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ACETIC ANHYDRIDE
CAS N°: 108-24-7

COVER PAGE**SIDS Initial Assessment Report**
for
6th SIAM

(Paris, 9-11 June 1997)

Chemical Name: Acetic Anhydride**CAS No.:** 108-24-7**Sponsor Country:** Canada

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HISTORY:

The SIDS Dossier was sent for review on March 1993. At the third SIDS Initial Assessment Meeting testing approval was given for a 13-week inhalation study with extensive evaluation of the bone marrow and respiratory and reproductive tracts. The results have been incorporated into the current SIAR.

no testing ()

testing ()

COMMENTS:

Deadline for circulation: March 7, 1997

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(To all National SIDS Contact Points and the OECD Secretariat)

SIDS INITIAL ASSESSMENT PROFILE

CAS Nr.	108-24-7
Chemical Name	Acetic anhydride
Structural formula	(CH ₃ CO) ₂ O

CONCLUSIONS AND RECOMMENDATIONS

It is currently considered of low priority for further work.

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

In the hydrosphere, Acetic anhydride is rapidly hydrolyzed (half-life 4.4 min.) to acetic acid which is readily biodegradable. In the atmosphere, it is converted to Acetic acid which is subject to photooxidative degradation (half-life 22 days). Toxicity to aquatic organisms is moderate (18 to 3400 mg/l), but it persists only for a short time due to its rapid hydrolysis to acetate/acetic acid. It has virtually no potential for bioaccumulation (log Kow = -0.27). The PEC/PNEC ratio is much less than 1, indicating that acetic anhydride has a low potential for risk to the environment.

The critical effect for Acetic anhydride is irritancy at the site of contact. Because of its well-known corrosive and irritating effects on the eyes, skin and respiratory tract and low odor threshold, procedures, equipment (e.g. goggles, gloves, respirators), training and engineering controls (closed systems) have already been in place for many years to prevent exposure. Levels of acetic anhydride in facilities where it is produced and used in the manufacture of cellulose acetate esters are below 1 ppm 8 hr. time-weighted average (4.2 mg/m³). It is suggested that member country occupational exposure limits be revisited based on the additional results from a 90 day test, reported in the SIAR. Acetic anhydride is used exclusively as a chemical intermediate and there is no indication that its use is in general practice in the consumer industry.

IF FURTHER WORK IS RECOMMENDED, SUMMARISE ITS NATURE

OECD HIGH PRODUCTION VOLUME CHEMICALS PROGRAM

SIDS INITIAL ASSESSMENT REPORT

ACETIC ANHYDRIDE CAS NO. 108-24-7

1. IDENTITY

Acetic Anhydride	CAS No. 108-24-7
Synonyms:	acetanhydride; acetic acid; anhydride; acetic oxide; acetyl anhydride; acetyl oxide; acetyl acetate
Molecular Formula:	C ₄ H ₆ O ₃
Structural Formula:	(CH ₃ CO) ₂ O
Molecular Weight:	102.09
Boiling point (760 mmHg):	138.6°C (282°F)
Freezing point:	-73°C (-100°F)
Vapor pressure:	4mm Hg at 20°C; 100 mm Hg at 36°C
Odor Threshold:	0.14 ppm
Flammable limits in air, percent by volume:	LEL = 2.8% at 81°C; 2% at 20°C UEL = 12.4% at 129°C; 10.2% at 20°C
Flash point:	52.5-53°C (closed cup); 124-130°F
Autoignition Temperature:	315-331°C (629°F)
Specific gravity:	1.082 - 1.083 (at 20°C)
Vapor density:	3.5 (air = 1)
Solubility in water:	Decomposes; 2.6 wt% at 20°C
Evaporation Rate:	0.46 (BuAc = 1.0)
Stability:	Stable in dry air

Acetic anhydride is a colorless, mobile, combustible liquid with a pungent acetic acid odor. It is primarily manufactured for captive use in production of cellulose acetate and related products, but is also marketed as a >98% purity reagent, for example, used in manufacturing pharmaceuticals. The major impurity in acetic anhydride is acetic acid. Acetic anhydride reacts violently with water to produce acetic acid and heat.

2. GENERAL INFORMATION ON EXPOSURE

2.1 General Discussion

Production capacities available for North America and Western Europe are given in Table I.

Table I. 1995 Acetic Anhydride Production Capacities (1)

Region	Thousand Metric Tons
Canada	70
Mexico	87
United States	1223

Acetic anhydride is manufactured in North America by two processes. Most of the production uses the ketene - acetic acid technology, which involves thermal cracking acetic acid to ketene and the subsequent reaction of the ketene with additional acetic acid to form acetic anhydride. Methyl acetate carbonylation is a second route. Some acetic acid is produced as a co-product in the methyl acetate carbonylation process.

Acetic anhydride used as a reagent in manufacturing acetate esters, acetylation of pharmaceuticals, end-capping polyacetal homopolymers, and other reactions is consumed in the reaction step. Reactions of acetic anhydride with hydroxyl groups yield the corresponding acetate ester with coproduction of acetic acid. Acetylation of amines produce acetamides such as TAED (tetraacetythylenediamine), which is used as a perborate bleach activator. Acetic anhydride is used to acetylate salicylic acid to aspirin and p-aminophenol to acetaminophen.

Most of the acetic anhydride production is consumed in manufacturing cellulose acetate esters. Cellulose acetate esters include cellulose diacetate, cellulose triacetate and mixed esters (propionates, butyrates). In the manufacture of cellulose acetate, one acetyl group from each acetic anhydride molecule reacts with the cellulose and the other acetyl group is converted to acetic acid which can be recycled back to make more acetic anhydride or be used to produce other acetic acid derivatives. Shredded pure alpha cellulose is typically soaked in aqueous acetic acid before the treated pulp is acetylated with a 60-40 mixture of acetic acid and acetic anhydride using a dilute sulfuric acid catalyst. Cellulose acetate fibers are recovered as tow or as filament yarn. Filters are made from a blend of tow and plasticizer. Cellulose acetate filament yarns are used in apparel and home furnishings. Cellulose triacetate is used in photographic film and pressure sensitive tapes. U.S. consumption of acetic anhydride in 1993, for example, was distributed in major end uses as follows in Table 2. This is generally representative of consumption in North America

Table 2. U.S. Consumption of Acetic Anhydride (Percentages) (1)

Cellulose Acetate Esters						
Filter Tow	Filament Yarn	Flake Export	Miscellaneous	Aspirin	Acetaminophen	Other
42%	18%	13%	12%	1%	2%	12%

Acetic anhydride reacts with water forming acetic acid and, therefore, can be used as a dehydration reagent.

2.2. Production releases

Celanese Canada, Edmonton (this plant produces both acetic anhydride and cellulose acetate)

Emissions Total (Annual Emission Estimate)

Storage 7 tons

Fugitive 4 tons

Amount released per day 30 kg/day (Assumes plant operates 365 days/year)

These releases are all to the atmosphere. Any release to water goes to deepwell injection. Due to hydrolysis this would only be present and detectable as acetic acid. Any releases in this manner are expected to be minimal.

2.3 Release from use

2.3.1 Release from cellulose acetate production

The major downstream use is in Cellulose Acetate Production, where Acetic Anhydride is an intermediate.

The release numbers given in 2.2. are for the Celanese Canada Edmonton facility as a whole, and so include both production and use. Although no definitive numbers are available, given the nature of the Cellulose Acetate Process any emissions are expected to be small (<10% of total emissions) and due to hydrolysis, in the form of acetic acid.

2.3.2 Release from consumer use

Acetic anhydride is used as a reactive intermediate. When reacted, for example to make cellulose acetate, it is not regenerated in use. Because it is reactive and readily hydrolyzed, its presence in end use products is not possible. See Section 4.1.2 for further information.

2.3.3 Widespread release

General widespread release is not an applicable scenario for acetic anhydride. It is used only as a captive, reactive intermediate.

2.4 Information on Safe Handling

In case of accidental release, ignition sources should be eliminated. Leaking containers should be placed in a well-ventilated area with spill containment. If fire potential exists, blanket spill with alcohol-type aqueous film-forming foam or use water spray to disperse vapors. Clean-up methods may include use of absorbent materials or a vacuum truck. Runoff into storm sewers and ditches which lead to natural waterways should be avoided by spill containment.

Storage of acetic anhydride containers should be with adequate ventilation and the containers should be closed when not in use. Contact with eyes, skin or clothing, and breathing acetic anhydride vapor should be avoided. Soiled clothing should be decontaminated thoroughly before re-use and contaminated leather clothing should be destroyed. Workers should wash thoroughly with soap and water after handling acetic anhydride containers.

Acetic anhydride should be stored away from heat, sparks, and flame sources, and should not be stored with incompatible materials. Incompatible materials include water; aqueous alkalis such as caustic soda solution; alcohols; glycols; hydrogen peroxide, perchloric acid, nitric acid, chromium trioxide, and other oxidizing agents; amines; boric acid. Acetic anhydride reacts with water to form acetic acid and heat.

3. ENVIRONMENT

3.1 Environmental Exposure

3.1.1 General Discussion

In natural bodies of water, acetic anhydride hydrolyses according to a first-order reaction to acetic acid. On the basis of experimentally determined rate constants (2), one can calculate half-lives, $t_{1/2}$, of 4.4 min. (at 25°C) and 8.1 min. (at 15°C).

This hydrolytic degradation to acetic acid also occurs in the atmosphere. On the basis of an experimentally determined rate constant, for the degradation of acetic acid through reaction with photochemically formed OH-radicals in the atmosphere a half-life of 22 days has been calculated (3). However, on account of its high solubility, acetic acid will be rapidly washed out of the atmosphere.

In the static Zahn-Wellens test of biodegradability, acetic acid is degraded to more than 95% within 5 days (4). In the respirometer test (22 - 24 hours in modified MITI test) acetic acid is degraded to 99% (5).

For acetic anhydride an n-octanol/water partition coefficient, $\log P_{ow}$, of -0.27 has been calculated, while for acetic acid a $\log P_{ow}$ of -0.17 has been experimentally determined (6,7). Neither value gives any indication of a potential for bioaccumulation.

3.1.2 Predicted Environmental Concentration

Given the volume of acetic anhydride released to the atmosphere annually the steady state concentrations using Mackay fugacity model ChemCan IV for the region of northern Alberta can be estimated. Releases to this 378 000 km² area result in 2.4×10^{-15} mg/m³ in air, 2.33×10^{-9} µg/g in soil, 1.8×10^{-11} g/m³ in water, and 1.9×10^{-14} g/m³ in sediment assuming a residence time in air of 2.42 days and 75.1 days in water for this region. Overall reaction persistence is estimated at 0.107 hrs. The concentration for water can be used as a PEC in the calculation (i.e. $PEC = 1.7 \times 10^{-11}$ mg/L).

As previously noted, the by-product of acetic anhydride is acetic acid. It is quickly biodegraded and does not bioaccumulate ($\log P_{ow} = -0.17$). It is less toxic in comparable aquatic species than acetic anhydride and in its neutralized form (acetate) it plays an important role in the metabolism of all species.

3.2 Effects on the Environment (6,7)

The results of various laboratory tests with aquatic organisms, in which the toxic threshold concentrations for acetic anhydride were found to be about half those for acetic acid, suggest an initial toxic effect, so long as not all of the substance has hydrolyzed to acetic acid (during the first few minutes).

For protozoa the toxic threshold concentration for acetic anhydride is between 30 and 735 mg/l (8,9,10):

Chilomonas paramecium, 48-hour Toxic Threshold Concentration = 395 mg/l
(cell multiplication inhibition test)

Entosiphon sulcatum, 72-hour Toxic Threshold Concentration
(5% Effect Concentration = EC₅) = 30 mg/l

(cell multiplication inhibition test)

Uronema parduzci, Toxic Threshold Concentration = 735 mg/l
(limited details; test duration not specified)

The toxic threshold concentration for bacteria (source: domestic wastewater treatment plant), as determined in the 24-hour fermentation-tube test, was $\geq 2,500$ mg/l. The endpoint was inhibition of respiration and the parameter measured was oxygen consumption (11,4). In the cell proliferation inhibition test (16 hrs.) with *Pseudomonas putida* a toxic threshold concentration (3% Effect Concentration = EC₃) of 1,150 mg/l was found (12).

In the cell multiplication inhibition test (8 days), the following toxic threshold concentrations (EC₃) were determined:

Microcystis aeruginosa (cyanobacteria): 18 mg/l (13)
Scenedesmus quadricauda (green algae): 3,400 mg/l (14)

In a 5-day study with *Chlorella pyrenoidosa* (algae) using chlorophyll reduction as the endpoint, 16.6% to 96.6% reduction was noted compared to the controls over the concentration range 50 mg/l to 400 mg/l (15).

For *Daphnia magna* the following effective concentrations for immobilization were determined (16):

	test medium not neutralized	neutralized to protect against pH lowering by released acetic acid
24-hour EC ₀ =	47 mg/l;	1370mg/l
24 hour EC ₅₀ =	55 mg/l;	3200mg/l
24-hour EC ₁₀₀ =	68 mg/l;	5900mg/l

With respect to fish toxicity, the following lethal concentrations were determined for the golden orfe (*Leuciscus idus*) (17):

48-hour LC₀ = 216 and 252 mg/l
48-hour LC₅₀ = 265 and 279 mg/l
48-hour LC₁₀₀ = 324 mg/l

3.3 Initial Assessment for the Environment

To determine the PNEC, the chronic lowest effect level of 18 mg/L is taken and divided by 2 to obtain an estimated NOEC of 9 mg/L based on guidance from the OECD SIDS Manual (June 1997). Applying a safety factor of 100 (because chronic NOECs are not available for the other trophic levels) provides a PNEC of 0.09 mg/L. Because chronic NOECs are not available for *Daphnia* or fish a comparison must be made between the PNEC derived from the lowest acute value. The lowest acute effect level is for *Daphnia* at 55 mg/L. Applying a safety factor of 500 because chronic data is available for algae and the substance is not persistent gives a PNEC of 0.11 mg/L which is slightly higher than the PNEC derived from chronic data. Therefore, using the PEC derived from the fugacity model the ratio would be as follows:

$$\text{PEC/PNEC} = 1.7 \times 10^{-11} \text{ mg/L} / 0.09 \text{ mg/L} = 1.9 \times 10^{-10}$$

The PEC/PNEC ratio is much less than 1 indicating that acetic anhydride has a low potential for risk to the environment. Acetic anhydride exhibits only moderate aquatic toxicity (18 to 3400 mg/L and essentially no bioaccumulation potential ($\log K_{ow} = -0.27$). Due to the very short half-life of acetic anhydride (4.4 min. @25 C) and its rapid breakdown to acetate/acetic acid (normally present in the environment and readily biodegradable), environmental concentrations are expected to be negligible. Therefore, acetic anhydride is considered to have low potential for risk to the environment.

