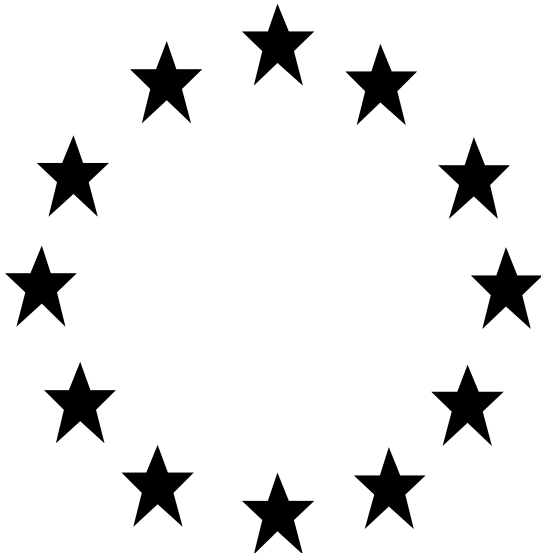

Draft Assessment Report (DAR)

- public version -

Initial risk assessment provided by the rapporteur Member State United Kingdom for the existing active substance

POTASSIUM HYDROGEN CARBONATE

of the fourth stage of the review programme referred to in Article 8(2) of Council Directive 91/414/EEC

Volume 3, Annex B, part 2, B.6

August 2008

B.6 TOXICOLOGY AND METABOLISM

B.6.1 Adsorption, Distribution, Excretion and Metabolism (Toxicokinetics) (Annex IIA, 5.1)

See Volume 1

B.6.2 Acute Toxicity Including Irritancy And Skin Sensitization (Annex IIA 5.2)

The acute oral, dermal and inhalation toxicity, the skin and eye irritation potential and the skin sensitisation potential of potassium bicarbonate were evaluated. The results of these investigations are summarised below.

B.6.2.1 Acute oral toxicity

Acute oral toxicity was investigated in the rat (S.M. Glaza, 1993). The test substance was described as Product 5649, Potassium Bicarbonate - Lot 1268M2, a white powder. Purity : USP Grade Potassium Bicarbonate 99.86 % Potassium Bicarbonate. The study was GLP and carried out in compliance with OECD 401. A single gavage dose of 1500, 2500, 3500 or 5000 mg/kg bw was administered to 5/sex Crl : CD®BR. Mortalities were seen within 24 hours at ≥ 2500 mg/kg bw/day. Clinical signs of toxicity included hypoactivity, staggered gait, soft stool, dark-stained urogenital area, and death. All mortality occurred within 1 day of test material administration. All surviving animals returned to a normal appearance by Day 2. Test material-related lesions at necropsy were limited to coloration changes in the gastric mucosa of the stomach.

The estimated oral LD_{50} values are :

Males: 3 706 mg/kg bw [2 680 to 5 124 mg/kg bw – 95% confidence limits]

Females: 2 064 mg/kg bow [1 569 to 2 715 mg/kg bow – 95% confidence limits]

Sexes combined: 2 825 mg/kg bow [2 222 to 3 592 mg/kg bow – 95% confidence limits]

B.6.2.2 Acute dermal toxicity

Acute dermal toxicity was investigated in the rabbit (S.M. Glaza, 1993). The test substance was described as Product 5649, Potassium Bicarbonate - Lot 1268M2, a white powder. Purity: USP Grade Potassium Bicarbonate 99.86 % Potassium Bicarbonate. The study was GLP and carried out in compliance with OECD 402. The test substance was applied to the health skin of 5/sex New Zealand albino rabbits were dosed dermally with a single topical application at a level of 2 000 mg/kg of body weight. No mortalities were observed during the test period. Dermal irritation consisted of slight to moderate erythema and slight oedema, atonia, and desquamation. No other dermal irritation was observed. All animals appeared clinically normal throughout the study. The estimated dermal LD_{50} for male and female rabbits was determined to be greater than 2 000 mg/kg.

B.6.2.3 Acute inhalation toxicity

Acute inhalation toxicity was investigated in the rabbit (R Shapiro, 1993). The study was GLP and carried out in compliance with OECD 403. The test substance was Biocode # 5692, Potassium Bicarbonate - Lot 3140M3, described as a white crystalline powder. Purity : 99.99 % Potassium Bicarbonate. Five/sex rats were exposed to the test atmosphere for 4½ hours at a gravimetric chamber concentration of 4.88 mg/L.

No mortalities occurred as a result of exposure. The gravimetric chamber concentration was 4.88 ± 0.60 mg/L with approximately 1% of the particles below 1 micron and 25 % below 3 microns. The mass median aerodynamic diameter was approximately 4.7 microns.

All animals recovered from clinical signs within 24 hours and gained weight over the 14-day observation period. Gross necropsy findings at terminal sacrifice were generally unremarkable. The acute (4½ hour) inhalation LC_{50} was greater than 4.88 mg/L.

B.6.2.4 Primary skin irritation

The primary dermal irritation potential of Product 5649, Potassium Bicarbonate was evaluated with 6 rabbits under 4-hour semi-occluded conditions. The test material produced only very slight erythema reactions in two animals and a very slight oedema reaction in one animal. No other dermal irritation was observed. All irritation cleared by the 48-hour observation. The average of the 24-, 48- and 72-hour scores is 0.05 for erythema and eschar formation, and 0.00 for oedema formation.

B.6.2.5 Primary eye irritation

The primary eye irritation potential of Product 5649, Potassium Bicarbonate, was evaluated when instilled into the eye of six rabbits. The test material produced iridal involvement in one animal and moderate to severe conjunctival irritation in all six animals. All treated eyes had returned to a normal appearance by Day 7 after treatment. On the basis of reactions observed and the criteria specified in Council Directive 67/548/EEC, Potassium Bicarbonate does not need to be classified.

B.6.2.6 Skin sensitisation

The delayed contact hypersensitivity potential of Product 5649, Potassium Bicarbonate, was evaluated in albino guinea pigs. The test material, when applied as a 0.2-g dose (moistened with deionised water), did not elicit any dermal reactions at challenge. Based on these results, this test material is not considered to be a dermal sensitiser in guinea pigs.

B.6.2.7 Inhalation

Please see 6.2.3 above.

B.6.2.8 Summary of acute toxicity including irritancy and sensitisation.

The acute toxicity of potassium bicarbonate was low via the oral, dermal and inhalation routes. Minimal reversible skin irritancy was observed. Potassium bicarbonate caused significant conjunctival irritation which reversed within 7 days. There was no evidence of dermal sensitisation.

B.6.3 Short-Term Toxicity

B.6.3.1 Sodium bicarbonate and human health.

