2,3-EPOXYPROPYLTRIMETHYLAMMONIUM CHLORIDE

CAS No: 3033-77-0

EINECS No: 221-221-0

SUMMARY RISK ASSESSMENT

Final report 2008

Finland

FINAL APPROVED VERSION

The summary of the risk assessment of 2,3-Epoxypropyltrimethylammonium chloride has been prepared by the National Product Control Agency for Welfare and Health, in co-operation with the Finnish Environment Institute.

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PREFACE

This report provides a summary, with conclusions, of the risk assessment report of the substance 2,3-Epoxypropyltrimethylammonium chloride (EPTAC) that has been prepared by Finland in the context of Council Regulation (EEC) No. 793/93 on the evaluation and control of existing substances. For detailed information on the risk assessment principles and procedures followed, the underlying data and the literature references the reader is referred to the comprehensive Final Risk Assessment Report (Final RAR) that can be obtained from the European Chemicals Bureau1. The Final RAR should be used for citation purposes rather than this present Summary Report.

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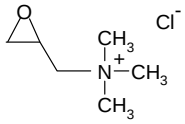
EUSES Calculations can be viewed as part of the report at the website of the European Chemicals Bureau: http://ecb.jrc.it

1. GENERAL SUBSTANCE INFORMATION

1.1. IDENTIFICATION OF THE SUBSTANCE

CAS Number: 3033-77-0
EINECS Number: 222-221-0
IUPAC Name: 2,3-Epoxypropyltrimethylammonium chloride
Molecular formula: $C_6H_{14}NOCl$



Structural formula:
Molecular weight: 151.66
Synonyms: EPTAC, Oxiranemethanaminium, N,N,N-trimethyl chloride, Glycydyltrimethylammonium chloride

1.2. PURITY/IMPURITIES, ADDITIVES

The typical concentration of technical EPTAC is 70-75 % water solution. The solubility of the substance limits higher water concentrations. Main impurities are:

Table 1.1 EPTAC impurities

CAS-No:	Name:	Contents:
3327-22-8	3-chlorohydroxypropyltrimethylammonium chloride (CHPTAC)	< 4 %
34004-36-9	2,3-dihydroxypropyltrimethylammonium chloride (diol)	< 3.5 %
55636-09-4	1.3-propanediaminium, 2-hydroxy-N,N,N,N',N',N'-hexamethyl-, dichloride	< 1.5 %
91725-36-9	(3-hydroxypropenyl)trimethylammonium chloride	< 0.2%
106-96-8	Epichlorohydrin	< 10 ppm

In order to prevent or minimize hydrolysis, the commercial EPTAC products contain a small quantity of CHPTAC (max. 4 wt-%, typically 1-2 wt-%). In addition, EPTAC is kept under controlled temperature during storage and transport (Raisio Chemicals, 2004b).

1.3. PHYSICO-CHEMICAL PROPERTIES

Pure EPTAC is at 20 °C and 101.3 kPa a solid substance, which is highly flammable. However, EPTAC is marketed and used as a non-flammable water solution. The physico-chemical analyses were performed in accordance with the EEC-guidelines. The reports

contained GLP compliance statements and quality assurance statements. Summary of the physico-chemical data is presented in Table 1.2.

Table 1.2 Summary of physico-chemical properties

Property	Value
Physical state	solid
Melting point	118 °C - 126 °C
Boiling point	Boiling point could not be determined because the substance decomposed in the range of the melting point 118 °C and 126 °C.
Relative density	1.178
Vapour pressure	$< 10^{-3}$ Pa
Water solubility	852.0 ± 16.7 g/l
Partition coefficient n-octanol/water (log value)	Pow < 0.05 or log Pow < -1.3
Partition coefficient organic carbon-water	Koc 53.8 l/kg
Granulometry	-
Conversion factors	-
Flash point	138 °C (70%), 155°C (75 %)
Autoflammability	Not self-ignitable
Flammability	Classified as highly flammable*
Explosive properties	No explosive properties
Oxidizing properties	Not likely oxidising
Viscosity	-
Henry's constant	<1.78 · 10-7 Pa m3/mol
Surface tension	73 mN/m

* EPTAC is sold only in water solution which is not expected to be flammable.

1.4. CLASSIFICATION

The substance is not yet officially classified at the community level according to the Dir. 67/548/EEC. However, EPTAC has been proposed to the 31st ATP with the following phrases:

Classification: Carc. Cat. 2; R45, Muta Cat 3; R68, Repro. Cat 3; R62, Xn; R21/22-R48/22, Xi; R41-43, R52-53

S-phrases: S: 53-45-61

Labelling: T, R:52/53

2. GENERAL INFORMATION ON EXPOSURE

In 2002 there were two producers of EPTAC within EU. Furthermore there was also import of EPTAC into EU. The total consumption volume of EPTAC, including production, import and export was 3866 tons in 1996, 5240 tons in 1999 and 6153 tons in 2001. A significant decrease in the EPTAC use volumes was observed in 2002 and 2003 (5237 and 3937 t, respectively).

The main use of EPTAC was for cationisation of starches (99% in 2001). Cationised starches are added in paper to give paper better surface quality and to improve paper strength. Only a small volume of EPTAC was used for quaternisation of other products such as guar, cellulose derivates and protein. The total number of sites using EPTAC or CHPTAC was 22 in 2001. Volumes of EPTAC used by single plant ranged from 8.5 tons to 1611 tons and CHPTAC from 2.9 tons to 7947 tons in 2001.

