(3-CHLORO-2-HYDROXYPROPYL)TRIMETHYLAMMONIUM CHLORIDE

CAS No: 3327-22-8

EINECS No: 222-048-3

SUMMARY RISK ASSESSMENT

Final report 2008

Finland

FINAL APPROVED VERSION

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

Contact (human health): National Product Control Agency for Welfare and Health
Chemicals Department
Mr. Marko Kuittinen
e-mail: Marko.Kuittinen@sttv.fi
Fax: +358 (9) 3967 2768

Contact (environment): Finnish Environment Institute
Expert Services Department
Chemicals Division
Mrs Jaana Heiskanen
e-mail:Jaana.K.Heiskanen@ymparisto.fi
Fax: +358 (20) 490 2591

Date of Last Literature Search :	**2003**
Review of report by MS Technical Experts finalised:	**5/2008**
Final report:	**2008**

PREFACE

This report provides a summary, with conclusions, of the risk assessment report of the substance (3-Chloro-2-hydroxypropyl)trimethylammonium chloride (CHPTAC) 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.

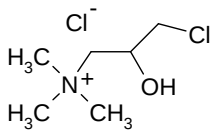
CONTENTS

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: 3327-22-8
EINECS Number: 222-048-3
IUPAC Name: (3-Chloro-2-hydroxypropyl)trimethylammonium chloride
Molecular formula: $C_6H_{15}ONCl_2$



Structural formula:
Molecular weight: 188.10 g/mol
Synonyms: CHPTAC, 1-Propanaminium, 3-chloro-2-hydroxy-N,N,N-trimethyl chloride

1.2. PURITY/IMPURITIES, ADDITIVES

The typical concentration of technical CHPTAC is 50-70 % water solution. The solubility of the substance limits higher water concentrations. Main impurities are:

Table 1.1: CHPTAC impurities

CAS No.	Chemical Name	Content
34004-36-9	2,3-dihydroxypropyltrimethylammonium chloride (diol)	< 1.5 %
55636-09-4	Bis/trimethylammoniumchloride)-2-hydroxypropane	1.3 - 4 %
106-89-8	Epichlorohydrin	<10 ppm
96-23-1	1,3-dichloro-2-propanol	< 20 ppm, exceptionally < 50 ppm

The pH in the commercial product is slightly acidic, typically 3-5. In such acidic pH CHPTAC is resistant against hydrolysis and does not need any special stabilizing agent.

1.3. PHYSICO-CHEMICAL PROPERTIES

Pure CHPTAC is at 20 °C and 101.3 kPa a solid and water-soluble substance. 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	180.5 °C
Boiling point	190 °C - 209 °C
Relative density	1.11
Vapour pressure	$< 10^{-3}$ Pa
Water solubility	835.2 $\pm$ 9.9 g/l
Partition coefficient n-octanol/water (log value)	$P_{ow} < 0.03$ or $\log P_{ow} < -1.5$
Granulometry	-
Conversion factors	-
Flash point	-
Autoflammability	Not self-ignitable
Flammability	Not highly flammable
Explosive properties	No explosive properties
Oxidizing properties	Not likely oxidising
Viscosity	-
Henry's constant	$< 2.25 \cdot 10^{-7}$ Pa m^3/mol
Surface tension	72.8 mN/m

1.4. CLASSIFICATION

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

Classification: Carc. Cat 3, R40, R52-53

Labelling: Xn, R:40-52/53

S-phrases: S: 36/37-61

2. GENERAL INFORMATION ON EXPOSURE

CHPTAC was produced at five sites within the EU in 1996. Production volumes for the five producers ranged from 187 to 8360 tons per plant during 1994-1996. In 1998 one plant ceased its production. Total production volume in 1996 was 21 069 t and in 1999 slightly higher i.e. 22 847 tons. Total consumption volume including both import and export was 20 960 tons in 1996, 23 087 tons in 1999 and 23 695 tons in 2001.

