

FOREWORD

INTRODUCTION

Category of Methanolates

CAS N°:

Sodium: 124-41-4

Potassium: 865-33-8

SIDS Initial Assessment Report

For

SIAM 22

Paris, France, 18–21 April 2006

- | | |
|---|---|
| 1. Chemical Name: | Category of Methanolates: Sodium methanolate, potassium methanolate |
| 2. CAS Number: | 124-41-4
865-33-8 |
| 3. Sponsor Country: | Germany
Contact Point:
BMU (Bundesministerium für Umwelt, Naturschutz und Reaktorsicherheit)
Contact person:
Prof. Dr. Ulrich Schlottmann
Postfach 12 06 29
D-53048 Bonn |
| 4. Shared Partnership with: | Methanolate consortium: BASF AG, Germany, Degussa AG, Germany, E.I. DUPONT DE NEMOURS AND COMPANY, USA, KEMIRA Oyj, Finland |
| 5. Roles/Responsibilities of the Partners: | - |
| <ul style="list-style-type: none"> • Name of industry sponsor /consortium | Methanolate consortium: BASF AG, Germany, Degussa AG, Germany, E.I. DUPONT DE NEMOURS AND COMPANY, USA, KEMIRA Oyj, Finland
Contact:
Degussa AG Germany
Dr. Sylvia Jacobi
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| <ul style="list-style-type: none"> • Process used | The BUA Peer Review Process: see page after next |
| 6. Sponsorship History | |
| <ul style="list-style-type: none"> • How was the chemical or category brought into the OECD HPV Chemicals Programme? | By ICCA HPV initiative |
| 7. Review Process Prior to the SIAM: | last literature search (update):
23 November 2005 (Human Health): databases Medline, towline; all subject related data bases of STN, DIMDI, Dialog, search profile CAS-No. and special search terms |

- 03 November 2005 (Ecotoxicology): databases CA, biosis; search profile CAS-No. and special search terms OECD/ICCA
- 8. Quality check process:** IUCLID was used as a basis for the SIDS dossier. All data were checked and validated by BUA. A final evaluation of the human health part has been performed by the Federal Institute for Risk Assessment (BfR) and of the ecotoxicological part by the Federal Environment Agency (UBA).
- 9. Date of Submission:** Deadline for circulation: 20 January 2006
- 10. Date of last Update:** Last literature search (update) of sponsor company: CAS-No. and special search terms
- Sodium methanolate: July 27, 2005: DIMDI, STN, Dialog, Beilstein
- Potassium methanolate: August, 3, 2005, DIMDI, STN, Beilstein.
- 11. Comments:** **OECD/ICCA - The BUA* Peer Review Process**
- Qualified BUA personnel (toxicologists, ecotoxicologists) perform a quality control on the full SIDS dossier submitted by industry. This quality control process follows internal BUA guidelines/instructions for the OECD/ICCA peer review process and includes:
- a full (or update) literature search to verify completeness of data provided by industry in the IUCLID/HEDSET
 - Review of data and assessment of the quality of data
 - Review of data evaluation
 - Check of adequacy of selection process for key studies for OECD endpoints, and, where relevant, for non-OECD endpoints by checking original reports/publications
 - Review of key study description according robust summaries requirements; completeness and correctness is checked against original reports/publications (if original reports are missing: reliability (4), i.e. reliability not assignable)
 - Review of validity of structure-activity relationships
 - Review of full SIDS dossier (including SIAR, SIAP and proposal for conclusion and recommendation for further work)
 - In case of data gaps, review of testing plan or rationale for not testing.

*BUA (GDCh-Beratergremium für Alstoffe): Advisory Committee on Existing Chemicals of the Association of German Chemists(GDCh)

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	124-41-4 865-33-8
Chemical Name	Category of Methanolates: Sodium methanolate, Potassium methanolate
Structural Formula	$\text{H}_3\text{C-O}^- \text{Na}^+; \text{H}_3\text{C-O}^- \text{K}^+$

SUMMARY CONCLUSIONS OF THE SIAR**Category Justification**

The production and use pattern of sodium and potassium methanolates are comparable. The two chemicals have very similar physical and chemical properties. In contact with water they react very fast, quantitative and exothermic to methanol and the corresponding alkali hydroxides.

One mol of sodium or potassium methanolate (54.02 g or 70.13 g) yields one mol of methanol (32.04 g) and sodium- or potassium hydroxide (40 g or 56.11 g) respectively.

Due to the very high pK_a -value of methanol of 15.5, the equilibrium is on the side of the reaction products. Toxicological and ecotoxicological studies of methanol and sodium and potassium hydroxide are therefore relevant for these products as well. The main toxicological characteristic is the corrosivity to skin and mucous membranes that limits the possibility of exposure to methanol and warrants strict exposure controls. In the environment, both effects through pH-changes by the hydroxides and effects of methanol need to be considered.

For potassium hydroxide SIAM 13, and for sodium hydroxide SIAM 14 concluded: "Environment and Human Health: no further work is recommended if sufficient control measures are in place to avoid significant human and environmental impact, including prevention of accidental exposure. Due to the corrosivity of the substance, no further studies are required under SIDS program."

For methanol, SIAM 19 decided that, in terms of human health, this chemical is a candidate for further work. In the US, further work is being performed regarding the use and refinement of pharmacokinetic models for extrapolating animal data to human. Methanol exhibits potential hazardous properties for human health (neurological effects, CNS depression, ocular effects, reproductive and developmental effects, and other organ toxicity). The effects of methanol on the CNS and retina in humans only occur at doses at which formate accumulates due to a rate-limiting conversion to carbon dioxide. In primates, formate accumulation was observed at methanol doses greater than 500 mg/kg bw (which would require a sodium methanolate dose of more than 840 mg/kg bw and a potassium methanolate dose of greater than 1000 mg/kg bw). Repeated exposure to such high dose levels of methanolates that are already in the acutely toxic range is highly unlikely due to their corrosive properties. The only exposure situation for sodium and potassium methanolate that could perhaps lead to methanol and formate blood levels resulting in acute neurophysiological and visual disturbances would be accidental dermal exposure to corrosive concentrations that could lead at the same time to an uptake of toxic amounts of methanol through the skin. For this exposure situation the post SIDS work for methanol is considered relevant as well and no specific work on sodium and potassium methanolate is considered necessary. In terms of the environment, methanol is currently of low priority for further work, due to its low hazard profile.

Human Health

The predominant effect of sodium and potassium methanolate on humans is their corrosivity to skin and mucous membranes, due to the rapid and exothermic reaction with tissue water yielding alkaline hydroxides. The abiotic hydrolysis of sodium and potassium methanolates with tissue water results in the hydroxides formation of sodium and potassium ions respectively, hydroxide ions and methanol. Exposure to non-irritant levels of methanolates via the dermal or inhalation route is not expected to lead to relevant uptake of the ionic degradation products sodium or potassium ions or hydroxide ions in amounts that would exceed the normal physiological levels.

The sodium ion is a normal constituent of the blood and an excess is excreted in the urine. Uptake of sodium following exposure to sodium methanolate can be considered negligible compared to the uptake of sodium via food (3.1 to 6 g/day).

Potassium ions are normal constituents of body fluids. K^+ plays an essential role in human physiology, but starts to be toxic at plasma concentrations of 250 mg/l. Its concentration in blood is regulated principally by renal excretion/re-absorption and controlled by an effective feed-back auto-regulation system. A systemic intoxication by potassium methanolate is not expected as the uptake will be limited by the corrosive properties of the substance. Exposure to hydroxide ions from sodium or potassium methanolate exposure could potentially increase the pH of the blood and lead to alkalosis. However, the pH of the blood is regulated between narrow ranges pH 7.0 to 7.8 and an excessive pH of the blood is prevented by the bicarbonate buffer system, respiration and renal compensation mechanisms.

SIAM 19 concluded for methanol: "Methanol is readily absorbed by inhalation, ingestion and dermal contact and partitions rapidly and equally throughout the organism in relation to the water content of organs and tissues. A small amount is excreted unchanged by the lungs and kidneys. Half-lives of methanol in the body are roughly 2.5 to 3 hours at doses less than 100 mg/kg bw. At high doses disproportionate increases of the parent compound in blood are obtained in rodents, but not in humans. On the other hand, in humans the metabolite formate accumulates at high doses. This important difference mirrors the different enzymes and enzyme capacities involved in the oxidative pathway from methanol to carbon dioxide. Specifically, two different rate limiting processes have been identified: in rodents, high doses (after inhalation of 2.5 – 3.3 mg/l) lead to the saturation of catalase, resulting in the accumulation of methanol whereas formate levels remain low, whereas in primates (especially humans), the parent compound is well oxidized and does not accumulate, but formate increases disproportionately. From studies in humans and monkeys exposed to concentrations of 0.26 – 2.6 mg/l (administered for 6 to 8 hours), it can be concluded that methanol remains close to 50 mg/l in blood. At inhalation exposures of 2.6 mg/l, rats also exhibit methanol blood levels that are not much higher (at about 80 mg/l), whereas the level in mice was 400 mg/l. At a higher inhalation exposure (6.5 mg/l), humans show the lowest blood methanol level (at 140 mg/l), followed by monkeys, rats, and mice, with the level in mice being more than 10 times higher than humans. Formate accumulation in primates has been observed at methanol doses greater than 500 mg/kg."

The corresponding dose levels for sodium and potassium methanolate that would lead to accumulation of formate in primates would be 840 and 1000 mg/kg bw. Such dose levels are already in the acutely toxic dose range. Due to the corrosive nature of the methanolates it is unlikely that repeated exposure to methanolates could result in an uptake of toxic doses of methanol. The only exposure situation for sodium and potassium methanolate that could perhaps lead to methanol and formate blood levels resulting in acute neurophysiological and visual disturbances would be accidental dermal exposure to corrosive concentrations that could lead at the same time to an uptake of toxic amounts of methanol through the skin. It has been assumed that an inhalation exposure to methanol of 260 mg/m³ for 8 hours does not lead to any adverse effects. This exposure level corresponds to a systemic dose of 2600 mg methanol/d (assuming an inhalation volume of 10 m³ during an 8-hour working day) or 37 mg/kg bw day (for a 70 kg human). It would require doses of 44.4 and 65 mg/kg bw of sodium or potassium methanolate, respectively, to achieve a systemic dose of 2600 mg methanol/d. The rate of dermal uptake for methanol was reported to be 0.192 mg/cm²/min. Accidental exposure of both hands (850 cm²) to sodium or potassium methanolate for one minute resulting in corrosive effects could then theoretically additionally lead to an uptake of methanol exceeding the dose level of 37 mg/kg bw. Such an exposure situation does however not reflect any human exposure situation under normal handling conditions as precautions are taken because of the corrosivity of the substances.

No signs of toxicity were observed in rats exposed to a dust enriched atmosphere of sodium methanolate for 8 hours, the dermal LD₅₀ of a 50 % aqueous solution was > 2000 mg/kg bw in rats. Skin necrosis was observed in this study. After oral administration the acute toxicity is dependent on the local tissue concentration and the dose rate of the substance and its degradation product sodium hydroxide. The LD₅₀ in water or water soluble solvents was between 800 and 1687 mg/kg bw, when administered in corn oil the LD₅₀ was 2037 mg/kg bw. The acute toxicity is consistent with that of sodium hydroxide and it can be assumed that the primary mode of action is local irritation/corrosion at the site of first contact.

For potassium methanolate no data are available, but due to the reaction with water and the liberation of hydroxide ions and the alkaline reaction the mode of action will be the same and the acute toxicity will be comparable to that of sodium methanolate and potassium hydroxide. The acute toxicity of both substances is mediated by their alkalinity and the hydroxide ion.

Sodium methanolate was highly corrosive to rabbit skin and eyes. For potassium methanolate no studies are available. Due to its alkaline reaction and exothermic reaction with water it will be similarly corrosive. Based on the skin and eye irritation data it can be assumed that both methanolates will also cause irritation/corrosion to the mucous membranes of the upper respiratory tract in case of an exposure via the inhalation route.

As the corrosivity is mediated by the exothermic liberation of sodium or potassium hydroxide the data for the two hydroxides may be important for the evaluation of this endpoint as well. For sodium hydroxide it was concluded that based on the animal data a NaOH solution of 8 % can be considered corrosive. Based on human data concentrations of 0.5 to 4 % were irritating to the skin and concentrations slightly lower than 0.5 % were con-

sidered non-irritating. Potassium hydroxide is corrosive at concentrations of about 2 % and higher. Between 0.5 % and 2 % it is irritating.

From the data of the hydrolysis products it can be concluded that sodium and potassium methanolate are not expected to have a notable skin sensitization potential.

No data on repeated dose toxicity of sodium and potassium methanolate are available. The tolerable dose levels will be determined by the corrosive nature of the substances. At non-irritant concentrations, the K^+ or Na^+ ions, and the OH^- ions are unlikely to have any adverse effects. The specific ocular and CNS toxicity of methanol in primates is based on the accumulation of formate in blood. Formate accumulation in primates has been observed at methanol doses greater than 500 mg/kg. The corresponding dose levels for sodium and potassium methanolate that would lead to accumulation of formate in primates would be 840 and 1000 mg/kg bw. Such dose levels are already in the acutely toxic dose range. Due to the corrosive nature of the methanolates it is very unlikely that exposure to methanolates could result in an uptake of toxic doses of methanol.

No data on mutagenicity of sodium or potassium methanolate are available with the exception of one negative Ames assay with a limited number of strains conducted with sodium methanolate. Due to the rapid hydrolysis of methanolates in *in vitro* test systems and tissue water *in vivo*, data for the hydrolysis products are relevant for methanolates as well. For sodium and potassium hydroxide there is no evidence for a mutagenic potential. For methanol the weight of evidence suggests that the substance is unlikely to have any relevant mutagenic activity. Therefore it can be concluded that there is no concern with regard to a mutagenic activity of sodium or potassium methanolate.

No data are available on the carcinogenicity of sodium and potassium methanolate. For potassium hydroxide it was concluded at SIAM 13 that there is no evidence of carcinogenicity in exposure situations that are relevant for humans. There was no evidence for a carcinogenic potential of methanol in two long-term inhalation studies on rats and mice. Based on the available data, there is therefore no concern for carcinogenicity of sodium and potassium methanolates.

No data are available on reproductive or developmental toxicity of sodium and potassium methanolate. For hydroxide, sodium and potassium ions, no relevant reproductive toxicity potential has been identified. For methanol reproductive and developmental toxicity effects have been described in rats, mice and monkeys. Blood methanol concentrations associated with serious developmental effects and reproductive toxicity in rodent studies are in the range associated with formate accumulation. It is unlikely that concentrations associated with serious developmental effects in rodents could be reached by administration of sodium or potassium methanolate to experimental animals, as those dose levels would be in the acutely toxic dose range and associated with massive local irritation at the site of first contact. The maximum tolerated dose in such studies is therefore likely to be below the dose that would result in methanol mediated developmental effects. In addition, for animal welfare reasons, it is not recommended to perform further animal studies with sodium and potassium methanolate.

Environment

Both sodium and potassium methanolate are white to yellowish organic solid salts that decompose above 300 °C (sodium methanolate) or at 300 °C (potassium methanolate). Sodium and potassium methanolate have a calculated vapor pressure of 6.39×10^{-6} hPa. On contact with water both substances decompose rapidly and exothermically under formation of methanol and the corresponding alkali hydroxides, sodium- or potassium hydroxide, respectively.

Photodegradation of methanol by hydroxyl radicals takes place with a half-life of 17 - 18 days. For the partitioning in the environmental compartments the hydrolysis products are of relevance. Sodium and potassium hydroxide are inorganic salts that partition predominantly into the water phase and will not adsorb to particulate matter or surfaces. For methanol it was concluded that based on the Henry's law constant of 0.461 Pa m³/mol it is not expected to significantly volatilize from the aquatic compartment and adsorption is not expected to be significant due to its high water solubility and low octanol-water partition coefficient. A distribution calculation performed with the Mackay level III model predicts that the air is the target environmental compartment for methanol. After rapid hydrolysis in water the relevant organic reaction product, methanol is readily biodegradable (76 – 82 % BOD removal after 5 days). As sodium and potassium methanolate react with water under formation of sodium or potassium hydroxide and methanol, an octanol-water partition coefficient cannot be experimentally established and bioaccumulation of the substances themselves is unlikely. Methanol will be the species that distributes into the octanol phase or could be taken up by organisms. For methanol the log K_{ow} was -0,74 indicating a low bioaccumulation potential. This was confirmed by experimental BCF-values below 10 that have been determined in different fish species.

The toxicity of sodium and potassium methanolate to aquatic organisms is mediated by their degradation products due to the rapid reaction with water yielding sodium or potassium hydroxide and methanol. The aquatic toxicity of methanol is low with acute EC₅₀ or LC₅₀ values > 10 000 mg/l and therefore its contribution to the methanolate toxicity is considered negligible. The limited data available for sodium methanolate are consistent with the aquatic toxicity of the alkali hydroxides. For sodium methanolate the acute toxicity to fish (48-h LC₅₀) for *Leuciscus idus melanotus* was 346 mg/l (equivalent to 256 mg/l of sodium hydroxide). The corresponding 48-h LC₅₀ value for sodium hydroxide was 189 mg/l the 96-h LC₅₀ for *Gambusia officinalis* was 125 mg/l for sodium hydroxide and 80 mg/l for potassium hydroxide. For invertebrates a 48-h LC₅₀ value of 40 mg/l (*Ceriodaphnia dubia*) and toxicity threshold concentrations (TTC) between 40 and 240 mg/l (*Daphnia magna*) were reported for sodium hydroxide. Lethal concentrations to molluscs of sodium hydroxide ranged between 150 mg/l (*Bulinus truncatus*, *Lymnea caillaudi*) and 450 mg/l (*Biomphalaria a. alexandria*), the 48-h LC₅₀ values for *Ophryotrocha* (marine polychaete) were between 33 and 100 mg/l. The 24-h EC₅₀ for algae (assimilation inhibition) was 302 mg/l for sodium methanolate. However, as concluded for sodium and potassium hydroxide already, acute toxicity data cannot be used to derive a PNEC or a PNEC_{added} for the compounds releasing hydroxide. Aquatic ecosystems are characterized by an alkalinity/pH and the organisms of the ecosystems are adapted to these specific natural conditions. Based on the natural alkalinity of waters, organisms will have different optimum pH conditions, ranging from poorly buffered waters with a pH of 6 or less to very hard waters with pH values up to 9. A lot of information is available about the relationship between pH and ecosystem structure and also natural variations in the pH of aquatic ecosystems have been quantified and reported extensively in ecological publications and handbooks. Normally a PNEC or a PNEC_{added} has to be derived from available ecotoxicity data. A PNEC_{added} is a PNEC which is based on the added concentrations of a chemical (added risk approach). Based on the available data it is not considered useful to derive a PNEC or PNEC_{added} for the sodium and potassium methanolate as their effect is based on hydroxide ions or a pH change. The natural pH of aquatic ecosystems can vary significantly and the sensitivity of aquatic ecosystems to a change of the pH can vary significantly between aquatic ecosystems. The change in pH due to anthropogenic OH⁻ addition through methanolate releases is influenced significantly by the buffer capacity of the exposed ecosystem.

Although a PNEC or PNEC_{added} was not calculated, there is a need to assess the environmental effect of an OH⁻ release through sodium or potassium methanolate release into the environment. Based on the pH and the buffer capacity of the effluent and receiving water and the dilution factor of the effluent, the pH of the receiving water after discharge can be calculated or its pH can be measured. The change in pH should be compared with the natural variation in pH of the receiving water. Based on this comparison it should be assessed if the pH change is acceptable.

To illustrate the procedure and to get an idea about the order of magnitude for a maximum anthropogenic addition, the maximum methanolate concentration will be calculated for 2 representative cases. According to Dir. 78/659/EEC, the pH of surface water for the protection of fish should be between 6 and 9. The 10th percentile and the 90th percentile of the bicarbonate concentration of 77 rivers of the world were 20 and 195 mg/l respectively. If it is assumed that only bicarbonate is responsible for the buffer capacity of the ecosystem and that an increase of pH to a value of 9 would be the maximum accepted value, then the maximum anthropogenic addition of sodium methanolate would be 1.4 mg/l and 8.2 mg/l (corresponding to 1.0 and 6.1 mg NaOH/l) and for potassium methanolate 1.1 mg/l and 10.4 mg/l (corresponding to 0.86 and 8.3 mg KOH/l) for bicarbonate concentrations of 20 and 195 mg/l respectively.

Sodium methanolate was moderately toxic to bacteria with a 24-hour EC₅₀ of 97 mg/l. The toxicity is likely mediated through a pH effect by the release of hydroxide ions.

There is only one study with potassium hydroxide available indicating a low level of terrestrial toxicity (90-day EC₅₀ in *Enchytraeus sp.* (> 95 % *Cogentia sphagnetorium*) of 850 mg/l (artificial soil)). The terrestrial toxicity will depend on the buffer capacity of the soil.

Exposure

European production volumes for sodium and potassium methanolate are above 1000 metric tonnes per year. The US-volume of sodium methanolate reported to US-EPA in 2002 by all US manufacturers and importers was between 4500 and 23 000 metric tonnes on a dry weight basis. Sodium and potassium methanolate are widely used in the chemical industry as intermediates, for example for the production of formic acid or the transesterification of fatty acid esters. One other major use is in biodiesel production as transesterification catalysts. Because of the predominant production and use in chemical industry under controlled conditions, environmental exposure from production and use is considered low. Furthermore due to the sensitivity of the substances to moisture it is unlikely that the products themselves enter the environment during production and use as they are immediately hydrolyzed to methanol and sodium or potassium hydroxide. Theoretically, the environment could be exposed to residues of the catalysts in consumer products. However, given the sensitivity of methanolates to moisture it is likely that any residual levels would rapidly hydrolyze under formation of methanol and sodium and potassium hydroxide.

In production and uses in chemical industry for which descriptions are available, from the process description very low occupational exposure is anticipated. As the majority of the products are used as intermediates in the chemical industry a controlled exposure situation is anticipated.

There is no information on possible consumer exposure for potassium methanolate. The only information available on sodium methanolate is from the Nordic Product Register of 2003, where consumer products are listed for Norway and Sweden (no details available on use or use concentrations). Theoretically, consumers could be exposed to residues of the catalysts in consumer products. However, given the sensitivity of methanolates to moisture it is likely that any residual levels would rapidly hydrolyze under formation of methanol and sodium and potassium hydroxide. Both products are listed in the Inventory of Processing Aids for food as catalysts for interesterified food oils of the Codex Alimentarius with residual levels below 1 mg/kg.

Sodium methanolate is contained in Nordic Product Registers for 2003: In Finland, 7 preparations for manufacture of chemicals and chemical products with a tonnage of 228 tonnes are listed. In Norway, 152 products with a total tonnage of 33.0 tonnes are listed, 6 of which are consumer products with a tonnage of 0.1 tonnes. Industrial uses listed in Norway are manufacture of chemicals and chemical products with a tonnage of 32.9 tonnes. In Sweden, 6 preparations with a tonnage of 51.0 tonnes are listed with information on industrial use from 2001 (4 preparation with a tonnage of 51.0 tonnes for process regulators), and 2 preparations are consumer preparations in which sodium methanolate is not added intentionally. Potassium methanolate is listed in Nordic Product Registers for Norway and Finland in 2003, but all data are confidential. However, given the sensitivity of methanolates to moisture it is likely that any residual levels would rapidly hydrolyze under formation of methanol and sodium and potassium hydroxide.

RECOMMENDATION AND RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

Human Health: The chemicals in this category are currently of low priority for further work. The human health hazard is characterized by the rapid and exothermic degradation of the chemicals to methanol and the corresponding alkali hydroxides with known corrosivity. Based on data presented by the Sponsor country, exposure is well controlled in occupational settings, and exposure of consumers is negligible. Countries may wish to investigate exposure scenarios with potential human exposure.

Environment: The chemicals in this category are currently of low priority for further work due to their rapid degradation in the environment via hydrolysis. The reaction products (methanol, potassium hydroxide and sodium hydroxide) have been evaluated within the OECD SIDS program for their hazardous properties and have been considered of low priority for further work for the environment.