4. HUMAN HEALTH

4.1 Human Exposure

4.1.1 Occupational Exposure

The OSHA PEL, MAK value and ACGIH TLV for acetic anhydride is currently 5 ppm (8-hr. TWA). The internal Hoechst Celanese and Celanese Canada Workplace Exposure Level (WEL) is 1 ppm (8-hr. TWA). In a typical acetic anhydride production facility there are fewer than 100 workers. Based on industrial hygiene monitoring data obtained at the Celanese Canada Edmonton plant and at the Hoechst Celanese U.S. plants, inhalation exposure is below published and internal workplace exposure guidelines. This applies both to acetic anhydride production and the major use (cellulose acetate production). Specific information from industrial hygiene monitoring records at the Celanese Canada Edmonton Plant (acetic anhydride and cellulose acetate production) is provided next.

Most often exposure has been monitored by measuring acetic acid concentration in the air. The method has a limit of detection of less than 0.1 ppm. Based on 110 air sample measurements per year over the last six years, in various job categories with exposure to acetic anhydride, workers were exposed 90 m% of the time to less than 0.1 to 0.4 ppm.

Hoechst Celanese and Celanese Canada developed and are currently phasing in newer methodology for specific acetic anhydride monitoring with a limit of detection of 0.07 ppm. Results at Hoechst Celanese U.S. facilities are comparable to those previously discussed for Celanese Canada. For example over the last year, using the new method 70 air sample measurements indicated acetic anhydride levels were in the range: < 0.07 ppm (limit of detection) to 0.35 ppm. Levels in most of the samples (55) were below the limit of detection.

Dermal and oral exposure would not be anticipated to be significant routes of exposure under standard occupational practice, because of protective procedures and equipment used.

4.1.2 Other Exposure Scenarios

Given acetic anhydride's use as a captive intermediate which is completely reacted in use coupled with its very short half-life, consumer or widespread environmental exposure scenarios are not likely. Neither Celanese Canada, the sole Canadian manufacturer, nor the Celanese Chemicals Division, one of the largest U.S. producers, sell acetic anhydride for consumer applications. European manufacturers of acetic anhydride (BP, Hoechst and Wacker-Chemie) were queried regarding sales to consumer-related applications, but indicated no sales for consumer applications. It is important to note that acetic anhydride sales are tightly controlled and end uses recorded by manufacturers under regulations to prevent chemical diversion to illegal drug synthesis. The International Data Summary for Acetic Anhydride in the SRI Chemical Economics Handbook (1)

did not mention any consumer applications or markets for acetic anhydride. Based on this recent input, there is no indication that its use is in general practice internationally in the consumer industry.

Note: Though there was reference to the possible use of acetic anhydride in shoe leather cleaner and in insecticide in Germany, though requested from the German representative (Dr. Hertel, Director, BGVV) by the CEFIC Acetyls Sector Technical Committee Chairman (Mr. Steve Williams), information was not provided for reasons of confidentiality.

4.2 Effects on Human Health

The initial data gaps identified during dossier preparation were: subchronic toxicity, reproductive toxicity and in vivo mutagenicity. Based on the physical/chemical properties of acetic anhydride, its metabolite (acetic acid) plus data from a subchronic inhalation/reproductive toxicity range-finding study, the testing program discussed next was presented at the February, 1995 SIAM Meeting in Williamsburg, Virginia and approved. A 90-day subchronic inhalation study in male and female rats with an additional 90-day recovery phase to assess reversibility provided the foundation for the program. Also included was a comprehensive, microscopic assessment of the reproductive organs plus standard cytogenetic analysis of the bone marrow. Results are described next in the pertinent sections.

a) Single exposure

Acetic anhydride is corrosive to the skin, eyes and mucous membranes. Acute toxicity values are listed below (6,7,18):

Oral LD ₅₀ :	1.8 g/kg (rats);
Dermal LD ₅₀ :	4.0 g/kg (rabbits);
Inhalation LC ₅₀ :	approximately 400 ppm (1680 mg/m ³ ; rats, 6 hrs., vapor)

No skin sensitization studies of acceptable quality are available. In a 1940 study using intracutaneous injection, a response claimed to be indicative of sensitization reaction was reported for guinea pigs receiving a 25% solution in olive oil. Given the corrosive nature of acetic anhydride, coupled with animal welfare considerations, further testing would be difficult to justify (19).

Acute overexposure in humans has been observed to cause severe eye, skin and respiratory tract irritation (6,7). The potential for occupational asthma may be raised when a chemical is an anhydride irritating to the respiratory system. The IUCLID document (6) lists two reports of human irritation from inhalation exposure to acetic anhydride; one in 1967 and one in 1992. In the event this or other information indicates sufficient need, comprehensive analyses with modern techniques would have been employed to further explore this area. However, this is beyond the scope of the SIDS/SIAR process.

b) Repeated exposure

One early study (20) using the inhalation route in animals was poorly reported and of uncertain validity. Insufficient detail was available from this report to draw reliable conclusions about the effects of repeated inhalation exposure to acetic anhydride. Therefore, new inhalation studies were conducted.

Acetic anhydride is highly irritating and readily hydrolyzes to acetic acid. Therefore, local toxicity at site of contact is observed, but not systemic toxicity. This is demonstrated by the following inhalation studies.

In a two-week inhalation study (18), respiratory tract irritation was reported in rats exposed for 6 hrs./day, 5 days per week (or less) to 25, 100 or 400 ppm acetic anhydride vapor. Mortality (40%) was observed in the 400 ppm group after the first 6-hr. exposure period and additional exposures were not conducted in this group.

In a 13-week inhalation study (21), rats were exposed for 6 hrs./day, 5 days/week to 1, 5 or 20 ppm acetic anhydride vapor. Each group contained 15 male and 15 female animals. The study was conducted under OECD and U.S. EPA TSCA GLPs. Clinical observations of eye and respiratory tract irritation and reduced body weights were observed primarily at 20 ppm. Microscopic examination of tissues revealed signs of irritation of minimal severity in the respiratory tract (nasal passages; larynx; trachea) in most animals at the 5 ppm level. At 20 ppm, all animals showed minimal to moderate respiratory tract irritation (nasal passages; larynx; trachea; lungs). The changes seen were predominantly localized inflammatory lesions with subsequent areas of epithelial hyperplasia and/or squamous metaplasia. Since the respiratory system is the target, further details from the microscopic examination of these tissues are given next for the 5 ppm (intermediate dosage) and 20 ppm (high dosage) groups.

Nasal lesions were primarily located in the anterior portion of the nose and comprised varying, predominantly minimal, degrees of hyperplasia of the respiratory epithelium, frequently with increased goblet cell prominence. Inflammation was associated with the respiratory epithelium and also the presence of granular eosinophilic inclusions within the respiratory epithelium, possibly representative of globule leucocytes. In the transitional epithelium lining anterior portions of the nasal turbinates, hyperplasia, squamous metaplasia and inflammation, occasionally with areas of erosion, were seen together with the presence of granular eosinophilic inclusions which may represent the presence of globule leucocytes. These latter inclusions were more evident in animals from the intermediate dosage group than in those from the high dosage group where transitional epithelial squamous metaplasia was more prominent. In general olfactory epithelium was unaffected by the acetic anhydride inhalation. Various amounts of exudative inflammatory cell accumulation, predominantly minimal in degree, were seen in the nasal passages of high dosage group animals and of a single male intermediate group animal.

In the larynx, inflammatory infiltration, squamous metaplasia of the ventral epithelium and hyperplasia of the epithelium covering the arytenoid processes, frequently with varying degrees of erosion or ulceration, were seen in the majority of animals from the high dosage group as well as occasional animals from the intermediate dosage group. In general these changes were of minimal to moderate severity. In the trachea, epithelial hyperplasia was seen at various sites, including at the carina, in the majority of animals from the high dosage group and in a proportion of intermediate dosage group animals. Also seen were epithelial squamous metaplasia at the carina, eosinophilic epithelial inclusions and inflammatory infiltration of the lamina propria. These changes were predominantly of a minimal degree of severity. Finally in the lungs, changes included the presence of occasional perivascular inflammatory cells, increased prominence of bronchus-associated lymphoid tissue (BALT), small foci of fibrosis in the walls of the alveolar ducts and increased prominence of alveolar macrophages. Changes were predominantly of minimal severity.

Systemic effects were not observed at 5 or 20 ppm. No effects (locally on the respiratory system or systemically) were detected at 1 ppm. In animals exposed to the same three dosage levels of acetic anhydride for 13 weeks and then allowed a 13-week period without exposure, significant recovery from irritation effects was reported. In summary, the effects were consistent with those typical of substances which act as local/site-of-contact irritants. The NOEL was concluded to be 1 ppm (4.2 mg/m³).

c) Reproductive toxicity

Acetic anhydride caused adverse reproductive effects in a screening study (18) with female rats exposed to the highly irritating, maternally toxic dose of 100 ppm vapor during gestation. Comparison was made with the unexposed females also sacrificed at Day 13 post coitum. Four out of five females were pregnant in each group. Two females which received 100 ppm showed total resorption of their litters, compared to none in the concurrent control group. The other two pregnant females in this group were supporting live litters of comparable size with those of the unexposed concurrent control group. At 100 ppm, severe respiratory tract irritation and bodyweight reduction were observed in the maternal animals. No developmental or reproductive effects were seen at 25 ppm even though substantial irritation of the respiratory tract was observed in maternal animals. The NOEL for developmental/reproductive effects was considered to be 25 ppm.

No significant adverse effects were observed on comprehensive, microscopic examination (21) of the reproductive organs of male and female rats exposed to acetic anhydride vapor for 13 weeks for 6 hrs./day, 5 days/week. The procedure was enhanced over what is routinely done histologically in subchronic studies. In particular, microscopic assessment of the testes was made with reference to the stages of the cycle of the seminiferous epithelium. The dose levels were 1 ppm, 5 ppm and 20 ppm.

As indicated previously, acetic anhydride is rapidly hydrolyzed to acetic acid. Acetic acid did not cause developmental toxicity in oral studies with rabbits, rats or mice at dose levels up to 1.6g 5% acetic acid/kg/day administered during days 6-18 (rabbit) or 6-15 (rats, mice) of gestation (26).

d) Genetic toxicity

In vitro tests: no evidence of mutagenicity in the Ames test (bacteria), with and without activation (22,23,24). Results in the mouse lymphoma gene mutation assay (25) were equivocal without metabolic activation and not mutagenic with metabolic activation. The equivocal result may be due to acidification of the culture medium. This equivocal response has been reported in mouse lymphoma assays for organic acids. *In vivo* test: not mutagenic (21); rats exposed via inhalation for 13 weeks at doses up to 20 ppm were without effects on bone marrow (micronucleus assay).

e) Other

Carcinogenicity

No data are currently available. Systemic effects are not expected given the ready hydrolysis of acetic anhydride to acetate/acetic acid. This is further supported by the lack of a mutagenic response in the bone marrow of rats exposed to acetic anhydride vapor for 13 weeks.

4.3 Initial Assessment for Human Health

4.3.1 Occupational (Workers)

The lowest NOEL, 1 ppm (4.2 mg/m³), is based on a recent subchronic study via the most relevant exposure route, inhalation. At the LOEL, 5 ppm (21mg/m³), minimal and reversible respiratory tract irritation was observed, but no systemic toxicity. In vivo genotoxicity and developmental toxicity studies did not reveal specific effects at higher concentrations (20-25 ppm).

Workplace exposure monitoring information is available from plants producing acetic anhydride and from plants using it. Exposure levels are low because procedures and equipment plus worker training programs are in place which provide protection. Therefore, acetic anhydride is considered of low potential for risk to man.

4.3.2 Other

Given its use pattern (captive intermediate, completely reacted in use) and rapid hydrolysis (half-life 4.4 min. @ 25 C in non-human study) to normal body metabolite (acetate), consumer or widespread environmental exposure are not significant scenarios for human exposure to acetic anhydride.

5. CONCLUSIONS AND RECOMMENDATIONS

5.1 Conclusions and 5.2 Recommendations

a) Environment

Acetic Anhydride is used solely as an intermediate for chemical synthesis where it is completely reacted. In the hydrosphere, acetic anhydride is rapidly hydrolyzed (half-life 4.4 min.) to acetic acid which is readily biodegradable. In the atmosphere, it is converted to acetic acid which is subject to photooxidative degradation (half-life 22 days). Toxicity to aquatic organisms is moderate (18 to 3400 mg/l), but it persists only for a short time due to its rapid hydrolysis to acetate/acetic acid. It has virtually no potential for bioaccumulation ($\log K_{ow} = -0.27$). The PEC/PNEC ratio was much less than one (1.9×10^{-10}). Therefore, acetic anhydride has a low potential for exposure and is considered to be currently of low priority for further environmental work in the SIDS context.

b) Human Health

The critical effect for acetic anhydride is irritancy at the site of contact. Because of its well-known corrosive and irritating effects on the eyes, skin and respiratory tract and low odor threshold, procedures, equipment (e.g., goggles, gloves, respirators), training and engineering controls have already been in place for many years to prevent exposure. Industrial hygiene monitoring data indicates that levels of acetic anhydride are below 1 ppm 8-hr. time-weighted-average (4.2 mg/m³) in facilities where acetic anhydride is produced and where the major use of acetic anhydride takes place. Acetic anhydride is used exclusively as a chemical intermediate and there is no indication that its use is in general practice in the consumer industry. It is suggested that occupational exposure limits be revisited based on the additional testing reported in this SIAR. Acetic anhydride is considered to be currently of low priority for further health-related work in the SIDS context.