CHPTAC is almost totally used for cationisation of starch. From the total consumption volume 95 % was used for cationisation of starch in 2001 and 5 % for synthesis of carnitine salts (1-Propanaminium, 3-carboxy-2-hydroxy-N,N,N-trimethyl salts), quaternisation of guar, protein (and/or protein derivatives) and cellulose.). Cationised starches are added in paper to give paper better surface quality and to improve paper strength. The total number of sites using CHPTAC or EPTAC was 22 in 2001. Volumes of CHPTAC used by single plant ranged from 2.9 tons to 7947 tons in 2001 and EPTAC from 8.5 tons to 1611 tons.

3. ENVIRONMENT

3.1. ENVIRONMENTAL EXPOSURE

3.1.1. Environmental releases

CHPTAC may be released into the environment during its production and industrial use but also during use of EPTAC (2,3-epoxypropyltrimethylammonium chloride, CAS 3033-77-0). 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 releases of EPTAC independent of which 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.

Exposure is assessed for six scenarios:

1) Production
2) Cationisation of starch with CHPTAC and EPTAC (industrial use scenario 1)
3) Use of starch with residual CHPTAC in paper making (industrial use scenario 2, cases 1-3)
   - high grade board for books, case 2
   - printing and writing paper, case 3
   - food grade board, case 3
4) Residual CHPTAC and EPTAC in paper recycling (industrial use scenario 3)
5) Use of starch residual CHPTAC in formulation of Alkyl Ketene emulsions (AKD) (industrial use scenario 4)
6) Other uses of CHPTAC and EPTAC (industrial use scenario 5)

3.1.2. Environmental fate

CHPTAC is highly soluble in water (835.2 ± 9.9 g/l at 20°C), has low vapour pressure (10^{-3} Pa at 20 - 150°C) and low log K_{ow} (< -1.5). Calculated Henry's law constant of < $2.25 \cdot 10^{-7}$ Pa m^3/mol indicates that CHPTAC does not volatize from water to air.

Under aqueous conditions, CHPTAC undergoes abiotic degradation to form EPTAC with half-life of 21 days at 12°C and pH 7.8. As the degradation product EPTAC is more toxic than CHPTAC, all CHPTAC releases at regional and continental scale has been converted to EPTAC and taken into account in the regional and continental assessment in EPTAC Risk Assessment Report.

In standard OECD studies (a modified Sturm test, OECD 301B, and an STP simulation study, OECD 303A), CHPTAC was not readily biodegradable, although there was some evidence in other non-standard tests. The mean primary degradation of CHPTAC was 28 ± 14.3 % in the OECD 303A simulation study, from which the removal rate constant was calculated to be 0.065 h^{-1}, which is close to the value 0.1 h-1 applicable to substances considered as inherently biodegradable. In this risk assessment CHPTAC can be regarded as inherently biodegradable, but not fulfilling the criteria set in the TGD. No degradation studies have been carried out for CHPTAC in soil. As the substance is regarded as inherently biodegradable but not fulfilling the criteria, a degradation half-life of 300 day in soil will be assumed.

CHPTAC is expected to have a low bioaccumulation potential to biota. Bioconcentration factors (BCFs) were calculated for fish and worm (1.41 l/kg and 3.36 kg/kg) based on the log K_{ow} (<-1.5). Adsorption to sludge at the wastewater treatment plant is assumed to be low. Base on known properties of the substance, CHPTAC is expected to distribute mainly to receiving water.

3.1.3. Environmental concentrations

Local concentrations

Based on site-specific information there are three production sites where no emissions to waste water treatment plant exist. In addition, the production of CHPTAC was ceased at site A2 in 1998. For the remaining production site A1, small releases to waste water will occur. Local concentration in freshwater from this site has been calculated by taking biodegradation (30.6%) and adsorption (0.8 %) into account at the municipal WWTP.

For the cationisation of starch (industrial use scenario 1) $PECs_{local}$ have been calculated from the measured WWTP effluent concentrations (nine sites). Concerning three sites where no monitoring data was available PECs have been calculated by using the release factor of 2.2 %, which is from a another starch cationisation plant. In addition 30.6 % biodegradation and 0.8 % adsorption have been taken into account.