SIDS Initial Assessment Report

1 IDENTITY

1.1 Identification of the Substance

Substance	Sodium methanolate	Potassium methanolate
CAS Number:	124-41-4	865-33-8
IUPAC Name:	Sodium methanolate	Potassium methanolate
Molecular Formula:	CH ₃ NaO	CH ₃ KO
Structural Formula:	H ₃ C-O ⁻ Na ⁺	H ₃ C-O ⁻ K ⁺
Molecular Weight:	54.02 Dalton	70.13 Dalton
Synonyms	Methanol, sodium salt; sodium methylate; methoxysodium; sodium methoxide; Natriummethanolat; Natriummethylat	Methanol, potassium salt; potassium methylate; methoxy potassium; potassium methoxide; Kaliummethanolat; Kaliummethylat

1.2 Purity/Impurities/Additives

Both, sodium and potassium methanolate are white to yellowish solids. Sodium methanolate has a typical purity of 98 % (w/w) and potassium methanolate of 97 % (w/w). Both substances are marketed either as powders or as solutions in methanol (25 to 30 % for sodium methanolate and 32 % for potassium methanolate respectively) (BASF AG, 2001; Degussa, 1998 a; Degussa, 2002; Degussa 2004a; Degussa 2005d). Impurities in the solid material from the production process include sodium hydroxide and sodium carbonate (≤ 2 % (w/w) combined impurities) for sodium methanolate (Degussa, 1998a) and potassium hydroxide and potassium carbonate (≤ 1 % (w/w) combined impurities) in the case of potassium methanolate (Degussa, 2002).

1.3 Physico-Chemical properties

Table 1 Summary of physico-chemical properties

Substance	Sodium methanolate	Potassium methanolate	Comment/Reference (sodium methanolate / potassium methanolate)
Property	Value	Value	
Physical state/color	Solid/white/	Solid/white to yellowish	Degussa, 1998°; Degussa, 2002
Melting point	300 °C Decomposition > 127 °C	300 °C (decomposition)	CRC 2001, IPCS 2001; BASF AG, 2002, 2003
Boiling point	n.a.	n.a.	Decomposes already below the melting temperature.
Density	1.3 g/cm ³ (20 °C)	1.7 g/cm ³ *	Degussa, 2005°; Roempp, 2003
Bulk density (20 °C)	0.45 g/cm ³	0.95 g/cm ³	Degussa, 1998°; Degussa, 2002
Vapor pressure (25 °C)	0.000639 Pa	0.000639 Pa	Calculated; Degussa, 2003°; Degussa, 2003 b
Water solubility	Decomposition, hydrolysis to methanol and sodium hydroxide	Decomposition, hydrolysis to methanol and potassium hydroxide	Sax, 2000; IPCS, 2001 ; Sax, 2000
Partition coefficient n-octanol/water (log value)	-0.74 (Methanol)	-0.74 (Methanol)	Due to rapid hydrolysis in water to methanol and sodium or potassium hydroxide, only the log K _{ow} of methanol is relevant. OECD, 2004
Henry's law constant	0.461 Pa m ³ /mol (Methanol)	0.461 Pa m ³ /mol (Methanol)	Due to rapid hydrolysis in water to methanol and sodium or potassium hydroxide, only the Henry's law constant of methanol is relevant. OECD, 2004
Autoignition temperature	50 - 60 °C	90 - 100 °C	Degussa, 2005°; Degussa, 2004
pKa	15.5 (Methanol)	15.5 (Methanol)	Friedrich, Sonnefeld, and Jansen, 1998

n.a.: Not applicable; *) Temperature not reported but 20 °C assumed

Sodium and potassium methanolate both react very fast, quantitative and exothermic with water under formation of methanol and sodium or potassium hydroxide respectively (Leal and de Matos, 1991).

1.4 Category Justification

The production and use pattern of sodium and potassium methanolates are comparable. The two chemicals have very similar physical and chemical properties. In contact with water they react very fast, quantitative and exothermic to methanol and the corresponding alkali hydroxides (Leal and de Matos, 1991).



One mol of sodium or potassium methanolate (54.02 g or 70.13 g) yields one mol of methanol (32.04 g) and sodium- or potassium hydroxide (40 g or 56.11 g) respectively.

Due to the very high pKa-value of methanol of 15.5 (Friedrich, Sonnefeld, and Jansen, 1998), the equilibrium is on the side of the reaction products. Toxicological and ecotoxicological studies of methanol and sodium and potassium hydroxide are therefore relevant for these products as well.

The main toxicological characteristic is the corrosivity to skin and mucous membranes that warrants strict exposure controls. The corrosivity also determines the maximum tolerable dose in any animal experiment. The maximum applicable dose level of methanol derived from the methanolates will therefore be considerably lower in experiments with methanolates than in experiments with methanol itself.

In the environment, both effects through pH-changes by the hydroxides, and effects of methanol need to be considered.

For potassium hydroxide SIAM 13 and for sodium hydroxide SIAM 14 concluded: "Environment and Human Health: no further work is recommended if sufficient control measures are in place to avoid significant human and environmental impact, including prevention of accidental exposure. Due to the corrosivity of the substance, no further studies are required under the SIDS program." (OECD, 2001, 2002).

For methanol, SIAM 19 decided, in terms of human health, that this chemical is a candidate for further work. In the US, further work is being performed regarding the use and refinement of pharmacokinetic models for extrapolating animal data to human. Methanol exhibits potential hazardous properties for human health (neurological effects, CNS depression, ocular effects, reproductive and developmental effects, and other organ toxicity). The effects of methanol on the CNS and retina in humans only occur at doses at which formate accumulates due to a rate-limiting conversion to carbon dioxide. In primates, formate accumulation was observed at methanol doses greater than 500 mg/kg bw (which would require a sodium methanolate dose of more than 840 mg/kg bw and a potassium methanolate dose of greater than 1000 mg/kg bw). Repeated exposure to such high dose levels, of methanolates, that are already in the acutely toxic range is highly unlikely due to their corrosive properties. The only exposure situation for sodium and potassium methanolate that could perhaps lead to methanol and formate blood levels resulting in acute neurophysiological and visual disturbances would be accidental dermal exposure to corrosive concentrations that could lead at the same time to an uptake of toxic amounts of methanol through the skin. For this exposure situation the post SIDS work for methanol is considered relevant as well and no specific work on sodium and potassium methanolate is considered necessary. In terms of the environment, methanol is currently of low priority for further work, due to its low hazard profile.

Data Availability For Sodium- And Potassium Methanolate

The available data for both members of the category are summarized in the following table. Data of the degradation products are mentioned as well were they are used as a surrogate for data on the methanolates.

Table 2 Data availability

OECD SIDS Endpoint	Sodium methanolate 124-41-4	Potassium methanolate 865-33-8	Sodium hydroxide 1310-73-2	Potassium hydroxide 1310-58-3	Methanol 67-56-1
Physicochemical Properties					
Melting point	✓	✓	✓	✓	✓
Boiling point	n.a.	n.a.	✓	✓	✓
Density	✓	✓	✓	✓	✓
Vapor pressure	✓ (calculated)	✓ (calculated)	✓ (calculated)	-	✓
Partition Coefficient	n.a.	n.a.	n.a.	n.a.	✓
Water solubility	n.a.	n.a.	✓	✓	✓
Fate					
Biodegradation	-	-	n.a.	n.a.	✓
Photodegradation	✓ calculated	✓ calculated	n.a.	n.a.	✓ calculated
Hydrolysis	✓	✓	n.a.	n.a.	n.a.
Fugacity	- *	- *	✓ estimation	✓ estimation	✓ calculation
Bioaccumulation	-	-	n.a.	n.a.	✓
Ecotoxicological data					
Acute Fish Toxicity	✓	-	✓	✓	✓
Acute Daphnia Toxicity	-	-	✓	✓	✓
Algae Toxicity	✓	-	-	✓	✓
Toxicity to microorganisms	✓	-	-	✓	✓
Toxicity to soil dwelling organisms				✓	-
Toxicological data					
Acute Toxicity	Oral: ✓ Dermal: ✓ Inhalation: ✓	Oral: - Dermal: - Inhalation -	Oral: ✓ Dermal: ✓ Inhalation ✓	Oral: ✓ Dermal: - Inhalation -	Oral: ✓ Dermal: ✓ Inhalation ✓
Repeated Dose Toxicity	-	-	✓	✓	✓
Genotoxicity, <i>in vitro</i> Ames	✓	-	✓	✓	✓
Genotoxicity, <i>in vitro</i> Cytogenetic test	-	-			✓
Genotoxicity <i>in vivo</i>	-	-	✓	✓	✓
Reproductive Toxicity	-	-	-	✓	✓
Developmental Toxicity	-	-	-	-	✓
Additional data					
Skin irritation	✓	-	✓	✓	✓
Eye irritation	✓	-	✓	✓	✓
Skin sensitization	-	-	✓	✓	✓
Toxicokinetic data	-	-	-	-	✓
Carcinogenicity	-	-	-	-	✓

* only data for methanol applicable

2 GENERAL INFORMATION ON EXPOSURE

2.1 Production Volumes and Use Pattern

2.1.1 Production

Both methanolates are produced in Europe in amounts greater than 1000 metric t/year. The US-volume of sodium methanolate reported to US-EPA in 2002 by all US manufacturers and importers was between 4500 and 23 000 metric tonnes on a dry weight basis (DuPont de Nemours, 2005).

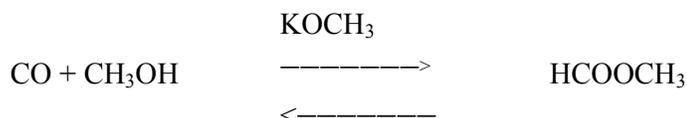
Methanolates can be produced from reaction of sodium metal or sodium hydroxide with methanol or by electrolysis using sodium or potassium salts that are reduced electrochemically and then reacted with methanol. From those reactions solutions of the methanolates in methanol are obtained that are either marketed or used as such or the alcohol is removed by distillation and the solid products are obtained (Markolwitz and Ruwwe, 2003).

Sodium and potassium methanolate are produced in closed continuous reactors (Kemira, 2005; DuPont de Nemours, 2005). The 22 to 30 weight percent solution for sodium methanolate (DuPont de Nemours, 2005; Degussa, 2004), and the 25 to 32 % weight percent solution for potassium methanolate (Kemira, 2005; Degussa, 2004) are continuously withdrawn from the reactor, either into ISO-storage tanks or transport containers. Transport of the methanolate solutions is performed by rail cars, tank trucks, or metal drums under an inert atmosphere (e.g. nitrogen) to avoid contact with moisture (Kemira, 2005; DuPont de Nemours, 2005; Markolwitz and Ruwwe, 2003). Filling operations are performed with special pumps and devices that exclude the contact with atmospheric moisture and also prevent any environmental or human exposure with the products (Markolwitz and Ruwwe, 2003). Solid sodium and potassium methanolate are marketed and transported in steel drums and smaller amounts in double bags (BASF AG, 1997; Degussa, 1998a; Degussa, 2002).

2.1.2 Processing and use

Sodium and potassium methanolate are used mainly as intermediates for chemical synthesis in the chemical industry and are involved in a variety of reactions, such as alkylation, arylation, acylation, solvolysis of esters, condensation and elimination reactions, isomerization, rearrangements, transfer hydrogenation, Wittig reactions and redox reactions (BASF AG, 2004). Those reactions are used in many different areas, as the production of agrochemicals, photochemicals, silanes or silicones, cosmetic raw materials, pharmaceuticals, colorants, food processing (e.g. as catalyst in the esterification of edible oils for margarine production), optical brighteners, flavors and fragrances, plastics and antioxidants (Degussa, 2004a; Markolwitz and Ruwwe, 2003).

Part of the production volume of the producers represented in the ICCA Methanolate consortium is used as internal intermediate for the synthesis of other chemicals; another part is sold to industrial customers. One major use of potassium methanolate is the synthesis of formic acid, in which potassium methanolate catalyzes the reaction and gradually reacts with water to potassium formate. (BASF AG, 2004; Kemira, 2005)



Another major application is the preparation of fatty acid methyl esters by transesterification of raw materials such as palm oil or coconut oil. The products obtained are further processed by hydrogenation and distillation to give fatty alcohols and serve as starting materials for inter alia surfactants (Markolwitz and Ruwwe, 2003).

Both sodium methanolate and potassium methanolate are used in the production of biodiesel as transesterification catalyst. Triglycerides of e.g. rapeseed or soybean oil are reacted with methanol under catalysis of the methanolates to glycerol and fatty acid methyl esters (Degussa, 2004a; Markolwitz and Ruwwe, 2003; BASF AG, 2004; DuPont de Nemours, 2005; Kemira, 2005).

Both products are listed in the Inventory of Processing Aids for food as catalysts for interesterified food oils of the Codex Alimentarius with residual levels below 1 mg/kg (Codex Alimentarius, 1989).

Sodium methanolate is contained in Nordic Product Registers for 2003 (SPIN, 2005): In Finland, 7 preparations for manufacture of chemicals and chemical products with a tonnage of 228 tonnes but no consumer products are listed. In Norway, 152 products with a total tonnage of 33.0 tonnes are listed, 6 of which are consumer products with a tonnage of 0.1 tonnes. Industrial uses listed in Norway are manufacture of chemicals and chemical products with a tonnage of 32.9 tonnes. In Sweden, 6 preparations with a tonnage of 51.0 tonnes are listed with information on industrial use from 2001 (4 preparation with a tonnage of 51.0 tonnes for process regulators), and 2 consumer preparations in which sodium methanolate is not added intentionally.

Potassium methanolate is listed in Nordic Product Registers for Norway and Finland in 2003 (SPIN, 2005) but all data are confidential.

2.2 Environmental Exposure and Fate

2.2.1 Sources of Environmental Exposure

Due to the sensitivity to moisture it is unlikely that the products themselves enter the environment during production and use as they are immediately hydrolyzed to methanol and sodium or potassium hydroxide (Friedrich, Sonnefeld, and Jansen, 1998).

From production there are no routine releases of sodium and potassium methanolate into waste water or air. By-product methanol and/or hydrogen are burned in a flare. (DuPont de Nemours, 2005; Kemira, 2005). Spills are absorbed and incinerated (DuPont de Nemours, 2005). Theoretically, the environment could be exposed to residues of the catalysts in consumer products. However, given the sensitivity of methanolates to moisture it is likely that any residual levels would rapidly hydrolyze under formation of methanol and sodium and potassium hydroxide.

The formic acid process that uses potassium methanolate is also closed and continuous (Kemira, 2005). Most of the other internal processes in which the products are used for chemical synthesis are also closed and there are no releases of methanolates from those processes (DuPont de Nemours, 2005).

For biodiesel production sodium or potassium methanolates are provided in methanolic solution. This solution is introduced into the transesterification process via closed system. At the end of the reaction, the catalyst is removed by neutralization e.g. with hydrochloric acid. (Markolwitz and Ruwwe, 2003). Thus entries into the environment of the methanolates are not to be expected from this process.

2.2.2 Photodegradation

Hydroxyl-radical mediated photodegradation in air was calculated for potassium and sodium methanolate using the AOPWIN program (version 1.91). The half-life was calculated to be approximately 19 days for both potassium and sodium methanolate (Degussa, 2005b; Degussa, 2005c). The relevant species that would be expected to occur in the air compartment would however, be methanol for which a half life of about 17 to 18 days was reported (OECD, 2004).

2.2.3 Stability in Water

In contact with water sodium and potassium methanolate react very rapidly, quantitatively and exothermically to methanol and the corresponding alkali hydroxides (Leal and de Matos, 1991).



Due to the very high pKa-value of methanol of 15.5 (Friedrich, Sonnefeld, and Jansen, 1998), the equilibrium is on the side of the reaction products under environmentally relevant conditions. The reaction products, alkali metal ions and methanol are stable in water while hydroxide ions can be subject to neutralization reactions depending on the buffer capacity of the carbonate/bicarbonate buffer systems (OECD, 2001, 2002, 2004).

2.2.4 Transport between Environmental Compartments

Due to the rapid hydrolysis of sodium and potassium methanolates in water the relevant species subject to environmental distribution are the degradation products sodium and potassium hydroxide respectively and methanol. For the hydroxides it was concluded that they will be found predominantly in the aquatic compartment as alkali metal and hydroxide ions and will not adsorb on particulate matter or surfaces (OECD, 2001, 2002). For methanol it was concluded that based on the Henry's law constant of 0.461 Pa m³/mol it is not expected to significantly volatilize from the aquatic compartment and adsorption to soil is not expected to be significant due to its high water solubility and low octanol-water partition coefficient (OECD, 2004). A distribution calculation performed with the Mackay Level III fugacity model using the emission rates derived from the releases into water, air and soil (79 658, 1531, and 658 tonnes respectively) reported in the U.S. Toxic Release inventory for 2001 predicts that the air is the target environmental compartment for methanol (OECD, 2004).

2.2.5 Biodegradation

After rapid hydrolysis of methanolates in water the relevant organic reaction product, methanol is subject to biodegradation. It was concluded that methanol is readily biodegradable based on the result of standard tests that show 76 - 82 percent removal of BOD after 5 days. Methanol will biodegrade readily in surface water, subsurface aquatic or soil systems under both aerobic and anaerobic conditions (OECD, 2004).

2.2.6 Bioaccumulation

As sodium and potassium methanolate react with water under formation of sodium or potassium hydroxide and methanol, an octanol-water partition coefficient cannot be experimentally established and bioaccumulation of the substances themselves is unlikely. Methanol will be the species that distributes to the octanol phase or could be taken up by organisms. For methanol experimental

BCFs of < 10 have been measured in fish species indicating a low bioaccumulation potential as was to be expected from its high water solubility and low octanol-water partition coefficient (OECD, 2004).

2.3 Human Exposure

2.3.1 Occupational Exposure

Due to the production in closed systems including filling operations occupational exposure during production is considered to be very low. (DuPont de Nemours, 2005; Kemira, 2005; Markolwitz, and Ruwwe, 2003). Special sampling valves have been reported to be used for sampling by one producer making exposure unlikely during sampling operations as well. As the majority of the products are used as intermediates in the chemical industry a controlled exposure situation is anticipated. Also for the use in biodiesel production from the process description a very low occupational exposure is anticipated (Markolwitz and Ruwwe, 2003). Due to the corrosivity of the materials it can be expected that adequate personal protective equipment is used wherever the material is handled. This has been confirmed for the production process (DuPont de Nemours, 2005; Kemira, 2005).

2.3.2 Consumer Exposure

There is no information on possible consumer exposure for potassium methanolate. The only information available on sodium methanolate is from the Nordic Product Register of 2003 (SPIN, 2005), where consumer products are listed for Norway and Sweden (no details available on use or use concentrations). Theoretically, consumers could be exposed to residues of the catalysts in consumer products. However, given the sensitivity of methanolates to moisture it is likely that any residual levels would rapidly hydrolyze under formation of methanol and sodium and potassium hydroxide. Both products are listed in the Inventory of Processing Aids for food as catalysts for interesterified food oils of the Codex Alimentarius with residual levels below 1 mg/kg (Codex Alimentarius, 1989).

3 HUMAN HEALTH HAZARDS

3.1 Effects on Human Health

The predominant effect of sodium and potassium methanolate on humans is their corrosivity to skin and mucous membranes, due to the rapid and exothermic reaction with tissue water yielding alkaline hydroxides.

3.1.1 Toxicokinetics, Metabolism and Distribution

The abiotic hydrolysis of sodium and potassium methanolates with tissue water results in the formation of sodium and potassium ions respectively, hydroxide ions and methanol. Information on the toxicokinetics, metabolism and distribution data of sodium hydroxide, potassium hydroxide and methanol can be found in the respective OECD SIDS dossiers (OECD, 2001, OECD, 2002, OECD, 2004).

Exposure to non irritant levels of methanolates via the dermal or inhalation route is not expected to lead to relevant uptake of the ionic degradation products sodium or potassium ions or hydroxide ions in amounts that would exceed the normal physiological levels.

Exposure to hydroxide ions from sodium or potassium methanolate exposure could potentially increase the pH of the blood and lead to alkalosis. However, the pH of the blood is regulated between narrow ranges (pH 7.0 to 7.8) and an excessive pH of the blood is prevented by the bicarbonate buffer system, respiration and renal compensation mechanisms (OECD 2001, OECD, 2002).

The sodium ion is a normal constituent of the blood and an excess is excreted in the urine (OECD, 2002). Uptake of sodium following exposure to sodium methanolate can be considered negligible compared to the uptake of sodium via food (3.1 to 6 g/day; OECD, 2002). For sodium hydroxide it was concluded in SIAM 14 "under normal handling and use conditions (non-irritating) neither the concentration of sodium in the blood nor the pH of the blood will be increased and therefore NaOH is not expected to be systemically available in the body." (OECD, 2002)

Potassium ions are normal constituents of body fluids. K^+ plays an essential role in human physiology, but starts to be toxic at plasma concentrations of 250 mg/l. Its concentration in blood is regulated principally by renal excretion/re-absorption and controlled by an effective feed-back auto-regulation system (OECD, 2001). A systemic intoxication by potassium methanolate is not expected. For potassium hydroxide SIAM 13 concluded: "Under normal handling and use conditions (non-irritating) neither the concentration of potassium in the blood nor the pH of the blood will be increased above normal limits and therefore KOH is not expected to cause systemically toxic levels in the blood. The renal excretion of K^+ can be elevated and the OH^- ion is neutralised by the bicarbonate buffer system in the blood."

OECD (2004) concluded for methanol at SIAM 19: "Methanol is readily absorbed by inhalation, ingestion and dermal contact and partitions rapidly and equally throughout the organism in relation to the water content of organs and tissues. A small amount is excreted unchanged by the lungs and kidneys. Half-lives of methanol in the body are roughly 2.5 to 3 hours at doses less than 100 mg/kg bw. At high doses disproportionate increases of the parent compound in blood are obtained in rodents, but not in humans. On the other hand, in humans the metabolite formate accumulates at high doses. This important difference mirrors the different enzymes and enzyme capacities involved

in the oxidative pathway from methanol to carbon dioxide. Specifically, two different rate limiting processes have been identified: in rodents, high doses (after inhalation of 2.5 – 3.3 mg/l) lead to the saturation of catalase, resulting in the accumulation of methanol whereas formate levels remain low, whereas in primates (especially humans), the parent compound is well oxidized and does not accumulate, but formate increases disproportionately.

From studies in humans and monkeys exposed to concentrations of 0.26 – 2.6 mg/l (administered for 6 to 8 hours), it can be concluded that methanol remains close to 50 mg/l in blood. At inhalation exposures of 2.6 mg/l, rats also exhibit methanol blood levels that are not much higher (at about 80 mg/l), whereas the level in mice was 400 mg/l. At a higher inhalation exposure (6.5 mg/l), humans show the lowest blood methanol level (at 140 mg/l), followed by monkeys, rats, and mice, with the level in mice being more than 10 times higher than humans. Formate accumulation in primates has been observed at methanol doses greater than 500 mg/kg bw.”

The corresponding dose levels for sodium and potassium methanolate that would lead to accumulation of formate in primates would be 840 and 1000 mg/kg bw. Such dose levels are already in the acutely toxic dose range. Due to the corrosive nature of the methanolates it is unlikely that exposure to methanolates could result in an uptake of toxic doses of methanol.

3.1.2 Acute Toxicity

Acute toxicity data are only available for sodium methanolate. As the toxicity is related to the corrosive properties of the substance, similar results can be expected for potassium methanolate.

Studies in Animals

Inhalation

Only limited inhalation toxicity studies are available. Rats were exposed for 8 hours to an enriched atmosphere of the volatile components of a 30 % solution of sodium methanolate in methanol at 20 °C. 200 l air/hour was pumped through a 5 cm layer of the product at 20 °C. No effects were observed in the animals following the exposure (BASF AG, 1978a; well documented, non-GLP). It is likely that the animals in this study were exposed to methanol rather than to sodium methanolate. After exposure of rats to a dust enriched atmosphere (200 l air per hour were piped through a 5 cm layer of the product) for 8 hours no mortality, no clinical symptoms and no macroscopic organ changes were observed (BASF AG, 1979a; well documented, Non-GLP). As no signs of irritation were observed it is likely that irritant exposure levels could not be reached using this method.

Due to the high alkalinity and corrosive nature of potassium methanolate and sodium and potassium hydroxide no acute inhalation studies were performed with these substances. It is very unlikely that through inhalation exposure to sodium or potassium methanolate air concentrations could be reached that would be in the range of causing methanol toxicity. The tolerable exposure will be limited by the highly corrosive properties of the substance.

Dermal

A non-GLP, but well documented acute dermal toxicity study with 50 % aqueous sodium methanolate in rats revealed a low acute toxicity (> 2000 mg/kg bw) via the dermal route. As the study was performed in aqueous solution, in fact the hydrolysis products have been tested. No deaths occurred at 1000 and 2000 mg/kg bw. Clinical signs reported included irregular breathing and bad general condition. Skin necrosis was observed after the 24 hour application period. This finding is in accordance with the corrosivity of the test substance. (BASF AG, 1979b)

Due to the high alkalinity and corrosive nature of potassium methanolate and sodium and potassium hydroxide no acute dermal studies were performed with these substances.

