganic salt and therefore the vapour pressure can be considered negligible. Its water solubility is 96 g/l at 20°C. Grades with different average particle size diameters (d_{50}) are placed on the market. The average particle size diameter of the different sodium bicarbonate grades can range between 15 and 300 µm.

Human Health

Oral LD_{50} values were higher than 4,000 mg/kg bw, and an inhalation study in rats using a concentration of 4.74 mg/l inhalable dust produced no deaths.

There are no directly relevant studies on repeated dose exposure, however, knowledge of prior use and available literature does not indicate any adverse effects of long-term use of exposure via any route. *In vitro* bacterial and mammalian cell tests showed no evidence of genotoxic activity. As with other sodium salts, high doses of sodium bicarbonate promote carcinoma formation in rat urinary bladder after pre-exposure to initiator or BBN. However, when rats were only exposed to sodium bicarbonate no carcinogenic effect on the urinary bladder was found. Based on the available information there are no indications that sodium bicarbonate has carcinogenic effects.

Sodium bicarbonate has a long history of use in foodstuff, feed and industrial processes. The bicarbonate ion is a normal constituent in vertebrates, as the principal extracellular buffer in the blood and interstitial fluid is the bicarbonate buffer system. Excess sodium and bicarbonate ions are readily excreted in the urine. It is therefore assumed that normal handling and use will not have any adverse effects. The consequences of accidental or excessive oral ingestion have been described in a number of publications. Acute oral ingestion by the patients may result in a ruptured stomach due to excessive gas development. Acute or chronic excessive oral ingestion may cause metabolic alkalosis, cyanosis and hypernatraemia. These conditions are usually reversible, and will not cause adverse effects.

Environment

Acute NOEC values to fish and daphnids are higher than 1,000 mg/l. The 21-day NOEC to *Daphnia magna* is higher than 576 mg/l. The acute toxicity of sodium bicarbonate for aquatic organisms could be based on a high osmotic pressure. This is a very general effect of salts as soon as their concentration in water exceeds a certain level.

Both sodium and bicarbonate are present naturally present in aquatic ecosystems. For sodium the 10^{th}- and 90^{th}-percentile were 1.5 and 68 mg/l, respectively, based on a total number of 75 rivers. For bicarbonate the 10^{th}- and 90^{th}-percentile were 20 and 195 mg/l, respectively, based on a total number of 77 rivers. Because the natural pH, bicarbonate and sodium concentration (and also their fluctuations in time) varies significantly between aquatic ecosystems, it is not considered useful to derive a generic PNEC or $PNEC_{added}$. To assess the potential environmental effect of a sodium bicarbonate discharge, the increase in sodium, bicarbonate and pH should be compared with the natural values and their fluctuations and based on this comparison it should be assessed if the anthropogenic addition is acceptable.

The production and use of sodium bicarbonate could potentially result in an emission of sodium bicarbonate to aquatic and terrestrial ecosystems. However, for most applications the bicarbonate will be digested (animal feeding, human food, pharmaceuticals) or treated by a waste water treatment plant (detergents and household cleaning products) and will not be directly emitted to the ecosystems. In order to determine if the production and use of sodium bicarbonate really results in a significant emission of bicarbonate, an evaluation of the complete, inorganic and organic carbon cycle would be required.

Aquatic sodium emissions originating from uses of sodium bicarbonate are probably small compared to other sources. It is clear that an environmental hazard assessment of sodium should not only evaluate all natural and anthropogenic sources of sodium but should also evaluate all other ecotoxicity studies with sodium salts, which is beyond the scope of this report.

Exposure

Sodium bicarbonate is produced on all continents of the world and the global number of production sites is estimated to be 30-50. The estimated total amount of sodium bicarbonate used in 2001 is 2 million tonnes.

Sodium bicarbonate is used as animal feed additive, human food additive and it is used in pharmaceuticals. It is also used for the production of other chemicals and it used in cosmetics and detergents and other household cleaning products. It is present in a large number of consumer products but the pure product is also available to consumers.

RECOMMENDATION

The chemical is currently of low priority for further work.

RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

This chemical is currently considered of low priority for further work because of its low hazard potential.

FULL SIDS SUMMARY

CAS N° 144-55-8		PROTOCOL	RESULTS
PHYSICO-CHEMICAL			
2.1 2.2	Melting point Boiling point	No data No data	Decomposition Decomposition
2.3	Density	No data	2.159 (at 20ºC)
2.4	Vapour pressure	No data	Negligible, ionizable inorganic compound
2.5	Partition coefficient	No data	Not relevant, ionizable inorganic compound
2.6	Water solubility	No data	69 g/l (at 0ºC) 96 g/l (at 20ºC) 165 g/l (at 60ºC)
2.11	Oxidising properties	No data	Not oxidizing
2.12	Additional remarks	Mild alkaline compound with a pH of 8.4 in a 0.1N aqueous solution at 25°C	
ENVIRONMENTAL FATE AND PATHWAY			
3.1.1	Photodegradation	Not applicable	
3.1.2	Stability in water	The sodium ion will not adsorb to particulate matter, but remains in the aqueous phase. In water the bicarbonate ions will re-equilibrate until an equilibrium is established. The main equilibria are: $HCO_3^- \leftrightarrow CO_3^{2-} + H^+$ pKa = 10.33 $CO_2 + H_2O \leftrightarrow HCO_3^- + H^+$ pKa = 6.33 The carbonate will finally be incorporated into the inorganic and organic carbon cycle.	
3.2	Monitoring data	UNEP (1995) reported the bicarbonate concentration for a total number of 77 rivers in North-America, South-America, Asia, Africa, Europe and Oceania. The 10th-percentile, mean and 90th-percentile were 20, 106 and 195 mg/l, respectively. The sodium concentration was reported for a total number of 75 rivers in North and South America, Africa, Asia, Europe and Oceania, with a 10th-percentile of 1.5 mg/l, mean of 28 mg/l and 90th-percentile of 68 mg/l (UNEP, 1995).	
3.3	Transport and Distribution	Not applicable.	
3.5	Biodegradation	Not applicable, as it is an inorganic compound.	
ECOTOXICOLOGY		**SPECIES**	**PROTOCOL** / **RESULTS**
4.1	Acute/prolonged toxicity to fish	Rainbow trout (*Oncorhynchus mykiss*)	Flow-through test, 96-hour exposure, FIFRA Guideline 72-1, GLP study NOEC: 2,300 mg/L LC50: 7,700 mg/L
		Bluegill sunfish *Lepomis macrochirus*	Flow-through test, 96-hour exposure, FIFRA Guideline 72-1, GLP study NOEC: 5,200 mg/L LC50: 7,100 mg/L

4.2	Acute toxicity to aquatic invertebrates	*Daphnia magna* (age<24H)	48 hr immobilisation test (flow through), FIFRA Guideline 72-2, GLP study	NOEC: 3,100 mg/L EC50: 4,100 mg/L
		Daphnia magna	Various static 48 hr immobilisation tests in public literature	EC50> 1000 mg/L
		Ceriodaphnia dubia (age<24H)	Two static 48 hr immobilisation tests in public literature	EC50 1,075 mg/L EC50 1,020 mg/L
4.3	Toxicity to aquatic plants e.g. algae	At a concentration of 45 mg/L, sodium bicarbonate is beneficial for algal growth.		
4.5.2	Chronic toxicity to aquatic invertebrates	21 days NOEC to *Daphnia magna* (survival and offspring) > 576 mg/L		
4.6	Toxicity to terrestrial organisms	Honeybee (*Apis mellifera*), 48 hours acute toxicity (FIFRA guideline 141-1, GLP Study): NOEC: 24 µg/bee, LC50> 24 µg/bee		

MAMMALIAN TOXICOLOGY		**SPECIES**	**PROTOCOL**	**RESULTS**
5.1.1	Acute Oral	Rat	No data	LD50: 4220 mg/kg bw
			No data	LD50: 4310 mg/kg bw
			No data	LD50: 4400 mg/kg bw
			No data	LD50: 5820 mg/kg bw
			No data	LD50: 6290 mg/kg bw
			No data	LD50: 8290 mg/kg bw
		Rat	EPA-FIFRA 40 CFR 160, GLP study	LD50: >4000 mg/kg bw
		Rat	GLP study	LD50: 7334 mg/kg bw
		Rat	EPA 16 CFR 1500.3C2(i)	LD50: >5000 mg/kg bw LD50: =5000 mg/kg bw LD50: <5000 mg/kg bw
5.1.2	Acute Inhalation	Rat	Whole-body exposure, 4.5 hours, particle size MMAD 2.8 µm. GLP study.	LC50: >4.74 mg/l
5.1.3	Acute Dermal	No data		
5.2.1	Skin irritation/corrosion	Rabbit Rabbit	GLP study 40 CFR 798.4470	Slightly irritating
5.2.2	Eye irritation/Corrosion	Rabbit	EPA TSCA 40 CFR 798.4500	Minimally irritating
		Rabbit	Draize test	Irritating (dose of 220 mg)

5.4	Repeated dose	Pig	1% NaHCO3 with/without 250 mg/kg bw Cu. Exposure period unknown.	LOAEL: 1% in feed.
5.5	Genetic Toxicity In vitro	*Salmonella typhimurium* *Salmonella typhimurium* *Salmonella typhimurium* Chinese hamster fibroblast cell line *Escherichia coli*	Reverse mutation assay, +/- S9, max. 10 mg/plate, duplicate. Reverse mutation assay, +/- S9, duplicate or triplicate. Reverse mutation assay, +/- S9, 0.1-10 mg/plate. Chromosomal aberration test +/- S9, 1 mg/ml. DNA damage and repair test, +/- S9, max. 5000 µg with S9, max. 2500 µg without S9, five parallels.	No induction of mutation. No induction of mutation. No induction of mutation. No induction of DNA damage. No induction of DNA damage.
5.6	Genetic Toxicity In vivo	No data available		
5.7	Carcinogenicity	Rat	Exposed for 104 weeks in feed to 1.25% sodium o-phenylphenol (OPP-Na) + 0.64% NaHCO3, 1.25% OPP + 0.32% NaHCO3, 1.25% OPP + 0.16% NaHCO3, 1.25% OPP or 0.64% NaHCO3.	No carcinogenic effects of NaHCO3 alone.
5.8	Reproduction Toxicity	No data available		
5.9	Development / Teratogenicity	Mouse, rat and rabbit	Exposed via oral intubation during days 6-15 of gestation.	NOAEL = 580 mg/kg bw (mouse) NOAEL = 340 mg/kg bw (rat) NOAEL = 330 mg/kg bw (rabbit)
5.11	Human experience	A number of cases of unintentional overdosing have been reported in the medical literature. In acute cases the patients suffer from a ruptured stomach due to excessive gas development. A stomach rupture occurred only after an extreme excess of food and drink followed by the use of excess (greater than recommended) amount of sodium bicarbonate. Acute or chronic over-ingestion may cause metabolic alkalosis, cyanosis and hypernatremia.		

SIDS Initial Assessment Report

1. IDENTITY

Name:	Sodium bicarbonate
CAS number:	144-55-8
EINECS number:	205-633-8
Molecular formula:	$NaHCO_3$
Molecular weight:	84.01
Synonyms:	baking soda, bicarbonate of soda, carbonic acid monosodium salt, monosodium carbonate, sodium acid carbonate, sodium hydrogen carbonate (Lewis, 1996; Solvay, 1996; Budavari, 1997).

1.1 Composition

Sodium bicarbonate is a white, odourless, crystalline powder with a purity > 98 %. Impurities may include sodium carbonate (< 1 %), water (< 0.5 %), chloride (< 0.1 %), sulfate (< 0.1 %) and calcium (< 0.1 %). The purity and the impurity profile depends on the composition of the raw materials, the production process and the intended use of the product. For example the purity of the pharmaceutical grade must be higher than 99.0 % in Europe (Pharmacopée Européenne, 2001).

1.2 Physical chemical properties

Sodium bicarbonate starts decomposing when heated over 50°C, releasing CO_2, H_2O and Na_2CO_3, with total decomposition at 270°C and therefore a melting and boiling point cannot be determined (Budavari, 1997; Lide, 1994; McEvoy, 1994). Sodium bicarbonate is an inorganic salt and therefore the vapour pressure can be considered negligible. The density is 2.159 at 20°C (Budavari, 1997) and the water solubility is 69 g/l at 0°C, 96 g/l at 20°C and 165 g/l at 60°C (Solvay, 1996). The octanol water partition coefficient (log Pow) is not relevant for an inorganic substance which dissociates. Grades with different average particle size diameters (d_{50}) are placed on the market. The average particle size diameter of the different grades can range between 15 and 300 µm.

2. GENERAL INFORMATION ON EXPOSURE

Sodium bicarbonate is produced on all continents of the world and the global number of production sites is estimated to be 30-50.

Sodium bicarbonate is manufactured mainly via the Solvay process, using sodium chloride and calcium carbonate as raw materials. Calcium carbonate is heated in lime kilns, releasing carbon dioxide (CO_2) and calcium oxide (CaO). A sodium chloride solution is saturated with ammonia and fed directly into carbonation columns. Carbon dioxide from the lime kilns is purified and then passed into the ammoniated sodium chloride solution, producing a precipitate of crude sodium bicarbonate (Solvay, 1996; Johnson, 1987). This crude product is then purified in a second crystallisation step to obtain the sodium bicarbonate which is commercialised.

Different qualities of the sodium bicarbonate are produced based on the final use of the substance. Feed, food, pharmaceutical and technical grades are placed on the market.

Published information regarding the total amount of sodium bicarbonate used on a yearly basis does not seem to be available. The estimated total amount of sodium bicarbonate used in 2001 is 2 million tonnes (Solvay, personal communication, 2002). The predicted growth of the market for the coming years is 5-10% per year. The main global applications are:
-animal feeding (35%)
-human food (15%)
-pharmaceuticals (12%)
-production of other chemicals (10%)
-cosmetics (5%)
-detergents and other household cleaning products (5%)
-fume treatment (4 %)
-swimming pools (2%)
-others (12%)
(Solvay, personal communication, 2002).

In addition to the applications mentioned above, sodium bicarbonate is used in the paper, pulp and board industry, as a foaming and swelling agent, in laboratories, in flame retardants and fire preventing agents and other areas (Solvay, 1996; NTP Chemical Repository, 2001). It is used therapeutically as an antacid and a urinary/systemic alkaliser in humans and animals (Budavari, 1997). Sodium bicarbonate is used in domestic products like detergents and cleaning products, soap, toothpaste and cosmetics (Solvay, 1996). The product sodium bicarbonate (baking soda) is also available for consumers and it has been ingested for example to alleviate heartburn or to improve the digestion of food.

Sodium bicarbonate is classified by the U.S. Food and Drug Administration (FDA) as a 'Generally Recognised as Safe' (GRAS) ingredient in food with no other limitation than current good manufacturing practice (FDA, 1978; FDA, 1983). In the EU it is approved as a food additive (EU, 2000) and a feed ingredient (EU, 1998).

Because sodium bicarbonate is used very widely the major applications (e.g. human food, pharmaceutical, cosmetics, detergents) are expected to occur in all countries.

2.1 Environmental exposure and fate

The high water solubility and low vapour pressure indicate that sodium bicarbonate will be found predominantly in the aquatic environment. Sodium bicarbonate is present in the environment as sodium and bicarbonate ions, which implies that it will not adsorb on particulate matter or surfaces and will not accumulate in living tissues. It is obvious that both the sodium and bicarbonate ion have a wide natural occurrence (UNEP, 1995).

Background concentration of bicarbonate

If bicarbonate is dissolved in water a re-equilibration takes place according to the following equations:

$CO_2 + H_2O \leftrightarrow HCO_3^- + H^+$ (pKa1 = 6.35)

$HCO_3^- \leftrightarrow CO_3^{2-} + H^+$ (pKa2 = 10.33)

Only a small fraction of the dissolved CO_2 is present as H_2CO_3, the major part is present as CO_2. The amount of CO_2 in water is in equilibrium with the partial pressure of CO_2 in the atmosphere. The CO_2 / HCO_3^- / CO_3^{2-} equilibria are the major buffer of the pH of freshwater and seawater throughout the world.

Based on the above equations, CO_2 is the predominant species at a pH smaller than 6.35, while HCO_3^- is the predominant species at a pH in the range of 6.35-10.33 and CO_3^{2-} is the predominant species at a pH higher than 10.33.

The natural concentration of CO_2 / HCO_3^- / CO_3^{2-} in freshwater is influenced by geochemical and biological processes. Many minerals are deposited as salts of the carbonate ion and for this reason the dissolution of these minerals is a continuous source of carbonate in freshwater. Carbon dioxide is produced in aquatic ecosystems from microbial decay of organic matter. On the other hand plants utilise dissolved carbon dioxide for the synthesis of biomass (photosynthesis). Because many factors influence the natural concentration of CO_2 / HCO_3^- / CO_3^{2-} in freshwater, significant variations of the concentrations do occur.

If the pH is between 7 and 9 then the bicarbonate ion is the most important species responsible for the buffer capacity of aquatic ecosystems. UNEP (1995) reported the bicarbonate concentration for a total number of 77 rivers in North-America, South-America, Asia, Africa, Europe and Oceania. The 10^{th} – percentile, mean and 90^{th}-percentile were 20, 106 and 195 mg/l, respectively.

Background concentration of sodium

The sodium ion is ubiquitously present in the environment and it has been measured extensively in aquatic ecosystems. Sodium and chloride concentrations in water are tightly linked. They both originate from natural weathering of rock, from atmospheric transport of oceanic inputs and from a wide variety of anthropogenic sources. The sodium concentration was reported for a total number of 75 rivers in North and South America, Africa, Asia, Europe and Oceania, with a 10^{th} percentile of 1.5 mg/l, mean of 28 mg/l and 90^{th} percentile of 68 mg/l (UNEP, 1995).

Anthropogenic addition of sodium bicarbonate

The use of sodium bicarbonate could potentially result in an aquatic emission of sodium bicarbonate and it could locally increase the sodium and bicarbonate concentration in the aquatic environment. In contrast to sodium carbonate, sodium bicarbonate does not increase the pH of water to high and/or lethal levels. An addition of bicarbonate to water will converge the pH to a

value of 8.34. The value of 8.34 is equal to (pKa1 + pKa2)/2. In other words, if the initial pH of the receiving water is for example 7.0 then an addition of bicarbonate will increase the pH but it will never be higher than 8.34. However, if the initial pH of the receiving water is for example 9.0 then an addition of bicarbonate will decrease the pH but it will never be lower than 8.34.

For most applications the bicarbonate will be digested (animal feeding, human food, pharmaceuticals) or treated by a waste water treatment plant (detergents and household cleaning products) and will not be directly emitted to the ecosystems. In order to determine if the production and use of sodium bicarbonate really results in a significant emission of bicarbonate, an evaluation of the complete, inorganic and organic carbon cycle would be required. Specific analytical data or publications about the use of sodium bicarbonate and the related emissions of sodium and bicarbonate have not been found.

2.2 Human exposure

The production and use of sodium bicarbonate may result in inhalation, dermal and/or oral exposure.

Inhalation

Inhalation of sodium bicarbonate dust may occur due to occupational exposure to sodium bicarbonate. However, inhalation is normally considered negligible for consumer applications due to the low exposure duriation and due to the negligible dust formation for most of the products which contain sodium bicarbonate (e.g. pharmaceuticals, cosmetics, liquid cleaning products). Per 2002, sodium bicarbonate does not have a recommended exposure limit value in the German MAK list, the US TLV list, or the British HSE list.

Dermal exposure

Dermal exposure to sodium bicarbonate may occur during production and use of the (pure) product sodium bicarbonate. Humans may also be exposed dermally to sodium bicarbonate via cosmetic products, detergents or other products which contain sodium bicarbonate. Sodium bicarbonate is used in bath, skin and hair preparations in concentrations from $\leq$0.1% to >50%. The products may come in contact with the eyes, nasal mucosa and other parts of the body. These products may be expected to remain in contact with the skin for an hour and may be used repeatedly over a period of many years. The products with the highest concentrations are bath formulations, which are diluted.

Oral exposure

Sodium bicarbonate is used in many countries (e.g. USA and EU) as a food additive. Significant quantities of sodium bicarbonate will be taken up via food, but it should be realised that it is also naturally present in food.

Sodium bicarbonate is also used in oral care products (i.e. toothpaste). A small part of the toothpaste can be expected to be ingested during brushing and therefore it can result in chronic exposure to sodium bicarbonate.

Sodium bicarbonate is also used as an antacid, with an initial recommended dose (for adults) of 4 g, supplemented by 1-2 g every 4 hours if necessary (McEvoy, 1994). Sodium bicarbonate is used therapeutically to treat metabolic acidosis (deficiency of extracellular bicarbonate with pH < 7.2) secondary to loss of bicarbonate from the body, although this treatment regime is controversial. In

addition, it is used to increase urinary pH, and treat diarrhoea accompanied by substantial gastrointestinal bicarbonate loss (McEvoy, 1994).

A number of examples of metabolic dysfunction due to excessive oral intake are reported in the medical literature (e.g., Brown, 1981; Mennen, 1988; Robertson, 1988; Wechsler *et al.*, 1990; Thomas and Stone, 1994; Perrone *et al.*, 1995; Fitzgibbons, 1999). In cases involving acute overdosing, the patients have generally ingested over-the counter antacids containing high concentrations of sodium bicarbonate or baking soda (pure $NaHCO_3$, not intended for direct consumption), primarily to alleviate heartburn. Doses of 4 to 40 g have resulted in acute, excessive development of CO_2-gas, and a ruptured stomach (Barna, 1986; Brismar, 1986; Lazebnik, 1986; Tonetti, 1988; Downs, 1989). A stomach rupture occurred only after an extreme excess of food and drink followed by the use of excess (greater than recommended) amount of sodium bicarbonate.

3. HUMAN HEALTH HAZARDS

$NaHCO_3$ has been used for many applications, in large number of countries and for a long period of time. A separate section on skin and eye irritation/corrosion has been included in the SIAR because several good quality studies were available although irritation/corrosion is not a SIDS element. The potential carcinogenicity of sodium bicarbonate was also assessed in a separate section.

3.1 Toxicokinetics, metabolism and mechanism of action

The major extracellular buffer in the blood and the interstitial fluid of vertebrates is the bicarbonate buffer system, described by the following equation:

$H_2O + CO_2 <=> H_2CO_3 <=> H^+ + HCO_3^-$

Carbon dioxide from the tissues diffuses rapidly into red blood cells, where it is hydrated with water to form carbonic acid. This reaction is accelerated by carbonic anhydrase, an enzyme present in high concentrations in red blood cells. The carbonic acid formed dissociates into bicarbonate and hydrogen ions. Most of the bicarbonate ions diffuse into the plasma. Since the ratio of H_2CO_3 to dissolved CO_2 is constant at equilibrium, pH may be expressed in terms of bicarbonate ion concentration and partial pressure of CO_2 by means of the Henderson-Hasselbach equation:

$pH = pk + \log[HCO_3^-]/ \alpha P_{CO2}$

The blood plasma of man normally has a pH of 7.40. Should the pH fall below 7.0 or rise above 7.8, irreversible damage may occur. Compensatory mechanisms for acid-base disturbances function to alter the ratio of HCO_3^- to PCO_2 , returning the pH of the blood to normal. Thus, metabolic acidosis may be compensated for by hyperventilation and increased renal absorption of HCO_3^-. Metabolic alkalosis may be compensated for by hypoventilation and the excess of HCO_3^- in the urine (Johnson and Swanson, 1987). Renal mechanisms are usually sufficient to restore the acid-base balance (McEvoy, 1994). The uptake of sodium, via exposure to sodium bicarbonate, is much less than the uptake of sodium via food. Therefore, sodium bicarbonate is not expected to be systemically available in the body. Furthermore it should be realised that an oral uptake of sodium bicarbonate will result in a neutralisation in the stomach due to the gastric acid.

3.2 Acute toxicity

Oral toxicity

Animal data

The available acute oral toxicity studies with animals are presented in Table 1. Crl:CD BR rats received sodium bicarbonate by gavage, females at levels of 3,000, 3,500 and 4,000 mg/kg bw, and males at levels of 3,000, 4,000 for 4,500 mg/kg bw (Glaza, 1993). One female administered 4,000 mg/kg bw died during the first day, the necropsy revealed only a red eroded area in the glandular mucosa of the stomach. The few animals with clinical signs of toxicity (soft stool, hypoactivity and staining of the urogenital area) showed no adverse clinical signs from day 2 forward. Necropsy did not reveal any substance-specific effects. This study was performed according to the EPA-FIFRA 40 CFR 160 and EPD-TSCA 40 CFR 792 (GLP standards). LD_{50} was not reported, but can be considered as higher than 4,000 mg/kg bw.

The LD_{50} of sodium bicarbonate in Crl:CD BR rats was assessed by dosing males and females with 5,000, 7,000 or 9,000 mg/kg bw, with 5 rats per group per dose (Glaza, 1992).
All animals that survived to the end of the observation period, exhibited body weight gain. Clinical signs of toxicity included hypoactivity, staggered gait, shallow breathing and soft stool during the first day after exposure. Among the rats that died, several had gas in the gastro-intestinal (GI) tract, and spleen lesions. Estimated oral LD50 for males was 7,937 mg/kg bw, for females 6,618 mg/kg bw and the sexes combined: 7,334 mg/kg bw. The GLP guidelines of the EPA-TSCA 40 CFR 792 were followed as appropriate.

In a study by Wakatama (1979), 5 groups consisting of 5 male and 5 female Sprague-Dawley rats, respectively, were exposed to the same dose level of sodium bicarbonate, to determine mortality. The identity of the substances was unknown to the study director. A dose of 5,000 mg/kg bw of the test substance was administered by gavage, as a 50% w/v dilution in water. Mortality varied strongly between the groups, with 2/10, 1/10, 4/10, 6/10 and 5/10 dying during the observation period, respectively. The clinical signs of toxicity included lethargy, ataxia, diarrhoea and a hunched posture. Surviving animals regained a normal appearance within day 2, and less than half of the rats in each group had pathological effects. The findings included yellow fluid or test material in the stomach and/or intestines, and red intestine or stomach walls. The authors concluded that in 3 of 5 groups the test substances were "not orally toxic" i.e. LD_{50} >5,000 mg/kg bw. In the remaining 2 of 5 groups the test substance was considered "orally toxic" by the authors of this study. LD_{50} <5,000 mg/kg bw for the group with 6/10 dead animals, and LD_{50} =5,000 mg/kg bw, for the group in which 5/10 rats died. This study was performed in accordance with the EPA 16 CFR 1500.3C2(i).

Table 1: Results of acute oral toxicity studies

Species	Result	Reliability[1]	Reference
Rat	LD_{50} >4,000 mg/kg bw	(1): GLP compliant. Comparable to guideline study.	Glaza, 1993
Rat	LD_{50} = 7,334 mg/kg bw.	(1): GLP compliant guideline study.	Glaza, 1992
Rat	Results of five identical LD_{50} tests with dosing of 5,000 mg/kg bw: 3/5: LD_{50} >5,000 mg/kg bw 1/5: LD_{50} =5,000 mg/kg bw 1/5: LD_{50} <5,000 mg/kg bw	(2): Guideline study but several test conditions and a description of the test substance was missing.	Wakatama, 1979
Rat	LD_{50} =4,220-4,400 mg/kg bw (20% slurry of $NaHCO_3$ in water) LD_{50} =5,820-6,290 mg/kg bw (50% slurry in water) LD_{50} =8,290 mg/kg bw (50% slurry of $NaHCO_3$ in corn oil)	(2): Acceptably documented publication that meets basic scientific principles.	Griffith, 1964

[1] Reliability (1) = valid without restrictions, (2) = valid with restrictions, (3) = invalid, (4) = not assignable (Klimisch HJ et al., 1997).

Human data

There have been a number of cases where excessive ingestion has caused moderate to severe toxic effects. The most prevalent symptoms are excessive carbon dioxide production, metabolic alkalosis, cyanosis, hypernatraemia and diuresis (Brown, 1981; AMA, 1994). Although absorption of unneutralised $NaHCO_3$ is known to cause alkalosis (Goodman and Gilman, 1995), this acid-base disturbance is usually transient in individuals with normal renal function, as the base excess will rapidly be excreted. The urinary pH can, however, be elevated by up to 1 unit, affecting tubular

reabsorption and urinary elimination of weak acids and bases (Goodman and Gilman, 1995). The minimum dose causing adverse effects will vary strongly according to age and health condition, but for antacid use it is inadvisable to ingest more than 4 grams/dose (Gosselin, 1976).

Inhalation toxicity

A total number of 5 male and 5 female Sprague-Dawley rats were exposed whole-body by inhalation for 4.5 hrs to sodium bicarbonate (Wnorowski, 1992a). The measured (gravimetric) chamber concentration was 4.74+/-1.03 mg/l, and particle size MMAD 2.8 µm (2.7+/-1.77 and 2.9+/-2.04 µm). There was no mortality. During the first hour of exposure, reduced movement and hunched posture was noted for most animals. Test substance was observed on the fur within the second day after exposure, ocular and/or nasal discharge was observed in 6/10 rats. All the animals were apparently healthy from day 2 or 3, and gained body weight during the observation period. There were no remarkable findings during necropsy. EPA GLP regulations were complied with.

Conclusion

The LD_{50} studies presented indicate low acute oral toxicity in rats, with LD_{50} values varying from >4,000 mg/kg bw up to 7,334 mg/kg bw. The inhalation toxicity study indicated a low toxic potential, as 4.74 mg/l induced adverse effects only temporarily. Considering the history of human use of sodium bicarbonate, the effects of oral exposure are well known due to accidental and intentional ingestion by humans, and it is considered safe to ingest up to 4 g/dose.

3.3 Skin irritation

The skin irritation potential of sodium bicarbonate was examined by Wnorowski (1992b), who exposed 3 male and 3 female New Zealand albino rabbits. A quantity of 0.5 g of moistened test substance was applied to clipped skin and covered by a semi-occlusive patch. After four hours, the exposed area was wiped clean. The average erythema score one hour after exposure terminated, was 0.7, and 0.2 after 24 hrs. The average oedema score was 0.2 one hour after exposure termination. All effects had reversed by day 2, and the authors classified the substance as slightly irritating, based on the Primary Dermal Irritation Index of 0.3. This study was done according to EPA GLP guidelines 40 CFR 798.4470.

Conclusion

Sodium bicarbonate causes reversible slight erythema and oedema in the skin of rabbits dosed with 0.5 g as a moistened solid in one study. The skin irritation potential is therefore low.

3.4 Ocular irritation

An amount of 0.1 g sodium bicarbonate was instilled into the right eye of 9 New Zealand albino rabbits (Wnorowski, 1992c). The eyes of 3 animals were irrigated with 30 ml of physiological saline 20-30 seconds after installation, while the eyes of the remaining six rabbits were not irrigated. Ocular lesions were evaluated at 1, 24, 48 and 72 hrs and 4 days post-installation. The results showed that 3/3 rabbits with unwashed eyes and 2/3 with washed eyes had conjunctivitis for at least 48 hours. The ocular irritation cleared from washed and unwashed eyes by days 3 and 4, respectively. The 24-hour Maximum Mean Total Score (MMTS) for washed eyes was 2.0 (practically non-irritating) and for unwashed eyes 8.3 (minimally irritating). All procedures followed the EPA TSCA 40 CFR 798.4500 guidelines.

The sensitivity of New Zealand albino rabbits to sodium bicarbonate was tested to assess the influence of alkalinity in ocular injury (Murphy, 1982). An amount of 0.1 ml solid $NaHCO_3$ (weight unknown) was applied to the right eye of 2 groups of 6 rabbits each. The eyes of the animals in one group were not rinsed after treatment; in the other group, the treated eye was washed 30 sec after instillation for a total of 2 minutes with 300 ml of tap water. For all animals the left eye served as control. The rabbits were observed for lesions, which were graded at 1 hr and day 1, 2, 3 and 7 after instillation. $NaHCO_3$ produced conjunctivitis that lasted until day 7 in all animals tested. Irrigation did not results in less lesions, indicating that alkalinity is only one of several factors causing ocular damage. The authors conclude, according to their own scoring system based on the methodology of Draize, that $NaHCO_3$ is irritating to the rabbit eye (Murphy, 1982).

Conclusion

Different results were obtained for the eye irritation potential of $NaHCO_3$. Based on a standard guideline study, instillation of 0.1 g was minimally irritating for unwashed eyes. Based on study with a lower reliability (2), a dose of 0.1 ml applied to the eye as a solid induced lasting conjunctivitis. Based on the results, it is likely that sodium bicarbonate is a minimal or mild ocular irritant.

3.5 Repeated dose toxicity

Oral toxicity

This study was set up with the intention of examining the mechanisms by which the dietary buffers widely used in livestock production exert their effect (Tucker, 1993). The influence of ruminal infusion of various amounts of $NaHCO_3$ on ruminal and systemic acid-base status and mineral metabolism was measured extensively. There were no adverse effects of sodium bicarbonate.

A study was conducted with 112 growing-finishing pigs (crossbred Yorkshire x Hampshire x Duroc) to evaluate the interactive effects of dietary sodium bicarbonate (1%) and excess dietary Cu (250 mg/kg diet) on growth, liver Cu accumulation and incidence of gastric ulceration (Southern, 1993). The pigs were exposed to a basal diet B (control), B + 250 mg/kg Cu, B + 1% sodium bicarbonate or B + 250 mg/kg Cu + 1% sodium bicarbonate. Sodium bicarbonate decreased dressing percentage but increased the incidence of gastric ulceration. The dressing percentage is the warm carcass weight divided by the live weight (as percentage). The LOAEL was 1% $NaHCO_3$ in feed.

Dermal and inhalation toxicity

No animal data are available on repeated dose toxicity studies by dermal or inhalation exposure routes for sodium bicarbonate.

Conclusion

Adequate repeated dose toxicity studies are not available and therefore a NOAEL or LOAEL has not been determined. None of the repeated dose studies were done in the rat, the species recommended, and the relevance of the results for humans is limited due to the way in which the studies were done. However, in humans there is a long history of sodium bicarbonate use as an antacid in doses up to 4 g without adverse effects of long-term use, although it is recommended not to use high doses of pure sodium bicarbonate instead of antacids (Gosselin, 1976; McEvoy, 1994).