Releases due to residual levels of CHPTAC in the cationised starch used in the production of paper and board (industrial use scenario 2, case 1) have been estimated to be 6.85 kg/day from the wet-end use at plant which produces 800 000 tons board per year. Predicted concentration was calculated to be 0.0110 mg/l (i.e. 11.0 µg/l) in the surface water. For comparison, local concentration was also calculated for a smaller mill which resulted PEC value of 0.0248mg/l (i.e. 24.8µg/l).

CHPTAC releases from production of printing and writing paper (case 2) have been estimated to be 5.165 kg/day. For this case a local concentration of 0.0083mg/l (i.e. 8.3µg/l) has been calculated for surface water and for a smaller mill PEC_{local} was 0.0199 mg/l (i.e. 19.9µg/l).

As the dosage used for food grade board purpose (case 3) is usually lower than in cases 1 and 2, no local estimation has been carried out.

Releases due to residual levels of CHPTAC in recovered printing and writing paper material used in recycling plant (incl. deinking process) have been estimated to be 0.049 kg/day (industrial use scenario 3). CHPTAC 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 1.2 µg/l in the surface water.

At the AKD formulation plant the release of cationic starch could be 15 t/y, when using an TGD emission factor of 2 % to waste water. The concentration of CHPTAC in the receiving water was calculated to be 0.77 µg/l.

Industry has provided monitoring data on two small sites, which use CHPTAC 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, which has provided site-specific information on releases. A local PEC for surface water from this site was calculated to be 9.67 µg/l.

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 CHPTAC. The acute toxicity test results of CHPTAC 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 0.51 mg/l with an assessment factor of 10. This results a PNEC of 51 µg/l for the fresh water organisms.

According to the TGD an assessment factor of 100 could be use to derive PNEC when emission takes place only a few times a year i.e. an intermittent release. This may happen as a result of batch process. In extrapolating to such a PNEC only short-term effects need to be considered. Thus, PNEC will be derived using the lowest acute EC50 164 mg/l and the assessment factor of 100. This results a $PNEC_{aquatic}$ of 1640 µg/l for intermittent use.

PNEC for micro-organisms can be derived from the activated sludge respiration inhibition test. As no EC_{50}-value could be found in the test with the highest concentration tested, a test concentration of 1032 mg/l, where 10 % inhibition was observed, will be used as EC_{10}-value for the PNEC derivation. 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 103 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 0.116 mg/kg, when using fresh water toxicity data for CHPTAC and a suspended matter-water partition coefficient (2.62 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 0.068 mg/kg**,** when using fresh water toxicity data for CHPTAC and a soil-water partition coefficient (2.26 m^3/m^3).

Atmosphere

There is no toxicity data available on CHPTAC via atmospheric exposure. Concerning abiotic effects CHPTAC 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 CHPTAC. However, as CHPTAC has low vapour pressure and small Henry's law constant, it is not expected that CHPTAC could have effect on global warming.

3.2.2. PBT assessment

According to existing data and assessment of inherent PBT -properties it can be concluded that CHPTAC can not be regarded as a PBT-substance nor vPvB –substance since it does not meet the B criterion. CHPTAC is considered potentially persistent under neutral and acidic aquatic environmental conditions, thus meeting the screening P-criterion. Also T-criterion can be seen fulfilled regarding human toxicity endpoints due to toxicity of the degradation product of CHPTAC.

3.3. RISK CHARACTERISATION

3.3.1. Aquatic compartment and sediment

Local risk characterisation

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

CHPTAC is mainly used for starch cationisation, where at four starch cationisation sites risk ratios are higher than one. Starch cationisation sites presented in Tables 3.1 and 3.2 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 CHPTAC 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 3.1: Site-specific PECs in surface water and sediment (based on measured CHPTAC effluent conc.) and corresponding PEC/PNEC ratios from starch cationisation.