3. ENVIRONMENT

3.1. ENVIRONMENTAL EXPOSURE

3.1.1. Environmental releases

EPTAC may be released into the environment during its production and industrial use. EPTAC releases have also been monitored from waste water during use of CHPTAC (3-Chloro-2-hydroxypropyl-trimethylammonium chloride) (CAS-3327-22-8). During main use of EPTAC and CHPTAC i.e. cationisation of starch the process conditions are very alkaline (pH > 10) and therefore most of the chemical, EPTAC or CHPTAC, is in form of EPTAC which is the reactive form. This leads to a release of EPTAC despite which of the chemical is used. Thus EPTAC releases from use of EPTAC and CHPTAC will be considered at the local scale in the risk assessment of EPTAC. Furthermore releases of EPTAC are likely due to conversion of CHPTAC to EPTAC in the environment.

Exposure is assessed for six scenarios:
1) production
2) cationisation of starch with EPTAC and CHPTAC (industrial use scenario 1)
3) use of starch with residual EPTAC in paper making (industrial use scenario 2, cases 1-3)
- high grade board for books, case 1
- printing and writing paper, case 2
- food grade board, case 3

4) residual EPTAC and CHPTAC in paper recycling (industrial use scenario 3)
5) use of starch residual EPTAC in formulation of Alkyl Ketene emulsions (AKD) (industrial use scenario 4)
6) other uses of EPTAC and CHPTAC (industrial use scenario 5)

3.1.2. Environmental fate

EPTAC is highly soluble in water (852.0 ± 16.7 g/l at 20°C), has low vapour pressure (< 10^{-3} Pa at 22 – 80°C) and low log K_{ow} (< -1.3). Calculated Henry's law constant of <1.78 * 10^{-7} Pa m^3/mol indicates that EPTAC does not volatize from water to air.

Under aqueous conditions, EPTAC hydrolyses to DIOL (2,3-dihydroxypropyltrimethyl-ammonium chloride) with half-life of 177 days at 12°C and pH 7.8. Therefore hydrolysis is not expected to be an important removal process of EPTAC in the environment.

No valid ready biodegradation studies are available for EPTAC. In an inherent biodegradation test conducted according to OECD 302B, using non-adapted sludge, EPTAC was not inherently biodegradable. In an STP simulation test conducted according to OECD 303A, the mean primary degradation was 15 ± 9.7 %, from which the removal rate constant for EPTAC was calculated to be 0.035 h^{-1}. In this risk assessment EPTAC can be regarded as inherently biodegradable but not fulfilling the criteria set in the TGD. No degradation studies have been carried out for EPTAC in soil and a degradation half-life of 300 days in soil is assumed.

EPTAC is expected to have a low bioaccumulation potential to biota. Bioconcentration factors (BCFs) were calculated for fish and worm (1.41 l/kg and 3.34 kg/kg) based on the log Kow (<-1.3). Adsorption to sludge at the wastewater treatment plant is assumed to be low. Based on known properties of the substance, EPTAC is expected to distribute primarily to receiving water.

3.1.3. Environmental concentrations

Local concentrations

According to the data provided by the industry there are no releases to the water at the production stage or they are negligible.

For the cationisation of starch (industrial use scenario 1) $PECs_{local}$ have been calculated from the measured WWTP effluent concentrations. Concerning three sites where no monitoring data was available PECs have been calculated by using a release factor of 1.32 %, which is from another starch cationisation plant. In addition biodegradation of 19.2 % and adsorption of 0.6 % have been taken into account in the calculation of PEC_{local}.

Releases due to residual levels of EPTAC in the cationised starch used in the production of board (industrial use scenario 2, case 1) have been estimated to be 1.161 kg/day from the wet-end use. Predicted concentration was calculated to be 3.99 µg/l in the surface water. For comparison, local concentration was also calculated for a smaller mill which resulted PEC value of 6.69 µg/l.

EPTAC releases to water from production of printing and writing paper (case 2) have been estimated to be 0.881 kg/d. For this case a local predicted concentration of 3.49 µg/l was calculated for surface water and for a smaller mill PEC_{local} was 5.79 µg/l.

As the dosage used for food grade board purpose (case 3) is usually lower than in high grade for books and printing and writing paper, no local estimation has been carried out.

Releases due to residual levels of EPTAC in recovered printing and writing paper material used in recycling plant (incl. deinking process) have been estimated to be 0.05 kg/day (industrial use scenario 3). EPTAC concentration in the surface water has been calculated

according to Emission scenario document (ESD) on pulp, paper and board industry (Environment Agency, draft December 2004). PEC_{local} was calculated to be 3.19 µg/l in the surface water.

At the AKD formulation plant (industrial use scenario 4) the release of cationic starch could be 15 t/y, when using an TGD emission factor of 2 % to waste water. PEC local was calculated to be 1.82 µg/l.

Industry has provided monitoring data on two small sites, which use EPTAC for quaternisation of substances other than starch (industrial use scenario 5). Based on site-specific data concentrations in marine water were low. Majority of the volume in this industrial use scenario is used by one site (CHPTAC user), which has provided site-specific information on releases. A local PEC for surface water from this site was 7.45 µg/l.

Regional concentrations

Table 3.1 shows the calculated PECs for air, water, soil and sediment at the regional scale.