Sodium bicarbonate is already recognised as 'GRAS' in food with no other limitation than current good manufacturing practice (FDA, 1983). In addition, sodium bicarbonate is an important extracellular buffer in vertebrates and is therefore readily regulated in the body. Therefore, additional testing for repeated dose toxicity is not deemed necessary.

3.6 Genetic toxicity

In vitro

Ishidate et al. (1984) assessed the mutagenicity of $NaHCO_3$ in Salmonella/microsome assays and chromosomal aberration tests *in vitro*. Reverse mutation assays using *S. typhimurium* strains TA92, TA94, TA98, TA100, TA1535 and TA1537 were carried out according to the Ames test. An S9 mix prepared from the liver of Fischer rats pre-treated with polychlorinated biphenyls was used as metabolic activation. Cells cultured overnight were pre-incubated with both the test sample and the S-9 mix for 20 min at 37°C before plating. The number of revertant colonies was scored after incubation at 37°C for 2 days. Duplicate plates were used for a total of six concentrations (of which only the highest was stated), with a maximum dose of 10 mg/plate. The results were negative.
The chromosomal aberration test was performed with a Chinese hamster fibroblast cell line, without metabolic activation. The test conditions and results were poorly reported but the results of the tests were negative.

The genotoxic activity and potency of sodium bicarbonate was assessed in the Ames reversion test and in a bacterial DNA-repair test (De Flora et al., 1984). The reverse mutation test was performed with *S. typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538. A S9 mix was prepared, containing 10% liver S9 fractions from Aroclor-treated Sprague-Dawley rats. The compound was tested with each strain, both with and without S9 metabolic activation. The concentrations tested are not specified, but extend up to the solubility or toxicity limit. Tests were performed in duplicate or triplicate plates, and all results were negative.
Three isogenic *E. coli* strains were used in the DNA damage and repair assay: WP2 (wild-type, repair-proficient), WP67 (*uvrA- polA-*) and CM871 (*uvrA- recA- LexA-*). The test substance was incubated with the bacteria in growth medium in microtiter plates for 16 hrs at 37°C. If necessary (by high turbidity due to the compound concentration or chemical precipitation), microdrops from the plates were subcultured on agar plates and grown for 8-24 hrs. Concentrations up to the solubility or toxicity limit were tested with a maximum of 2,500 µg without S9 and 5,000 µg with S9 metabolic activation in five separate experiments, where all results were negative.

Conclusion

None of the mutagenicity tests were performed according to guidelines. However, all the results were negative and more or less well documented. Furthermore sodium bicarbonate is naturally present in cells and the structure does not indicate a genotoxic potential. Therefore, sodium bicarbonate is considered to be not genotoxic.

3.7 Carcinogenicity

A valid carcinogenicity study has been reported by Fukushima et al. (1989). In this study male Fischer 344 rats were fed with 0.64% $NaHCO_3$ in the diet and they were exposed for 104 weeks. The liver, kidney and bladder were removed after gross examination, fixed and used for histological examination. Although the survival was not decreased, the final body weight of the exposed male rats was lower compared to the control. However, the $NaHCO_3$ exposed animals did not have a

significant increase in the number of tumours. Papillary or nodular hyperplasia and papilloma incidence did not differ from the control group incidence. A restriction of this study is that it has only been conducted in male rats and not in female rats.

Several invalid studies performed with rats have shown $NaHCO_3$ has bladder carcinogenesis promoting properties, observed as papilloma, hyperplasia and/or tumours when administered in feed in the relatively high concentrations of 0.375%-3% (Fukushima et al., 1988; Lina, 1989; Cohen, 1995; Mori et al., 1997). These effects are only seen in combination with the initiators *N*-butyl-*N*-(4-hydroxybutyl)nitrosamine (BBN) and a possible promotor (*o*-phenylphenate). However, the tumour promoting effect can be explained by unspecific general effects due to the high pH of the urine, the increased sodium concentration of the urine or due to the formation of crystals in the bladder. These effects only occur at high doses and after repeated exposure. Similar effects have been reported for other sodium salts (Lina, 1989; Cohen, 1995).

Conclusion

As with other sodium salts, high doses of sodium bicarbonate promote carcinoma formation in rat urinary bladder after pre-exposure to initiator or BBN, but this can be explained by unspecific general effects due to the high pH of the urine, the increased sodium concentration of the urine or due to the formation of crystals in the bladder. No carcinogenic effects were found in a valid study when male Fischer 344 rats were exposed to sodium bicarbonate alone. There is no convincing substantiation of $NaHCO_3$ having carcinogenic effects.

3.8 Reproduction toxicity

Developmental toxicity

Aqueous solutions of sodium bicarbonate were administered daily via oral intubation to pregnant mice at doses ranging from 5.8 to 580 mg/kg bw during days 6-15 of gestation. The fetuses were examined for the presence of external congenital abnormalities, detailed visceral abnormalities and for skeletal defects. The test substance did not affect implantation nor the survival of dams and foetuses. The number of abnormalities seen in either soft or skeletal tissues of the test group did not differ from the number occurring spontaneously in the sham-treated controls. Similar negative results were reported for rats and rabbits for daily doses from 3.4-340 mg/kg bw and 3.3-330 mg/kg bw, respectively (FDA, 1974).

Conclusion

Sodium bicarbonate did not induce developmental effects when administered orally at the following doses: 580 mg/kg bw (mice), 340 mg/kg bw (rats) and 330 mg/kg bw (rabbits). Furthermore the substance will usually not reach the foetus when the exposure to sodium bicarbonate is sufficiently low, as it does not become systemically available.

4. HAZARDS TO THE ENVIRONMENT

4.1 Aquatic effects

The pH dependent equilibrium between CO_2 , HCO_3^- and CO_3^{2-} that is outlined in paragraph 2.1 should be kept in mind when the aquatic effects of sodium bicarbonate are evaluated. HCO_3^- is the predominant species at a pH in the range of 6.35-10.33. Because the pH of the dilution water of aquatic toxicity tests is normally lest than 8.34, an addition of sodium bicarbonate will increase the pH but not significantly higher than a value of 8.34 (see section 2.1). The results of aquatic toxicity tests with sodium bicarbonate are summarized in Table 2.

Table 2: Results of aquatic toxicity tests with sodium bicarbonate

Species	EC50 (mg/l)	NOEC (mg/l)	Reliability[A]	Reference
Rainbow trout (*Oncorhynchus mykiss*)	7,700 (96h)	2300 (96 h)	1	Machado, 1993a
Bluegill sunfish *(Lepomis macrochirus)*	7,100 (96 h)	5,200 (96 h)	1	Machado, 1993b
Bluegill sunfish *(Lepomis macrochirus)*	8,250 - 9,000 (96 h)		4	Cairns and Scheier, 1959
Daphnia magna	4,100 (48 h)	3,100 (48 h)	1	Putt, 1993
Daphnia magna (age<24 hrs)	1,268 (48 h)		2	Hoke, 1992
Daphnia magna (age 6-7 days)	> 1,781 (age 6 days, 48 h) > 1,730 (age 7 days,48 hr)		2	Hoke, 1992
Daphnia magna	1,640 mg/l (48 h)		2	Mount et al., 1997
Ceriodaphnia dubia (age< 24 hrs)	1,075 mg/l (48 h)		2	Hoke, 1992
Ceriodaphnia dubia	1,020 (48 h)		2	Mount et al., 1997
Daphnia magna	>576 (21-day, chronic study)		2	Leblanc and Surprenant, 1984
Aquatic plants e.g. algae	A concentration of 45 mg/l is beneficial for algal growth (63 days exposure)		4	Dickman, 1973

[A] Reliability : 1 = valid without restrictions, 2 = valid with restrictions, 3 = invalid, 4 = not assignable. Klimisch et al. (1997).

Effects on fish

In a 96-hr acute flow-through test with rainbow trout (*Oncorhynchus mykiss*) a NOEC of 2,300 mg/l and a LC_{50} of 7,700 mg/l were determined (Machado, M.W., 1993a). The test was conducted under GLP conditions and according to FIFRA Guideline Reference number 72-1.

In a 96-hr acute flow-through test with bluegill sunfish (*Lepomis macrochirus*) a NOEC of 5,200 mg/l and a LC_{50} of 7,100 mg/l were determined (Machado, M.W., 1993b). The test was conducted under GLP conditions and according to FIFRA Guideline Reference number 72-1.

A toxicity test with 50 bluegill sunfish (*Lepomis macrochirus*) exposed to sodium bicarbonate and 10 control fish was performed by Cairns and Scheier (1959). The 96-hr TL_m (concentration at which 50% of organism would be expected to survive, equal to LC_{50}) was 8,250 mg/l for small fish, 8,600 mg/l for medium fish and 9,000 mg/l for large fish. The study was performed before OECD guidelines 203 came into force, but was well described.

Effects on invertebrates

In a 48-hr acute flow-through test with *Daphnia magna* a NOEC of 3,100 mg/l and a LC_{50} of 4,100 mg/l were determined (Putt, A.E., 1993). The test was conducted under GLP conditions and according to FIFRA Guideline Reference number 72-2.

The 48-hr acute aquatic toxicity of sodium bicarbonate to *Daphnia magna* and *Ceriodaphnia dubia* was determined by Hoke et al. (1992) with a method according to USEPA (1985). The reported nominal 48-hr LC_{50} value of *Daphnia magna* less than 24 hours old at the beginning of the test was 1,268 mg/l. The nominal 48-hr LC_{50} to *Ceriodaphnia dubia* (of less than 24 hours old at the beginning of the test), reported in the same article had an average value of 1,075 mg/l.
More recently, Mount et al. (1997) determined acute aquatic 24-hr and 48-hr toxicity of various salts (and combinations of salts) to *Daphnia magna* and *Ceriodaphnia dubia* for the development of a predictive tool. The method was according to USEPA (1991). HCO_3^- concentrations in the stock solutions were determined indirectly by the measurement of phenolphthalein alkalinity. As HCO_3^- is the predominate carbonate species present in the pH range of interest (pH 6.5-9.0), alkalinity equivalents were converted directly to HCO_3^- concentration. Test results were reported as nominal values. The reported mean 48-hr LC_{50} to *Daphnia magna* was 1,640 mg/l (1,170 – 2,030 mg/l). The reported mean 48-hr LC_{50} to *Ceriodaphnia dubia* was 1,020 mg/l (880 – 1,170 mg/l). Both values are very similar to the ones that were determined by Hoke et al. (1992).

Leblanc and Surprenant (1984) carried out a (chronic) reproduction test with *Daphnia magna*. Test solutions were prepared to contain the appropriate concentrations of salts to yield a total hardness of 170 mg/l $CaCO_3$ (USEPA 1975). At the tested concentration $NaHCO_3$ of 576 mg/l the survival was 100% and the cumulative number of offspring per female did not significantly differ from the control. This demonstrates that the 21-day *Daphnia magna* NOEC is higher than 576 mg/l. Although the study is not carried out according to OECD 202, it is very well described.

Effects on aquatic plants / algae

Standard toxicity tests with algae or aquatic plants have not been found, but test medium for acute algae tests contain 50 mg/l sodium bicarbonate. Dickman (1973) exposed glass slides to a portion of a small stream with an addition of sodium bicarbonate to a concentration of 45 mg/l for a period of 63 days. An increasing algal standing crop compared to the controls was found. Except for a small increase of Cyanophycea species, no shift in species was determined.

Although a high quality standard algal toxicity test (performed according to current standard guidelines) with sodium bicarbonate is not available there seems to be no need for further testing
because the medium for algal tests contains already sodium bicarbonate. A further addition of sodium bicarbonate will increase the growth of the algae, while a growth reduction (osmotic effect) will probably be found at very high concentrations (>1 g/l). It should be realised also that a further algal test will not refine a risk assessment (see below).

Conclusions

Acute NOEC values of fish and *Daphnia* in GLP studies were higher than 1,000 mg/l. *Daphnia magna* exposed to a $NaHCO_3$ concentration of 576 mg/l for 21 days had a 100 % survival and showed no significant decrease in offspring and it was demonstrated that a concentration of 45 mg/l was beneficial for algal growth. The acute toxicity of sodium bicarbonate for fish and water fleas could be based on a high osmotic pressure. This is a very general effect of salts as soon as their concentration in water exceeds a certain level.

UNEP (1995) reported the bicarbonate concentration for a total number of 77 rivers in North-America, South-America, Asia, Africa, Europe and Oceania. The 10^{th}-percentile, mean and 90^{th}-percentile were 20, 106 and 195 mg/l, respectively. For sodium the 10^{th}-percentile, mean and 90^{th}-percentile were 1.5, 28 and 68 mg/l, respectively, based on a total number of 75 rivers. Based on these data it is evident that aquatic organisms are tolerant to sodium bicarbonate concentrations in 10-100 mg/l range. This is confirmed by the composition of most aquatic test media because sodium bicarbonate concentrations in most media used in OECD tests are 30-300 mg/l.

Furthermore it should be realised that inorganic carbon is essential for growth of plants and algae. In general, the productivity of aquatic ecosystems increases if the amount of inorganic carbon in the water increases (Bloemendaal et al., 1988). This will certainly be the case under carbon limited conditions.

As described in paragraph 2.1, HCO_3^- is in equilibrium with CO_3^{2-} and CO_2 in water, dependent on the pH. An anthropogenic addition of sodium bicarbonate to water will not only increase the sodium and bicarbonate concentration but can also increase the pH to a value of 8.3. Beause the natural pH, bicarbonate and also the sodium concentration (and their fluctuations in time) varies significantly between aquatic ecosystems, it is not considered useful to derive a generic PNEC or $PNEC_{added}$. For example an anthropogenic addition of 20 mg/l could affect an aquatic ecosystem with a background concentration of 20 mg/l. The primary production (plants, algae) of the aquatic ecosystem could increase. On the other hand an anthropogenic addition of 20 mg/l could not significantly affect an aquatic ecosystem with a background concentration of 150 mg/l.

To assess the potential environmental effect of a sodium bicarbonate discharge, the increase in sodium, bicarbonate and pH should be compared with the natural values and their fluctuations and based on this comparison it should be assessed if the anthropogenic addition is acceptable.

4.2 Terrestrial effects

Toxicity tests that determined the effect of sodium bicarbonate on terrestrial organisms are not available.

4.3 Other environmental effects

In a 48-hr acute test with honeybees (*Apis mellifera*) a NOEC of 24 µg/bee and a LC_{50} of >24 µg/bee were determined (Collins, M.K., 1999). The NOEC of 24 microgram per bee is equal to the highest treatment level. The test was conducted under GLP conditions and according to FIFRA Guideline Reference number 141-1. The test substance was a 100 % grade of sodium bicarbonate.

5. CONCLUSIONS

Conclusions

Human health hazard

Oral LD_{50} values were higher than 4,000 mg/kg bw, and an inhalation study in rats using a concentration of 4.74 mg/l inhalable dust produced no deaths.
There are no directly relevant studies on repeated dose exposure, however, knowledge of prior use and available literature does not indicate any adverse effects of long-term use of exposure via any route. *In vitro* bacterial and mammalian cell tests showed no evidence of genotoxic activity. As with other sodium salts, high doses of sodium bicarbonate promote carcinoma formation in rat urinary bladder after pre-exposure to initiator or BBN. However, when rats were only exposed to sodium bicarbonate no carcinogenic effect on the urinary bladder was found. Based on the available information there are no indications that sodium bicarbonate has carcinogenic effects.

Sodium bicarbonate has a long history of use in foodstuff, feed and industrial processes. The bicarbonate ion is a normal constituent in vertebrates, as the principal extracellular buffer in the blood and interstitial fluid is the bicarbonate buffer system. Excess sodium and bicarbonate ions are readily excreted in the urine. It is therefore assumed that normal handling and use will not have any adverse effects. The consequences of accidental or excessive oral ingestion have been described in a number of publications. Acute oral ingestion by the patients may result in a ruptured stomach due to excessive gas development. Acute or chronic excessive oral ingestion may cause metabolic alkalosis, cyanosis and hypernatraemia. These conditions are usually reversible, and will not cause adverse effects.

Hazards to the environment

Acute NOEC values to fish and daphnids are higher than 1,000 mg/l. The 21-day NOEC to *Daphnia magna* is higher than 576 mg/l. The acute toxicity of sodium bicarbonate for aquatic organisms could be based on a high osmotic pressure. This is a very general effect of salts as soon as their concentration in water exceeds a certain level.

Both sodium and bicarbonate are present naturally present in aquatic ecosystems. For sodium the 10^{th}- and 90^{th}-percentile were 1.5 and 68 mg/l, respectively, based on a total number of 75 rivers.
For bicarbonate the 10^{th}- and 90^{th}-percentile were 20 and 195 mg/l, respectively, based on a total number of 77 rivers. Beause the natural pH, bicarbonate and sodium concentration (and also their fluctuations in time) varies significantly between aquatic ecosystems, it is not considered useful to derive a generic PNEC or $PNEC_{added}$. To assess the potential environmental effect of a sodium bicarbonate discharge, the increase in sodium, bicarbonate and pH should be compared with the natural values and their fluctuations and based on this comparison it should be assessed if the anthropogenic addition is acceptable.

The production and use of sodium bicarbonate could potentially result in an emission of sodium bicarbonate to aquatic and terrestrial ecosystems. However, for most applications the bicarbonate will be digested (animal feeding, human food, pharmaceuticals) or treated by a waste water treatment plant (detergents and household cleaning products) and will not be directly emitted to the ecosystems. In order to determine if the production and use of sodium bicarbonate really results in a significant emission of bicarbonate, an evaluation of the complete, inorganic and organic carbon cycle would be required.

Aquatic sodium emissions originating from uses of sodium bicarbonate are probably small compared to other sources. It is clear that an environmental hazard assessment of sodium should not only evaluate all natural and anthropogenic sources of sodium but should also evaluate all other ecotoxicity studies with sodium salts, which is beyond the scope of this report.

5.2 Recommendations

This chemical is currently considered of low priority for further work because of its low hazard potential.

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I U C L I D Data Set

Existing Chemical	:	ID: 144-55-8
CAS No.	:	144-55-8
EINECS Name	:	sodium hydrogencarbonate
EC No.	:	205-633-8
TSCA Name	:	Carbonic acid monosodium salt
Molecular Formula	:	CHO3.Na

Producer related part

Company	:	Solvay S.A.
Creation date	:	02.05.2002

Substance related part

Company	:	Solvay S.A.
Creation date	:	02.05.2002
Status	:	
Memo	:	
Printing date	:	11.02.2003
Revision date	:	
Date of last update	:	10.02.2003
Number of pages	:	
Chapter (profile)	:	
Reliability (profile)	:	
Flags (profile)	:	

1.0.1 APPLICANT AND COMPANY INFORMATION

Type	:	lead organisation
Name	:	Solvay S.A.
Contact person	:	Mr. A.G. Berends
Date	:	
Street	:	Rue de Ransbeek 310
Town	:	1120 Brussels
Country	:	Belgium
Phone	:	+ 32 2 264 3398
Telefax	:	+ 32 2 264 2990
Telex	:	
Cedex	:	
Email	:	albert.berends@solvay.com
Homepage	:	http://www.solvay.com
Remark	:	The IUCLID and the other parts of the SIDS dossier were prepared on behalf of a consortium of sodium bicarbonate producers. Both the ESAPA (European Soda Ash Producers Association) and the Japanese Soda Industry Association were involved in the project. The cooperating companies are mentioned below.

08.05.2002

Type	:	cooperating company
Name	:	ASAHI GLASS CO., LTD.
Contact person	:	Mr. I. Katsuji
Date	:	
Street	:	1-12-1 Yurakucho Chiyoda-ku
Town	:	100-8405 Tokyo
Country	:	Japan
Phone	:	
Telefax	:	
Telex	:	
Cedex	:	
Email	:	Katsuji-Itoh@om.agc.co.jp
Homepage	:	

08.05.2002

Type	:	cooperating company
Name	:	Brunner Mond & Company
Contact person	:	Mr. M. Thorpe
Date	:	
Street	:	Winnington Lane, PO Box 4
Town	:	CW8 4DT Northwich
Country	:	United Kingdom
Phone	:	+ 44 1606 724000
Telefax	:	+ 44 1606 724433
Telex	:	
Cedex	:	
Email	:	mac.thorpe@brunnermond.com
Homepage	:	

08.05.2002

Type	:	cooperating company
Name	:	Church & Dwight Co, Inc.
Contact person	:	Mr. S. Lajoie
Date	:	
Street	:	469 North Harrison Street
Town	:	NJ 08543 Princeton
Country	:	United States

Phone :
Telefax :
Telex :
Cedex :
Email :
Homepage :
03.05.2002

Type : cooperating company
Name : Novacarb
Contact person : Mr. D. Jacob
Date :
Street : Usine de la Madeleine
Town : F - 54410 Laneuveville
Country : France
Phone : + 33 83 184460
Telefax : + 33 83 184461
Telex :
Cedex :
Email : dominique.jacob@eu.rhodia.com
Homepage :
08.05.2002

Type : cooperating company
Name : SODA MATWY
Contact person : Mr. B. Miakota
Date :
Street : ul. Fabryczna 4
Town : 88-101 Inowroclaw
Country : Poland
Phone : + 48 3541424
Telefax : + 48 124567
Telex :
Cedex :
Email : dzial_rozwoju-inwestycji@izch.com.pl
Homepage :
08.05.2002

Type : cooperating company
Name : Soda Sanayii A.S.
Contact person : Mr. E. Erturk
Date :
Street : Is Kuleleri Kule-3
Town : 80620-4 Levent-Istanbul
Country : Turkey
Phone : + 90 212 503647
Telefax : + 90 212 504647
Telex :
Cedex :
Email : eerturk@sisecam.com.tr
Homepage :
08.05.2002

Type : cooperating company
Name : Sodawerk Staßfurt GmbH & Co KG
Contact person : Mr. G. Witte
Date :
Street : An der Löderburger Bahn 4a
Town : 39418 Staßfurt
Country : Germany

Phone	:	+ 49 3925 608260
Telefax	:	+ 49 3925 263379
Telex	:	
Cedex	:	
Email	:	g.witte@sodawerk.de
Homepage	:	

08.05.2002

Type	:	cooperating company
Name	:	Tokuyama Corporation
Contact person	:	Mr. S. Moriyama
Date	:	
Street	:	3-1 Shibya 3-Chome, Shibuya-Ku
Town	:	150-8383 Tokyo
Country	:	Japan
Phone	:	+ 81 3 3499 8478
Telefax	:	+ 81 3 3499 8967
Telex	:	
Cedex	:	
Email	:	s-moriyama@tokuyama.co.jp
Homepage	:	

08.05.2002

Type	:	cooperating company
Name	:	Tosoh Corporation
Contact person	:	Mr. M. Akazawa
Date	:	
Street	:	3-8-2 Shiba, Minato -Ku
Town	:	105-8263 Tokyo
Country	:	Japan
Phone	:	
Telefax	:	
Telex	:	
Cedex	:	
Email	:	akazawa@tosoh.co.jp
Homepage	:	

08.05.2002

1.0.2 LOCATION OF PRODUCTION SITE, IMPORTER OR FORMULATOR

1.0.3 IDENTITY OF RECIPIENTS

1.0.4 DETAILS ON CATEGORY/TEMPLATE

1.1.0 SUBSTANCE IDENTIFICATION

IUPAC Name	:	Sodium bicarbonate
Smiles Code	:	
Molecular formula	:	NaHCO3
Molecular weight	:	84.01
Petrol class	:	

08.05.2002

1.1.1 GENERAL SUBSTA NCE INFORMATION

Purity type	:	typical for marketed substance
Substance type	:	Inorganic

Physical status : Solid
Purity : > 98 % w/w
Colour : White
Odour : no odour
Remark : The purity of the technical grade is > 98 %. The purity of the marketed substance will be higher for certain applications (e.g. food additive, feed additive, pharmaceutical applications).
31.05.2002

Purity type : typical for marketed substance
Substance type : Inorganic
Physical status : Solid
Purity : > 99 % w/w
Colour : White
Odour : no odour
Remark : Purity for Pharmaceutical/food grades.
30.07.2002 (66)

1.1.2 SPECTRA

1.2 SYNONYMS AND TRADENAMES

baking soda
20.02.2002 (9)

bicarbonate of soda
13.02.2002 (43)

carbonic acid monosodium salt
13.02.2002 (43)

monosodium carbonate
13.02.2002 (43)

Sbc
Remark : This is an abbreviation which is used frequently.
13.06.2002

sodium acid carbonate

13.02.2002 (9)

sodium hydrogen carbonate
20.02.2002 (43)

1.3 IMPURITIES

Purity : typical for marketed substance
CAS-No : 497-19-8
EC-No : 207-838-8
EINECS-Name : sodium carbonate
Molecular formula : Na2CO3
Value : < 1 % w/w
31.05.2002

Purity : typical for marketed substance

CAS-No : 7732-18-5
EC-No : 231-791-2
EINECS-Name : water
Molecular formula : H2O
Value : < .5 % w/w
31.05.2002

Purity : typical for marketed substance
CAS-No :
EC-No :
EINECS-Name : chloride
Molecular formula : Cl
Value : < .1 % w/w
31.05.2002

Purity : typical for marketed substance
CAS-No :
EC-No :
EINECS-Name : sulfate
Molecular formula : SO4
Value : < .1 % w/w
31.05.2002

Purity : typical for marketed substance
CAS-No : 7440-70-2
EC-No : 231-179-5
EINECS-Name : calcium
Molecular formula : Ca
Value : < .1 % w/w
31.05.2002

1.4 ADDITIVES

Purity type : typical for marketed substance
CAS-No : 1592-23-0
EC-No : 216-472-8
EINECS-Name : calcium distearate
Molecular formula : Ca(C18H35O2)2
Value : < 1 % w/w
Function of additive : Anticaking agent
Remark : This additive is only present in certain grades. Depending on the particle size distribution and the application, calcium distearate is used sometimes to prevent anticaking (anticlogging) and to improve the free-flowing properties.
31.05.2002

Purity type : typical for marketed substance
CAS-No : 7758-87-4
EC-No : 231-840-8
EINECS-Name : tricalcium bis(orthophosphate)
Molecular formula : Ca3(PO4)2
Value : < 1 % w/w
Function of additive : Anticaking agent
Remark : This additive is only present in certain grades. Depending on the particle size distribution and the application, tricalcium bis(orthophosphate) is used sometimes to prevent anticaking (anticlogging) and to improve the free-flowing properties.
31.05.2002

1.5 TOTAL QUANTITY

Quantity : ca. 2000000 - tonnes produced in 2001
Remark : About 2 million tonnes were produced in 2001. The expected growth of the market is 5-10% for the coming years.

14.05.2002

1.6.1 LABELLING

Labelling : no labelling required (no dangerous properties)
Specific limits :
30.07.2002

1.6.2 CLASSIFICATION

Classified : no classification required (no dangerous properties)
Class of danger :
R-Phrases :
Specific limits :
1st Concentration :
2nd Concentration :
3rd Concentration :
4th Concentration :
5th Concentration :
6th Concentration :
7th Concentration :
8th Concentration :
1st Classification :
2nd Classification :
3rd Classification :
4th Classification :
5th Classification :
6th Classification :
7th Classification :
8th Classification :
30.07.2002

1.6.3 PACKAGING

1.7 USE PATTERN

Type of use : type
Category : Use in closed system
08.05.2002

Type of use : type
Category : Use resulting in inclusion into or onto matrix
08.05.2002

Type of use : type
Category : Wide dispersive use
Remark : < 10 %.
08.05.2002

Type of use : industrial
Category : Basic industry: basic chemicals
08.05.2002

Type of use : industrial
Category : Leather processing industry
08.05.2002

Type of use : industrial
Category : Paper, pulp and board industry
08.05.2002

Type of use : industrial
Category : Personal and domestic use
08.05.2002

Type of use : industrial
Category : Polymers industry
08.05.2002

Type of use : industrial
Category : Textile processing industry
08.05.2002

Type of use : use
Category : Cleaning/washing agents and disinfectants
Remark : Cleaning agent (metals , building materials)
08.05.2002

Type of use : use
Category : Cosmetics
08.05.2002

Type of use : use
Category : Flame retardants and fire preventing agents
08.05.2002

Type of use **:** use
Category **:** Foaming agents
08.05.2002

Type of use **:** use
Category **:** Food/foodstuff additives
Remark **:** Sodium bicarbonate is not only used as a feed additive (for animal feed) but it is also used as a food additive (human food). These applications are the most important applications of sodium bicarbonate.
13.06.2002

Type of use **:** use
Category **:** Laboratory chemicals
08.05.2002

Type of use **:** use
Category **:** pH-regulating agents
08.05.2002

Type of use **:** use
Category **:** Pharmaceuticals
08.05.2002

Type of use : use
Category : Tanning agents
08.05.2002

Type of use : use
Category : other
Remark : Swelling agent for plastics foams
08.05.2002

1.7.1 DETAILED USE PATTERN

1.7.2 METHODS OF MANUFACTURE

Origin of substance : Synthesis
Type : Production
Remark : The ammonia-soda process was developed by Ernest Solvay in his laboratory in 1863. Named after its inventor, the Solvay process uses sodium chloride (common salt, NaCl) and calcium carbonate (limestone, CaCO3) as raw materials and converts them into calcium chloride (CaCl2) and sodium carbonate (washing soda, sal soda or soda ash, Na2CO3).

Calcium carbonate is heated in lime kilns, releasing carbon dioxide (CO2) and calcium oxide (quicklime, CaO). Salt in the form of a sodium chloride solution is saturated with ammonia and fed directly into carbonation columns. Carbon dioxide from the lime kilns is purified and then passed into the ammoniated sodium chloride solution, producing a precipitate of sodium bicarbonate.

NaCl + NH3 + H2O + CO2 -> NaHCO3 + NH4Cl

08.05.2002 (66)

1.8 REGULATORY MEASURES

1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES

Type of limit : MAK (DE)
Limit value :
Remark : not mentioned in the German MAK list
08.05.2002

Type of limit : TLV (US)
Limit value :
Remark : not mentioned in TLV list ACGIH
08.05.2002

1.8.2 ACCEPTABLE RESIDUES LEVELS

1.8.3 WATER POLLUTION

1.8.4 MAJOR ACCIDENT HAZARDS

1.8.5 AIR POLLUTION

1.8.6 LISTINGS E.G. CHEMICAL INVENTORIES

1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS

1.9.2 COMPONENTS

1.10 SOURCE OF EXPOSURE

1.11 ADDITIONAL REMARKS

1.12 LAST LITERATURE SEARCH

Type of search	:	Internal and External
Chapters covered	:	3, 4, 5
Date of search	:	05.09.2000
Remark	:	A literature search has been done in 1994 by the industry to prepare the IUCLID in the context of 'Council Regulation (EEC) No. 793/93 on the Evaluation and Control of the Risks of Existing Subs tances'. This IUCLID has been published by the European Chemicals Bureau. An additional literature search has been done in 2000 by Solvay. It covered the period 1994-2000. The following databases were used: AQUIRE, BIODEG, BIOLOG, CCRIS, CHRIS, DART/ETIC, DATALOG, ENVIROFATE, GENETOX, GIABS, HSDB SUBSET, IRIS, MEDLINE TOXICOLOGY SUBSET, NIOSHTIC SUBSET , PHYTOTOX, RISKLINE, RTECS, TERRETOX, TSCATS, TOXCENTER and TOXLINE.

08.01.2003

1.13 REVIEWS

2.1 MELTING POINT

Remark : Not applicable. Sodium bicarbonate decomposes when it is heated above 50 °C (begins to lose CO2).

08.05.2002 (9)

2.2 BOILING POINT

Remark : Not applicable. Sodium bicarbonate decomposes when it is heated (begins to lose CO2).

20.02.2002 (9) (44)

2.3 DENSITY

Type : relative density
Value : = 2.159 at 20 °C
Remark : Density is 2.159 at 20 degrees Celcius. Real density 2.22 kg/dm3, apparent relative density 0.65-1.2 kg/dm3 according to particle size.

13.06.2002 (66)

2.3.1 GRANULOMETRY

Remark : Grades with different average particle size diameters (d50) are placed on the market. The average particle size diameter of the different grades can range between 15 and 300 µm.

31.05.2002

2.4 VAPOUR PRESSURE

Remark : Sodium bicarbonate is an inorganic solid and for this reason the vapour pressure of sodium bicarbonate is negligible. Furthermore it is technically not possible to determine the vapour pressure.

08.05.2002 (66)

2.5 PARTITION COEFFICIENT

Remark : The octanol/water coefficient is not relevant for an inorganic substance which dissociates.

20.02.2002 (44)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in :
Value : ca. 96 g/l at 20 °C
pH value : ca. 8.4
concentration : 50 g/l at °C

Temperature effects	:	The water solubility increases with temperature. Water solubility is 69 g/l at 0 °C and 165 g/l at 60 °C.
Examine different pol.	:	
pKa	:	at 25 °C
Description	:	
Stable	:	
Deg. product	:	
Method	:	
Year	:	
GLP	:	no
Test substance	:	no data
Remark	:	pH 8.4 in a 1% solution.

13.06.2002 (44) (66)

Solubility in	:	other: alcohol
Value	:	at °C
pH value	:	
concentration	:	at °C
Temperature effects	:	
Examine different pol.	:	
pKa	:	at 25 °C
Description	:	
Stable	:	
Remark	:	Insoluble in alcohol.

22.02.2002 (9) (66)

2.6.2 SURFACE TENSION

2.7 FLASH POINT

Remark : Not applicable.
20.02.2002

2.8 AUTO FLAMMABILITY

Remark : Not flammable. Not a fire hazard.
20.02.2002

2.9 FLAMMABILITY

Remark : Not flammable. Not combustible.
03.03.1994

2.10 EXPLOSIVE PROPERTIES

Remark : Not explosive.
25.04.2002

2.11 OXIDIZING PROPERTIES

Remark : No oxidizing properties.
20.02.2002

2.12 DISSOCIATION CONSTANT

2.13 VISCOSITY

2.14 ADDITIONAL REMARKS

3.1.1 PHOTODEGRADATION

Remark : Not applicable
08.05.2002

3.1.2 STABILITY IN WATER

Type : abiotic
t1/2 pH4 : at °C
t1/2 pH7 : at °C
t1/2 pH9 : at °C
Remark : In water, sodium bicarbonate dissociates into sodium and bicarbonate.