Potassium bicarbonate has been reviewed by the US EPA with respect to safety as a food additive and has been granted GRAS (Generally Regarded As Safe) status. The US EPA has determined that no tolerances (or residue limits) are required for potassium bicarbonate when used on food crops as an inert ingredient. This material is found ubiquitously in the environment and is a major component of normal human physiology. As a salt of a weak acid (carbonic acid), potassium bicarbonate will dissociate in an aqueous environment into the anions (bicarbonate (HCO_3^{-1}) and carbonate (CO_3^{-2}) and the positively charged cation, potassium. The potential effects on the human body are therefore from the anion and cation independently and their metabolism and physiological function in the human body is well understood [1].

The average adult (70 kg) daily burden of potassium is approximately 140 g. It is the predominant intracellular cation and plays a vital role in maintenance of electrical excitability of nerve and muscle tissue. It also has an important role in genesis and correction of imbalances of acid-base metabolism, in regulating cellular water content and in regulating blood pressure. Intracellular potassium concentration far exceeds extracellular concentration

[1] Goodman, A., and Gillmans, A., (eds). The Pharmacological Basis of Therapeutics. NY., 8th Edition, Pergamon Press, NY, Toronto, London. 1990.

in mammals and this high concentration gradient from cell to extracellular fluid is very tightly controlled even during extreme degrees of total body potassium surfeit or deficit. Concentration within the plasma is very tightly controlled. The body continually takes in potassium as it is not stored in any tissue (other than in association with glucagen) and is continually lost in the urine. The normal status is 147 mg/liter blood (4.8 mEq/liter). The kidney is the primary system responsible for maintenance of both intracellular and plasma potassium concentrations. The second adaptive response to high potassium intake is extrarenal by distribution to various tissues. A number of endocrine systems are involved through the action of insulin and aldosterone. These systems act together to effectively maintain correct potassium balance even in the face of significant potassium loading. A healthy male is estimated to excrete approximately 2000 mg/day in the urine. The minimum daily requirement is therefore somewhat in excess of 2000 mg/kg in adult individuals (who are not perspiring, not subject to fear or anxiety, and do not have diarrhoea). Some sources (US Academy of Sciences) indicate a daily requirement up to 4500 mg/day in individuals with normal kidney function, and in the absence of other compromising medical conditions.

The bicarbonate anion is the principle buffer of the extracellular compartment in all mammalian organisms, including man. Based on the interrelationship between bicarbonate and carbon dioxide, the body is able to adjust to dramatic shifts in total amount of acid or base produced in a variety of circumstances, either endogenously or exogenously. The amount in the serum is closely maintained at around 26 mEq./L, while the urinary concentrations are variable and dependent upon urinary pH.
Potassium bicarbonate is widely used as an over the counter antacid and the US FDA has set the maximum daily dosage limit at 200 mEq of bicarbonate ion for persons up to 60 years of age and 100 mEq for persons of 60 years or older.

A number of publications were presented which were of some general but limited relevance to human hazard evaluation and risk assessment of potassium bicarbonate. The physiology of both potassium and bicarbonate in the human body are extensively documented and the systems for dealing with excess of either are also well documented in the medical literature. In this context data generated by high exposures of experimental animals are not considered to be very relevant to human hazard evaluation or risk assessment. Those of some interest are summarised below.

B.6.3.2 Summary of experimental data submitted

B.6.3.2.1.

Lina B.A.R., Kuijpers M.H.M. (2004) : Toxicity and carcinogenicity of acidogenic or alkalogenic diets in rats ; effects of feeding NH4Cl, KHCO3 or KCl. Published report : Food and Chemical Toxicology 42 (2004) 135-153.

The effects of diet-induced acid-base disturbances were examined in 4-week, 13-week and 18-month toxicity studies, and in a 30-month carcinogenicity study (Lina and Kuijpers, 2003). The sub-chronic data are summarised here.

The 4-week study:

Rats were fed a natural ingredient diet (controls), supplemented with 2% or 4% KHCO3 (base-forming diets), or with 2% or 4% NH4Cl (acid-forming diets). Only the KHCO3 will be reported here. KHCO3 elevated base excess in the blood and urinary pH and decreased urinary net acid excretion. Clinical condition and death rate were not affected. The feeding of high levels of each salt resulted in growth retardation and increased water intake and urinary volume. Plasma potassium and urinary potassium excretion were increased with KHCO3.Standard haematological and clinical chemistry parameters were not affected.

The 13-week study:

NH4Cl induced the expected metabolic acidosis in the rats.The feeding of KHCO3 induced effects opposite to NH4Cl, by elevating base excess in blood and urinary pH and decreasing urinary net acid excretion.The feeding of K+ and Cl- as 3% KCl (additional control group) in

amounts equimolar to those provided by 4% KHCO3 and 2.1% NH4Cl, respectively, did not affect the acid-base balance, because the base-forming character of K+ was compensated by the acid-forming character of the Cl. Treatment with KHCO3 and KCl resulted in similarly increased plasma potassium levels. The plasma chloride concentration was increased with NH4Cl but not with equimolar amounts of KCl.The increased potassium levels in the plasma of rats fed KHCO3 or KCl were associated with hypertrophy of the adrenal zona glomerulosa and increased potassium excretion. The concentration of potassium in plasma has been shown to be a powerful regulator of aldosterone secretion. A high rate of potassium directly stimulates the secretion of aldosterone that in turn stimulates potassium excretion in the distal nephron.The hypertrophy of the zona glomerulosa observed with either KHCO3, KCl and NH4Cl is ascribed to chronic stimulation of the adrenal cortex by either K+ or by NH4Cl induced acidosis.

B.6.3.2.2

De Groot A.P., Feron V.J. and Immel H.R. (1988): Induction of hyperplasia in the bladder epithelium of rats by a dietary excess of acid or base : implications for toxicity/carcinogenicity testing.Published report : Food and Chemical Toxicology 26 (5) 425-434, 1988.

In previous studies, an increased incidence of hyperplasia was observed in the epithelium of the urinary bladder of rats fed cereal-based stock diet supplemented with 6% monosodium glutamate (MSG) for 3 months. Hyperplasia of the bladder epithelium was induced not only by feeding MSG, but also by feeding 5% of the alkalizing salt KHCO3, both in purified diet (acid casein supplemented with methionine)and in stock (cereal based open formula diet) diet. In the current study two experiments were carried out. In the first, groups of 10 male rats were fed unsupplemented stock diet or this diet containing 6% MSG, or 6% MSG + 1.6% NaHCO3, or 6% MSG + 1.0% NH4Cl, or 2.5% KHCO3 for 13 weeks. In the second experiment the effects of a high level of an alkalizing salt (5% KHCO3) in stock diet and in purified diet and the changes induced by a high level of an acidifying agent (5% NH4Cl), were compared in a 13-week feeding study.The rats were gradually accustomed to the high levels of the supplements by feeding 1% in week 1, 2% in wk 2, 3% in wk 3, 4% in wk 4 and 5, and 5% from wk 6 to wk 13.