Due to the severe corrosivity sodium and potassium methanolate it is very unlikely that dermal exposure of humans to sodium or potassium methanolate would lead to an uptake of methanol that would be sufficiently high to cause acute methanol toxicity.

Oral

An aqueous solution of sodium methanolate (10 to 20 %) was tested for its acute toxicity according to OECD guideline 401 and GLP in male and female Sprague-Dawley rats. The LD₅₀ was 1687 mg/kg bw. Animals of all dose groups showed symptoms of hunched posture lethargy and decreased respiration rate. Macroscopic findings at necropsy in animals that died during the study included red lungs pale, dark or patchy pale discoloration of the liver and at doses from 1587 mg/kg bw severe hemorrhage and rugae of the glandular gastric epithelium as well as occasional adherence of the stomach to the liver. In animals killed at termination occasional white foci in the non-glandular stomach and adherence of the stomach to the liver was also observed (Degussa, 1988a).

Sodium methanolate was administered as a 2.15 to 10 % aqueous solution (volume administered 10 ml/kg) to male and female Sprague-Dawley rats by gavage at dose levels between 215 and 1000 mg/kg bw. All animals of the 1000 mg/kg dose group died while animals dosed up to 681 mg/kg bw survived. Clinical symptoms of dyspnea and apathy were observed in all dose groups, at 316 mg/kg bw yellow discoloration of the urine was observed and disturbances of posture and gait were observed from 681 mg/kg bw. Macroscopic findings were only observed in the animals that died during the study and included dilatation and discoloration of the right heart, acute congestive hyperemia, atonic stomach and intestines, fluid stomach and intestinal content and diffuse reddening and vascular injection of the forestomach. The study was well documented, but non-GLP (BASF AG, 1978b).

As both studies mentioned above were performed with aqueous solutions of sodium methanolate, in fact the hydrolysis products have been tested.

Two other studies tested the acute oral toxicity to rats of suspensions of solid sodium methanolate in non-aqueous solutions. An LD₅₀ value of 800 mg/kg bw was reported in a study using Lutrol as a solvent. No characteristic symptoms were observed in this study. Macroscopic findings were only reported in the animals that died during the study and included acute dilatation of the right heart and congestive hyperemia as well as ulcerating gastritis, bleeding in the forestomach, thickened walls of the glandular stomach, adhesions between stomach and liver atonic intestine with bloody content, hydrothorax and partly blood colored ascites. (BASF AG, 1979b). This study is a well documented non-GLP study.

In another well documented non-GLP study a suspension of sodium methanolate in corn oil was administered to male and female Sprague Dawley rats. In this study an LD₅₀ of 2037 mg/kg bw was obtained. Labored breathing, weakness, wet and stained perianal area as well as chromodacryorrhea and ruffled fur were observed in all animals. Macroscopic findings were not reported in the reference. (Dupont de Nemours, 1982).

The difference between the two studies in non-aqueous solvents is probably due to their different lipophilicity. Lutrol is hydrophilic and readily dissolved in the aqueous gastric fluid liberating the dispersed test substance that will hydrolyze immediately delivering the hydrolysis products at a relative high concentration to the stomach tissue. This leads to the relative severe signs of irritation and corrosivity. The lipophilic corn oil on the other hand can be expected to release the test substance more slowly from the administered bolus leading to a lower tissue concentration of the hydrolysis products and less damage to the gastric mucosa.

The symptomatology and macroscopic findings in all studies are consistent with the corrosive nature of the substance and sodium hydroxide as the corrosive hydrolysis product. The differences in toxicity can probably be explained with the difference concentrations and dose rates of the delivery of the substance and its degradation products to the tissues of the gastrointestinal tract. The order of magnitude of the LD₅₀ is consistent with that of sodium hydroxide for which LD₅₀ values between 325 and higher than 500 mg/kg bw have been reported (OECD, 2002). It is unlikely that methanol contributes much to the acute toxicity observed in the above studies as in most of the studies in rodents methanol toxicity was approximately one order of magnitude lower (OECD, 2004).

For potassium methanolate no data are available. Due to the reaction with water and the liberation of hydroxide ions and the alkaline reaction the mode of action will be the same and the acute toxicity will be comparable to that of sodium methanolate and potassium hydroxide. For potassium hydroxide acute oral toxicity values between 273 and 1230 mg/kg body weight were reported (OECD, 2001). These are also consistent with the data for sodium hydroxide and sodium methanolate supporting the evidence for a common hydroxide ion mediated mode of action.

With regard to a possible methanol toxicity in humans through oral uptake of sodium or potassium methanolate it should be considered that doses that would lead to deaths in humans (300 to 1000 mg methanol/kg bw. correspond to sodium and potassium methanolate doses between 507 to 1690 and 657 to 2190 mg/kg bw respectively. Such dose levels would already cause considerable irritation of the mucous membranes in the oral cavity, pharynx and gastrointestinal tract and humans are unlikely to be exposed orally to such dose levels.

Conclusion

No signs of toxicity were observed in rats exposed to a dust enriched atmosphere of sodium methanolate for 8 hours, the dermal LD₅₀ of a 50 % aqueous solution was > 2000 mg/kg bw in rats. Skin necrosis was observed in this study. After oral administration the acute toxicity is dependent on the local tissue concentration and the dose rate of the substance and its degradation product sodium hydroxide. The rat LD₅₀ in water or water soluble solvents was between 800 and 1687 mg/kg bw, when administered in corn oil the LD₅₀ was 2037 mg/kg bw. The acute toxicity is consistent with that of sodium hydroxide and it can be assumed that the primary mode of action is local irritation/corrosion at the site of first contact.

For potassium methanolate no data are available, but due to the reaction with water and the liberation of hydroxide ions and the alkaline reaction the mode of action will be the same and the acute toxicity will be comparable to that of sodium methanolate and potassium hydroxide. The acute toxicity of both substances is mediated by their alkalinity and the hydroxide ion.

Skin Irritation

Studies in Animals

A 30 % sodium methanolate solution in methanol was highly corrosive to the skin of rabbits when exposed for 1 to 15 minutes. Necrosis was already observed after an exposure time of 1 minute. A severe pain reaction was observed shortly after the application of the test substance (BASF AG, 1979b) (well documented non-GLP study). In another study on 2 rabbits (well documented, no GLP) a 80 % solution of sodium methanolate in water was highly corrosive after 3 minutes of exposure to the skin and resulted in necrosis that was irreversible after the 8-day post exposure observation period (BASF AG, 1979b). In a standard skin irritation/corrosion test according to EPA OPP 81-5 and GLP solid sodium methanolate moistened with water was applied to the skin of 6 rabbits for 4 hours under semi occluded conditions. Due to severe necrosis at all application sites

the study was terminated one hour after removal of the patches for humane reasons. (Degussa, 1988b).

For potassium methanolate no studies are available. Due to its alkaline reaction and exothermic reaction with water it will be similarly highly corrosive to skin.

Eye Irritation

Studies in Animals

In a preliminary non-GLP study with two rabbits 50 ml of undiluted sodium methanolate were administered to the eyes. Already after one hour severe corneal opacity and a grey discoloration of the nictating membranes was observed. The effects were irreversible within the 8-day observation period. The substance was corrosive to rabbit eye (BASF AG, 1978a).

For potassium methanolate no studies are available. Due to its alkaline reaction and exothermic reaction with water it will be similarly corrosive to the eye.

Conclusion

Sodium methanolate was highly corrosive to rabbit skin and eyes. For potassium methanolate no studies are available. Due to its alkaline reaction and exothermic reaction with water it will be similarly corrosive. Based on the skin and eye irritation data it can be assumed that both methanolates will also cause irritation/corrosion to the mucous membranes of the upper respiratory tract in case of an exposure via the inhalation route.

As the corrosivity is mediated by the exothermic liberation of sodium or potassium hydroxide the data for the hydroxides may be important for the evaluation of this endpoint as well. For sodium hydroxide OECD 2002 concluded that based on the animal data a NaOH solution of 8 % can be considered corrosive. Based on human data concentrations of 0.5 to 4 % were irritating to the skin and concentrations slightly lower than 0.5 % were considered non-irritating. For potassium hydroxide OECD 2001 that KOH is a corrosive at concentrations of about 2 % and higher. Between 0.5 % and 2 % it is irritating.

Sensitization

No data with regard to skin sensitization are available for sodium and potassium methanolate. The abiotic hydrolysis of sodium and potassium methanolates with tissue water results in the formation of sodium and potassium ions respectively and methanol. For sodium hydroxide, a study with human volunteers did not indicate a skin sensitization potential (OECD, 2002), and no allergic skin reactions were observed in an intracutaneous skin sensitization test with potassium hydroxide on guinea pigs according to the Landsteiner and Jacobs method (OECD, 2001). For methanol, a guinea pig maximization test gave no evidence of contact sensitization after induction and challenge doses of 50 percent (OECD, 2004).

Conclusion

From the data of the hydrolysis products it can be concluded that sodium and potassium methanolate are not expected to have a notable skin sensitization potential.

3.1.3 Repeated Dose Toxicity

No data are available on repeated dose toxicity of sodium and potassium methanolate. The abiotic hydrolysis of sodium and potassium methanolates with tissue water results in the formation of

sodium and potassium ions respectively, hydroxide ions and methanol. Therefore the data of the hydrolysis products are relevant for the methanolates as well.

Hydroxide ions

The neutralization of OH⁻ by gastric HCl and the quick and efficient pH regulation mechanism of extracellular fluids (buffer capacity of extra cellular body fluids, respiratory and renal compensation mechanisms), prevents an alkalosis due to OH⁻ ions after sodium- or potassium methanolate dosage in non-irritant concentrations (see also section 3.1.1).

Sodium ions

The hazard of repeated human exposure to sodium has been focused on the effects of sodium on the prevention and control of hypertension. A dietary salt intake of 2.0 to 3.0 g was reported to be a moderately restricted intake; 3.1 to 6.0 g was reported as normal intake, while a dietary intake of > 6 g of sodium ions per day was considered an excessive intake (OECD, 2002). An intake of 6 g per day for a 60 kg individual would correspond to a daily dose of 100 mg/kg bw of sodium ions per day. To reach an excessive intake of sodium from exposure to sodium methanolate and intake of more than 235 mg sodium methanolate/kg bw per day would be needed. Given the corrosive properties of the substance it is unlikely that humans would be exposed to such dose levels under normal use conditions.

Potassium ions

Studies in Animals

From a two year dietary study in mice with potassium chloride a NOAEL of > 955 mg K⁺/kg bw/day was derived (OECD, 2001).

Studies in Humans

For potassium ions NOAEL in humans of 46 and 56.6 mg/kg bw/day have been suggested from human studies with potassium chloride based on lowering effects on the systolic and diastolic blood pressure (OECD, 2001). The human NOAEL would correspond to between 82 mg/kg and 101 mg potassium methanolate/kg bw. The rat NOAEL corresponds to 1709 mg/kg bw. Given the corrosive properties of the substance it is unlikely that humans would be exposed to such dose levels under normal use conditions.

Methanol

For methanol a number of repeated dose studies in different species have been described in OECD, 2004.

The following conclusion was drawn on Methanol toxicity in OECD, 2004. "In a whole body inhalation study in monkeys exposed to 0.013, 0.13, and 1.3 mg/l 21 hours per day 7 days per week for 7, 19, and 29 months, several general clinical signs as well as degenerative effects in the brain (at 0.13 and 1.3 mg/l), slight peripheral nerve damage (at 0.13 and 1.3 mg/l), very slight degeneration of the optic nerve (concentrations not noted), increased fat granules and slight fibrosis in the liver (all concentrations), and Sudan positive granules in the kidney were observed (at 0.13 and 1.3 mg/l). Also, a slight myocardial disorder (at 0.13 and 1.3 mg/l) and localized effects in the trachea and possible slight fibrosis in the lungs (concentrations not noted) were observed. Although the statistical significance of the effects cannot be verified from the study report, the number of effects and systems affected indicate a relationship with methanol.

In another whole body inhalation study in monkeys exposed up to 20 days for 21 hours per day, coma and lethality were observed at concentrations > 9.1 mg/l/day. In the brain, necrosis of the

basal ganglia and cerebral edema were observed at 6.5 mg/l/day and at 3.9 mg/l/day, hyperplasia and fibrosis around myelin sheaths of the basal ganglia as well as a slight to moderate increase in astroglia cells were observed. The optic nerve showed atrophy at > 3.9 mg/l/day, along with reduction in myelin fibers. In the liver, fibrosis was observed at 6.5 mg/l/day and mild fatty degeneration was observed at 3.9 mg/l/day. In the kidney, partly vacuolated hyaline degeneration was observed at 6.5 mg/l/day.

In rats exposed to methanol up to 6.5 mg/l for 6 hours per day, five days per week for 28 days, no adverse effects were observed except local nasal irritation and increased relative spleen weights, which were observed only at the middle dose. The estimated blood level of methanol was about 250 mg/l under this condition.

In a whole body inhalation study in mice exposed for 12 months to concentrations of 0.013, 0.13, and 1.3 mg/l per day, slight changes in clinical signs, body and organ weights, and some changes in histopathology were observed. In rats exposed in the same manner, slight changes in body weight and organ weights were observed at the highest dose. In rats, gavage doses of 100, 500, and 2500 mg/kg bw/day for 90 days resulted in increased liver enzymes and reduced brain weights at the highest dose resulting in a NOAEL of 500 mg/kg/day.”

Conclusion

No data on repeated dose toxicity of sodium and potassium methanolate are available. Due to the immediate hydrolysis of the substances the toxicity of the hydrolysis products K^+ or Na^+ ions, OH^- ions and methanol is considered relevant. The tolerable dose levels will be determined by the corrosive nature of the substances. At non-irritant concentrations the toxicity of K^+ or Na^+ ions and OH^- ions are unlikely to contribute to the effects to be expected after repeated exposure. The specific ocular and CNS toxicity of methanol in primates is based on the accumulation of formate in blood. Formate accumulation in primates has been observed at methanol doses greater than 500 mg/kg. (OECD, 2004). The corresponding dose levels for sodium and potassium methanolate that would lead to accumulation of formate in primates would be 840 and 1000 mg/kg bw. Such dose levels are already in the acutely toxic dose range. Due to the corrosive nature of the methanolates it is unlikely that exposure to methanolates could result in an uptake of toxic doses of methanol.

3.1.4 Mutagenicity

No data are available on the mutagenicity of potassium methanolate. A limited GLP-Ames assay with sodium methanolate in only three strains of *S. thyphimurium* TA 97, TA98 and TA100 with and without metabolic activation at concentration up to 5000 µg/plate did not show any increase in revertants. (Degussa, 1987). The abiotic hydrolysis of sodium and potassium methanolates either in aqueous culture media or in vitro test systems or with tissue water results in the formation of sodium or potassium hydroxide and methanol. Therefore the data of the hydrolysis products are relevant for the methanolates as well. For sodium and potassium hydroxide there was no evidence of a mutagenic activity (OECD, 2001, 2002). For methanol the majority of the *in vitro* assays available were negative with the exception of a positive result in a mouse lymphoma assay, an ambiguous result in one Ames assay for strain 102 and an ambiguous result in the DNA damage and repair assay. Of the eleven *in vivo* assays (all micronucleus and cytogenicity assay and one *Drosophila* SLRL assay) all were negative except one cytogenetic assay for which limited information was available, that was positive for aneuploidy, SCE, and micronuclei (OECD, 2004).

Conclusion

No data on mutagenicity of sodium or potassium methanolate are available with the exception of one negative Ames assay with a limited number of strains conducted with sodium methanolate. Due to the rapid hydrolysis of methanolates in *in vitro* test systems and tissue water *in vivo*, data for the hydrolysis products are relevant for methanolates as well. For sodium and potassium hydroxide there is no evidence for a mutagenic potential. For methanol the weight of evidence suggests that the substance is unlikely to have any relevant mutagenic activity. Therefore it can be concluded that there is no concern with regard to a mutagenic activity of sodium or potassium methanolate.

3.1.5 Carcinogenicity

No data are available on carcinogenicity of sodium and potassium methanolate. The abiotic hydrolysis of sodium and potassium methanolates with tissue water results in the formation of sodium and potassium hydroxide respectively and methanol. Therefore the data of the hydrolysis products are relevant for the methanolates as well. No data on the carcinogenicity of sodium hydroxide are available. For potassium hydroxide it was concluded that there is no evidence of KOH to be carcinogenic in exposure situations that are relevant for humans (OECD, 2001). Only at repeated exposure to highly irritant concentrations leading to a prolonged inflammatory response local carcinogenicity due to a non-genotoxic mechanism by direct hyperplasia as a consequence of severe tissue damage could occur, as described in an old mouse skin painting study (25 to 46 weeks of exposure) with irritant concentrations of KOH (3 - 6 %) (OECD, 2001). Methanol was tested in two long-term whole body inhalation studies (24 months in rats and 18 months in mice for 20 and 19 hours per day respectively), up to concentrations of 1.3 mg/l. There was no evidence of a carcinogenic potential. (OECD, 2004).

Conclusion

No data are available on the carcinogenicity of sodium and potassium methanolate. For potassium hydroxide it was concluded at SIAM 13 that there is no evidence of carcinogenicity in exposure situations that are relevant for humans. There was no evidence for a carcinogenic potential of methanol in two long-term inhalation studies on rats and mice. Based on the available data, there is therefore no concern for carcinogenicity of sodium and potassium methanolates.

3.1.6 Toxicity for Reproduction

No data are available on toxicity to reproduction or development of sodium and potassium methanolate. The abiotic hydrolysis of sodium and potassium methanolates with tissue water results in the formation of sodium and potassium ions respectively, hydroxide ions and methanol. Therefore the data of the hydrolysis products are relevant for the methanolates as well.

For reasons outlined in section 3.1.1 and 3.1.3 hydroxide ions will not be systemically available to the developing embryo or fetus or the reproductive organs. No effects on the developing embryo or fetus or on reproduction have been observed with potassium salts. The calculated NOAEL for the potassium ion is > 164 mg/kg bw of K^+ (the highest dose administered in developmental studies in rats and mice and a one generation study in mice) (OECD, 2001). For sodium ions no relevant potential for developmental or reproductive toxicity was expected (OECD, 2002).

For methanol the following conclusions on toxicity to reproduction were drawn (OECD, 2004): "Monkeys. In monkeys, parents were exposed via inhalation prior to and during breeding as well as during pregnancy to doses of 0.26, 0.78, and 2.34 mg/l. Wasting syndrome was observed at the

highest dose. Mild neurobehavioral effects in offspring as well as some vaginal bleeding and unproductive labor in mothers were observed at all concentrations. However, due to the normal variance in and the low number of animals, the observed findings are somewhat difficult to interpret.

Rats. Several inhalation studies in rats resulted in a variety of effects in offspring due to prenatal and/or postnatal dosing. In a 2-generation whole body inhalation reproductive study in which rats were exposed for 19 - 20 hours/day, decreased brain weights in the first generation offspring (F1) resulted in a NOAEL of 0.13 mg/l. In a developmental study in which rats were exposed by whole body inhalation on gestation days 1 to 19 at the two lowest doses and days 7 to 15 at the highest dose for 7 hours/day, malformations and fetal weight changes resulted in a LOAEL of 6.5 mg/l/day (the lowest dose tested). A second whole-body inhalation developmental study in which rats were exposed on gestation days 7 to 17 for 23 hours/day, malformations, increased fetal resorptions, and decreased numbers of live fetuses were observed, resulting in a NOAEL of 1.3 mg/l/day.

Mice. In a study of reproductive effects, there was an insignificant increase in morphological anomalies in spermatozoa in male mice at 1000 mg/kg/day after oral dosing for five weeks. A developmental whole body inhalation study in mice exposed on gestation days 6 to 15 for 7 hrs/day resulted in developmental effects including increased exencephaly and cleft palate, fully resorbed fetuses, decreased numbers of live pups, and decreased body weights; this study resulted in a NOAEL of 1.3 mg/l/day. Oral studies in mice resulted in various malformations at 4000 mg/kg-bw/day (the LOAEL) and higher; no NOAELs could be established from these studies.

Humans. No epidemiological studies in humans have been located to demonstrate that there is a link between methanol exposure and an increased incidence of fetal malformations or developmental impairment.

Rodent data on reproductive and developmental toxicity are relevant for humans despite the known differences in methanol metabolism between rodents and humans. Rodents are adequate models for human exposure to methanol at levels where formate does not accumulate. However, blood methanol concentrations associated with serious teratogenic effects and reproductive toxicity observed in the rodent studies are in the range associated with formate accumulation, which is likely to result in metabolic acidosis and visual and clinical effects in humans. Other effects (e.g., subtle neurological effects observed in primates) are exhibited at lower inhalation concentrations and lower methanol blood levels. “

It is unlikely that concentrations associated with serious developmental effects in rodents could be reached by administration of sodium or potassium methanolate to experimental animals, as those dose levels would be in the acute toxic dose range and associated with massive local irritation at the site of first contact. The maximum tolerated dose in such studies is therefore likely to be below the dose that would result in methanol mediated developmental effects. In addition for animal welfare reasons it is not recommended to perform further animal studies with sodium and potassium methanolate.

Conclusion

No data are available on reproductive or developmental toxicity of sodium and potassium methanolate. The abiotic hydrolysis of sodium and potassium methanolates with tissue water results in the formation of sodium and potassium ions respectively, hydroxide ions and methanol. For hydroxide ions, sodium and potassium ions no relevant reproductive toxicity potential has been identified. For methanol reproductive and developmental toxicity effects have been described in rats, mice and monkeys. Blood methanol concentrations associated with serious developmental effects and reproductive toxicity in rodent studies are in the range associated with formate accumulation. It is unlikely that concentrations associated with serious developmental effects in rodents could be reached by administration of sodium or potassium methanolate to experimental

animals, as those dose levels would be in the acute toxic dose range and associated with massive local irritation at the site of first contact. The maximum tolerated dose in such studies is therefore likely to be below the dose that would result in methanol mediated developmental effects. In addition for animal welfare reasons it is not recommended to perform further animal studies with sodium and potassium methanolate.

3.2 Initial Assessment for Human Health

The predominant effect of sodium and potassium methanolate on humans is their corrosivity to skin and mucous membranes, due to the rapid and exothermic reaction with tissue water yielding alkaline hydroxides.

The abiotic hydrolysis of sodium and potassium methanolates with tissue water results in the formation of sodium and potassium ions respectively, hydroxide ions and methanol.

Exposure to non irritant levels of methanolates via the dermal or inhalation route is not expected to lead to relevant uptake of the ionic degradation products sodium or potassium ions or hydroxide ions in amounts that would exceed the normal physiological levels.

The sodium ion is a normal constituent of the blood and an excess is excreted in the urine (OECD, 2002). Uptake of sodium following exposure to sodium methanolate can be considered negligible compared to the uptake of sodium via food (3.1 to 6 g/day; OECD, 2002).

Potassium ions are normal constituents of body fluids. K^+ plays an essential role in human physiology, but starts to be toxic at plasma concentrations of 250 mg/l. Its concentration in blood is regulated principally by renal excretion/re-absorption and controlled by an effective feed-back auto-regulation system (OECD, 2001). A systemic intoxication by potassium methanolate is not expected as the uptake will be limited by the corrosive properties of the substance.

Exposure to hydroxide ions from sodium or potassium methanolate exposure could potentially increase the pH of the blood and lead to alkalosis. However, the pH of the blood is regulated between narrow ranges pH 7.0 to 7.8 and an excessive pH of the blood is prevented by the bicarbonate buffer system, respiration and renal compensation mechanisms (OECD, 2001, 2002).

OECD (2004) concluded for methanol: "Methanol is readily absorbed by inhalation, ingestion and dermal contact and partitions rapidly and equally throughout the organism in relation to the water content of organs and tissues. A small amount is excreted unchanged by the lungs and kidneys. Half-lives of methanol in the body are roughly 2.5 to 3 hours at doses less than 100 mg/kg bw. At high doses disproportionate increases of the parent compound in blood are obtained in rodents, but not in humans. On the other hand, in humans the metabolite formate accumulates at high doses. This important difference mirrors the different enzymes and enzyme capacities involved in the oxidative pathway from methanol to carbon dioxide. Specifically, two different rate limiting processes have been identified: in rodents, high doses (after inhalation of 2.5 – 3.3 mg/l) lead to the saturation of catalase, resulting in the accumulation of methanol whereas formate levels remain low, whereas in primates (especially humans), the parent compound is well oxidized and does not accumulate, but formate increases disproportionately."