Table 3.1 Regional PECs in air, water and soil

Compartment	PEC regional
Surface water (total)	1.79 [µg/l]
Surface water (dissolved)	1.79 [µg/l]
Sea water (total)	0.166 [µg/l]
Air (total)	9.46×10^{-14} [mg/m^{-3}]
Agricultural soil (total)	3.31×10^{-5} [mg/kg wwt]
Pore water of agricultural soils	3.1×10^{-5} [mg/l]
Natural soil (total)	4.84×10^{-6} [mg/kg wwt]
Industrial soil (total)	1.28×10^{-3} [mg/kg wwt]
Sediment (total)	3.38×10^{-3} [mg/kg wwt]
Sea water sediment (total)	3.1×10^{-4} [mg/kg wwt]

3.2. EFFECTS ASSESSMENT

3.2.1. Calculation of Predicted No Effect Concentration (PNEC)

Aquatic compartment (incl. sediment)

There is a full base set available on short term toxicity with EPTAC. The acute toxicity test results of EPTAC show clearly that Daphnia is the most sensitive species of the species tested. There are long term NOECs for algae and Daphnia and it is very unlikely that a chronic fish test would give a lower NOEC than the Daphnia test. Accordingly the PNEC will be derived from the 21 day Daphnia reproduction rate NOEC of 0.16 mg/l with an assessment factor of 10. This results a $PNEC_{aquatic}$ of 16 µg/l.

PNEC for micro-organisms can be estimated from the activated sludge respiration inhibition test. An EC_{10}-value of 443 could be derived from the test, and according to TGD an

assessment factor of 10 should be used for a EC_{10}- or NOEC –value from this kind of test. This results a PNEC of 44.3 mg/l for micro-organisms.

$PNEC_{sediment}$ has been estimated by using $PNEC_{aquatic}$ as there are no tests with sediment organisms. $PNEC_{sediment}$ will be 0.0313 mg/kg, when using fresh water toxicity data for EPTAC and a suspended matter- water partition coefficient (2.25 m^3/m^3).

Terrestrial compartment

No toxicity studies have been carried out for terrestrial organisms. Therefore $PNEC_{soil}$ has been estimated by using $PNEC_{aquatic}$. $PNEC_{soil}$ will be 0.0170 mg/kg**,** when using fresh water toxicity data for EPTAC and a soil-water partition coefficient (1.81 m^3/m^3).

Atmosphere

There is no toxicity data available on EPTAC via atmospheric exposure. Concerning abiotic effects EPTAC is not expected to have effects on stratospheric ozone depletion, tropospheric ozone formation or acidification since it evaporates from the water very slowly.

Possible impact of a substance on global warming could be estimated from its IR adsorption characteristis and its atmospheric lifetime. Such information is not available on EPTAC. However, as EPTAC has low vapour pressure and small Henry's law constant, it is not expected that EPTAC could have effect on global warming.

Secondary poisoning

It seems likely, that EPTAC would not bioconcentrate in high degree. Therefore assessment of secondary poisoning was not carried out.

3.2.2. PBT assessment

According to existing data and assessment of inherent PBT –properties, it can be concluded that EPTAC can not be regarded as a PBT-substance nor a vPvB –substance, as it does not meet the B criterion. The screening level P-criterion is fulfilled. T-criterion is fulfilled based on human toxicity endpoints, but not for ecotoxicological endpoints.

3.3. RISK CHARACTERISATION

3.3.1. Aquatic compartment and sediment

Local risk characterisation

There are no risks to aquatic compartment from production of EPTAC.

EPTAC is mainly used for starch cationisation, where at five starch cationisation sites risk ratios are higher than one. Starch cationisation sites presented in Tables 3.2 and 3.3 are all using wet process. In addition there are also four sites which produce cationised starch with

dry process and three sites with wet process but without releases to water. As there are no releases of EPTAC to water from these sites, the risk ratios from these sites to aquatic environment are zero i.e. there are no risks from these sites.

Table 3.2: Site-specific PECs in surface water and sediment and corresponding PEC/PNEC ratios from starch cationisation. At these sites EPTAC has been measured from the waste water effluent.

Site	$PEC_{aquatic}$ (µg/l)	$PEC_{sediment}$ (mg/kg)	$PEC/PNEC_{aquatic (\& sediment)}$
CHPTAC users			
B3	< 3.12	< 6.1E-03	< 0.195
B4	< 18.6	< 0.0363	< 1.16
B5	10.6(average)	0.0207	0.661
B14	5.79	0.0113	0.36
B16	< 7.35	< 0.014	< 0.46
B17	< 10.16	< 0.0198	< 0.635
B18	< 1.82	< 3.56E-03	< 0.114
B21	< 13.24	< 0.0258	< 0.826
B25	< 65.4	< 0.128	< 4.09

Table 3.3: Site-specific PECs in surface water and sediment and corresponding PEC/PNECratios from starch cationisation. At these sites EPTAC has not been measured from the waste water, but there are other site-specific information available.

Site	$PEC_{aquatic}$ (µg/l)	$PEC_{sediment}$ (mg/kg)	$PEC/PNEC_{aquatic (\& sediment)}$
EPTAC users			
B9	218	0.426	13.6
B19[1)]	-	-	-
CHPTAC users			
B10	143	0.279	8.93
B23	4291	8.37	268
B26[2)]	-	-	-

[1)] *This site has been closed at the end of 2002
[2)] This site has been closed in 2004

For all other uses than starch cationisation i.e. industrial use scenarios 2, 3, 4 and 5 PEC/PNEC ratios for surface water and sediment are lower than 1 indicating no concern for the aquatic compartment.

Regional risk characterisation

There is no risk at regional level in surface water and sediment.

Wastewater treatment plant

PEC/PNEC ratios are lower than 1 for all use scenarios. As there are no releases from EPTAC production sites to waste water treatment plants, risk ratios are zero for production.

Conclusions for the aquatic compartment (including marine environment)

Conclusion (iii) There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

Conclusion (iii) applies to surface water and sediment from cationisation of starch with wet process (Industrial use scenario 1) at the local scale (i.e. sites B4, B9, B10, B23 and B25).