In the first experiment, feeding 2.5% KHCO3 for 13 weeks had the effect of reducing growth rate (slight), increasing relative kidney weight (statistically significant $p<0.01$), increased urinary pH, and an increase in moderate grade diffuse epithelial hyperplasia of the urinary bladder and intra-epithelial cysts. In the second experiment, upon supplementing stock diet or purified diet with KHCO3, the expected increase in HCO3- ion concentration was observed, as well as decreases in total titratable acid and net acid concentration. Moreover there was considerable decrease in NH4+ ion concentration in these supplemented groups. Treatment-related changes were seen in the urinary bladder epithelium. These changes comprised various forms and degrees of epithelial hyperplasia and very small intra-epithelial cyst. An increased incidence and severity of hyperplasia occurred in each of the two groups receiving KHCO3. More severe, papillomatous hyperplasia was present in one rat fed KHCO3 in stock diet (cereal based open formula diet) and in two rats fed NH4Cl in the purified diet (acid casein supplemented with methionine). Both the incidence and the degree of the epithelial changes indicated a more marked effect of KHCO3 in the stock diet than in the purified diet.

These findings showed that hyperplasia of the bladder epithelium of rats can be induced both by acidifying and by alkalizing the urine through manipulation of the acid-base balance of the basal diet through excess of either NH4Cl or KHCO3.

B.6.4. Genotoxicity (Annex IIA, 5.4)

It is reported in the Church & Dwight, 1994 paper, submitted by the notified, that potassium carbonate has been tested and found to be negative in assays conducted with Saccharomyces cerreviseae, strain D4 and (Ames test) Salmonella typhimurium, stains TA-92, TA-1535, TA-100, TA-1537, TA-94, TA-137, or TA-1538. The tests were conducted with and without liver microsome fraction and several of the studies were also conducted with activation assays prepared from liver, lungs and testes of mice, rats and monkeys. The actual studies or study

summaries were not submitted.

B.6.5 Long Term Toxicity And Carcinogenicity (Annex IIA, 5.5)

B.6.5.1

A review by S.M. Cohen of the data on carcinogenicity of sodium salts (sodium saccharin, sodium ascorbate) and the mechanism involved was presented. The sodium and potassium of salts of various anions including sodium saccharin, sodium ascorbate, sodium bicarbonate, potassium bicarbonate and potassium carbonate have been shown to be non-genotoxic promoters of bladder carcinogenicity in the male rat. Since this paper was prepared (1994), it has been demonstrated that potassium bicarbonate also can act as a weak initiator of bladder tumors in the rat (summarised below in B.6.5.2). These results are consistent with the known nongenotoxic mechanism of bladder carcinogenesis in the rat. This mechanism involves long-term alteration (elevation) of urinary pH, formation of urinary crystals and calculi leading to transitional epithelial cell damage and proliferation. Male rats had been previously shown to be most sensitive to this effect of salts of weak acids. The high urinary protein of male rats was considered the main factor in this sex difference. An epigenetic mechanism was elucidated which is dose-dependent with a threshold effect (no-observed-effect level of 1% (≈ 0.5 g/kg/day) in the rat diet. This has been established as the no-effect level for sodium on the various urothelial changes, whether proliferative, tumor enhancement, or carcinogenicity. This mechanism is not considered to be of relevence to man. A recent publication on this subject is summarised below and demonstrates that both male and female rats are sensitive to this effect.

B.6.5.2 18-month and 30-month feeding study in the rat

Lina B.A.R., Kuijpers M.H.M. (2004) : Toxicity and carcinogenicity of acidogenic or alkalogenic diets in rats ; effects of feeding NH4Cl, KHCO3 or KCl.Published report : Food and Chemical Toxicology 42 (2004) 135-153.

18-month and 30-month studies.

15/sex rats 18-month study) and 50/sex rats (30-month) study) were fed a natural ingredient diet (controls), supplemented with 2% or 4% KHCO3 (base-forming diets), or with 1% or 2.1% NH4Cl (acid-forming diets). Additional controls were fed 3% KCl (neutral diet providing K+ and Cl- in amounts equimolar to those in the 4% KHCO3 diet and the 2.1% NH4Cl diet, respectively).

Conclusions:

NH4Cl induced the expected metabolic acidosis, as shown by decreased base excess in blood, decreased urinary pH and increased urinary net acid excretion. KHCO3 induced the opposite effects. Clinical condition and death rate were not affected. The feeding of high levels of each salt resulted in growth retardation and increased water intake and urinary volume. Plasma potassium and urinary potassium excretion were increased with KHCO3 and KCl. Plasma chloride was increased with NH4Cl, but not with KCl. Urinary calcium and phosphate excretion were increased with NH4Cl, but there were no indications that bone minerals were involved (weight, calcium content and fat free solid of the femur were not affected). Standard haematological and clinical chemistry parameters were not affected. Kidney weights were increased with 2.1% NH4Cl. Hypertrophy of the adrenal zona glomerulosa occurred with KHCO3, KCl and NH4Cl, due to chronic stimulation of the adrenal cortex by either K+ or by NH4Cl-induced acidosis. An early onset (from week 13) of oncocytic tubules was noted in the kidneys of rats fed KHCO3 and, after 30 months, the incidence of this lesion was much higher than the background incidence in ageing controls. No progression to oncocytomas was noted. KCl showed only slight effects on the early onset of oncocytic tubules (from 18 months). In contrast, the severity of nephrosis and the incidence of oncocytic tubules were decreased with 2.1% NH4Cl, suggesting a protective effect of acidosis. The feeding of KHCO3 resulted in hyperplasia, papillomas and carcinomas of the urinary bladder. With KCl only a slight increase in proliferative urothelial lesions was noted. Apart from these pre-neoplastic and neoplastic lesions in the urinary bladder, there were no treatment-related differences in tumour response among the groups.

In summary, it may be concluded that most of the observed changes can be regarded as physiological adaptations to the feeding of acid-, base-forming or neutral salt, and that the rats showed a remarkable adaptive capacity to life-long exposure to the acid or base load. Adverse effects were noted with KHCO3, and to a far lesser extent with KCl, and consisted of renal oncocytic tubules, and hyperplastic and neoplastic lesions of the urinary bladder.