From studies in humans and monkeys exposed to concentrations of 0.26 – 2.6 mg/l (administered for 6 to 8 hours), it can be concluded that methanol remains close to 50 mg/l in blood. At inhalation exposures of 2.6 mg/l, rats also exhibit methanol blood levels that are not much higher (at about 80 mg/l), whereas the level in mice was 400 mg/l. At a higher inhalation exposure (6.5 mg/l), humans show the lowest blood methanol level (at 140 mg/l), followed by monkeys, rats, and mice, with the level in mice being more than 10 times higher than humans. Formate accumulation in primates has been observed at methanol doses greater than 500 mg/kg."

The corresponding dose levels for sodium and potassium methanolate that would lead to accumulation of formate in primates would be 840 and 1000 mg/kg bw. Such dose levels are already in the acutely toxic dose range. Due to the corrosive nature of the methanolates it is unlikely that repeated exposure to methanolates could result in an uptake of toxic doses of methanol. The only exposure situation for sodium and potassium methanolate that could perhaps lead to methanol and formate blood levels resulting in acute neurophysiological and visual disturbances would be accidental dermal exposure to corrosive concentrations that could lead at the same time to an uptake of toxic amounts of methanol through the skin. It has been assumed that an inhalation exposure to methanol of 260 mg/m³ for 8 hours does not lead to any adverse effects (OECD, 2004). This exposure level corresponds to a systemic dose of 2600 mg methanol/d (assuming an inhalation volume of 10 m³ during an 8-hour working day) or 37 mg/kg bw day (for a 70 kg human). It would require doses of 44.4 and 65 mg/kg bw of sodium or potassium methanolate respectively, to achieve a systemic dose of 2600 mg methanol/d. The rate of dermal uptake for methanol was reported to be 0.192 mg/cm²/min. Accidental exposure of both hands (850 cm²) to sodium or potassium methanolate for one minute resulting in corrosive effects could then theoretically additionally lead to an uptake of methanol exceeding the dose level of 37 mg/kg bw. Such an exposure situation does however not reflect any human exposure situation under normal handling conditions as precautions are taken because of the corrosivity of the substances.

No signs of toxicity were observed in rats exposed to a dust enriched atmosphere of sodium methanolate for 8 hours, the dermal LD₅₀ of a 50 % aqueous solution was > 2000 mg/kg bw in rats. Skin necrosis was observed in this study. After oral administration the acute toxicity is dependent on the local tissue concentration and the dose rate of the substance and its degradation product sodium hydroxide. The LD₅₀ in water or water soluble solvents was between 800 and 1687 mg/kg bw, when administered in corn oil the LD₅₀ was 2037 mg/kg bw. The acute toxicity is consistent with that of sodium hydroxide and it can be assumed that the primary mode of action is local irritation/corrosion at the site of first contact.

For potassium methanolate no data are available, but due to the reaction with water and the liberation of hydroxide ions and the alkaline reaction the mode of action will be the same and the acute toxicity will be comparable to that of sodium methanolate and potassium hydroxide. The acute toxicity of both substances is mediated by their alkalinity and the hydroxide ion.

Sodium methanolate was highly corrosive to rabbit skin and eyes. For potassium methanolate no studies are available. Due to its alkaline reaction and exothermic reaction with water it will be similarly corrosive. Based on the skin and eye irritation data it can be assumed that both methanolates will also cause irritation/corrosion to the mucous membranes of the upper respiratory tract in case of an exposure via the inhalation route.

As the corrosivity is mediated by the exothermic liberation of sodium or potassium hydroxide the data for the two hydroxides may be important for the evaluation of this endpoint as well. For sodium hydroxide OECD 2002 concluded that based on the animal data a NaOH solution of 8 % can be considered corrosive. Based on human data concentrations of 0.5 to 4 % were irritating to the skin and concentrations slightly lower than 0.5 % were considered non-irritating. Potassium hydroxide is corrosive at concentrations of about 2 % and higher. Between 0.5 % and 2 % it is irritating.

From the data of the hydrolysis products it can be concluded that sodium and potassium methanolate are not expected to have a notable skin sensitization potential.

No data on repeated dose toxicity of sodium and potassium methanolate are available. The tolerable dose levels will be determined by the corrosive nature of the substances. At non-irritant concentrations, the K⁺ or Na⁺ ions and the OH⁻ ions are unlikely to have any adverse effects. The

specific ocular and CNS toxicity of methanol in primates is based on the accumulation of formate in blood. Formate accumulation in primates has been observed at methanol doses greater than 500 mg/kg. (OECD, 2004). The corresponding dose levels for sodium and potassium methanolate that would lead to accumulation of formate in primates would be 840 and 1000 mg/kg bw. Such dose levels are already in the acutely toxic dose range. Due to the corrosive nature of the methanolates it is very unlikely that exposure to methanolates could result in an uptake of toxic doses of methanol.

No data on mutagenicity of sodium or potassium methanolate are available with the exception of one negative Ames assay with a limited number of strains conducted with sodium methanolate. Due to the rapid hydrolysis of methanolates in *in vitro* test systems and tissue water *in vivo*, data for the hydrolysis products are relevant for methanolates as well. For sodium and potassium hydroxide there is no evidence for a mutagenic potential. For methanol the weight of evidence suggests that the substance is unlikely to have any relevant mutagenic activity. Therefore it can be concluded that there is no concern with regard to a mutagenic activity of sodium or potassium methanolate.

No data are available on the carcinogenicity of sodium and potassium methanolate. For potassium hydroxide it was concluded at SIAM 13 that there is no evidence of carcinogenicity in exposure situations that are relevant for humans. There was no evidence for a carcinogenic potential of methanol in two long-term inhalation studies on rats and mice. Based on the available data, there is therefore no concern for carcinogenicity of sodium and potassium methanolates.

No data are available on reproductive or developmental toxicity of sodium and potassium methanolate. For hydroxide, sodium and potassium ions, no relevant reproductive toxicity potential has been identified. For methanol reproductive and developmental toxicity effects have been described in rats, mice and monkeys. Blood methanol concentrations associated with serious developmental effects and reproductive toxicity in rodent studies are in the range associated with formate accumulation. It is unlikely that concentrations associated with serious developmental effects in rodents could be reached by administration of sodium or potassium methanolate to experimental animals, as those dose levels would be in the acutely toxic dose range and associated with massive local irritation at the site of first contact. The maximum tolerated dose in such studies is therefore likely to be below the dose that would result in methanol mediated developmental effects. In addition, for animal welfare reasons, it is not recommended to perform further animal studies with sodium and potassium methanolate.

4 HAZARDS TO THE ENVIRONMENT

4.1 Aquatic Effects

A limited number of toxicity studies are available for sodium methanolate. However, in the aquatic environment due to the rapid hydrolysis of the compounds the toxicity of the degradation products, sodium and potassium hydroxide and methanol are relevant.

Acute Toxicity Test Results

Toxicity to fish

A 48-hour static fish toxicity test with *Leuciscus idus melanotus* was performed with sodium methanolate according to DIN 38412 part 15 (non-GLP, no analytical monitoring). The 48-h LC₅₀ was 346 mg/l (Degussa, 1988c).

Toxicity to algae

A 24-hour test in the alga *Scenedesmus subspicatus* was performed with sodium methanolate according to DIN 38412 part 12 (no GLP, no analytical monitoring). The EC₅₀ for assimilation inhibition was calculated to be 302 mg/l, the EC₁₀ was 24 mg/l and the EC₉₀ 3800 mg/l (Degussa, 1989a).

Additional results to the hydrolyses products are listed in Table 3

Table 3 Toxicity of hydrolysis products to aquatic organisms

Species	Parameter	Effects	Reference
Sodium hydroxide:			
<i>Leuciscus idus melanotus</i> <i>Gambusia affinis</i> (fish)	48h-LC ₅₀ 96h-LC ₅₀	189 mg/l 125 mg/l	OECD, 2002
<i>Ceriodaphnia dubia</i> <i>Daphnia magna</i> (invertebrate)	48h-LC ₅₀ TTC*	40 mg/l 40 – 240 mg/l	OECD, 2002
<i>Biomphalaria a. alexandrina</i> <i>Bulinus truncatus</i> <i>Lymnea caillaudi</i> (mollusca)	Lethal concentrations	450 mg/l 150 mg/l 150 mg/l	OECD, 2002
<i>Ophryotrocha diadema</i> (marine polychaete)	48h-LC ₅₀	33 - 100 mg/l	OECD, 2002
Potassium hydroxide:			
<i>Gambusia affinis</i> <i>Poecilia reticulata</i> (fish)	96h-LC ₅₀ 24h-LC ₅₀	80 mg/l 165 mg/l	OECD, 2001
Methanol:			
Different fish species	96h-LC ₅₀	15 400 – 29 400 mg/l	OECD, 2004
<i>Daphnia magna</i> (invertebrate)	Several 24h- and 48h-EC ₅₀ 24h-EC ₅₀	> 10 000 mg/l 21 400 mg/l	OECD, 2004
<i>Chlorella pyrenoidosa</i> (algae)	10 – 14d- ErC ₅₀	28 440 mg/l	OECD, 2004

* toxicity threshold concentration

Chronic Toxicity Test Results

Only one chronic toxicity study which was not considered reliable (reliability 3) was reported for NaOH. An adverse effect on survival rate, growth and fecundity as well as the quality of progeny was found in *Lebistes reticulatus* between 25 and 100 mg/l of NaOH (OECD, 2002).

Toxicity to Microorganisms

The inhibition of bacterial metabolism in a bacterial mixed culture according to DIN 38412 part 12 was studied with sodium methanolate. The 24-hour EC₅₀ was 97 mg/l, the EC₁₀ 38 mg/l and the EC₉₀ 246.9 mg/l.

Sodium hydroxide

The 15-minute-EC₅₀ for *Photobacterium phosphoreum* in the Microtox system was 22 mg/l. The test medium was 2 % NaCl indicating that the medium was not buffered. The effect of NaOH on

motility of the protozoan *Tetrahymena thermophila* was studied microscopically. When 1 % NaOH was diluted 62 times the motility was higher than 90 % of control cell motility (highest tolerated dose, HTD). This would be equal to a NaOH concentration of 161 mg/l. (OECD, 2002)

Potassium hydroxide

The 15-minute-EC₅₀ for *Photobacterium phosphoreum* in the Microtox system was 22 mg/l. The test medium was 2 % NaCl indicating that the medium was not buffered. (OECD, 2001).

Methanol

The lowest toxic limit concentrations have been reported to be at 6600 mg/l in a cell multiplication test for 16 hours using two *Pseudomonas* species according to German Standard Procedures DEV L8) (OECD, 2004).

Conclusion

The toxicity of sodium and potassium methanolate to aquatic organisms is mediated by their degradation products due to the rapid reaction with water yielding sodium or potassium hydroxide and methanol. The aquatic toxicity of methanol is low with acute EC₅₀ or LC₅₀ values > 10 000 mg/l and therefore its contribution to the methanolate toxicity is considered negligible. Sodium methanolate was moderately toxic to bacteria with a 24-hour EC₅₀ of 97 mg/l. The toxicity is likely mediated through a pH effect by the release of hydroxide ions. The limited data available for sodium methanolate are consistent with the aquatic toxicity of the alkali hydroxides. However, as concluded for sodium and potassium hydroxide already (see OECD, 2001, 2002), acute toxicity data cannot be used to derive a PNEC or a PNEC_{added} for the compounds releasing hydroxide. Aquatic ecosystems are characterized by an alkalinity/pH and the organisms of the ecosystems are adapted to these specific natural conditions. Based on the natural alkalinity of waters, organisms will have different optimum pH conditions, ranging from poorly buffered waters with a pH of 6 or less to very hard waters with pH values up to 9. A lot of information is available about the relationship between pH and ecosystem structure and also natural variations in the pH of aquatic ecosystems have been quantified and reported extensively in ecological publications and handbooks.

4.2 Terrestrial Effects

No studies on terrestrial effects of sodium or potassium methanolate are available. Due to the rapid hydrolysis of the compounds the toxicity of the degradation products, sodium and potassium hydroxide and methanol are relevant. For sodium hydroxide and methanol no studies on terrestrial effects are available. For potassium hydroxide a 90-day EC₅₀ value of 850 mg/l (artificial soil) for *Enchytraeus sp.* (> 95 % *Cogentia sphagnetorium*) was reported (OECD, 2001). The effect of KOH was not correlated to pH but to an increase of conductivity.

Conclusion

There is only one study with potassium hydroxide available indicating a low level of terrestrial toxicity. The terrestrial toxicity will depend on the buffer capacity of the soil.

4.3 Other Environmental Effects

No data are available.

4.4 Initial Assessment for the Environment

Both sodium and potassium methanolate are white to yellowish organic solid salts that decompose above 300 °C (sodium methanolate) or at 300 °C (potassium methanolate). Sodium and potassium methanolate have a calculated vapor pressure of 6.39×10^{-6} hPa. On contact with water both substances decompose rapidly and exothermically under formation of methanol and the corresponding alkali hydroxides, sodium- or potassium hydroxide, respectively. Photodegradation of methanol by hydroxyl radicals takes place with a half-life of 17 - 18 days. For the partitioning in the environmental compartments the hydrolysis products are of relevance. Sodium and potassium hydroxide are inorganic salts that partition predominantly into the water phase and will not adsorb to particulate matter or surfaces. For methanol it was concluded that based on the Henry's law constant of $0.461 \text{ Pa m}^3/\text{mol}$ it is not expected to significantly volatilize from the aquatic compartment and adsorption is not expected to be significant due to its high water solubility and low octanol-water partition coefficient. A distribution calculation performed with the Mackay level III model predicts that the air is the target environmental compartment for methanol. After rapid hydrolysis in water the relevant organic reaction product, methanol is readily biodegradable (76 – 82 % BOD-removal after 5 days). As sodium and potassium methanolate react with water under formation of sodium or potassium hydroxide and methanol, an octanol-water partition coefficient cannot be experimentally established and bioaccumulation of the substances themselves is unlikely. Methanol will be the species that distributes into the octanol phase or could be taken up by organisms. For methanol the $\log K_{OW}$ was -0,74 indicating a low bioaccumulation potential. This was confirmed by experimental BCF-values below 10 that have been determined in different fish species.

The toxicity of sodium and potassium methanolate to aquatic organisms is mediated by their degradation products due to the rapid reaction with water yielding sodium or potassium hydroxide and methanol. The aquatic toxicity of methanol is low with acute EC_{50} or LC_{50} values $> 10\,000 \text{ mg/l}$ and therefore its contribution to the methanolate toxicity is considered negligible. The limited data available for sodium methanolate are consistent with the aquatic toxicity of the alkali hydroxides. For sodium methanolate the acute toxicity to fish (48-h LC_{50}) for *Leuciscus idus melanotus* was 346 mg/l (equivalent to 256 mg/l of sodium hydroxide). The corresponding 48-h LC_{50} value for sodium hydroxide was 189 mg/l , the 96-h LC_{50} for *Gambusia officinalis* was 125 mg/l for sodium hydroxide and 80 mg/l for potassium hydroxide. For invertebrates a 48-h LC_{50} value of 40 mg/l (*Ceriodaphnia dubia*) and toxicity threshold concentrations (TTC) between 40 and 240 mg/l (*Daphnia magna*) were reported for sodium hydroxide. Lethal concentrations to molluscs of sodium hydroxide ranged between 150 mg/l (*Bulinus truncatus*, *Lymnea caillaudi*) and 450 mg/l (*Biomphalaria a. alexandria*), the 48-h LC_{50} values for *Ophryotrocha* (marine polychaete) were between 33 and 100 mg/l . The 24-h EC_{50} for algae (assimilation inhibition) was 302 mg/l for sodium methanolate. However, as concluded for sodium and potassium hydroxide already (see OECD, 2001, 2002), acute toxicity data cannot be used to derive a PNEC or a $PNEC_{added}$ for the compounds releasing hydroxide. Aquatic ecosystems are characterized by an alkalinity/pH and the organisms of the ecosystems are adapted to these specific natural conditions. Based on the natural alkalinity of waters, organisms will have different optimum pH conditions, ranging from poorly buffered waters with a pH of 6 or less to very hard waters with pH values up to 9. A lot of information is available about the relationship between pH and ecosystem structure and also natural variations in the pH of aquatic ecosystems have been quantified and reported extensively in ecological publications and handbooks.

Normally a PNEC or a $PNEC_{added}$ has to be derived from available ecotoxicity data. A $PNEC_{added}$ is a PNEC which is based on the added concentrations of a chemical (added risk approach). Based on the available data it is not considered useful to derive a PNEC or $PNEC_{added}$ for the sodium and potassium methanolate as their effect is based on hydroxide ions or a pH change, because:

- The natural pH of aquatic ecosystems can vary significantly
- The sensitivity of aquatic ecosystems to a change of the pH can vary significantly between aquatic ecosystems.
- The change in pH due to anthropogenic OH⁻ addition through methanolate releases is influenced significantly by the buffer capacity of the exposed ecosystem.

Although a PNEC or PNEC_{added} was not calculated, there is a need to assess the environmental effect of an OH⁻ release through sodium or potassium methanolate release into the environment. Based on the pH and the buffer capacity of the effluent and receiving water and the dilution factor of the effluent, the pH of the receiving water after discharge can be calculated or its pH can be measured. The change in pH should be compared with the natural variation in pH of the receiving water. Based on this comparison it should be assessed if the pH change is acceptable (see OECD, 2001).

To illustrate the procedure and to get an idea about the order of magnitude for a maximum anthropogenic addition, the maximum methanolate concentration will be calculated for 2 representative cases. According to Dir. 78/659/EEC, the pH of surface water for the protection of fish should be between 6 and 9. The 10th percentile and the 90th percentile of the bicarbonate concentration of 77 rivers of the world were 20 and 195 mg/l respectively. If it is assumed that only bicarbonate is responsible for the buffer capacity of the ecosystem and that an increase of pH to a value of 9 would be the maximum accepted value, then the maximum anthropogenic addition of sodium methanolate would be 1.4 mg/l and 8.2 mg/l (corresponding to 1.0 and 6.1 mg NaOH/l) and for potassium methanolate 1.1 mg/l and 10.4 mg/l (corresponding to 0.86 and 8.3 mg KOH/l) for bicarbonate concentrations of 20 and 195 mg/l respectively.

Sodium methanolate was moderately toxic to bacteria with a 24-hour EC₅₀ of 97 mg/l. The toxicity is likely mediated through a pH effect by the release of hydroxide ions.

There is only one study with potassium hydroxide available indicating a low level of terrestrial toxicity (90-day EC₅₀ in *Enchytraeus sp.* (> 95 % *Cogentia sphagnetorium*) of 850 mg/l (artificial soil)). The terrestrial toxicity will depend on the buffer capacity of the soil.

5 RECOMMENDATIONS

Human Health

The chemicals are currently of low priority for further work. The human health hazard is characterized by the rapid and exothermic degradation of the chemicals to methanol and the corresponding alkali hydroxides with known corrosivity. Based on data presented by the Sponsor country, exposure is well controlled in occupational settings, and exposure of consumers is negligible. Countries may wish to investigate exposure scenarios with potential human exposure.

Environment

The chemicals are currently of low priority for further work due to their rapid degradation in the environment via hydrolysis. The reaction products (methanol, potassium hydroxide and sodium hydroxide) have been evaluated within the OECD SIDS program for their hazardous properties and have been considered of low priority for further work for the environment.

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I U C L I D

Data Set

Existing Chemical : ID: 124-41-4
CAS No. : 124-41-4
EINECS Name : sodium methanolate
EC No. : 204-699-5
TSCA Name : Methanol, sodium salt
Molecular Formula : CH₃ONa
Structural Formula : CH₃-O Na

Producer related part
Company : Degussa AG
Creation date : 04.06.2000

Substance related part
Company : Degussa AG
Creation date : 04.06.2000

Status :
Memo :

Printing date : 28.06.2006
Revision date : 19.11.2003
Date of last update : 28.06.2006

Number of pages : 39

Chapter (profile) : Chapter: 1.0.1, 1.0.2, 1.0.4, 1.1.0, 1.1.1, 1.2, 1.3, 1.4, 1.5, 1.6.1, 1.6.2, 1.7, 1.7.1, 1.7.2, 1.8, 1.8.1, 1.8.2, 1.8.3, 1.8.4, 1.8.5, 1.8.6, 1.9.1, 1.9.2, 1.10, 1.11, 1.12, 1.13, 2, 3, 4, 5, 6, 10

Reliability (profile) : Reliability: without reliability, 1, 2, 3, 4
Flags (profile) : Flags: without flag, non confidential, SIDS

1.0.1 APPLICANT AND COMPANY INFORMATION

Type : cooperating company
Name : BASF AG
Contact person :
Date :
Street : Carl-Bosch-Strasse 38
Town : D-67056 Ludwigshafen
Country : Germany
Phone : +49 621 60 44712
Telefax : +49 621 60 44711
Telex :
Cedex :
Email :
Homepage :

24.10.2005

Type : other: contact point
Name : Degussa AG - ZN Wolfgang
Contact person : Dr. Wilfried Mayr/Dr. S. Jacobi
Date :
Street : Rodenbacher Chaussee 4
Town : 63457 Hanau
Country : Germany
Phone : +49 6181 59 4139
Telefax : +49 6181 59 2083
Telex :
Cedex :
Email :
Homepage :

24.10.2005

Type : cooperating company
Name : Du Pont de Nemours & Co., Inc.
Contact person :
Date :
Street : Elkton Road, P.O. Box 50
Town : 19714 Delaware, Newark
Country : United States
Phone :
Telefax :
Telex :
Cedex :
Email :
Homepage :

24.10.2005

1.0.2 LOCATION OF PRODUCTION SITE, IMPORTER OR FORMULATOR**1.0.4 DETAILS ON CATEGORY/TEMPLATE**

Comment : Sodium methanolate, 124-41-4; potassium methanolate, 865-33-8

Remark : The category of alkali methanolates, sodium and potassium methanolates has been defined because of the similar properties of both substances their fast and exothermic decomposition in water under formation of methanol and sodium or potassium hydroxide respectively. Where data are lacking for one of the members of the category they can reasonably be substituted by data of the other member of the category due to the structural similarity. Furthermore due to the instability of the substances for most endpoints the data of the degradation products are relevant.

The production and use pattern of sodium and potassium methanolates are comparable. The two chemicals have very similar physico-chemical and chemical properties. In contact with water they react very fast, quantitative and exothermic to methanol and the corresponding alkali hydroxides (Leal and de Matos, 1991).

$X-O-CH_3 + H_2O \rightarrow CH_3OH + OH^- + X^+$ (with $X = Na^+$ or K^+)

One mole of sodium or potassium methanolate (54.02 g or 70.13 g) yields one mol of methanol (32.04 g) and sodium- or potassium hydroxide (40 g or 56.11 g) respectively.

Due to the very high pKa-value of methanol of 15.5, the equilibrium is on the side of the reaction products. Toxicological and ecotoxicological studies of methanol and sodium and potassium hydroxide are therefore relevant for these products as well. The main toxicological characteristics is the corrosivity to skin and mucous membranes that warrants strict exposure controls. The corrosivity also determines the maximum tolerable dose in any animal experiment. The maximum applicable dose level of methanol derived from the methanolates will therefore be considerably lower in experiments with methanolates than in experiments with methanol itself. In the environment, both effects through pH-changes by the hydroxides and effects of methanol need to be considered.