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Additional information sources (not included in SIDS).

- a. CEH-Stanford Research Institute International Data Summary 603.5000 A.
- b. IUCLID (1996): International Uniform Chemical Information Database.
- c. Acetic Anhydride: 2 Weeks Repeat Dose Inhalation Toxicity Study in Male and Time-Mated Female Rats. Huntingdon Report HST 400/942606 (October 13, 1994).
- d. Acetic Anhydride: 13-week Inhalation Toxicity Study in Rats. Huntingdon Report HST 411/961219 (August 27, 1996).
- e. BUA-Stoffbericht No. 70 (1991).

SIDS PROFILE

1.1	CAS NO.	108-24-7
1.2	Chemical Name	Acetic Anhydride
1.5	Structural Formula	(CH ₃ CO) ₂ O
	Other Chemical Identity Information	Synonyms: Acetic Oxide Acetyl Oxide Ethanoic Anhydride
3.0	Sources and Levels of Exposure	<p>The potential for exposure exists during manufacture, processing and distribution.</p> <p>Environment: In the hydrosphere, acetic anhydride is rapidly hydrolyzed (half-life 4.4 min.) to acetic acid which is readily biodegradable. In the atmosphere, it is converted to acetic acid which is subject to photooxidative degradation (half-life 22 days). Toxicity to aquatic organisms is moderate (18 to 3400 mg/l), but it persists only for a short time due to its rapid hydrolysis to acetate/acetic acid. It has virtually no potential for bioaccumulation (log K_{ow} = -0.27).</p> <p>Human: Because of its well-known corrosive and irritating effects on the eyes, skin and respiratory tract and low odor threshold; procedures, equipment (e.g., goggles, gloves, respirators), training and engineering controls (closed systems) have already been in place for many years to prevent occupational exposure. Levels of acetic anhydride in facilities where it is produced and used in the manufacture of cellulose acetate esters are well below 1 ppm (4.2 mg/m³). Acetic anhydride is used exclusively as a chemical intermediate and not in consumer applications.</p>
3.1	Production Range	<p>Production capacities in thousand metric tons available for North America and Western Europe are as follows:</p> <p>Canada - 70; Mexico - 87; United States - 1223; Western Europe - 539. In Canada, about 90% is consumed internally at the site of production.</p>
3.3	Categories and Types of Use	Used as an intermediate in the manufacture of pharmaceuticals, agricultural chemicals and cellulose acetate.
	Issues for Discussion (Identify, if any)	See Attachment 1.

Attachment 1

Health:

Because of the irritating and unstable nature of acetic anhydride, a conventional testing approach is not recommended. Since acetic anhydride readily hydrolyzes to acetic acid in water (half-life about 3 minutes), systemic toxicity is unlikely and emphasis will be placed on toxicity at the site of contact for the most relevant route of potential human exposure. Because a repeated inhalation exposure study of acceptable quality is not available, a 90-day vapor inhalation study in the rat via OECD guidelines is recommended. Emphasis will be placed on effects in the upper respiratory tract and subsequent reversibility.

Appropriate studies on reproductive and developmental toxicity are not available for acetic anhydride. A teratology study conducted with an acetic acid solution was negative. This result combined with a careful evaluation of the gonads in the proposed 90-day inhalation study is considered to provide sufficient information.

Results from gene mutation studies in vitro with acetic anhydride have been negative except for one equivocal response. Studies assessing chromosomal aberrations are not available. An in vitro chromosomal aberration study is not recommended because the published literature indicates that acidic materials lower culture medium pH resulting in artifacts. Cytogenetic evaluation of bone marrow from animals in the 90-day inhalation study will be conducted.

Because of the corrosive nature of acetic anhydride and the minimal potential for prolonged exposure, the need for testing should be evaluated in light of animal welfare concerns before proceeding.

Environmental:

Acceptable acute studies are available for fish, invertebrates and algae. Since acetic anhydride hydrolyzes quickly to a well-studied material of low toxicity (acetic acid/acetate) additional studies to assess ecotoxicity, environmental fate and biodegradation are not recommended.

Study CAS No: 108-24-7 (Status of database prior to initiation of testing in 1993)		Info Avail	GLP	OECD Study	Other Study	Estim. Methods	Accept- able	SIDS Testing Req'd
		Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N
PHYSICAL-CHEMICAL								
2.1	Melting Point	Y					Y	N
2.2	Boiling Point	Y					Y	N
2.3	Vapour Pressure	Y					Y	N
2.4	Partition Coefficient	N						N
2.5	Water Solubility	Y					Y	N
OTHER STUDIES RECEIVED								
ENVIRONMENTAL FATE/ BIODEGRADATION								
4.1.1	Aerobic biodegradability	Y					Y	N
4.1.3.1	Hydrolysis	Y					Y	N
4.1.3.2	Photodegradability	N						N
4.3	Env. Fate/ Distribution	N						N
4.4	Env. Concentration	N						N
OTHER STUDIES RECEIVED		N						
ECOTOXICOLOGY								
5.1	Acute Toxicity Fish	Y					Y	N
5.2	Daphnia	Y					Y	N
5.3	Algae	Y					Y	N
5.6.1	Terrest. Organisms	N						N
5.6.2	Terrest. Plants	N						N
5.6.3	Avians	N						N
5.6.4	Avian Reproduction	N						N
OTHER STUDIES RECEIVED		N						
TOXICOLOGY								
6.1	Acute Oral	Y					Y	N
	Acute Dermal	Y					Y	N
	Acute Inhalation	Y					Y	N
6.2	Skin Irritation	Y					Y	N
	Eye Irritation	Y					Y	N
6.3	Skin Sensitization	Y					Y	N
6.4	Repeated Dose	Y					N	Y
6.5	Genetic Toxicity							
	Gene Mutation	Y	Y				Y	N
	Chromosomal Aberrations	N					N	Y
6.7	Reproductive and Developmental Toxicity	Y					Y	N
OTHER STUDIES RECEIVED		Y						

**Summary of Responses to the OECD Request for
Available Data on HPV Chemicals**

o. General Information

Name of Sponsor Country CANADA
Contact point (name, address, telephone and telefax)
Mr. Mark Lewis
Commercial Chemicals Evaluation Branch
Environment Canada
351 St. Joseph Blvd.
Ottawa, Ontario K1A 0H3
CANADA
Telephone: 1-819-953-7199
Telefax: 1-819-953-4936

Name of Lead Organization CELANESE

1. Chemical Identity

***1.1 CAS number 108-24-7**

***1.2 Name (give the name supplied by OECD)**

Acetic Anhydride

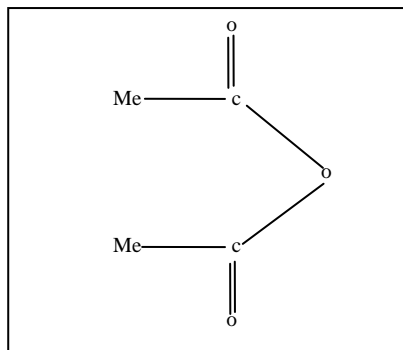
1.3 Common Synonyms

Acetic oxide, acetyl oxide, ethanoic anhydride, ethanoic anhydride, acetyl ether

1.4 Empirical Formula

$C_4H_6O_3$ (m.w. 102.9)

***1.5 Structural Formula**



ACETIC ANHYDRIDE

1.6 Purity of Industrial Product**1.6.1 Degree of purity (percentage by weight/volume)**

Acetic Anhydride 95.0% - 99.0% (HCC-MSDS)

1.6.2 Identity of major impurities

Acetic Acid (CAS No. 94-19-7) 4% maximum (HCC-MSDS)

1.6.3 Essential additives (stabilizing agents, inhibitors, other additives), if applicable

Not applicable.

2. Physical-Chemical Data***2.1 Melting or Decomposition Point**

-73.1 °Centigrade

Method (e.g., OECD, others):

GLP: YES []
NO []

Comments:

Reference: CRC Handbook of Chemistry and Physics, 65th ed., Robert C. Weast, ed. 1984, CRC Press Inc., Boca Raton, Florida. p. C-70

***2.2 Boiling Point**

(including temperature of decomposition, if relevant).

138-140.5 °C (at 760 mm Hg) 1013 hPa

Method (e.g., OECD, others):

GLP: YES []
NO []

Comments:

Reference: IUCLID (1996)

***2.3 Vapour Pressure**

7.2 hPa at 25.4 °C (calculated)

Method (e.g., OECD, others):

GLP: YES []
NO []

Comments: Calculations based on 1 Atmosphere = 101,325 N/m³ 1 kPa = 1000 N/m³

Reference: IUCLID (1996)

***2.4 Partition co-efficient n-Octanol/water**

log Pow = -0.27

Method: calculated [X]

measured []
 GLP: YES []
 NO []

Analytical Method:

Comments (e.g., is the compound surface active or dissociative?): Acetic anhydride hydrolyzes quickly to acetic acid which is very water soluble (see section 4.1.3)

Reference: IUCLID (1996)

*2.5 Water Solubility

120 g/l at °C (with hydrolysis)

Method (e.g., OECD, others):

GLP: YES []
 NO []

Analytical Method:

Comments (e.g., the detection limit for insoluble substances):

Reference: DATENBLATT' ALTSTOFFE' (Data sheet on 'Old Materials') May 2, 1988, Hoechst AG.

2.6 Flash point (liquids)

49.4 °C closed cup [X] 65.5 °C open cup [X]

Method (e.g., OECD, others including references to the standard test used):

Tag open cup = ASTM D1310

Tag closed cup = ASTM D56

GLP: YES []
 NO []

Comments: Flash point open cup reported as 150 °F conversion $C^{\circ} = 5/9 (F^{\circ} - 32)$

Reference: Closed cup: The Condensed Chemical Dictionary, 10th ed. Gessner G. Hawley ed. 1981, Van Nostrand Reinhold Company, New York, p. 6-7

Open cup: Hygienic Guide Series Acetic Anhydride. American Industrial Hygiene Association Journal 32:66-67 (1971)

2.7 Flammability (solid/gases)

Method (e.g., OECD, others):

GLP: YES []
 NO []

Test results:

Comments:

References:

2.8 pH in water

pH at mg/l (water)

pKa

Method (e.g., OECD, others):

GLP: YES []
 NO []

Comments: Acetic anhydride hydrolyzes quickly to acetic acid which has a pKa of 4.76 (see section 4.1.3)

Reference:

2.9 Other data e.g., relative density, surface tension (of aqueous solution), fat solubility, explosivity, oxidizing properties and particle size distribution.

Autoignition temperature: 330°C

Reference: IUCLID (1996).

Lower Explosive Limit: 2.0% (by volume in air) at 20°C

Reference: IUCLID (1996).

Upper Explosive Limit: 10.2% (by volume in air) at 20°C

Reference: IUCLID (1996).

Specific gravity: 1.082-1.083 (20/20 °C)

Reference: The Condensed Chemical Dictionary, 10th ed. Gessner G. Hawley editor, 1981, Van Nostrand Reinhold Company, New York, p. 6-7 and IUCLID (1996).

3. Source of Exposure

3.1 Production levels expressed as tonnes per annum

Information on production levels should be provided in ranges (e.g., 100-1000 tonnes, etc.) per responder or country and the date for which those ranges apply should be given.

Production capacities available for North America and Western Europe are given in Table I.

**Table I. 1995 Acetic Anhydride Production Capacities
(1.Stanford Research Institute)**

Region	Thousand Metric Tons
Canada	70
Mexico	87
United States	1223
Western Europe	539

3.2 Processes

Describe sources of potential human or environmental exposure including workplace concentrations and emission data (in % release), if available, for both manufacturing and user areas.

Production releases

Celanese Canada, Edmonton (this plant produces both acetic anhydride and cellulose acetate)

Emissions Total (Annual Emission Estimate)

Storage 7 tons

Fugitive 4 tons

Amount released per day 30 kg/day (Assumes plant operates 365 days/year)

These releases are all to the atmosphere. Any release to water goes to deepwell injection. Due to hydrolysis this would only be present and detectable as acetic acid. Any releases in this manner are expected to be minimal.

Release from use**Release from cellulose acetate production**

The major onstream use is in Cellulose Acetate Production, where Acetic Anhydride is an intermediate.

The release numbers given in above are for the Celanese Canada Edmonton facility as a whole, and so include both production and use. Although no definitive numbers are available, given the nature of the Cellulose Acetate Process any emissions are expected to be small (<10% of total emissions) and due to hydrolysis, in the form of acetic acid.

Release from consumer use

Acetic anhydride is used as a reactive intermediate. When reacted, for example to make cellulose acetate, it is not regenerated in use. Because it is reactive and readily hydrolyzed, its presence in end use products is not possible.

Widespread release

General widespread release is not an applicable scenario for acetic anhydride. It is used only as a captive, reactive intermediate.

Acetic anhydride is commercially manufactured by several routes. The most widely used process is the addition of ketene to glacial acid. In the ketene process, acetic acid is dehydrated to ketene and then further reacted with additional acetic acid to produce the anhydride. This route is used extensively to recycle acetic acid generated when acetic anhydride is used to acetylate cellulose to produce cellulose acetate. Methyl acetate carbonylation is a second route. Some acetic acid is produced as a co-product in the methyl acetate carbonylation process. About 90% of acetic anhydride production is consumed internally as a reactant at the site of production. The potential for exposure exists during manufacture, processing and distribution. Because of the irritating nature of this material, facilities, equipment and handling procedures are designed to minimize exposure. Acetic anhydride hydrolyzes quickly and, therefore, presence in the environment is not projected.