B 6.6 Reproduction And Developmental Toxicity Studies (Annex IIA. 5.6)

No data specific to potassium bicarbonate has been submitted. A review of the status of sodium bicarbonate with respect to reproductive toxicity was considered relevant to this point. The current US FDA GRAS report (1975) was referred to in which a number of studies were considered. It was reported that sodium bicarbonate did not induce teratogenic effects when administered orally at the following doses : 580 mg/kg/day (mice) day 6 through 15 of gestation, 340 mg/kg/day (rats) 6 through 15, and 330 mg/kg/day (rabbits) day 6 through 18 of gestation. A study carried out with potassium carbonate was also reported. In this study the administration of up to 290 mg per kg to pregnant mice and up to 180 mg per kg to pregnant rat for 10 consecutive days (day 6 through day 15 of gestation) had no clearly discernible effect on nidation or on maternal or fetal survival. The number of abnormalities in either soft or skeletal tissues of the test group did not differ from the number occurring in the sham-treated controls (Church & Dwight Co-Anonymous 1, 1994; Church & Dwight Co-Anonymous 2, 1994).

B.6.7 Delayed Neurotoxicity studies (annex 11a, 5.7)

There were no observations in short-term animal studies indicating a requirement for neurotoxicity testing.

B.6.8 Further Toxicological Studies (Annex IIA, 5.8)

No toxicity studies on metabolites need to be conducted since potassium bicarbonate is rapidly disassociated in the mammalian organism to the cation K+ and the anion HCO3-.

B.6.9 Medical Data And Information (Annex IIA, 5.9)

B.6.9.1 Report on medical surveillance on manufacturing plant personal

The notified has reported that there have been no cases of unexpected effects.

B.6.9.2 Report on clinical cases and poisoning incidents

No cases of poisoning have been reported by the company

B.6.9.3 Observations on exposure of the general population and epidemiological studies

Lindinger et al (2000) studied the acute response of the kidneys in correcting plasma volume, acid-base, and ion disturbances resulting from NaHCO3 and KHCO3 ingestion. Renal excretion of ions and water was studied in five men after ingestion of 3.57 mmol/kg body mass of sodium bicarbonate (NaHCO3) and, in a separate trial , potassium bicarbonate (KHCO3).

In the KHCO3 trial, arterial plasma K+ concentration rapidly increased from 4.25±0.10 to a peak of 7.17±0.13 mEq/L 140 min after the beginning of ingestion. This increase resulted in a pronounced, transient diuresis, with cumulative urine output at 270 min similar to the volume ingested, natriuresis and a pronounced kaliuresis that was maintained until the end of the experiment. Cumulative (above basal) renal K+ excretion at 270 min accounted for 26±5% of ingested K+. The kidneys were important in mediating rapid corrections of substantial portions of the fluid and electrolytes disturbances from ingestion of KHCO3 and NaHCO3 solutions.

Dietary intake by humans of alkalinizing potassium salts has been demonstrated to exert profound beneficial effects on calcium balance, bone mineralization, predisposition to calcium

oxalate nephrolithiasis, and overall nitrogen balance. Dietary sodium restriction has also been shown to improve calcium balance, bone mineralization, and the effectiveness of neuro-humoral defences against orthostatic hypotension (Fettman, 2000).

B.6.9.4 Clinical signs and symptoms of poisoning and details of clinical tests

No acute health effects are known from potassium bicarbonate. At high single or daily contacts slight skin or eye irritation may occur.

B.6.9.5 First aid measures, therapeutic regimes

On contamination remove to fresh air. Wash with plenty of water and soap in the case of skin contact. Wash with plenty of water in the case of eye contact. No specific toxic symptoms known. Symptomatic medical treatment.

B.6.9.6 Expected effects and duration of poisoning as a function of the type, level and duration of exposure or ingestion. Expected effects and duration of poisoning as a function of varying time periods between exposure or ingestion and commencement of treatment

Overdose : Confusion; irregular or slow heartbeat; numbness or tingling in hands, feet or lips; shortness of breath or difficult breathing; paralysis of arms and legs, blood pressure drop; convulsions, coma, cardiac arrest.

B.6.10 Summary Of Mammalian Toxicology And Proposed Adi, Aoel, Arfd And Drinking Water Limit (Annex IIA, 5.10)

B.6.10.1 Toxicological properties.

B.6.10.2 Allowed Daily Intake (ADI)

It has been proposed by the notified that as potassium bicarbonate is available and extensively used as an over-the-counter antacid preparation, an ADI is not required. This approach is considered acceptable.

B.6.10.3 Drinking Water Limit.

Not relevant.

B.6.10.4 Acceptable Operator Exposure Level (AOEL)

The notifier has proposed using the Normal Daily Requirement (NDR) for potassium as the AOEL, without a safety factor. This is in the region of 3,500 gms/adult person/day and equivalent ot 8.96 gms potassium bicarbonate/day and 128 mg potassium bicarbonate/kg bw/day. As the estimate of operator exposure using the UK POEM is 5.8 mg/kg/day without PPE, exposure to potassium bicarbonate from pesticidal use will not impact on potassium balance in the human body.

B.6.10.5 Acute Reference Dose (ARfD)

Due to the low acute toxic potential of potassium bicarbonate, the allocation of an ARfD was not considered required.

B.6.10.6 Proposal for labelling.

According to the data presented potassium bicarbonate does not require classification.

B.6.11 Acute Toxicity Including Irritancy And Skin Sensitization Of Preparations (Annex IIIA, 7.1)

B.6.11.1 Acute Toxicity

B.6.11.1.1 Acute oral toxicity in the rat.

Report: Single Dose Oral Toxicity in Rats / LD50 in Rats.
Author: Cerven D. R
Date of Report: 1995
Report Identity: N° MB 95-4666 A.

Testing Facility: [redacted]

GLP: Yes
Test Substance: Fungicide 2346-102, a white powder, Lot 2386-118.
Guidelines: EPA Guidelines 81-1 (EPA GLP 40 CFR Part 160); OECD 401
Deviations: None
Acceptable: Yes

Materials and Methods:

Five healthy male and five healthy female Wistar Albino rats were given a single oral dose of Fungicide 2346-102, suspended in distilled water, at a dose level of 5.0 g/kg of body weight, and were observed for 14 days.

Finding:

The deaths occurred by Day 1 and were preceded by physical signs of diarrhea, lethargy, coma, ataxia, dyspnea, soiling of the anogenital area and wetness of body areas. Necropsy of the dead animals revealed abnormalities of the lungs, liver, kidneys, spleen and gastrointestinal tract as well as wetness and red or brown staining of the nose/mouth area, and brown staining, wetness and soiling of the anogenital area. Physical signs noted in survivors included diarrhea, soiling of the anogenital area, lethargy, ataxia and wetness of the anogenital area. Body weight changes and necropsy results of survivors were normal.
The number of animals that died and the time of death are summarised in Table B.6.11.1.1-1

Table B.6.11.1.1-1 Acute oral toxicity of ARMICARB 85SP to the rat

Dose (mg/kg)	Males (Died/Treated)	Time to death	Females (Died/Treated)	Time to Death
1.0	0/5	-	0/5	-
2.0	0/5	-	0/5	-
2.5	1/5	day 1	2/5	day 1
3.0	2/5	4h/day 1	5/5	2h/day 1
5.0	5/5	4h/day 1	5/5	2h/day 1

Conclusion:

The LD50 and 95% confidence intervals were :
males – 2.9 (2.5 – 3.3) g/kg
females : 2.6 (2.3 – 2.9) g/kg
combined : 2.7 (2.5 – 2.9) g/kg.
According to Council Directive 99/45/EC and Commission Directive 2001/59/EC (adaptation to 67/548/EEC) no classification is required.