From these five starch cationisation sites, which have risk ratio higher than one, two sites (B4, B25) have monitoring data on EPTAC releases to waste water. The detection limit of EPTAC from waste water effluent (0.7 - 10 mg/l) is rather high compared to PNEC (0.016 mg/l l). Use of lower detection limit might decrease risks from these two sites. For those three sites where no monitoring data is available (B9, B10, B23), releases have been calculated with an actual emission factor from a starch cationisation site with highest release factor (1.32 %). Biodegradation at the WWTP has been assumed to take place at these sites.

The PNEC for water and sediment has been calculated from the chronic NOEC for Daphnia using an assessment factor of 10. Refinement of PNEC is therefore not possible with the dataset currently available.

Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.

Conclusion (ii) applies to fresh water and sediment from production of EPTAC and cationisation of starch with dry process for seven sites (B6, B11, B12, B13, B15, B22 and B28) and with wet process for seven sites (B3, B5, B14, B16, B17, B18 and B21) (Industrial use 1). Conclusion (ii) also applies to paper and board scenario (Industrial use 2), paper recycling (Industrial use 3), AKD formulation (Industrial use 4) and other uses of CHPTAC and EPTAC (Industrial use 5). Conclusion applies also to waste water treatment plants and marine environment from all scenarios.

3.3.2. Terrestrial compartment

There are no monitoring data available on concentrations of EPTAC in soil and therefore terrestrial concentrations have been calculated from measured concentrations in aquatic compartment. As there are neither toxicity studies for terrestrial organisms $PNEC_{soil}$ has been estimated from aquatic toxicity studies.

Conclusions for the terrestrial compartment

Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those, which are being applied already.

Conclusion applies to production and all use scenarios.

3.3.3. Atmosphere

No quantitative risk assessment has been carried out for the atmospheric compartment due to lack of effect data via air.
Due to low volatility of EPTAC no significant exposure to the atmosphere is expected.
EPTAC releases to air are likely during cationisation of starch as a residue in the starch dust. However, based on a few measurements releases are fairly low.

Conclusions for the atmosphere

Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.

Conclusion applies to production and all use scenarios.

3.3.4. Secondary poisoning

It seems likely, that EPTAC would not bioconcentrate in high degree. Therefore no assessment of secondary poisoning has been carried out.

4. HUMAN HEALTH

4.1. OCCUPATIONAL EXPOSURE

According to the information received from the industry, many companies have detailed guidelines for handling and management of these two cationising chemicals. In these cases if instructions are strictly followed, the exposure may be significantly lower than estimated here as a reasonable worst case.

Inhalation exposure

The inhalation exposure data used in this risk assessment is summarised in table 4.1 A.

As EPTAC is a non-volatile organic salt handled in water solutions, inhalation exposure to this chemical does not occur. In loading operations where 75% water solution of this chemical is handled, EASE estimation for exposure is 0-0.05 mg/m3 (0-0.08 ppm). Measurements have confirmed that the concentration was below the detection limit of the method of 0.08 mg/m^3.

During the use in dry cationisation workers may be exposed to the dust containing residual amounts of cationising chemicals. In maintenance and clean-up work EASE calculations gave results of 0.0008 mg/m3 for EPTAC and 0.02 mg/m3 for CHPTAC with the estimated residual amounts of 15 mg/kg and 450 mg/kg, respectively. In bagging the estimated exposure concentrations were 0.00002 mg/m3 and 0.0005 mg/m3, respectively. Based on the total dust measurements in bagging, the reasonable worst case exposure concentrations would be 0.00008 mg/m^3 for EPTAC and 0.002 mg/m^3 for CHPTAC.

The particle size of dry cationised starch is not known. Native potato starch has the particle size between 10 to 100 µm.

Dermal exposure

The dermal exposure data used in this risk assessment is summarised in table 4.1 B.

The EPTAC manufacturing process is an enclosed system with breaches for product sampling, tanker or silo filling and some maintenance activities.

Using the EASE model, dermal exposure during sampling was estimated to be in the range of 15 to 150 mg/person/day. Typical exposure level is likely to be in the lower end of the range as the activity takes about five minutes to complete making the exposure time to about 30 minutes per shift.

Analysing samples may expose workers in the laboratory to this chemical in the range of 30 to 300 mg/person/day according to the EASE modelling. This activity lasts about four hours daily.

In maintenance and cleanup work EASE estimation for dermal exposure is 0 to 63 mg/person/day. In loading and sampling after loading the range was 0 to 30 mg/person/day.

In wet cationisation process workers may expose to liquids containing EPTAC about 3%. EASE estimation gave the range of 0.5 to 5 mg/person/day in sampling 1-10 mg/person/day in laboratory work.

In dry cationisation exposure may happen to solid or dust of cationised starch containing residual amounts of cationising chemicals. EASE gave highest estimations in bagging operations where the range was 0.001 to 0.01 mg/person/day for EPTAC and 0.04 to 0.4 mg/person/day for CHPTAC.

If personal protection is properly worn exposure to EPTAC can be assumed low. Main risks of exposure are in sampling of process materials, analysing and performing maintenance tasks. Contamination of work sites and careless use and handling of gloves may expose worker to this chemical. Bagging operations of dry cationised starch expose workers to dust containing residual amounts of this chemical.

Since EPTAC is a genotoxic carcinogen, more analytical data is not considered essential at this stage, but the estimated occupational exposure are sufficient for the purpose of the risk assessment

Table 4.1 A: Summary of inhalation exposure data of 2,3-epoxypropyltrimethylammonium chloride (EPTAC) and (3-chloro-2-hydroxypropyl) trimethylammonium chloride (CHPTAC).