Bicarbonate re-equilibrates according to the following equations:
HCO_3^- <--> CO_3^{2-} + H^+ pKa = 10.33
$CO_2 + H_2O$ <--> HCO_3^- + H^+ pKa = 6.35

Only a small fraction of the dissolved CO_2 is present as H_2CO_3, the major part is present as CO_2. The amount of CO_2 in water is in equilibrium with the partial pressure of CO_2 in the atmosphere. The CO_2 / HCO_3^- / CO_3^{2-} equilibria are the major buffer of the pH of freshwater throughout the world.

08.05.2002

3.1.3 STABILITY IN SOIL

3.2.1 MONITORING DATA

Type of measurement : background concentration
Media : surface water
Concentration :
Method :
Remark : The sodium and bicarbonate ion are both naturally occurring in the environment.

UNEP (1995) reported the sodium concentration for a total number of 75 rivers in North-America, South-America, Asia, Africa, Europe and Oceania. The 10th-percentile, mean and 90th-percentile were 1.5, 28 and 68 mg/l, respectively.

UNEP (1995) reported the bicarbonate concentration for a total number of 77 rivers in North-America, South-America, Asia, Africa, Europe and Oceania. The 10th-percentile, mean and 90th-percentile were 20, 106 and 195 mg/l, respectively.

08.05.2002 (72)

3.2.2 FIELD STUDIES

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Remark : Sodium bicarbonate is an inorganic substance and therefore standard computer models can not be used to determine the transport or distribution

between environmental compartments.

Solid sodium bicarbonate has a negligible vapour pressure and for this reason it will not be distributed to the atmosphere.

If sodium bicarbonate is emitted to water it will remain in the water phase. If the pH is decreased then carbonic acid (H_2CO_3 or CO_2) can be formed. If the concentration of carbon dioxide water is above the water solubility limit, the carbon dioxide will distribute to the atmosphere.

If sodium bicarbonate is emitted to soil it can escape to the atmosphere as CO_2 (see above), precipitate as a metal carbonate, form complexes or stay in solution.

08.05.2002

3.3.2 DISTRIBUTION

Remark : See 3.1.2 and 3.3.1.
14.05.2002

3.4 MODE OF DEGRADATION IN ACTUAL USE

08.05.2002

3.5 BIODEGRADATION

Contact time :
Degradation : = (±) % after
Result :
Remark : Sodium bicarbonate is a substance which can not be oxidized or biodegraded by microorganisms. A biodegradation test would not generate valid or useful data.

08.05.2002

3.6 BOD5, COD OR BOD5/COD RATIO

Remark : Not applicable; see 3.5.
08.05.2002

3.7 BIOACCUMULATION

Remark : Not bioaccumulable. Log Pow is not applicable for an inorganic compound which dissociates.

14.05.2002

3.8 ADDITIONAL REMARKS

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	flow through
Species	:	*Lepomis macrochirus* (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
NOEC	:	= 5200 measured/nominal
LC50	:	= 7100 calculated
Limit test	:	no
Analytical monitoring	:	yes
Method	:	EPA OPP 72-1
Year	:	1993
GLP	:	yes
Test substance	:	other TS: Sodium bicarbonate
Method	:	METHOD FOLLOWED: EPA OPP 72-1 DEVIATIONS FROM GUIDELINE: Fish were fed in the 48 hours prior to the study. GLP: Yes STATISTICAL METHODS: Moving average angle analysis, probit analysis and nonlinear interpolation with 95% confidence intervals calculated by binominal probability. METHOD OF CALCULATION: the 24-, 48-, 72- and 96-hour median LC50 values were estimated from derived mortality data at the measured concentrations using the described statistical methods which were available in a computer programme. If two or more statistical methods produced acceptable results, then the method which yielded the smallest 95% confidence interval was selected. ANALYTICAL METHODS: The Sodium concentration was determined, using the technique "multiple known standard additions" using an Orion Model 960 Ion Analyzer, equiped with a sodium probe, a stirrer and an automatic dispenser.
Result	:	RESULTS: EXPOSED - Nominal/ measured concentrations in mg A.I./ L Nominal: 780 Mean Measured (SD):740 (190) Nominal: 1300 Mean Measured (SD):1200 (49) Nominal: 2200 Mean Measured (SD):2700 (550) Nominal: 3600 Mean Measured (SD):5200 (2200) Nominal: 6000 Mean Measured (SD):6300 (390) Nominal: 10000 Mean Measured (SD):9400 (1100) - Concentration / response curve: Mean percentage mortality (of vessel A and B) after 96 hours: Control: 5 % 740 mg A.I./L: 0 % 1200 mg A.I./L: 10 % 2700 mg A.I./L: 5 % 5200 mg A.I./L: 0 % 6300 mg A.I./L: 20 % 9400 mg A.I./L: 100 % - Other effects: At 6000 mg A.I./L all of the surviving fish were observed lethargic, two of the surviving fish were observed to be dark RESULTS: TEST WITH REFERENCE SUBSTANCE: No test with reference substance RESULTS: CONTROL - Number/percentage of animals showing adverse effects: 5 % mortality in the control.
Test substance	:	Purity 99.9 %, Church & Dwight Co. Inc. Lot no 2F332
Reliability	:	(1) valid without restriction GLP test
Flag	:	confidential

13.06.2002 (46)

Type	:	flow through
Species	:	*Oncorhynchus mykiss* (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
NOEC	:	= 2300 measured/nominal
LC50	:	= 7700 calculated
Limit test	:	no
Analytical monitoring	:	yes
Method	:	EPA OPP 72-1
Year	:	1993
GLP	:	yes
Test substance	:	other TS: Sodium bicarbonate
Method	:	METHOD FOLLOWED: EPA OPP 72-1 DEVIATIONS FROM GUIDELINE: N one reported GLP: Yes STATISTICAL METHODS: Moving average angle analysis, probit analysis and nonlinear interpolation with 95% confidence intervals calculated by binominal probability. METHOD OF CALCULATION: the 24-, 48-, 72- and 96-hour median LC50 values were estimated from derived mortality data at the measured concentrations using the described statistical methods which were available in a computer programme. If two or more statistical methods produced acceptable results, then the method which yielded the smallest 95% confidence interval was selected. ANALYTICAL METHODS: The Sodium concentration was determined, using the technique "multiple known standard additions" using an Orion Model 960 Ion Analyzer, equiped with a sodium probe, a stirrer and an automatic dispenser.
Result	:	RESULTS: EXPOSED - Nominal/measured concentrations: Nominal: 780 Mean Measured (SD):920 (43) Nominal: 1300 Mean Measured (SD):1300 (57) Nominal: 2200 Mean Measured (SD):2300 (78) Nominal: 3600 Mean Measured (SD):3800 (160) Nominal: 6000 Mean Measured (SD):6500 (230) Nominal: 10000 Mean Measured (SD):10000 (150) - Concentration / response curve: Control: 0 % 920 mg A.I./L: 0 % 1300 mg A.I./L: 0 % 2300 mg A.I./L: 0 % 3800 mg A.I./L: 5 % 6500 mg A.I./L: 10 % 10000 mg A.I./L: 100 % - Effect concentration vs. test substance solubility: Not reported - Other effects: At 6500 mg A.I./L all of the surviving fish exhibited partial loss of equilibrium. RESULTS: CONTROL - Number/percentage of animals showing adverse effects: 0 RESULTS: TEST WITH REFERENCE SUBSTANCE No test with reference substance has been carried out.
Test substance	:	Purity 99.9 %, Church & Dwight Co. Inc. Lot no 2F332
Reliability	:	(1) valid without restriction GLP test with full report
Flag	:	confidential

13.06.2002 (47)

Type	:	static

Species	:	*Gambusia affinis* (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
NOEC	:	= 5600
LC50	:	= 7550
LC100	:	= 10000
Limit test	:	
Analytical monitoring	:	no
Method	:	other
Year	:	1957
GLP	:	no
Test substance	:	no data
Remark	:	LC50 after 24 hour is 7700 mg/l; after 48 hour 7550 mg/l.
Test condition	:	Temp. 20-22 degrees Celsius; pH range 7.3-9.2; turbidity 185-200 ppm.The fishes were collected from Stillwater Creek in Payne County, Okla, adult females.
Reliability	:	(4) not assignable

14.05.2002 (74)

Type	:	static
Species	:	*Lepomis macrochirus* (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
LC50	:	= 8250 - 9000
Limit test	:	
Analytical monitoring	:	no data
Method	:	other: Recommendations of Committee on Research were followed
Year	:	1959
GLP	:	no
Test substance	:	other TS: Sodium bicarbonate
Method	:	METHOD FOLLOWED: A toxicity test with 50 bluegill sunfish exposed to sodium carbonate/ sodium bicarbonate and 10 control fish. Immediately before the introduction of the fish and at the end of the 24, 48, 72 and 96 hour test periods, the pH of the test solution was determined. At the end of the 24, 48, 72 and 96 hours a mortality count was taken. Recommendations of Committee on Research, Subcommittee on Toxicity, Section III, Federation of Sewage and Industrial Wastes Associations were followed. These are described in the following article: Douderoff, C. et al. (1951) Bio-Assay methods for the evaluation of acute toxicity of industrial wastes to fish. Sewage and Industrial Wastes 23 (11): 1380-1397 DEVIATIONS FROM GUIDELINE: Not applicable GLP: No STATISTICAL METHODS: Not reported METHOD OF CALCULATION: Not reported ANALYTICAL METHODS: Not reported
Remark	:	The LC50 value as well as the conditions are the same as Patrick and Cairns (1968). Above that, Cairns is author of both studies. Therefore it is assumed that this article refers to the same study.
Result	:	RESULTS: EXPOSED - Nominal/measured concentrations: Not reported - Effect data (Mortality): LC50 is dependant on the size of the fish. Small fish: approx. 3.88 cm, 0.96 gram: LC50 = 8250 mg/l. Medium fish: approx. 6.09 cm, 2.80 gram: LC50 = 8600 mg/l. Large fish: approx. 14.24 cm, 54.26 gram: LC50 = 9000 mg/l. - Concentration / response curve: Not reported - Effect concentration vs. test substance solubility: Not reported - Other effects: This is a test of carbonate to bicarbonate ratio RESULTS: CONTROL

- Number/percentage of animals showing adverse effects: zero
- Nature of adverse effects: No losses in the control

RESULTS: TEST WITH REFERENCE SUBSTANCE
- Concentrations: Not reported
- Results: Not reported

Test condition : TEST ORGANISMS
- Strain: Not reported
- Supplier: A private fish hatchery in Pennsylvania and the Pennsylvania Fish Commission
- Age/size/weight/loading: Age not reported

Small fish: approx. 3.88 cm, 0.96 gram
Medium fish: approx. 6.09 cm, 2.80 gram
Large fish: approx. 14.24 cm, 54.26 gram
fish were weighed wet
Experiments with small and medium fish: 10 fish per container
Experiments with large fish: 5 fish per container
- Feeding: Until 36 hours prior to testing, fish were fed daily with chopped, freshly cooked shrimp (15 min. in boiling water).
- Pretreatment: Acclimatizarion seven days in large aquarium
- Feeding during test: Not fed

STOCK AND TEST SOLUTION AND THEIR PREPARATION
- Other procedures: From a concentrated stock solution (2000x) the chemical was pipetted directly into five gallons of distilled water in order to prevent precipitation of the chemicals.

STABILITY OF THE TEST CHEMICAL SOLUTIONS: Not reported
REFERENCE SUBSTANCE: Not reported
DILUTION WATER
- Source: Distilled water
- Aeration: Firstly aerated with CO_2 to insure proper solution of the chemical. Compressed air was then forced through the solution to reduce the CO_2 and bring the dissolved oxygen to the test level.
- Alkalinity: Not reported,
- Hardness: Not reported
- Salinity: Not reported
- TOC: Not reported
- TSS: Not reported
- pH: Not reported
- Oxygen content: 5-9 ppm
- Conductance: Not reported
- Holding water: Not reported

TEST SYSTEM
- Concentrations: Not reported
- Dosing rate: Not reported
- Exposure vessel type: 5 gallon glass jars with cork stoppers
- Number of replicates, fish per replicate: 1 replicate, 10 fish per replicate in experiments with small and medium fish. 5 fish per replicate in experiments with large fish.
- Test temperature: 19 - 21 degrees Celsius
- Dissolved oxygen: 5-9 ppm
- pH: Determined, but not reported
- Adjustment of pH: Not reported
- Intensity of irradiation: Not reported
- Photoperiod: Not reported

DURATION OF THE TEST: 96 hours
TEST PARAMETER: Cessation of gill movement and lack of response to a mechanical stimulus for a period of 5 minutes.
SAMPLING: Every 24 hours
MONITORING OF TEST SUBSTANCE CONCENTRATION: Not reported

Test substance : SOURCE: Baker
PURITY: Chemically pure

IMPURITY/ADDITIVE/ETC.:
Common name: Sodium bicarbonate
- CAS number: 144-55-8
- Function: None
ANY OTHER INFORMATION: Not reported.

Reliability : (4) not assignable
This is not a toxicity test, but a test of pH related to the carbonate/bicarbonate ratio. However, the pH used was not indicated. Therefore it cannot be determined what the proportion carbonate/bicarbonate was. More information would be needed.

13.06.2002 (10)

Type : static
Species : *Lepomis macrochirus* (Fish, fresh water)
Exposure period : 96 hour(s)
Unit : mg/l
LC50 : = 8600
Limit test :
Analytical monitoring : no
Method : other: Recommendations of Committee on Research were followed
Year : 1968
GLP : no
Test substance : other TS: Sodium bicarbonate
Method : Recommendations of Committee on Research, Subcommittee on Toxicity, Section III, Federation of Sewage and Industrial Wastes Associations were followed. These are described in the following article:
Douderoff, C. et al. (1951) Bio-Assay methods for the evaluation of acute toxicity of industrial wastes to fish.
Sewage and Industrial Wastes 23 (11): 1380-1397
Remark : The LC50 value as well as the conditions are the same as Cairns and Scheer (1959). Above that, Cairns is author of both studies. Therefore it is assumed that this article refers to the same study.
Test condition : TEST ORGANISMS
- Strain: Not reported
- Supplier: Not reported
- Wild caught: Not reported
- Age/size/weight/loading: Not reported
- Feeding: No feeding during test
- Pretreatment: Not reported
- Feeding during test: No feeding during test

STOCK AND TEST SOLUTION AND THEIR PREPARATION
- Other procedures: Not reported

STABILITY OF THE TEST CHEMICAL SOLUTIONS: Not reported
REFERENCE SUBSTANCE: Not reported
DILUTION WATER
- Source: Not reported
- Aeration: Not reported
- Alkalinity: Not reported
- Hardness: Not reported
- Salinity: Not reported
- TOC: Not reported
- TSS: Not reported
- pH: Not reported
- Oxygen content: Not reported
- Conductance: Not reported
- Holding water:

TEST SYSTEM
- Test type: Static, 96 hour test
- Concentrations: Not reported
- Dosing rate: Not reported

- Renewal of test solution: Not reported
- Exposure vessel type: Not reported
- Number of replicates, fish per replicate: Not reported
- Test temperature: 16-20 degrees Celsius
- Dissolved oxygen: 5-9 ppm
- pH: Not reported
- Adjustment of pH:
- Intensity of irradiation: Not reported
- Photoperiod: Not reported

DURATION OF THE TEST: 96 hours
TEST PARAMETER: mortality
SAMPLING: Not reported
MONITORING OF TEST SUBSTANCE CONCENTRATION: Not reported

Test substance : A.C.S. grade Sodium bicarbonate, no further details reported
Reliability : (4) not assignable
14.05.2002 (58)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type	:	flow through
Species	:	*Daphnia magna* (Crustacea)
Exposure period	:	48 hour(s)
Unit	:	mg/l
NOEC	:	= 3100 measured/nominal
EC50	:	= 4100 calculated
Analytical monitoring	:	yes
Method	:	EPA OPP 72-2
Year	:	1993
GLP	:	yes
Test substance	:	other TS: Sodium bicarbonate
Method	:	METHOD FOLLOWED: EPA OPP 72-2 DEVIATIONS FROM GUIDELINE: Alkalinity in the controls were not measured at test initiation, but at test termination. GLP: Yes STATISTICAL METHODS: Moving average angle analysis, probit analysis and nonlinear interpolation with 95% confidence intervals calculated by binominal probability. METHOD OF CALCULATION: the 24-, 48-, 72- and 96-hour median LC50 values were estimated from derived mortality data at the measured concentrations using the described statistical methods which were available in a computer programme. If two or more statistical methods produced acceptable results, then the method which yielded the smallest 95% confidence interval was selected. ANALYTICAL METHODS: The Sodium concentration was determined, using the technique "multiple known standard additions" using an Orion Model 960 Ion Analyzer, equiped with a sodium probe, a stirrer and an automatic dispenser.
Result	:	RESULTS: EXPOSED - Nominal/measured concentrations: - Nominal/ measured concentrations in mg A.I./ L Nominal: 780 Mean Measured (SD):630 (57) Nominal: 1300 Mean Measured (SD):1100 (81) Nominal: 2200 Mean Measured (SD):1800 (190) Nominal: 3600 Mean Measured (SD):3100 (280) Nominal: 6000 Mean Measured (SD):5400 (400) - Concentration / response curve: Mean percentage mortality (of vessel A and B) after 96 hours:

Control: 5 %
630 mg A.I./L: 0 %
1100 mg A.I./L: 0 %
1800 mg A.I./L: 5 %
3100 mg A.I./L: 0 %
5400 mg A.I./L: 100 %
- Effect concentration vs. test substance solubility:Not reported
- Other effects: Not reported
RESULTS CONTROL: No effects
RESULTS: TEST WITH REFERENCE SUBSTANCE
Not reported

Test substance : Purity 99.9 %, Church & Dwight Co. Inc. Lot no 2F332
Reliability : (1) valid without restriction GLP test with full report
GLP test with full report
Flag : confidential
13.06.2002 (61)

Type : static
Species : *Daphnia magna* (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
EC50 : = 1640 measured/nominal
Analytical monitoring : yes
Method : other: EPA/600/4-91/002 (USEPA 1991)
Year : 1997
GLP : no
Test substance : other TS: Sodium bicarbonate
Method : METHOD FOLLOWED: USEPA (1991), Methods for measuring the acute toxicity of effluents to freshwater and marine organisms, 4th ed. EPA/600/4-91/002., U.S. Environmental Protection Agency, Washington DC.
DEVIATIONS FROM GUIDELINE: Daphnids were fed during the test. Preliminary tests with and without feeding had shown that this would not influence the results GLP: No
STATISTICAL METHODS: Stepwise logistic multiple regression using the LR program within BMDP statistical software
METHOD OF CALCULATION: Data was entered into a database using Paradox 3.1 software (Borland International, Scotts Valley, CA, USA). Via the statistical methods LC50s were determined.
ANALYTICAL METHODS: Bicarbonate ion concentrations were determined indirectly by phenolphtalein alkalinity. As bicarbonate is the predominate carbonate species present in the pH range of interest (pH 6.5-9.0), alkalinity equivalents were converted directly to bicarbonate concentration.
Result : RESULTS: EXPOSED
- Nominal/measured concentrations: All ions concentrations measured in the stock solutions were compared to nominal values. If the measured concentrations differed from the nominal value by more than 20%, the actual measured concentrations were substituted for the nominal concentrations.
- Effect data (Immobilisation):
48H EC50 = 1640 (1170-2030) mg/L
- Concentration / response curve: Not reported
- Effect concentration vs. test substance solubility: Not reported
- Other effects: Not reported
RESULTS CONTROL: Not reported
RESULTS: TEST WITH REFERENCE SUBSTANCE
Not reported
Test substance : Reagent grade NaHCO3 (Sigma Chemical Company, St Louis, MO, USA)
Reliability : (2) valid with restrictions No GLP, reliability 2 based on the fact that an EPA standard method has been followed.
No GLP, reliability 2 based on the fact that an EPA standard method has

been followed.

14.05.2002 (55)

Type	:	Static
Species	:	*Daphnia magna* (Crustacea)
Exposure period	:	48 hour(s)
Unit	:	mg/l
EC50	:	= 1268 measured/nominal
Analytical monitoring	:	No
Method	:	other: EPA/600/4-85/013 (USEPA 1985)
Year	:	1992
GLP	:	no
Test substance	:	other TS: Sodium bicarbonate
Method	:	METHOD FOLLOWED: USEPA (1985), Methods for measuring the acute toxicity of effluents to freshwater and marine organisms. EPA/600/4-85/013., U.S. Environmental Protection Agency, ORD, EMSL, Cincinnati, OH, 216p. DEVIATIONS FROM GUIDELINE: Not reported GLP: No STATISTICAL METHODS: Not reported METHOD OF CALCULATION: Not reported ANALYTICAL METHODS: Not reported
Remark	:	The reported nominal 48 H LC50 value of *Daphnia magna* less than 24 hours old at the beginning of the test was 1,268 mg/L. The 48 H LC50 values of 6 and 7 days old daphnids (at the beginning of the test) were also determined and had average nominal values of 1,781 mg/L and 1,730 mg/L respectively.
Result	:	RESULTS: EXPOSED - Nominal/measured concentrations: Results are reported as nominal concentrations - Effect data (Immobilisation): reported 48H LC 50 15.1 +/- 2.2 mmol/L (=1268 mg/L) - Concentration / response curve: Not reported - Cumulative immobilisation: Not reported - Effect concentration vs. test substance solubility: Not reported - Other effects: Not reported RESULTS CONTROL: Not reported RESULTS: TEST WITH REFERENCE SUBSTANCE Not reported
Test substance	:	Baker reagent-grade NaHCO3
Reliability	:	(2) valid with restrictions No GLP, reliability 2 based on the fact that an EPA standard method has been followed. No GLP, reliability 2 based on the fact that an EPA standard method has been followed.

14.05.2002 (36)

Type	:	static
Species	:	*Ceriodaphnia sp*. (Crustacea)
Exposure period	:	48 hour(s)
Unit	:	mg/l
EC50	:	= 1075 measured/nominal
Analytical monitoring	:	no
Method	:	other
Year	:	1992
GLP	:	no
Test substance	:	other TS: Sodium bicarbonate
Method	:	METHOD FOLLOWED: USEPA (1985), Methods for measuring the acute toxicity of effluents to freshwater and marine organisms.

EPA/600/4-85/013., U.S. Environmental Protection Agency, ORD, EMSL, Cincinnati, OH, 216p.
DEVIATIONS FROM GUIDELINE: Not reported
GLP: No
STATISTICAL METHODS: Not reported
METHOD OF CALCULATION: Not reported
ANALYTICAL METHODS: Not reported

Result : RESULTS: EXPOSED
- Nominal/measured concentrations: Results are reported as nominal concentrations
- Effect data (Immobilisation):
reported 48H LC 50 12.8 +/- 1.5 mmol/L (=1075 mg/L)
- Concentration / response curve: Not reported
- Cumulative immobilisation: Not reported
- Effect concentration vs. test substance solubility: Not reported
- Other effects: Not reported
RESULTS CONTROL: Not reported
RESULTS: TEST WITH REFERENCE SUBSTANCE
Not reported

Test substance : Baker reagent-grade NaHCO3

Reliability : (2) valid with restrictions No GLP, reliability 2 based on the fact that an EPA standard method has been followed.
No GLP, reliability 2 based on the fact that an EPA standard method has been followed.

14.05.2002 (36)

Type : static
Species : *Ceriodaphnia sp.* (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
EC50 : = 1020 measured/nominal
Analytical monitoring : yes
Method : other: EPA/600/4-91/002 (USEPA 1991)
Year : 1997
GLP : no
Test substance : other TS : Sodium bicarbonate

Method : METHOD FOLLOWED: USEPA (1991), Methods for measuring the acute toxicity of effluents to freshwater and marine organisms, 4th ed. EPA/600/4-91/002., U.S. Environmental Protection Agency, Washington DC.
DEVIATIONS FROM GUIDELINE: Daphnids were fed during the test. Preliminary tests with and without feeding had shown that this would not influence the results
GLP: No
STATISTICAL METHODS: Stepwise logistic multiple regression using the LR program within BMDP statistical software
METHOD OF CALCULATION: Data was entered into a database using Paradox 3.1 software (Borland International, Scotts Valley, CA, USA). Via the statistical methods LC50s were determined.
ANALYTICAL METHODS: Bicarbonate ion concentrations were determined indirectly by phenolphtalein alkalinity. As bicarbonate is the predominate carbonate species present in the pH range of interest (pH 6.5-9.0), alkalinity equivalents were converted directly to bicarbonate concentration.

Result : RESULTS: EXPOSED
- Nominal/measured concentrations: All ions concentrations measured in the stock solutions were compared to nominal values. If the measured concentrations differed from the nominal value by more than 20%, the actual measured concentrations were substituted for the nominal concentrations.
- Effect data (Immobilisation):

48H EC50 = 1020 (880-1170) mg/L
- Concentration / response curve: Not reported
- Effect concentration vs. test substance solubility: Not reported
- Other effects: Not reported
RESULTS CONTROL: Not reported
RESULTS: TEST WITH REFERENCE SUBSTANCE
Not reported

Test substance : Reagent grade NaHCO3 (Sigma Chemical Company, St Louis, MO, USA)
Reliability : (2) valid with restrictions
No GLP, reliability 2 based on the fact that an EPA standard method has been followed.

14.05.2002 (55)

Type :
Species : *Daphnia magna* (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
EC50 : = 2350
Analytical monitoring : no
Method : other
Year : 1946
GLP : no
Test substance : other TS: Sodium bicarbonate
Method : METHOD FOLLOWED: Not reported
DEVIATIONS FROM GUIDELINE: Not applicable
GLP: No
STATISTICAL METHODS: Not reported
METHOD OF CALCULATION: Not reported
ANALYTICAL METHODS: Not reported
Result : RESULTS: EXPOSED
- Nominal/measured concentrations: Not reported
- Effect data (Mortality):
Reported as "Threshold concentration". It is not really clear whether this is a LOEC or EC50: 2350 ppm
- Concentration / response curve: Not reported
- Effect concentration vs. test substance solubility: Not reported
- Other effects: Not reported
RESULTS: CONTROL
Not reported
RESULTS: TEST WITH REFERENCE SUBSTANCE
Not reported
Test condition : TEST ORGANISMS
- Strain: Not reported
- Supplier: Not reported
- Wild caught: Not reported
- Age/size/weight/loading: Not reported
- Feeding: Not reported
- Pretreatment: Not reported
- Feeding during test: Not reported
STOCK AND TEST SOLUTION AND THEIR PREPARATION
- Other procedures: Not reported
STABILITY OF THE TEST CHEMICAL SOLUTIONS: Not reported
REFERENCE SUBSTANCE: Not reported
DILUTION WATER
- Source: Lake Erie
- Aeration: Not reported
- Alkalinity: Not reported
- Hardness: Not reported
- Salinity: Not reported
- TOC: Not reported

- TSS: Not reported
- pH: Not reported
- Oxygen content: Not reported
- Conductance: Not reported
- Holding water: Not reported

TEST SYSTEM
- Test type: Not reported
- Concentrations: Not reported
- Dosing rate: Not reported
- Renewal of test solution: Not reported
- Exposure vessel type: Not reported
- Number of replicates, fish per replicate: Not reported
- Test temperature: Not reported
- Dissolved oxygen: Not reported
- pH: Not reported
- Adjustment of pH: Not reported
- Intensity of irradiation: Not reported
- Photoperiod: Not reported

DURATION OF THE TEST: Not reported
TEST PARAMETER: Not reported
SAMPLING: Not reported
MONITORING OF TEST SUBSTANCE CONCENTRATION: Not reported

Test substance : Sodium bicarbonate, no further details reported
Reliability : (4) not assignable
14.05.2002 (3)

Type :
Species : other aquatic worm: *Polycelis nigra*
Exposure period : 48 hour(s)
Unit : g/l
NOEC : = 7.14
Analytical monitoring : no
Method : other
Year : 1941
GLP : no
Test substance : as prescribed by 1.1 - 1.4
Test condition : Temperature 15-18 degrees Celsius. PH 8.0 by adding about 4% HCl. The solutions are every 12 hours renewed. No further details reported.
Reliability : (4) not assignable
14.05.2002 (40)

Type :
Species : other aquatic crustacea: *Mesocyclops leuckarti*
Exposure period : 24 hour(s)
Unit : mg/l
LC50 : = 1786.5
Analytical monitoring : no
Method : other
Year : 1982
GLP : no
Test substance : as prescribed by 1.1 - 1.4
Remark : Calculated by probit analysis according Finney (1952).
Test condition : Temperature range 23-27 degrees Celsius.
Reliability : (4) not assignable
The data included in the publication is not extensive enough to assign reliability (2). Sodium bicarbonate exposed *M. leuckarti* were used as a control group.
14.05.2002 (51)

Type :

Species	:	other: Culex sp.
Exposure period	:	48 hour(s)
Unit	:	mg/l
EC50	:	= 2000
Analytical monitoring	:	no
Method	:	other
Year	:	1965
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	LC50 after 24 hour is 2000 mg/l.
Test condition	:	Mosquito larvae, mostly Culex pipiens, obtained from puddles in a ditch on the campus, Louisiana State University, Baton Rouge. Tested in Reference Dilution Water (Dowden, 1960).
Reliability	:	(4) not assignable

14.05.2002 (21)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species	:	other algae: *Nitzschia linearis* W. Sm.
Endpoint	:	
Exposure period	:	5 day(s)
Unit	:	mg/l
EC50	:	= 650
Limit test	:	
Analytical monitoring	:	no
Method	:	other
Year	:	1968
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	EC50= 50% reduction in number of cells produced.

14.05.2002 (58)

Species	:	other algae: mixture of green algae
Endpoint	:	
Exposure period	:	63 day(s)
Unit	:	mg/l
NOEC	:	> 45
Limit test	:	
Analytical monitoring	:	yes
Method	:	other
Year	:	1973
GLP	:	no
Test substance	:	other TS: Sodium bicarbonate
Method	:	Glass slides were exposed to a portion of a small stream with an addition of Sodium bicarbonate to a concentration of 45 mg/L for a period of 63 days.
Remark	:	The biomass increased slightly more rapid in the treated slides.
Test condition	:	Flow-through system; pH = 7.0; Bicarbonate concentrations determined at beginning and end of the study by A.P.H.A.(1965) standard method and Hach chemicals. Mixture of green algae tested, composed mainly of: *Mougeotia sp.,Oedogonium sp., Zygnema sp., Bulbochaete sp., Nitzschia sp., Achnanthes sp., Navicula sp., Neidium sp., Gomphonema sp., Stephanodiscus sp., Fragilaria sp., Synedra sp.* and *Pinnularia sp.*.
Reliability	:	(4) not assignable The study was performed to assess the effects of adding sodium bicarbonate to a small stream on algae. This is not a toxicity test and is therefore assigned reliability (4).

14.05.2002 (14)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

Species	:	*Daphnia magna* (Crustacea)
Endpoint	:	other: Survival and reproduction rate
Exposure period	:	21 day(s)
Unit	:	mg/l
NOEC	:	> 576 measured/nominal
Analytical monitoring	:	no
Method	:	other
Year	:	1984
GLP	:	no
Test substance	:	other TS: Sodium bicarbonate
Method	:	METHOD FOLLOWED: Chronic, 3 week limit-test with *Daphnia magna*. One concentration: 576 mg/L. Ten daphnids (<24 hours)per replicate were exposed in two replicate solutions. Three times a week the daphnids were transferred to newly prepared test sdutions. Survival was assessed and offspring were counted on each day that the daphnids were transferred to fresh medium. The test was terminated after 3 weeks. DEVIATIONS FROM GUIDELINE: Not applicable GLP: No STATISTICAL METHODS: Not applicable METHOD OF CALCULATION: Percentage survival and offspring were compared with the control. ANALYTICAL METHODS: None.
Remark	:	No influence on reproduction observed. Offspring/female is resp. 65 and 69; control resp. 69 and 63, according Steel & Torrie (1960) analysis of variance.
Result	:	RESULTS: RANGE FINDING TEST: Not applicable RESULTS: EXPOSED - Nominal/measured concentrations: Only 1 nominal concentration was tested (together with 1 control) - Effect data: Control: 100% survival, resp. 69 and 63 offspring/female in the replicates 576 mg/L: 100 % survival, resp. 65 and 69 offspring/female in the replicates - Concentration / response curve: Not applicable - Effect concentration vs. test substance solubility: Not reported - Other effects: Not reported RESULTS: CONTROL - Number/percentage of animals showing adverse effects: zero - Nature of adverse effects: Not applicable RESULTS: TEST WITH REFERENCE SUBSTANCE Not reported STATISTICAL RESULTS: Not applicable
Source	:	TNO Voeding AJ Zeist
Test condition	:	TEST ORGANISMS - Strain: Not reported - Supplier: EG&G, Bionomics - Age: < 24 hours old - Feeding: During the test each 1 L test solution was supplied with 1.5 mL of a 2 mg/L Strike fish food suspension and 1.0 mL of a unicellular green algae suspension (*Selenastrum capricornutum*, 1x10E+7 cells/mL) - Pretreatment: Not reported - Feeding during test: see above

- Controls: Two replicate controls, consisting of standard hard water (170 mg/L CaCO3)
STOCK AND TEST SOLUTION AND THEIR PREPARATION
- Other procedures: Not reported
STABILITY OF THE TEST CHEMICAL SOLUTIONS: Not reported
REFERENCE SUBSTANCE: Not reported
DILUTION WATER
- Source: Deionized well water
- Aeration: Not reported
- Alkalinity: 115 +/- 10 mg/L as CaCO3
- Hardness: 170 mg/L CaCO3
- Salinity: Not reported
- TOC: Not reported
- TSS: Not reported
- pH: 7.9 - 8.3
- Oxygen content: Not reported
- Conductance: 600 +/- 100 micro mhos/cm
No further details, except for the NaHCO3 level, which was as a test substance added three times the required amount, quality meets criteria described in U.S. EPA (1975) Methods for acute toxicity tests with fish, macroinvertebrates and amphibians. Ecol. Res. Ser.