B.6.11.1.2 Acute dermal toxicity in the rabbit.

Report: Single Dose dermal Toxicity in Rabbits / LD50 in Rabbits.
Author: Cerven D. R
Date of Report: 1995
Report Identity: N° MB 95-4666 B.
Testing Facility: [redacted]

GLP: Yes
Test Substance: Fungicide 2346-102, a white powder, Lot 2386-118, purity not specified.
Guidelines: EPA Guidelines 81-2 (EPA GLP 40 CFR Part 160); OECD 402
Deviations: Environmental conditions not specified.
Acceptable: Yes

Materials and Methods:

Five healthy male and five healthy female New Zealand albino rabbits were dosed dermally with Fungicide 2346-102, at 5.0 g/kg of body weight. The test article was applied to the prepared site (dorsal area of the trunk, approximately 10% of the body surface, clipped free of hair), moistened with distilled water and covered with a four layered surgical gauze patch. The torso was wrapped with plastic which was secured with non-irritation tape. The test article was kept in contact with the skin for 24 hours.

Findings:

There were no mortalities. Instances of few faeces and diarrhoea were noted during the observation period. Draize dermal scores, well defined to severe on Day 1, were severe on Day 7, and absent to normal by Day 14. Additionally, instances of moderate to severe eschar, shiny areas of skin and poor hair regrowth, indicative of injuries in depth were noted on days 7 and 14. Body weight changes were normal in 8/10 animals. One male and one female lost weight during the first week of the study but returned to normal by Day 14. Necropsy revealed treated skin abnormalities (the nature of the abnormalities was not specified).

Conclusion:

The LD50 is greater than 5.0 g/kg of body weight. According to Council Directive 99/45/EC and Commission Directive 2001/59/EC (adaptation to 67/548/EEC) no classification is required.

B.6.11.1.3 Acute inhalation toxicity in the rat.

Report:	Inhalation Toxicity in Rats.
Author:	Cerven D. R
Date of Report:	1995
Report Identity:	N° MB 95-4709 E.
Testing Facility:	[redacted]
GLP:	Yes
Test Substance:	Fungicide 2346-102, a white powder, Lot 2386-118, purity not specified.
Guidelines:	EPA Guidelines 81-3 (EPA GLP 40 CFR Part 160); OECD 403
Deviations:	None
Acceptable:	Yes

Materials and Methods:

Five Wistar Albino rats of each sex were exposed (whole-body) to an aerosol atmosphere of Fungicide #2346-135 at a concentration of 2.3 mg/L for a period of 4 hours. Following exposure, the animals were returned to individual housing and observed for 14 days. All rats were monitored hourly during the 4 hour exposure period, again at one hour following exposure and once daily thereafter for 14 days for toxicity and pharmacological effects. The rats were observed twice daily for mortality. Body weights were recorded prior to exposure, weekly and at death or termination in the survivors. All animals were examined for gross pathology.

Findings:

An aerosol was generated using a Venturi Dust Generator and the particle analysis is given below.

Table B.6.11.1.3-1: Particule size analysis

Sample No.	Sampling time minutes	MMAD (microns)[1]	SD[2]
I	1	3.20	2.45
II	1	2.91	2.27

[1)] mass median aerodynamic diameter
[2)] geometric standard deviation

All animals survived the exposure to 2.3 mg/l for four hours. Body weight was not affected in 9/10 animals and was reduced in one female during the second week of observation. Physical signs noted through day 1 included wetness of body areas, lethargy, dyspnea, piloerection, red and brown staining of the nose/mouth area, wetness of the nose/mouth area, licking inside of mouth, hunched posture, coating of the fur with test article, ocular abnormalities and laboured breathing. All animals appeared normal from day 2 through day 14. There were no abnormalities at necropsy.

Conclusions:

The LC50 was greater than 2.3 mg/L, the maximum concentration obtained.
No classification is required.

B.6.11.1.2 Acute dermal toxicity in the rabbit.

Report: Primary Dermal Irritation in Albino Rabbits..
Author: Kieffer, L.
Date of Report: 1995
Report Identity: N° MB 95-4666 C.
Testing Facility: [redacted]
GLP: Yes
Test Substance: Fungicide 2346-102, a white powder, Lot 2386-118, purity not specified.
Guidelines: EPA Guidelines 81-5 (EPA GLP 40 CFR Part 160); OECD 404
Deviations: Environmental conditions not specified.
Acceptable: Yes

Materials and Methods:

Six healthy New Zealand albino rabbits (4 males – 2 females) were dosed dermally with Fungicide 2346-102. The test article (0.5 g) was applied semi-occluded to one intact site/rabbit (dorsal area clipped free of hair, approximately 10 cm²) and covered with a four layered 6 cm² surgical gauze patch moistened with distilled water. The test article was kept in contact with skin for 4 hours. The dermal reactions were scored at 30 to 60 minutes after removal of wrapping and again at 24, 48 and 72 hours. The skin was also evaluated for ulceration and necrosis, or any evidence of tissue destruction at these time periods. Body weights were recorded pre-test. The primary irritation index was calculated.

Result:

Application of Fungicide2346-102 / ARMICARB 85SP to the skin of rabbits under 4-hour semi-occluded conditions resulted in only very slight erythema reactions (grade 1) in three animals and a very slight edema reaction(grade 1) in one animal at the notation 30-60 mn. These reactions had reversed by 24 hours. The mean score of the 24-, 48- and 72-hour notations is 0.00 for erythema and eschar formation, and 0.00 for edema formation.

Conclusion:

On the basis of the degree of skin reactions observed, and the criteria specified in Council Directive 67/548/EEC, Fungicide2346-102 / ARMICARB 85SP does not classify as a skin irritant.

B.6.11.1.5 Eye irritation in the rabbit.