Scenario	Frequency Days/year	Duration Hours/day	EPTAC				CHPTAC			
			Reasonable worst case		Typical concentration		Reasonable worst case		Typical concentration	
			Unit mg/m³	Method[2]	Unit mg/m³	Method [2]	Unit mg/m³	Method [2]	Unit mg/m³	Method [2]
Production (EPTAC conc. 75%)										
Loading/Unloading	Daily	2	0.04[3]	Measured	-	-	-	-	-	-
			0.05	EASE	-	-	-	-	-	-
Use in dry cationisation or wet cationisation with drying (EPTAC conc. 15 mg/kg, CHPTAC conc. 450 mg/kg for RWC; EPTAC 3 mg/kg, CHPTAC 12 mg/kg for typical)										
Bagging	Daily	Shift length	0.00008	Measured	0.00006	Measured-	0.002	Measured	0.00003	Measured
			0.00002	EASE	0.000002[4]	EASE	0.0005	EASE	0.000006[4]	EASE
Maintenance and clean-up work	Weekly		0.0008	EASE	0.00002[4]	EASE	0.02	EASE	0.00006[4]	EASE

1: Full shift, short term, etc.
2: Measured, EASE, Expert judgment, Calculated, etc.

3: half of the detection limit

4: using the 50th percentile of the residual level in starch and the middle of the EASE estimate in bagging and the lower estimate of EASE in maintenance and clean-up

Note: The exposure scenario "Use of products with residual EPTAC" was left out from the table as it is considered negligible.

Table 4.1 B: Summary of dermal exposure data of 2,3-epoxypropyltrimethylammonium chloride (EPTAC) and (3-chloro-2-hydroxypropyl)trimethylammonium chloride (CHPTAC).

Scenario	Frequency Days/year	Duration Hours/ day	Contact level (EASE)	Level of exposure (mg/cm²/day)	Exposed area (cm²)	EPTAC		CHPTAC		Method [2]
						RWC mg/p/day	Typical conc. mg/p/day	RWC mg/p/day	Typical conc. mg/p/day	
Production (EPTAC conc. 75%)										
Sampling	Daily	0.5	Intermittent	0.075-0.75	210	150	15[b]	-	-	EASE
Laboratory work	Daily	4	Intermittent	0.075-0.75	420	300	30[b]	-	-	EASE
Maintenance and clean-up	Weekly	4	Incidental	0-0.075	840	63	6[b]	-	-	EASE
Loading/Unloading	Daily	2	Incidental	0-0.075	420	30	3[b]	-	-	EASE
Use in wet cationisation (EPTAC conc. 3% in starch slurry)										
Sampling	Daily	0.5	Intermittent	0.003-0.03	210	5	0.6[b]	-	-	EASE
Laboratory work	Daily	4	Intermittent	0.003-0.03	420	10	1.3[b]	-	-	EASE
Maintenance work	Weekly	4	Incidental	0-0.003	840	3	0.3[b]	-	-	EASE
Filling (end-product EPTAC 15 mg/kg, CHPTAC 450 mg/kg, RWC, EPTAC 3 mg/kg, CHPTAC 12 mg/kg, typ	Daily	8	Incidental	0-0.1 cat. starch	420	0.0006	0.00006[a]	0.02	0.00025[a]	EASE
Use in dry cationisation or wet cationisation with drying (EPTAC conc. 15 mg/kg, CHPTAC 450 mg/kg for RWC; EPTAC 3 mg/kg, CHPTAC 12 mg/kg for typical) There was not enough information for EASE estimations for wet cationising with drying. The scenarios were assessed by applying the dry cationisation scenario.										
Sampling	Daily	0.5	Intermittent	0.1-1 cat.starch	210	0.003	0.00006[b]	0.1	0.00025[b]	EASE
Laboratory work	Daily	6	Intermittent	0.1-1 cat. starch	420	0.006	0.0001[b]	0.2	0.0005[b]	EASE
Maintenance work	Weekly	4	Incidental	0-0.1 cat. starch	840	0.001	0.000025[b]	0.04	0.0001[b]	EASE
Clean-up work	Daily	2	Intermittent	0.1-1 cat. starch	840	0.01	0.00025[b]	0.4	0.001[b]	EASE
Bagging	Daily	8	Intermittent	0.1-1 cat.starch	840	0.01	0.00025[b]	0.4	0.005	EASE

1: Full shift, short term, etc., 2: Measured, EASE, Expert judgment, Calculated, etc; a: middle of the EASE estimate used; b: lower estimate or one tenth of the upper estimate of EASE used. Note: The exposure scenario "Use of products with residual EPTAC" was left out from the table as it is considered negligible.

4.2. CONSUMER AND INDIRECT EXPOSURE

Consumer exposure to EPTAC is negligible. Residues in cosmetics, such as shampoos and shower gels, which expose skin or scalp cause the greatest consumer exposure. Lesser sources of exposure are skin exposure from paper, books or oral exposure from food packaging residues. The following table summarises the exposure ranges from different sources.

Table 4.2 Consumer exposure to EPTAC

Product	Scenario	Total exposure
Food packaging	Transfer to product from wet packaging	0.0000012 µg/kg bw
Children's books	Small children chewing a book, which can lead to ingestion or skin exposure.	0.006 µg/kg bw
Copy paper and news papers	Skin exposure from paper surface.	0.009 µg/ kg bw
Cosmetics	EPTAC residues in cosmetic products expose skin and scalp. Rinse-off products	0.007-0.29 µg/kg bw 0.07-2.9 ng/kg bw.