TEST SYSTEM
- Test type: 3 week static-renewal chronic test
- Concentrations: 0 (control), 576 mg/L
- Dosing rate: Not applicable
- Renewal of test solution: Three times a week, daphnids were transferred to freshly prepared test solutions.
- Exposure vessel type: 250 mL beaker containing 200 mL test solution
- Number of replicates, individuals per replicate: Two replicates, 10 daphnids per replicate
- Test temperature: Not reported
- Dissolved oxygen: Not reported
- pH: Not reported
- Adjustment of pH:Not reported
- Intensity of irradiation: Not reported
- Photoperiod: Not reported
DURATION OF THE TEST: 3 weeks
ENDPOINTS ASSESSED: Mortality and offspring
SAMPLING: Three times a week (when transfer to fresh medium took place)
MONITORING OF TEST SUBSTANCE CONCENTRATION: No

Test substance : Sodium bicarbonate, no further details reported
Reliability : (2) valid with restrictions
No GLP, but the test is well described

14.05.2002 (42)

4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES

Species : other
Endpoint : mortality
Exposure period : 48 hour(s)
Unit : other

NOEC	:	= 24 measured/nominal
LC50	:	> 24 calculated
Method	:	EPA OPP 141-1
Year	:	1999
GLP	:	yes
Test substance	:	other TS: Sodium bicarbonate
Method	:	METHOD FOLLOWED: Acute toxicity test with honeybees (*Apis mellifera*) acording to FIFRA Guideline 141-1. DEVIATIONS FROM GUIDELINE: The temperature ranged from 29-33 degrees Celsius instead of 31-33 degrees Celsius. GLP: Yes STATISTICAL METHODS: Not applicable METHOD OF CALCULATION: At the highest tested concentration, no mortality was recorded. No calculation was required. ANALYTICAL METHODS: All samples were analyzed for Sodium bicarbonate by adding methyl red TS indicator solution and titrating with HCl according to standard USP methods (USP, 1994): U.S. Pharmacopeia, 1994, United States Pharmacopeial Convention, Inc., Rockyville, Maryland, Vol. 23.
Result	:	Results are expressed as microgram per bee. The NOEC of 24 microgram per bee is equal to the highest treatment level and expressed as a mean measured concentration. RESULTS: EXPOSED - Nominal/measured concentrations: Nominal test concentrations: 1.6, 3.1, 6.2, 13 and 25 microgram per bee, plus non-dosed and surfactant control Mean measured test concentrations: 1.6, 3.0, 6.0, 13 and 24 microgram per bee, plus non-dosed and surfactant control - Effect data (Mortality): Following 48 hours of exposure, mortality of 3.0% was observed in the surfactant control and the 6.0 and 13 microgram/bee treatment. No mortality or sublethal effects (e.g. lethargy) were onserved among bees exposed to any of the remaining treatment levels or non-dosed controls. - Concentration / response curve: Not applicable RESULTS: CONTROL - Number/percentage of animals showing adverse effects: zero - Nature of adverse effects: not applicable RESULTS: TEST WITH REFERENCE SUBSTANCE Not reported
Test substance	:	Sodium bicarbonate, Purity 100 %, Church & Dwight Co. Inc. Lot no 8F065
Reliability	:	(1) valid without restriction
Flag	:	confidential

14.05.2002 (12)

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

In Vitro/in vivo : *In vivo*
Type : Toxicokinetics
Species : mouse
Number of animals
Males :
Females :
Doses
Males :
Females :
Vehicle : no data
Route of administration : i.p.
Exposure time :
Product type guidance :
Decision on results on acute tox. tests :
Adverse effects on prolonged exposure :
Half-lives : 1st:
2nd:
3rd:
Toxic behaviour :
Deg. product :
Method :
Year :
GLP : no data
Test substance : other TS: sodium bicarbonate
Result : The intraperitoneal injection of an unknown concentration of sodium [14C] bicarbonate into CFW mice was followed by assays (after 24 and 48 hrs and 1, 2, 4 and 12 weeks) of blood, spleen, liver, kidneys, lungs, brain, jejenum, muscle, skin, hair and long bones. More than 90% of the total radioactivity injected was lost via the respiratory route in one hour. At 24 hrs, most of the radioactivity in the blood was in noncarbonate form. Specific activity in long bones parallelled that in the blood for up to 12 weeks.
The radioactivity of the compound injected into a pregnant mouse was fixed in the foetal tisssues more rapidly than in the maternal tissues.
Variable and transient responses in erythrocyte counts and hemoglobin levels in mice to orally administered sodium bicarbonate was reported.
Reliability : (4) not assignable
Only secondary literature.

13.06.2002 (27)

In Vitro/in vivo : In vivo
Type : Toxicokinetics
Species : rat
Number of animals
Males :
Females :
Doses
Males :
Females :
Vehicle :
Route of administration : i.p.
Exposure time :
Product type guidance :
Decision on results on acute tox. tests :
Adverse effects on prolonged exposure :
Half-lives : 1st:
2nd:

3rd.:

Toxic behaviour :
Deg. product :
Method :
Year :
GLP : no data
Test substance : other TS: sodium bicarbonate
Result : Rapid absorption was demonstrated in rats after intraperitoneal injection of less than 1 mg sodium [14C] bicarbonate. Expired radioactivity reached a maximum specific activity within 4-10 minutes, and by 13-16 minutes the specific activity was reduced by half.

In a further study, rats were fasted for 24 hrs and given lactate by stomach tube, followed by 5 intraperitoneal injections of sodium [11C] bicarbonate made at 30 min intervals. The animals were sacrificed 1-half hour later and about 60% of the label was accounted for. The livers were removed and the glycogen extracted; 0.3-1.1% of the administered carbon-11 was present in the glycogen. Urine contained 1.3% of the dose and over 50% of the dose was accounted for by respiratory [11C] carbon dioxide. The authors calculated that one out of eight carbon atoms present in the glycogen was derived from the bicarbonate carbon.
Reliability : (4) not assignable
Only secondary literature.

14.05.2002 (27)

In Vitro/in vivo : In vivo
Type : Metabolism
Species : rat
Number of animals
Males :
Females :
Doses
Males : 672 mg/kg
Females :
Vehicle :
Route of administration : i.p.
Exposure time :
Product type guidance :
Decision on results on acute tox. tests :
Adverse effects on prolonged exposure :
Half-lives : 1st.:
2nd.:
3rd.:
Toxic behaviour :
Deg. product :
Method :
Year :
GLP : no data
Test substance : other TS: sodium bicarbonate
Result : Sodium bicarbonate has been reported to affect citrate metabolism in the kidneys of rats. An intraperitoneal injection of 672 mg/kg into 4 male rats caused a threefold rise in tissue citrate levels of the kidney and a smaller but significant rise in the citrate levels in the liver.
Reliability : (4) not assignable
Only secondary literature.

14.05.2002 (27)

In Vitro/in vivo : In vivo
Type : Toxicokinetics
Species : human

Number of animals
Males :
Females :
Doses
Males :
Females :
Vehicle :
Method :
Year :
GLP :
Test substance : other TS: sodium bicarbonate
Result : In man, at plasma bicarbonate levels below 24 mM, virtually all bicarbonate entering the renal tubules is reabsorbed. Above this level the excess bicarbonate is excreted. Oral administration of sodium bicarbonate at 1 g/kg as a single dose increased sodium excretion and increased blood chloride concentration and urine chloride excretion. This study demonstrates that the carbonate and bicarbonate ions enter and are constituents of the normal metabolic pathways of man.
Reliability : (4) not assignable
Only secondary literature.

14.05.2002 (27)

5.1.1 ACUTE ORAL TOXICITY

Type : LD50
Value : > 4000 mg/kg bw
Species : rat
Strain : other: Crl:CD BR
Sex : male/female
Number of animals : 30
Vehicle : water
Doses : Females: 3000, 3500, 4000 mg/kg bw. Males: 3000, 3500, 4500 mg/kg bw.
Method : other
Year : 1993
GLP : yes
Test substance : other TS: sodium bicarbonate
Method : METHOD FOLLOWED: EPA-FIFRA 40 CFR 160
DEVIATIONS FROM GUIDELINE: Not reported.
GLP: Yes.
STATISTICAL METHODS: Not reported.
METHOD OF CALCULATION: Not reported.
ANALYTICAL METHODS: Not reported.
Result : MORTALITY: one female dosed with 4000 mg/kg died.
- Time of death: The animal died within 24 hours of administration.
- Number of deaths at each dose: 1/5 females dosed with 4000 mg/kg died.
CLINICAL SIGNS: All the surviving animals gained weight during the postexposure observation period. The clinical signs of toxicity included soft stool, hypoactivity, dark-stained urogenital area. The surviving animals returned to a normal appearance by day 2. Of the females dosed with 3500mg/kg, 4/5 had soft stool, 1/5 had a dark-stained urogenital area and 1/5 exhibited hypoactivity, within the first day. Among the females dosed with 4000 mg/kg, 1/5 had soft stool and 1/5 was hypoactive during the first day. Among the males dosed with 4500 mg/kg, 1/5 had soft stool and 1/5 was hypoactive during the first day.
NECROPSY FINDINGS: In the female that died on day 0, a single erosion was found in the glandular mucosa of the stomach near the pylorus. An enlarged pelvis was present in the right kidney of a male given 3000 mg/kg, both mandibular lymph nodes were enlarged in a male given 4000 mg/kg,

and multiple opaque areas were on the parietal surface of the spleen in a male and a female given 4000 mg/kg.
POTENTIAL TARGET ORGANS: Not reported.
SEX-SPECIFIC DIFFERENCES: Not reported.

The no observable adverse effects level (NOAEL) is 4,000 mg/kg in males and 3,000 mg/kg in females.

Test condition : TEST ORGANISMS: Crl:CD BR rats.
- Source: Charles River Laboratories, Inc.
- Age: Young adult, no further detalis were given.
- Weight at study initiation: 234-299 g.
- Controls: Not reported.

ADMINISTRATION: Oral, by gavage.
- Doses: 5 males in each of three groups were dosed with 3000, 4000 or 4500 mg/kg, respectively. 5 females in each of three groups were dosed with 3000, 3500 or 4000 mg/kg, respectively.
- Doses per time period: Only one dose was given.
- Volume administered or concentration: The test material was mixed with distilled water to form a uniform suspension, and administered at a volume of 10.0 ml/kg bw.
- Post dose observation period: 14 days.

EXAMINATIONS: The rats were observed for mortality twice daily. Clinical signs were registered at approximately 1, 2.5, and 4 hrs after test material administration, and daily thereafter for at least 14 days. The body weight was registered before experimental initiation, at 7 and 14 days after administration, and at death.

Test substance : SOURCE: Church & Dwight Co., Inc., Old Fort, OH, USA.
PURITY: 99.9%.
IMPURITY/ADDITIVE/ETC.: Arsenic < 2 ppm. Heavy metals < 5 ppm. Loss on drying < 0.25%. Chloride < 0.015%. Sulfate < 0.015%.
ANY OTHER INFORMATION: Lot No. 063095F.

Reliability : (1) valid without restriction
Comparable to guideline study.

07.01.2003 (32)

Type : LD50
Value : = 7334 mg/kg bw
Species : rat
Strain : other: Crl:CD BR
Sex : male/female
Number of animals : 30
Vehicle : water
Doses : 5000, 7000, 9000 mg/kg bw
Method : other: EPA guideline
Year : 1992
GLP : yes
Test substance : other TS: sodium bicarbonate
Method : METHOD FOLLOWED: Not reported.
DEVIATIONS FROM GUIDELINE: Not reported.
GLP: Yes.
STATISTICAL METHODS: The LD50 value for males, females and the sexes combined was determined by a computer program using a modified Behrens-Reed-Muench cumulant method.
ANALYTICAL METHODS: Not reported.

Result : MORTALITY:
- Time of death: The time of death is listed by dose. 7,000 mg/kg: day 1. 9,000 mg/kg: day 1.
- Number of deaths at each dose: Mortality is listed by dose. 7,000 mg/kg: 2/5 males, 3/5 females. 9,000 mg/kg: 3/5 males, 5/5 females.

CLINICAL SIGNS: Animals that survived to the end of the observation period, exhibited body weight gain. Clinical signs of toxicity included hypoactivity, staggered gait, shallow breathing and soft stool. All surviving animals had a normal appearance by day 2.
NECROPSY FINDINGS: Among animals dosed with 5000 mg/kg, 3/10 had lesions in the spleen (multiple raised, grey areas on parietal surface and 1/10 a cyst in the spleen. Of the animals dosed with 7,000 mg/kg, 5/10 had one or more portions of the gastro-intestinal tract distended with gas, 1/10 had multiple, slightly raised tan areas in the spleen, 1/10 had a tan area in the heart. Along animals dosed with 9000 mg/kg, 2/10 had multiple tan, grey slightly raised areas, 6/10 had one or more portions of the gastro-intestinal tract distended with gas, one of these had large submandibular nodes. In 1/10 the glandular mucosa of the stomach had dark red areas.
POTENTIAL TARGET ORGANS: Not reported.
SEX-SPECIFIC DIFFERENCES: Not reported.

Estimated oral LD50:
male: 7,937 mg/kg bw
95% confidence limits - 5,284-8,290 mg/kg bw

Female: 6, 618 mg/kg bw
95% confidence limits - 5,284-8,290 mg/kg bw

Sexes combined: 7,334 mg/kg bw
95% confidence limits - 6,203-8,669 mg/kg bw

Test condition : TEST ORGANISMS: Crl:CD BR albino rat.
- Source: Charles River Laboratories, Inc.
- Age: The animals were described as young adults.
- Weight at study initiation: 208-264 g.
- Controls: Not reported.
ADMINISTRATION: Oral by gavage.
- Doses: 5000, 7,000 and 9,000 mg/kg bw, with five males and five females in each dose group.
- Doses per time period: One dose only.
- Volume administered or concentration: The test material was mixed with distilled water, and administered in a volume of 10 ml/kg bw.
- Post dose observation period: 14 days.
EXAMINATIONS: Clinical signs and mortality were registered at approximately 1, 2.5, and 4 hrs after test material administration, and twice daily thereafter for at least 14 days. The body weight was registered before experimental initiation, at 7 and 14 days after administration, or at death when survival exceeded one day.

Test substance : SOURCE: Not reported.
PURITY: Not reported.
IMPURITY/ADDITIVE/ETC.: Not reported.
ANY OTHER INFORMATION: Not reported.

Reliability : (1) valid without restriction
EPA guideline study.

07.01.2003 (31)

Type : LD50
Value :
Species : rat
Strain : Sprague-Dawley
Sex : male/female
Number of animals : 50
Vehicle : water
Doses : 5000 mg/kg bw
Method : other: EPA 16 CFR 1500.3C2 (i)
Year : 1979

GLP : no
Test substance : other TS: sodium bicarbonate
Method : METHOD FOLLOWED: EPA 16 CFR 1500.3C2 (i).
DEVIATIONS FROM GUIDELINE: Not reported.
GLP: No, the research was executed before the existence of GLP.
STATISTICAL METHODS: Not reported.
METHOD OF CALCULATION: Not reported.
ANALYTICAL METHODS: Not reported.
Result : MORTALITY:
- Time of death: Listed by identity code. #5059: mortality occurred within 24 hrs of test substance administration.
#5060: mortality occurred within 4 hrs of substance administration. #5061: mortality within 24 hrs of test substance administration. #5062: mortality within 48 hrs of substance administration. #5063: mortality occurred within 48 hours.
- Number of deaths at each dose: The number of deaths is listed by identity code. #5059: 2/10 #5060: 1/10. #5061: 4/10. #5062: 6/10. #5063: 5/10.
CLINICAL SIGNS: All surviving animals experienced a body weight gain, and showed no apparent clinical signs from day 2 until the study was terminated .#5059: 3/10 were lethargic, 1/10 had ataxia during the first day. #5060: 10/10 were lethargic, 2/9 had ataxia, 1/9 was ataxic with diarrhoea and 1/9 had ataxia, diarrhoea and a hunched posture. #5061: 1/10 had ataxia and diarrhoea, 4/10 had ataxia, 1/10 was observed with ataxia, a hunched posture and pilo-erection, 2/10 had prostration, and 1/10 had ataxia, tremors and diarrhoea. #5062: all the animals were lethargic, 1/10 had ataxia and diarrhoea, 1/10 had prostration, 3/10 had ataxia, 1/10 had ataxia, diarrhoea and a hunched posture, 1/10 had pilo-erection, prostration, 1/10 had ataxia. #5063: 1/10 had a hunched posture, 4/10 had ataxia, 1/10 had ataxia and a hunched posture, 1/10 had a hunched posture, diarrhoea and ataxia, 1/10 had ataxia, a hunched posture and pilo-erection.
NECROPSY FINDINGS:
#5059: 1/10 had yellow fluid in intestines, and 1/10 had test material in the stomach, which was pyloric red.
#5060: 1/10 had a yellow fluid in the stomach and intestines.
#5061: 1/10 had test material in the stomach and the stomach wall was red. 3/10 had a red pyloric and intestines, and test material in stomach.
#5062: 2/10 had test material in the stomach and the stomach wall was red. 3/10 had hemorrhagic pyloric section and test material in stomach. 1/10 had a yellow fluid in the stomach and red intestinal lining. 1/10 had terst material in the stomach and red intestine walls.
#5063: 2/10 had test material in the stomach, and red pyloric section. 1/10 had yellow fluid in the intestines, 2/10 in the stomach and intestines.
POTENTIAL TARGET ORGANS: Not reported.
SEX-SPECIFIC DIFFERENCES: Not reported.

In this study five groups of 10 rats in each (5 males and 5 females) were exposed to the same dose level of 5 unidentified substances, to determine mortality. The substances (all sodium bicarbonate from the same source) were given individual codes: #5059, #5060, #5061, #5062 and #5063.

The report authors concluded:
#5059 is not orally toxic
#5060 is not orally toxic
#5061 is not orally toxic
#5062 is orally toxic
#5063 is orally toxic
Test condition : TEST ORGANISMS: Sprague-Dawley rats.
- Source: Taconic Farms, Inc., Germantown, NY, USA.

- Age: Not reported.
- Weight at study initiation: Not reported.
- Controls: Not reported.
ADMINISTRATION:
- Doses: 5000 mg/kg
- Doses per time period: 1 oral dose.
- Volume administered or concentration: 50% w/v dilution in tap water.
- Post dose observation period: 14 days.
EXAMINATIONS: Animals were observed for mortality and overt signs of toxicity frequently during the day of dosing and at least once daily for 14 days thereafter. The rats that died during the observation period were given a necropsy examination for grass organ pathology, this was performed on the surviving animals after the observation period. The body weight data was recorded initially and at termination of the study for the survivors.

Test substance : SOURCE: Not reported.
PURITY: Not reported.
IMPURITY/ADDITIVE/ETC.: Not reported.
ANY OTHER INFORMATION: Not reported.

Reliability : (1) valid without restriction
Guideline study but several test conditions and a description of the test substance was missing.

06.08.2002 (73)

Type : LD50
Value : ca. 4220 - 8290 mg/kg bw
Species : Rat
Strain : Sprague-Dawley
Sex : male/female
Number of animals : 60
Vehicle : other: water or corn oil
Doses : not reported
Method : other
Year : 1964
GLP : No
Test substance : other TS: sodium bicarbonate
Method : METHOD FOLLOWED: Not reported.
GLP: No, research executed before existence of GLP.
STATISTICAL METHODS: Not reported.
METHOD OF CALCULATION:Conform OECD 401.
ANALYTICAL METHODS: Not reported.
Remark : Remark:
The study was an interlaboratory test with six laboratories to assess the influence of the method on the results. They were to determine the acute oral LD50 for albino rats by administering a 20% slurry of $NaHCO_3$ in water, a 50% slurry of $NaHCO_3$ in water, or a 50% slurry of $NaHCO_3$ in corn oil.

By the administration of 20% slurry in water: the number of animals was 5 (laboratory A), 10 (laboratory B) or 20 (laboratory C), and the LD50 4220, 4310, and 4400 mg/kg bw, respectively. The results were a function of the test procedure as well as the substance.

By administration of 50% slurry in water: the number of animals was 10 (laboratory D) and 5 (laboratory E), and the LD50 6290 and 5820 mg/kg bw, respectively. Laboratory D used animals of both sex, while laboratory E used only males.

By administration of 50% slurry in corn oil: 10 male rats were exposed (laboratory F), and LD50 was 8290 mg/kg bw. The LD50 was higher than for a 50% slurry in water, possibly due to a slower absorption rate of the

water soluble NaHCO3 from the corn oil into the circulation.

Result : No details reported.

Test condition : TEST ORGANISMS: rat
- Source: Not reported.
- Age: Not reported.
- Weight at study initiation: 200-300g
- Controls: Not reported.

ADMINISTRATION:
- Doses: Not reported.
- Doses per time period: Single intragastrical (gavage) dose.
- Volume administered or concentration: Not reported.
- Post dose observation period: 14 days.

EXAMINATIONS: Not reported.

Test substance : SOURCE: Not reported.
PURITY: Not reported.
IMPURITY/ADDITIVE/ETC.: Not reported.
ANY OTHER INFORMATION: Not reported.

Reliability : (2) valid with restrictions
Acceptably documented publication which meets basic scientific principles.

13.06.2002 (35)

Type : LD50

Value : ca. 7570 - 8900 mg/kg bw

Species : Rat

Strain : Wistar

Sex : no data

Number of animals :

Vehicle : no data

Doses :

Method :

Year : 1968

GLP : No

Test substance : other TS: sodium bicarbonate

Result : NaHCO3 was administered by gavage. LD50 values were:
7570 mg/kg bw (fasted rats on wire floored cages)
8460 mg/kg bw (fasted rats bedded on wood shavings)
8900 mg/kg bw (fed rats)

Of ten adult white rats (fasted for 24 hrs) given 5000 mg/kg bw via gavage, one animal died within 6 hrs of administration. There were no toxic effects on the remaining rats.

Reliability : (4) not assignable
The result are retrieved from a secondary source. The article by Johnsonwas published in 1987, while the original article was published in 1968.

13.06.2002 (39)

5.1.2 ACUTE INHALATION TOXICITY

Type : other: limit test

Value : > 4.74 mg/l

Species : Rat

Strain : Sprague-Dawley

Sex : male/female

Number of animals : 10

Vehicle : other: none

Doses : 4.74 mg/l

Exposure time : 4.5 hour(s)

Method : other: EPA/TSCA CFR part 798.1150

Year : 1992

GLP : Yes
Test substance : other TS: sodium bicarbonate
Method : METHOD FOLLOWED: EPA/TSCA 40 CFR Part 798.1150
DEVIATIONS FROM GUIDELINE: Not reported.
GLP: Yes.
STATISTICAL METHODS: Not reported.
METHOD OF CALCULATION: Not reported.
ANALYTICAL METHODS: Not reported.
Result : MORTALITY:
- Time of death: there was no mortality, and the animals were sacrificed after 14 days of observation. LC50 >4.74 mg/l.
- Number of deaths at each dose: No mortality.
CLINICAL SIGNS: during the first hour of exposure, reduced movement and hunched posture were noted for most animals. At exposure termination test substance was observed on the fur of two animals, while the same was observed in all the remaining rats on the one or two after exposure termination.
Ocular and/or nasal discharge was observed in 6/10 rats within one day after exposure. 6/10 rats were active and health the from day 2 after exposure, and the remaining animals likewise from day 3. All the animals gained body weight during the observation period (body weight males at 14 days, 311-341 g; body weight females at 14 days, 254-267 g).
NECROPSY FINDINGS: the general findings at gross necropsy were unremarkable. One male and one female had moderately red lung tissue, while one male had slightly red lung tissue.
POTENTIAL TARGET ORGANS: Respiratory tract, lungs.
SEX-SPECIFIC DIFFERENCES: Not reported.
Test condition : TEST ORGANISMS: Sprague-Dawley rats.
- Source: Hilltop Lab Animals, Scottdale, PA.
- Age: the report states that the rats were young adults, but the exact age is not given.
- Weight at study initiation: The weight-range for males was 224-239 g, and 219-226 g for females.
- Number of animals: 5 males and 5 females were used in this study.
- Controls: None.
ADMINISTRATION:
- Type of exposure: The rats were exposed by inhalation for 4,5 hrs.
- Concentrations: the measured (gravimetric) chamber concentration was 4.74 +/-1.03 mg/l.
- Particle size: MMAD in two samplings of two minutes duration, was (1) 2.9 +/- 1.77 micrometres SD and (2) 2.7 +/- 2.04 micrometres SD, respectively.
- Type or preparation of particles: the test substance was ground for 24 hours in a ball mill prior to aerosolisation. Thereafter it was sieved through a 425 micron screen to separate it from the grinding medium and any other large particles which remained.
EXAMINATIONS: body weight was measured prior to exposure and on days 1,7 and 14. Animals were observed before exposure commenced, every 15 min during the first exposure hour, and every 15 min thereafter through exposure termination. The animals were individually examined on removal from the chamber. In-chamber animal observations were limited due to the accumulation of test substance on the walls of the chamber which obscured visualisation.
Test substance : SOURCE: Not reported.
PURITY: > 99.5%
IMPURITY/ADDITIVE/ETC.: Not reported.
ANY OTHER INFORMATION: the test substance was ground for 24 hours in a ball mill prior to testing.
Reliability : (1) valid without restriction
Guideline study.

14.05.2002 (77)

5.1.3 ACUTE DERMAL TOXICITY

5.1.4 ACUTE TOXICITY, OTHER ROUTES

Type	:	other: Brain damage
Value	:	= 10 ml/kg bw
Species	:	rabbit
Strain	:	other: Japanese white
Sex	:	no data
Number of animals	:	45
Vehicle	:	no data
Doses	:	7% NaHCO3 in doses of 10, 30, 50 or 100 ml/kg bw
Route of admin.	:	i.p.
Exposure time	:	
Method	:	other
Year	:	1981
GLP	:	no
Test substance	:	other TS: sodium bicarbonate
Method	:	METHOD FOLLOWED: Not reported. GLP: No, research executed before existence of GLP. STATISTICAL METHODS: Not reported. METHOD OF CALCULATION: Not reported. ANALYTICAL METHODS: Not reported.
Result	:	MORTALITY: - Time of death: within two hours - Number of deaths at each dose: none (10 ml), 1 (30 ml), 6 (50 ml), 5 (100 ml). Survival: 100%, 88%, 33% and 44%, respectively. CLINICAL SIGNS: Not reported. NECROPSY FINDINGS: All animals died of brain damage by haemorraging. Half of the newborn rabbits injected with 7% NaHCO3 at 10 ml/kg, i.p., had intracranial haemorrhage at 335 mOsm/L. When the hyperosmolality reached 392 mOsm/L (50 ml/kg), intracranial haemorrhage was observed in all cases. POTENTIAL TARGET ORGANS: Only the brain was examined. SEX-SPECIFIC DIFFERENCES: Not reported.
Test condition	:	TEST ORGANISMS: Japanese white rabbits. - Source: Not reported. - Age: 1 day. - Weight at study initiation: 25-80 g. - Controls: (1) 2 unexposed rabbits, 2 in each group injected i.p. with (2) 50 ml and (3) 100 ml saline, respectively. ADMINISTRATION: - Doses: (7% NaHCO3 in doses of 10, 30, 50 or 100 ml/kg bw) was administered i.p. with 9 animals in each group. - Post dose observation period: No. EXAMINATIONS: Morphological examination of the brain.
Test substance	:	SOURCE: Not reported. PURITY: Not reported. IMPURITY/ADDITIVE/ETC.:Not reported. ANY OTHER INFORMATION: Not reported.
Reliability	:	(3) invalid Unsuitable test system, as the solution was administered intraperitoneal. Insufficient documentation for assessment, as the study was carried out to assess the correlation between hyperosmolality and brain damage. NaHCO3 was used as a hypertonic solution.

14.05.2002 (68)

Type	:	other: brain damage
Value	:	

Species	:	Rabbit
Strain	:	other: Japanese white
Sex	:	no data
Number of animals	:	27
Vehicle	:	no data
Doses	:	7% NaHCO3 (group 1), 7% NaHCO3 + 10% hypoxia (group 2), 10% hypoxia (group 3)
Route of admin.	:	Infusion
Exposure time	:	
Method	:	Other
Year	:	1981
GLP	:	No
Test substance	:	other TS: sodium bicarbonate
Method	:	METHOD FOLLOWED: Not reported. GLP: No, research executed before existence of GLP. STATISTICAL METHODS: Not reported. METHOD OF CALCULATION: Not reported. ANALYTICAL METHODS: Not reported.
Result	:	MORTALITY: - Time of death: Within two hours. - Number of deaths at each dose: The drip continued until death due to hyperosmolality, within two hours, in group 1 and 2. 4 of 5 survived in group 3. CLINICAL SIGNS: Not reported. NECROPSY FINDINGS: All the young rabbits exposed to 7% NaHCO3 died with hyperosmolality at over 380 mOsm/L (the mean was 462 mOsm/L) after the drip infusion. The mean for group 2 was 393 mOsm/l and for group 3, 300 mOsm/l. pH rose with the start of drip infusion and showed strong alkalosis. Fatal intracranial hemorrhage was induced by hyperosmolality and was enhanced by the combination of hypoxia and immaturity. POTENTIAL TARGET ORGANS: Only the brain was examined. SEX-SPECIFIC DIFFERENCES: Not reported.
Test condition	:	TEST ORGANISMS: Japanese white rabbits. - Source: Not reported. - Age: Not reported. - Weight at study initiation: 1-1.5 kg - Controls: In group 3 the animals were in a hypoxic environment for 3 hrs. ADMINISTRATION: - Doses: The hypertonic solution was administered continously via an ear vein, 20-60 ml/kg/hr. Group 1 (12 rabbits) received no additional treatment. Group 2 (10 rabbits) and 3 (5 rabbits) were subjected to 10% hypoxic hypoxia (group 2 for 1 hr, group 3 for 3 hrs). It is not known how long the drip lasted, although mortality was assessed after two hours. - Post dose observation period: 2 hrs EXAMINATIONS: morphological observations of the brain.
Test substance	:	SOURCE: Not reported. PURITY: Not reported. IMPURITY/ADDITIVE/ETC.:Not reported. ANY OTHER INFORMATION: Not reported.
Reliability	:	(3) invalid Unsuitable test system, as the solution was administered intravenously. Insufficient documentation for assessment, as the study was carried out to assess the correlation between hyperosmolality and brain damage. NaHCO3 was used as a hypertonic solution.

14.05.2002 (68)

Type	:	other: instillation in the trachea
Value	:	
Species	:	Rabbit

Strain	:	no data
Sex	:	no data
Number of animals	:	2
Vehicle	:	no data
Doses	:	4 cc/kg of 1.87% or 3.75% solution
Route of admin.	:	Other
Exposure time	:	48 hour(s)
Method	:	Other
Year	:	1961
GLP	:	No
Test substance	:	other TS: sodium bicarbonate
Method	:	METHOD FOLLOWED: Not reported. GLP: No, research executed before existence of GLP. STATISTICAL METHODS: Not reported. METHOD OF CALCULATION: Not reported. ANALYTICAL METHODS: Not reported.
Result	:	MORTALITY: None. CLINICAL SIGNS: Not reported. NECROPSY FINDINGS: The animals exposed to NaHCO3 alone sustained some mononuclear infiltration, but no damage. NaHCO3 did not protect the lung tissue from HCl, but did not cause any damage either. POTENTIAL TARGET ORGANS: Lungs, respiratory tract. SEX-SPECIFIC DIFFERENCES: Not reported.
Test condition	:	TEST ORGANISMS: White rabbit - Source: Not reported. - Age: Not reported. - Weight at study initiation: 1.95-4.4 kg - Controls: 2 rabbits exposed to NaHCO3 alone were control animals in this study to assess the lung damage following inhalation of vomit (as hydrochloric acid causes lesions) and whether instillation of neutral/alkaline liquids is an efficient treatment. The control animals were instilled with 4 cc/kg bw 1.87% and 4 cc/kg bw 3.75% sodium bicarbonate, respectively. ADMINISTRATION: The rabbits were anesthetised and instilled with hydrochloric acid in the trachea by intubation, they were then turned from side to side to ensure dispersion of the liquid in both lungs. Two minutes later a NaHCO3 solution was instilled in the lungs. - Doses: One animal received 4 cc/kg bw HCl (pH 1.6) and 1.36 cc/ kg bw 7.5% NaHCO3, one received 4 cc/kg bw HCl (pH 1.6) and 2 cc/kg bw 1.87% NaHCO3, and 8 rabbits received 4 cc/kg bw HCl (pH 1.8) and 2 cc/kg bw directly in each lung of 7.5% NaHCO3 solution. - Post dose observation period: None. The animals were sacrificed after 48 hours. EXAMINATIONS: The respiratory tract and lungs were examined for type and extent of lesions.
Test substance	:	SOURCE: Not reported. PURITY: Not reported. IMPURITY/ADDITIVE/ETC.:Not reported. ANY OTHER INFORMATION: Not reported.
Reliability	:	(3) invalid The test system was unsuitable, as the solution of NaHCO3 was instilled in the trachea and lungs of rabbits, to assess the damage caused by HCl with and without NaHCO3. There is insufficient documentation for assessment. Only two rabbits were exposed to NaHCO3 alone, and there were no control animals that were not instilled with any solutions. It is therefore unsure what caused the mononuclear infiltration observed .