Report:	Primary eye irritation/corrosion in Albino Rabbits..
Author:	Kieffer, L.
Date of Report:	1995
Report Identity:	N° MB 95-4666 D.
Testing Facility:	[redacted]
GLP:	Yes
Test Substance:	Fungicide 2346-102, a white powder, Lot 2386-118, purity not specified.
Guidelines:	EPA Guidelines 81-4 (EPA GLP 40 CFR Part 160); OECD 405
Deviations:	Environmental conditions not specified.
Acceptable:	Yes

Materials and Methods:

Six healthy New Zealand albino rabbits (4 males – 2 females) were dosed with Fungicide 2346-102. The test article (0.1 mL) was into the conjunctival sac of one eye of each rabbit. Ocular responses were recorded at 1 hour post dose and on Days 1, 2, 3, 4 and 7. Sodium fluorescein was used to determine corneal effects on Day 1. Body weights were recorded pre-test. Scoring was carried out in accordance with the Draize method, and the mean irritation indices at 24, 48 and 72 hours, for the six rabbits, were calculated.

Results:

There was no corneal opacity noted at any observation period. Iritis (grade 1), noted in 4/6 eyes, was cleared by 72 hours. Moderate to severe conjunctival erythema (grade 1 to 3) was noted in 6/6 eyes by 24 hours, resolved to mild to moderate by 72 and was fully resolved by Day 7. Severe chemosis occurred in 5/6 animals within 1 hour. Moderate chemosis was recorded in all animals by 24 hours and resolved in 2/6 by72 hours, and in 6/6 by day 7. There were no abnormal physical signs noted during the observation period.

Table B.6.11.1.5-1: Eye irritation of rabbits by Fungicide2346-102 / ARMICARB 85SP. Individual and mean eye irritation scores according to Draize

Item	Reading hours/days	Rabbit number 1	2	3	4	5	6	Mean scores 24-72 h
Cornea								
- degree of opacity	1 h	0	0	0	0	0	0	
- area of involvement		0	0	0	0	0	0	
- degree of opacity	24 h	0	0	0	0	0	0	
- area of involvement		0	0	0	0	0	0	
- degree of opacity	48 h	0	0	0	0	0	0	
- area of involvement		0	0	0	0	0	0	
- degree of opacity	72 h	0	0	0	0	0	0	
- area of involvement		0	0	0	0	0	0	
- degree of opacity	4 d	0	0	0	0	0	0	
- area of involvement		0	0	0	0	0	0	
- degree of opacity	7 d	0	0	0	0	0	0	0.00
- area of involvement		0	0	0	0	0	0	
Iris	1 h	1	1	0	1	1	0	
	24 h	1	0	0	1	1	0	
	48 h	0	0	0	1	1	0	
	72 h	0	0	0	0	0	0	0.28
	4 d	0	0	0	0	0	0	
	7 d	0	0	0	0	0	0	
Conjunctiva								
- redness	1 h	1	1	2	1	2	1	
- chemosis		3	3	3	3	3	2	
- discharge		3	3[a]	2	2	2	2[a]	
- redness	24 h	2	2	2	3	3	2	
- chemosis		2	2	2	2	2	2	
- discharge		2	2	2	2	2	2	Redness 2.11
- redness	48 h	2	2	2	2	3	2	
- chemosis		1	2	1	2	2	1	chemosis1 .61
- discharge		1	2	0	1	2	1	
								discharge 0.78
- redness	72 h	1	1	1	1	2	1	
- chemosis		1	2	0	2	2	0	
- discharge		0	0	0	0	1	0	
- redness	4 d	0	1	0	1	2	0	
- chemosis		1	1	0	1	1	0	
- discharge		0	0	0	0	0	0	
- redness	7 d	0	0	0	0	0	0	
- chemosis		0	0	0	0	0	0	
- discharge		0	0	0	0	0	0	

Conclusion:

Instillation of 0.1 mls of Armicarb 85 SP caused significant conjunctival irritation which resolved relatively slowly over a period of 7 days. Classification is not indicated according to the criteria outlined in EU 91/414. However, attention should be drawn to the significant irritancy potential by use of appropriate safety phrases.

B.6.11.1.5 Dermal sensitisation.

Report: Delayed Contact Dermal Sensitization Test (Buehler Method).
Author: Newcombe, T., 1995.
Date of Report: 1995
Report Identity: N° MB 95-4666 F.
Testing Facility: [redacted]
GLP: Yes
Test Substance: Fungicide 2346-102, a white powder, Lot 2386-118, purity not specified.
Guidelines: EPA Guidelines 81-6 (EPA GLP 40 CFR Part 160); OECD 406
Deviations: Environmental conditions not specified.
Acceptable: Yes

Materials and Methods:

An irritation screening study was conducted to determine the irritation threshold of the test material. Fifteen healthy male Hartley albino guinea pigs were assigned to the study. Ten guinea pigs (Group 1) received three topical inductions over a three week period of 100% concentration of moistened test article. Five guinea pigs (Group 2) served as the naïve control for the test article treated animals during the induction period. Two weeks following the third induction, Group 1 and 2 were challenge with a 75% concentration of the moistened test article.Skin reactions of the animals in Group 1 were recorded at 24 and 48 hours following each induction dose. The skin reactions of all animals were recorded at 24, 48 and 72 hours following the challenge dose (grade 0 to 3). Two indices were calculated from the erythema scores :The incidence index was calculated by counting the number of animals showing an erythema response (1 or greater) for a specified time period and dividing by the number of animals examined at that time period. The severity index was calculated by adding the erythema scores for a specified time period and dividing by the number of scores added. A score of 1 or greater at challenge in 20% or more of the animals is indicative of a sensitizing response. Body weights were recorded pre-test, the day following the last induction and the day following the challenge application. The animals were observed once daily for mortality and toxicity.

Results:

All animals appeared normal throughout the study. Body weight changes were normal. Erythema was absent to moderate during the induction phase. The test article was used as received and moistened with 0.1 mL of distilled water. Erythema (grade 1) was recoreded in1/10 animals at 24 hours only. Erythema was absent in the controls. The test article was used as a 75% dilution in distilled water. The positive control animals were considered to have been sensitised with mild to moderate erythema recorded at the 0.1% w/w concentration of DNCB in acetone at challenge.

Conclusion:

According to the criteria the test substance was negative under the above conditions and classification was not required.

B.6.11.1.6 Summary of acute toxicity of the preparation.

The acute toxicity of Armicarb 85 SP was very similar to that of the active ingredient, potassium bicarbonate. Toxicity was low via the oral, dermal and inhalation routes. Significant dermal irritation was seen in the dermal toxicity study following 24 hour semi-

occluded exposure. It was not irritating to the skin following acute (4 hour) exposure. Armicarb 85 SP caused significant conjunctival irritation which reversed within 7 days. There was no evidence of dermal sensitisation.