Reference: Chemical Economics Handbook, Menlo Park, CA, SRI International, Section 603.5000A (1996)

Occupational Exposure

The OSHA PEL, MAK value and ACGIH TLV for acetic anhydride is currently 5 ppm (8-hr. TWA). The internal Hoechst Celanese and Celanese Canada Workplace Exposure Level (WEL) is 1 ppm (8-hr. TWA). In a typical acetic anhydride production facility there are fewer than 100 workers. Based on industrial hygiene monitoring data obtained at the Celanese Canada Edmonton plant and at the Hoechst Celanese U.S. plants, inhalation exposure is below published and internal workplace exposure guidelines. This applies both to acetic anhydride production and the major use (cellulose acetate production). Specific information from industrial hygiene monitoring records at the Celanese Canada Edmonton Plant (acetic anhydride and cellulose acetate production) is provided next.

Most often exposure has been monitored by measuring acetic acid concentration in the air. The method has a limit of detection of less than 0.1 ppm. Based on 110 air sample measurements per year over the last six years, the 90% tolerance levels for the various operations with exposure to acetic anhydride are: 0.1 to 0.4 ppm acetic acid. These data apply to workers involved in both acetic acid production and cellulose acetate production. It is important to understand the industrial hygiene use of the term "tolerance level". Tolerance levels are not averages. For example, a 90% tolerance level of 0.4 ppm acetic acid means that in that job category, workers are exposed 90% of the time to 0.4 ppm acetic acid or less. There is also a method specific for acetic anhydride, but it is less sensitive, and has not been used routinely, i.e., the limit of detection is less than 0.3 ppm to 0.5 ppm. Using this method, representative 1997 data for ten air sample measurements collected within the last six months indicate eight values at or below the limit of detection, one value at 0.6 ppm and one value at 1 ppm.

Hoechst Celanese and Celanese Canada developed and are currently phasing in newer methodology for specific acetic anhydride monitoring with a limit of detection of 0.07 ppm. Results at Hoechst Celanese U.S. facilities are comparable to those previously discussed for Celanese Canada. For example over the last year, using the new method 70 air sample measurements indicated acetic anhydride levels were in the range: < 0.07 ppm (limit of detection) to 0.35 ppm. Most of the samples (55) were below the limit of detection.

Dermal and oral exposure would not be anticipated to be significant routes of exposure under standard occupational practice, because of protective procedures and equipment used.

Other Exposure Scenarios

Given acetic anhydride's use as a captive intermediate which is completely reacted in use coupled with its very short half-life, consumer or widespread environmental exposure scenarios are not applicable.

3.3 Information concerning Uses (including categories and types of uses expressed in percentage terms)

Examples of use categories are dyestuffs, intermediates, solvents, adhesives, building material agents, detergents, cleaning agents, fertilizers, plastic agents, surface treatment agents, etc.

Acetic anhydride used as a reagent in manufacturing acetate esters, acetylation of pharmaceuticals, end-capping polyacetal homopolymers, and other reactions is consumed

in the reaction step. Reactions of acetic anhydride with hydroxyl groups yield the corresponding acetate ester with coproduction of acetic acid. Acetylation of amines produce acetamides such as TAED (tetraacetythylenediamine), which is used as a perborate bleach activator. Acetic anhydride is used to acetylate salicylic acid to aspirin and p-aminophenol to acetaminophen.

Most of the acetic anhydride production is consumed in manufacturing cellulose acetate esters. Cellulose acetate esters include cellulose diacetate, cellulose triacetate and mixed esters (propionates, butyrates). In the manufacture of cellulose acetate, one acetyl group from each acetic anhydride molecule reacts with the cellulose and the other acetyl group is converted to acetic acid which can be recycled back to make more acetic anhydride or be used to produce other acetic acid derivatives. Shredded pure alpha cellulose is typically soaked in aqueous acetic acid before the treated pulp is acetylated with a 60-40 mixture of acetic acid and acetic anhydride using a dilute sulfuric acid catalyst. Cellulose acetate fibers are recovered as tow or as filament yarn. Filters are made from a blend of tow and plasticizer. Cellulose acetate filament yarns are used in apparel and home furnishings. Cellulose triacetate is used in photographic film and pressure sensitive tapes. U.S. consumption of acetic anhydride in 1993, for example, was distributed in major end uses as follows in Table 2. This is generally representative of consumption in North America

**Table 2. U.S. Consumption of Acetic Anhydride (Percentages)
(1.Stanford Research Institute)**

Cellulose Acetate Esters						
Filter Tow	Filament Yarn	Flake Export	Miscellaneous	Aspirin	Acetaminophen	Other
42%	18%	13%	12%	1%	2%	12%

Acetic anhydride reacts with water forming acetic acid and, therefore, can be used as a dehydration reagent.

Reference: Chemical Economics Handbook, Menlo Park, CA, SRI International, Section 603.5000A (1996)

Types of uses are divided into three: industrial use (open system and closed system), public use and export. Essentially all for industrial use (closed system).

3.4 Options for disposal

Mode of disposal (e.g., incineration, release to sewage system) for each category and type of use, if appropriate; recycling possibility.

Preferred method is incineration, deepwell injection or biological treatment in a government approved facility.

3.5 Other remarks

Reference:

4. **Environmental Fate and Pathways**

Reporting of studies should give the test method, test conditions (lab versus field studies), test results (e.g., % degradation in specified time period) and reference. Information on breakdown products (transient and stable) should be provided when available.

4.1 **Degradability (biotic and abiotic)**

4.1.1 **Biodegradability**

Test substance: Acetic Anhydride
 Test type: aerobic , anaerobic
 Test medium: water/activated sludge
 In the case of poorly soluble chemicals, treatment given (nature, concentration, etc.):
 Test method (e.g., OECD, others): Directive 84/449/EEC, C.7 "Biotic degradation - modified MITI test"
 GLP YES
 NO
 Test results: 578 mg/l related to COD (Chemical Oxygen Demand).
 After 22-24 hrs.: 99% elimination.
 Comments: pH 5.5-6.9
 Reference: Placak, Ruchhoft (1947): Public Health Reports, XVII. The utilization of organic substrates by activated sludge, Vol. 62, 697-716

4.1.1 **Biodegradability**

Test substance: Acetic Anhydride
 Test type: aerobic , anaerobic
 Test medium: water/activated sludge, industrial, non-adapted
 In the case of poorly soluble chemicals, treatment given (nature, concentration, etc.):
 Test method (e.g., OECD, others): OECD Guideline 302 B "Inherent Biodegradability: Modified Zahn-Wellens Test" 1975
 GLP YES
 NO
 Test results: 95% biodegradation (acetic acid) after 5 days.
 Comments:
 Reference: Hoechst AG study reported in IUCLID (1996).

4.1.2 **Sewage Treatment**

Information on treatability of the substance: Expected to be readily treatable.
 Reference: BUA - Stoffbericht No. 70 (1991)

4.1.3 **Stability in air (e.g., photodegradability) and in water (e.g., hydrolysis)**

Test substance: Acetic Anhydride
 Test method or estimation method (e.g. OECD, others): Not specified.
 If available, information on degradation products, dissociation constants and half-life should be given.
 GLP YES
 NO

Test results: Hydrolyzes in water to form acetic acid.
 Percentage of degradation after certain period: 50% hydrolysis in water after 4.4 minutes at 25°C; 50% hydrolysis in water after 8.1 minutes at 15°C.
 Reference: IUCLID (1996)

4.1.3 Stability in air (e.g., photodegradability) and in water (e.g., hydrolysis)

Test substance: Acetic Acid
 Test method or estimation method (e.g. OECD, others): Calculated (Atkinson).
 If available, information on degradation products, dissociation constants and half-life should be given.
 GLP YES
 NO
 Test results: Photodegradation in atmosphere with hydroxyl radicals.
 Percentage of degradation after certain period: 50% after 21.7 days.
 Reference: IUCLID (1996)

4.1.4 Identification of main mode of degradability in actual use

Comment: Acetic anhydride hydrolyzes to acetic acid which is biodegraded to carbon dioxide.
 Reference:

4.2 Bioaccumulation

Test substance:
 Test method (e.g., OECD, others):
 • Type of test: static , semi-static , flow-through
 • Other (e.g., field test)
 GLP YES
 NO
 Test results:
 Bioaccumulation factor:
 Calculated results:
 Method of calculation:
 Comments: Calculated $\log P_{ow} = -0.27$ indicates virtually no potential for bioaccumulation.
 Reference: IUCLID (1996)

4.3 Transport and distribution between environmental compartments including estimated environmental concentrations and distribution pathways

This information may be provided by industry or by public authorities. It should be indicated whether the calculation is on a global basis or is site-specific, and whether it is based on laboratory measurements or filed observations.

Type of transport and distribution processes between compartments (e.g., air, water, soil):

Estimation of environmental concentrations:

- results of the estimation
- summary of the method (or model) used

Given the volume of acetic anhydride released to the atmosphere annually the steady state concentrations using Mackay fugacity model ChemCan IV for the region of northern Alberta can be estimated. Releases to this 378 000 km² area result in 2.4×10^{-15} mg/m³ in air, 2.33×10^{-9} µg/g in soil, 1.8×10^{-11} g/m³ in water, and 1.9×10^{-14} g/m³ in sediment assuming a residence time in air of 2.42 days and 75.1 days in water for this region. Overall reaction persistence is estimated at 0.107 hrs. The concentration for water can be used as a PEC in the calculation (i.e. PEC = 1.7×10^{-11} mg/L).

Reference: Environment Canada (1997)

4.4 Monitoring data (environment)

Test substance: Acetic Anhydride

The Celanese workplace exposure level is 1 ppm (8 hr. TWA). Levels off-site would be projected to be much lower.

Indicate whether the data are measurements of background concentrations or measurements at contaminated sites:

- air	(µg/m ³) in	as of 19..
- surface water	(µg/l) in	as of 19..
- ground water	(µg/l) in	as of 19..
- soil sediment	(µg/g) in	as of 19..
- biota*	(µg/g) in	as of 19..
*(specify species)		
- food	(µg/g)in	as of 19..

Reference:

5. Ecotoxicological Data

5.1 Toxicity to fish

5.1.1 Results of acute tests

Test substance: Acetanhydrit (Acetic anhydride)

Test species: Golden Orfe (*Leuciscus idus*)

Test method (e.g., OECD, others): Methodology reported briefly in reference. Parallel studies performed at two labs.

- Type of test: static [], semi-static [], flow-through []
- Other (e.g., field test) []

GLP YES []
NO []

Test results:

48 hr. LC₀ = 216 mg/l, 252 mg/l

48 hr. LC₅₀ = 265 mg/l, 279 mg/l
 48 hr. LC₁₀₀ = 324 mg/l, 324 mg/l
 LC₅₀ or EC₅₀ - values after 24, 48, 72 and 96 hours and method used to calculate these values
 Comments: Study published in German, results in tabular form.
 Reference: Juhnke, I, and D. Ludemann. Ergebnisse der Untersuchung von 200 chemischen Verbindungen auf Akute Fischtoxizität mit dem Goldorfenfest. Z. Wasser Abwasser Forsch. 11 (5)161, 1978.

5.1.2 Results of long-term tests e.g., prolonged toxicity, early life-stage

Test substance:
 Test species:
 Test method: (e.g., OECD, others):
 • Type of test: static [], semi-static [], flow-through []
 • Other (e.g., field test) []
 GLP YES []
 NO []
 Test results:
 Maximum concentration at which no effect was observed within the period of the test.
 Minimum concentration at which effect was observed within the period of the test.
 Comments:
 Reference:

5.2 Toxicity to daphnids

5.2.1 Results of acute tests

Test substance: Acetanhydrid (acetic anhydride)
 Test species: *Daphnia magna* Straus IRCHA
 Test method: (e.g., OECD, others): (Detailed methodology of the “improved” standardized procedure are in reference).
 GLP YES []
 NO []
 Test results:
 EC₅₀ - values after 24 and 48 hours, and method used to calculate these values (values reported here are without neutralization)
 24 hr. LC₅₀ = 55 mg/l (95% confidence interval 53-58 mg/l)
 24 hr. LC₀ = 47 mg/l
 24 hr. LC₁₀₀ = 68 mg/l
 Comments: Document published in German with English abstract.
 Reference: Bringmann, G., and R. Kuhn. Results of Toxic Action of Water Pollutants on *Daphnia magna* Straus Tested by an Improved Standardized Procedure. Z. Wasser Abwasser Forsch. 15, 1-7, 1982.

5.2.2 Results of long-term tests e.g., reproduction

Test substance:
 Test species:
 Test method: (e.g., OECD, others):
 • Type of test: static [], semi-static [], flow-through []

- Other (e.g., field test) []
- GLP YES []
 NO []

Test results:

Maximum concentration at which no effect was observed within the period of the test.

Minimum concentration at which effect was observed within the period of the test.

Comments:

Reference:

*5.3 Toxicity to algae

Test substance: Acetic anhydride

Test species: *Scenedesmus quadricauda*

Test method (e.g., OECD, others): Cell-multiplication inhibition test (8 days), detailed methodology in reference.

GLP YES []
 NO []

Test results: Toxicity threshold = 3,400 mg/l

Reference: Bringmann, G. and R. Kuhn. Comparison of the Toxicity Thresholds of Water Pollutants to Bacteria, Algae, and Protozoa in Cell Multiplication Inhibition Test, Water Research 14(3) p. 231, 1980.

*5.3 Toxicity to algae

Test substance: Acetic anhydride

Test species: *Chlorella pyrenoidosa*

Test method (e.g., OECD, others): Chlorophyll reduction (5 days)

GLP YES []
 NO []

Test results: 16.6% to 96.6% reduction was noted compared to the controls over the concentration range 50 mg/l to 400 mg/l.

Comments:

Reference: Gloyna, Thirumurthi (1967) : Water Sewage Works 114(3), 83-88.

5.4 Toxicity to other aquatic organisms

Test substance: Acetic anhydride

Test species: *Entosiphon sulcatum*

Test method (e.g., OECD, others): Cell multiplication inhibition test (72 hrs).