02.12.2005

(28) (33)

1.1.0 SUBSTANCE IDENTIFICATION

IUPAC Name : sodium methanolate
Smiles Code : [Na]OC
Molecular formula : CH₃NaO
Molecular weight : 54.02
Petrol class :

02.12.2005

(19)

1.1.1 GENERAL SUBSTANCE INFORMATION

Purity type : typical for marketed substance
Substance type : organic
Physical status : solid
Purity : ca. 98 % w/w
Colour : white
Odour :

1.2 SYNONYMS AND TRADENAMES

Methanol, sodium salt

Methoxysodium**Natriummethanolat****Natriummethylat****sodium methoxide****sodium methylate****1.3 IMPURITIES**

Purity : typical for marketed substance
CAS-No : 1310-73-2
EC-No : 215-185-5
EINECS-Name : sodium hydroxide
Molecular formula :
Value : < 2 % w/w

Remark : Content sodium hydroxide and sodium carbonate combined: < 2%.
 02.12.2005 (19)

Purity : typical for marketed substance
CAS-No : 497-19-8
EC-No : 207-838-8
EINECS-Name : sodium carbonate
Molecular formula :
Value : < 2 % w/w

Remark : Content sodium hydroxide and sodium carbonate combined: < 2%
 02.12.2005 (19)

1.4 ADDITIVES**1.5 TOTAL QUANTITY****1.6.1 LABELLING**

Labelling : as in Directive 67/548/EEC
Specific limits : no
Symbols : F, C, ,
Nota : , ,
R-Phrases : (11) Highly flammable
 (14) Reacts violently with water
 (34) Causes burns

1. GENERAL INFORMATION

ID: 124-41-4

DATE: 28.06.2006

S-Phrases : (1/2) Keep locked up and out of reach of children
 (8) Keep container dry
 (16) Keep away from sources of ignition - No smoking
 (26) In case of contact with eyes, rinse immediately with plenty of water and seek medical advice
 (43) In case of fire, use powder, dry sand. Never use water
 (45) In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible)

Remark : Last update MSDS Chapter 15 "Labelling and Classification" on 2003-08-21.
 S1/2 = labelling as consumer product

29.03.2006

(23)

1.6.2 CLASSIFICATION

Classified : as in Directive 67/548/EEC
Class of danger : corrosive
R-Phrases : (34) Causes burns
Specific limits : no

02.12.2005

(23)

Classified : as in Directive 67/548/EEC
Class of danger : highly flammable
R-Phrases : (11) Highly flammable
Specific limits : no

02.12.2005

(23)

Classified : as in Directive 67/548/EEC
Class of danger :
R-Phrases : (14) Reacts violently with water
Specific limits : no

02.12.2005

(23)

1.7 USE PATTERN

Type of use : type
Category : Non dispersive use

Type of use : industrial
Category : Chemical industry: used in synthesis

Type of use : use
Category : Intermediates

1. GENERAL INFORMATION

ID: 124-41-4

DATE: 28.06.2006

1.7.1 DETAILED USE PATTERN**1.7.2 METHODS OF MANUFACTURE****1.8 REGULATORY MEASURES****1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES****1.8.2 ACCEPTABLE RESIDUES LEVELS****1.8.3 WATER POLLUTION**

Classified by : KBwS (DE)
Labelled by : KBwS (DE)
Class of danger : 1 (weakly water polluting)

Country : Germany
Remark : Substance number 1155, classified in Annex 2.
 02.12.2005 (5) (9)

1.8.4 MAJOR ACCIDENT HAZARDS

Legislation : Stoerfallverordnung (DE)
Substance listed : yes
No. in Seveso directive :

Country : Germany
Remark : Annex I; Nr.:10a
 02.12.2005 (39)

1.8.5 AIR POLLUTION**1.8.6 LISTINGS E.G. CHEMICAL INVENTORIES****1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS**

Type : degradation product in water
CAS-No : 67-56-1
EC-No : 200-659-6
EINECS-Name : methanol
IUCLID Chapter :

02.12.2005

1. GENERAL INFORMATION

ID: 124-41-4

DATE: 28.06.2006

Type : degradation product in water
CAS-No : 1310-73-2
EC-No : 215-185-5
EINECS-Name : sodium hydroxide
IUCLID Chapter :

02.12.2005

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 : 22.08.2000

15.09.2005

Type of search : Internal and External
Chapters covered : 3, 4, 5
Date of search : 24.06.2003

Remark : CIS, DIMDI, STN

Type of search : Internal and External
Chapters covered : 3, 4, 5
Date of search : 27.07.2005

Remark : DIMDI, STN, Dialog
27.07.2005

1.13 REVIEWS

2.1 MELTING POINT

Value : > 300 °C
Decomposition : yes, at 70 °C
Sublimation :
Method : other: no data
Year : 2000
GLP : no data
Test substance : other TS

Remark : Dangerous degradation products: Methanol, sodium hydroxide.
Reliability : (4) not assignable
 Database and handbook data.

12.01.2006 (9)

Value : 300 °C
Sublimation :
Method : other: no data
Year : 2003
GLP : no data
Test substance : other TS: No data

Reliability : (2) valid with restrictions
 Handbook data
Flag : Critical study for SIDS endpoint

04.08.2005 (12)

Value : > 300 °C
Decomposition : yes, at 127 °C
Sublimation :
Method : other: no data
Year : 2000
GLP : no data
Test substance : other TS

Remark : Dangerous degradation products: Methanol, sodium hydroxide.
Reliability : (4) not assignable
 Database and handbook data.

05.05.2006 (36)

Decomposition : yes, at >= 50 °C
Sublimation :
Method : other: no data
Year : 2003
GLP : no data
Test substance : other TS: no data

Result : Sodium methylate decomposes at heating from 50 °C onwards in the air.
Reliability : (4) not assignable
 Data base data

02.12.2005 (5)

Decomposition : yes, at > 127 °C
Sublimation :
Method : other: decomposition
Year :
GLP : no data
Test substance : other TS: no data

Reliability	:	(2) valid with restrictions Database and handbook data.	
Flag	:	Critical study for SIDS endpoint	
04.08.2005			(11) (32)
Decomposition	:	yes, at > 126 °C	
Sublimation	:		
Method	:	other: decomposition	
Year	:		
GLP	:	no data	
Test substance	:	other TS: no data	
Reliability	:	(4) not assignable Database and handbook data.	
05.05.2006			(30) (34)

2.2 BOILING POINT

Remark	:	Not applicable, decomposition at 126-127 °C. See melting point.
Flag	:	Critical study for SIDS endpoint
04.08.2005		

2.3 DENSITY

Type	:	density	
Value	:	ca. 1.3 g/cm ³ at 20 °C	
Reliability	:	(4) not assignable	
Flag	:	Critical study for SIDS endpoint	
11.01.2006			(23) (34)
Type	:	bulk density	
Value	:	450 kg/m ³ at 20 °C	
Remark	:	Determined at 20 °C by DIN 53466	
Result	:	Compacted bulk density: 600 kg/m ³ , determined by ISO 787/11.	
Reliability	:	(4) not assignable	
11.01.2006			(19)
Type	:	bulk density	
Value	:	= 500 - 600 kg/m ³ at °C	
Reliability	:	(4) not assignable	
11.01.2006			(5) (34)
Type	:	bulk density	
Value	:	ca. 500 kg/m ³ at °C	
Reliability	:	(4) not assignable	
15.09.2005			(23)

2.3.1 GRANULOMETRY

Type of distribution : Volumetric Distribution
Precentile : D90
Particle size : = .02822 mm
Passage 1 :
Particle size 1 :
Passage 2 :
Particle size 2 :
Passage 3 :
Particle size 3 :
Method : other: VDI 2263 part 1
Year : 2003
GLP : no data
Test substance : other TS: no data

Result :
 Passage 1: 5 %
 Particle size 1: = 107.8 µm
 Passage 2: 50 %
 Particle size 2: = 51.85 µm
 Passage 3: 95 %
 Particle size 3: = 17.21 µm

Reliability : (1) valid without restriction
 06.12.2005

(22)

2.4 VAPOUR PRESSURE

Value : .00000639 hPa at 25 °C
Decomposition :
Method : other (calculated): MPBPWIN (LOGKOW(c)) Program, Version 1.40,
 Syracuse Research Corporation, Merrill Lane, Syracuse, New York, 13210,
 U.S.A.
Year : 2003
GLP : no
Test substance :

Remark : The vapour pressure calculation was performed according to the modified
 Grain method which is proposed in Annex 1 of the EU method A.4.
 (92/69/EEC). From the result (6.39E-04 Pa) it can be concluded that no
 measurement is required because the calculated value is far below the
 detection limit of the available methods.

Result : Calculation result (modified Grain method): 6.39E-06 hPa

Reliability : (2) valid with restrictions
 Calculated data, internationally accepted method.

Flag : Critical study for SIDS endpoint

02.12.2005

(21)

2.5 PARTITION COEFFICIENT

Partition coefficient : octanol-water
Log pow : -3.18 at °C
pH value :
Method : other (calculated): KOWWIN (v1.67)
Year : 2004

2. PHYSICO-CHEMICAL DATA

ID: 124-41-4

DATE: 28.06.2006

GLP	:	no data	
Test substance	:	no data	
Reliability	:	(2) valid with restrictions	(10)
Partition coefficient	:	octanol-water	
Log pow	:	-.77 at °C	
pH value	:		
Method	:	other (calculated)	
Year	:	1995	
GLP	:	no	
Test substance	:	other TS: Methanol	
Reliability	:	(4) not assignable	(29)
02.12.2005			
Partition coefficient	:		
Log pow	:	-.74 at °C	
pH value	:		
Method	:		
Year	:		
GLP	:		
Test substance	:	other TS: Methanol	
Remark	:	As Sodium and potassium methylate react with water under formation of sodium hydroxide and methanol, an octanol-water partition coefficient cannot be experimentally established. Methanol will be the species that distributes to the octanol phase. Recommended value for Methanol	
Reliability	:	(2) valid with restrictions Scientifically verified data	(35)
12.01.2006			

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in Value	:	Water	
pH value concentration	:	at °C	
Temperature effects	:		
Examine different pol.	:		
pKa	:	at 25 °C	
Description	:	other: decomposition due to hydrolysis	
Stable	:	no	
Deg. product	:	yes	
Method	:	other: no data	
Year	:		
GLP	:	no data	
Test substance	:	other TS: no data	
Deg. products	:	1310-73-2 215-185-5 sodium hydroxide 67-56-1 200-659-6 methanol	
Reliability	:	(2) valid with restrictions Database and handbook data.	
Flag	:	Critical study for SIDS endpoint	(9) (32) (34) (36)
04.08.2005			

2. PHYSICO-CHEMICAL DATA

ID: 124-41-4

DATE: 28.06.2006

Solubility in Value : Organic Solvents
 : at °C
pH value concentration :
 : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description : other: soluble
Stable : yes
Deg. product :
Method : other: no data
Year :
GLP : no data
Test substance : other TS: no data

Remark : Soluble in methanol and ethanol.
Reliability : (2) valid with restrictions
 Handbook data

28.06.2006

(12)

Solubility in Value : Organic Solvents
 : at °C
pH value concentration :
 : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description : other: soluble
Stable :
Deg. product :
Method : other: no data
Year : 2000
GLP :
Test substance : other TS: no data

Remark : Soluble in methanol and ethanol, fats and esters.
Reliability : (4) not assignable
 Handbook data

05.05.2006

(36)

2.6.2 SURFACE TENSION

2.7 FLASH POINT

Value : 240 °C
Type :

Reliability : (4) not assignable

11.01.2006

(34)

2.8 AUTO FLAMMABILITY

Value : 50 - 60 °C at
Method : other:67/548/EWG, Appendix V, A.16
Year :

GLP	:		
Test substance	:		
Reliability	:	(4) not assignable	
Flag	:	Critical study for SIDS endpoint	
11.01.2006			(23)
Value	:	> 50 °C at	
Method	:	other: Directive 84/449/EEC, Appendix V, A.16	
Year	:		
GLP	:		
Test substance	:		
Remark	:	Self ignition temperature.	
Reliability	:	(4) not assignable	
11.01.2006			(5)

2.9 FLAMMABILITY

Result	:	flammable	
Result	:	flammable when exposed to heat or flame	
Reliability	:	(2) valid with restrictions	
		Handbook data	
04.07.2005			(30)
Result	:	highly flammable	
Method	:	other: 67/548/EWG, Appendix V, A.10	
Year	:		
GLP	:		
Test substance	:		
Reliability	:	(2) valid with restrictions	
12.01.2006			(32)

2.10 EXPLOSIVE PROPERTIES**2.11 OXIDIZING PROPERTIES****2.12 DISSOCIATION CONSTANT**

Acid-base constant	:	15.5	
Method	:	other	
Year	:	1998	
GLP	:	no data	
Test substance	:	other TS	
Method	:	The reaction rates of methanol and hydroxide ions or methylate and water with a standard nucleophil, methyl bromide were determined at different temperatures and with different methanol/water ratios. From these different reaction rates the equilibrium concentrations of methanolate and hydroxide ions and the equilibrium constant was determined.	
Remark	:	pKa of Methanol (CH ₃ OH --> CH ₃ OO ⁻)	

Test substance : Potassium methylate
Reliability : (2) valid with restrictions
 Well documented Scientific literature.
Flag : Critical study for SIDS endpoint
 02.12.2005 (28)

2.13 VISCOSITY

2.14 ADDITIONAL REMARKS

Memo : Auto ignition temperature
Result : Auto ignition temperature: 70 - 80 °C (32)

Memo : Ignition temperature
Result : Ignition temperature = 70 °C
Reliability : (4) not assignable (9)

Memo : Limiting oxygen concentration
Method : According to VDI 2263 part 1, chapter 2.4: Limiting oxygen concentration
Remark : Year: 2003 GLP: no
Result : The limiting oxygen concentration is 11.9 vol %, that means 43 vol % of the air have to be replaced by nitrogen.
Reliability : (1) valid without restriction (22)
 14.01.2004

Memo : Minimum ignition temperature (Emin)
Method : According to VDI 2263 part 1, chapter 2.5: Minimum ignition energy (modified Hartmann-apparatus with high voltage capacitor as ignition source).
Remark : Year 2003, GLP: no
Result : Minimum ignition energy (MIE):
 T [°C] Inductivity 1 mH
 25 10 < MIE < 30
 The test substance can be characterized as "normal ignitable".
Reliability : (1) valid without restriction
 German standard method (22)
 15.09.2005

3.1.1 PHOTODEGRADATION

Type	:	air	
Light source	:	Sun light	
Light spectrum	:	nm	
Relative intensity	:	based on intensity of sunlight	
INDIRECT PHOTOLYSIS			
Sensitizer	:	OH	
Conc. of sensitizer	:	500000 molecule/cm ³	
Rate constant	:	.00000000008296 cm ³ /(molecule*sec)	
Degradation	:	50 % after 19.3 day(s)	
Deg. product	:		
Method	:	other (calculated): AOPWIN (AOP(c)) Program, Version 1.91, Syracuse Research Corporation, Merrill Lane, Syracuse, New York, 13210, U.S.A.	
Year	:	2005	
GLP	:	no	
Test substance	:	other TS: no data	
Remark	:	Assumption for the calculation: 24 hours average concentration of OH radicals.	
Reliability	:	(2) valid with restrictions Calculated data, internationally accepted method.	
Flag	:	Critical study for SIDS endpoint	
02.12.2005			(10) (25)

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 contact with water sodium and potassium methanolate react very fast, quantitative and exothermic to methanol and the corresponding alkali hydroxides.	
Reliability	:	(2) valid with restrictions Well documented Scientific literature.	
Flag	:	Critical study for SIDS endpoint	
19.10.2005			(33)

3.1.3 STABILITY IN SOIL**3.2.1 MONITORING DATA****3.2.2 FIELD STUDIES****3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS**

Type	:	adsorption
Media	:	water - soil

3. ENVIRONMENTAL FATE AND PATHWAYS

ID: 124-41-4

DATE: 28.06.2006

Air	:	% (Fugacity Model Level I)	
Water	:	% (Fugacity Model Level I)	
Soil	:	% (Fugacity Model Level I)	
Biota	:	% (Fugacity Model Level II/III)	
Soil	:	% (Fugacity Model Level II/III)	
Method	:	other: (calculation): PCKOCWIN	
Year	:	2003	
Method	:	PC-KOC (c) Program, Version 1.66 Syracuse Research Corporation, Merrill Lane, Syracuse, New York, 13210, U.S.A., 2000, GLP: no	
Result	:	The soil or sediment adsorption coefficient (Koc) of Sodium methoxide was calculated as Koc = 1.	
Reliability	:	(3) invalid	
		Value uncertain, because of the ionic nature of the substance.	
06.12.2005			(20)
Type	:	other	
Media	:		
Air	:	% (Fugacity Model Level I)	
Water	:	% (Fugacity Model Level I)	
Soil	:	% (Fugacity Model Level I)	
Biota	:	% (Fugacity Model Level II/III)	
Soil	:	% (Fugacity Model Level II/III)	
Method	:		
Year	:		
Remark	:	Due to the rapid hydrolysis in water, yielding methanol and sodium hydroxide, the data for methanol are relevant.	
04.12.2005			(33) (35)

3.3.2 DISTRIBUTION

Media	:	air - biota - sediment(s) - soil - water
Method	:	Calculation according Mackay, Level III
Year	:	2005
Method	:	Mackay et al.: Chemosphere, 24, 695-717 (1992) and earlier publications.
Remark	:	Level III Program, Mackay, D., 2002, Version 2.70, Trent University The distribution of sodium methanolate is of limited relevance for the assessment of the environmental behaviour as due to the rapid hydrolysis in water, the relevant species subject to environmental distribution are the degradation products sodium hydroxide and methanol.
Result	:	Scenario 1 Scenario 2 Scenario 3 100 % Release
		100 % Release 100 % Release
		into air into water into soil
		[%] [%] [%]
		Compartment
		Air 18.0 0 0
		Water 3.50 100 0
		Soil 78.5 0 100
		Sediment 0 0 0
Test condition	:	The calculation was conducted with the following user entered parameters: Molar mass: 54.02 g/mol Ambient temperature: 25 °C Log Kow: -0.74 Vapour pressure: 1.00E-05 Pa [20 °C] Melting point: 127 °C Half-life in air: 464 hours

3. ENVIRONMENTAL FATE AND PATHWAYS

ID: 124-41-4

DATE: 28.06.2006

	Emission rate:	
	Scenario 1:	
	3000 kg/h into air, 0 kg/h into water and soil	
	Scenario 2:	
	3000 kg/h into water, 0 kg/h into air and soil	
	Scenario 3:	
	3000 kg/h into soil, 0 kg/h into water and air	
Reliability	:	(2) valid with restrictions
		Calculated data, internationally accepted method.
12.01.2006		(24)

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

Type	:	
Inoculum	:	other
Remark	:	As sodium methylate rapidly hydrolyzes in water to methanol and sodium hydroxide, the data of the hydrolysis products are relevant for this substance as well. SIDS dossiers, SIARs and SIAPs are available for the degradation products. Methanol is readily biodegradable (BOD5 is 76 - 82%). Biodegradability is not applicable for sodium hydroxide.
06.12.2005		(35) (38)

3.6 BOD5, COD OR BOD5/COD RATIO**3.7 BIOACCUMULATION**

Species	:	other: expert judgement
Exposure period	:	at °C
Concentration	:	
Remark	:	As sodium and potassium methanolate react with water under formation of sodium and potassium hydroxide and methanol, an octanol-water partition coefficient cannot be experimentally established and bioaccumulation of the substances themselves is unlikely.
02.12.2005		

3.8 ADDITIONAL REMARKS

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	static	
Species	:	Leuciscus idus melanotus (Fish, fresh water)	
Exposure period	:	48 hour(s)	
Unit	:	mg/l	
LC50	:	= 346 calculated	
Limit test	:	no	
Analytical monitoring	:	no	
Method	:	other: DIN 38412 part 15	
Year	:	1988	
GLP	:	no	
Test substance	:	other TS: Sodium Methylate	
Test substance	:	Sodium Methylate as prescribed by 1.1 - 1.4 of CAS 124-41-4	
Reliability	:	(4) not assignable	
		Short report only, no details available.	
05.05.2006			(16)

Remark	:	As sodium and potassium methylates rapidly hydrolyse in water to methanol and sodium or potassium hydroxide respectively, the data of the hydrolysis products are relevant for this substance as well. SIDS dossiers, SIAR and SIAP is available for the degradation products.	
Flag	:	Critical study for SIDS endpoint	
20.10.2005			(35) (37) (38)

Remark	:	As sodium methylate rapidly hydrolyses in water to methanol and sodium hydroxide, the data of the hydrolysis products are relevant for this substance as well. SIDS dossiers, SIAR and SIAP is available for both substances.	
Flag	:	Critical study for SIDS endpoint	
04.08.2005			(35) (38)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type	:	other	
Species	:		
Exposure period	:		
Unit	:		
Remark	:	As sodium and potassium methylates rapidly hydrolyse in water to methanol and sodium or potassium hydroxide respectively, the data of the hydrolysis products are relevant for this substance as well. SIDS dossiers, SIAR and SIAP is available for the degradation products.	
Flag	:	Critical study for SIDS endpoint	
19.10.2005			(35) (37) (38)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species	:	Scenedesmus subspicatus (Algae)	
Endpoint	:	other: assimilation inhibition	
Exposure period	:	24 hour(s)	

Unit	:	mg/l	
EC10	:	= 24.2 calculated	
EC50	:	= 302.2 calculated	
EC90	:	= 3800 calculated	
Limit test	:	no	
Analytical monitoring	:	no	
Method	:	other: DIN 38142 part 12	
Year	:	1989	
GLP	:	no	
Test substance	:	other TS: Sodium methylate	
Method	:	Assimilation inhibition test. Inhibition of oxygen liberation as a function of the concentration.	
Result	:	- Nominal/measured concentrations: nominal only - Effect data inhibition of the assimilation: - Concentration / response curve: EC50 = 302.2 mg/l EC10 = 24.2 mg/l EC90 = 3800 mg/l	
Test condition	:	TEST ORGANISMS - Strain: <i>Scenedesmus subspicatus</i> Chodat STOCK AND TEST SOLUTION AND THEIR PREPARATION - Vehicle, solvent: not stated - Concentration in vehicle/ solvent: 2 g/l STABILITY OF THE TEST CHEMICAL SOLUTIONS: Chemical reacts with water under formation of sodium hydroxide and methanol. DILUTION WATER: no data Duration: 24 h Statistical analysis: Probit analysis	
Test substance	:	Sodium Methylate as prescribed by 1.1 - 1.4 of CAS 124-41-4	
Reliability	:	(4) not assignable Short report only, no details available.	
05.05.2006			(18)
Remark	:	As sodium and potassium methylates rapidly hydrolyse in water to methanol and sodium or potassium hydroxide respectively, the data of the hydrolysis products are relevant for this substance as well. SIDS dossiers, SIAR and SIAP is available for the degradation products.	
19.10.2005			(35) (37) (38)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

Type	:	aquatic
Species	:	aerobic microorganisms
Exposure period	:	24 hour(s)
Unit	:	mg/l
EC10	:	= 38 calculated
EC50	:	= 96.9 calculated
EC90	:	= 246.9 calculated
Analytical monitoring	:	no
Method	:	other: DIN 38412 part 12
Year	:	1989
GLP	:	no
Test substance	:	other TS: Sodium methylate
Method	:	Inhibition of bacterial metabolism.
Test condition	:	- Bacteria mixed culture

STOCK SOLUTION: 1 g/l

STABILITY OF THE TEST CHEMICAL SOLUTIONS: unstable hydrolyses
under formation of sodium hydroxide and methanol.

STATISTICAL ANALYSIS:

Probit analysis

Test substance : Sodium Methylate as prescribed by 1.1 - 1.4 of CAS 124-41-4

Reliability : (4) not assignable
Short report only, no details available.

Flag : Critical study for SIDS endpoint

05.05.2006

(17)

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

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

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

Memo : More data are available on the degradation products methanol and sodium
and potassium hydroxide that are relevant for the assessment of the
ecotoxicological properties of methylates.

19.10.2005

(35) (37) (38)

5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

Remark

: The abiotic hydrolysis of sodium and potassium methanolates with tissue water results in the formation of sodium and potassium ions respectively, hydroxyl ions and methanol.

For sodium hydroxide it was concluded in SIAM 14 "under normal handling and use conditions (non-irritating) neither the concentration of sodium in the blood nor the pH of the blood will be increased and therefore NaOH is not expected to be systemically available in the body."

For potassium hydroxide SIAM 13 concluded: ". Under normal handling and use conditions (non-irritating) neither the concentration of potassium in the blood nor the pH of the blood will be increased above normal limits and therefore KOH is not expected to cause systemically toxic levels in the blood. The renal excretion of K⁺ can be elevated and the OH⁻ ion is neutralised by the bicarbonate buffer system in the blood."

For Methanol SIAM 19 concluded: "Methanol is readily absorbed by inhalation, ingestion and dermal contact and distributes rapidly throughout the body. Metabolism in humans, rodents, and monkeys contributes up to 98 percent of the clearance, with more than 90 percent of the administered dose is ultimately exhaled as carbon dioxide. Renal and pulmonary excretion contributes only about 2 - 3 percent. In humans, the half-life is approximately 2.5 - 3 hours at doses lower than 100 mg/kg. At higher doses, the half life can be 24 hours or more.

The mammalian metabolism of methanol occurs mainly in the liver, where methanol is converted to formaldehyde, which is in turn converted to formate. Formate is then finally converted to carbon dioxide and water. In humans and monkeys, the conversion to formaldehyde is mediated by alcohol dehydrogenase. In rodents, the reaction occurs mainly via a catalase-peroxide pathway. In rodents, the first step is rate limiting and methanol accumulates in the blood. In primates, the conversion of formate to carbon dioxide is rate-limiting, leading to a disproportionate increase of formate in the blood and sensitive target tissues (such as CNS and the retina).