14.05.2002 (4)

5.2.1 SKIN IRRITATION

Species	:	Rabbit
Concentration	:	.5 g
Exposure	:	Semiocclusive
Exposure time	:	4 hour(s)
Number of animals	:	6
Vehicle	:	water
PDII	:	.3
Result	:	slightly irritating
Classification	:	
Method	:	other: EPA 40 CFR 798.4470
Year	:	1992
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	METHOD FOLLOWED: EPA guidelines 40 CFR 798.4470. DEVIATIONS FROM GUIDELINE: Not reported. GLP: Yes. STATISTICAL METHODS: Not reported. METHOD OF CALCULATION: Not reported. ANALYTICAL METHODS: Not reported.
Result	:	AVERAGE SCORE - Erythema: 1 hour: 0.7. 24 hrs: 0.2. 48 hrs: 0. 72 hrs: 0. - Edema: 1 hour: 0.2. 24 hrs: 0. 48 hrs: 0. 72 hrs: 0. REVERSIBILITY: The effects were fully reversible. OTHER EFFECTS: Not reported. The Primary Dermal Irritation Index (PDII) was 0.3. The substance is slightly irritating.
Test condition	:	TEST ANIMALS: Rabbit. - Strain: New Zealand Albino. - Sex: 3 males and 3 females. - Source: Davidson's Mill Farm, S. Brunswick, NJ. - Age: Not reported. - Weight at study initiation: Not reported. - Number of animals: 6. - Controls: Not reported. ADMINISTRATION/EXPOSURE - Preparation of test substance: The test substance was moistened with distilled water prior to application. - Area of exposure: the application site was approximately 6 cm2 of skin clipped free of hair, either dorsal or lateral on the rabbit. - Occlusion: the test site was immediately after application covered with a 2-7/8 x 4-1/2 in adhesive-backed gauze patch which was loosely held in contact with the skin by use of a semi-occlusive elastic cloth overwrap. - Vehicle: Distilled water. - Concentration in vehicle: 0.5 g test substance per 0.5 ml distilled water. - Total volume applied: 0.5 ml. - Postexposure period: 72 hrs. - Removal of test substance: the patches were removed after 4 hrs of exposure at which time the test sites were gently wiped clean of any residual test substance. EXAMINATIONS - Scoring system: The skin lesions were scored according to the Draize scoring system. The average erythema and oedema scores for the 1, 24, 48 and 72 hrs scoring intervals were added. The resultant value was divided by the number of evaluation intervals (4). - Examination time points: Skin sites were evaluated at approximately 30-60 minutes, 24, 48 and 72 hrs after patch removal and scored.

Test substance	:	SOURCE: Not reported. PURITY: > 99.5% IMPURITY/ADDITIVE/ETC.: Not reported. ANY OTHER INFORMATION: Not reported.
Reliability	:	(1) valid without restriction Guideline study.
14.05.2002		(78)
Species	:	Rabbit
Concentration	:	.5 g
Exposure	:	Semiocclusive
Exposure time	:	24 hour(s)
Number of animals	:	6
Vehicle	:	other:none
PDII	:	
Result	:	not irritating
Classification	:	
Method	:	other
Year	:	1972
GLP	:	No
Test substance	:	other TS: sodium bicarbonate
Method	:	METHOD FOLLOWED: Not reported. DEVIATIONS FROM GUIDELINE:Not reported. GLP: No, the experiment was performed before the GLP standard was established. STATISTICAL METHODS:Not reported. METHOD OF CALCULATION: Not reported. ANALYTICAL METHODS: Not reported.
Result	:	AVERAGE SCORE - Erythema: Not reported. - Edema: Not reported. REVERSIBILITY: Not reported. OTHER EFFECTS: Not reported. None of the animals had signs of skin irritation.
Test condition	:	TEST ANIMALS: Rabbit. - Strain: Not reported. - Sex: Not reported. - Source: Not reported. - Age: Not reported. - Weight at study initiation: Not reported. - Number of animals: 6 - Controls: Not reported. ADMINISTRATION/EXPOSURE - Preparation of test substance: Not reported. - Area of exposure: Abraded and non-abraded clipped skin on the back - Occlusion: Semi-occluded, with gauze patches. - Vehicle: Not reported. - Total volume applied: 0.5 g of test substance applied. - Concentration in vehicle: Not reported. - Postexposure period: Observation at 0, 48 and 72 hrs after removing the patch. - Removal of test substance: After 24 hrs exposure. EXAMINATIONS - Scoring system: Not reported. - Examination time points: Not reported.
Test substance	:	SOURCE: Not reported. PURITY: Solid, purity not reported. IMPURITY/ADDITIVE/ETC.: Not reported. ANY OTHER INFORMATION: Not reported.

Reliability	:	(4) not assignable The information is taken from a secondary literature source. The article by Johnson was published in 1987, while the original article was published in 1972.
13.06.2002		(39)
Species	:	Rabbit
Concentration	:	.5 g
Exposure	:	Occlusive
Exposure time	:	24 hour(s)
Number of animals	:	6
Vehicle	:	other: solid
PDII	:	
Result	:	not irritating
Classification	:	
Method	:	other
Year	:	1972
GLP	:	No
Test substance	:	other TS: sodium bicarbonate
Method	:	METHOD FOLLOWED: Not reported. GLP: No, the study was perfomed before the GLP standard was established. STATISTICAL METHODS: Not reported. METHOD OF CALCULATION: Not reported. ANALYTICAL METHODS: Not reported.
Result	:	AVERAGE SCORE - Erythema: Not reported. - Edema: Not reported. REVERSIBILITY: Not reported. OTHER EFFECTS: Not reported. No skin lesions were observed.
Test condition	:	TEST ANIMALS:Rabbit. - Strain: Albino. - Sex: Not reported. - Source: Not reported. - Age: Not reported. - Weight at study initiation: Not reported. - Number of animals: 6 - Controls: Not reported. ADMINISTRATION/EXPOSURE - Preparation of test substance: Not reported. - Area of exposure: Abraded and non-abraded clipped skin on the back. - Occlusion: Yes. - Vehicle: Not reported. - Concentration in vehicle: Not reported. - Total volume applied: 0.5 g of test substance was applied. - Postexposure period: Observation for 48 hrs after removing the patch. - Removal of test substance: After 24 hrs exposure. EXAMINATIONS - Scoring system: Not reported. - Examination time points: Not reported.
Test substance	:	SOURCE: Not reported. PURITY: Solid, purity not reported. IMPURITY/ADDITIVE/ETC.:Not reported. ANY OTHER INFORMATION: Not reported.
Reliability	:	(4) not assignable The information is taken from a secondary literature source. The article by Johnson was published in 1987, while the original article was published in 1972.
13.06.2002		(39)

5.2.2 EYE IRRITATION

Species	:	Rabbit
Concentration	:	.1 g
Dose	:	.1 other: g
Exposure time	:	
Comment	:	other: eyes were irrigated 20-30 seconds after instillation, or not at all during the test period.
Number of animals	:	9
Vehicle	:	None
Result	:	slightly irritating
Classification	:	
Method	:	other: EPA/TSCA guidelines 40 CFR 798.4500
Year	:	1992
GLP	:	Yes
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	METHOD FOLLOWED: EPA/TSCA guidelines 40 CFR 798.4500. DEVIATIONS FROM GUIDELINE: Not reported. GLP: Yes. STATISTICAL METHODS: Not reported. METHOD OF CALCULATION: Not reported. ANALYTICAL METHODS: Not reported.
Result	:	AVERAGE SCORE - Cornea: 0/6 (unwashed eye) and 0/3 (washed eye) at all evaluations. - Iris: Unwashed eyes: 1 hr, 1/6; 24 hrs, 0/6; 48 hrs, 0/6; 72 hrs 0/6; 4 days, 0/6. Washed eyes: 1 hr, 1/3; 24 hrs, 0/3; 48 hrs, 0/3; 72 hrs 0/3; 4 days, 0/3. - Conjuntivae (Redness): According to the applied assessment system, conjunctivae consists of hyperaemia, chemosis and discharge. Unwashed eyes: 1 hr, 6/6; 24 hrs, 6/6 ; 48 hrs, 6/6; 72 hrs 1/6; 4 days, 0/6. Washed eyes: 1 hr, 3/3; 24 hrs, 2/3; 48 hrs, 1/3; 72 hrs 0/3; 4 days, 0/3. - Conjuntivae (Chemosis): See above. - Overall irritation score: The 24 hour Maximum Mean Total Score (MMTS) for the washed eyes was 2.0 (practically non-irritating). The 24 hour Maximum Mean Total Score (MMTS) for the unwashed eyes was 8.3 (minimally irritating). The authors classified the substance as practically non-irritating to the washed eye and minimally irritating to the unwashed eye. DESCRIPTION OF LESIONS: No corneal opacity was noted during the study. One washed and one unwashed eye exhibited iritis one hour after installation only. All treated eyes had conjunctivitis. The incidence and severity of irritation decreased with time. All ocular irritation cleared from the washed and unwashed eyes by days 3 and 4, respectively. REVERSIBILITY: The effects were fully reversible. OTHER EFFECTS: Not reported.
Test condition	:	TEST ANIMALS: Rabbit. - Strain: New Zealand Albino. - Sex: 4 males and 5 females. - Source: Davidson's Mill Farm, South Brunswick, NJ. - Age: Not reported. - Weight at study initiation: Not reported. - Number of animals: 9. - Controls: The left eye of each rabbit remained untreated and served as control. ADMINISTRATION/EXPOSURE - Preparation of test substance: The test substance was instilled undiluted. - Amount of substance instilled: 0.1 gram. - Vehicle: None. - Postexposure period: The treated eyes of the rabbits were irrigated with 30 ml of physiological saline approximately 20-30 seconds after installation

of the test substance. The eyes of the remaining six rabbits were not irrigated. The rabbits were observed for four days.
EXAMINATIONS
- Ophtalmoscopic examination: the incidence of irritation was evaluated by corneal opacity, iritis and conjunctival irritation.
- Scoring system:Ocular lesions were evaluated by the method of Draize et al. The eye scores were further classified by the system of Kay and Calandra, modified.
- Observation period: Ocular lesions were evaluated at 1, 24, 48 and 72 hrs and at 4 days post-installation.
- Tool used to assess score: Not reported.

Test substance : SOURCE: Not reported.
PURITY: > 99.5%
IMPURITY/ADDITIVE/ETC.: Not reported.
ANY OTHER INFORMATION: Not reported.

Reliability : (1) valid without restriction
Guideline study.

14.05.2002 (79)

Species : Rabbit
Concentration : 100 other: % w/v
Dose : .1 ml
Exposure time :
Comment : Other
Number of animals : 12
Vehicle : None
Result : Irritating
Classification :
Method : other
Year : 1982
GLP : No
Test substance : other TS: sodium bicarbonate
Method : METHOD FOLLOWED: Not reported.
GLP: No, research was executed before the existence of GLP.
STATISTICAL METHODS: Not reported.
METHOD OF CALCULATION: Not reported.
ANALYTICAL METHODS: Not reported.

Remark : The article is published in 1982, while the studies were performed in 1973 and 1974.

Result : AVERAGE SCORE
- Cornea: Not reported.
- Iris: Not reported.
- Conjuntivae (Redness): Not reported.
- Conjuntivae (Chemosis): Not reported.
- Overall irritation score: Not reported.

DESCRIPTION OF LESIONS:
NaHCO3 produced conjunctivitis which lasted th rough day 7 in all animals tested. There was no corneal opacity.
REVERSIBILITY: Conjuntivitis lasted the entire test period, 7 days.
OTHER EFFECTS: Not reported.

Test condition : TEST ANIMALS: Rabbit.
- Strain: New Zealand albino.
- Sex: Both.
- Source: Zartman Frams, PA, USA.
- Age: Not reported.
- Weight at study initiation: 2-2.5 kg.
- Number of animals: 12, 2 groups of 6 in each.
- Controls: The left eye was used as control.

ADMINISTRATION/EXPOSURE
Amount of substance instilled: The equivalent of 0.1 ml solid. Equivalent of

0.1 ml solid NaHCO3 was applied to the right eye. The eyes of the animals in one group were not rinsed after treatment; in the other group, the treated eye was washed for 2 minutes with tap water, starting 30 sec after instillation of NaHCO3.
- Vehicle: None.
- Postexposure period: No.
EXAMINATIONS
- Ophtalmoscopic examination: The animals were observed for lesions, which were graded at 1 hr and day 1, 2, 3 and 7 after instillation. Gross examination.
- Scoring system: based on Draize, 1= severe, 2=moderate, 3=irritant, 4=non-irritant.
- Observation period: 7 days.
- Tools used to assess score: Not reported.

Test substance : SOURCE: Not reported.
PURITY:Not reported.
IMPURITY/ADDITIVE/ETC.:Not reported.
ANY OTHER INFORMATION: Not reported.

Reliability : (2) valid with restrictions
Comparable to guideline study with acceptable restrictions.

07.01.2003 (56)

Species : Rabbit
Concentration : .1 other:molar
Dose : 11 other: ml/hr
Exposure time : 3 hour(s)
Comment :
Number of animals : 2
Vehicle : other: phosphate buffered saline.
Result : not irritating
Classification :
Method : other
Year : 1967
GLP : No
Test substance : other TS: sodium bicarbonate
Method : METHOD FOLLOWED: Not reported.
GLP: No, research was executed before the existence of GLP.
STATISTICAL METHODS: Not reported.
METHOD OF CALCULATION: Not reported.
ANALYTICAL METHODS: Not reported.

Result : AVERAGE SCORE
- Cornea: Not reported.
- Iris: Not reported.
- Conjuntivae (Redness): Not reported.
- Conjuntivae (Chemosis): Not reported.
- Overall irritation score: Not reported.

DESCRIPTION OF LESIONS:
None.
REVERSIBILITY: Not reported.
OTHER EFFECTS: NaHCO3 did not cause any lesions.

Test condition : TEST ANIMALS: Rabbit
- Strain: New Zealand white.
- Sex: Not reported.
- Source: NIH production center.
- Age: Not reported.
- Weight at study initiation: Approximately 2 kg.
- Number of animals: 2.
- Controls: Not reported.

ADMINISTRATION/EXPOSURE
- Preparation of test substance: Adjusted to approach osmolar

concentration of 0.46, optimal for corneal tissue.
- Amount of substance instilled: the eye was irrigated with 0.1M of the test solution continously for 3 hours, at at least 11 ml/hr. The pH was adjusted to 7.0-7.5 to avoid pH-related lesions.
- Vehicle: Not reported.
- Postexposure period: No.
EXAMINATIONS
- Ophtalmoscopic examination: eyes were fixed, embedded in paraffin and sections were cut and stained for microscopic examination.
- Scoring system: loss of corneal transparency +/-
- Observation period: No.
- Tool used to assess score: Not reported.
DESCRIPTION OF LESIONS:
NaHCO3 did not induce lesions.

Test substance : SOURCE: Not reported.
PURITY: Not reported.
IMPURITY/ADDITIVE/ETC.:Not reported.
ANY OTHER INFORMATION: Not reported.

Reliability : (3) invalid
There were relevant methodological deficiencies. The study was performed on rabbit cornea to replace the use of rabbit gingival (gum) tests. The scoring system was extremely poor, only "lesions" were registered as adverse effects. The cornea of rabbits was irrigated with a NaHCO3 for only 3 hours, and there was no post-exposure observation period.

14.05.2002 (62)

Species : Rabbit
Concentration :
Dose : .09 other: grams
Exposure time :
Comment :
Number of animals : 6
Vehicle : other:solid
Result : not irritating
Classification :
Method : other
Year : 1972
GLP : no
Test substance : other TS: sodium bicarbonate
Method : METHOD FOLLOWED: Draize' method of ocular irritation scoring.
DEVIATIONS FROM GUIDELINE: Not reported.
GLP: No, the study was executed before the existence of GLP standard.
STATISTICAL METHODS: Not reported.
METHOD OF CALCULATION: Not reported.
ANALYTICAL METHODS: Not reported.

Result : AVERAGE SCORE
- Cornea: Not reported.
- Iris: Not reported.
- Conjuntivae (Redness): One animal had slight conjunctival redness at 48 hrs post instillation, three animals had slight conjunctival redness at 48 and 72 hrs, and 2 animals had slight conjunctival redness at 24, 48, and 72 hrs.
- Conjuntivae (Chemosis): one of the two animals with redness also had slight conjunctival chemosis and discharge at 24 hrs.
- Overall irritation score: Not irritating.
DESCRIPTION OF LESIONS: See average score.
REVERSIBILITY: Not reported.
OTHER EFFECTS: Not reported.

Test condition : EXAMINATIONS
- Ophtalmoscopic examination: corneal opacity
- Scoring system: Ocular irritation was scored according to the scale by

Draize.
- Observation period: 3 days
TEST ANIMALS: Albino rabbit.
- Strain: Not reported.
- Sex: Not reported.
- Source: Not reported.
- Age: Not reported.
- Weight at study initiation: Not reported.
- Number of animals: 6
- Controls: The left eye served as control.
ADMINISTRATION/EXPOSURE
- Preparation of test substance: Not reported.
- Amount of substance instilled: 0.086 g into one eye.
- Vehicle: None.
- Postexposure period: Treated and control eyes were examined every 24 hrs for a period of 3 days.
EXAMINATIONS
- Ophtalmoscopic examination: Ocular irritation was evaluated.
- Scoring system: Irritation was scored according to the scale of Draize.
- Observation period: Three days.
- Tool used to assess score: Not reported.

Test substance : SOURCE: Not reported.
PURITY: Not reported.
IMPURITY/ADDITIVE/ETC.:Not reported.
ANY OTHER INFORMATION: Not reported.

Reliability : (4) not assignable
The information is taken from a secondary literature source.
The article by Johnson was published in 1987, while the original article was published in 1972.

14.05.2002 (39)

Species : Rabbit
Concentration :
Dose : .1 ml
Exposure time :
Comment :
Number of animals : 6
Vehicle : no data
Result : not irritating
Classification :
Method : other
Year :
GLP : No
Test substance : other TS: sodium bicarbonate
Method : METHOD FOLLOWED: Not reported.
DEVIATIONS FROM GUIDELINE: Not reported.
GLP: No, the study was performed before the existance of GLP standard.
STATISTICAL METHODS:Not reported.
METHOD OF CALCULATION: Not reported.
ANALYTICAL METHODS: Not reported.

Result : AVERAGE SCORE
- Cornea: Not reported.
- Iris: Not reported.
- Conjuntivae (Redness): Not reported.
- Conjuntivae (Chemosis): Not reported.
- Overall irritation score: Not reported.
DESCRIPTION OF LESIONS: No ocular lesions were observed.
REVERSIBILITY: Not reported.
OTHER EFFECTS: Not reported.
The test substance did not induce ocular irritation in any of the rabbits.

Test condition	:	TEST ANIMALS: Albino rabbit. - Strain: Not reported. - Sex: Not reported. - Source: Not reported. - Age: Not reported. - Weight at study initiation:Not reported. - Number of animals: 6 - Controls: One eye served as control. ADMINISTRATION/EXPOSURE - Preparation of test substance: Not reported. - Amount of substance instilled: 0.1 ml into one eye. - Vehicle: Not reported. - Postexposure period: 7 days. EXAMINATIONS - Ophtalmoscopic examination: The rabbits were observed for signs of eye irritation. - Scoring system: Not reported. - Observation period: 7 days. - Tool used to assess score: Not reported.
Test substance	:	SOURCE: Not reported. PURITY: Not reported. IMPURITY/ADDITIVE/ETC.:Not reported. ANY OTHER INFORMATION: Not reported.
Reliability	:	(4) not assignable The information is taken from a secondary literature source. The article by Johnson was published in 1987, while the original article was published in 1972.

14.05.2002 (39)

5.3 SENSITIZATION

5.4 REPEATED DOSE TOXICITY

Type	:	
Species	:	cattle
Sex	:	female
Strain	:	other: Jersey and Holstein
Route of admin.	:	oral feed
Exposure period	:	2 weeks after 1 wk adjustment and 1 wk adaptation
Frequency of treatm.	:	twice daily
Post exposure period	:	
Doses	:	basal feed plus 1.7% NaHCO3
Control group	:	yes
Method	:	
Year	:	1984
GLP	:	no
Test substance	:	other TS: sodium bicarbonate
Method	:	METHOD FOLLOWED: Not reported. DEVIATIONS FROM GUIDELINE: Not reported. GLP: Not reported. STATISTICAL METHODS:Not reported. METHOD OF CALCULATION: Not reported. ANALYTICAL METHODS:Not reported.
Remark	:	Animal were living in hot weather conditions, with depression of feed intake. Inclusion of NaHCO3 under these conditions increased feed intake, but because of group feeding procedures, little precision was possible in a statistical test for these large differences.

Addition of NaHCO3 adds both an anion and a cation, so their effects are confounded. This addition resulted in greater respiration rate and body temperature, higher urine pH, increased blood glucose, higher blood potassium, lower blood gases (except for pO2), lower base excess, and higher percentages of protein and total solids in milk. The authors feel that the large effect on feed intake was real and is important for sustaining milk production during high ambient temperatures.

Test substance : SOURCE: Not reported.
PURITY: Not reported.
IMPURITY/ADDITIVE/ETC.:Not reported.
ANY OTHER INFORMATION: Not reported.

Reliability : (4) not assignable
The original reference of this data was not available, as the text was prepared in the previous IUCLID update.

14.05.2002 (64)

Type	:	
Species	:	cattle
Sex	:	female
Strain	:	other: Holstein
Route of admin.	:	other: intraruminal
Exposure period	:	no data
Frequency of treatm.	:	twice daily 2 to 4 hrs post feeding
Post exposure period	:	
Doses	:	0, 29, 57.9, 86.8 g/l
Control group	:	yes
Method	:	
Year	:	1993
GLP	:	no data
Test substance	:	other TS: sodium bicarbonate

Method : METHOD FOLLOWED: Not reported.
GLP: Not reported.
STATISTICAL METHODS: linear model ANOVA for sampling times for ruminal values; DMI (dry matter intake), milk production and milk composition were evaluated for wk 2. Cow, period, treatment and residual errors were included in the model. Contrasts were employed to evaluate linear, quadratic and cubic effects of the quantity of NaHCO3 infused.
METHOD OF CALCULATION: Not reported.
ANALYTICAL METHODS: Not reported.

Result : LOAEL: 29 g/l.

The intention with the study was to examine the mechanisms by which the dietary buffers widely used in livestock production excert their effect.
Specifically the influence of ruminal infusion of various amount of NaHCO3 on ruminal and systemic acid-base status and mineral metabolism. Infusion of buffer increased ruminal fluid buffering capacity transiently at 4.5 hrs post-feeding but otherwise did not markedly affect ruminal acid-base status.
Systemic acid-base status was unaffected by the buffer primarily because renal excretion of base successfully reduced systemic base load.
Urine volume increased in response to NaHCO3 infusion.
Buffer infusion increased urinary excretion of Na, Mg, and K but decreased Ca excretion for 12 hrs post feeding; Cl excretion was not affected.
Buffer infusion tended to increase total volatile fatty acids in ruminal fluid.
The authors' data indicate that homeostatic mechanisms can eliminate exogenous base via the kidneys; hence, acid-base status was not perturbed by infusion of NaHCO3.
The authors further claim that increased excretion of Mg and K with buffer infusion indicates that the dietary requirements for these minerals may be increased by NaHCO3.
The diuresis accompanying large doses of NaHCO3 may increase dietary

requirements for some minerals. There was little effects on milk production or composition.

Test condition : TEST ORGANISMS
- Age: Pluriparious, age not specified.
- Weight at study initiation: Not reported.
- Number of animals: 4

ADMINISTRATION / EXPOSURE
- Duration of test/exposure: 2 weeks.
- Type of exposure: Ruminal infusion.
- Post exposure period: Not reported.
- Vehicle: Water.
- Concentration in vehicle: 0, 29, 57.9, 86.8 g/l. 3.8 l in total was dosed 2 times daily.

SATELLITE GROUPS AND REASONS THEY WERE ADDED: None.

CLINICAL OBSERVATIONS AND FREQUENCY:
- Clinical signs: Not reported.
- Mortality: Not reported.
- Body weight: Not reported.
- Food consumption: Dry matter index (DMI) kg/d was registered once every week.The cattle was allowed to feed for two hours two times per 24 hours, at 03.00 and 15.00.
- Water consumption: Not reported.
- Haematology: blood was collected via the jugular vein, 7 ml every 30 min. after feeding for 12 hrs in total. It was analysed for pH, pO2, pCO2; plasma creatinine, Cl, Na, K, Ca and Mg.
- Biochemistry: Not reported.
- Urinalysis: Parameters were measured every day at feeding and every 30 min thereafter for 12 hrs: total urine volume, Ca, Mg, Ca, K, pH.

ORGANS EXAMINED AT NECROPSY (MACROSCOPIC AND MICROSCOPIC):
- Macroscopic: Not performed.
- Microscopic: Not performed.

OTHER EXAMINATIONS: analysis of ruminal fluid pH, Cl, Ca, Mg, Na and K was measured every day at feeding and every 30 min thereafter for 12 hrs. Milk production was also monitored, and samples were analysed once per week for protein and fat content.

STATISTICAL METHODS: linear model ANOVA for sampling times for ruminal values; DMI (dry matter intake), milk production and milk composition were evaluated for wk 2. Cow, period, treatment and residual errors were included in the model. Contrasts were employed to evaluate linear, quadratic and cubic effects of the quantity of $NaHCO_3$ infused.

Test substance : SOURCE: Not reported.
PURITY: Not reported.
IMPURITY/ADDITIVE/ETC.:Not reported.
ANY OTHER INFORMATION: Not reported.

Reliability : (3) invalid
Unsuitable and not relevant test system. The study was perfomed to assess the buffer mechanisms of $NaHCO_3$ in cattle, and was not intended to cause adverse effects. The use of cattle is not common in toxicity tests, and little is known about adverse effects of test substances in comparison to humans or other more widely used test animals like the rat

14.05.2002 (71)

Type :
Species : other: chicken
Sex : no data
Strain : no data
Route of admin. : drinking water
Exposure period : 5-6 days
Frequency of treatm. : continously

Post exposure period	:	up to 1 week observation
Doses	:	0, 0.6%, 1.2%, 2.0%, 2.4% in water
Control group	:	yes
LOAEL	:	= .6 %
Method	:	other
Year	:	1936
GLP	:	no
Test substance	:	other TS: sodium bicarbonate
Method	:	METHOD FOLLOWED: Not reported. DEVIATIONS FROM GUIDELINE: The study was performed before the existence of OECD guidelines. GLP: The study was perfomed before the existence of GLP. STATISTICAL METHODS: Not reported. METHOD OF CALCULATION: Not reported. ANALYTICAL METHODS: Not reported.
Result	:	LOAEL chickens: 0.6% in water LOAEL cockerels: 2.4% in water 0.6% sodium bicarbonate given in the drinking water caused chickens to drink more water than normal and produced moist droppings. Chickens 2 weeks old developed pale and small and kidneys from this dosage, but chickens three weeks old and older were not noticeably injured. 1.2% of sodium carbonate caused chickens to drink more water than those fed the 0.6% solution. Chickens 2 -8 weeks old was seriously injured by this dosage within 1-3 days and deaths occurred within this time. 2.4% solution reduced water consumption below normal for chickens under 4 weeks of age. The injurious effects of this dosage were noted within a day and deaths occurred within 3 days. Mature cockerels were injured with a 2.4% solution, but were not affected by a 1.2% solution. It was apparent that the younger the chickens the more susceptible they were to injury. Kidneys from chickens affected by feeding of sodium bicarbonate became pale, swollen and engorged with urates. The kidney tubules showed degenerative and exudative changes indicating severe injury. Chickens affected by feeding of sodium bicarbonate showed an increased in kidney weight, and increase of approximately four times in uric acid per gram of kidney and in uric acid in the blood.
Test condition	:	TEST ORGANISMS - Age: Test 1, 2 weeks. Test 2, 3 weeks. Test 3, 3 or 8 weeks. Test 4, 4 weeks. Test 5, app. 1 year. Test 6, 6-8 weeks. - Weight at study initiation: Not reported. - Number of animals: Three groups of 22 in test 1. Four groups of unknown size in test 2. Six groups of unknown size in test 3. 15 chickens in test 4. Two groups of 3 cockerels in test 5. Six chickens in test 6. ADMINISTRATION / EXPOSURE - Duration of test/exposure: 1-11 days in test 1. 6 days in test 2. Not reported for test 3. Three days in test 4. Five days for test 5. At least four days in test 6. - Type of exposure: NaHCO3 dissolved in drinking water. - Post exposure period: In test 1 and 2, surviving chickens were observed for several days after the exposure ended. - Vehicle: Water. - Concentration in vehicle: Test 1, 0.6% or 1.2%. Test 2, 0.6%, 1.2% or 2%. Test 3, 2%. Test 4, 1.2%. Test 5, 1.2% or 2.4%. Test 6, 2%. SATELLITE GROUPS AND REASONS THEY WERE ADDED: Not

reported.
CLINICAL OBSERVATIONS AND FREQUENCY:
- Clinical signs: General well being and activity checked daily.
- Mortality: Daily.
- Body weight: Not reported.
- Food consumption: Not reported.
- Water consumption: Reported for test 1 and 2.
- Ophthalmoscopic examination: Not reported.
- Haematology: Mg. uric acid in the blood was measured in test 3, after sacrifice.
- Biochemistry: Not reported.
- Urinalysis: Chickens have a cloaca, i.e. the urine and faeces are excreted in a single dropping.

ORGANS EXAMINED AT NECROPSY (MACROSCOPIC AND MICROSCOPIC):
- Macroscopic: Kidneys.
- Microscopic: Kidneys.

OTHER EXAMINATIONS: The concentration (in mg/g kidney) of uric acid deposited in the kidneys of chick in test 3 was registered.
STATISTICAL METHODS: Not reported.

Test substance : SOURCE: Not reported.
PURITY: Not reported.
IMPURITY/ADDITIVE/ETC.:Not reported.
ANY OTHER INFORMATION: Not reported.

Reliability : (3) invalid
The documentation is insufficient for assessment, as little information is given on individual animals, clinical data, etc. The doses are very high, and it is unsure whether the results give an accurate picture of the exposure effects at a lower, more realistic, dose level.

14.05.2002 (76)

Type	:	
Species	:	other: chicken
Sex	:	no data
Strain	:	Leghorn
Route of admin.	:	drinking water
Exposure period	:	75 days
Frequency of treatm.	:	continously
Post exposure period	:	no data
Doses	:	0.5% in feed
Control group	:	yes
LOAEL	:	= .5 %
Method	:	other
Year	:	1981
GLP	:	no
Test substance	:	other TS: sodium bicarbonate

Method : METHOD FOLLOWED: Not reported.
DEVIATIONS FROM GUIDELINE: Not reported.
GLP: The study was perfomed before the existence of GLP.
STATISTICAL METHODS: Not reported.
METHOD OF CALCULATION: Not reported.
ANALYTICAL METHODS: Not reported.

Result : NOAEL (NOEL), LOAEL (LOEL): 0.5% in feed.
ACTUAL DOSE RECEIVED BY DOSE LEVEL BY SEX
- Time of death: No mortality.
- Number of deaths at each dose: No mortality.

TOXIC RESPONSE/EFFECTS BY DOSE LEVEL:
- Mortality and time to death: No mortality.
- Clinical signs: Not reported.
- Body weight gain: Not reported.

- Food/water consumption: Not reported.
- Ophthalmoscopic examination: Not reported.
- Clinical chemistry: Not reported.
- Haematology: A gradual rise in total protein (significant on day 45 of exposure), nonprotein nitrogen and uric acid (both significant on day 15 of exposure) in comparison to the control group was reported.
- Urinalysis: The animals had exsessive watery droppings following NaHCO3 exposure.
- Organ weights:Not reported.
- Gross pathology: Not reported.
- Histopathology: Not reported.
- Other: Not reported.

STATISTICAL RESULTS: Not reported.

Test condition : TEST ORGANISMS Leghorn chickens.
- Age: Not reported.
- Weight at study initiation: Not reported.
- Number of animals: 10 in the exposed group and 10 in the control group.

ADMINISTRATION / EXPOSURE
- Duration of test/exposure: 75 days.
- Type of exposure: Oral.
- Post exposure period: Not reported.
- Vehicle: Feed.
- Concentration in vehicle: 0.5%
- Total volume applied: Not reported.
- Doses: Not reported.

SATELLITE GROUPS AND REASONS THEY WERE ADDED: Not reported.

CLINICAL OBSERVATIONS AND FREQUENCY:
- Clinical signs: Not reported.
- Mortality: Not reported.
- Body weight: Not reported.
- Food consumption: Not reported.
- Water consumption: Not reported.
- Ophthalmoscopic examination: Not reported.
- Haematology: Blood samples were drawn every 15 days and pooled samples were analysed for total protein, nonprotein nitrogen and uric acid.
- Biochemistry: Not reported.
- Urinalysis: Not reported.

ORGANS EXAMINED AT NECROPSY (MACROSCOPIC AND MICROSCOPIC):
- Macroscopic: Not reported.
- Microscopic: Not reported.

OTHER EXAMINATIONS: Not reported.

STATISTICAL METHODS: Not reported.

Test substance : SOURCE: Not reported.

PURITY: Not reported.

IMPURITY/ADDITIVE/ETC.:Not reported.

ANY OTHER INFORMATION: Not reported.

Reliability : (4) not assignable

This information is from a secondary source. The article of Johnson was published in 1987, while the original was published in 1981.

13.06.2002 (39)

Type :
Species : Pig
Sex : male/female
Strain : other: crossbred Yorkshire x Hampshire x Duroc
Route of admin. : oral feed
Exposure period : Unknown
Frequency of treatm. : Continously

Post exposure period	:	
Doses	:	0 and 1% sodium bicarbonate in feed. (App. 30 g/d.)
Control group	:	Yes
LOAEL	:	= 1 %
Method	:	
Year	:	1993
GLP	:	no data
Test substance	:	other TS: sodium bicarbonate
Method	:	METHOD FOLLOWED: Not reported. GLP: Not reported. STATISTICAL METHODS:Not reported. METHOD OF CALCULATION: Not reported. ANALYTICAL METHODS: Not reported.
Result	:	LOAEL: 1% NaHCO3 in feed, ca. 30 g/d. Stomachs of pigs in trial 1 were evaluated for ulceration and severity of ulceration. The scoring system range runs from 1-4 with 1=normal, 2=cornification, 3=erosion and 4=ulcer. Sodium bicarbonate decreased (P< .01) dressing percentage but increased (P<.06) the incidence of gastric ulceration. The ulcer scores were: 1.9 for control and 3.0 for NaHCO3 treated animals. Dietary Cu increased (P<.01) liver Cu concentrations and this response was not significantly affected (P>.10) by dietary sodium bicarbonate.
Test condition	:	TEST ORGANISMS - Age: Not reported. - Weight at study initiation: The average in trial 1: 57 kg (finishing pigs). The average in trial 2: 32 kg (growing pigs). - Number of animals: 112 in total. Each treatment was replicated 4 (trial 1) or 3 (trial 2) times with four pigs per replicate. ADMINISTRATION / EXPOSURE - Duration of test/exposure: Not reported. - Type of exposure: Oral in feed. - Post exposure period: No. - Vehicle: Feed. - Concentration in vehicle: 1% NaHCO3 and/or 250 mg/kg Cu. - Doses: Pigs received a basal diet B (diet 1), B + 250 mg/kg Cu (diet 2), B + 1% sodium bicarbonate (diet 3) or B + 250 mg/kg Cu + 1% sodium bicarbonate (diet 4). SATELLITE GROUPS AND REASONS THEY WERE ADDED: Not reported. CLINICAL OBSERVATIONS AND FREQUENCY: - Clinical signs: Not reported. - Mortality: None. - Body weight: determined at the initiation and termination of the treatment. - Food consumption: Registered daily. - Water consumption: Not reported. - Ophthalmoscopic examination: Not reported. - Haematology: Not reported. - Biochemistry: A liver sample was taken for Cu analysis, microgram/g dry tissue. - Urinalysis: Not reported. ORGANS EXAMINED AT NECROPSY (MACROSCOPIC AND MICROSCOPIC): - Macroscopic: Stomachs were examined for ulceration in trial 1. - Microscopic: Stomach, liver. OTHER EXAMINATIONS: Not reported. STATISTICAL METHODS: Data from trial 1 and 2 were pooled. Data was analysed by "analysis of variance procedures" not further defined. Treatment variances for the liver Cu data were Log transformed (ln[y+1]) for statistical analysis. The gastric ulcer data were square-root transformed for

statistical analysis.