- Type of test: static [], semi-static [], flow-through []
- Other (e.g., field observation) []

GLP YES []
 NO []

Test results: EC₅ Toxicity threshold = 30 mg/l

Comments:

Reference: Bringmann, G. and R. Kuhn. Comparison of the Toxicity Thresholds of Water Pollutants to Bacteria, Algae, and Protozoa in Cell Multiplication Inhibition Test, Water Research 14(3) p. 231, 1980.

5.4 Toxicity to other aquatic organisms

Test substance: Acetic anhydride
 Test species: *Chilomanas paramaecium*
 Test method (e.g., OECD, others): Cell multiplication inhibition test (48 hrs.) (detailed methodology in reference)
 GLP YES []
 NO []
 Test results: Toxicity threshold = 395 mg/l
 Comments:
 Reference: Bringmann et al. (1980) : Z. Wasser Abwasser Forsch. 13(5), 170-173.

5.4 Toxicity to other aquatic organisms

Test substance: Acetic anhydride
 Test species: *Uronema parduzci*
 Test method (e.g., OECD, others): Cell multiplication inhibition test (detailed methodology in reference)
 GLP YES []
 NO []
 Test results: Toxicity threshold = 735 mg/l
 Comments:
 Reference: Bringmann, Kuehn(1981) : Gass-Wasserfach, Wasser-Abwasser 122(7), 308-313

5.5 Toxicity to bacteria

Test substance: Acetic anhydride
 Test species: *Pseudomonas putida*
 Single species tests such as "Microtox Photobacterium luminescence test" and tests on overall processes such as nitrification or soil respiration are included in this item.
 Test method (e.g., OECD, others): Cell multiplication inhibition test (16 hrs.) (detailed methodology in reference)
 • Type of test: static [], semi-static [], flow-through []
 • Other (e.g., field observation) []
 GLP YES []
 NO []
 Test results: EC₃ Toxicity Threshold = 1,150 mg/l
 Comments:
 Reference: Bringmann, G. and R. Kuhn. Comparison of the Toxicity Thresholds of Water Pollutants to Bacteria, Algae, and Protozoa in Cell Multiplication Inhibition Test, Water Research 14(3) p. 231, 1980.

5.5 Toxicity to bacteria

Test substance: Acetic anhydride
 Test species: *Microcystis aeruginosa (cyanobacteria)*
 Test method (e.g., OECD, others): Cell multiplication inhibition test (8 days) (detailed methodology in reference)
 • Type of test: static [], semi-static [], flow-through []
 • Other (e.g., field observation) []

GLP YES []
 NO []
 Test results: EC₃ Toxicity Threshold = 18 mg/l
 Comments:
 Reference: Bringmann (1975) : Gesund.-Ing. 96(9), 238-241.

5.5 Toxicity to bacteria

Test substance: Acetic anhydride
 Test species: bacteria (source: domestic wastewater treatment plant)
 Test method (e.g., OECD, others): 24-hour fermentation-tube test.
 The endpoint was inhibition of respiration and the parameter measured was oxygen consumption.
 GLP YES []
 NO []
 Test results: EC₃ Toxicity Threshold ≥ 2,500 mg/l
 Comments:
 Reference: Hoechst AG Study cited in IUCLID (1996).

*5.6 Toxicity to terrestrial organisms

Comments: Because of the unstable nature of acetic anhydride, a conventional testing approach is not recommended. Acetic anhydride hydrolyzes quickly to a well-studied material of low toxicity (acetic acid/acetate).

5.6.1 Toxicity to soil dwelling organisms

Test substance:
 Test species:
 Test method: (e.g., OECD, others):
 GLP YES []
 NO []
 Test results: LC₅₀ (at 7 and 14 days for earthworms)
 Comments:
 Reference:

5.6.2 Toxicity to plants

Test substance:
 Test species:
 Test method: (e.g., OECD, others):
 GLP YES []
 NO []
 Test results: EC₅₀ for 7 and 14 days or LC₅₀
 Maximum concentration at which no effect was observed within the period of the test.
 Minimum concentration at which effect was observed within the period of the test.
 Comments:
 Reference:

5.6.3 Toxicity to birds

Test substance:

Test species:

Test method: (e.g., OECD, others):

GLP YES []

NO []

Test results: LD₅₀ (acute), LC₅₀ (subacute)

Maximum concentration at which no effect was observed within the period of the test (semi-chronic or chronic).

Minimum concentration at which effect was observed within the period of the test (semi-chronic or chronic).

Comments:

Reference:

5.7 Biological Effects Monitoring (including biomagnification)

Studies on variation of predominant species in certain ecosystems and monitoring of biological effects (e.g., thinning of eggshell) etc. are included.

Test substance:

Organism or ecosystem studied:

Effects monitored:

Information on monitoring conditions (water characteristics: suspended matter, pH, temperature, hardness) (Soil/sediment characteristics: % organic matter, clay content).

Test results:

Chemical analysis:

Comments:

Reference:

5.8 Biotransformation and kinetics in environmental species

Under this item, studies on absorption, distribution, metabolism and excretion etc. should be given.

6. Toxicological Data (oral, dermal and inhalation, as appropriate)

Where observations on humans are available, e.g., irritation, these should be entered in the appropriate "Comments" section.

*6.1 Acute toxicity

6.1.1 Acute oral toxicity

Test substance: Acetic anhydride

Test species/strain: rat/albino Wistar rats (typical strain used by Smyth)

Test method: (e.g., OECD, limit test, fixed dose test): Described in: Smyth, H.F. and Carpenter, C.P. Journal of Industrial Hygiene and Toxicology, 26(8), 269-273, 1944.

GLP YES []

NO [X]

Test results: LD₅₀ = 1.78 g (1.48-2.43)

LD₅₀ or other measure of acute toxicity (e.g. in case of fixed-dose test)

Discriminating dose (for fixed dose only):

Comments:

Reference: Smyth, H.F., Jr., Carpenter, C.P. and Weil, Range-finding Toxicity Data: List IV. AMA Arch Ind Hyg Occup Med, 4, p. 119, 1951.

6.1.2 Acute inhalation toxicity

Test substance: Acetic anhydride

Test species/strain: rat

Test method: (e.g., OECD, EC, limit test):

GLP YES []

NO []

Test results: LC₅₀ = 1000 ppm/4h = 4240 mg/m³/4 h

Comments:

Reference: DATENBLATT 'ALTSTOFFE' (Data sheet on 'Old Materials') May 2, 1988, Hoechst AG

6.1.2 Acute inhalation toxicity

Test substance: Acetic anhydride

Test species/strain: rat / Wistar typically used

Test method: (e.g., OECD, EC, limit test):

GLP YES []

NO []

Test results: 1000 ppm / 4 hrs = 0/6 mortality after 14 days

2000 ppm / 4 hrs = 6/6 mortality after 14 days

Comments: Other qualitative inhalation toxicity information indicates that saturated vapor caused no deaths when rats were exposed for 5 minutes (Smyth), but 15 minute exposure (Union Carbide Data Sheet, 1963) was fatal. (BIBRA Toxicity Profile, 11/89)

Reference: Smyth, H.F., Jr., Carpenter, C.P. and Weil, Range-finding Toxicity Data: List IV. AMA Arch Ind Hyg Occup Med, 4, p. 119, 1951.

6.1.3 Acute dermal toxicity

Test substance: Acetic anhydride

Test species/strain: rabbit

Test method: (e.g., OECD, EC, limit test):

GLP YES []

NO []

Test results: LD₅₀ = 4000 mg/kg

Comments: Information found in NIOSH Registry of Toxic Effects of Chemical Substances, (RTECS), 4/15/91

Reference: Original reference cited in RTECS was Union Carbide Data Sheet [8/7/63]

6.2 Corrosiveness/irritation

6.2.1 Skin Irritation

Test substance: Acetic anhydride
 Test species/strain: albino rabbits
 Test method: (e.g., OECD, others): Described in: Smyth, H.F. and Carpenter, C.P. Journal of Industrial Hygiene and Toxicology, 26(8). 269-273, 1944.
 GLP YES []
 NO []
 Test results: gives a score of 2 out of a maximum possible score of 10 after 24 hrs.
 Comments:
 Reference: Smyth, H.F., Jr., Carpenter, C.P. and Weil, Range-finding Toxicity Data: List IV. AMA Arch Ind Hyg Occup Med, 4, p. 119, 1951.

6.2.1 Skin Irritation

Test substance: Acetic anhydride
 Test species/strain: human
 Test method: (e.g., OECD, others): description of incidental exposure
 GLP YES []
 NO []
 Test results: Severe burns and vesiculation of human skin have been reported from liquid splashes, and concentrated vapor produced primary irritation.
 Comments: Reported in ACGIH Documentation of Threshold Limit Values and Biological Exposure Indices 6th ed., 1991.
 Reference: U.S. Department of Labor, Occupational Safety and Health Administration: Industrial Exposure and Control of Technologies for OSHA Regulated Hazardous Substances, Vol. 1, pp. 10-13, USDOL/OSHA, Washington, DC (March 1989)

6.2.1 Skin Irritation

Test substance: Acetic anhydride
 Test species/strain: rabbit
 Test method: (e.g., OECD, others): Covered 24 hr. application of the neat liquid to rabbits, or 540 mg. open applied to rabbit skin.
 GLP YES []
 NO []
 Test results: Burns and blisters observed after 24 hrs. Mild irritation observed after open application.
 Comments: Reported in ACGIH Documentation of Threshold Limit Values and Biological Exposure Indices 6th ed., 1991.
 Reference: U.S. Department of Labor, Occupational Safety and Health Administration: Industrial Exposure and Control of Technologies for OSHA Regulated Hazardous Substances, Vol. 1, pp. 10-13, USDOL/OSHA, Washington, DC (March 1989)

6.2.2 Eye Irritation

Test substance: 10% solution Acetic Anhydride
 Test species/strain: Corneal epithelial cells in tissue culture from New Zealand White rabbits

Test method:	(e.g., OECD, others): Protocol developed by authors to examine the effects of test agent on the ability of epithelial cells to migrate and recover a wound in-vitro.
GLP	YES [] NO []
Test results:	0.01% of test material (0.1 mM) permitted wound closure. 0.1% test solution inhibited wound closure, and 0.3 to 1.0% was cytotoxic.
Comments:	Protocol was developed to provide an in vitro method to predict ocular irritancy. Comparison of known irritancy provided validation. Authors found that chemicals that are irritating due to extremes in pH (Acetic anhydride or NaOH) were found to be less irritating in test system because they were buffered by the medium.
Reference:	Simmons, S.J., Jumblatt, M.M. and A.H. Neufeld. Corneal Epithelial Wound Closure in Tissue Culture: An in Vitro Model for Ocular Irritancy. Toxicology and Applied Pharmacology 88:13-23, 1987.

6.2.2 Eye Irritation

Test substance:	Acetic anhydride
Test species/strain:	humans
Test method: (e.g., OECD, others):	
GLP	YES [] NO []
Test results:	
Comments:	16 cases of corneal burns reported; most healed rapidly, 3 slowly, and 1 resulted in vision loss.
Reference:	McLaughlin, R.S. Am. J. Ophthal. 29:1355, 1946.

6.2.2 Eye Irritation

Test substance:	Acetic anhydride
Test species/strain:	humans
Test method: (e.g., OECD, others):	Incidental exposures
GLP	YES [] NO []
Test results:	
Comments:	“The symptoms are constant conjunctival irritation with reddening and lacrimation which appears even at concentrations lower than the maximum allowable (acetic anhydride: 5 ppm). Higher concentrations give way to depression of the central nervous system; still higher concentrations give way to depression of the central nervous system with drowsiness, dizziness and narcosis.”
Reference:	Baldi, G. Patologia Professionale da Acetone, E. Derivati Alogenati, Acido Acetico, Anidride Acetica, Cloruro Di Acetile, Acetil Acetone, La Medicina Del Lavoro, 44(10), 413-414, 1953.

6.2.2 Eye Irritation

Test substance:	Acetic anhydride
Test species/strain:	albino rabbits

Test method: (e.g., OECD, others): Described in: Smyth, H.F. and Carpenter, C.P. Journal of Industrial Hygiene and Toxicology, 26(8). 269-273, 1944.

GLP YES []
NO []

Test results: give a score of 9 out of a maximum possible score of 10 after 24 hrs.

Comments:

Reference: Smyth, H.F., Jr., Carpenter, C.P. and Weil, Range-finding Toxicity Data: List IV. AMA Arch Ind Hyg Occup Med, 4, p. 119, 1951.

6.2.2 Eye Irritation

Test substance: Acetic anhydride

Test species/strain: rabbits

Test method: (e.g., OECD, others):

GLP YES []
NO []

Test results: A 1% solution caused injury to rabbit eye

Comments: Information from BIBRA Toxicity Profile Acetic Anhydride 11/89 and RTECS, 1991

Reference: Original reference cited by BIBRA and RTECS was Union Carbide Data Sheet, 1963.

6.3 Skin sensitization

Test substance: Acetic anhydride

Test species: Guinea pigs

Test method (e.g., OECD, others): Guinea pigs were given twice weekly intracutaneous injections of 0.05 ml of a solution in olive oil for 2-2.5 weeks.

GLP YES []
NO []

Test results: A local response claimed to be indicative of a sensitization reaction was produced when, not more than 2 weeks after the induction regime, a 25% solution was applied dermally and the skin was "scratched through the solution" and examined.
Number of animals with skin reaction at challenge not specified.
Number of animals with skin reaction in control group at challenge not specified.

Comments:

Reference: Jacobs, J.L., Immediate Generalized Skin Reactions in Hypersensitive Guinea Pigs. Proc. Soc. Exptl. Biol. Med. 43: 641, 1940.

6.4 Repeated dose toxicity

Test substance: Acetic anhydride

Test species: Male Albino Rat

Test method (e.g., OECD, others): Rats were exposed to continuous inhalation of vapors containing 2.5, 0.1, and 0.03 mg/m³.

GLP YES []
NO []

Test results: At 2.5 mg/m³ there was a decrease in vitamin C content of the liver, kidneys, and adrenals; in addition there was a decrease in

coproporphyrin and blood albumin. Cholinesterase activity was raised at 2.5 and 01 mg/m³.