The reasonable worst case exposure to be taken to the risk characterisation is a daily dermal dose of 0.29 µg/kg of b.w.

Table 4.3 Indirect human exposure to EPTAC, averages based on the EUSES estimations (local scenario) for nine monitored sites.

Source of exposure and concentration	Local daily dose (mg/kg of b.w)	Regional daily dose (mg/kg of b.w)
Drinking water, 15.12 µg/l (average of nine sites)	0.0005 (nine sites)	5.12E-05
Fish, 0.0206 mg/kg in wet weight	0.000034	4.16E-06
Leaf crops	0.0013	1.74E-07
Root crops	1.11E-05	1.58E-07
Meat	2.04E-08	3.39E-10
Milk	3.81E-07	6.32E-09
Air	2.48E-06	2.7E-14
Total	**0.0019**	**5.57E-05**

4.3. EFFECTS ASSESSMENT: HAZARD IDENTIFICATION AND DOSE (CONCENTRATION)- RESPONSE (EFFECT) ASSESSMENT

4.3.1. Toxicokinetics, metabolism and distribution

In the absence of data for inhalation, 75% absorption is assumed. For oral route, an assumption of 50 % is used. Based on the findings in the *in vitro* skin penetration assay, a maximum penetration rate of 0.685 % was reached in the human skin. Since it is recommended by the TGD that the dose retained is the skin should also be taken in consideration 5 % would then be more appropriate (0.685+ (0.685 x 6.8)). However, this factor does not take into account the amount retained in the stratum corneum. Accounting for the amount retained in the stratum corneum the average absorbed ranged between 0.1-15 %. Taking the highest percentage retained in the stratum corneum would probably be too conservative, due to factors like exfoliation, washing and other processes in which the substance is lost to outside. Moreover, the epidermal uptake is likely to occur slowly because of high water solubility (>800 g/l) and a log P of less than zero. Therefore, an absorption percentage of 6 % will be taken for the risk characterisation.

4.3.2. Acute toxicity

The LD50 value for acute oral toxicity is 1080 mg/kg when expressed as pure substance. Dermal toxicity test is available only in rabbit. The study results indicated that dermal acute toxicity LD50-value is probably 1500-3000 mg/kg. Based on a study in which rats were exposed to an EPTAC concentration of 8.17 mg/l for 7-hour the 4-hr-LC50 value is above 5 mg/l, which is the limit for classification. The classification and labelling working group has agreed to classify EPTAC Xn;R22/21.

4.3.3. Irritation, Corrosivity and sensitisation

EPTAC is a severe eye irritant when 70 % solution is applied. Classification and labelling working group has agreed to classify EPTAC Xi;R41.

Although severe signs of skin irritation are seen in the Degussa-study (1981), the results of this assay are not considered relevant when drawing a conclusion on skin irritation of EPTAC. The method of the study is non-guideline and the exposure time is six times of the normally used. Based on a study conducted according to OECD guideline, EPTAC is not a skin irritant.

Based on the findings in the skin irritation study EPTAC is not corrosive.

Based on the positive test results in guinea-pig maximisation tests and the patch tests in humans it can be concluded that EPTAC is sensitiser by skin contact. Classification and labelling working group has agreed to classify EPTAC Xi; R43.

4.3.4. Mutagenicity

EPTAC causes mutations in *E. coli* WP2 and S. typhimurium 1535, 1537 and 100 but not in 1538 or 98. These mutations did not require metabolic activation to occur. The evidence from the bacterial mutagenicity tests suggests that EPTAC act as a direct point mutagen by base pair substitution but not frame shift mutation. In addition, tests in two yeast strains have demonstrated that EPTAC can cause gene conversion in two different gene loci. The positive response in the liver UDS test gives indications of increased DNA damage in mammalian cells as well. In addition, a well-correlated dose-related increase of sister chromatid exchanges in the Chinese hamster V79 cells was seen.

Damage to chromosomes has been shown to occur in mammalian test systems *in vitro* and *in vivo*. The results of the in vitro chromosome aberration tests in both rat liver cells and Hamster ovary cells showed that both the frequency of aberrations per cell, with or without gaps, and the percentage of cells with all aberrations increased with the dose. In vivo, there was also a clear statistically significant increase of micronucleated PCE in females 24 hours after the administration in both sexes.

Positive results in vitro and in vivo show that in addition to causing point mutations in bacterial systems, EPTAC has clastogenic or aneugenic potential in mammalian cells as well. Moreover, microscopic examination in the 28-day test showed that there were abnormal mitosis and polyploid nuclei in the kidney proximal tubule cells at doses 10 mg/kg or higher, which could be indicative of a genotoxic event. In addition, atrophy of testes and especially of ovaries was seen at 31.6 mg/kg after 28-day of exposure increasing the possibility that EPTAC is also a germ cell mutagen.

EPTAC is a mutagen in somatic cells *in vivo*. Based on the evidence seen in a 28 day study, EPTAC also reaches the gonads, thus making it likely that EPTAC is also a germ cell mutagen. Classification and labelling working group has agreed to classify EPTAC Muta. Cat. 3; R68.

4.3.5. Carcinogenicity

EPTAC is a local carcinogen when applied on mouse skin at 1 % concentration (estimated dose applied on the skin: ~50 mg/kg/application). There is some indication that EPTAC could also cause some systemic tumours (e.g. lung or mammary tumours) when applied to mouse skin as a 1 % solution. However, the relevance of these tumours to the treatment is uncertain. Moreover, it is possible that oral intake could have occurred during the experiment. Based on in vitro skin absorption data from CHPTAC, the dermal penetration property of EPTAC is ca. 45 % or 29% in mouse skin at a concentration of 0.1% and 1% respectively, while in human skin it is less than 6%. Regardless of this, it is difficult to completely disregard the relevance of the systemic tumours. Furthermore, as EPTAC has direct mutagenic potential, which does not seem to be inactivated by mammalian metabolising systems, carcinogenic properties could be expected. Classification and labelling working group has agreed to classify EPTAC Carc. Cat 2; R45.