In humans, when exposed via inhalation up to an air concentration of 0.065 mg/L, no increase of blood methanol is expected. Up to 0.26 mg/L (single or repeated exposure), the methanol blood level is likely to increase 2 to 4-fold above the endogenous methanol concentration in humans, but still remains significantly below 10 mg/L. Air concentrations up to 1.6 mg/L resulted in similar blood methanol among rats, monkeys, and humans. However, above 1.6 mg/L, a steep exponential increase occurs in rats, a smaller exponential increase occurs in monkeys, and humans exhibit a linear relationship between air concentrations and blood methanol levels.

Baseline levels of formate in blood are about 3 to 19 mg/L (0.07 - 0.4 mM) in humans. Toxic blood formate concentrations are reported to be 220 mg/L and higher (> 5 mM formate). Inhalation of about 1.20 mg methanol/L for 2 hours contributed only insignificantly to the internal formate pool in monkeys (in the µM-range), whereas formate accumulation has been observed in primates at methanol doses greater than 500 mg/kg."

Flag
05.05.2006

: Critical study for SIDS endpoint

(35) (37) (38)

5.1.1 ACUTE ORAL TOXICITY

Type	:	LD50	
Value	:	= 1500 mg/kg bw	
Species	:	rat	
Strain	:	no data	
Sex	:	no data	
Number of animals	:		
Vehicle	:	other: Lutrol	
Doses	:	no data	
Method	:	other: no data	
Year	:	1978	
GLP	:	no	
Test substance	:	other TS: Sodiummethylate 30% in Methanol	
Result	:	Symptoms: uncharacteristic. Pathology: Macroscopic findings: Heart: acute dilatation (right side), acute congestive hyperaemia. Stomach: profound haemorrhagic gastritis, adhesions in forestomach and glandular stomach. Intestine: diarrhoea, blood, haemorrhagic enteritis. Sero-fibroic peritonitis. Abdomen: blood coloured ascites.	
Test condition	:	TEST ORGANISMS: rats ADMINISTRATION: gavage, 0.928 to 46.4% solution in Lutrol (G/V). Observation period: 14 days	
Reliability	:	(2) valid with restrictions Well documented report, details missing, preliminary study only.	
24.10.2005			(1)
Type	:	LD50	
Value	:	= 800 mg/kg bw	
Species	:	rat	
Strain	:	no data	
Sex	:	no data	
Number of animals	:		
Vehicle	:	other: Lutrol	
Doses	:	not specified	
Method	:	other: not specified	
Year	:	1979	
GLP	:	no	
Test substance	:	other TS: Sodium methylate	
Result	:	Symptoms: uncharacteristic. At the beginning of the observation period body weight reduction. Pathology: Macroscopic changes in animals that died during the study: Heart: acute dilatation (right), acute congestive hyperaemia. Stomach: extended ulcerating gastritis, bleeding in the forestomach. Wall of glandular stomach thickened. Intraabdominal adhesions between stomach and liver. Intestine: atonic, diarrhoea, bloody content. Hydrothorax and partly blood coloured ascites.	
Test condition	:	Administration of 0.43 to 14.7% (G/V) suspension of crystalline sodium methylate in Lutrol. Observation period: 14 days	
Test substance	:	Sodium methylate as prescribed by 1.1 - 1.4 of CAS 124-41-4	
Reliability	:	(2) valid with restrictions Well documented report, details missing.	

Flag : Critical study for SIDS endpoint
05.08.2005 (3)

Type : LD50
Value : = 2037 mg/kg bw
Species : rat
Strain : Sprague-Dawley
Sex : male
Number of animals : 10
Vehicle : other: corn oil
Doses : 1500, 1800, 2250, 2380, 2600, 3400 mg/kg bw
Method : other: similar to OECD Guide-line 401
Year : 1982
GLP : no data
Test substance : other TS: sodium methylate

Result : MORTALITY:
Dose [mg/kg bw] Mortality
3400 10/10
2600 10/10
2380 8/10
2250 2/10
1800 5/10
1500 1/10
- Time of death: up to 14 days after dosing
CLINICAL SIGNS:
All dose levels: labored breathing, weakness, wet and stained perianal area, chromodacryorrhea, ruffled fur.
from 1800 mg/kg bw: salivation and lethargy
from 2380 mg/kg bw: Ataxia
from 2600 mg/kg bw: lacrimation
Body weight: loss from day 9

Test condition : TEST ORGANISMS: Male Sprague Dawley rats crl:CD
- Age: young adult
- Weight at study initiation: 238 - 252
ADMINISTRATION:
- concentration: 20 to 30% Suspension in corn oil by gavage
- Volume administered: 1.83 to 2.7 ml
- Post dose observation period: 14 days
EXAMINATIONS: clinical observations, body weight

Reliability : (2) valid with restrictions
Comparable to guideline study, no necropsy findings reported, no data on GLP

Flag : Critical study for SIDS endpoint
18.08.2005 (27)

Type : LD50
Value : = 1687 mg/kg bw
Species : rat
Strain : Sprague-Dawley
Sex : male/female
Number of animals : 10
Vehicle : water
Doses : 1000, 1260, 1587, 2000 mg/kg bw
Method : OECD Guide-line 401 "Acute Oral Toxicity"
Year : 1988
GLP : yes
Test substance : other TS: Sodium methylate

Remark : As the substance was tested in aqueous solution and sodium methylate

Result	<p>hydrolyses rapidly to methanol and sodium hydroxide, in fact the hydrolysis products have been tested.</p> <p>: MORTALITY:</p> <table border="0"> <tr> <td>Dose [mg/kg bw]</td> <td>Mortality</td> </tr> <tr> <td>2000</td> <td>8/10</td> </tr> <tr> <td>1587</td> <td>2/10</td> </tr> <tr> <td>1260</td> <td>1/10</td> </tr> <tr> <td>1000</td> <td>1/10</td> </tr> </table> <p>LD50 males: 1844 mg/kg bw LD50 females: 1682 mg/kg bw LD50 combined: 1687 mg/kg bw - Time of death: most deaths occurred between days 1 and 6 after treatment.</p> <p>CLINICAL SIGNS: All animals: hunched posture, pilo-erection, decreased respiration rate (1 to 4 h after dosing). Some of the symptoms were observed up to days 6 to 9 in surviving animals of the 1587 mg/kg bw group and up to day 11 in those of the high dose group. Additional symptoms at 1587 mg/kg bw: lethargy, ptosis pallor of the extremities, red/brown staining around the snout, emaciation (females, from day 6).</p> <p>Body weights: In most of the animals body weight gain was noted. Isolated cases of body weight loss or reduced bw gain were reported.</p> <p>NECROPSY FINDINGS: Common abnormalities of animals that died during the study: red lungs, pale or dark or patchy pallor of livers. At 1587 and 2000 mg/kg bw: severe haemorrhage and rugae of the glandular gastric epithelium. Occasional adherence of stomach to the liver. In the surviving animals killed at termination occasional findings were white foci in the non-glandular gastric epithelium and adherence of the stomach to the liver.</p>	Dose [mg/kg bw]	Mortality	2000	8/10	1587	2/10	1260	1/10	1000	1/10
Dose [mg/kg bw]	Mortality										
2000	8/10										
1587	2/10										
1260	1/10										
1000	1/10										
Test condition	<p>: TEST ORGANISMS: male and female Sprague-Dawley CFY rats - Source: Interfauna (UK) Ltd. Wyton - Age: 5 to 8 weeks - Weight at study initiation: Males: 122 to 145 g, females: 120 to 142 g</p> <p>ADMINISTRATION - Concentration: 100 - 200 mg/ml - Volume administered: 10 ml/kg bw - Post dose observation period: 14 days</p> <p>EXAMINATIONS: Clinical observations Body weights Gross necropsy findings</p>										
Test substance	<p>: Sodium methylate</p>										
Reliability	<p>: (1) valid without restriction Guideline study, GLP</p>										
Flag	<p>: Critical study for SIDS endpoint</p>										
24.10.2005	(15)										
Type	<p>: LD100</p>										
Value	<p>: = 1000 mg/kg bw</p>										
Species	<p>: rat</p>										
Strain	<p>: Sprague-Dawley</p>										
Sex	<p>: male/female</p>										
Number of animals	<p>: 10</p>										

Vehicle	:	water
Doses	:	215, 316, 464, 681, 1000 mg/kg
Method	:	other: comparable to OECD Guide-line 401
Year	:	1978
GLP	:	no
Test substance	:	other TS: Sodium methylate
Remark	:	As the substance was tested in aqueous solution and sodium methylate hydrolyses rapidly to methanol and sodium hydroxide, in fact the hydrolysis products have been tested.
Result	:	Mortality: All animals of the 1000 mg/kg bw. group died between 1 h and 1 day p.a. Symptoms: All dose groups: dyspnea, apathy from 316 mg/kg additionally yellow discoloration of the urine. from 681 mg/kg: spastic and staggered gait. at 1000 mg/kg: anomalous posture, atonia, reddening of skin, loss of pain reflex, narcotic condition. Pathology Macroscopic examination: Animals that were killed after termination of the study did not reveal any macroscopic organ changes. Animals that died during the study: Dilatation of right heart, discoloration of right ventricle, acute congestive hyperaemia. Stomach: atonic, fluid stomach content, forestomach: diffuse reddening, vascular injection. Intestines: atonic, diarrhoea.
Test condition	:	TEST ORGANISMS: males and female Sprague Dawley rats - Source: Herilan, Eggersmann KG - Initial body weight: males: 220-230 g, females: 180-200g - Number of animals: 5 males, 5 females per dose group ADMINISTRATION: - Type of exposure: gavage, Volume 10 ml/kg - Concentrations: 2.15, 3.16, 4.64, 6.81, 10 % (G/V) 14 Days observation period. EXAMINATIONS: Symptoms Mortality Body weight development Macroscopic examination at termination or after death of the animals.
Test substance	:	Sodium Methylate as prescribed by 1.1 - 1.4 of CAS 124-41-4
Reliability	:	(2) valid with restrictions Well documented study.
Flag	:	Critical study for SIDS endpoint
05.12.2005		(2)

5.1.2 ACUTE INHALATION TOXICITY

Type	:	other: acute inhalation risk test (IRT)
Value	:	
Species	:	rat
Strain	:	no data
Sex	:	no data
Number of animals	:	12
Vehicle	:	
Doses	:	atmosphere enriched with volatile parts at 20 °C
Exposure time	:	8 hour(s)
Method	:	other: according to Smyth et al.: Am. Ind. Hyg. Ass. J. 23, 95-107, 1962

Year : 1978
GLP : no
Test substance : other TS: Sodium methylate 30% in Methanol

Result : Mortality: no animal died during the study.
 No clinical symptoms and no macroscopic organ changes at termination of the study were observed.

Test condition : TEST ORGANISMS: Rats
 Number: 12
 ADMINISTRATION:
 - Type of exposure: inhalation of an atmosphere enriched with the volatile components at 20 °C. 200 l/h air were piped through a 5 cm layer of the product.

Reliability : (2) valid with restrictions
 Well documented report, details missing.

Flag : Critical study for SIDS endpoint
 05.08.2005 (1)

Type : other: acute inhalation risk test (IRT)
Value :
Species : rat
Strain : no data
Sex : no data
Number of animals : 12
Vehicle :
Doses : dust enriched atmosphere at room temperature
Exposure time : 7 hour(s)
Method : other: IRT
Year : 1979
GLP : no
Test substance : other TS: Sodium methylate

Result : No mortality.
 No symptoms were observed during the study.
 Pathological examination at termination of the study did not reveal any macroscopic organ changes.

Test condition : Inhalation of an dust enriched atmosphere at room temperature. 200 l air/hour were piped through a 5 cm layer of the product.

Test substance : Sodium methylate as prescribed by 1.1 - 1.4 of CAS 124-41-4

Reliability : (2) valid with restrictions
 Well documented report, details missing.

Flag : Critical study for SIDS endpoint
 05.08.2005 (3)

5.1.3 ACUTE DERMAL TOXICITY

Type : LD50
Value : > 2000 mg/kg bw
Species : rat
Strain : Sprague-Dawley
Sex : male/female
Number of animals : 6
Vehicle : water
Doses : 1000, 2000 mg/kg bw
Method : other
Year : 1979
GLP : no
Test substance : other TS: Sodium methylate 50% aqueous solution

Remark	:	As the substance was tested in aqueous solution and sodium methylate hydrolyses rapidly to methanol and sodium hydroxide, in fact the hydrolysis products have been tested.
Result	:	MORTALITY: No deaths occurred at either dose level CLINICAL SIGNS: irregular breathing and bad general condition. Skin: necrosis after the 24 hour application. NECROPSY FINDINGS: No macroscopic organ changes apart from the skin necrosis were observed.
Test condition	:	TEST ORGANISMS: male and female Sprague-Dawley rats, SPF - Source: Hagemann, Extertal - Weight at study initiation: males: 220 g, females 190 g ADMINISTRATION: as 50% solution in water - Area covered: 50 cm ² - Occlusion: yes, 24 hours - Vehicle: water - Concentration in vehicle: 50% - Doses: 1000 and 2000 mg/kg bw - Removal of test substance: after 24 hours with lukewarm water or water/lutrol EXAMINATIONS: Mortality within 14 days Clinical symptoms Necropsy and macroscopic examination at termination.
Test substance	:	Sodium methylate krist., BASF tested as 50% solution in water
Reliability	:	(2) valid with restrictions Well documented study.
Flag	:	Critical study for SIDS endpoint
23.08.2005		(4)

5.1.4 ACUTE TOXICITY, OTHER ROUTES

Type	:	LD50
Value	:	= 40 mg/kg bw
Species	:	mouse
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Route of admin.	:	i.p.
Exposure time	:	
Method	:	other: not specified
Year	:	1979
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	Symptoms: uncharacteristic, in the beginning of the observation period body weight reduction. Deaths occurred within the whole of first week of the experiment. No macroscopic findings at necropsy.
Source	:	BASF AG Ludwigshafen
Test condition	:	Administration of 0.43 to 14.7 % (G/V) suspensions i.p. Observation period: 14 days.
Test substance	:	Natriummethylat krist. 0,43 - 14,7 %ige Suspension in Lutrol (G/V).
05.08.2005		(3)

5. TOXICITY

ID: 124-41-4

DATE: 28.06.2006

Type : LD50
Value : ca. 130 mg/kg bw
Species : mouse
Strain :
Sex :
Number of animals :
Vehicle : other: Lutrol
Doses :
Route of admin. : i.p.
Exposure time :
Method : other: not specified
Year : 1978
GLP : no
Test substance : other TS

Source : BASF AG Ludwigshafen
Test condition : Administration of 0.928 to 46.4% solutions in Lutrol.
 Observation time: 14 days
Test substance : Natriummethylat Loesung 30 % in Methanol als 0,93 - 46,4
 %ige Loesung in Lutrol (G/V).

05.08.2005 (1)

5.2.1 SKIN IRRITATION

Species : rabbit
Concentration : undiluted
Exposure : no data
Exposure time :
Number of animals : 2
Vehicle :
PDII :
Result : corrosive
Classification : highly corrosive (causes severe burns)
Method : other: not specified
Year : 1978
GLP : no
Test substance : other TS: Sodium methylate 30% in Methanol

Result : Exposure 1 min:
 Symptoms after 24 h:
 slight necrosis, moderate erythema and oedema
 Symptoms after 8 days:
 moderate necrosis and desquamation
 Exposure 5 min:
 Symptoms after 24 h:
 moderate necrosis, moderate erythema and oedema.
 After 8 days: moderate extended necrosis
 15 min: very severe necrosis persisting after 8 days.
 Severe pain reaction shortly after the application of the test substance.

Test condition : Exposure time 1 to 15 min.
Reliability : (2) valid with restrictions
 Well documented report, details missing.

Flag : Critical study for SIDS endpoint
 24.10.2005 (1)

Species : rabbit
Concentration : 80 %
Exposure : no data

Exposure time	:	3 minute(s)
Number of animals	:	2
Vehicle	:	water
PDII	:	
Result	:	highly corrosive
Classification	:	highly corrosive (causes severe burns)
Method	:	other: similar to OECD Guide-line 404
Year	:	1979
GLP	:	no
Test substance	:	other TS: Sodium methylate
Result	:	Primary irritation score
		3 min:
		Erythema: 2 (2/2 animals)
		Oedema: 0 (2/2 animals)
		24 h
		Erythema: 2 extended patchy necrosis (1/2 animals)
		2 patchy necrosis (1/2 animals)
		Oedema: 2 (2/2 animals) extended in 1 animal
		48 h
		Erythema: 3 extended patchy necrosis (1/2 animals)
		4 very severe necrosis (1/2 animals) (parchment-like)
		Oedema: 2 (2/2 animals) extended in 1 animal
		8 days:
		Erythema: 4 Necrosis (2/2 animals) (leather-like)
		Oedema: 1 (2/2 animals)
Test substance	:	Sodium methylate as prescribed by 1.1 - 1.4 of CAS 124-41-4
Reliability	:	(2) valid with restrictions
		Well documented report, details missing.
Flag	:	Critical study for SIDS endpoint
05.08.2005		(3)
Species	:	rabbit
Concentration	:	undiluted
Exposure	:	Semiocclusive
Exposure time	:	4 hour(s)
Number of animals	:	6
Vehicle	:	water
PDII	:	
Result	:	corrosive
Classification	:	corrosive (causes burns)
Method	:	EPA OPP 81-5
Year	:	1988
GLP	:	yes
Test substance	:	other TS: Sodium methylate
Result	:	Severe necrosis, sunken green coloured was observed at all treatment sites 1 hour after removal of the patches. The study was terminated for humane reasons and the material considered corrosive to rabbit skin.
Test condition	:	TEST ANIMALS: Rabbits
		- Strain: New Zealand white
		- Sex: Male
		- Source: David Percival Ltd. U.K.
		- Age: 12 to 16 weeks
		- Weight at study initiation: 2.4 to 2.9 g
		- Number of animals: 6
		ADMINISTRATION/EXPOSURE

- Preparation of test substance: Powder moistened with water.
 - Area of exposure: 5 cm²
 - Occlusion: semi-occlusive
 - Total volume applied: 0.5 g moistened with 0.5 ml of distilled water
 - Postexposure period: none, study was terminated 1 h after removal of the patch
 - Removal of test substance: after 4 h with water
 Examinations: only after 1 hour
 Scoring system: Draize, 1959
 - Examination time points: 1 hour
Test substance : Sodium methylate as prescribed by 1.1 - 1.4 of CAS 124-41-4
Reliability : (1) valid without restriction
 Guideline study under GLP
Flag : Critical study for SIDS endpoint
 24.10.2005 (14)

5.2.2 EYE IRRITATION

Species : rabbit
Concentration : undiluted
Dose : 50 ml
Exposure time :
Comment :
Number of animals : 2
Vehicle :
Result : corrosive
Classification : risk of serious damage to eyes
Method : other: not specified
Year : 1978
GLP : no
Test substance : other TS: Sodium methylate 30% in Methanol

Result : After 1 h:
 Grey discoloration of the nictating membrane. Severe corneal opacity.
 Severe pain reaction after application of the test substance.
 After 24 h:
 Grey discoloration of the nictating membrane and the conjunctiva (partly).
 Moderate conjunctival redness, slight oedema, severe corneal opacity.
 Necrosis of the edges of the eye lids.
 After 8 days:
 Severe necrosis, severe suppuration, eyelids shrunken.
Reliability : (2) valid with restrictions
 Well documented report, details missing.
Flag : Critical study for SIDS endpoint
 05.08.2005 (1)

5.3 SENSITIZATION

Type : other
Species :

Remark : As sodium and potassium methylates rapidly hydrolyse in water to methanol and sodium or potassium hydroxide respectively, the data of the hydrolysis products are relevant for this substance as well. SIDS dossiers, SIARs and SIAPs are available for the degradation products.
 19.10.2005 (35) (37) (38)

5.4 REPEATED DOSE TOXICITY

Method : other: rational
Year :
GLP :
Test substance :

Remark : No data on repeated dose toxicity of sodium and potassium methanolate are available. The tolerable dose levels will be determined by the corrosive nature of the substances. At sub irritant concentrations the toxicity of K⁺ or Na⁺ ions and OH⁻ ions are unlikely to contribute to the effects to be expected after repeated exposure. The specific ocular and CNS toxicity of methanol in primates is based on the accumulation of formate in blood. Formate accumulation in primates has been observed at methanol doses greater than 500 mg/kg. The corresponding dose levels for sodium and potassium methanolate that would lead to accumulation of formate in primates would be 840 and 1000 mg/kg bw. Such dose levels are already in the acutely toxic dose range. Due to the corrosive nature of the methanolates it is unlikely that exposure to methanolates could result in an uptake of toxic doses of methanol.

02.12.2005

(35) (37) (38)

5.5 GENETIC TOXICITY 'IN VITRO'

Type : other
System of testing :
Test concentration :
Cycotoxic concentr. :
Metabolic activation :
Result :
Method :
Year :
GLP :
Test substance :

Remark : As sodium and potassium methylates rapidly hydrolyse in water to methanol and sodium or potassium hydroxide respectively, the data of the hydrolysis products are relevant for this substance as well. SIDS dossiers, SIARs and SIAPs are available for the degradation products.

Due to the rapid hydrolysis of methanolates in in vitro test systems and tissue water in vivo, data for the hydrolysis products are relevant for methanolates as well. For sodium and potassium hydroxide there is no evidence for a mutagenic potential. For methanol the weight of evidence suggests that the substance is unlikely to have any relevant mutagenic activity. Therefore it can be concluded that there should at present be no concern with regard to a mutagenic activity of sodium or potassium methanolate.

02.12.2005

(35) (37) (38)

Type : Ames test
System of testing : S. typhimurium TA97, 98, 100
Test concentration : 8 - 5000 µg/plate
Cycotoxic concentr. : > 5000 µg/plate
Metabolic activation : with and without
Result : negative
Method : other: comparable to OECD Guide-line 471, but 3 strains only tested

Year	:	1987	
GLP	:	yes	
Test substance	:	other TS: Sodium methanolate	
Result	:	GENOTOXIC EFFECTS: - With metabolic activation: none - Without metabolic activation: none PRECIPITATION CONCENTRATION: 5000 µg/plate CYTOTOXIC CONCENTRATION: - With metabolic activation: > 5000 µg/plate - Without metabolic activation: > 5000 µg/plate	
Test condition	:	SYSTEM OF TESTING: Bacterial gene mutation assay - Species/cell type: S. Typhimurium TA97 TA98, TA100, - Deficiencies/Proficiencies: His deficient - Metabolic activation system: Arochlor induced rat liver post.mitochondrial fraction (S9). Pre-Test for toxicity in TA 100 Solvent: water - Concentrations: 8, 40, 200, 1000, 5000 µg/plate - Number of replicates: 3 - Positive controls: 2-nitrofluorene (TA98 - S9), sodium azide (TA100 - S9), 9-aminoacridine (TA97, -S9), 2-aminoanthracene (all strains + S9) - Negative control groups: solvent: water CRITERIA FOR EVALUATING RESULTS: twofold increase in revertants compared to concurrent controls indicates positive result. STATISTICAL METHODS: F-test and regression analysis in case of positive results.	
Reliability	:	(2) valid with restrictions 3 strains only tested	
Flag 07.12.2005	:	Material Safety Dataset, Critical study for SIDS endpoint	(13)
Reliability 07.12.2005	:	(2) valid with restrictions	

5.6 GENETIC TOXICITY 'IN VIVO'

Type	:	other	
Species	:		
Sex	:		
Strain	:		
Route of admin.	:		
Exposure period	:		
Doses	:		
Result	:		
Method	:		
Year	:		
GLP	:		
Test substance	:		
Remark	:	As sodium and potassium methylates rapidly hydrolyse in water to methanol and sodium or potassium hydroxide respectively, the data of the hydrolysis products are relevant for this substance as well. SIDS dossiers, SIARs and SIAPs are available for the degradation products.	
19.10.2005			(35) (37) (38)

5.7 CARCINOGENICITY

Species : other
Sex :
Strain :
Route of admin. :
Exposure period :
Frequency of treatm. :
Post exposure period :
Doses :
Result :
Control group :
Method :
Year :
GLP :
Test substance :

Remark : As sodium and potassium methylates rapidly hydrolyse in water to methanol and sodium or potassium hydroxide respectively, the data of the hydrolysis products are relevant for this substance as well. SIDS dossiers, SIARs and SIAPs are available for the degradation products.
 19.10.2005 (35) (37) (38)

5.8.1 TOXICITY TO FERTILITY

Type : other
Species :
Sex :
Strain :
Route of admin. :
Exposure period :
Frequency of treatm. :
Premating exposure period
 Male :
 Female :
Duration of test :
No. of generation studies :
Doses :
Control group :

Remark : As sodium and potassium methylates rapidly hydrolyse in water to methanol and sodium or potassium hydroxide respectively, the data of the hydrolysis products are relevant for this substance as well. SIDS dossiers, SIARs and SIAPs are available for the degradation products.
 19.10.2005 (35) (37) (38)

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species : other
Sex :
Strain :
Route of admin. :
Exposure period :
Frequency of treatm. :

5. TOXICITY

ID: 124-41-4

DATE: 28.06.2006

Duration of test :
Doses :
Control group :

Remark : As sodium and potassium methylates rapidly hydrolyse in water to methanol and sodium or potassium hydroxide respectively, the data of the hydrolysis products are relevant for this substance as well. SIDS dossiers, SIARs and SIAPs are available for the degradation products.