Site	PEC_{local} (µg/l)	$PEC_{sediment}$ (mg/kg)	$PEC/PNEC_{aquatic\ (\&\ sediment)}$
CHPTAC users			
B3	< 1.14	< 2.59E-03	< 0.023
B4	< 16.8	< 0.0382	< 0.329
B5	7.5	0.017	0.146

Site	PEC_{local} (µg/l)	$PEC_{sediment}$ (mg/kg)	PEC/PNEC $_{aquatic\ (\&\ sediment)}$
B14	4	9.11E-03	0.078
B17	< 8.37	< 0.0191	< 0.16
B21	14	0.0318	0.274
B25	90.9	0.207	1.78
EPTAC users			
B16	< 7.12	< 0.0162	< 0.14
B 18	< 3.95E-05	< 9E-05	< 7.75E-04
B 19	-	-	- *

* This site has been closed at the end of 2002

Table 3.2: Site-specific PECs in surface water and sediment and corresponding PEC/PNECratios from starch cationisation. At these sites CHPTAC have not been measured from the waste water, but there are other site-specific information available.

Site	PEC_{local} (µg/l)	$PEC_{sediment}$ (mg/kg)	PEC/PNEC $_{aquatic\ (\&\ sediment)}$
CHPTAC users			
B10	251	0.572	4.92
B23	7549	17.2	148
B26 [1)]	-	-	-
EPTAC users			
B9	383	0.875	7.53

1) 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 one indicating no concern for the aquatic compartment.

Regional risk characterisation

Regional risk characterisation has not been carried out as the risks posed by CHPTAC at the regional scale will be considered in the risk assessment of EPTAC.

Wastewater treatment plant

For CHPTAC production sites the PEC/PNEC ratios for micro-organisms at WWTP are lower than one. PEC/PNEC ratios are lower than 1 for all use scenarios, and therefore there is no risk to micro-organisms.

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 for four sites with wet process (Industrial use 1) at the local scale (i.e. sites B9, B10, B23 and B25).

From these four starch cationisation sites, which have risk ratio higher than one, only one site (B25) has monitoring data on CHPTAC releases to waste water. However, the detection limit of CHPTAC from waste water effluent (2 mg/l) has been rather high compared to PNEC (0.051 mg/l l). Use of lower detection limit might decrease risks from this site. For those three sites where no monitoring data is available (B9, B10 and B23), releases have been calculated with an actual emission factor from a starch cationisation site with highest release factor (2.2 %). 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, cationisation of starch for seven sites with dry process (B6, B11, B12, B13, B15, B22 and B28) and for eight sites with wet process (B3, B4, B5, B14, B16, B17, B18, B21) (Industrial use 1), 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 CHPTAC 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.

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 CHPTAC no significant exposure to the

atmosphere is expected. CHPTAC 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.

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 CHPTAC would not bioconcentrate in high degree (see section 3.1.7). 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.

4.1.1. Inhalation exposure

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

As CHPTAC is a non-volatile organic salt handled in water solutions, inhalation exposure to this chemical does not occur. In loading operations where 70% water solution of this chemical is handled, EASE estimation for exposure is 0-0.04 mg/m3 (0-0.07 ppm).

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.

4.1.2. Dermal exposure

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

The CHPTAC manufacturing process is a closed 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 60 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 0.5-5 mg/person/day in sampling and 1 to 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 CHPTAC 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.

Table 4.1A: 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/m[3]	Method[2]	Unit mg/m[3]	Method [2]	Unit mg/m[3]	Method [2]	Unit mg/m[3]	Method [2]
Production										
Loading/Unloading (CHPTAC conc. 70%)	Daily	2	-	-	-	-	0.04[3]	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 EASE estimate in bagging and lower estimate of EASE in maintenance and clean-up

Table 4.1B: 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 (CHPTAC conc. 70%)										
Sampling	Daily	0.5	Intermittent	0.07-0.7	210	-	-	150	15[b]	EASE
Laboratory work	Daily	4	Intermittent	0.07-0.7	420	-	-	300	30[b]	EASE
Maintenance and clean-up	Weekly	4	Incidental	0-0.07	840	-	-	60	6[b]	EASE
Loading/Unloading	Daily	2	Incidental	0-0.07	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-prod. 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 15 mg/kg, CHPTAC conc. 450 mg/kg for RWC; EPTAC conc. 3 mg/kg, CHPTAC conc. 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	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 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

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.

Most of the indirect exposure was estimated to come from leaf crops and drinking water.