B.6.11.1.6-1 Summary of acute toxicity of Armicarb 85 SP

Parameter	Species	Result	Classification	Reference
Acute oral toxicity	Rat	(♂)LD50 = 2 600 mg/kg (♀)LD50 = 2 700 mg/kg (combined) LD50 = 2 900 mg/kg	Not required	Cerven D. R. (1995)
Acute dermal toxicity	Rat	LD50 : > 5 000 mg/kg	Not required	Cerven D. R. (1995)
Acute inhalation toxicity	Rat	LC50–4 hour : > 2.3 mg/L	Not required	Cerven D. R. (1995)
Skin irritation	Rabbit	Non irritant	Not required	Kieffer L. (1995)
Eye irritation	Rabbit	Moderate, reversible irritant	Not required	Cerven D. R. (1995)
Skin sensitisation (Buehler test)	Guinea-pigs	Not sensitising	Not required	Newcomb T. (1995)

B.6.12 Dermal Absorption (Annex IIA, 7.3)

In absence of specific data, the UK model requires use of 10% percutaneous absorption default value and 1% default value for penetration through gloves (based on ARMICARB 85SP being a solid formulation), and a value of 100 % for dermal absorption from the formulation during mixing/loading and spraying.

B.6.13 Toxicological Data On Non-Active Substances (Annex IIIA, 7.4 And Point 4 Of The Introduction)

No data.

B.6.14 Exposure Data (Annex IIIA, 7.2)

ARMICARB 85SP is intended for use on vines / powdery mildew and apples / scab. The amount used is 2 125-5 100 grams of active ingredient/ha/treatment with a maximum of 8 applications, and spray interval of 8-10 days.
All the calculations will be made using the maximum used dose i.e. 5 100 g of potassium bicarbonate/ha (i.e. 6 kg ARMICARB 85SP / ha).

Table B.14-1: Recommended use rate and details on application

Crop			Spray volume	Maximum in-use conc. of a.i.	Application technique
	Kg product/ha	G a.i./ha	(L/ha)		
Apples	6.0	5100	500-1000L	8.5	Tractor-mounted/trailed broadcast air-assisted sprayer
Vines	6.0	5100	200-600 L	25.5	Tractor-mounted/trailed broadcast air-assisted sprayer, low volume

The calculation parameters (worst case) for APPLES are as follows :

Area treated per day	15 ha for the calculations using the German Model and the UK-POEM.
Work rate per day	6 hours
Application dose	4 250 g a.i./ha
Spray volume	500 L/ha - Not relevant for the German model
Packaging	25 kg - Not relevant for the German model
Standard operator body weight	70 kg for the calculations using the German Model and 60 kg for the calculations using the modified UK-POEM.

The calculation parameters (worst case) for VINES are as follows :

Area treated per day	15 ha for the calculations using the German Model and the UK-POEM.
Work rate per day	6 hours
Application dose	4 250 g a.i./ha
Spray volume	200 L/ha - Not relevant for the German model
Packaging	25 kg - Not relevant for the German model
Standard operator body weight	70 kg for the calculations using the German Model and 60 kg for the calculations using the modified UK-POEM.

Calculations were made using the UK-POEM and the German Model as follows:

UK-POEM	No-PPE	Mixing/loading Application	No gloves No gloves
	PPE	Mixing/loading Application	Gloves No gloves
German model	No PPE	Mixing/loading Application	No gloves No gloves
	PPE	Mixing/loading Application	Gloves No gloves

Table B.14-2: Summary of exposure estimates and risk quotients.

Model	PPE	Estimated exposure (mg/kg/day)	AOEL (mg/kg/day)	% of AOEL
Apple				
UK-POEM	no PPE	4.68	128	3.66
	PPE (gloves during mixing/loading	2.96	128	2.32
German model	no PPE	2.01	128	1.57
	PPE (gloves during mixing/loading/spraying	1.36	128	1.06
Vines				
UK-POEM	no PPE	5.78	128	4.52
	PPE (gloves during spraying)	4.06	128	3.18
German model	no PPE	2.01	128	1.57
	PPE (gloves during mixing/loading/spraying)	1.36	128	1.063

The AOEL is not exceeded in any of the use scenarios outlined above with or without PPE.

6.15 Refereneces Relied On.

Annex point/ reference number	Author(s)	Year	Title Source (where different from company) Company name, Report No., GLP status (where relevant) published or not	Data protection claimed	Owner
IIA 5.1/01	Cohen S.	1994	Review of the Carcinogenic Risk of Bicarbonates and Carbonates.University of Nebraska Medical Center, 600 South 42nd Street, Omaha, NE 68198-3135. Not GLP, Unpublished	No	Armand Products Company
IIA 5.1/02	Church & Dwight Co-Anonymous1	1994	ArmicarbTM, A safe and efficacious Pest Management Alternative.Dossier submitted by Church & Dwight Co, Inc. to US EPA for review under Safer Pesticide Policy. Not GLP, Unpublished	No	Armand Products Company
IIA 5.1/03	Church & Dwight Co-Anonymous2	1994	Food Grade Sodium Bicarbonate, and Potassium Carbonate : A Safe and efficacious Pest Management Alternatives.Dossier submitted by Church & Dwight Co, Inc. to US EPA for review under Reduced-Risk Pesticide Initiative. Not GLP, Unpublished	No	Armand Products Company
IIA 5.2.1	Glaza S. M.	1993	Acute Oral Toxicity Study of Product 5649 Potassium Bicarbonate Lot # 1268M2 in Rats. [redacted] Report N° HWI 30100993 GLP, Unpublished	Yes	Armand Products Company.
IIA 5.2.2	Glaza S. M.	1993	Acute Dermal Toxicity of Product 5649, Potassium Bicarbonate - Lot # 1268M2 in Rabbits [redacted] Report N° HWI 30100994. GLP, Unpublished	Yes	Armand Products Company.

Annex point/ reference number	Author(s)	Year	Title Source (where different from company) Company name, Report No., GLP status (where relevant) published or not	Data protection claimed	Owner
IIA 5.2.3	Shapiro R.	1993	EPA Acute Inhalation Limit Test : Potassium Bicarbonate, Lot # 3140M3 [redacted] Report No T-2630. GLP, Unpublished	Yes	Armand Products Company.
IIA 5.2.4	Glaza S. M.	1993	Primary Dermal Irritation Study of Product 5649, Potassium Bicarbonate, Lot # 1268M2 in rabbits.[redacted] Report No HWI 30100995. GLP, Unpublished	Yes	Armand Products Company.
IIA 5.2.5	Glaza S. M.	1993	Primary Eye Irritation Study of Product 5649, Potassium Bicarbonate, Lot # 1268M2 in rabbits [redacted] Report No HWI 30100996. GLP, Unpublished	Yes	Armand Products Company.
IIA 5.2.6	Glaza S. M.	1993	Dermal Sensitization Study of Product 5649, Potassium Bicarbonate, Lot # 1268M2 in guinea pigs- Closed Patch Technique [redacted] Report No HWI 30100997. GLP, Unpublished	Yes	Armand Products Company.
IIA 5.3.1	Lina B.A.R.,Kuijpers M.H.M.	2004	Toxicity and carcinogenicity of acidogenic or alkalogenic diets in rats ; effects of feeding NH4Cl, KHCO3 or KCl.Food and Chemical Toxicology 42 (2004) 135-153. Report No : not stated Not GLP, Published	No	-