Dose or concentration at which no toxic effects were observed:

0.03 mg/m³

Comments: Very little experimental detail was described in this report. Rationale is not given for the investigation of the indicated endpoints.

Reference: Takhirov, M.T. Hygienic Standards for Acetic Acid and Acetic Anhydride in Air. Gig Sanit 34(6):722-725, 1969.

6.4 Repeated dose toxicity

Test substance: Acetic anhydride

Test species: Rats

Test method (e.g., OECD, others): Rats were exposed to inhalation of vapors containing 0, 25, 100 or 400 ppm for 6 hrs./day, 5 days/week for 2 weeks.

GLP YES

NO

Test results: Respiratory tract irritation at all levels; 40% mortality at 400 ppm after one, 6-hour exposure period.

Dose or concentration at which no toxic effects were observed: None

Comments:

Reference: Acetic Anhydride: 2 Weeks Repeat Dose Inhalation Toxicity Study in Male and Time-Mated Female Rats. Huntingdon Report HST 400/942606 (October 13, 1994).

6.4 Repeated dose toxicity

Test substance: Acetic anhydride

Test species: Rat

Test method (e.g., OECD, others): Rats were exposed to inhalation of vapors containing 0, 1, 5 or 20ppm for 6 hrs/day, 5 days/week for 13 weeks.

GLP YES

NO

Test results: Clinical observations of eye and respiratory tract irritation and reduced body weights were observed primarily at 20 ppm. Microscopic examination of tissues revealed signs of irritation of minimal severity in the respiratory tract (nasal passages; larynx) in most animals at the 5 ppm level. At 20 ppm, all animals showed minimal to moderate respiratory tract irritation (nasal passages; larynx; trachea; lungs). Systemic effects were not observed at 5 or 20 ppm. No effects were detected at 1 ppm. In animals exposed to the same levels of acetic anhydride for 13 weeks and then allowed a 13-week period without exposure, significant recovery from irritation effects was reported. In summary, the effects were consistent with those typical of substances which act as local/site-of-contact irritants. The NOEL was concluded to be 1 ppm (4.2 mg/m³).

Dose or concentration at which no toxic effects were observed: 1 ppm

Comments: Additional 13 week recovery groups included to assess reversibility.

Reference: Acetic Anhydride: 13-week Inhalation Toxicity Study in Rats. Huntingdon Report HST 411/961219 (August 27, 1996).

6.5 Genetic toxicity

6.5.1 Bacterial test: Ames Salmonella / Microsome Plate

Test substance: Acetic anhydride
 Test species/strain: Salmonella typhimurium TA-1535, TA-1537, TA-1538, TA-98, ATA-100
 Test method: (e.g., OECD, others): Litton Bionetics, Inc. Protocol DMT-100
 GLP YES
 NO
 Test results: Acetic anhydride did not demonstrate genetic activity in any of the test strains with or without activation.
 Minimum concentration of test substance at which toxicity to bacteria was observed:
 with metabolic activation: 0.1 µl / plate
 without metabolic activation: 1.0 µl / plate
 Concentration of the test compound resulting in precipitation:
 Genotoxic effects: All strains

	+	?	-
with metabolic activation:	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>
without metabolic activation:	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>

Comments:
 Reference: Litton Bionetics, Sponsored by Celanese Corporation, Mutagenic Evaluation of C-62 (Acetic Anhydride) in Salmonella / Microsome Plate Test, Genetics Assay #3855, 1979. Unpublished Report.

6.5.1 Bacterial test: Modification of the Ames Test for Bacterial Mutagens

Test substance: Acetic anhydride
 Test species/strain: Salmonella typhimurium G46, TA-100, C3076, TA-1537, D3052, TA-1538, TA-98 and E. coli WP2 and WP2 uvrA.
 Test method: (e.g., OECD, others): Bacterial Mutagen Screen on Gradient Plates; methodology described in report, and in Cline, J.C. and R.E. McMahon. Detection of chemical mutagens. Use of concentration gradient plates in a High Capacity Screen. Res. Commun. Chem. Pathol. Pharmacol. 16:523, 1977.
 GLP YES
 NO
 Test results: Acetic anhydride did not demonstrate genetic activity in any of the test strains with or without activation.
 Minimum concentration of test substance at which toxicity to bacteria was observed:
 with metabolic activation: not reported
 without metabolic activation: not reported
 Concentration of the test compound resulting in precipitation:
 Genotoxic effects: All strains

	+	?	-
with metabolic activation:	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>
without metabolic activation:	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>

Comments: Rat liver S9 used preparation described in reference.
 Reference: McMahon, R.E, J.C. Cline, and C.Z. Thompson. Assay of 855 Test Chemicals in Ten Tester strains Using a Modification of the Ames Test for Bacterial Mutagens, Cancer Research 39:682, 1979.

6.5.1 Bacterial test: Salmonella Preincubation Assay

Test substance: Acetic anhydride (Aldrich Chemical 99+ % purity)
 Test species/strain: Salmonella typhimurium TA-1535, TA-1537, TA-97, TA-100
 Test method: (e.g., OECD, others): (NTP Protocol)
 GLP YES
 NO
 Test results: Acetic anhydride did not demonstrate genetic activity in any of the test strains with or without activation.
 Minimum concentration of test substance at which toxicity to bacteria was observed:
 190 µg/plate
 with metabolic activation (rat liver S-9 Aroclor induced): 900.0 µg/plate
 (Hamster liver S-9 Aroclor induced): 1000 µg/plate
 Concentration of the test compound resulting in precipitation:
 Genotoxic effects: All strains

	+	?	-
with metabolic activation:	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>
without metabolic activation:	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>

Comments:
 Reference: Mortelmans, et al. Salmonella Mutagenicity Tests: II. Results From the Testing of 270 Chemicals, Environmental Mutagenesis. 8(sup 7) 1-119, 1986.

6.5.1 Bacterial test: Salmonella/Mammalian Microsome Plate Incorporation Mutagenicity Assay

Test substance: Acetic anhydride
 Test species/strain: Salmonella typhimurium TA-98, TA-100, TA-1535, TA-1537, TA-1538
 Test method: (e.g., OECD, others): Ames Assay
 GLP YES
 NO
 Test results: Acetic anhydride was negative with or without Aroclor induced rat and hamster liver microsomes.
 Minimum concentration of test substance at which toxicity to bacteria was observed:
 without metabolic activation: 667 µg/plate
 with metabolic activation (rat and hamster liver S-9 Aroclor induced): 3333 µg/plate
 Concentration of the test compound resulting in precipitation:
 Genotoxic effects: All strains

	+	?	-
with metabolic activation:	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>
without metabolic activation:	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>

Comments: Unpublished study sponsored by the National Cancer Institute
 Reference: Cameron T.P. Salmonella Mammalian Microsome Plate Incorporation Mutagenicity Assay (Ames Test) NCI-MA #C21, 1985.

6.5.2 Non-bacterial in vitro test: Mouse Lymphoma Mutagenesis Assay

Test substance: Acetic anhydride
 Type of cell used: L5178Y TK+/-Mouse Lymphoma
 Test method: (e.g., OECD, others): Standard test method described in reference.
 GLP YES
 NO
 Test results: Acetic anhydride produced a slight increase in mutant frequency without metabolic activation characterized as an equivocal response. No increase in mutant frequency was reported with activation.
 Lowest concentration producing cell toxicity:
 without metabolic activation: 0.1 µg/ml
 with metabolic activation: 0.05 µg/ml
 Genotoxic effects:

	+	?	-
with metabolic activation:	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>
without metabolic activation:	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>

 Comments: This unpublished study was sponsored by the NCI.
 Reference: Cameron T.P. Mouse Lymphoma Mutagenesis Assay with #83634 Acetic Anhydride (ML-NCI #142).

6.5.2 Non-bacterial in vitro test

Test substance: Acetic anhydride
 Type of cell used: rabbit liver cells
 Test method: (e.g., OECD, others): Test method described in reference. Method to assess the effect of increasing concentrations of acetic anhydride on chromatin.
 GLP YES
 NO
 Test results: Increased acetic anhydride concentrations resulted in increased acetylation and subsequent modification of tyrosyl and lysyl residue of chromatin protein. No conformational changes in DNA observed, and no dissociation of histone proteins.
 Lowest concentration producing cell toxicity:
 without metabolic activation:
 with metabolic activation:
 Genotoxic effects:

	+	?	-
with metabolic activation:	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
without metabolic activation:	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

 Comments: This study was undertaken to determine which regions of the DNA are accessible for acetylation and which are not.
 Reference: Simpson, R.T. Modification of Chromatin with Acetic Anhydride. Biochemistry 10(24)4466-4470, 1971.

6.5.2 Non-bacterial in vitro test

Test substance: Acetic anhydride
 Type of cell used: Bovine corpus luteum cells
 Test method: (e.g., OECD, others): Test method described in reference.
 GLP YES
 NO

Test results: Preincubation of bovine corpus luteum membranes with acetic anhydride inhibited 3H-labelled prostaglandin F₂-alpha binding by apparently totally abolishing all F₂-alpha receptors or severely reducing their affinities.

Lowest concentration producing cell toxicity:
 without metabolic activation:
 with metabolic activation:

Genotoxic effects:

	+	?	-
with metabolic activation:	[]	[]	[]
without metabolic activation:	[]	[]	[]

Comments: This was not an assay for genotoxicity. This study was undertaken to determine the mechanism of binding prostaglandin F₂-alpha to its receptor.

Reference: Rao, C.V. Prostaglandin F₂-alpha receptors in bovine corpus luteum cell membranes *Biochim. Biophys. Acta* 436: 170-182, 1976.

6.5.3 Non-bacterial test in vivo

Test substance: Acetic anhydride

Type of cell used: Rat

Test method: (e.g., OECD, others): Micronucleus/Bone Marrow subchronic exposure at 0, 1, 5 or 20 ppm for 6 hrs./day, 5 days /week for 13 weeks.

GLP YES [X]
 NO []

Test results: No effects

Lowest dose producing toxicity: 5 ppm
 Genotoxic effects: None

Comments: Positive Control included

Reference: Acetic Anhydride: 2 Weeks Repeat Dose Inhalation Toxicity Study in Male and Time-Mated Female Rats. Huntingdon Report HST 400/942606 (October 13, 1994).

6.6 Carcinogenicity

Test substance:

Test species/strain:

Test method (e.g. OECD, others):

GLP YES []
 NO []

Test results:

Comments:

Reference:

6.7 Reproductive and Developmental Toxicity

6.7.1 Reproductive Toxicity

Test substance: Acetic Anhydride

Test species/strain: Rats

Test method (e.g. OECD, others): Inhalation exposure of pregnant females to 0, 25, 100 or 400 ppm 6 hrs. /day, during days 6-15 of gestation.

GLP YES
NO

NOEL for P generation: 25 ppm
NOEL for F1 generation: 25 ppm
NOEL for F2 generation: Not applicable

Comments: Screening study

Reference: Acetic Anhydride: 2 Weeks Repeat Dose Inhalation Toxicity Study in Male and Time-Mated Female Rats. Huntingdon Report HST 400/942606 (October 13, 1994).

6.7.2 Teratogenicity/Developmental Toxicity

Test substance: Acetic Anhydride

Test species/strain: Rats

Test method (e.g. OECD, others): Inhalation exposure of pregnant females to 0, 25, 100 or 400 ppm 6 hrs. /day, during days 6-15 of gestation.

GLP YES
NO

Test results: Acetic anhydride caused fetotoxicity in a screening study with female rats exposed to the highly irritating, maternally toxic dose of 100 ppm vapor during gestation. At 100 ppm, severe respiratory tract irritation and bodyweight reduction were observed in the maternal animals. No developmental or reproductive effects were seen at 25 ppm even though substantial irritation of the respiratory tract was observed in maternal animals. The NOEL for developmental/reproductive effects was considered to be 25 ppm.

NOEL for maternal animals: None
NOEL for offspring: 25 ppm

Maternal general toxicity: Respiratory tract irritation; reduced body weight.

Comments: Additional Information:
No significant adverse effects were observed on comprehensive, microscopic examination of the reproductive organs of male and female rats exposed to acetic anhydride vapor for 13 weeks for 6 hrs./day, 5 days/week. In particular, microscopic assessment of the testes was made with reference to the stages of the cycle of the seminiferous epithelium. The dose levels were 1 ppm, 5 ppm and 20 ppm.

References: Acetic Anhydride: 2 Weeks Repeat Dose Inhalation Toxicity Study in Male and Time-Mated Female Rats. Huntingdon Report HST 400/942606 (October 13, 1994).
Acetic Anhydride: 13-Week Inhalation Toxicity Study in Rats. Huntingdon Report HST 411/961219 (August 27, 1996).

6.7.2 Teratogenicity/Developmental Toxicity

Test substance: Acetic Anhydride

Test species/strain: Mice/CD-1

Test method (e.g. OECD, others): Brief abstract did not report method in detail.

GLP YES

	NO []
Test results:	19 mg/kg body weight injected (i.p.) into mice on days 11 to 13 of pregnancy produced abnormalities in the offspring.
NOEL for maternal animals:	
NOEL for offspring:	
Maternal general toxicity:	
Pregnancy and litter data:	
Foetal data (live/dead, sex, external defects, soft tissue and skeletal defects)	
Comments:	No information in this brief abstract about maternal effects, or specific effects in offspring. Acetic acid, the hydrolysis product of acetic anhydride, was not teratogenic to rabbits in an oral study at doses up to 1.6 kg/day (vinegar) administered during Day 6 through Day 18 f gestation.
References:	Brown, N.A., et. al, The Relationship between Acylating Ability and Teratogenicity of Selected Anhydrides and Imides. Toxicology and Applied Pharmacology 45:361, 1978. FDRL, Teratologic Evaluation of FDA 71-78, apple cider vinegar (acetic acid) in rats, mice and rabbits, 1974.