Table 4.2. Consumer exposure to CHPTAC

Product	Scenario	Total exposure
Food packaging	Transfer to product from wet packaging	0.00003 µg/kg bw
Children's books	Small children chewing a book, which can lead to ingestion or skin exposure.	0.06-0.16 µg/kg bw
Copy paper and news papers	Skin exposure from paper surface.	0.6 µg/day
Cosmetics	CHPTAC residues in cosmetic products used on skin and scalp. Rinse-off products	0.007-0.29 µg/kg bw 0.07-2.9 ng/kg b.w

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 CHPTAC, averages based on the EUSES estimations (local scenario) for nine monitored sites.

Source of exposure and concentration	Daily dose (mg/kg of b.w)
Drinking water, 18.8 µg/l (average of nine sites)	0.0006 (nine sites)
Fish, 0.0223 mg/kg	0.000036 mg/kg
Leaf crops	0.00164
Root crops	$1.33E^{-5}$
Meat	$2.51E^{-8}$
Milk	$3.37E^{-7}$
Air	$3.09E^{-6}$
Total	**0.00229 mg/kg**

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. Based on the findings of the abiotic degradations test, it is assumed that up to almost 50 % of CHPTAC could be converted to EPTAC in 24 hours in pH 7.4. However, it should be kept in mind that the conversion is a reaction affected by a multitude of factors and that no direct conclusion can be drawn from it to in regards CHPTAC's behaviour to biological systems.

4.3.2. Acute toxicity

For oral acute toxicity, an LD50 of 2170 mg/kg and an LD50 dermal of >2348 mg/kg is taken to the risk characterisation. For dermal toxicity, an LD50 value of over 2000 mg/kg can be derived based on limit tests. Although there is relatively little data on acute toxicity via inhalation, based on available information it appears that toxicity via that route is low enough not to warrant classification. Based on limited data, no signs of toxicity were seen in rats exposed to 12.5 mg/l CHPTAC for seven hours.

4.3.3. Irritation

Skin

CHPTAC is not irritating based on the skin irritation tests described above. CHPTAC did not cause skin irritation.

Eye

CHPTAC caused slight irritation when administered at a maximum concentration of 65 %. The irritation scores are not sufficient to warrant classification according to the criteria. If tests were conducted with pure CHPTAC, higher irritation scores could be expected, possibly warranting classification.

4.3.4. Corrosivity

CHPTAC is not corrosive based on the results of irritation tests.

4.3.5. Sensitisation

CHPTAC is not a sensitiser.

4.3.6. Repeated dose toxicity

Based on an oral 28-day limit study, there were only slight morphological changes seen in the kidney proximal tubules. The microscopical changes in kidneys appear similar to those seen with EPTAC. In addition to the renal histopathological changes, there was a 20% increase in relative kidney weights in male animals. A slight decrease in left testis weight was noted when CHPTAC was administered dermally at a maximum dose of 5750 mg/kg/week. The 28-day study will be used for the determination of the lowest effect level and inhalation routes, because of the uncertainties in the definition of a reliable LOAEL from the two-year study, due to the dosing regime (twice a week). Moreover, the oral study used rat as the test animal, which is preferable species to mice. Based on the kidney changes seen in the 28-day study the LOAEL for CHPTAC after oral administration is 1085 mg/kg/day. For inhalation, a systemic LOAEL of 543 mg/kg will be used, based on the assumption that 50 % of the dose is absorbed from the gastro-intestinal tract.