Annex point/ reference number	Author(s)	Year	Title Source (where different from company) Company name, Report No., GLP status (where relevant) published or not	Data protection claimed	Owner
IIA 5.3.2/01	Lina B.A.R.,Kuijpers M.H.M.	2004	Toxicity and carcinogenicity of acidogenic or alkalogenic diets in rats ; effects of feeding NH4Cl, KHCO3 or KCl.Food and Chemical Toxicology 42 (2004) 135-153. Report No : not stated Not GLP, Published	No	-
IIA 5.3.2/02	De Groot A.P., Feron V.J.,Immel H.R.	1998	Induction of hyperplasia in the bladder epithelium of rats by a dietary excess of acid or base : implications for toxicity /carcinogenicity testing.Food and Chemical Toxicology 26 (5) 425-434, 1988. Report No : not stated Not GLP, Published.	No	-
IIA 5.3.3/02	Church & Dwight Co-Anonymous1	1994	ArmicarbTM , A safe and efficacious Pest Management Alternative. Dossier submitted by Church & Dwight Co, Inc. to US EPA for review under Safer Pesticide Policy. Not GLP, Unpublished	No	Armand Products Company
IIA 5.3.3/03	Church & Dwight Co-Anonymous2	1994	Food Grade Sodium Bicarbonate, and Potassium Carbonate : A Safe and efficacious Pest Management Alternatives. Dossier submitted by Church & Dwight Co, Inc. to US EPA for review under Reduced-Risk Pesticide Initiative. Not GLP, Unpublished	No	Armand Products Company
IIA 5.4	Church & Dwight Co-Anonymous1	1994	ArmicarbTM , A safe and efficacious Pest Management Alternative. Dossier submitted by Church & Dwight Co, Inc. to US EPA for review under Safer Pesticide Policy. Not GLP, Unpublished	No	Armand Products Company.

Annex point/ reference number	Author(s)	Year	Title Source (where different from company) Company name, Report No., GLP status (where relevant) published or not	Data protection claimed	Owner
IIA 5.5/01	Lina B.A.R., Kuijpers M.H.M.	2004	Toxicity and carcinogenicity of acidogenic or alkalogenic diets in rats ; effects of feeding NH4Cl, KHCO3 or KCl. Food and Chemical Toxicology 42 (2004) 135-153. Report No : not stated Not GLP, Published	No	-
IIA 5.5/02	Cohen S.	1994	Review of the Carcinogenic Risk of Bicarbonates and Carbonates. University of Nebraska Medical Center, 600 South 42nd Street, Omaha, NE 68198-3135. Not GLP, Unpublished	No	Armand Products Company.
IIA 5.5/03	Church & Dwight Co-Anonymous1	1994	ArmicarbTM, A safe and efficacious Pest Management Alternative. Dossier submitted by Church & Dwight Co, Inc. to US EPA for review under Safer Pesticide Policy. Not GLP, Unpublished	No	Armand Products Company.
IIA 5.6/01	Church & Dwight Co-Anonymous1	1994	ArmicarbTM, A safe and efficacious Pest Management Alternative. Dossier submitted by Church & Dwight Co, Inc. to US EPA for review under Safer Pesticide Policy. Not GLP, Unpublished	No	Armand Products Company.
IIA 5.6/02	Church & Dwight Co-Anonymous2	1994	Food Grade Sodium Bicarbonate and Potassium Carbonate: A Safe and efficacious Pest Management Alternatives. Dossier submitted by Church & Dwight Co, Inc. to US EPA for review under Reduced-Risk Pesticide Initiative. Not GLP, Unpublished	No	Armand Products Company.
IIA 5.9.3/04	Lindinger M.I. Franklin T.W. Lands L.C. Pedersen P.K. Welsh D.G. Heigenhauser G.J.	2000	$NaHCO_3$ and $KHCO_3$ ingestion rapidly increases renal electrolyte excretion in humans. J Appl. Physiol., 88:540-550, 2000. Report No : not stated Not GLP, Published	No	-

Annex point/ reference number	Author(s)	Year	Title Source (where different from company) Company name, Report No., GLP status (where relevant) published or not	Data protection claimed	Owner
IIA 5.11.1/01	Church & Dwight Co-Anonymous1	1994	ArmicarbTM, A safe and efficacious Pest Management Alternative. Dossier submitted by Church & Dwight Co, Inc. to US EPA for review under Safer Pesticide Policy. Not GLP, Unpublished	No	Armand Products Company.
IIA 5.11.1/02	Church & Dwight Co-Anonymous2	1994	Food Grade Sodium Bicarbonate and Potassium Carbonate: A Safe and efficacious Pest Management Alternatives. Dossier submitted by Church & Dwight Co, Inc. to US EPA for review under Reduced-Risk Pesticide Initiative. Not GLP, Unpublished	No	Armand Products Company.
IIA 5.11.3/01	Church & Dwight Co-Anonymous1	1994	ArmicarbTM, A safe and efficacious Pest Management Alternative. Dossier submitted by Church & Dwight Co, Inc. to US EPA for review under Safer Pesticide Policy. Not GLP, Unpublished	No	Armand Products Company.
IIIA 7.1.1/01	Cerven D	1995	Single Dose Oral Toxicity in Rats / LD_{50} in Rats [redacted] Report No : MB 95-4666 A GLP, Unpublished	Yes	Armand Products Company.
IIIA 7.1.2/01	Cerven D	1995	Acute Dermal Toxicity in Rabbits / LD_{50} in Rabbits [redacted] Report No : MB 95-4666 B GLP, Unpublished	Yes	Armand Products Company.
IIIA 7.1.3/01	Cerven D	1995	Inhalation Toxicity in Rats [redacted] Report No : MB 95-4709 E GLP, Unpublished	Yes	Armand Products Company.

Annex point/ reference number	Author(s)	Year	Title Source (where different from company) Company name, Report No., GLP status (where relevant) published or not	Data protection claimed	Owner
IIIA 7.1.4/01	Keiffer, L	1995	Primary Dermal Irritation in Albino Rabbits [redacted] Report No : MB 95-4666 C GLP, Unpublished	Yes	Armand Products Company.
IIIA 7.1.5/01	Cerven D	1995	Primary Eye Irritation/Corrosion in Albino Rabbits [redacted] Report No : MB 95-4666 D GLP, Unpublished	Yes	Armand Products Company.
IIIA 7.1.6/01	Newcombe T	1995	Delayed Contact Dermal Sensitization Test (Buehler Method) [redacted] Report No : MB 95-4666 F GLP, Unpublished	Yes	Armand Products Company.