6.8 Specific toxicities (Neurotoxicity, Immunotoxicity, etc.)

6.9 Toxicodynamics, toxico-kinetics

The activity of human hepatic, intestinal, and placental phosphatases was decreased by up to 80% when the enzymes were treated with 0.1M acetic anhydride in vitro. Acetic anhydride probably reduced the activity of these phosphatases by decreasing the positive charges due to ionizable amino groups on the enzyme molecules.

Reference: Moss, D.W. Comparative effects of Chemical Modification of Human Alkaline Phosphatases Biochem. J. 118(2):17-18, 1970.

7. Experience with Human Exposure (give full description of study design, effects of Accidental or Occupational Exposure, epidemiology)

The odor threshold and irritating concentration of Acetic Anhydride vapors in humans was reported.

0.56 mg/m³ = odor threshold low (lowest concentration odor first perceived)

1.44 mg/m³ = odor threshold high (highes concentration odor first perceived)

odor described as sharp, sour acid

Irritating concentration = 20.00 mg/m³

Reference: Ruth, J. Odor Threshold and Irritation Levels of Several Chemical Substances: A Review., Am. Ind. Hyg. Assoc. J. 47:A142-A151), 1986.

7. Experience with Human Exposure (give full description of study design, effects of Accidental or Occupational Exposure, epidemiology)

Aerosol of acetic acid and acetic anhydride was released from a reactor in an industrial accident exposing workers. All exposed workers complained of severe conjunctival and naso-pharyngeal irritation, harsh cough, and some of dyspnea. Of the 18 workers exposed, 14 were admitted to the hospital showing intense conjunctivitis and acute pharyngolaryngitis. 12 showed numerous corneal abrasions, 11 presented necrotic areas in the nasal mucosa, and 12 showed a spastic bronchitis. Two workers suffered first and second degree burns on the legs. Complete recovery occurred in 5-25 days.

Comment: Published in Italian with English summary.

Reference: Capellini, A. and Sartorelli, E. Episodio Di Intossicazione Collectiva Da Anidride Acetica Ed Acido Acetico, Med. lavoro 58: 108, 1967.

7.1 Biological Monitoring (including clinical studies, case reports, etc).

8. Recommended Precautions, Classification (use and/or transportation) and Safety Data Sheets.

In case of accidental release, ignition sources should be eliminated. Leaking containers should be placed in a well-ventilated area with spill containment. If fire potential exists, blanket spill with alcohol-type aqueous film-forming foam or use water spray to disperse vapors. Clean-up methods may include use of absorbent materials or a vacuum truck. Runoff into storm sewers and ditches which lead to natural waterways should be avoided by spill containment.

Storage of acetic anhydride containers should be with adequate ventilation and the containers should be closed when not in use. Contact with eyes, skin or clothing, and breathing acetic anhydride vapor should be avoided. Soiled clothing should be decontaminated thoroughly before re-use and contaminated leather clothing should be destroyed. Workers should wash thoroughly with soap and water after handling acetic anhydride containers.

Acetic anhydride should be stored away from heat, sparks, and flame sources, and should not be stored with incompatible materials. Incompatible materials include water; aqueous alkalis such as caustic soda solution; alcohols; glycols; hydrogen peroxide, perchloric acid, nitric acid, chromium trioxide, and other oxidizing agents; amines; boric acid. Acetic anhydride reacts with water to form acetic acid and heat.

9. Availability and reference(s) for existing review(s).

10. Name of responder. Celanese Canada

EXTRACT FROM IRPTC LEGAL FILES

file: 17.01 LEGAL rn : 100204
 systematic name:Acetic acid, anhydride
 common name :Acetic anhydride
 reported name :Acetic anhydride
 cas no :108-24-7 rtecs no :AK1925000
 area : ARG type : REG

subject	specification	descriptor
AIR	OCC	MPC

8H-TWA : 20 MG/M3 (5 PPM), 15MIN-STEL : 20 MG/M3 (5 PPM) (MAXIMUM 4
 TIMES/DAY WITH INTERVALS OF AT LEAST 60 MINUTES)
 entry date: OCT 1991 effective date: 29MAY1991

title: LIMIT VALUES FOR CHEMICAL SUBSTANCES IN THE WORKING
 ENVIRONMENT-RESOLUTION NO.444/1991 OF THE MINISTRY OF WORK AND SOCIAL
 SECURITY (AMENDING REGULATION DECREE NO. 351/1979 UNDER LAW NO.
 19587/1972: HYGIENE AND SAFETY AT WORK)
 original : ARGOB*, BOLETIN OFICIAL DE LA REPUBLICA ARGENTINA(ARGENTIAN
 OFFICIAL BULLETIN), 24170 , I , 1 , 1979
 amendment: ARGOB*, BOLETIN OFICIAL DE LA REPUBLICA ARGENTINA(ARGENTIAN
 OFFICIAL BULLETIN), 27145 , I , 4 , 1991

file: 17.01 LEGAL rn : 300526
 systematic name:Acetic acid, anhydride
 common name :Acetic anhydride
 reported name :Acetic anhydride
 cas no :108-24-7 rtecs no :AK1925000
 area : CAN type : REG

subject	specification	descriptor
AIR	OCC	TLV

TWA: ceiling limit - 5 ppm, 20 mg/m3. Prescribed by the Canada
 Occupational Safety and Health Regulations, under the Canada Labour Code
 (administered by the Department of Employment and Immigration). The
 regulations state that no employee shall be exposed to a concentration
 of an airborne chemical agent in excess of the value for that chemical
 agent adopted by ACGIH (American Conference of Governmental Industrial
 Hygienists) in its publication entitled: "Threshold Limit Value and
 Biological Exposure Indices for 1985-86". The regulations also state
 that the employer shall, where a person is about to enter a confined
 space, appoint a qualified person to verify by means of tests that the
 concentration of any chemical agent or combination of chemical agents
 will not result in the exposure of the person to a concentration in
 excess of the value indicated above. These regulations prescribe
 standards whose enforcement will provide a safe and healthy workplace.
 entry date: OCT 1994 effective date: 24MCH1994

amendment: CAGAAK, CANADA GAZETTE PART II, 128 , 7 , 1513 , 1994

file: 17.01 LEGAL rn : 301528
 systematic name:Acetic acid, anhydride
 common name :Acetic anhydride
 reported name :Acetic anhydride
 cas no :108-24-7 rtecs no :AK1925000
 area : CAN type : REG

subject	specification	descriptor
TRNSP		CLASS
LABEL		RQR
PACK		

Schedule II, List II - Dangerous Goods other than Explosives: PIN
 (Product Identification No.): UN1715. Class (8): Corrosive; Class (9.2):
 Hazard to environment. Special provisions: 109. Packing group II,
 (I=Great danger, III=Minor danger). Passenger Vehicles: 1 L. Prescribed
 by the Transportation of Dangerous Goods Regulations, under the
 Transportation of Dangerous Goods Act (administered by the Department of
 Transport). The act and regulations are intended to promote safety in
 the transportation of dangerous goods in Canada, as well as provide
 comprehensive regulations applicable to all modes of transport across
 Canada. These are based on United Nations recommendations. The act and
 regulations should be consulted for details. Information is entered
 under the proper shipping name found in the regulations; this may
 include general groups of chemical substances.
 entry date: OCT 1994 effective date: 02DEC1993

amendment: CAGAAK, CANADA GAZETTE PART II, 127 , 25 , 4056 , 1993

file: 17.01 LEGAL rn : 302312
 systematic name:Acetic acid, anhydride
 common name :Acetic anhydride
 reported name :Acetic anhydride
 cas no :108-24-7 rtecs no :AK1925000
 area : CAN type : REG

subject	specification	descriptor
USE	OCC	RQR
STORE		
LABEL		

Ingredient Disclosure List - Concentration: 1% weight/weight. The
 Workplace Hazardous Materials Information System (WHMIS) is a national
 system providing information on hazardous materials used in the
 workplace. WHMIS is implemented by the Hazardous Products Act and the
 Controlled Products Regulations (administered by the Department of
 Consumer and Corporate Affairs). The regulations impose standards on
 employers for the use, storage and handling of controlled products. The
 regulations also address labelling and identification, employee
 instruction and training, as well as the upkeep of a Materials Safety
 Data Sheet (MSDS). The presence in a controlled product of an ingredient
 in a concentration equal to or greater than specified in the Ingredient
 Disclosure List must be disclosed in the Safety Data Sheet.
 entry date: APR 1991 effective date: 31DEC1987

amendment: CAGAAK, CANADA GAZETTE PART II, 122 , 2 , 551 , 1988

file: 17.01 LEGAL rn : 400594
 systematic name:Acetic acid, anhydride
 common name :Acetic anhydride
 reported name :Acetic anhydride
 cas no :108-24-7 rtecs no :AK1925000
 area : CSK type : REG

subject	specification	descriptor
AIR	OCC	MAC

TWA: 20.0MG/M3; CLV: 40.0MG/M3 (CALCULATED AS ACETIC ACID)
 entry date: DEC 1991 effective date: MCH1985

title: DIRECTIVE NO. 46/1978 ON HYGIENIC REQUIREMENTS ON OCCUPATIONAL ENVIRONMENT

original : HPMZC*, HYGIENICKE PREDPISY MINISTERSTVA ZDRAVOTNICTVI
 CSR(HYGIENIC REGULATIONS OF MINISTRY OF HEALTH OF CSR), 39 ,
 , , 1978

amendment: HPMZC*, HYGIENICKE PREDPISY MINISTERSTVA ZDRAVOTNICTVI
 CSR(HYGIENIC REGULATIONS OF MINISTRY OF HEALTH OF CSR), 58 ,
 , , 1985

file: 17.01 LEGAL rn : 402626
 systematic name:Acetic acid, anhydride
 common name :Acetic anhydride
 reported name :Acetic anhydride
 cas no :108-24-7 rtecs no :AK1925000
 area : CSK type : REG

subject	specification	descriptor
EXPRT		RQR
IMPRT		RQR

EXPORT AND IMPORT OF THE SUBSTANCE IS POSSIBLE ONLY WHEN SPECIAL PERMISSION (LICENCE) IS GIVEN BY THE RELEVANT GOVERNMENTAL AUTHORITY.
 + Y MINISTERSTVA ZDRAVOTNICTVI

file: 17.01 LEGAL rn : 402626
 systematic name:Acetic acid, anhydride
 entry date: NOV 1994 effective date: 14SEP1994

title: THE DECREE OF FEDERAL MINISTRY OF FOREIGN TRADE NO. 560 ON CONDITIONS OF GIVING OF THE OFFICIAL PERMISSION FOR EXPORT AND IMPORT OF GOODS AND SERVICES

original : SZCFR*, , , 106 , 2762 , 1991

amendment: SZCZR*, , , 56 , 1785 , 1994

file: 17.01 LEGAL rn : 522106

!!! WARNING - not original IRPTC record - WARNING !!!

systematic name:Acetic acid, anhydride

common name :Acetic anhydride

reported name :Acetic anhydride

cas no :108-24-7

rtecs no :AK1925000

area : DEU

type : REG

subject	specification	descriptor
AQ		CLASS
USE	INDST	RQR

This substance is classified as moderately hazardous to water (Water Hazard Class: WHC 1). (There are 3 water hazard classes: WHC 3 = severely hazardous; WHC 2 = hazardous; WHC 1 = moderately hazardous; and the classification as "not hazardous to water"). The purpose of the classification is to identify the technical requirements of industrial plants which handle substances hazardous to water.

entry date: SEP 2001

effective date: 01JUN1999

title: Administrative Order relating to Substances Hazardous to Water (Verwaltungsvorschrift wassergefaehrdende Stoffe)

original : BUANZ*, Bundesanzeiger, 51 , 98a , 1 , 1999

file: 17.01 LEGAL rn : 540004

!!! WARNING - not original IRPTC record - WARNING !!!

systematic name:Acetic acid, anhydride

common name :Acetic anhydride

reported name :Acetic anhydride

cas no :108-24-7

rtecs no :AK1925000

area : DEU

type : REC

subject	specification	descriptor
AIR	OCC	MAK

MAK value (8-hour time-weighted average): 5 ml/m³ (ppm) or 21 mg/m³ (20 C, 1013 hPa). Peak limitation category I: Substance for which local irritant effects determine the MAK value; excursion factor = 1 (peak level is 1 x MAK). Pregnancy risk group IIc: No pregnancy risk group classification. Vapour pressure: 4 hPa at 20 C.

entry date: MAY 2001

title: List of MAK and BAT Values 2000. Maximum Concentrations and Biological Tolerance Values at the Workplace. (MAK- und BAT-Werte-Liste 2000. Maximale Arbeitsplatzkonzentrationen und Biologische Arbeitsstofftoleranzwerte.)

original : MPGFDf, Mitteilung der Senatskommission zur Pruefung gesundheitsschaedlicher Arbeitsstoffe, 36 , , , 2000

file: 17.01 LEGAL rn : 606762

systematic name:Acetic acid, anhydride

common name :Acetic anhydride

reported name :Acetic anhydride
 cas no :108-24-7 rtecs no :AK1925000
 area : GBR type : REG

subject	specification	descriptor
TRNSP	MARIN	RQR
AQ	MARIN	RSTR
AQ	EMI	RSTR

CATEGORY D SUBSTANCE: DISCHARGE INTO THE SEA IS PROHIBITED; DISCHARGE OF RESIDUAL MIXTURES IS SUBJECT TO RESTRICTIONS.

entry date: 1992 effective date: 06APR1987

title: THE MERCHANT SHIPPING (CONTROL OF POLLUTION BY NOXIOUS LIQUID SUBSTANCES IN BULK) REGULATIONS 1987, SCHEDULE 1

original : GBR SI*, STATUTORY INSTRUMENTS, 551 , , 15 , 1987

amendment: GBR SI*, STATUTORY INSTRUMENTS, 2604 , , 2 , 1990

file: 17.01 LEGAL rn : 911876
 systematic name:Acetic acid, anhydride
 common name :Acetic anhydride
 reported name :Acetic anhydride
 cas no :108-24-7 rtecs no :AK1925000
 area : KEN type : REG

subject	specification	descriptor
FOOD	ADDIT	PRMT

FOOD ADDITIVE PERMITTED AS STARCH MODIFYING AGENTS. FOOD PRODUCTS IN OR UPON WHICH IT IS PERMITTED AND MAXIMUM LEVELS OF USE ARE LISTED.