4.3.7. Mutagenicity

All in vitro tests mutagenicity tests conducted with CHPTAC have given a positive result. However, the interpretation of these results is somewhat complicated because the purity of the CHPTAC used was sometimes questionable. Looking at the results of the AMES tests, the typically positive strains TA1535 and TA100 are the same which were positive also with 2,3-epoxypropyltrimethylammonium chloride (EPTAC). There can be at least two explanations for this: If technical grade CHPTAC was used it contained approximately 2-3 % EPTAC as an impurity. Even when purified CHPTAC is used, it converts pH dependently to the more reactive epoxy form. At pH 9, approximately 80 % of CHPTAC are converted to EPTAC and at the typical *in vitro* test system pH, 7.5, up to 50 % conversion could occur ((Mendrala, 1984a), (Raisio Chemicals, 2004a)). Moreover, (Richold et al., 1982a) showed that when the vehicle for the substance was buffered to 4.0 or 5.5. No mutagenic activity was seen in TA1535, which was typically positive. Therefore, even if CHPTAC might not be a mutagen itself a partial conversion to the mutagenic EPTAC could occur in the body. However, it is unclear, how CHPTAC behaves on entering the body. There is no information about the possible toxicokinetic fate of this substance. In the mouse micronucleus test *in vivo*, the result was negative when almost pure (99.7 %) CHPTAC was administered to rats in a 69 % water solution with at pH 3-6. Since the test substance was administered by an intraperitoneal injection, at least a couple options of its fate can be envisaged. When given via the intraperitoneal route, a substance may enter the general circulation directly from the intraperitoneal space or it may also enter the liver via the portal vein and be biotransformed there before reaching rest of organs. Thus, CHPTAC may either enter the general circulation unchanged or it was biotransformed and extracted to the bile without ever entering the systemic circulation or the bone marrow. Because there is no toxicokinetic knowledge of CHPTAC it is difficult to draw any definitive conclusions of its mutagenicity in vivo. An additional in vivo mutagenicity test (e.g. UDS) in another tissue would help to solve this issue.

Table 4.4 Mutagenicity of CHPTAC in mammalian cells

Test system	Concentrations	Result	Reference
Clastogenic effects in lymphocyte chromosomes (*in vitro*)	from 0.016, 0.049, 0.148, 0.444, 1.333, 4.000 12.000 mg/ml	Positive	(Wilmer, 1984)
Rat liver UDS (*in vitro*)	0.001, 0.00316, 0.01, 0.0316, 0.1, 0.316, 1.0, 3.16 and 10 mg/ml	Positive	(Mendrala, 1984c)
Chinese hamster ovary cell mutation (*in vitro*)	0.1, 1.0, 5.0, 10.0, 25.0 and 50.0 mg/ml	Positive	(Mendrala, 1984b)
Mouse micronucleus test (*in vivo*)	147 mg/kg	Negative	(Degussa, 1992)

Conclusion

CHPTAC is an *in vitro* mutagen. Mutagenicity in vivo was negative in the mouse micronucleus test. Because only one study is available, there is uncertainty whether CHPTAC is an *in vivo* mutagen. No definitive conclusion can be drawn for this end-point at the moment. However, for the purposes of this risk assessment it is not seen necessary to produce further in vivo data on this end-point, because it is likely that this information would not help to refine the risk reduction measures.

4.3.8. Carcinogenicity

Under the conditions of exposure, CHPTAC is not a local carcinogen in mice when administered via skin but there is a possibility that it is a systemic carcinogen based on the increased incidence of bronchiolo-alveolar tumours. However, the evidence on the systemic tumours is relatively weak and partly confounded by the duration of the study, which was longer than usually. Because there is not enough information on the mutagenicity in vivo, a directly genotoxic non-threshold mode of action of these tumours cannot be ruled out. Classification and labelling working group agreed to classify CHPTAC as Xn; Carc. Cat. 3; R40.

4.3.9. Toxicity for reproduction

No definite conclusion can be drawn for reproductive toxicity at this state.

4.4. RISK CHARACTERISATION [1]

4.4.1. Risk characterisation for workers

Table 4.5 Overview of the conclusions with respect to occupational risk characterisation

[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.