4.3.6. Toxicity for reproduction

Although these results tell little of the effect on the reproductive performance itself they can be used to set an indicative NOAEL based on the rather severe morphological changes in the reproductive organs of both sexes. The 10mg/kg NOAEL obtained from the 28-day repeated dose toxicity study is selected for toxicity to reproduction.

It unlikely that any further information obtained about the possible toxicity to reproduction (fertility or development) by requiring additional testing would enhance the possible risk reduction measures needed by a genotoxic carcinogen. Classification and labelling working group has agreed to classify EPTAC Repro. Cat. 3; R62.

4.4. RISK CHARACTERISATION [1]

4.4.1. Risk characterisation for workers

Table 4.4 Overview of the conclusions with respect to occupational risk characterisation

		Acute toxicity		Sensitisation	Repeated dose toxicity Systemic		Mutagenicity	Carcinogenicity (MOE skin)	Reproductive toxicity
		Dermal	Inhalation		Dermal	Inhalation			
Production									
Sampling	MOS	11538	-	-	12	-	-	*[5]*	38
	Concl.		ii	iii	iii	ii	iii	iii	i on hold
Laboratory work	MOS	5769	-	-	6	-	-	*[2]*	19
	Concl.		ii	iii	iii	ii	iii	iii	i on hold
Maintenance	MOS	30000	-	-	32	-	-	*[11]*	100
	Concl.		ii	iii	ii	ii	iii	iii	i on hold
Loading/ Unloading and sampling after loading	MOS	50000	204250	-	79	1580	-	*[25]*	167
	Concl.	ii	ii	iii	ii	ii	iii	iii	i on hold
Use: Wet cationising									
Sampling	MOS	$4x10^5$	-	-	395	-	-	*[140]*	1250
	Concl.	ii	ii	iii	ii	ii	iii	iii	i on hold
Laboratory work	MOS	2x105	-	-	176	-	-	*[70]*	556
	Concl.	ii	ii	iii	ii	ii	iii	iii	i on hold
Maintenance	MOS	$5x10^5$	-	-	527	-	-	*[245]*	1667
	Concl.	ii	ii	iii	ii	ii	iii	iii	i on hold
Filling	MOS	$3x10^9$	-	-	$3x10^5$	-	-	*[$1x10^6$]*	$1.0x10^6$
	Concl.	ii	ii	iii	ii	ii	iii	iii	i on hold
Use: Dry cationising or wet cationising with drying									
Bagging	MOS	$2x10^8$	$8x10^6$	-	$2x10^5$	14364	-	*[$7x10^4$]*	$6x10^5$
	Concl.	ii	ii	iii	ii	ii	iii	iii	i on hold
Clean-up work	MOS	$2x10^8$	$1x10^7$	-	$2x10^5$	18433	-	*[$7x10^4$]*	$6x10^5$
	Concl.	ii	ii	iii	ii	ii	iii	iii	i on hold
Laboratory work	MOS	$3x10^8$	-	-	$3x10^5$	-	-	*[$7x10^5$]*	$1x10^6$

[1] Conclusion (i) There is a need for further information and/or testing.
Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.
Conclusion (iii) There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

	Concl.	ii	ii	**iii**	ii	ii	**iii**	**iii**	i on hold
Sampling	MOS	$5x10^8$	-	**-**	$6x10^5$	-	**-**	*[$2x10^5$]*	$2x10^6$
	Concl.	ii	ii	**iii**	ii	ii	**iii**	**iii**	i on hold
Maintenance work	MOS	$2x10^8$	$1x10^7$	**-**	$2x10^5$	18433	**-**	*[$7x10^4$]*	$6x10^5$
	Concl.	ii	ii	**iii**	ii	ii	**iii**	**iii**	ii

4.4.2. Risk characterisation for consumers

Table 4.5 Summary of risk characterisation for consumers

		Acute toxicity		Sensitisation	Repeated dose toxicity Systemic		Mutagenicity	Carcinogenicity	Reproductive toxicity
		Dermal	Inhalation		Dermal	Inhalation			
Food packages	MOS	Acute toxicity is not relevant in consumer exposure scenarios due to very low exposure. Conclusion ii in all scenarios.		-	Lowest MOS found in cosmetics scenario: MOS of 93000. Conclusion ii in all scenarios.		-	*[4.6x10^9]*	Lowest MOS found in cosmetics scenario: MOS of 290000. Conclusion i on hold in all scenarios.
	Concl.			ii			**ii**	**ii**	
Children's books	MOS			-			-	*[9.3x10^5]*	
	Concl.			ii			**ii**	**ii**	
Copy paper & newspapers	MOS			-			-	*[1.8x10^7]*	
	Concl.			ii			**ii**	**ii**	
Cosmetics	MOS			-			-	*[5.7x10^5]*	
	Concl.			ii			**ii**	**ii**	

4.4.3. Risk characterisation for exposure via the environment

Based on the calculations, drinking water appears to be the greatest source of exposure. However, currently the estimations have many uncertainties.

Table 4.6 Summary of risk characterisation for indirect exposure all exposures combined

		Acute toxicity		Sensitisation	Repeated dose toxicity Systemic		Mutagenicity	Carcinogenicity	Reproductive toxicity
		Dermal	Inhalation		Dermal	Inhalation			
Combined indirect exposure	MOS	Acute toxicity is not relevant in indirect exposure scenarios due to very low exposure. Conclusion ii.		-	MOS of 1580 Conclusion ii in all scenarios.		-	*[2800]*	MOS of 5000. Conclusion i on hold.