The experiment was conducted with growing-finishing pigs to evaluate the interactive effects of dietary sodium bicarbonate (1%) and excess dietary Cu (250 mg/kg diet) on growth, liver Cu accumulation and incidence of gastric ulceration. Each treatment was replicated 4 (trial 1) or 3 (trial 2) times with 4 pigs per replicate. At termination, 2 of each replicate in trial 1 and all pigs in trial 2 were killed. There is no information regarding the duration of the trials.

Test substance : SOURCE: Not reported.
PURITY: Not reported.
IMPURITY/ADDITIVE/ETC.:Not reported.
ANY OTHER INFORMATION: Not reported.

Reliability : (3) invalid
Unsuitable testing system. The experiment was conducted with growing-finishing pigs to evaluate the interactive effects of dietary sodium bicarbonate (1%) and excess dietary Cu (250 mg/kg diet) on growth, liver Cu accumulation and incidence of gastric ulceration. The dose is high and the use of pig as a test animal difficult to compare to the results of studies done on recommended test animals.

14.05.2002 (67)

5.5 GENETIC TOXICITY 'IN VITRO'

Type : Ames test
System of testing : TA 92, 94, 98, 100, 1535, 1537
Test concentration : max. 10 mg/plate
Cycotoxic concentr. : not reported
Metabolic activation : With
Result : Negative
Method : other: Ames; McCann and Yamasaki, 1975
Year : 1984
GLP : No
Test substance : other TS: sodium bicarbonate
Method : METHOD FOLLOWED: Ames.
GLP: No, the study was performed before the existence of GLP standard.
STATISTICAL METHODS: Not reported.
METHOD OF CALCULATION: Not reported.
ANALYTICAL METHODS: Not reported.
Result : GENOTOXIC EFFECTS:
- With metabolic activation: Negative.
- Without metabolic activation: Not performed.
PRECIPITATION CONCENTRATION: Not reported.
FREQUENCY OF EFFECTS: Not reported.
CYTOTOXIC CONCENTRATION:
- With metabolic activation:10 mg/plate.
- Without metabolic activation: Not performed.
TEST-SPECIFIC CONFOUNDING FACTORS: Not reported.
STATISTICAL RESULTS: Not reported.
Test condition : SYSTEM OF TESTING
- Species/cell type: S. typhimurium, TA 92, 94, 98, 100, 1535, 1537.
- Deficiences/Proficiences: his+
- Metabolic activation system: S9 mix, from livers of Fischer rats pretreated 5 days with polychlorinated biphenyls.
- Solvent: Phosphate buffer.
ADMINISTRATION:
- Dosing: max. 10 mg/plate, six doses. The remaining dose concentrations are unknown.

- Number of replicates: 2.
- Application: Not reported.
- Positive and negative control groups and treatment: The negative control groups were exposed to the solvent (phosphate buffer) or remained untreated. A positive control was not included.
- Pre-incubation time: 20 minutes at 37 degrees C.

DESCRIPTION OF FOLLOW UP REPEAT STUDY: Not reported.
CRITERIA FOR EVALUATING RESULTS: The result was considered positive if the number of colonies were double the number in the control.

Test substance : SOURCE: Samples were supplied by the Japanese Food Additives Association, Tokyo, J.
PURITY: 99.9%
IMPURITY/ADDITIVE/ETC.: Not reported.
ANY OTHER INFORMATION: Not reported.

Reliability : (2) valid with restrictions
Acceptable, well-documented publication which meets basic scientific principles.

07.01.2003 (38)

Type : other: Chromosomal aberration
System of testing : Chinese Hamster fibroblast cell line
Test concentration : max. 1 mg/ml
Cycotoxic concentr. : see below
Metabolic activation : without
Result : negative
Method : other
Year : 1984
GLP : no
Test substance : other TS: sodium bicarbonate
Method : METHOD FOLLOWED: Ishidate and Oshadima, 1977.
GLP: No, the study was performed before the existence of GLP standard.
STATISTICAL METHODS: Not reported.
METHOD OF CALCULATION: Not reported.
ANALYTICAL METHODS: Not reported.
Result : GENOTOXIC EFFECTS:
- With metabolic activation: Not performed.
- Without metabolic activation: Negative, 3% polyploidity, 3% structural aberrations.

FREQUENCY OF EFFECTS: Not reported.
PRECIPITATION CONCENTRATION: Not reported.
MITOTIC INDEX: Not reported.
CYTOTOXIC CONCENTRATION:
- With metabolic activation: Not performed.
- Without metabolic activation: 1 mg/ml caused 50% cell-growth inhibition.

TEST-SPECIFIC CONFOUNDING FACTORS: Not reported.
STATISTICAL RESULTS: Not reported.
Test condition : SYSTEM OF TESTING
- Species/cell type: Chinese hamster fibroblast cells (CHO)
- Deficiences/Proficiences: Not reported.
- Metabolic activation system: Not performed.
- Solvent: Physiological saline.
- No. of metaphases analyzed: 100 per sample.

ADMINISTRATION:
- Dosing: Max. 1 mg/ml. There were three doses in total, the two lower concentrations are not reported. The cells were exposed for 24 and 48 hrs.
- Number of replicates: Not reported.
- Application: Not reported.
- Positive and negative control groups and treatment: The negative control groups were untreated or solvent-treated cells (solvent was physiological saline). A positive control was not included.

- Pre-incubation time: Not reported.
DESCRIPTION OF FOLLOW UP REPEAT STUDY: Not reported.
CRITERIA FOR EVALUATING RESULTS: The results were negative if the incidence of aberrations was less than 4.9%, equivocal if 5.0 -9.9% and positive if more than 10.0%.

Test substance : SOURCE: Samples supplied by the Japanese Food Additives Association, Tokyo, J.
PURITY: 99.9%
IMPURITY/ADDITIVE/ETC.: Not reported.
ANY OTHER INFORMATION: Not reported.

Reliability : (3) invalid
Test conditions not reported in sufficient detail.

07.01.2003 (38)

Type : Ames test
System of testing : *S. typhimurium* TA 98, 100, 1535, 1537, 1538
Test concentration : not reported
Cycotoxic concentr. : not reported
Metabolic activation : with and without
Result : Negative
Method : other: Ames test
Year : 1984
GLP : No
Test substance : other TS: sodium bicarbonate
Method : METHOD FOLLOWED: Ames.
GLP: No, the study was performed before GLP standard existed.
STATISTICAL METHODS: Not reported.
METHOD OF CALCULATION: Not reported.
ANALYTICAL METHODS: The mutagenic potency was expressed by dividing the number of revertants in excess of controls by the corresponding amount of compound.
Result : GENOTOXIC EFFECTS:
- With metabolic activation: Negative.
- Without metabolic activation: Negative.
FREQUENCY OF EFFECTS: Not reported.
PRECIPITATION CONCENTRATION: Not reported.
MITOTIC INDEX: Not reported.
CYTOTOXIC CONCENTRATION:
- With metabolic activation: Not reported.
- Without metabolic activation: Not reported.
TEST-SPECIFIC CONFOUNDING FACTORS: Not reported.
STATISTICAL RESULTS: Not reported.
Test condition : SYSTEM OF TESTING
- Species/cell type: *S. typhimurium* , TA 98, 100, 1535, 1537,1538.
- Proficiencies/Deficiences: his+
- Metabolic activation system: S9 mix, from livers of Sprague-Dawley rats pretreated 5 days with Arochlor.
ADMINISTRATION:
- Dosing: Unknown, it is reported that dilutions ranged up to solubility or toxicity concentration.
- Number of replicates: 2-3.
- Application: Not reported.
- Positive and negative control groups and treatment: Thenegative control groups were exposed to the solvent (phosphate buffer) or untreated.
- Pre-incubation time: 20 minutes at 37 degrees C.
DESCRIPTION OF FOLLOW UP REPEAT STUDY: Not reported.
CRITERIA FOR EVALUATING RESULTS: The criteria for a positive result included a greater than 3-fold increase of induced vs spontaneous revertants.
Test substance : SOURCE: Britisch Chrome and Chem.

PURITY: Not reported.
IMPURITY/ADDITIVE/ETC.: Not reported.
ANY OTHER INFORMATION: Not reported.

Reliability : (3) invalid
Test conditions not reported in sufficient detail.

06.08.2002 (13)

Type : other: DNA-repair test in E. coli
System of testing : *E. coli* WP2, WP67, CM871
Test concentration : 2500 µg without S9, 5000 µg with S9 metabolic activation
Cycotoxic concentr. : The substance was tested up to toxicity or solubility limit.
Metabolic activation : with and without
Result : Negative
Method : other: Kada et al., 1980; McCarroll et al. 1981.
Year : 1984
GLP : No
Test substance : other TS: sodium bicarbonate
Method : METHOD FOLLOWED: Kada et al., 1980; McCarroll et al., 1981.
GLP: No, the study was performed before GLP existed.
STATISTICAL METHODS:
The genotoxic potency was calculated by relating the differences of MICs (minimal inhibitory concentration) in repair-deficient (rep-) and -proficient (rep+) strains to the corresponding nmoles of compound. For negative compounds the potency is 0 when the MICs are overlapping repair-deficient and -proficient bacteria.
METHOD OF CALCULATION: Not reported.
ANALYTICAL METHODS: Not reported.
Result : GENOTOXIC EFFECTS:
- With metabolic activation: Negative.
- Without metabolic activation: Negative.
FREQUENCY OF EFFECTS: Not reported.
PRECIPITATION CONCENTRATION: Not reported.
CYTOTOXIC CONCENTRATION:
- With metabolic activation:The substance was tested up to toxicity or solubility limit.
- Without metabolic activation: The substance was tested up to toxicity or solubility limit.
TEST-SPECIFIC CONFOUNDING FACTORS: Not reported.
STATISTICAL RESULTS: Not reported.
Test condition : SYSTEM OF TESTING
- Species/cell type: *E. coli* WP2, WP67, CM871.
- Deficiences/Proficiences: WP67: uvrA- polA-, CM871: uvrA- recA- lexA-, WP2: uvrA- .
- Metabolic activation system: S9 mix was prepared from livers of Sprague-Dawley rats pretreated 5 days with Arochlor.
- No. of metaphases analyzed: Not performed.
ADMINISTRATION:
- Dosing: The max. concentration with S9 activation was: 5000 µg/well. The max. concentration without S9 activation was: 2500 µg/well. The concentration was selected based on the toxicity or solubility of the compound. The solution was further diluted until 8 concentrations were made, with 6 well/dilution. In repeated assays only 4 solutions were used, based on the results o f the first assay, with 2 wells/ dilution.
- Number of replicates: 2
- Application: bacterial growth was assessed after 16 hrs at 37 degrees C.
- Positive and negative control groups and treatment: The negative control groups were exposed to the solvent (phosphate buffered saline, PBS) or S9 mix.
- Pre-incubation time: Not reported.
DESCRIPTION OF FOLLOW UP REPEAT STUDY: Not reported.

CRITERIA FOR EVALUATING RESULTS: A positive response was indicated by a dose-dependent (at least 3 doses) and reproducible increase in diameter in plates containing repair deficient bacteria, as compared to the repair proficient strain. If no inhibition could be detected even with the max possible concentration, the assay was repeated by pouring 50 µl in wells dug at the centra of agar plates. If no toxicity was observed the result was classified as no test (negative).

Test substance : SOURCE: Britisch Chrome and Chem.
PURITY: Not reported.
IMPURITY/ADDITIVE/ETC.: Not reported.
ANY OTHER INFORMATION: Not reported.

Reliability : (2) valid with restrictions
Acceptable, well-documented publication which meets basic scientific principles.

14.05.2002 (13)

Type : Ames test
System of testing : S. typhimurium TA97, 102
Test concentration : 0, 0.1, 0.5, 1, 5, 10 mg/plate
Cycotoxic concentr. : not reported
Metabolic activation : with and without
Result : Negative
Method : other: Ames test
Year : 1994
GLP : no data
Test substance : other TS: sodium bicarbonate
Method : METHOD FOLLOWED:Ames test.
DEVIATIONS FROM GUIDELINE: Not reported.
GLP: Not reported.
STATISTICAL METHODS:Not reported.
METHOD OF CALCULATION: Not reported.
ANALYTICAL METHODS: Not reported.
Result : GENOTOXIC EFFECTS:
- With metabolic activation: Negative.
- Without metabolic activation: Negative.
FREQUENCY OF EFFECTS: Not reported.
PRECIPITATION CONCENTRATION: Not reported.
CYTOTOXIC CONCENTRATION:
- With metabolic activation: Not reported.
- Without metabolic activation: Not reported.
TEST-SPECIFIC CONFOUNDING FACTORS: Not reported.
STATISTICAL RESULTS: Not reported.
Test condition : SYSTEM OF TESTING
- Species/cell type: *S. typhimirium* TA97, TA102.
- Deficiences/Proficiencies: his -
- Metabolic activation system: S9.
ADMINISTRATION:
- Dosing: 0, 0.1, 0.5, 1, 5, 10 mg/plate.
- Number of replicates: Not reported.
- Application: in distilled water.
- Positive and negative control groups and treatment: The positive controls were 50 µg 9-aminoacridine, 0.5 µg mitomycin C and 5 µg 2 - aminoantracene (all in DMSO). The negative control was distilled water.
- Pre-incubation time: 20 minutes.
DESCRIPTION OF FOLLOW UP REPEAT STUDY: Not reported.
CRITERIA FOR EVALUATING RESULTS: Not reported.
Test substance : SOURCE: Not reported.
PURITY: Not reported.
IMPURITY/ADDITIVE/ETC.:Not reported.
ANY OTHER INFORMATION: Not reported.

Reliability	:	(4) not assignable The article is written in Japanese, with an English abstract and a table with information on dose, the number of revertants per plate for TA97 and TA102, with and without S9-activation and solvent. It is therefore not possible to assess the conditions under which the study was performed.
14.05.2002		(28)
Type	:	Ames test
System of testing	:	*Salmonella typhimurium* TA1535, TA1537, TA1538 and *Saccharomyces cerevisia* D4e
Test concentration	:	
Cycotoxic concentr.	:	
Metabolic activation	:	with and without
Result	:	negative
Method	:	other
Year	:	1974
GLP	:	no
Test substance	:	other TS: sodium bicarbonate
Method	:	METHOD FOLLOWED: Not reported. DEVIATIONS FROM GUIDELINE: Not reported. GLP: The study was perfomed before the existence of GLP. STATISTICAL METHODS: Not reported. METHOD OF CALCULATION: Not reported. ANALYTICAL METHODS: Not reported.
Result	:	The suspension tests and plate tests were negative.
Test substance	:	SOURCE: Not reported. PURITY: Not reported. IMPURITY/ADDITIVE/ETC.:Not reported. ANY OTHER INFORMATION: Not reported.
Reliability	:	(4) not assignable This information is from a secondary source. The article of Johnson was published in 1987, while the original study was performed in 1974.
14.05.2002		(39)

5.6 GENETIC TOXICITY 'IN VIVO'

5.7 CARCINOGENICITY

Species	:	rat
Sex	:	male
Strain	:	Fischer 344
Route of admin.	:	oral feed
Exposure period	:	104 weeks
Frequency of treatm.	:	continously
Post exposure period	:	
Doses	:	2% sodium o-phenylphenol (OPP-Na), 1.25% OPP plus 0.64% $NaHCO_3$, 1.25% OPP plus 0.32% $NaHCO_3$, 1.25% OPP plus 0.16% $NaHCO_3$, 1.25% OPP or 0.64% $NaHCO_3$
Result	:	negative
Control group	:	yes
Method	:	
Year	:	1989
GLP	:	no data
Test substance	:	other TS: sodium bicarbonate
Method	:	METHOD FOLLOWED: Not reported. DEVIATIONS FROM GUIDELINE: Not reported. GLP: Not reported.

STATISTICAL METHODS: Data concerning incidence of lesions were analysed for statistial significance with the two-sided Fischer's exact probability test. Other data were analysed using Student's t-test.
METHOD OF CALCULATION: Not reported.
ANALYTICAL METHODS: Flame photometry for sodium and potassium. Cresolphthalein complexone method for calcium. Chloride meter for chloride. Modification of the phosphomolybdate method for phosphorus. Reaction with Calmagite for magnesium. Liver, kidney and bladder were removed after gross examinati on and fixed in 10% phosphate-buffered formalin solution (pH 6.8) and fixed. Liver and kidneys were weighed before fixation. Bladders were divided sagittaly for histological examination, weighed and each half cut in four strips for histological examination. The bladder, liver and kidneys were embedded in paraffin, sectioned and stained with hematoxylin and eosin. Animals that died during the experiment or became moribund were also autopsied and the bladder processed for histological examination.

Result : The study assessed the carcinogenic potential of OPP-Na and OPP in combination with NaHCO3. NaHCO3 alone did not have a carcinogenic effect on the urinary bladder of rats. Papillary or nodular hyperplasia and papilloma incidence did not differ from the control group incidence.
MORTALITY AND TIME TO DEATH: The percentage of survival in week 104 was: NaHCO3-exposed animals: 84% (26/31); control group: 73% (22/30). Time of death is not reported.
BODY WEIGHT GAIN: The final body weight was significantly lower in all treated groups than in the control group.
URINALYSIS: The urinary Na+ concentrations increased significantly with NaHCO3 exposure, compared to the control group 7. Potassium levels were increased significantly compared to the control group. NaHCO3 exposure also caused significantly elevated urinary pH concentrations.
ORGAN WEIGHTS: The relative weight (organ/body weight %) of kidneys and liver was significantly increased compared to the control.
GROSS PATHOLOGY: NaHCO3-exposed animals did not have a significant increase in the number of tumours, in comparison to the control group.
TIME TO TUMOURS:
The first bladder tumour was found in a rat that died in week 49. It is not known how many rats survived the full experimental period of 104 weeks.

Source : TNO Voeding AJ Zeist

Test condition : TEST ORGANISMS
- Age: 6 weeks.
- Weight at study initiation: Approximately 120 g.
- Number of animals: 216 in total, 31 in group 1-6 and 30 in group 7.

ADMINISTRATION / EXPOSURE
- Duration of test/exposure: 104 weeks.
- Type of exposure: Oral in feed.
- Post exposure period: No.

FOR ORAL STUDIES:
- Vehicle: Feed.
- Concentration in vehicle: Rats were given a diet containing 2% sodium o-phenylphenol (OPP-Na, group 1), 1.25% OPP plus 0.64% NaHCO3 (group 2), 1.25% OPP plus 0.32% NaHCO3 (group 3), 1.25% OPP plus 0.16% NaHCO3 (group 4), 1.25% OPP (group 5), 0.64% NaHCO3 (group 6) or no test substance (control group 7).
- Total volume applied: Not reported.
- Doses: As given above.

CLINICAL OBSERVATIONS AND FREQUENCY
- Body weight: Registered weekly up to week 14 and thereafter monthly for the remainder of the experiment.
- Food consumption: Registered monthly up to week 16, and every 3 months thereafter for the remainder of the experiment.

- Water consumption: Not reported.
- Clinical signs: Not reported.
- Mortality: It is not known how frequently mortality was registered.
- Macroscopic examination: Not reported.
- Ophthalmoscopic examination: Not reported.
- Haematology: Not reported.
- Clinical chemistry: Not reported.
- Urinalysis: Performed in week 58, 80, 96 for determination of sodium, potassium, calcium, chloride, phosphorus, and magnesium concentrations. Performed 10 times during the experiment to measure pH.

ORGANS EXAMINED AT NECROPSY (MACROSCOPIC AND MICROSCOPIC):
- Macroscopic: Liver, kidney and urinary bladder.
- Microscopic: Liver, kidney and urinary bladder.

OTHER EXAMINATIONS: Not reported.
STATISTICAL METHODS: data concerning incidence of lesions were analysed for statistial significance with the two-sided Fischer's exact probability test. Other data were analysed using Student's t-test.

Test substance : SOURCE: Wako Pure Chemical Ind., Osaka, Japan.
PURITY: Food additive grade.
IMPURITY/ADDITIVE/ETC.: Not reported.
ANY OTHER INFORMATION: Not reported.

Reliability : (2) valid with restrictions
Acceptable, well-documented publication which meets basic scientific principles.

08.01.2003 (29)

Species : Rat
Sex : Male
Strain : Fischer 344
Route of admin. : oral feed
Exposure period : 8 weeks
Frequency of treatm. : Continously
Post exposure period :
Doses : 2% sodium o-phenylphenol (OPP-Na), 1.25% OPP plus 0.64% NaHCO3, 1.25% OPP plus 0.32% NaHCO3, 1.25% OPP plus 0.16% NaHCO3, 1.25% OPP or 0.64% NaHCO3
Result : Negative
Control group : Yes
Method :
Year : 1989
GLP : no data
Test substance : other TS: sodium bicarbonate
Method : METHOD FOLLOWED: Not reported.
DEVIATIONS FROM GUIDELINE:Not reported.
GLP: Not reported.
STATISTICAL METHODS: Data concerning incidence of lesions were analysed for statistial significance with the two-sided Fischer's exact probability test. Other data were analysed using Student's t-test.
METHOD OF CALCULATION: Not reported.
ANALYTICAL METHODS: Flame photometry for sodium and potassium. Cresolphthalein complexone method for calcium. Chloride meter for chloride. Modification of the phosphomolybdate method for phosphorus. Reaction with Calmagite for magnesium. The animals were killed in week 8, and the bladder inflated with 2% glutaraldehyde in 0.1M cacodylate buffer (pH 7.4) and then processed for scanning electron microscopic examination.
Result : One group was exposed to 0.64% NaHCO3 alone.
URINALYSIS:
The pH, Na-concentration and urine volume was significantly increased in

the NaHCO3-exposed group, compared to the control. Osmolality decreased significantly in the exposed group.
HISTOPATHOLOGY: The surface of the superficial epithelial cells of the urinary bladder was normal.

Source : TNO Voeding AJ Zeist

Test condition : TEST ORGANISMS
- Age: 6 weeks.
- Weight at study initiation: Not reported.
- Number of animals: 35 in total, divided in seven groups of 5.

ADMINISTRATION / EXPOSURE
- Duration of test/exposure: 8 weeks.
- Type of exposure: Oral in feed.
- Post exposure period: No.

FOR ORAL STUDIES:
- Vehicle: Feed.
- Concentration in vehicle: Rats were given a diet containing 2% sodium o-phenylphenol (OPP-Na, group 1), 1.25% OPP plus 0.64% NaHCO3 (group 2), 1.25% OPP plus 0.32% NaHCO3 (group 3), 1.25% OPP plus 0.16% NaHCO3 (group 4), 1.25% OPP (group 5), 0.64% NaHCO3 (group 6) or no test substance (group 7).
- Total volume applied: Not reported.
- Doses: As above.

CLINICAL OBSERVATIONS AND FREQUENCY
- Body weight: Not reported.
- Food consumption:Not reported.
- Water consumption: Not reported.
- Clinical signs: Not reported.
- Mortality: Not reported.
- Macroscopic examination: Not reported.
- Ophthalmoscopic examination: Not reported.
- Haematology: Not reported.
- Clinical chemistry: Not reported.
- Urinalysis: pH was measured in week 2, 4, 6, 8.

Electrolytes were measured (Na, Na, Ca, Cl, P, Mg) in week 2, 4, 6, 8; and osmolality in week 4 and 8.
ORGANS EXAMINED AT NECROPSY (MACROSCOPIC AND MICROSCOPIC):
- Macroscopic: Urinary bladder.
- Microscopic: Urinary bladder.

STATISTICAL METHODS: Data concerning incidence of lesions were analysed for statistial significance with the two-sided Fischer's exact probability test. Other data were analysed using Student's t-test.

Test substance : SOURCE: Wako Pure Chemical Ind., Osaka, Japan.
PURITY: Food additive grade.
IMPURITY/ADDITIVE/ETC.:Not reported.
ANY OTHER INFORMATION: Not reported.

Reliability : (3) invalid
This study is invalid because the exposure period is only 8 weeks.

08.01.2003 (29)

Species : Rat
Sex : Male
Strain : Fischer 344
Route of admin. : oral feed
Exposure period : 70 days
Frequency of treatm. : Continously
Post exposure period :
Doses : ca. 2240 mg/kg bw/d (2.9% of diet)
Result :
Control group : Yes

Method	:	
Year	:	1995
GLP	:	no data
Test substance	:	other TS:sodium bicarbonate
Method	:	METHOD FOLLOWED: Not reported. DEVIATIONS FROM GUIDELINE: Not reported. GLP: Not reported. STATISTICAL METHODS: comparison of all data collected on body weight, consumption, urinary parameters were performed by the SAS general linear models procedure and Duncan's multiple range test. Labelling indices determined by bromodeoxyuridine were compared by Student's t-test and histologic results were compared using Fischer's exact test. METHOD OF CALCULATION: Not reported. ANALYTICAL METHODS:Not reported.
Result	:	LOAEL: ca. 2240 mg/kg bw/d (2.9% NaHCO3 in feed) ACTUAL DOSE RECEIVED BY DOSE LEVEL BY SEX - Time of death: No mortality. - Number of deaths at each dose: None. TOXIC RESPONSE/EFFECTS BY DOSE LEVEL: - Mortality and time to death: No mortality. - Histopathology: 3/10 rats had simple hyperplasia in the bladder, while kidneys and forestomach were normal. Scanning electron microscopy (SEM) revealed 9/10 animals with severe and 1/10 with less severe changes in the bladder epithelium i.e. proliferation. The increase in bladder weight is assumed to be a secondary effect of the increased concentration of salt (sodium) in the diet causing the rats to drink more water, and resulting in larger urine production. The reduced creatinine concentration corresponded to an increase in urine volume. The increase in pH is likewise a secondary effect of the increase in HCO_3^- in the urine.
Source	:	TNO Voeding AJ Zeist
Test condition	:	TEST ORGANISMS - Age: 5 weeks. - Weight at study initiation: Not reported. - Number of animals: 10 in each group of NaHCO3-exposed and control. ADMINISTRATION / EXPOSURE - Duration of test/exposure: 70 days. - Type of exposure: Oral in feed. - Post exposure period: No. Rats were injected i.p. with 100 mg/kg bw bromodeoxyuridine (BrdU) 1 hr before sacrifice, to assess the uptake due to unusual levels of DNA repair. - Vehicle: Feed. - Concentration in vehicle: 2.9% - Doses: 2240 mg/kg bw/d. (Equimolar to saccharin, the substance to which NaHCO3 was compared.) SATELLITE GROUPS AND REASONS THEY WERE ADDED: Not reported. CLINICAL OBSERVATIONS AND FREQUENCY: - Clinical signs: Not reported. - Mortality: Daily. - Body weight: Rats were weighed on day 0, 7, 14, 28, 42, 56 and 70 of the experiment. - Food consumption: Recorded over 7 day intervals beginning on day 7, 21, 35, 49 and 63. - Water consumption: Recorded over 7 day intervals beginning on day 7, 21, 35, 49 and 63. - Ophthalmoscopic examination: Not performed. - Haematology: Not performed.

- Biochemistry: Not performed.
- Urinalysis: Urine was collected during week 4 and 10 of the experiment. Analysed for ph in week 4 and 10, and volume, creatinine and sodium in week 10.
ORGANS EXAMINED AT NECROPSY (MACROSCOPIC AND MICROSCOPIC):
- Macroscopic: urinary bladder, kidney, forestomach.
- Microscopic: urinary bladder, kidney, forestomach.
OTHER EXAMINATIONS: Not reported.
STATISTICAL METHODS: See "Method".

Test substance : SOURCE: Sigma Chemical Co., St. Louis, MO, USA
PURITY: Not reported.
IMPURITY/ADDITIVE/ETC.:Not reported.
ANY OTHER INFORMATION: Not reported.

Reliability : (3) invalid
This study is invalid because the exposure period is only 70 days.

08.01.2003 (11)

Species : Rat
Sex : Male
Strain : Fischer 344
Route of admin. : oral feed
Exposure period : 32 weeks
Frequency of treatm. : continously
Post exposure period :
Doses : 0, 0.375, 0.75, 1.5, 3% of feed
Result : negative
Control group : yes
Method :
Year : 1988
GLP : no data
Test substance : other TS: sodium bocarbonate
Method : METHOD FOLLOWED: Not reported.
GLP: Not reported.
STATISTICAL METHODS: Data concerning incidences of lesions were analysed for statistical significance with the two-sided Fischer's probability test. Other data were analysed using Student's t test.
METHOD OF CALCULATION: Not reported.
ANALYTICAL METHODS: Flame photometry for sodium and potassium. Crezolphthalein complexone method for calcium. Chloride meter for chloride. Modification of the phosphomolybdate method for phosphorus. Reaction with Calmagite for magnesium. Bladders were inflated by intraluminal injection with 10% phosphate-buffered formalin solution and fixed. Then divided sagittaly, weighed and each half cut in four strips for histological examination.
Urinary bladder lesions were counted by light microscopy.

Result : The incidence of papillary or nodular hyperplasia, papillomas, number of tumours, urinary bladder weight. Urinary pH and Na-concentration increased in rats fed NaHCO3 only if they had been pretreated with BBN. There were no similar results in animals only fed NaHCO3.

Source : TNO Voeding AJ Zeist

Test condition : TEST ORGANISMS
- Age: 6 weeks.
- Weight at study initiation: The mean body weight in exposure groups was: 121-124g +/- 3-6g.
- Number of animals: 220 in total, 20 in group 1-10 and 10 in group 11 and 12.
ADMINISTRATION / EXPOSURE
- Duration of test/exposure: The animals were preexposed to BBN for 4 weeks, and thereafter treated for 32 weeks.

- Type of exposure: Oral in feed.
- Post exposure period: No.
FOR ORAL STUDIES:
- Vehicle: Feed.
- Concentration in vehicle: 0 (control, group 1), 0.375% NaHCO3 (2), 0.75% NaHCO3 (3), 1.5% NaHCO3 (4), 3% NaHCO3 (5), 5% AsA (6), 0.375% NaHCO3 + 5% AsA (7), 0.75% NaHCO3 + 5% AsA (8), 1.5% NaHCO3 + 5% AsA (9), 3% NaHCO3 + 5% AsA (10).
- Total volume applied: Not reported.
- Doses: As indicated in "concentration in vehicle".
CLINICAL OBSERVATIONS AND FREQUENCY
- Body weight: Registered weekly up to week 14, every other week from week 16-36.
- Food consumption: Registered weekly up to week 14, every other week from week 16-36.
- Water consumption: Registered weekly up to week 14, every other week from week 16-36.
- Clinical signs: Not reported.
- Mortality: Not reported.
- Macroscopic examination: Not reported.
- Ophthalmoscopic examination: Not reported.
- Haematology: Not reported.
- Clinical chemistry: Not reported.
- Urinalysis: Performed in week 12, 24, 32, 36. Total ascorbic acid, Na, K, Ca, Cl, P, Mg was analysed.
ORGANS EXAMINED AT NECROPSY (MACROSCOPIC AND MICROSCOPIC):
- Macroscopic: Urinary bladder.
- Microscopic: Urinary bladder.
- OTHER EXAMINATIONS: Not reported.
STATISTICAL METHODS: two-sided Fischer's exact probability test incidence and number of hyperplasia, papillomas and carcinomas Student's t test: body weight gain, absolute urinary bladder weight, food consumption, total NaHCO3 intake, incidence and number of hyperplasia, papillomas and carcinomas, average urinary pH and Na-ion concentration.

Test substance : SOURCE: Wako Pure Chemical Ind., Osaka, Japan.
PURITY: Food additive grade.
IMPURITY/ADDITIVE/ETC.:Not reported.
ANY OTHER INFORMATION: Not reported.

Reliability : (3) invalid
The test system is unsuitable for assessing the carcinogen potential of NaHCO3, as the rats have been pre-treated with BBN.

25.04.2002 (30)

Species	:	rat
Sex	:	male
Strain	:	Fischer 344
Route of admin.	:	oral feed
Exposure period	:	4 weeks
Frequency of treatm.	:	continously
Post exposure period	:	
Doses	:	0, 3% NaHCO3, 3% NaHCO3 and 5% L-ascorbic acid (AsA)
Result	:	negative
Control group	:	yes
Method	:	
Year	:	1988
GLP	:	no data
Test substance	:	other TS: sodium bicarbonate
Method	:	METHOD FOLLOWED: Not reported. GLP: Not reported.

STATISTICAL METHODS: Student's t test.
METHOD OF CALCULATION: Not reported.
ANALYTICAL METHODS: Urinary bladders were excised, inflated, and fixed in 10% phosphate-buffered formalin and embedded in paraffin. Epithelial cells incorporating BrdUrd were demostrated in histological sections by the avidin-biotin-peroxidase complex immunohistochemical method with anti-BrdUrd monoclonal antibody. Numbers of labeled cells per 1000 cells were counted under the light microscope and labelling indexes expressed as percentage values.