19.10.2005 (35) (37) (38)

5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES**5.9 SPECIFIC INVESTIGATIONS****5.10 EXPOSURE EXPERIENCE****5.11 ADDITIONAL REMARKS**

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- (20) Degussa AG (2003). unpublished report, Estimation of the Soil or Sediment Adsorption Coefficient of Sodium methylate CAS-No.: 124-41-4 by Quantitative Structure Activity Relationship (QSAR-Method = Calculation)
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ID: 124-41-4

DATE: 28.06.2006

-
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in der Fassung der Bekanntmachung vom 8. Juni 2005
(BGBl. I Nr. 33 vom 16.06.2005 S. 1598)

I U C L I D

Data Set

Existing Chemical : ID: 865-33-8
CAS No. : 865-33-8
EINECS Name : potassium methanolate
EC No. : 212-736-1
Molecular Weight : 70.14
Structural Formula : CH3-OK
Molecular Formula : CH3O.K

Producer related part

Company : Degussa AG
Creation date : 18.06.2001

Substance related part

Company : Degussa AG
Creation date : 18.06.2001

Status :
Memo : Überarbeitungsversion

Printing date : 28.06.2006
Revision date : 28.06.2004
Date of last update : 08.05.2006

Number of pages : 34

Chapter (profile) : Chapter: 1.0.1, 1.0.2, 1.0.4, 1.1.0, 1.1.1, 1.2, 1.3, 1.4, 1.5, 1.6.1, 1.6.2, 1.7, 1.7.1, 1.7.2, 1.8, 1.8.1, 1.8.2, 1.8.3, 1.8.4, 1.8.5, 1.8.6, 1.9.1, 1.9.2, 1.10, 1.11, 1.12, 1.13, 2, 3, 4, 5, 6, 10

Reliability (profile) : Reliability: without reliability, 1, 2, 3, 4
Flags (profile) : Flags: without flag, non confidential, SIDS

1.0.1 APPLICANT AND COMPANY INFORMATION

Type : cooperating company
Name : BASF AG
Contact person :
Date :
Street : Karl-Bosch-Str
Town : 67056 Ludwigshafen
Country : Germany
Phone :
Telefax :
Telex :
Cedex :
Email :
Homepage :

16.09.2005

Type : other: contact point
Name : Degussa AG - ZN Wolfgang
Contact person : Dr. W. Mayr, Dr. S. Jacobi
Date :
Street : Rodenbacher Chaussee 4
Town : 63457 Hanau
Country : Germany
Phone : +49 6181 59 4139
Telefax : +49 6161 59 2083
Telex :
Cedex :
Email :
Homepage :

24.10.2005

Type : cooperating company
Name : Kemira Oy
Contact person :
Date :
Street : P.O.Box 330
Town : SF-00101 Helsinki
Country : Finland
Phone : 358 0 132 1504
Telefax : 358 0 132 1619
Telex :
Cedex :
Email :
Homepage :

24.10.2005

1.0.2 LOCATION OF PRODUCTION SITE, IMPORTER OR FORMULATOR**1.0.4 DETAILS ON CATEGORY/TEMPLATE**

Comment : Sodium methanolate, 124-41-4; potassium methanolate, 865-33-8

- Remark** : The category of alkali methanolates, sodium and potassium methanolates has been defined because of the similar properties of both substances their fast and exothermic decomposition in water under formation of methanol and sodium or potassium hydroxide respectively.
Where data are lacking for one of the members of the category they can reasonably be substituted by data of the other member of the category due to the structural similarity. Furthermore due to the instability of the substances for most endpoints the data of the degradation products are relevant.
- The production and use pattern of sodium and potassium methanolates are comparable. The two chemicals have very similar physico-chemical and chemical properties. In contact with water they react very fast, quantitative and exothermic to methanol and the corresponding alkali hydroxides (Leal and de Matos, 1991).

$$X-O-CH_3 + H_2O \rightarrow CH_3OH + OH^- + X^+ \text{ (with } X = Na^+ \text{ or } K^+)$$
One mole of sodium or potassium methanolate (54.02 g or 70.13 g) yields one mol of methanol (32.04 g) and sodium- or potassium hydroxide (40 g or 56.11 g) respectively.
Due to the very high pKa-value of methanol of 15.5, the equilibrium is on the side of the reaction products. Toxicological and ecotoxicological studies of methanol and sodium and potassium hydroxide are therefore relevant for these products as well. The main toxicological characteristics is the corrosivity to skin and mucous membranes that warrants strict exposure controls. The corrosivity also determines the maximum tolerable dose in any animal experiment. The maximum applicable dose level of methanol derived from the methanolates will therefore be considerably lower in experiments with methanolates than in experiments with methanol itself. In the environment, both effects through pH-changes by the hydroxides and effects of methanol need to be considered.
- 02.12.2005 (20) (21)

1.1.0 SUBSTANCE IDENTIFICATION

- IUPAC Name** : potassium methanolate
Smiles Code : [K]OC
Molecular formula : CH₃OK
Molecular weight : 70.13
Petrol class :

02.12.2005

1.1.1 GENERAL SUBSTANCE INFORMATION

- Purity type** : typical for marketed substance
Substance type : organic
Physical status : solid
Purity : ca. 97 % w/w
Colour : white
Odour :

16.09.2005

(13)

1.2 SYNONYMS AND TRADENAMES

Kaliummethanolat

16.09.2005

Kaliummethylat

16.09.2005

methanol, potassium salt**methoxy potassium**

16.09.2005

potassium methoxide**1.3 IMPURITIES**

Purity : typical for marketed substance
CAS-No : 1310-58-3
EC-No : 215-181-3
EINECS-Name : potassium hydroxide
Molecular formula :
Value : < 1 % w/w

Remark : <= 1% potassium hydroxide and potassium carbonate combined.
Flag : Critical study for SIDS endpoint

02.12.2005

(13)

Purity : typical for marketed substance
CAS-No : 584-08-7
EC-No : 209-529-3
EINECS-Name : potassium carbonate
Molecular formula :
Value : < 1 % w/w

Remark : <= 1% potassium hydroxide and potassium carbonate combined.
Flag : Critical study for SIDS endpoint

02.12.2005

(13)

1.4 ADDITIVES**1.5 TOTAL QUANTITY****1.6.1 LABELLING**

Labelling : as in Directive 67/548/EEC
Specific limits : no
Symbols : F, C, ,
Nota : A, ,
R-Phrases : (11) Highly flammable
 (14) Reacts violently with water
 (34) Causes burns

1. GENERAL INFORMATION

ID: 865-33-8

DATE: 28.06.2006

S-Phrases : (1/2) Keep locked up and out of reach of children
 (8) Keep container dry
 (16) Keep away from sources of ignition - No smoking
 (26) In case of contact with eyes, rinse immediately with plenty of water and seek medical advice
 (43) In case of fire, use use powder, dry sand. Never use water
 (45) In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible)

Remark : Index No. 603-040-00-2
 02.12.2005 (1) (6) (16)

1.6.2 CLASSIFICATION

Classified : as in Directive 67/548/EEC
Class of danger : corrosive
R-Phrases : (34) Causes burns
Specific limits :

Classified : as in Directive 67/548/EEC
Class of danger : highly flammable
R-Phrases : (11) Highly flammable
Specific limits :

Classified : as in Directive 67/548/EEC
Class of danger :
R-Phrases : (14) Reacts violently with water
Specific limits :

1.7 USE PATTERN

Type of use : type
Category : Non dispersive use

Type of use : industrial
Category : Chemical industry: used in synthesis

Type of use : use
Category : Intermediates

1.7.1 DETAILED USE PATTERN**1.7.2 METHODS OF MANUFACTURE**

1.8 REGULATORY MEASURES**1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES****1.8.2 ACCEPTABLE RESIDUES LEVELS****1.8.3 WATER POLLUTION**

Classified by : KBwS (DE)
Labelled by : KBwS (DE)
Class of danger : 1 (weakly water polluting)

Country : Germany
Remark : Substance number 2541, classified according to Annex 3
 02.12.2005 (1)

1.8.4 MAJOR ACCIDENT HAZARDS

Legislation : Stoerfallverordnung (DE)
Substance listed : yes
No. in Seveso directive :

Country : Germany
Remark : Annex 1, No. 10a
 02.12.2005 (1) (6) (27)

1.8.5 AIR POLLUTION**1.8.6 LISTINGS E.G. CHEMICAL INVENTORIES****1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS**

Type : degradation product in water
CAS-No : 67-56-1
EC-No : 200-659-6
EINECS-Name : methanol
IUCLID Chapter :

16.09.2005

Type : degradation product in water
CAS-No : 1310-58-3
EC-No : 215-181-3
EINECS-Name : potassium hydroxide
IUCLID Chapter :

16.09.2005

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 : 27.02.2001

Remark : Datastar
03.08.2005

Type of search : Internal and External
Chapters covered : 3, 4, 5
Date of search : 03.08.2005

Remark : Update 02/2001
Hosts: STN, DIMDI, Dialog
03.08.2005

1.13 REVIEWS

2.1 MELTING POINT

Decomposition : yes, at ca. 300 °C

Remark : Storage under inert gas

Reliability : (4) not assignable

Flag : Critical study for SIDS endpoint

11.01.2006 (1) (22)

2.2 BOILING POINT

Decomposition :

Method : other

Year :

GLP :

Test substance :

Remark : Not applicable, decomposition at 300 °C. See melting point.

02.12.2005

2.3 DENSITY

Type : density

Value : 1.7 g/cm³ at °C

Reliability : (2) valid with restrictions

Flag : Data from handbook (Roempp)

: Critical study for SIDS endpoint (24)

Type : bulk density

Value : 750 kg/m³ at °C

Method :

Year :

GLP : no data

Test substance : no data

Reliability : (4) not assignable

11.01.2006 (22)

Type : bulk density

Value : ca. 950 kg/m³ at °C

Remark : Determined by DIN 53 466

Result : Compacted bulk density: 1100 kg/m³, determined by ISO 787/11.

Reliability : (4) not assignable

11.01.2006 (16)

2.3.1 GRANULOMETRY**2.4 VAPOUR PRESSURE**

Value : .00000639 hPa at 25 °C

Decomposition Method :
Year : 2003
GLP : no
Test substance :

Reliability : (2) valid with restrictions
 Calculated data, internationally accepted method.
Flag : Critical study for SIDS endpoint
 08.05.2006 (15)

2.5 PARTITION COEFFICIENT

Partition coefficient :
Log pow : -.74 at °C
pH value :
Method :
Year :
GLP :
Test substance : other TS: Methanol

Remark : As Sodium and potassium methylate react with water under formation of sodium hydroxide and methanol, an octanol-water partition coefficient cannot be experimentally established. Methanol will be the species that distributes to the octanol phase.
 Recommended value for Methanol
Reliability : (2) valid with restrictions
 Scientifically verified data
 12.01.2006 (23)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in Value : Water
 at °C
pH value concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description : other: decomposition due to hydrolysis
Stable : no
Deg. product : yes
Method : other: no data
Year :
GLP :
Test substance :
Deg. products : 1310-58-3 215-181-3 potassium hydroxide
 67-56-1 200-659-6 methanol

Reliability : (4) not assignable
Flag : Critical study for SIDS endpoint
 11.01.2006 (16) (22)

Solubility in Value : Organic Solvents
 330 g/l at 20 °C
pH value concentration : at °C
Temperature effects :

Examine different pol. :
pKa : at 25 °C
Description :
Stable :
Deg. product :
Method :
Year :
GLP : no data
Test substance : no data

Remark : Organic solvent: Methanol
Reliability : (4) not assignable
 11.01.2006

(22)

2.6.2 SURFACE TENSION

2.7 FLASH POINT

2.8 AUTO FLAMMABILITY

Value : 30 - 50 °C at
Method : other: DIN 51794
Year :
GLP : no data
Test substance : no data

Reliability : (4) not assignable
 11.01.2006

(22)

Value : ca. 50 - 60 °C at
Method : other: 67/548/EWG, Appendix V, A.16
Year :
GLP :
Test substance :

Reliability : (4) not assignable
 11.01.2006

(16)

Value : 90 - 100 °C at

Reliability : (2) valid with restrictions
 Data from handbook (Roempp)
Flag : Critical study for SIDS endpoint

(24)

2.9 FLAMMABILITY

Result : highly flammable
Method : other: 67/548/EWG, Appendix V, A.10
Year :
GLP :
Test substance :

Reliability : (4) not assignable
Flag : Critical study for SIDS endpoint
11.01.2006 (6) (16)

2.10 EXPLOSIVE PROPERTIES**2.11 OXIDIZING PROPERTIES****2.12 DISSOCIATION CONSTANT**

Acid-base constant : 15.5
Method : other
Year : 1998
GLP : no data
Test substance : other TS

Method : The reaction rates of methanol and hydroxide ions or methylate and water with a standard nucleophil, methyl bromide were determined at different temperatures and with different methanol/water ratios. From these different reaction rates the equilibrium concentrations of methanolate and hydroxide ions and the equilibrium constant was determined.

Remark : pKa of Methanol (CH₃OH --> CH₃OO⁻)
Test substance : Potassium methylate
Reliability : (2) valid with restrictions
Well documented Scientific literature.

Flag : Critical study for SIDS endpoint
02.12.2005 (20)

2.13 VISCOSITY**2.14 ADDITIONAL REMARKS**

3.1.1 PHOTODEGRADATION

Type	:	air
Light source	:	
Light spectrum	:	nm
Relative intensity	:	based on intensity of sunlight
INDIRECT PHOTOLYSIS		
Sensitizer	:	OH
Conc. of sensitizer	:	500000 molecule/cm ³
Rate constant	:	ca. .000000000008296 cm ³ /(molecule*sec)
Degradation	:	% after
Deg. product	:	
Method	:	other (calculated)
Year	:	2005
GLP	:	no
Test substance	:	other TS: no data
Method	:	Calculated AOPWIN (AOP(c)) Program, Version 2.1, Syracuse Research Corporation, Merrill Lane, Syracuse, New York, 13210, U.S.A., 2000
Remark	:	Assumption for the calculation: 24 hours average concentration of OH radicals.
Result	:	Half-life ca. 19 days.
Reliability	:	(2) valid with restrictions Calculated data, internationally accepted method.
Flag	:	Critical study for SIDS endpoint
02.12.2005		(17)

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 contact with water sodium and potassium methanolate react very fast, quantitative and exothermic to methanol and the corresponding alkali hydroxides.
Reliability	:	(2) valid with restrictions Well documented Scientific literature.
Flag	:	Critical study for SIDS endpoint
19.10.2005		(21)

3.1.3 STABILITY IN SOIL**3.2.1 MONITORING DATA****3.2.2 FIELD STUDIES****3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS**

Type	:	adsorption
-------------	---	------------

3. ENVIRONMENTAL FATE AND PATHWAYS

ID: 865-33-8

DATE: 28.06.2006

Media : water - soil
Air : % (Fugacity Model Level I)
Water : % (Fugacity Model Level I)
Soil : % (Fugacity Model Level I)
Biota : % (Fugacity Model Level II/III)
Soil : % (Fugacity Model Level II/III)
Method : other: (calculation): PCKOCWIN (PC-KOC (c)) Program, Version 1.66, Syracuse Research Corporation, Merrill Lane, Syracuse, New York, 13210, U.S.A., 2000
Year : 2003
Remark : GLP: no
Result : The soil or sediment adsorption coefficient (Koc) of Potassium methoxide was calculated as Koc = 1.
Reliability : (3) invalid
 Value uncertain, because of the ionic nature of the substance.

04.12.2005 (14)

Type : other
Media :
Air : % (Fugacity Model Level I)
Water : % (Fugacity Model Level I)
Soil : % (Fugacity Model Level I)
Biota : % (Fugacity Model Level II/III)
Soil : % (Fugacity Model Level II/III)
Method :
Year :
Remark : Due to the rapid hydrolysis in water, yielding methanol and potassium hydroxide, the data for methanol are relevant.

04.12.2005 (21) (23)

3.3.2 DISTRIBUTION

Media : air - biota - sediment(s) - soil - water
Method : Calculation according Mackay, Level III
Year : 2005
Method : Mackay et al.: Chemosphere, 24, 695-717 (1992) and earlier publications.
Remark : Level III Program, Mackay, D., 2002, Version 2.70, Trent University
 The distribution of potassium methanolate is of limited relevance for the assessment of the environmental behaviour as due to the rapid hydrolysis in water, the relevant species subject to environmental distribution are the degradation products potassium hydroxide and methanol.

Result :

	Scenario 1	Scenario 2	Scenario 3	100 % Release
100 % Release	100 % Release			
	into air	into water	into soil	
	[%]	[%]	[%]	
Compartment				
Air	89.3	0	0	
Water	0.46	100	0	
Soil	10.2	0	100	
Sediment	0	0	0	

Test condition : The calculation was conducted with the following user entered parameters:
 Molar mass: 70.13 g/mol
 Ambient temperature: 25 °C
 Log Kow: -0.74
 Vapour pressure: 6.39E-04 Pa [20 °C]
 Melting point: 300 °C

3. ENVIRONMENTAL FATE AND PATHWAYS

ID: 865-33-8

DATE: 28.06.2006

	Half-life in air: 464 hours	
	Emission rate:	
	Scenario 1:	
	3000 kg/h into air, 0 kg/h into water and soil	
	Scenario 2:	
	3000 kg/h into water, 0 kg/h into air and soil	
	Scenario 3:	
	3000 kg/h into soil, 0 kg/h into water and air	
Reliability	:	(2) valid with restrictions
		Calculated data, internationally accepted method.
12.01.2006		(18)

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

Type	:	
Inoculum	:	other
Remark	:	As potassium methylate rapidly hydrolyzes in water to methanol and potassium hydroxide, the data of the hydrolysis products are relevant for this substance as well. SIDS dossiers, SIARs and SIAPs are available for the degradation products. Methanol is readily biodegradable (BOD5 is 76-82%). Biodegradability is not applicable to potassium hydroxide.
04.12.2005		(23) (25)

3.6 BOD5, COD OR BOD5/COD RATIO**3.7 BIOACCUMULATION**

Species	:	other: expert judgement
Exposure period	:	at °C
Concentration	:	
Remark	:	As sodium and potassium methanolate react with water under formation of sodium and potassium hydroxide and methanol, an octanol-water partition coefficient cannot be experimentally established and bioaccumulation of the substances themselves is unlikely.
02.12.2005		

3.8 ADDITIONAL REMARKS

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type : static
Species : Leuciscus idus melanotus (Fish, fresh water)
Exposure period : 48 hour(s)
Unit : mg/l
LC50 : = 346 calculated
Limit test : no
Analytical monitoring : no
Method : other: DIN 38412 part 15
Year : 1988
GLP : no
Test substance : other TS: Sodium Methylate

Test substance : Sodium Methylate as prescribed by 1.1 - 1.4 of CAS 124-41-4
Reliability : (4) not assignable
 Short report only, no details available.

05.05.2006 (10)

Remark : As sodium and potassium methylates rapidly hydrolyse in water to methanol and sodium or potassium hydroxide respectively, the data of the hydrolysis products are relevant for this substance as well. SIDS dossiers, SIAR and SIAP is available for the degradation products.

Flag : Critical study for SIDS endpoint
 20.10.2005 (23) (25) (26)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type : other
Species :
Exposure period :
Unit :

Remark : As sodium and potassium methylates rapidly hydrolyse in water to methanol and sodium or potassium hydroxide respectively, the data of the hydrolysis products are relevant for this substance as well. SIDS dossiers, SIAR and SIAP is available for the degradation products.

Flag : Critical study for SIDS endpoint
 19.10.2005 (23) (25) (26)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species : Scenedesmus subspicatus (Algae)
Endpoint : other: assimilation inhibition
Exposure period : 24 hour(s)
Unit : mg/l
EC10 : = 24.2 calculated
EC50 : = 302.2 calculated
EC90 : = 3800 calculated
Limit test : no
Analytical monitoring : no
Method : other: DIN 38142 part 12
Year : 1989
GLP : no

Test substance	: other TS: Sodium methylate	
Method	: Assimilation inhibition test. Inhibition of oxygen liberation as a function of the concentration.	
Result	: - Nominal/measured concentrations: nominal only - Effect data inhibition of the assimilation: - Concentration / response curve: EC50 = 302.2 mg/l EC10 = 24.2 mg/l EC90 = 3800 mg/l	
Test condition	: TEST ORGANISMS - Strain: Scenedesmus subspicatus Chodat STOCK AND TEST SOLUTION AND THEIR PREPARATION - Vehicle, solvent: not stated - Concentration in vehicle/ solvent: 2 g/l STABILITY OF THE TEST CHEMICAL SOLUTIONS: Chemical reacts with water under formation of sodium hydroxide and methanol. DILUTION WATER: no data Duration: 24 h Statistical analysis: Probit analysis	
Test substance Reliability	: Sodium Methylate as prescribed by 1.1 - 1.4 of CAS 124-41-4 : (4) not assignable Short report only, no details available.	
05.05.2006		(12)
Remark	: As sodium and potassium methylates rapidly hydrolyse in water to methanol and sodium or potassium hydroxide respectively, the data of the hydrolysis products are relevant for this substance as well. SIDS dossiers, SIAR and SIAP is available for the degradation products.	
19.10.2005		(23) (25) (26)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

Type	: aquatic	
Species	: aerobic microorganisms	
Exposure period	: 24 hour(s)	
Unit	: mg/l	
EC10	: = 38 calculated	
EC50	: = 96.9 calculated	
EC90	: = 246.9 calculated	
Analytical monitoring	: no	
Method	: other: DIN 38412 part 12	
Year	: 1989	
GLP	: no	
Test substance	: other TS: Sodium methylate	
Method	: Inhibition of bacterial metabolism.	
Test condition	: - Bacteria mixed culture STOCK SOLUTION: 1 g/l STABILITY OF THE TEST CHEMICAL SOLUTIONS: unstable hydrolyses under formation of sodum hydroxide and methanol. STATISTICAL ANALYSIS: Probit analysis	
Test substance Reliability	: Sodium Methylate as prescribed by 1.1 - 1.4 of CAS 124-41-4 : (4) not assignable Short report only, no details available.	