entry date: SEP 1982

title: THE FOOD, DRUGS AND CHEMICAL SUBSTANCES (FOOD LABELLING, ADDITIVES AND STANDARDS) REGULATIONS, 1978

original : GSKEN*, KENYA GAZETTE SUPPLEMENT NO. 40, SPECIAL ISSUE (LEGISLATIVE SUPPLEMENT NO. 27), 40 , , 404 , 1978

file: 17.01 LEGAL rn : 1010076
 systematic name:Acetic acid, anhydride
 common name :Acetic anhydride
 reported name :Acetic anhydride
 cas no :108-24-7 rtecs no :AK1925000
 area : MEX type : REG

subject	specification	descriptor
AIR	OCC	MXL

AT ANY WORKPLACE WHERE THIS SUBSTANCE IS PRODUCED, STORED OR HANDLED A MAXIMUM PERMISSIBLE LEVEL OF 20MG/M3 (5PPM) MUST BE OBSERVED FOR A PERIOD OF 8 HOURS.

entry date: DEC 1991 effective date: 28MAY1984

title: INSTRUCTION NO.10 RELATED TO SECURITY AND HYGIENIC CONDITIONS AT WORKPLACES. (INSTRUCTIVO NO. 10, RELATIVO A LAS CONDICIONES DE SEGURIDAD E HIGIENE DE LOS CENTROS DE TRABAJO).

original : DOMEX*, DIARIO OFICIAL, , , , 1984

file: 17.01 LEGAL rn : 1122194
 systematic name:Acetic acid, anhydride
 common name :Acetic anhydride
 reported name :Acetic anhydride
 cas no :108-24-7 rtecs no :AK1925000
 area : RUS type : REG

subject	specification	descriptor
AIR	AMBI	MAC

0.1 MG/M3 1X/D, 0.03 MG/M3 AV/D

entry date: SEP 1985

effective date: AUG1984

amendment: PDKAV*, PREDELNO DOPUSTIMYE KONTSENTRATSII (PDK)
 ZAGRYAZNYAYUSHCHIKH VESHCHESTV V ATMOSFERNOM VOZDUKHE
 NASELENNYKH MEST (MAXIMUM ALLOWABLE CONCENTRATIONS (MAC) OF
 CONTAMINANTS IN THE AMBIENT AIR OF RESIDENTIAL AREAS),
 3086-84 , , , 1984

file: 17.01 LEGAL rn : 1200246
 systematic name:Acetic acid, anhydride
 common name :Acetic anhydride
 reported name :Acetic anhydride
 cas no :108-24-7 rtecs no :AK1925000
 area : SWE type : REG

subject	specification	descriptor
AIR	OCC	HLV

CLV (15MIN-TWA): 20MG/M3 (5PPM).

entry date: 1992

effective date: 01JUL1991

title: HYGIENIC LIMIT VALUES.

original : AFS***, ARBETARSKYDDSSSTYRELSENS FOERFATTNINGSSAMLING, 1990:13
 , , 5-64 , 1990

file: 17.01 LEGAL rn : 1309009
 systematic name:Acetic acid, anhydride
 common name :Acetic anhydride
 reported name :Acetic anhydride
 cas no :108-24-7 rtecs no :AK1925000
 area : USA type : REG

subject	specification	descriptor
CLASS	INDST	RQR
AIR	EMI	RQR
AQ	EMI	RQR

5000 (2270); Summary - RELEASES OF THIS HAZARDOUS SUBSTANCE, IN QUANTITIES EQUAL TO OR GREATER THAN ITS REPORTABLE QUANTITY (RQ), REPORTED AS >LBS (KG)|, ARE SUBJECT TO REPORTING TO THE NATIONAL RESPONSE CENTER UNDER THE COMPREHENSIVE ENVIRONMENTAL RESPONSE, COMPENSATION, AND LIABILITY ACT. (#)- RQ IS SUBJECT TO CHANGE
 entry date: SEP 1991 effective date: 1990
 title: CERCLA: LIST OF HAZARDOUS SUBSTANCES AND REPORTABLE QUANTITIES
 original : CFRUS*, CODE OF FEDERAL REGULATIONS, 40 , 302 , 4 , 1990
 amendment: CFRUS*, CODE OF FEDERAL REGULATIONS, 40 , 302 , 4 , 1990

file: 17.01 LEGAL rn : 1313006
 systematic name:Acetic acid, anhydride
 common name :Acetic anhydride
 reported name :Acetic anhydride
 cas no :108-24-7 rtecs no :AK1925000
 area : USA type : REG

subject	specification	descriptor
AQ	EMI	RQR
AQ	GRND	RQR
AQ	MARIN	RQR

5000 (2270) LBS (KG); Summary - FOR PURPOSES OF SECTION 311 OF THE CLEAN WATER ACT THE FOLLOWING HAZARDOUS SUBSTANCES IN QUANTITIES GIVEN SHALL NOT BE DISCHARGED INTO OR UPON THE NAVIGABLE WATERS OF THE UNITED STATES OR ADJOINING SHORELINES, WATERS OF THE CONTIGUOUS ZONE, OR OUTER DEEP WATERS WHICH MAY AFFECT NATURAL RESOURCES BELONGING TO THE UNITED STATES.
 entry date: SEP 1991 effective date: 1986
 title: REPORTABLE QUANTITIES OF HAZARDOUS SUBSTANCES; CLEAN WATER ACT, SECTION 311
 original : FEREAC, FEDERAL REGISTER, 51 , , 34547 , 1986
 amendment: CFRUS*, CODE OF FEDERAL REGULATIONS, 40 , 117 , 3 , 1991

file: 17.01 LEGAL rn : 1325090
 systematic name:Acetic acid, anhydride
 common name :Acetic anhydride
 reported name :Acetic anhydride
 cas no :108-24-7 rtecs no :AK1925000
 area : USA type : REC

subject	specification	descriptor
SAFTY	OCC	MXL
USE	OCC	MXL

1000 PPM

entry date: OCT 1991

effective date: JUN1990

title: POCKET GUIDE TO CHEMICAL HAZARDS

original : XPHPAW, US PUBLIC HEALTH SERVICE PUBLICATION, 90 , 117 , 30 ,
1990

amendment: XPHPAW, US PUBLIC HEALTH SERVICE PUBLICATION, 90 , 117 , 30 ,
1990

file: 17.01 LEGAL rn : 1340117

systematic name:Acetic acid, anhydride

common name :Acetic anhydride

reported name :Acetic anhydride

cas no :108-24-7

rtecs no :AK1925000

area : USA

type : REC

subject	specification	descriptor
AIR	OCC	TLV

Ceiling Limit 5 ppm, 21 MG/M3; Summary - THIS THRESHOLD LIMIT VALUE IS INTENDED FOR USE IN THE PRACTICE OF INDUSTRIAL HYGIENE AS A GUIDELINE OR RECOMMENDATION IN THE CONTROL OF POTENTIAL HEALTH HAZARDS.

entry date: DEC 1991

effective date: 1989

title: THRESHOLD LIMIT VALUES

original : ACGIH*, AMERICAN CONFERENCE OF GOVERNMENT INDUSTRIAL
HYGIENISTS, , , 11 , 1989

amendment: ACGIH*, AMERICAN CONFERENCE OF GOVERNMENT INDUSTRIAL
HYGIENISTS, , , 11 , 1991

file: 17.01 LEGAL rn : 1407164

systematic name:Acetic acid, anhydride

common name :Acetic anhydride

reported name :Acetic anhydride

cas no :108-24-7

rtecs no :AK1925000

area : EEC

type : REG

subject	specification	descriptor
EXPRT		RQR
IMPRT		RQR
SALE		RQR

THE SUBSTANCE IS LISTED IN CATEGORY 2. THE OPERATORS ENGAGED IN THE IMPORT, EXPORT OR TRANSIT OF THE SUBSTANCE ARE REQUIRED TO REGISTER AND UPDATE WITH THE COMPETENT AUTHORITIES THE ADDRESSES OF THE PREMISES FROM WHICH THEY MANUFACTURE OR TRADE IN THE SUBSTANCE. THE EXPORTATION OF THE SUBSTANCE IS SUBJECT TO AUTHORIZATIONS ISSUED IN ACCORDANCE WITH THE PROVISION LAID DOWN BY THE COMPETENT AUTHORITY OF THE MEMBER STATE. THE PROVISIONS FOR DOCUMENTATION, NOTIFICATION AND LABELLING OF THE SUBSTANCE ARE LAID DOWN.

entry date: AUG 1995

effective date: 01JUL1991

AND ARTICLES INTENDED TO COME INTO CONTACT WITH FOODSTUFFS. THE USE OF THE SUBSTANCE IS SUBJECT TO THE RESTRICTIONS SPECIFIED THEREIN. PLASTIC MATERIALS AND ARTICLES SHALL NOT TRANSFER THEIR CONSTITUENTS TO FOODSTUFFS IN QUANTITIES EXCEEDING 10MG/DM2 OF SURFACE AREA OF MATERIAL OR ARTICLE OR 60 MG/KG OF FOODSTUFFS IN THE SPECIFIED CASES. VERIFICATION OF COMPLIANCE WITH THE MIGRATION LIMITS SHALL BE CARRIED OUT IN ACCORDANCE WITH DIRECTIVES 82/711/EEC AND 85/572/EEC.
 entry date: SEP 1995 effective date: 01JAN1991

title: COMMISSION DIRECTIVE OF 23 FEBRUARY 1990 RELATING TO PLASTICS MATERIALS AND ARTICLES INTENDED TO COME INTO CONTACT WITH FOODSTUFFS (90/128/EEC)

original : OJEC**, OFFICIAL JOURNAL OF THE EUROPEAN COMMUNITIES, L75 , , 19 , 1990

amendment: OJEC**, OFFICIAL JOURNAL OF THE EUROPEAN COMMUNITIES, L90 , , 26 , 1993

file: 17.01 LEGAL rn : 1470360

!!! WARNING - not original IRPTC record - WARNING !!!

systematic name:Acetic acid, anhydride

common name :Acetic anhydride

reported name :Acetic anhydride

cas no :108-24-7

rtecs no :AK1925000

area : EEC

type : REG

subject	specification	descriptor
MANUF	INDST	CLASS
IMPRT	INDST	CLASS

The substance is included in a list of existing substances produced or imported within the Community in quantities exceeding 1000 tonnes per year. - A system of data reporting by any manufacturer who has produced or any importer who has imported the substance, as such or in a preparation, in quantities exceeding 10 tonnes per year is established.
 entry date: AUG 1999 effective date: 04JUN1993

title: Council Regulation (EEC) No 793/93 of 23 March 1993 on the evaluation and control of the risks of existing substances

original : OJECFC, Official Journal of the European Communities, L84 , , 1 , 1993

file: 17.01 LEGAL rn : 1660005

!!! WARNING - not original IRPTC record - WARNING !!!

systematic name:Acetic acid, anhydride

common name :Acetic anhydride

reported name :Acetic anhydride

cas no :108-24-7

rtecs no :AK1925000

area : IMO

type : REG

subject	specification	descriptor
AQ	EMI	RSTR
TRNSP	MARIN	RQR

 Category D substance: Noxious liquid substances which if discharged into the sea from tank cleaning or deballasting operations would present a recognizable hazard to either marine resources or human health and therefore require some attention in operational conditions. - Category D substances are practically non-toxic to aquatic life (TLm of 100 ppm or more, but less than 1000 ppm) or are categorized because of other special characteristics. - The discharge into sea of substances in Category D or ballast water, tank washings, or other residues or mixtures containing such substances shall be prohibited, except when the discharge is made under specified conditions. - Technical requirements for reception facilities and cargo unloading terminal arrangements in the ports are given.
 entry date: JUN 1999 effective date: 03MCH1996

title: Regulations for the Control of Pollution by Noxious Liquid Substances in Bulk (Annex II of MARPOL 73/78)
 original : MARPO*, International Convention for the Prevention of Pollution from Ships, 1973, as modified by the Protocol of 1978 relating thereto (MARPOL 73/78), Consolidated Edition, , , 1997

file: 17.01 LEGAL rn : 1661575
 !!! WARNING - not original IRPTC record - WARNING !!!
 systematic name:Acetic acid, anhydride
 common name :Acetic anhydride
 reported name :Acetic anhydride
 cas no :108-24-7 rtecs no :AK1925000
 area : IMO type : REC

subject	specification	descriptor
TRNSP	MARIN	CLASS
LABEL		RQR
PACK		RQR

UN No. 1715. Class: 8 = Corrosive substance. Subsidiary risk: 3 = Flammable liquid. Packing group: II = Medium danger.
 entry date: NOV 2000 effective date: 01JAN2001

title: IMDG Code - Dangerous Goods List
 original : IMDGC*, International Maritime Dangerous Goods Code, Amendment 30-00, Volume 2 , , , 2000

file: 17.01 LEGAL rn : 1760575
 !!! WARNING - not original IRPTC record - WARNING !!!
 systematic name:Acetic acid, anhydride
 common name :Acetic anhydride
 reported name :Acetic anhydride
 cas no :108-24-7 rtecs no :AK1925000
 area : UN type : REC

subject	specification	descriptor
TRNSP	MARIN	CLASS
LABEL		RQR
PACK		RQR

TRNSP	CLASS
LABEL	RQR
PACK	RQR

UN No. 1715. Class: 8 = Corrosive substance. Subsidiary risk: 3 =
Flammable liquid. Packing group: II = Medium danger.
entry date: NOV 2000

title: UN Orange Book - Dangerous Goods List
original : !RTDGFK, Recommendations on the Transport of Dangerous Goods
prepared by the United Nations Committee of Experts on the
Transport of Dangerous Goods, 11th revised ed., , , 1999