Result : MORTALITY AND TIME TO DEATH: No mortality.
HISTOPATHOLOGY: Significant increases in BrdUrd uptake over untreated control group values were observed for NaHCO3 treatment. The labelling index (%) for animals fed 3% NaHCO3 was statistically significantly different from the control. No exposure-related effects were observed in rats that had not been pretreated with BBN.

Source : TNO Voeding AJ Zeist

Test condition : TEST ORGANISMS
- Age: 6 weeks.
- Weight at study initiation: Not reported.
- Number of animals: 5 in each of four groups, 20 in total.

ADMINISTRATION / EXPOSURE
- Duration of test/exposure: 4 weeks.
- Type of exposure: Oral in feed.
- Post exposure period: No. The rats were injected i.p. with bromodeoxyuridine (BrdUrd), 150 mg/kg 1 hour before sacrifice. Epithelial cells labelled with BrdUrd were counted and labelling indices expressed as percentage values.

FOR ORAL STUDIES:
- Vehicle: Feed.
- Concentration in vehicle: 3% NaHCO3.
- Total volume applied: Not reported.
- Doses: 3% NaHCO3 (group 1), 5% AsA (L-ascorbic acid) (group 2), 3% NaHCO3 + 5% AsA (group 3) or no supplements (control group 4).

CLINICAL OBSERVATIONS AND FREQUENCY
- Body weight: Registered every week for the duration of the exposure.
- Food consumption: Registered every week for the duration of the exposure.
- Water consumption: Registered every week for the duration of the exposure.
- Clinical signs: Not reported.
- Mortality: Not reported.
- Macroscopic examination:Not reported.
- Ophthalmoscopic examination: Not reported.
- Haematology: Not reported.
- Clinical chemistry: Not reported.
- Urinalysis: Measurement of: pH in week 2, 4, 6, 8.

Electrolytes (Na, Na, Ca, Cl, P, Mg) in week 2, ,4, 6, 8.
Osmolality in week 4 and 8.
ORGANS EXAMINED AT NECROPSY (MACROSCOPIC AND MICROSCOPIC):
- Macroscopic: Urinary bladder.
- Microscopic: Urinary bladder.

OTHER EXAMINATIONS: Not reported.
STATISTICAL METHODS: Student's t test.

Test substance : SOURCE: Wako Pure Chemical Ind., Osaka, Japan.
PURITY: Food additive grade.
IMPURITY/ADDITIVE/ETC.:Not reported.
ANY OTHER INFORMATION: Not reported.

Reliability : (3) invalid
The test system is unsuitable for assessing the carcinogen potential of

NaHCO3, as the rats have been pre-treated with BBN.

25.04.2002 (30)

Species	:	Rat
Sex	:	Male
Strain	:	Wistar
Route of admin.	:	oral feed
Exposure period	:	32 weeks
Frequency of treatm.	:	continously
Post exposure period	:	
Doses	:	control diet (group 1) or this diet supplemented with equimolar amounts of the following minerals: 2.34% NaCl (group 2), 2.98% KCl (group 3), 3.36% NaHCO3 (group 4), 1.68% NaHCO3 + 2% KHCO3 (group 5), or 4% KHCO3 (group 6)
Result	:	
Control group	:	yes
Method	:	
Year	:	1989
GLP	:	no data
Test substance	:	other TS: sodium bicarbonate
Method	:	METHOD FOLLOWED: Not reported. DEVIATIONS FROM GUIDELINE: Not reported. GLP: Not reported. STATISTICAL METHODS: The results were evaluated by analysis of variance techniques followed by Dunnett's multiple comparison test (body weights) or by the LSD test (food and water intake, urianlyses). Urinary pH values were analysed with the Mann/Whitney U-test. Data on microscopical lesions were analysed with the two-sided Fischer exact probability test (incidences) or Student's t-test. METHOD OF CALCULAT ION: Not reported. ANALYTICAL METHODS: At the end of week 37, all rats were killed and the urinary bladders were inflated by intraluminal injection of a neutral, aqueous phosphate buffered 10% solution of formaldehyde and removed. The urinary bladder was processed for microscopy by conventional methods, step-sectioned (~10 sections/bladder) at 5 microm, stained with haematoxylin and eosin and examined by light microscopy. In addition the total length of of the basement membrane was measured by morphometry and the number of lesions/10 cm of basement membrane calculated.The lesions found in the urinary bladder epithelium were classified into simple hyperplasia, papillary or nodular hyperplasia, papilloma and carcinoma.
Result	:	The incidence of papillary or nodular hyperplasia, papillomas and carcinomas increased in rats fed NaHCO3 only if they had been pretreated with BBN. There was no control group with animals fed NaHCO3 that had not been pretreated with BBN.
Source	:	TNO Voeding AJ Zeist
Test condition	:	TEST ORGANISMS - Age: 5 weeks. - Weight at study initiation: Not reported. - Number of animals: 120 in total, 20 in each of 6 groups. ADMINISTRATION / EXPOSURE - Duration of test/exposure: The rats were pre-exposed to 0.05% N-butyl-N-(4-hydroxybutyl)nitrosamine (BBN) in drinking water for four weeks to initiate tumour formation, and then exposed for 32 weeks. - Type of exposure: Oral in feed. - Post exposure period: No. FOR ORAL STUDIES: - Vehicle: Feed. - Concentration in vehicle: Rats were fed with a control diet (group 1) or diet supplemented with equimolar amounts of the following minerals: 2.34%

NaCl (group 2), 2.98% KCl (group 3), 3.36% NaHCO3 (group 4), 1.68% NaHCO3 + 2% KHCO3 (group 5), or 4% KHCO3 (group 6).
- Total volume applied: Not reported.
- Doses: See above.

CLINICAL OBSERVATIONS AND FREQUENCY
- Body weight: It is reported that is was "measured periodically", with no further details.
- Food consumption:It is reported that is was "measured periodically", with no further details.
- Water consumption: It is reported that is was "measured periodically", with no further details.
- Mortality: Not reported.
- Macroscopic examination: Not reported.
- Ophthalmoscopic examination: Not reported.
- Haematology: Not reported.
- Clinical chemistry: Not reported.
- Urinalysis: Performed in week 9, 13, 24, 36. Volume, density, Na, K, Cl, Ca, Mg, P and S were measured.

ORGANS EXAMINED AT NECROPSY (MACROSCOPIC AND MICROSCOPIC):
- Macroscopic: Urinary bladder.
- Microscopic: Urinary bladder.

OTHER EXAMINATIONS: Not reported.
STATISTICAL METHODS: Analysis of variance techniques followed by Dunnett's multiple comparison test (body weight) or by the LSD test (food/water intake, urinalyses). Urinary pH values analysed with the Mann/Whitney U-test. Data on microscopical lesions were analyses with the two-sided Fischer exact probability test (incidences) or Student's t-test.

Test substance : SOURCE: British Drug House, UK.
PURITY: > 99.9%
IMPURITY/ADDITIVE/ETC.:Not reported.
ANY OTHER INFORMATION: Not reported.

Reliability : (3) invalid
The test system is unsuitable for assessing the carcinogen potential of NaHCO3, as the rats have been pre-treated with BBN.

13.06.2002 (45)

Species : rat
Sex : male
Strain : other: Fischer 344 and ODS/Shi-od/od
Route of admin. : oral feed
Exposure period : 32 weeks
Frequency of treatm. : continously
Post exposure period :
Doses : 3% NaHCO3 + 5% AsA (group 1 and 5), 3% NaHCO3 (group 2 and 6), 5% AsA (group 3 and 7), or basal diet alone (controls, group 4 and 8)
Result :
Control group : yes
Method :
Year : 1997
GLP : no data
Test substance : other TS: sodium bicarbonate
Method : METHOD FOLLOWED: Not reported.
GLP: Not reported.
STATISTICAL METHODS:Statistical analyses of incidences of histopathological lesions were performed with the Fischer's exact probability test. After testing for homogeneity by Bartlett's test, the other data were evaluated by either (1) the F-test for analysis of variance, and then the Sheffe's test, or (2) the Kruskal-Wallis test using rank sum and chi-square analysis, and then the Dunn's test.
METHOD OF CALCULATION: Not reported.

ANALYTICAL METHODS: At the end of week 34, all rats were killed under ether anaesthesia. The urinary bladders were inflated with 10% phosphate buffered formalin solution (pH 7.4) through the urethra and sliced into strips (12 per bladder) for routine processing and histological examination of sections stained with haematoxylin and eosin. For quantitative analysis, urinary bladder lesions were classified into papillomas and carcinomas, and numbers counted per urinary bladder.

Result : MORTALITY AND TIME TO DEATH: Two ODS rats in group 4 died because of puelonephritis and prostatitis, without urinary bladder tumours, in week 25 and 33 respectively.
CLINICAL SIGNS: 11 and 12 F344 rats in group 5 and 6, respectively, exhibited haematuria. ODS rats showed no scorbutic signs such as abnormal gait, eyelids stained with brown liquid, and no signs of toxicity due to the chemical treatments in any groups.

The addition of 3% NaHCO3 to the diet promoted urinary bladder carcinogenesis induced by BBN pretreatment in the F344 rat strain. In the ODS rat strain, no promoting activity was observed, despite comparable changes in urinary pH and Na urinary concentration. ODS rats are resistant to sodium L-ascorbate (Na-AsA) promoting effects, as opposed to male F344 rats who can synthesise alpha2µ-globuin in addition to AsA. The results indicate that ODS rats are also resistant to the modifying effects of NaHCO3 and/or AsA on two-stage urinary bladder carcinogenesis after BBN treatment. There were no groups that received NaHCO3 without pretreament with BBN.

Source : TNO Voeding AJ Zeist

Test condition : TEST ORGANISMS
- Age: 6 weeks
- Weight at study initiation: ODS rats, 174-178g+/- 23g. F344 rats, 142-143g+/-5-6g.
- Number of animals: 60 ODS, 15 in each group 1-4. 60 F344 rats, 15 in each group 5-8.

ADMINISTRATION / EXPOSURE
- Duration of test/exposure: The rats were pre-exposed 2 weeks to BBN, thereafter exposed 32 weeks to the test substances.
- Type of exposure: The rats received drinking water containing 0.05% N-butyl-N-(hydroxybutyl)nitrosamine (BBN) for two weeks, and were thereafter fed basal diet supplemented with the test substances.
- Post exposure periode: No.

FOR ORAL STUDIES:
- Vehicle: Feed.
- Concentration in vehicle: 3% NaHCO3 and/or 5% AsA.
- Total volume applied: Not reported.
- Doses: 3% NaHCO3 + 5% AsA (group 1 and 5), 3% NaHCO3 (group 2 and 6), 5% AsA (group 3 and 7), or basal diet alone (controls, group 4 and 8).
- Removal of test substance: Not reported.

CLINICAL OBSERVATIONS AND FREQUENCY
- Body weight: Measured 'periodically', however it is not detailed how frequently.
- Food consumption:Measured 'periodically', however it is not detailed how frequently.
- Water consumption: Measured 'periodically', however it is not detailed how frequently.
- Clinical signs: Not reported.
- Mortality: Not reported.
- Macroscopic examination:Not reported.
- Ophthalmoscopic examination: Not reported.
- Haematology: Not reported.
- Clinical chemistry: Not reported.

- Urinalysis: Performed in week 10, 22 and 32. The pH, total ascorbic acid concentration and sodium concentration were registered.
ORGANS EXAMINED AT NECROPSY (MACROSCOPIC AND MICROSCOPIC):
- Macroscopic: Urinary bladder.
- Microscopic: Urinary bladder.
OTHER EXAMINATIONS: Not reported.
STATISTICAL METHODS: Statistical analyses of incidences of histopathological lesions were performed with the Fisher exact probaility test. After testing for homogeneity by Bartlett's test, the other data were evaluated by either (1) the F-test for analysis of variance, and then the Scheffe's test, or (2) the Kruskal -Wallis test using rank sum and chi-square analysis, and then the Dunn's test.

Test substance : SOURCE: Wako Pure Chemicals Industries Ltd., Osaka, J
PURITY: Not reported.
IMPURITY/ADDITIVE/ETC.:Not reported.
ANY OTHER INFORMATION: Not reported.

Reliability : (3) invalid
The test system is unsuitable for assessing the carcinogen potential of NaHCO3, as the rats have been pre-treated with BBN.

07.01.2003 (54)

5.8.1 TOXICITY TO FERTILITY

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species	:	Mouse
Sex	:	Female
Strain	:	CD-1
Route of admin.	:	Gavage
Exposure period	:	Day 6 - day 15 of gestation
Frequency of treatm.	:	Once daily
Duration of test	:	
Doses	:	0, 5.8, 27, 125 and 580 mg/kg
Control group	:	Yes
Method	:	
Year	:	1974
GLP	:	No
Test substance	:	other TS: sodium bicarbonate
Method	:	METHOD FOLLOWED: Not reported. GLP: No, the study was executed before the existence of GLP STATISTICAL METHODS: Not reported. METHOD OF CALCULATION: Not reported. ANALYTICAL METHODS: Not reported.
Result	:	NOAEL (NOEL): 580 mg/kg ACTUAL DOSE RECEIVED BY DOSE LEVEL BY SEX: Not reported. TOXIC RESPONSE/EFFECTS BY DOSE LEVEL:

Dose (mg/kg):	Sham	Aspirin	5.8	27	125	580
Pregnancies	24	24	21	22	23	20
Died or aborted	0	0	0	0	0	0
Live litters	24	24	20	22	23	20
Implant sites	277	295	232	271	270	229
Resorptions	12	8	20	1	6	7
Live fetuses	265	285	208	266	261	220
Dead fetuses	0	2	4	4	3	2
Fetus weight (g)	0.92	0.88	0.90	0.86	0.88	0.90

- Effects on offspring: 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.

Test condition : TEST ORGANISMS
- Strain: Albino CD-1 outbred mice.
ADMINISTRATION / EXPOSURE
- Type of exposure: By oral intubation.
- Duration of test/exposure: Sodium bicarbonate was administered from day 6-15 of gestation.
- Treatment: 0, 5.8, 27, 125 and 580 mg/kg
- Control group and treatment: The females were dosed with the indicated dosages by oral intubation; the controls were sham treated. A positive control was included dosed with 150 mg Aspirin/kg.
- Vehicle: Water.
- Total volume applied: Not reported.
MATING PROCEDURES: 25 virgin adult female mice per test group were mated with young adult males, and observation of the vaginal sperm plug was considered day 0 of gestation.
STANDARDIZATION OF LITTERS: Not reported.
PARAMETERS ASSESSED DURING STUDY P AND F1:
- Clinical observations: Body weights were recorded on Days 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.
- Estrous cycle: Not reported.
- Sperm examination: Not reported.
PARAMETERS ASSESSED DURING STUDY F1 AND F2: Not applicable.
OFFSPRING: One-third of the fetuses of each litter underwent detailed visceral examinations employing the Wilson technique. The remaining two-thirds were cleared in KOH, stained with alizarin red S dye and examined for skeletal defects.
ORGANS EXAMINED AT NECROPSY (MACROSCOPIC AND MICROSCOPIC):
On day 17 all dams were subjected to Caesarean section and the number of implantation sites, resorption sites and live and dead fetuses were recorded. The body weights of the live pups was also recorded. The urogenital tract was examined in detail for anatomical normality. All fetuses were examined grossly for the presence of external congenital abnormalities.
OTHER EXAMINATIONS: Not reported.
STATISTICAL METHODS: Not reported.

Test substance : No data on test substance reported.

Reliability : (2) valid with restrictions
Acceptable, well documented study which meets basic scientific principles.

10.02.2003 (24)

Species	:	rat
Sex	:	female
Strain	:	Wistar
Route of admin.	:	gavage
Exposure period	:	Day 6 - day 15 of gestation
Frequency of treatm.	:	Once daily
Duration of test	:	
Doses	:	0, 3.4, 15.8, 73.3 and 340 mg/kg
Control group	:	yes
Method	:	
Year	:	1974
GLP	:	no
Test substance	:	other TS: sodium bicarbonate
Method	:	METHOD FOLLOWED: Not reported.

GLP: No, the study was executed before the existence of GLP
STATISTICAL METHODS: Not reported.
METHOD OF CALCULATION: Not reported.
ANALYTICAL METHODS: Not reported.

Result : NOAEL (NOEL): 340 mg/kg
ACTUAL DOSE RECEIVED BY DOSE LEVEL BY SEX: Not reported.
TOXIC RESPONSE/EFFECTS BY DOSE LEVEL:

Dose (mg/kg):	Sham	Aspirin	3.4	15.8	73.3	340
Pregnancies	20	24	20	21	21	22
Died or aborted	1	0	0	0	0	0
Live litters	19	19	20	21	21	22
Implant sites	226	277	239	268	238	254
Resorptions	5	93	3	0	0	1
Live fetuses	221	183	236	268	237	251
Dead fetuses	0	1	0	0	1	2
Fetus weight (g)	3.57	2.53	3.66	3.80	3.85	3.72

- Effects on offspring: 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.

Test condition : TEST ORGANISMS
- Strain: Albino Wistar derived rats.
ADMINISTRATION / EXPOSURE
- Type of exposure: By oral intubation.
- Duration of test/exposure: Sodium bicarbonate was administered from day 6-15 of gestation.
- Treatment: 0, 3.4, 15.8, 73.3 and 340 mg/kg
- Control group and treatment: The females were dosed with the indicated dosages by oral intubation; the controls were sham treated with the vehicle at a level equivalent to the group receiving the highest test dose. A positive control was included dosed with 250 mg Aspirin/kg.
- Vehicle: Water.
- Total volume applied: At a dosage level of < 250 mg/kg the test material was dosed at 1 ml/kg. At a dosage of 340 mg/kg the test material was dosed at 2 ml/kg.
MATING PROCEDURES: 25 virgin adult female rats per test group were mated with young adult males, and observation of the vaginal sperm plug was considered day 0 of gestation.
STANDARDIZATION OF LITTERS: Not reported.
PARAMETERS ASSESSED DURING STUDYP AND F1:
- Clinical observations: Body weights were recorded on Days 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.
- Estrous cycle: Not reported.
- Sperm examination: Not reported.
PARAMETERS ASSESSED DURING STUDY F1 AND F2: Not applicable.
OFFSPRING: One-third of the fetuses of each litter underwent detailed visceral examinations employing the Wilson technique. The remaining two-thirds were cleared in KOH, stained with alizarin red S dye and examined for skeletal defects.
ORGANS EXAMINED AT NECROPSY (MACROSCOPIC AND MICROSCOPIC):
On day 20 all dams were subjected to Caesarean section and the number 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 was examined in detail for anatomical normality. All fetuses were examined grossly for the presence of external congenital abnormalities.

OTHER EXAMIN ATIONS: Not reported.
STATISTICAL METHODS: Not reported.

Test substance : No data on test substance reported.
Reliability : (2) valid with restrictions
Acceptable, well documented study which meets basic scientific principles.
10.02.2003 (24)

Species : Rabbit
Sex : female
Strain : Dutch
Route of admin. : gavage
Exposure period : Day 6 - day 18 of gestation
Frequency of treatm. : Once daily
Duration of test :
Doses : 0, 3.3, 15.3, 71,2 and 330 mg/kg
Control group : yes
Method :
Year : 1974
GLP : no
Test substance : other TS: sodium bicarbonate
Method : METHOD FOLLOWED: Not reported.
GLP: No, the study was executed before the existence of GLP
STATISTICAL METHODS: Not reported.
METHOD OF CALCULATION: Not reported.
ANALYTICAL METHODS: Not reported.
Result : NOAEL (NOEL): 330 mg/kg
ACTUAL DOSE RECEIVED BY DOSE LEVEL BY SEX: Not reported.
TOXIC RESPONSE/EFFECTS BY DOSE LEVEL:

Dose (mg/kg):	Sham	6-AN	3.3	15.3	71.2	330
Pregnancies	11	17	13	12	11	12
Corpora Lutea	137	159	154	151	149	168
Died or aborted	1	1	0	0	1	0
Live litters	9	15	13	12	9	12
Implant sites	45	100	77	78	57	71
Resorptions	7	22	3	4	7	5
Live fetuses	38	77	74	74	50	66
Dead fetuses	0	1	0	0	0	0
Fetus weight (g)	43.1	36.1	37.5	37.7	41.7	39.2

- Effects on offspring: 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.

Test condition : TEST ORGANISMS
- Strain: Dutch-belted rabbits.
ADMINISTRATION / EXPOSURE
- Type of exposure: By oral intubation.
- Duration of test/exposure: Sodium bicarbonate was administered from day 6-18 of gestation.
- Treatment: 0, 3.3, 15.3, 71,2 and 330 mg/kg
- Control group and treatment: The females were dosed with the indicated dosages by oral intubation; the controls were sham treated with the vehicle at a level equivalent to the group receiving the highest test dose. A positive control was included dosed on Day 9 with 2.5 mg/kg of 6-aminonicotinamide.
- Vehicle: Water.
- Total volume applied: At a dosage level of < 250 mg/kg the test material was dosed at 1 ml/kg. At a dosage of 330 mg/kg the test material was dosed at 2 ml/kg.

MATING PROCEDURES: On Day 0, each doe was given an injection of 0.4 ml of human chorionic gonadotropin. Three hours later, each doe was inseminated artificially with 0.3 ml diluted semen from a proven donor.
STANDARDIZATION OF LITTERS: Not reported.
PARAMETERS ASSESSED DURING STUDY P AND F1:
- Clinical observations: Body weights were recorded on Days 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.
- Estrous cycle: Not reported.
- Sperm examination: Not reported.
PARAMETERS ASSESSED DURING STUDY F1 AND F2: Not applicable.
OFFSPRING: 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 KOH, stained with alizarin red S dye and examined for skeletal defects.
ORGANS EXAMINED AT NECROPSY (MACROSCOPIC AND MICROSCOPIC):
On day 29 all does were subjected to Caesarean section and the number 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 was examined in detail for anatomical normality. In addition all fetuses were examined grossly for the presence of external congenital abnormalities.
OTHER EXAMINATIONS: Not reported.
STATISTICAL METHODS: Not reported.

Test substance : No data on test substance reported.
Reliability : (2) valid with restrictions
Acceptable, well documented study which meets basic scientific principles.

10.02.2003 (24)

Species : rat
Sex : female
Strain : Sprague-Dawley
Route of admin. : drinking water
Exposure period : Day 15 - day 20 of gestation
Frequency of treatm. : NaHCO3 was administered in drinking water
Duration of test :
Doses : 2 %
Control group :
Method :
Year : 1993
GLP : no
Test substance : other TS: sodium bicarbonate
Method : METHOD FOLLOWED: Not reported.
GLP: No.
STATISTICAL METHODS: see TS.
METHOD OF CALCULATION: Not reported.
ANALYTICAL METHODS: Not reported.
Result : NOAEL (NOEL), LOAEL (LOEL): Not possible to assess.
ACTUAL DOSE RECEIVED BY DOSE LEVEL BY SEX: Not reported.
TOXIC RESPONSE/EFFECTS BY DOSE LEVEL:
- Clinical biochemistry findings incidence and severity: Females treated with NaHCO3 gained weight comparable to vehicle controls throughout the experiment. No maternal deaths or physical signs of toxicity were seen during the experiment. Treatment with NaHCO3 resulted in an average maternal blood pH of 7.43 which was slightly alkalotic compared to the controls maintained with tap water.
- Number of implantations: There was no effect of NaHCO3 on the number of implants, % resorptions, or number of live fetuses per litter.

- Litter size and weights: The average body weights of live fetuses in the NaHCO3 treated group was comparable to the control group.
- Effects on offspring: No treatment-related external abnormalities were seen in the group treated with NaHCO3.

Test condition : TEST ORGANISMS
- Strain: Nulliparous female Sprague-Dawley rats, Crj:CD(SD).
- Source: Charles River Japan, Inc.

ADMINISTRATION / EXPOSURE
- Type of exposure: Oral, via drinking water.
- Duration of test/exposure: Sodium bicarbonate was given from day 15 of gestation.
- Treatment: 2 % NaHCO3.
- Control group and treatment: Two groups were given 0.5 % aqueous methylcellulose on day 16 of gestation by gavage and were given either tap water (control group) or 2 % NaHCO3 solution as drinking water.
- Vehicle: tap water.
- Concentration in vehicle: 2 %.
- Total volume applied: Unknown.

MATING PROCEDURES: Females were allowed to mate, at +/- 12 weeks of age with adult males of the same strain in a ration of 1:1. Mating was confirmed next morning by the presence of spermatozoa in vaginal saline lavages and the day was designated as day 0 of gestation.
STANDARDIZATION OF LITTERS: Not reported.
PARAMETERS ASSESSED DURING STUDY P AND F1:
- Clinical observations: Physical signs of toxicity were monitored daily. Maternal body weights were recorded daily and their water consumption was also checked daily. Blood samples were collected 4 hours after treatment with methylcellulose and pH and pCO2 were measured anaerobically.
- Estrous cycle: Not reported.
- Sperm examination: Not reported.

PARAMETERS ASSESSED DURING STUDY F1 AND F2: Not applicable.
OFFSPRING: All fetuses were weighed, sexed and examined externally. After evisceration, all fetuses were fixed and stained with alizarin red S for subsequent skeletal examination which was limited to the evaluation of wavy ribs.
ORGANS EXAMINED AT NECROPSY (MACROSCOPIC AND MICROSCOPIC):
On day 20 of gestation, all females were euthanatized and reproductive status of each female was examined. Implants were counted and classified as a live fetus, dead fetus or resorption.
OTHER EXAMINATIONS: Not reported.
STATISTICAL METHODS: Blood gas parameters were statistically analyzed by Student's t-test. Maternal body weight gain and reproductive parameters were analyzed with one-way analysis of variance.

Test substance : No data on test substance reported.
Reliability : (3) invalid
Documentation insufficient for assessment.

10.02.2003 (57)

Species : mouse
Sex : female
Strain : Swiss
Route of admin. : i.p.
Exposure period : 7th to 9th day of pregnancy
Frequency of treatm. : daily
Duration of test :
Doses : 2% NaHCO3
Control group : other: saline solution or untreated

Method :
Year : 1986
GLP : no
Test substance : other TS: sodium bicarbonate
Method : METHOD FOLLOWED: Not reported.
DEVIATIONS FROM GUIDELINE: Not reported.
GLP: No, the study as executed before the existence of GLP.
STATISTICAL METHODS:Not reported.
METHOD OF CALCULATION: Not reported.
ANALYTICAL METHODS: Not reported.
Result : NOAEL (NOEL), LOAEL (LOEL): Not possible to assess.
ACTUAL DOSE RECEIVED BY DOSE LEVEL BY SEX: Not reported.
TOXIC RESPONSE/EFFECTS BY DOSE LEVEL:
- Gross pathology incidence and severity: There were 2 resorption sites in total in the two females, compared to 2 resorption sites in 3 saline treated controls.
- Number of implantations: 22
- Litter size and weights: There were 20 viable foetuses in total from two females. In the control groups 27 foetuses were counted in 3 saline treated females, and 17 foetuses in 2 untreated females.
- Effects on offspring: In the NaHCO3 group, hematomas were found in 4 foetuses (of a total of 20); no other abnormalities were found. The increased incidence of hematomas may be incidental, as in the groups tested with a drug (the only which 2% NaHCO3 was added to), hematomas were also observed. No abnormalities were observed in the other control groups.

STATISTICAL RESULTS: Not reported.
Test condition : TEST ORGANISMS
ADMINISTRATION / EXPOSURE
- Type of exposure: Intraperitoneal.
- Duration of test/exposure: The mice were exposed i.p. on day 7, 8 and 9 of pregnancy, and sacrificed on day 14 of the pregnancy.
- Treatment: 2% NaHCO3 i.p. Volume is unknown.
- Control group and treatment: In this study (an experiment to test certain drugs for teratogenicity) the NaHCO3 group of animals was considered a control group together with a group receiving saline and an untreated group.
- Vehicle: Unknown.
- Concentration in vehicle: 2%
- Total volume applied: Unknown.

MATING PROCEDURES: The breeding groups consisted of six females and two males in each cage, females were examined in the morning and afternoon for evidence of mating. Females with fresh vaginal plugs were isolated and the date noted as the first day of pregnancy.
STANDARDIZATION OF LITTERS: Not reported.
PARAMETERS ASSESSED DURING STUDY P AND F1:
- Clinical observations: Not reported.
- Estrous cycle: Not reported.
- Sperm examination: Not reported.

PARAMETERS ASSESSED DURING STUDY F1 AND F2:
- Clinical observations and frequency: Not reported.
- Others: Not reported.

OFFSPRING: Not reported.
ORGANS EXAMINED AT NECROPSY (MACROSCOPIC AND MICROSCOPIC):
- Organ weights P and F1:Not reported.
- Histopathology P and F1: Animals (P) were killed on the fourteenth day of pregnancy, and the uteri removed. The uterus was examined for implantation sites, viable fetuses and resorption sites. Viable foetuses (F1) were examined for grossly visible malformations. Histological preparations were made of selected foetuses.
- Histopathology F1 not selected for mating, F2: Not reported.

OTHER EXAMINATIONS: Not reported.
STATISTICAL METHODS: Not reported.

Test substance : SOURCE: Not reported.
PURITY: Not reported.
IMPURITY/ADDITIVE/ETC.: Not reported.
ANY OTHER INFORMATION: Not reported.

Reliability : (3) invalid
Documentation insufficient for assessment. Very few of the parameters measured in a guideline test were monitored in this study. The volume injected and vehicle is unknown. Only two animals were used in each exposure group.

10.02.2003 (6)

Species : Rat
Sex : Female
Strain : other: Dahl rats
Route of admin. : oral unspecified
Exposure period : 5 days before breeding and during pregnancy
Frequency of treatm. : Daily
Duration of test :
Doses : 1.43 %
Control group : other: saline solution
Method :
Year : 1993
GLP : No
Test substance : other TS: sodium bicarbonate
Method : METHOD FOLLOWED: Not reported.
GLP: No.
STATISTICAL METHODS: see TS.
METHOD OF CALCULATION: Not reported.
ANALYTICAL METHODS: Not reported.

Result : NOAEL (NOEL), LOAEL (LOEL): Not possible to assess.
ACTUAL DOSE RECEIVED BY DOSE LEVEL BY SEX: Not reported.
TOXIC RESPONSE/EFFECTS BY DOSE LEVEL:
- Clinical biochemistry findings incidence and severity:
The bicarbonate diet had only a moderate effect on blood pressure of salt-resistant females. Net maternal weight gain was greatest in females fed a bicarbonate diet.
- Number of implantations: 387
- Litter size and weights: Litter sizes were comparable in all groups.
- Effects on offspring: In salt-sensitive animals there were significant negative correlations between mean arterial pressure of females and body weight of newborns in all dietary groups. In salt-sensitive newborns the bicarbonate diet increased significantly the water content in heart, kidney and liver in comparison with the group on low-salt diet. Relative heart and kidney protein contents were lowered in salt-sensitive rats on a bicarbonate diet. Relative DNA content was lowered after a bicarbonate diet in both genotypes.

Test condition : TEST ORGANISMS
- Strain: Inbred Dahl salt-sensitive (DS/JR) and salt-resistant (DR/JR) rats.
- Source: Institute of Physiology, Prague.
ADMINISTRATION / EXPOSURE
- Type of exposure: Oral, via diet.
- Duration of test/exposure: 5 days before breeding and during pregnancy.
- Treatment: 1.43 % $NaHCO_3$.
- Control group and treatment: In the control group both females and males were fed a standard nutritionally-balanced low-salt diet containing 0.3 % NaCl. High salt group received diet containing 8 % NaCl.
- Vehicle: Unknown.

- Concentration in vehicle: 1.43 %.
- Total volume applied: Unknown.
MATING PROCEDURES: Males and females were left together for three nights.
STANDARDIZATION OF LITTERS: Not reported.
PARAMETERS ASSESSED DURING STUDY P AND F1:
- Clinical observations: Systolic, diastolic and mean arterial pressures of dams were measured on the first day after delivery.
- Estrous cycle: Not reported.
- Sperm examination: Not reported.
PARAMETERS ASSESSED DURING STUDY F1 AND F2: Not applicable.
OFFSPRING: Not reported.
ORGANS EXAMINED AT NECROPSY (MACROSCOPIC AND MICROSCOPIC):
- Newborn rats of both sexes were weighed and decapitated within 18 hours after birth. Hearts, kidneys (both left and right pooled) as well as livers were excised, weighed and stored at -70 degrees C until their protein and DNA contents were determined.
OTHER EXAMINATIONS: Protein content was assayed in the homogenate by the method of Lowry (1951) and DNA content by the method of Burton (1956).
STATISTICAL METHODS: All data were expressed as means +/- SEM and evaluated by one-way analysis of variance. The linear regression analysis was employed for the evaluation of the relationships between blood pressure of mothers and body weight of newborns.

Test substance : No data on test substance reported.
Reliability : (3) invalid
Documentation insufficient for assessment.

10.02.2003 (19)

5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

5.9 SPECIFIC INVESTIGATIONS

Endpoint : other: effect of bicarbonate intake on physical performance at high intensities
Study descr. in chapter :
Reference : Horswill, C.A., Effects of Bicarbonate, Citrate, and Phosphate Loading on Performance. Int. J. Sport Nutr., suppl., S111-S119, 1995.
Type :
Species : human
Sex : no data
Strain :
Route of admin. : oral
No. of animals :
Vehicle : other: solution or capsule
Exposure period :
Frequency of treatm. : single dose or several doses taken over several hours.
Doses : 0.1-0.5 g/kg
Control group : no data specified
Observation period : no data
Result :
Method : other
Year : 1995
GLP : no data
Test substance : other TS: sodium bicarbonate
Result : This paper reviews the theoretical mechanisms whereby bicarbonate may enhance physical performance at high intensities. Ingested bicarbonate

elevates the bicarbonate concentration in the extracellular space, but not the intracellular space. The mechanism by which bicarbonate loading exerts its influence may be through the elevation of the extracellular bicarbonate concentrations, which then increases rate of efflux of H+ from the intracellular space. Others claim that the ingested sodium changes the strong-ion difference, and that this change, not the bicarbonate per se, produces the increase in blood buffering capacity. The typical protocol employed to administer a sodium bicarbonate buffer was a dose of 0.1-6.0 mmol/kg given as a single oral dose (solution or capsule), either as one dose 1 hr before performance, or as repeated doses taken over several hours before performance. A positive correlation was found between bicarbonate dosage and the extent of improvement in performance, using data generated from mean values reported in the literature. 0.3 g/kg is the apparent minimum effective dose. The ergogenic effects of bicarbonate appear to be most consistent either when exercise protocols involve repeated sprints that are interspersed with short recovery periods or when protocols commence at submaximal intensities, becoming progressively more difficult, and culminate at near-maximum levels. During a performance the blood bicarbonate system becomes the primary mechanism for buffering H+ only after the subject reaches the anaerobic threshold. Despite the existing results it hasn't yet been conclusively demonstrated that buffers can improve sport performance.