Flag : Critical study for SIDS endpoint
05.05.2006 (11)

4.5.1 CHRONIC TOXICITY TO FISH**4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES****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****4.7 BIOLOGICAL EFFECTS MONITORING****4.8 BIOTRANSFORMATION AND KINETICS****4.9 ADDITIONAL REMARKS**

Memo : More data are available on the degradation products methanol and sodium and potassium hydroxide that are relevant for the assessment of the ecotoxicological properties of methylates.
19.10.2005 (23) (25) (26)

5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

- Remark** : The abiotic hydrolysis of sodium and potassium methanlates with tissue water results in the formation of sodium and potassium ions respectively, hydroxyl ions and methanol.
- For sodium hydroxide it was concluded in SIAM 14 "under normal handling and use conditions (non-irritating) neither the concentration of sodium in the blood nor the pH of the blood will be increased and therefore NaOH is not expected to be systemically available in the body."
- For potassium hydroxide SIAM 13 concluded: ". Under normal handling and use conditions (non-irritating) neither the concentration of potassium in the blood nor the pH of the blood will be increased above normal limits and therefore KOH is not expected to cause systemically toxic levels in the blood. The renal excretion of K⁺ can be elevated and the OH⁻ ion is neutralised by the bicarbonate buffer system in the blood."
- For Methanol SIAM 19 concluded: "Methanol is readily absorbed by inhalation, ingestion and dermal contact and distributes rapidly throughout the body. Metabolism in humans, rodents, and monkeys contributes up to 98 percent of the clearance, with more than 90 percent of the administered dose is ultimately exhaled as carbon dioxide. Renal and pulmonary excretion contributes only about 2 - 3 percent. In humans, the half-life is approximately 2.5 - 3 hours at doses lower than 100 mg/kg. At higher doses, the half life can be 24 hours or more.
- The mammalian metabolism of methanol occurs mainly in the liver, where methanol is converted to formaldehyde, which is in turn converted to formate. Formate is then finally converted to carbon dioxide and water. In humans and monkeys, the conversion to formaldehyde is mediated by alcohol dehydrogenase. In rodents, the reaction occurs mainly via a catalase-peroxide pathway. In rodents, the first step is rate limiting and methanol accumulates in the blood. In primates, the conversion of formate to carbon dioxide is rate-limiting, leading to a disproportionate increase of formate in the blood and sensitive target tissues (such as CNS and the retina).
- In humans, when exposed via inhalation up to an air concentration of 0.065 mg/L, no increase of blood methanol is expected. Up to 0.26 mg/L (single or repeated exposure), the methanol blood level is likely to increase 2 to 4-fold above the endogenous methanol concentration in humans, but still remains significantly below 10 mg/L. Air concentrations up to 1.6 mg/L resulted in similar blood methanol among rats, monkeys, and humans. However, above 1.6 mg/L, a steep exponential increase occurs in rats, a smaller exponential increase occurs in monkeys, and humans exhibit a linear relationship between air concentrations and blood methanol levels.
- Baseline levels of formate in blood are about 3 to 19 mg/L (0.07 - 0.4 mM) in humans. Toxic blood formate concentrations are reported to be 220 mg/L and higher (> 5 mM formate). Inhalation of about 1.20 mg methanol/L for 2 hours contributed only insignificantly to the internal formate pool in monkeys (in the µM-range), whereas formate accumulation has been observed in primates at methanol doses greater than 500 mg/kg."
- Flag** : Critical study for SIDS endpoint
05.05.2006 (23) (25) (26)

5.1.1 ACUTE ORAL TOXICITY

Type	:	LD50	
Value	:	= 1500 mg/kg bw	
Species	:	rat	
Strain	:	no data	
Sex	:	no data	
Number of animals	:		
Vehicle	:	other: Lutrol	
Doses	:	no data	
Method	:	other: no data	
Year	:	1978	
GLP	:	no	
Test substance	:	other TS: Sodiummethylate 30% in Methanol	
Result	:	Symptoms: uncharacteristic. Pathology: Macroscopic findings: Heart: acute dilatation (right side), acute congestive hyperaemia. Stomach: profound haemorrhagic gastritis, adhesions in forestomach and glandular stomach. Intestine: diarrhoea, blood, haemorrhagic enteritis. Sero-fibroic peritonitis. Abdomen: blood coloured ascites.	
Test condition	:	TEST ORGANISMS: rats ADMINISTRATION: gavage, 0.928 to 46.4% solution in Lutrol (G/V). Observation period: 14 days	
Reliability	:	(2) valid with restrictions Well documented report, details missing, preliminary study only.	
24.10.2005			(2)
Type	:	LD50	
Value	:	= 800 mg/kg bw	
Species	:	rat	
Strain	:	no data	
Sex	:	no data	
Number of animals	:		
Vehicle	:	other: Lutrol	
Doses	:	not specified	
Method	:	other: not specified	
Year	:	1979	
GLP	:	no	
Test substance	:	other TS: Sodium methylate	
Result	:	Symptoms: uncharacteristic. At the beginning of the observation period body weight reduction. Pathology: Macroscopic changes in animals that died during the study: Heart: acute dilatation (right), acute congestive hyperaemia. Stomach: extended ulcerating gastritis, bleeding in the forestomach. Wall of glandular stomach thickened. Intraabdominal adhesions between stomach and liver. Intestine: atonic, diarrhoea, bloody content. Hydrothorax and partly blood coloured ascites.	
Test condition	:	Administration of 0.43 to 14.7% (G/V) suspension of crystalline sodium methylate in Lutrol. Observation period: 14 days	
Test substance	:	Sodium methylate as prescribed by 1.1 - 1.4 of CAS 124-41-4	
Reliability	:	(2) valid with restrictions Well documented report, details missing.	
Flag	:	Critical study for SIDS endpoint	
05.08.2005			(4)
Type	:	LD50	

Value	:	= 2037 mg/kg bw	
Species	:	rat	
Strain	:	Sprague-Dawley	
Sex	:	male	
Number of animals	:	10	
Vehicle	:	other: corn oil	
Doses	:	1500, 1800, 2250, 2380, 2600, 3400 mg/kg bw	
Method	:	other: similar to OECD Guide-line 401	
Year	:	1982	
GLP	:	no data	
Test substance	:	other TS: sodium methylate	
Result	:	MORTALITY:	
		Dose [mg/kg bw]	Mortality
		3400	10/10
		2600	10/10
		2380	8/10
		2250	2/10
		1800	5/10
		1500	1/10
		- Time of death: up to 14 days after dosing	
		CLINICAL SIGNS:	
		All dose levels: labored breathing, weakness, wet and stained perianal area, chromodacryorrhea, ruffled fur.	
		from 1800 mg/kg bw: salivation and lethargy	
		from 2380 mg/kg bw: Ataxia	
		from 2600 mg/kg bw: lacrimation	
		Body weight: loss from day 9	
Test condition	:	TEST ORGANISMS: Male Sprague Dawley rats cri:CD	
		- Age: young adult	
		- Weight at study initiation: 238 - 252	
		ADMINISTRATION:	
		- concentration: 20 to 30% Suspension in corn oil by gavage	
		- Volume administered: 1.83 to 2.7 ml	
		- Post dose observation period: 14 days	
		EXAMINATIONS: clinical observations, body weight	
Reliability	:	(2) valid with restrictions	
		Comparable to guideline study, no necropsy findings reported, no data on GLP	
Flag	:	Critical study for SIDS endpoint	
18.08.2005			(19)
Type	:	LD50	
Value	:	= 1687 mg/kg bw	
Species	:	rat	
Strain	:	Sprague-Dawley	
Sex	:	male/female	
Number of animals	:	10	
Vehicle	:	water	
Doses	:	1000, 1260, 1587, 2000 mg/kg bw	
Method	:	OECD Guide-line 401 "Acute Oral Toxicity"	
Year	:	1988	
GLP	:	yes	
Test substance	:	other TS: Sodium methylate	
Remark	:	As the substance was tested in aqueous solution and sodium methylate hydrolyses rapidly to methanol and sodium hydroxide, in fact the hydrolysis products have been tested.	
Result	:	MORTALITY:	
		Dose [mg/kg bw]	Mortality
		2000	8/10

1587 2/10
1260 1/10
1000 1/10

LD50 males: 1844 mg/kg bw
LD50 females: 1682 mg/kg bw
LD50 combined: 1687 mg/kg bw
- Time of death: most deaths occurred between days 1 and 6 after treatment.

CLINICAL SIGNS:

All animals: hunched posture, pilo-erection, decreased respiration rate (1 to 4 h after dosing).

Some of the symptoms were observed up to days 6 to 9 in surviving animals of the 1587 mg/kg bw group and up to day 11 in those of the high dose group.

Additional symptoms at 1587 mg/kg bw: lethargy, ptosis pallor of the extremities, red/brown staining around the snout, emaciation (females, from day 6).

Body weights: In most of the animals body weight gain was noted. Isolated cases of body weight loss or reduced bw gain were reported.

NECROPSY FINDINGS:

Common abnormalities of animals that died during the study: red lungs, pale or dark or patchy pallor of livers.

At 1587 and 2000 mg/kg bw: severe haemorrhage and rugae of the glandular gastric epithelium. Occasional adherence of stomach to the liver. In the surviving animals killed at termination occasional findings were white foci in the non-glandular gastric epithelium and adherence of the stomach to the liver.

Test condition : TEST ORGANISMS: male and female Sprague-Dawley CFY rats
- Source: Interfauna (UK) Ltd. Wyton
- Age: 5 to 8 weeks
- Weight at study initiation:
Males: 122 to 145 g, females: 120 to 142 g

ADMINISTRATION

- Concentration: 100 - 200 mg/ml
- Volume administered: 10 ml/kg bw
- Post dose observation period: 14 days

EXAMINATIONS:

Clinical observations
Body weights
Gross necropsy findings

Test substance : Sodium methylate
Reliability : (1) valid without restriction

Flag : Guideline study, GLP
: Critical study for SIDS endpoint

24.10.2005

(9)

Type : LD100
Value : = 1000 mg/kg bw
Species : rat
Strain : Sprague-Dawley
Sex : male/female
Number of animals : 10
Vehicle : water
Doses : 215, 316, 464, 681, 1000 mg/kg
Method : other: comparable to OECD Guide-line 401
Year : 1978
GLP : no
Test substance : other TS: Sodium methylate

Remark	:	As the substance was tested in aqueous solution and sodium methylate hydrolyses rapidly to methanol and sodium hydroxide, in fact the hydrolysis products have been tested.
Result	:	Mortality: All animals of the 1000 mg/kg bw. group died between 1 h and 1 day p.a. Symptoms: All dose groups: dyspnea, apathy from 316 mg/kg additionally yellow discoloration of the urine. from 681 mg/kg: spastic and staggered gait. at 1000 mg/kg: anomalous posture, atonia, reddening of skin, loss of pain reflex, narcotic condition. Pathology Macroscopic examination: Animals that were killed after termination of the study did not reveal any macroscopic organ changes. Animals that died during the study: Dilatation of right heart, discoloration of right ventricle, acute congestive hyperaemia. Stomach: atonic, fluid stomach content, forestomach: diffuse reddening, vascular injection. Intestines: atonic, diarrhoea.
Test condition	:	TEST ORGANISMS: male and female Sprague Dawley rats - Source: Herilan, Eggersmann KG - Initial body weight: males: 220-230 g, females: 180-200g - Number of animals: 5 males, 5 females per dose group ADMINISTRATION: - Type of exposure: gavage, Volume 10 ml/kg - Concentrations: 2.15, 3.16, 4.64, 6.81, 10 % (G/V) 14 Days observation period. EXAMINATIONS: Symptoms Mortality Body weight development Macroscopic examination at termination or after death of the animals.
Test substance	:	Sodium Methylate as prescribed by 1.1 - 1.4 of CAS 124-41-4
Reliability	:	(2) valid with restrictions Well documented study.
Flag	:	Critical study for SIDS endpoint
05.12.2005		(3)

5.1.2 ACUTE INHALATION TOXICITY

Type	:	other: acute inhalation risk test (IRT)
Value	:	
Species	:	rat
Strain	:	no data
Sex	:	no data
Number of animals	:	12
Vehicle	:	
Doses	:	atmosphere enriched with volatile parts at 20 °C
Exposure time	:	8 hour(s)
Method	:	other: according to Smyth et al.: Am. Ind. Hyg. Ass. J. 23, 95-107, 1962
Year	:	1978
GLP	:	no
Test substance	:	other TS: Sodium methylate 30% in Methanol
Result	:	Mortality: no animal died during the study. No clinical symptoms and no macroscopic organ changes at termination of the study were observed.
Test condition	:	TEST ORGANISMS: Rats

	Number: 12	
	ADMINISTRATION:	
	- Type of exposure: inhalation of an atmosphere enriched with the volatile components at 20 °C. 200 l/h air were piped through a 5 cm layer of the product.	
Reliability	: (2) valid with restrictions	
	Well documented report, details missing.	
Flag	: Critical study for SIDS endpoint	
05.08.2005		(2)
Type	: other: acute inhalation risk test (IRT)	
Value	:	
Species	: rat	
Strain	: no data	
Sex	: no data	
Number of animals	: 12	
Vehicle	:	
Doses	: dust enriched atmosphere at room temperature	
Exposure time	: 7 hour(s)	
Method	: other: IRT	
Year	: 1979	
GLP	: no	
Test substance	: other TS: Sodium methylate	
Result	: No mortality. No symptoms were observed during the study. Pathological examination at termination of the study did not reveal any macroscopic organ changes.	
Test condition	: Inhalation of an dust enriched atmosphere at room temperature. 200 l air/hour were piped through a 5 cm layer of the product.	
Test substance	: Sodium methylate as prescribed by 1.1 - 1.4 of CAS 124-41-4	
Reliability	: (2) valid with restrictions	
	Well documented report, details missing.	
Flag	: Critical study for SIDS endpoint	
05.08.2005		(4)

5.1.3 ACUTE DERMAL TOXICITY

Type	: LD50	
Value	: > 2000 - mg/kg bw	
Species	: rat	
Strain	: Sprague-Dawley	
Sex	: male/female	
Number of animals	: 6	
Vehicle	: water	
Doses	: 1000, 2000 mg/kg bw	
Method	: other	
Year	: 1979	
GLP	: no	
Test substance	: other TS: Sodium methylate 50% aqueous solution	
Remark	: As the substance was tested in aqueous solution and sodium methylate hydrolyses rapidly to methanol and sodium hydroxide, in fact the hydrolysis products have been tested.	
Result	: MORTALITY: No deaths occurred at either dose level CLINICAL SIGNS: irregular breathing and bad general condition. Skin: necrosis after the 24 hour application. NECROPSY FINDINGS: No macroscopic organ changes apart from the skin necrosis were observed.	

Test condition : TEST ORGANISMS: male and female Sprague-Dawley rats, SPF
 - Source: Hagemann, Extertal
 - Weight at study initiation: males: 220 g, females 190 g
 ADMINISTRATION: as 50% solution in water
 - Area covered: 50 cm²
 - Occlusion: yes, 24 hours
 - Vehicle: water
 - Concentration in vehicle: 50%
 - Doses: 1000 and 2000 mg/kg bw
 - Removal of test substance: after 24 hours with lukewarm water or water/lutrol
 EXAMINATIONS:
 Mortality within 14 days
 Clinical symptoms
 Necropsy and macroscopic examination at termination.

Test substance : Sodium methylate krist., BASF tested as 50% solution in water

Reliability : (2) valid with restrictions
 Well documented study.

Flag : Critical study for SIDS endpoint

23.08.2005

(5)

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.2.1 SKIN IRRITATION

Species : rabbit
Concentration : undiluted
Exposure : no data
Exposure time :
Number of animals : 2
Vehicle :
PDII :
Result : corrosive
Classification : highly corrosive (causes severe burns)
Method : other: not specified
Year : 1978
GLP : no
Test substance : other TS: Sodium methylate 30% in Methanol

Result : Exposure 1 min:
 Symptoms after 24 h:
 slight necrosis, moderate erythema and oedema
 Symptoms after 8 days:
 moderate necrosis and desquamation
 Exposure 5 min:
 Symptoms after 24 h:
 moderate necrosis, moderate erythema and oedema.
 After 8 days: moderate extended necrosis
 15 min: very severe necrosis persisting after 8 days.
 Severe pain reaction shortly after the application of the test substance.

Test condition : Exposure time 1 to 15 min.
Reliability : (2) valid with restrictions
 Well documented report, details missing.

Flag : Critical study for SIDS endpoint

24.10.2005

(2)

Species : rabbit
Concentration : 80 %

Exposure	:	no data	
Exposure time	:	3 minute(s)	
Number of animals	:	2	
Vehicle	:	water	
PDII	:		
Result	:	highly corrosive	
Classification	:	highly corrosive (causes severe burns)	
Method	:	other: similar to OECD Guide-line 404	
Year	:	1979	
GLP	:	no	
Test substance	:	other TS: Sodium methylate	
Result	:	Primary irritation score	
		3 min:	
		Erythema: 2 (2/2 animals)	
		Oedema: 0 (2/2 animals)	
		24 h	
		Erythema: 2 extended patchy necrosis (1/2 animals)	
		2 patchy necrosis (1/2 animals)	
		Oedema: 2 (2/2 animals) extended in 1 animal	
		48 h	
		Erythema: 3 extended patchy necrosis (1/2 animals)	
		4 very severe necrosis (1/2 animals) (parchment-like)	
		Oedema: 2 (2/2 animals) extended in 1 animal	
		8 days:	
		Erythema: 4 Necrosis (2/2 animals) (leather-like)	
		Oedema: 1 (2/2 animals)	
Test substance	:	Sodium methylate as prescribed by 1.1 - 1.4 of CAS 124-41-4	
Reliability	:	(2) valid with restrictions	
		Well documented report, details missing.	
Flag	:	Critical study for SIDS endpoint	
05.08.2005			(4)
Species	:	rabbit	
Concentration	:	undiluted	
Exposure	:	Semiocclusive	
Exposure time	:	4 hour(s)	
Number of animals	:	6	
Vehicle	:	water	
PDII	:		
Result	:	corrosive	
Classification	:	corrosive (causes burns)	
Method	:	EPA OPP 81-5	
Year	:	1988	
GLP	:	yes	
Test substance	:	other TS: Sodium methylate	
Result	:	Severe necrosis, sunken green coloured was observed at all treatment sites 1 hour after removal of the patches. The study was terminated for humane reasons and the material considered corrosive to rabbit skin.	
Test condition	:	TEST ANIMALS: Rabbits	
		- Strain: New Zealand white	
		- Sex: Male	
		- Source: David Percival Ltd. U.K.	
		- Age: 12 to 16 weeks	
		- Weight at study initiation: 2.4 to 2.9 g	
		- Number of animals: 6	
		ADMINISTRATION/EXPOSURE	

	- Preparation of test substance: Powder moistened with water.
	- Area of exposure: 5 cm ²
	- Occlusion: semi-occlusive
	- Total volume applied: 0.5 g moistened with 0.5 ml of distilled water
	- Postexposure period: none, study was terminated 1 h after removal of the patch
	- Removal of test substance: after 4 h with water
	Examinations: only after 1 hour
	Scoring system: Draize, 1959
	- Examination time points: 1 hour
Test substance	: Sodium methylate as prescribed by 1.1 - 1.4 of CAS 124-41-4
Reliability	: (1) valid without restriction
	Guideline study under GLP
Flag	: Critical study for SIDS endpoint
24.10.2005	(8)

5.2.2 EYE IRRITATION

Species	: rabbit
Concentration	: undiluted
Dose	: 50 ml
Exposure time	:
Comment	:
Number of animals	: 2
Vehicle	:
Result	: corrosive
Classification	: risk of serious damage to eyes
Method	: other: not specified
Year	: 1978
GLP	: no
Test substance	: other TS: Sodium methylate 30% in Methanol
Result	: After 1 h: Grey discoloration of the nictating membrane. Severe corneal opacity. Severe pain reaction after application of the test substance. After 24 h: Grey discoloration of the nictating membrane and the conjunctiva (partly). Moderate conjunctival redness, slight oedema, severe corneal opacity. Necrosis of the edges of the eye lids. After 8 days: Severe necrosis, severe suppuration, eyelids shrunken.
Reliability	: (2) valid with restrictions Well documented report, details missing.
Flag	: Critical study for SIDS endpoint
05.08.2005	(2)

5.3 SENSITIZATION

Type	: other
Species	:
Remark	: As sodium and potassium methylates rapidly hydrolyse in water to methanol and sodium or potassium hydroxide respectively, the data of the hydrolysis products are relevant for this substance as well. SIDS dossiers, SIARs and SIAPs are available for the degradation products.
19.10.2005	(23) (25) (26)

5.4 REPEATED DOSE TOXICITY

Method : other: rational
Year :
GLP :
Test substance :

Remark : No data on repeated dose toxicity of sodium and potassium methanolate are available. The tolerable dose levels will be determined by the corrosive nature of the substances. At sub irritant concentrations the toxicity of K⁺ or Na⁺ ions and OH⁻ ions are unlikely to contribute to the effects to be expected after repeated exposure. The specific ocular and CNS toxicity of methanol in primates is based on the accumulation of formate in blood. Formate accumulation in primates has been observed at methanol doses greater than 500 mg/kg. The corresponding dose levels for sodium and potassium methanolate that would lead to accumulation of formate in primates would be 840 and 1000 mg/kg bw. Such dose levels are already in the acutely toxic dose range. Due to the corrosive nature of the methanolates it is unlikely that exposure to methanolates could result in an uptake of toxic doses of methanol.

02.12.2005

(23) (25) (26)

5.5 GENETIC TOXICITY 'IN VITRO'

Type : other
System of testing :
Test concentration :
Cycotoxic concentr. :
Metabolic activation :
Result :
Method :
Year :
GLP :
Test substance :

Remark : As sodium and potassium methylates rapidly hydrolyse in water to methanol and sodium or potassium hydroxide respectively, the data of the hydrolysis products are relevant for this substance as well. SIDS dossiers, SIARs and SIAPs are available for the degradation products.

Due to the rapid hydrolysis of methanolates in in vitro test systems and tissue water in vivo, data for the hydrolysis products are relevant for methanolates as well. For sodium and potassium hydroxide there is no evidence for a mutagenic potential. For methanol the weight of evidence suggests that the substance is unlikely to have any relevant mutagenic activity. Therefore it can be concluded that there should at present be no concern with regard to a mutagenic activity of sodium or potassium methanolate.

02.12.2005

(23) (25) (26)

Type : Ames test
System of testing : S. typhimurium TA97, 98, 100
Test concentration : 8 - 5000 µg/plate
Cycotoxic concentr. : > 5000 µg/plate
Metabolic activation : with and without
Result : negative
Method : other: comparable to OECD Guide-line 471, but 3 strains only tested
Year : 1987
GLP : yes

Test substance	:	other TS: Sodium methanolate
Result	:	<p>GENOTOXIC EFFECTS:</p> <ul style="list-style-type: none"> - With metabolic activation: none - Without metabolic activation: none <p>PRECIPITATION CONCENTRATION: 5000 µg/plate</p> <p>CYTOTOXIC CONCENTRATION:</p> <ul style="list-style-type: none"> - With metabolic activation: > 5000 µg/plate - Without metabolic activation: > 5000 µg/plate
Test condition	:	<p>SYSTEM OF TESTING: Bacterial gene mutation assay</p> <ul style="list-style-type: none"> - Species/cell type: S. Typhimurium TA97 TA98, TA100, - Deficiencies/Proficiencies: His deficient - Metabolic activation system: Arochlor induced rat liver post.mitochondrial fraction (S9). <p>Pre-Test for toxicity in TA 100</p> <p>Solvent: water</p> <ul style="list-style-type: none"> - Concentrations: 8, 40, 200, 1000, 5000 µg/plate - Number of replicates: 3 - Positive controls: 2-nitrofluorene (TA98 - S9), sodium azide (TA100 - S9), 9-aminoacridine (TA97, -S9), 2-aminoanthracene (all strains + S9) - Negative control groups: solvent: water <p>CRITERIA FOR EVALUATING RESULTS: twofold increase in revertants compared to concurrent controls indicates positive result.</p> <p>STATISTICAL METHODS: F-test and regression analysis in case of positive results.</p>
Reliability	:	(2) valid with restrictions 3 strains only tested
Flag 07.12.2005	:	Material Safety Dataset, Critical study for SIDS endpoint

(7)

5.6 GENETIC TOXICITY 'IN VIVO'

Type	:	other
Species	:	
Sex	:	
Strain	:	
Route of admin.	:	
Exposure period	:	
Doses	:	
Result	:	
Method	:	
Year	:	
GLP	:	
Test substance	:	
Remark	:	As sodium and potassium methylates rapidly hydrolyse in water to methanol and sodium or potassium hydroxide respectively, the data of the hydrolysis products are relevant for this substance as well. SIDS dossiers, SIARs and SIAPs are available for the degradation products.
19.10.2005		(23) (25) (26)

5.7 CARCINOGENICITY

Species	:	other
Sex	:	
Strain	:	
Route of admin.	:	
Exposure period	:	

Frequency of treatm. :
Post exposure period :
Doses :
Result :
Control group :
Method :
Year :
GLP :
Test substance :

Remark : As sodium and potassium methylates rapidly hydrolyse in water to methanol and sodium or potassium hydroxide respectively, the data of the hydrolysis products are relevant for this substance as well. SIDS dossiers, SIARs and SIAPs are available for the degradation products.
 19.10.2005 (23) (25) (26)

5.8.1 TOXICITY TO FERTILITY

Type : other
Species :
Sex :
Strain :
Route of admin. :
Exposure period :
Frequency of treatm. :
Premating exposure period
 Male :
 Female :
Duration of test :
No. of generation studies :
Doses :
Control group :

Remark : As sodium and potassium methylates rapidly hydrolyse in water to methanol and sodium or potassium hydroxide respectively, the data of the hydrolysis products are relevant for this substance as well. SIDS dossiers, SIARs and SIAPs are available for the degradation products.
 19.10.2005 (23) (25) (26)

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species : other
Sex :
Strain :
Route of admin. :
Exposure period :
Frequency of treatm. :
Duration of test :
Doses :
Control group :

Remark : As sodium and potassium methylates rapidly hydrolyse in water to methanol and sodium or potassium hydroxide respectively, the data of the hydrolysis products are relevant for this substance as well. SIDS dossiers, SIARs and SIAPs are available for the degradation products.
 19.10.2005 (23) (25) (26)

5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES**5.9 SPECIFIC INVESTIGATIONS****5.10 EXPOSURE EXPERIENCE****5.11 ADDITIONAL REMARKS**

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