4.5. HUMAN HEALTH (PHYSICO-CHEMICAL PROPERTIES)

4.5.1. Effects assessment: Hazard identification

Explosivity

EPTAC is not explosive.

Flammability

EPTAC is highly flammable as a pure powder but is sold in water solution which is not flammable.

Oxidizing potential

EPTAC is not oxidising.

4.5.2. Risk characterisation

Workers

Flammability is not a concern because EPTAC is normally handled as a 50-70% water solution. Conclusion ii is drawn.

Consumers

EPTAC is not sold to consumer. Conclusion ii.

Humans exposed via the environment

Not relevant.

RESULTS [2]

4.6. ENVIRONMENT

Conclusions for the aquatic compartment (including marine environment)

Conclusion (iii) There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

Conclusion (iii) applies to surface water and sediment from cationisation of starch with wet process (Industrial use scenario 1) at local scale for 5 sites (i.e. sites B4, B9, B10, B23 and B25).

From these five starch cationisation sites, which have risk ratio higher than one, two sites (B4, B25) have monitoring data on EPTAC releases to waste water. The detection limit of EPTAC from waste water effluent (0.7-10 mg/l) is rather high compared to PNEC (0.016 mg/l). Use of lower detection limit might decrease risk from these two sites. For those three sites where no monitoring data is available (B9, B10, B23), releases have been calculated with an actual emission factor from a starch cationisation site with highest release factor (1.32 %). Biodegradation at the WWTP has been assumed to take place at these sites.

The PNEC for water and sediment has been calculated from the chronic NOEC for Daphnia using an assessment factor of 10. Refinement of PNEC is therefore not possible with the dataset currently available.

Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.

Conclusion (ii) applies to fresh water and sediment from production of EPTAC and cationisation of starch with dry process for seven sites (B6, B11, B12, B13, B15, B22 and B28) and with wet process for seven sites (B3, B5, B14, B16, B17, B18 and B21) (Industrial use 1). Conclusion (ii) also applies to paper and board scenario (Industrial use 2), paper recycling (Industrial use 3), AKD formulation (Industrial use 4) and other uses of CHPTAC and EPTAC (Industrial use 5). Conclusion applies also to waste water treatment plants and marine environment from all scenarios.

Conclusions for the atmosphere and terrestrial compartment

Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.

Conclusion applies to production and all use scenarios.

[2] Conclusion (i) There is a need for further information and/or testing.
Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.
Conclusion (iii) There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

4.7. HUMAN HEALTH

Human health (toxicity)

Workers

Conclusion (iii) There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

Conclusion (iii) applies all worker exposure scenarios because of concerns for mutagenicity, carcinogenicity and sensitisation.

Conclusion (iii) also applies in relation to concerns from repeat dose toxicity for sampling and laboratory work during production of EPTAC.

Conclusion (i) There is a need for further information and/or testing.

There is a need to further investigate the reproductive toxicity in a 2-generation fertility test and a developmental toxicity test. However, since EPTAC is a genotoxic carcinogen, this property alone is sufficient to lead to the strictest measures for risk management in work places. Therefore, ***conclusion i on hold*** is drawn for all scenarios.

Consumers

Conclusion (**ii)** There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.

Conclusion (ii) applies to all scenarios.

Humans exposed via the environment

Conclusion (**iii)** There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account..

Although the modelled exposure figure is likely to be an over estimate, risks can not be excluded as the substance EPTAC is identified as a non-threshold carcinogen thus Conclusion (iii) is drawn for mutagenicity and carcinogenicity. However, the risk assessment indicates that risks are already very low. This should be taken into account when considering the adequacy of existing controls and the feasibility and practicability of further specific risk reduction measures.

Combined exposure
Combined exposure was not assessed because of low additional impact to human health.

Human health (risks from physico-chemical properties)

Conclusion (**ii)** There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.

Conclusion (ii) applies to all scenarios.

The report provides the summary of the comprehensive risk assessment of the substance 2,3-Epoxypropyltrimethylammonium chloride (EPTAC) It has been prepared by Finland in the frame of Council Regulation (EEC) No. 793/93 on the evaluation and control of the risks of existing substances, following the principles for assessment of the risks to man and the environment, laid down in Commission Regulation (EC) No. 1488/94.

The evaluation considers the emissions and the resulting exposure to the environment and the human populations in all life cycle steps. Following the exposure assessment, the environmental risk characterisation for each protection goal in the aquatic, terrestrial and atmospheric compartment has been determined.
The environmental risk assessment concludes that there is concern for the aquatic ecosystem (including marine environment) from exposure arising from cationisation of starch with wet process at local scale for five sites. There is no concern for the atmosphere, the terrestrial ecosystem and micro-organisms in the sewage treatment plant.

For human health the scenarios for occupational exposure, consumer exposure and humans exposed via the environment have been examined and the possible risks have been identified.
The human health risk assessment concludes that there is concern for workers with regard to mutagenicity, carcinogenicity and sensitisation from all worker scenarios and with regard to repeated dose toxicity from sampling and laboratory work during production of EPTAC. There is also concern for humans exposed via the environment with regard to carcinogenicity and mutagenicity, however the risks are very low. For consumers and for human health (physico-chemical properties) there is no concern.

The conclusions of this report will lead to risk reduction measures to be proposed by the Commission's committee on risk reduction strategies set up in support of Council Regulation (EEC) N. 793/93.