Source : TNO Voeding AJ Zeist
Test substance : SOURCE: Not reported.
PURITY: Not reported.
IMPURITY/ADDITIVE/ETC.:Not reported.
ANY OTHER INFORMATION: Not reported.

25.04.2002 (37)

Endpoint : other: effects on anaerobic excercise
Study descr. in chapter :
Reference : McNaughton, L.R., Sodium bicarbonate ingestion and its effects on anaerobic exercise of various durations. J. of Sports Sciences, vol. 10: 425-435, 1992.
Type :
Species : human
Sex : male
Strain :
Route of admin. : oral
No. of animals :
Vehicle : other: 400 ml low-energy, artificially sweetened, flavoured drink
Exposure period :
Frequency of treatm. : single dose
Doses : 0.3 g/kg bw NaHCO3
Control group : yes
Observation period :
Result :
Method : other
Year : 1992
GLP : no data
Test substance : other TS: sodium bicarbonate
Result : During high-intensity, short-duration exercise, the requirements for energy are mainly provided by anaerobic glycolysis. This type of exercise is associated with increasing amounts of lactic acid and a rise in hydrogen ions, which decreases blood and muscle pH leading to fatigue. This study examines which anaerobic exercise generations can be influenced by bicarbonate buffering, which is believed to improve the amount of work that can be done anaerobically.

Test subjects underwent a total of 3 test sessions, 1 control, 1 placebo (0.3

g/kg CaCO3) and a 0.3 g/kg dose of NaHCO3. Blood samples were taken at 0 and 90 minutes, and immediately following the exercise test. The blood was analysed for paO2, pH, HCO3- and base excess. Immediately preceding the test, the subjects ingested one of two liquids, the placebo or NaHCO3. The exercise test consisted of pedalling an ergometer for 10, 30, 120 or 240s, the subjects not knowing how long the test would last and being instructed to exert a maximum effort and accomplish maximum amount of work for the full time period. The ingestion of NaHCO3 had no effects on the work undertaken or on the peak power achieved, neither in the 10 seconds test, nor in the 30 seconds test. In the 120- and 240 second test, the work output and peak power achieved was significantly higher for the group ingesting NaHCO3 than for the control and placebo test groups. Likewise, the pH was significantly lower in this group. Post-excersise levels of blood lactate were significantly higher in the group ingesting NaHCO3 after the 120s and 240s trials, than in the control and placebo groups.

Source : TNO Voeding AJ Zeist
Test substance : SOURCE: Not reported.
PURITY: Not reported.
IMPURITY/ADDITIVE/ETC.:Not reported.
ANY OTHER INFORMATION: Not reported.

16.04.2002 (50)

5.10 EXPOSURE EXPERIENCE

Type of experience : Human - Medical Data
Remark : The common dose as antiacid in adult humans is 1 to 4 g. The pH of saturated aqueous solution may range from 8 -9. Not caustic like sodium carbonate.
In neutralising gastric acid, distention and possible damage or rupture of the stomach may occur from carbon dioxide release. Large doses, particularly in patients with renal insufficiency, have produced systemic alkalosis and/or expansion in the extracellular fluid volume with edema.

14.05.2002 (34)

Type of experience : Human - Medical Data
Remark : When applied as a medicinal drug for IV administration, NaHCO3 is incompatible with: ACTH, alcohol 5% with dextrose 5%, anileridine HCl, calcium chloride, calcium gluconate, codeine phosphate, aqueous insulin, levarterenol bitartrate, levorphanol tartrate, magnesium sulfate, meperidine HCl, methadone HCl, methicillin sodium, oxytetracyclin HCl, pentobarbital sodium, procain HCl, promazin HCl, protein hydrolysate (incompatible in 5% dextrose injection), lactated Ringer's injection, Ringer's injection, sodium lactate (1/6 M) injection, streptomycin sulfate, tetracyclin HCl, thiopental sodium, vancomycin HCl, vitamin B complex with ascorbic acid.

Compatible with:
dextrose in saline water or 2,5% in half-strength lactated Ringer's injection, (NaHCO3 is reported to be incompatible in lactated Ringer's injection, Ringer's injection and sodium lactate injection) Ringer's injection, sodium chloride injection, sodium lactate (1/6 M) injection. Cephalothin sodium, kanamycin sulfate, methicillin sodium, penicillin G buffered, pentobarbital sodium, tetracycline HCl.
Reliability : (4) not assignable
Only secondary literature.

14.05.2002 (48)

Type of experience : Human - Medical D ata
Remark : Excess sodium bicarbonate is emptied rapily into the small intestine where

it is absorbed.
Sodium bicarbonate is not recommended for long-term use (as antacid therapy) because of its short duration of action and its alkalosis producing properties.
Although alkalosis is not usually a problem in relatively healthy patients, sodium bicarbonate may cause volume expansion, hypertension, and edema in patients with renal insufficiency, hypertension or congestive heart failure.
Doses: 300 mg to 2 gm per dose.

Reliability : (4) not assignable
The original reference of this data was not available, as the text was prepared in the previous IUCLID update.

14.05.2002 (53)

Type of experience : Human - Medical Data
Remark : Use: Administration of sodium bicarbonate is generally reserved for the treatment of severe acidosis (e.g. arterial pH less than 7-7.15 or serum bicarbonate concentration of 8 mEq/l or less). Used in treating diabetic ketoacidosis, NaHCO3 should only be administered to partially correct the acidosis (e.g. to arterial pH of about 7.2) to avoid rebound metabolic alkalosis as ketones are metabolised.
It is not generally recommended to administer NaHCO3 after a cardiac arrest. Excessive administration during resuscitation may result in metabolic alkalosis and subsequent impairment of oxygen release from hemoglobin to tissues, and sodium and water overload with subsequent hypernatremia and hyperosmolality. Adverse effects: gastric distention and flatulence.
Metabolic alkalosis in patients with reduced renal function.
Large doses of sodium bicarbonate tend to increase sodium and water retention, leading to edema.

Reliability : (4) not assignable
Only secondary literature.

14.05.2002 (49)

Type of experience : Human - Medical Data
Remark : Sodium bicarbonate is completely absorbed orally and usually is excreted within three to four hours. Carbon dioxide formation in the stomach may be bothersome.
The maximum sodium tolerance is 250 mEq/m2/24 hrs in healthy persons (&gm of NaHCO3 contains 11.9 mEq of sodium). Sodium bicarbonate must be used with caution in edematous patients with sodium retaining disorders.
Prolonged administration of average doses (300 mg to 1.8 g, one to four times daily) in patients with normal renal function may cause systemic alkalosis with irritability, neuromuscular excitability, and tetany.

Reliability : (4) not assignable
The original reference of this data was not available, as the text was prepared in the previous IUCLID update.

14.05.2002 (2)

Type of experience : Human - Medical Data
Result : Use:
Sodium bicarbonate is used to treat metabolic acidosis secondary to loss of bicarbonate from the body.

Adverse reactions and precautions:
Excessive amounts of sodium bicarbonate may cause metabolic alkalosis and hypernatremia. Rapid alkalisation may precipitate tetany in hypocalcemic patients and cause cardiotoxicity and paralysis in hypokalemic patients. Too rapid administration produces a transient elevation of PCO2, and CO2 diffuses into the cells and cerebrospinal fluid more rapidly than bicarbonate, resulting in intracellular and central nervous

system acidosis. If administered in excess, NaHCO3 increases production of lactate, worsens cardiac output and decreases blood pressure in patients with lactic acidosis. Should be given cautiously to patients with congestive heart failure or other edematous or sodium-retaining conditions, oliguria or anuria. NaHCO3 injection is classified in FDA pregnancy category C.

Drug interactions:
Patients receiving corticosteroids may retain excessive sodium if NaHCO3 is given. Alkalization of the urine by NaHCO3 may decrease the renal clearance of organic bases (e.g. amphetamines, ephedrine, flecainide, quinine).
Conversely, the degree of ionisation and renal clearance of organic acids (e.g. chlorpropamide, phenobarbital, salicylates) may be increased. The renal clearance of lithium also may be accelarated by the increased renal sodium load.

Reliability : (4) not assignable
Only secondary literature.

10.02.2003 (1)

Type of experience : Human
Remark : NaHCO3 USP was considered slight irritating on scarified human skin when applied as 10% solution in water or as a 10% dilution in another solid.
It was considered as markedly irritating when used as a 100% pure powder on scarified skin.
Reliability : (4) not assignable
The original reference of this data was not available, as the text was prepared in the previous IUCLID update.

14.05.2002 (23)

Type of experience : other: Federal Register GRAS evaluation
Remark : The Food and Drug Administration (FDA) approved sodium bicarbonate as generally recognised as safe (GRAS) as a direct human food ingredient. This final ruling was effective from 19 December 1983, replacing a proposed rule dated 13 June 1978. Sodium bicarbonate was simultaneously approved as a GRAS indirect food substance. The safety of these ingredients has been evaluated under the comprehensive safety review conducted by the agency.
Reliability : (4) not assignable
Only secondary literature.

14.05.2002 (26) (27)

Type of experience : other: Federal Register GRAS literature assessment
Result : This report summarises the available scientific literature from 1920 to 1972, related to the 'safety'of carbonates as a food ingredients. Chemical information, biological data and biochemical aspects of carbonates are given in a 137 p. summary containing 874 references. The studies pertaining to sodium bicarbonate are mainly from the 1930s and 1940s, and are therefore considered as unreliable for assessing the possible adverse effects of sodium bicarbonate.
Reliability : (4) not assignable
Only secondary literature.

14.05.2002

Type of experience : Direct observation, clinical cases
Remark : PERSONS EXPOSED: A 4 kg., 4-month old girl.
EXPOSURE
- Reason of exposure: As a home remedy.
- Type of exposure: Oral.
- Duration of exposure: One dosing.
- Exposure concentrations / dose: 30 mEq/kg of NaHCO3

- Other information: Not reported.
EXAMINATIONS: Physical, hematology.
TREATMENT: Symptoms were easily corrected by infusion (i.v.) of saline solutions and 5% dextrose.
OTHER: Not reported.
FINDINGS
- Clinical signs: Cyanosis, hypernatremia, acute metabolic alcalosis and apnea, moderate respoiratory distress.
- Results of examinations: The clinical impression of acute volume depletion (dehydration) was most likely due to acute intraintestinal sequestration of fluids and osmotic diuresis.
- Effectivity of medical treatment: Good.
- Outcome: Full recovery. The levels of serum sodium, potassium, chloride, bicarbonate, hematocrit, glucose and BUN had normalised by the following day.
OTHER: Not reported.

Reliability : (3) invalid
Relevant methodological deficiencies. Case report described/evaluated by staff treating the patient.

11.04.2002 (8)

Type of experience : Direct observation, clinical cases
Result : Letter to the editor: Sodium bicarbonate taken with a heavy meal can cause a stomach burst, which is potentially life threatening. Antacid preparations frequently contain high concentrations of sodium, some with a recommended dose of 53-1402 mg sodium (recommended daily maximum dose is 1272-4974 mg). Frequent intake of certain brands of antacid may lead to high sodium intake, and use of antacids low in sodium is recommended by the author.

Reliability : (3) invalid
Relevant methodological deficiencies. Case report described/evaluated by staff treating the patient.

11.04.2002 (5)

Type of experience : Direct observation, clinical cases
Remark : PERSONS EXPOSED: A 7.5 week old boy.
EXPOSURE
- Reason of exposure:
The mother had been adding two "pinches" (dose unknown) of baking soda ($NaHCO_3$) to the food mixture each time she prepared to food formula. Before the clinical symptoms, the boy had been administered half a table spoon of $NaHCO_3$ (dose:9.2 to 14.5 mEq/kg).
- Type of exposure: Oral.
- Duration of exposure: Not reported.
- Exposure concentrations / dose: App. 9.2 to 14.5 mEq/kg.
- Other information: The patient had a 36 hr history of vomiting, diarrhea and irritability.
EXAMINATIONS: Physical, haematology, urinalysis.
TREATMENT:Fluids IV (saline with dextrose).
OTHER: Not reported.
FINDINGS
- Clinical signs:
On admittance to the hospital the infant had a temperature of 38.5 C, pulse rate of 159, respiratory rate of 36 breaths/minute and a blood pressure of 100/70 mmHg. Physical examination revealed a flat anterior fontanel, teary eyes, and moist mucous membranes. He had symmetric hyperreflexia with mildly increased tone. His skin was thickened and dry (normal turgor) with some scaling, especially around the feet; in addition, minimal pretibial and pedal edema was present; other clinical features were normal.
- Results of examinations: In blood, electrolyte values were: sodium, 155

mEq/l; potassium 4.0 mEq/l; chloride 109 mEq/l; bicarbonate, 29 mmol/l; BUN 10 mg/dl; creatinine 0.5 mg/dl; glucose 94 mg/dl. Serum osmolality was 310 mOsm. Arterial pH 7.41, PCO2 was 48 mm Hg. Urinalysis revealed a specific gravity of 1.018 and a pH >8.5; urine osmolality was 804 mOsm, with urine sodium level> 300 mEq/l. Urine protein concentration was 65 mg/dl (dip stick method).
- Effectivity of medical treatment: Good. During the next 36 hrs, serum sodium level fell to 142 mEq/l, serum bicarbonate to 20 mmol/l; The urine pH fell to 6.5 and urine sodium to 84 mEq/l; urine protein concentration dropped to 6 mg/dl (dip stick method). The child recovered completely. The apparent proteinuria is probably due to false positive dipstick result related to urine pH. This is indicated by normal protein levels in the serum during intoxication.
- Outcome: Full recovery.
OTHER: Not reported.

Reliability : (3) invalid
Relevant methodological deficiencies. Case report described/evaluated by staff treating the patient.

14.05.2002 (75)

Result : PERSONS EXPOSED: A 43-year old man.
EXPOSURE
- Reason of exposure: He had eaten a meal of potatoes and herring pickled in vinegar, with carbonated water. He had taken 30 g NaHCO3 after the meal to avoid epigastralgia.
- Type of exposure: Oral.
- Duration of exposure: Acute.
- Exposure concentrations / dose: 30 g.
- Other information: The patient had previously been troubled by slight epigastralga and treated with antacids
EXAMINATIONS: Physical, radiography.
TREATMENT: The abdomen was emptied for gas, blood-stained fluid and undigested food, and irrigated with saline, and the rupture was sewn closed.
OTHER: Not reported.
FINDINGS
- Clinical signs: Severe abdominal pain.
- Results of examinations: The patient was admitted with a haematemesis, breathing difficulties, and a 5 cm. rupture in the stomach wall.
- Effectivity of medical treatment: Efficient.
- Outcome: Full recovery.
OTHER: The combination of the pickled food, carbonated water and overdose of sodium carbonate resulted in the enormous gas development, causing a ruptured stomach. The clinical picture was characteristic.

Reliability : (3) invalid
Relevant methodological deficiencies. Case report described/evaluated by staff treating the patient.

14.05.2002 (7)

Type of experience : Direct observation, clinical cases

Result : PERSONS EXPOSED: A 7 -year old girl.
EXPOSURE:The patient had inhaled chlorine fumes froma can of chlorine tablets used for a swimming pool.
EXAMINATIONS: Physical, haematology.
TREATMENT: She received one treatment of albuterol by hand heald nebuliser, and when this did not increase the O2 saturation to >90%, sodium bicarbonate solution (3.75%) by hand held nebuliser, 4.25 ml over 20 minutes. The patient improved dramatically, blood count and blood chemistry was normal three hours later.
OTHER: Not reported.
FINDINGS

- Clinical signs: She immediately started coughing and choking, and vomited several times. The vomit contained streaks of blood with mucus. She started having breathing difficulties, chest pain and burning in the throat. The patient had respiratory distress, nasal flaring, intercostals and subcostal retraction, frequent coughing, diminished breath sounds in both lungs.
- Results of examinations: Arterial blood gases: pH 7.4, PCO2 39 mm Hg, PO2 45 mm Hg.
- Effectivity of medical treatment: Efficient.
- Outcome: Full recovery.
OTHER: The effect of this treatment has been tested in clinical trials once, when three patients with mild respiratory symptoms improved significantly after treatment with sodium bicarbonate solution (3.75%) by hand held nebuliser. The mechanism of action is thought to be through neutralising HCl formed when chlorine gas comes into contact with water at the target tissues.

Reliability : (3) invalid
Relevant methodological deficiencies. Case report described/evaluated by staff treating the patient.

01.05.2002 (20)

Type of experience : Direct observation, clinical cases

Result : PERSONS EXPOSED: The case reports of two chronic alcoholics are presented, of a 39-year old man and a 49-year old immunocompromised female.
EXPOSURE
- Reason of exposure: Self-ingestion to alleviate heartburn.

- Type of exposure: Oral.
- Duration of exposure: Not reported. The man ingesting antacids and several tablespoons of baking soda daily. The woman had consumed a box of baking soda weekly.
- Exposure concentrations / dose: Not reported.
- Other information: Not reported.
EXAMINATIONS: Physical, haematology, cardiac evaluation.
TREATMENT: Both treated with saline and electrolytes.
OTHER: Not reported.
FINDINGS
- Clinical signs: The man experienced a week of general weakness, intermittent dizzy spells, headaches, cough, unconciousness. The female experienced altered level of conciousness.
- Results of examinations: The blood levels of natrium, potassium, chloride, CO2, creatinine, BUN, glucose calcium, PO4, hematocrit, hemoglobin, pH, pCO2, pO2, BE and HCO3-prompted questioning of both regarding consumption of antacids.
- Effectivity of medical treatment: The man's blood levels normalised after three days. The womans blood values were normal within 48 hours.
- Outcome: Full recovery.
OTHER:Elevation of serum bicarbonate causes metabolic alkalosis (MA) and alkalemia, generally caused by acid loss or base gain. An abnormal bicarbonate load induces a bicarbonate diuresis, which also causes loss of sodium, chloride, potassium and volume. Reduction in glomerular filtration rate (GFR) leads to alkalosis. Hypokalemia, hypochloremia and hypercalcemia contribute to impaired bicarbonate excretion. Both patients showed typical signs of MA and hypokalemia, including central nervous system dysfunction and cardiac dysrythmias.

Excessive oral ingestion of bicarbonate places patients at risk for a variety of metabolic derangements including metabolic alkalosis, hypokalemia, hypernatremia, and hypoxia. The clinical presentation will vary, ranging

from mild gastroenteritis to seizures, dysrythmias and cardiac pulmonary arrest. Chronic alcoholics are a group at particular risk, as dyspepsia is a common complaint. Comorbid diseases such as gastritis, alcoholic ketoacidosis, pancreatitis and alcohol withdrawal can also increase self-medication with antacids. Dehydration may confound and exacerbate the metabolic derangements caused by antacid overuse.

Reliability : (3) invalid
Relevant methodological deficiencies. Case report described/evaluated by staff treating the patient.

01.05.2002 (25)

Type of experience : Direct observation, clinical cases
Result : PERSONS EXPOSED: A 70-year old man.
EXPOSURE
- Reason of exposure: Ingestion to alleviate heartburn.
- Type of exposure: Oral.
- Duration of exposure: Acute.
- Exposure concentrations / dose: 12 g.
- Other information: The ingestion of sodium bicarbonate in water followed a large meal.

EXAMINATIONS: Physical, radiography, laparotomy.
TREATMENT: Operation and peritoneal lavage.
OTHER: Not reported.
FINDINGS
- Clinical signs: His abdomen rapidly distended, he had difficulty breathing and experienced sudden, severe epigastric pain. On admission he was in pain and dyspnoeic, with a 6 cm tear in the stomach.
- Results of examinations: Distended stomach, free intraperironeal food.
- Effectivity of medical treatment: Efficient.
- Outcome: Full recovery.

OTHER:
The build-up of gas in the stomach was caused by the sodium bicarbonate and water.

Reliability : (3) invalid
Relevant methodological deficiencies. Case report described/evaluated by staff treating the patient.

01.05.2002 (22)

Type of experience : Direct observation, clinical cases
Result : PERSONS EXPOSED: A 38-year old male.
EXPOSURE
- Reason of exposure: Ingestion to alleviate severe heartburn.
- Type of exposure: Oral.
- Duration of exposure: Acute.
- Exposure concentrations / dose: 1 tablespoon, exact dose unknown.
- Other information: The patient had eaten a heavy meal and took 1 tablespoon of sodium bicarbonate in a quarter glass of water to alleviate heartburn.

EXAMINATIONS: Physical, X-ray.
TREATMENT: Laparotomy.
OTHER: Not reported.
FINDINGS
- Clinical signs:The patient was admitted with severe upper abdominal pains and hematemesis.
- Results of examinations: The patient suffered a 10-cm rupture in the stomach, and had air and food particles in the peritoneal cavity.
- Effectivity of medical treatment: Effective.
- Outcome: Full recovery.

OTHER:
It is assumed that the sudden increase in intragastric pressure due to a

heavy meal and overdose of sodium bicarbonate caused the rupture. It is further recommended that is the oral use of sodium bicarbonate be discontinued, due to the high mortality rates associated with this lesion.

Reliability : (3) invalid
Relevant methodological deficiencies. Case report described/evaluated by staff treating the patient.

14.05.2002 (41)

Result : PERSONS EXPOSED: A 45 year old man.
EXPOSURE
- Reason of exposure: Ingestion to alleviate epigastric pain.
- Type of exposure: Oral.
- Duration of exposure: Acute.
- Exposure concentrations / dose: Not reported.
- Other information: The patient was admitted after eating an unknown amount of baking soda over the last days for epigastric pain. He had the history of peptic ulcer disease, alcohol abuse hypertension and a seizure disorder.

EXAMINATIONS: Physical, haematology, cardiac.
TREATMENT: After rescucitating the patient with CPR, the metabolic alkalosis was corrected using IV 0.25 N hydrochloric acid.
OTHER:
FINDINGS
- Clinical signs: The patient presented with complaints of burning pain in his arms and legs. He had a cardiopulmonary arrest, following resuscitation without administration of sodium bicarbonate.
- Results of examinations: The arterial blood gas revealed a pH of 7.73, pO2 of 51 mm Hg, and pCO2 of 52 mm Hg.
- Effectivity of medical treatment: Not sufficient.
- Outcome: The patient remained comatose as a result of severe and anoxic encephalopathy and died two weeks later.
OTHER: Not reported.

Reliability : (3) invalid
Relevant methodological deficiencies. Case report described/evaluated by staff treating the patient.

14.05.2002 (52)

Type of experience : Direct observation, clinical cases

Result : PERSONS EXPOSED: A 47 year old female.
EXPOSURE
- Reason of exposure: Unknown.
- Type of exposure: Oral.
- Duration of exposure: Not reported.
- Exposure concentrations / dose: Not reported.
- Other information: Not reported.
EXAMINATIONS: Physical, blood gases, urinalysis.
TREATMENT: She was rehydrated with 0.9% NaCl and K+ supplements and externally rewarmed, and recovered after 48 hours.
OTHER: Not reported.
FINDINGS
- Clinical signs: The patient presented with altered mental status, shallow respiration, profound hypochloremic metabolic alkalosis.
- Results of examinations: The patient was dehydrated, had metabolic alkalosis and altered emntal status.
- Effectivity of medical treatment: Metabolic and respiratory acid-base disturbances tend to compensate for each other, except for metabolic alkalosis where a respiratory acidosis would not be physiologic. Since metabolic alkalosis blunts the chemoreceptor stimulus to breathe, only

hypoxaemia stimulates respiration. Supplemental oxygen caused hypoventilation as it produced neither hypoxaemia nor acidosis. Decreased FiO2 reduced her ability to hypoventilate and her pO2 fell. With supplemental oxygen a near normal pH was maintained. The patient normalised over the following 48 hours.
- Outcome: Full recovery.
OTHER:

Reliability : (3) invalid
Relevant methodological deficiencies. Case report described/evaluated by staff treating the patient.

01.05.2002 (59)

Type of experience : Direct observation, clinical cases
Result : 2 case reports:
(1)
PERSONS EXPOSED: A three-month old girl.
EXPOSURE
- Reason of exposure: Not reported.
- Type of exposure: Oral.
- Duration of exposure: Not reported.
- Exposure concentrations / dose:Not reported.
- Other information: Dosing with medications or bicarbonate was suspected, but denied by the parents. The child formula contained Na 242 mEq/l, K 13 mEq/l, Cl 14 mEq/l and baking soda was found in a can for powdered child formula. The patient had a two-day history of mild diarrhoea and coughing.
EXAMINATIONS: Physical, haematology, urinalysis.
TREATMENT: She was treated for convulsions, and was sedated and mechanically ventillated for 2 1/2 days while lowering her serum sodium level. At this time she was still showing diffuse hypotonia.
OTHER: Not reported.
FINDINGS
- Clinical signs: The patient was admitted when she began to vomit, became lethargic, was afebrile, dehydrated.
- Results of examinations: High serum sodium level.
- Effectivity of medical treatment: Efficient.
- Outcome: Full recovery.
OTHER:

(2)
PERSONS EXPOSED: A 10 months old girl.
EXPOSURE
- Reason of exposure: Ingestion.
- Type of exposure: She was treated with syrup of ipecac for ingesting a single amaryllis leaf.
- Duration of exposure: Not reported.
- Exposure concentrations / dose:Not reported.
- Other information: After an initial trip to the ER she was sent home.
EXAMINATIONS: Not reported.
TREATMENT: Crisis intervention measures included CPR, at tracheal intubation, ECG, intracardeal adrenalin, chest X-ray, and administration of atropine, calcium, isuprel and NaHCO3 (50 mEq).
OTHER: Not reported.
FINDINGS
- Clinical signs: She vomited the following 48 hours, and at 52 hours, developed fever, lethargy and respiration arrest.
- Results of examinations: Not reported.
- Effectivity of medical treatment: Not sufficient.
- Outcome: The patient died.
OTHER: After death was pronounced, laboratory results were: glucose 24 mg%, BUN 35 mg%, Ca 28, Na 183 mEq/l, K 11.5 mEq/l, Cl 104mEq/l and

HCO3 53 mEq/l. At post mortem an infarcted distended stomach was found herniated into the left chest. A malpractice action (failure to recognize hypernatremic dehydration) was rapidly settled. Post mortem poisoning was concluded. It is suggested that baking soda can cause hypernatremia.

Reliability : (3) invalid
Relevant methodological deficiencies. Case report described/evaluated by staff treating the patient.

01.05.2002 (63)

Type of experience : Direct observation, clinical cases

Result : PERSONS EXPOSED: A 58 year old male.
EXPOSURE
- Reason of exposure: The patient said that he regularly ingested antacids to treat an ulcer.
- Type of exposure: Oral.
- Duration of exposure: Not reported.
- Exposure concentrations / dose: Not reported.
- Other information: The patient's medical history showed alcoholic oesophagitis and gastritis, and he admitted to chronic excessive consumption of alcohol.
EXAMINATIONS: Physical, cardiac, haematology.
TREATMENT: He was treated for 11 days with intravenous crystalloids and electrolyte replacement, and rehydrated.
OTHER:
FINDINGS
- Clinical signs: The patient presented with one week of dizziness and diarrhoea. He had treated himself by ingesting antacids.
- Results of examinations: He had pulse 108 beats/min, temperature 39.8C, non-tender hepatomegaly, regular tachycardia. Laboratory values: Na 136 mEq/l, K 2.5 mEq/l, Cl 77 mEq/l, CO2 content 41.4 mEq/l, creatinine 2.4 mg/dl, Mg 1.0 mg/dl, hematocrit 24.5%. Blood pH 7.55, 73 mm Hg, pCO2 49 mm Hg, CO2 44.5 mm/l, base excess of 17.
- Effectivity of medical treatment: The patient's blood levels and physical condition improved. Hematocrit, chloride and creatine levels normalised within 24 hrs of intravenous fluid therapy,and hypomagnesemia within 2 days. Seven days of intravenous and oral potassium replacement were required before resolution of hypokalemia.
- Outcome: Full recovery.
OTHER: The patient presented on 2 further occasions within three months, with metabolic alkalosis and electrolyte abnormalities, admitting to ingesting large amounts of sodium bicarbonate (10-12 oz in a five day periode and 4 oz within 24 hours, respectively). The laboratory values on the first admission are also consistent with HCO3 toxicity. On each of the three occasions, hospital admission was required to normalised levels of HCO3, pH and electrolyte values. The most commonly reported complication of HCO3 toxicity is the hypochloremic metabolic alkalosis, with many reports of HCO3 levels of 40 mEq/l and higher. Hypochloremia, by inhibiting renal excretion of HCO3, appears to play a significant role in the development of metabolic alkalosis in some patients with chronic bicarbonate toxicity. In volume-depleted patients in ingesting sodium HCO3, hypokalaemia results in renal absorption of sodium (and thereby HCO3 as well) to maintain volume. Hypokalaemia is a very common finding in metabolic alkalosis. Hypernatremia may also occur, and is responsible for the acute and chronic hypertensive conditions. High sodium intake occurring with HCO3 ingestion has also resulted in disruption of endocrine maintenance of sodium and potassium homeostasis. Abnormalities in calcium and phosphorus metabolism had also be reported to result from baking soda ingestion. Treatment of toxicity is usually limited to contrivance therapy with saline and, on a case-by-case basis, other electrolytes.

Reliability : (3) invalid

Relevant methodological deficiencies. Case report described/evaluated by staff treating the patient.

01.05.2002 (69)

Type of experience : Direct observation, clinical cases
Result : PERSONS EXPOSED: A 54 year old female.
EXPOSURE
- Reason of exposure: Ingestion of sodium bicarbonate to eliminate an unpleasant feeling of gastric pyrosis.
- Type of exposure: Oral.
- Duration of exposure: Not reported.
- Exposure concentrations / dose: Not reported.
- Other information: Not reported.

EXAMINATIONS: Not reported.
TREATMENT: Emergency surgery.
OTHER: Not reported.
FINDINGS
- Clinical signs: Gastric dilatation, stomach rupture.
- Results of examinations: Not reported.
- Effectivity of medical treatment: Not reported.
- Outcome: Not reported.

Reliability : (4) not assignable
Due to the fact that the article was written in Italian with an English abstract, it was not possible to extract more information.

14.05.2002 (70)

Type of experience : Human - Medical Data
Remark : Although absorption of unneutralised NaHCO3 is known to cause alkalosis, this acid-base disturbance is usually transient in individuals with normal renal function, as the base excess will rapidly be excreted. The urinary pH can, however, be elevated by up to 1 unit, affecting tubular reabsorption and urinary elimination of weak acids and bases.

07.01.2003 (33)

Type of experience : Human - Medical Data
Result : Text of Schenkel and Vorherr (1974): Sodium bicarbonate is a systemic antacid which may produce the "milk alkali syndrome" when used continuously in large activities. Because fetal kidneys cannot excrete an excess of bicarbonate sodium, metabolic alkalosis and edema may occur; a possible overload of the circulatory system may lead to congestive heart failure or to an increased blood pH in both mother and fetus which can be fatal.
Reliability : (4) not assignable
10.02.2003 (65)

5.11 ADDITIONAL REMARKS

Type : Other
Remark : In the EU, NaHCO3 may be used as a human food additive, E 500 ii, with the following restrictions:

a) NaHCO3 is permitted used as a food additive following the "quantum satis" principle (No maximum level is specified. However additives shall be used in accordance with good manufacturing practice, at a level not higher than is necessary to acheive the intended purpose and provided that they do not mislead the consumer.)

b) In cocoa and chocolate products as defined in Directive 73/241/EEC, the

maximum level of NaHCO3 permitted is 7% on dry matter without fat.

c) In partially dehydrated and dehydrated milk as defined in Directive 76/118/EEC, "quantum satis".

d) In soured-cream butter, "quantum satis".

e) In weaning foods, "quantum satis" (only as a rasing agent).

30.07.2002 (17)

Type : other
Remark : NaHCO3 may be used in the EU as an acidity regulator (E 500 II) in the complete feedingstuff of dogs and cats with a moisture content of maximum 12%. There are no specified restrictions with respect to content or other provisions. (Directive 70/524/EEC).

A later amendment states that it is compulsory to declare the sodium content related to the weight of the feed material. (Directive 98/67/EC).

30.07.2002 (16) (18)

Type : other
Result : NaHCO3 may be used as an active ingredient and as an additive in pharmaceutical products for oral administration (most forms) and parenteral administration (under special circumstances). The quality standard must fulfill those set in the "Pharmacopee Europeenne".

30.07.2002 (60)

Type : other
Remark : The specific purity criteria on the use of NaHCO3 as a food additive in the EU is laid down in Directive 2000/63/EC. It states that the purity must be not less than 99% on the anhydrous basis. Loss on drying: not more than 0.25% (over silica gel, 4 hrs).
Ammonium salts: no odour of ammonia detectable after heating.
Arsenic: Not more than 3 mg/kg.
Lead: Not more than 5 mg/kg.
Mercury: Not more than 1 mg/kg.

30.07.2002 (15)

6.1 ANALYTICAL METHODS

6.2 DETECTION AND IDENTIFICATION

7.1 FUNCTION

7.2 EFFECTS ON ORGANISMS TO BE CONTROLLED

7.3 ORGANISMS TO BE PROTECTED

7.4 USER

7.5 RESISTANCE

8.1 METHODS HANDLING AND STORING

8.2 FIRE GUIDANCE

8.3 EMERGENCY MEASURES

8.4 POSSIB. OF RENDERING SUBST. HARMLESS

8.5 WASTE MANAGEMENT

8.6 SIDE-EFFECTS DETECTION

8.7 SUBSTANCE REGISTERED AS DANGEROUS FOR GROUND WATER

8.8 REACTIVITY TOWARDS CONTAINER MATERIAL

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