		Acute toxicity		Sensitisation	Repeated dose toxicity Systemic		Mutagenicity	Carcinogenicity§	Reproductive toxicity
		Dermal	Inhalation		Dermal	Inhalation			
Production									
Sampling	MOS	>15384	-	-	4177	-	-	*523*	-
	Concl.	ii	ii	ii	ii	ii	i on hold	ii	i on hold
Laboratory work	MOS	>7692	-	-	2088	-	-	*211*	-
	Concl.	ii	ii	ii	ii	ii	i on hold	ii	i on hold
Maintenance	MOS	>2.2x10^5	-	-	10860	-	-	*1100*	-
	Concl.	ii	ii	ii	ii	ii	i on hold	ii	i on hold
Loading/ Unloading and sampling after loading	MOS	5.0x10^5	>3.1x10^5	-	27150		-	*2750*	-
	Concl.	ii	ii	ii	ii	ii	i on hold	ii	i on hold
Use Wet cationising									
Sampling	MOS	-	-	[0]	*-/ [395]*	-	-	[0]	*[-]*
	Concl.	ii	ii	[iii]	ii	ii	i on hold	iii	i on hold
Laboratory work	MOS	-	-	[0]	*-/ [176]*	-	-	[0]	*[-]*
	Concl.	ii	ii	[iii]	ii	ii	i on hold	iii	i on hold
Maintenance	MOS	-	-	[0]	*-/ [527]*	-	-	[0]	*[-]*
	Concl.	ii	ii	[iii]	ii	ii	i on hold	iii	i on hold
Filling	MOS	6.6x10^8	-	[0]	3.2x10^7 *[3.1x10^6]*	-	-	[0]	*[-]*
	Concl.	ii	ii	[iii]	ii	ii	i on hold	iii	i on hold
Use Dry cationising or wet cationising with drying									
Bagging	MOS	3.3x10^7	>6.3x10^6	[0]	1.6x10^6 *[1.8x10^5]*	2.6x10^6 *[7524]*	-	[0]	*[-]*
	Concl.	ii	ii	[iii]	ii	ii	i on hold	iii	i on hold
Clean-up work	MOS	3.3x10^8	>6.3x10^5	[0]	1.6x10^6 *[1.8x10^5]*	2.6x10^5 *[752]*	-	[0]	*[-]*
	Concl.	ii	ii	[iii]	ii	ii	i on hold	iii	i on hold
Laboratory work	MOS	6.6x10^7	-	[0]	3.2x10^6 *[3.1x10^5]*	-	-	[0]	*[-]*
	Concl.	ii	ii	[iii]	ii	ii	i on hold	iii	i on hold
Sampling	MOS	2.0x10^9	-	[0]	6.3x10^6 *[6.1x10^5]*	-	-	[0]	*[-]*
	Concl.	ii	ii	[iii]	ii	ii	i on hold	iii	i on hold
Maintenance work	MOS	3.3x10^8	>6.3x10^5	[0]	1.6x10^6 *[1.8x10^5]*	2.6x10^5 *[752]*	-	[0]	*[-]*
	Concl.	ii	ii	[iii]	ii	ii	i on hold	iii	i on hold

§Production scenario MOEs are based on a theoretical systemic benchmark dose obtained by extrapolation from one dermal carcinogenicity study in mice with CHPTAC. MOSs for use scenarios are based on data from EPTAC are shown in brackets.

4.4.2. Risk characterisation for consumers

In consumer exposure, exposure is only to negligible amount of residual CHPTAC or converted EPTAC.

Table 4.6 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 79000. Conclusion ii in all scenarios.		-	-	Lowest MOS found in cosmetics scenario: MOS of 120000. Conclusion i on hold.
	Concl.			ii			i on hold	ii	
Children's books	MOS			-			-	-	
	Concl.			ii			i on hold	ii	
Copy paper & newspapers	MOS			-			-	-	
	Concl.			ii			i on hold	ii	
Cosmetics	MOS			-			-	-	
	Concl.			ii			i on hold	ii	

4.4.3. Risk characterisation for exposure via the environment

Because no actual emission CHPTAC calculations were available, EUSES modelling was conducted to estimate indirect exposure resulting from cationising process. No degradation has been assumed in the model.

According to EUSES calculations, the combined daily internal dose is 1 ug/kg with the greatest exposures coming from leaf crops and drinking water. However, the assessed total exposure could be an overestimation.

Table 4.7 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 543000 Conclusion ii in all scenarios.		**-**	*[55000]*	24000* Conclusion i on hold.
	Concl.			ii			**ii**	**ii**	

* The MOS was derived using a controversial modelled exposure figure. Therefore this MOS is likely not likely to have relevance to the general population.

4.5. HUMAN HEALTH (PHYSICO-CHEMICAL PROPERTIES)

4.5.1. Effects assessment: Hazard identification

Explosivity

CHPTAC is not explosive.

Flammability

CHPTAC is not flammable.

Oxidizing potential

CHPTAC is not oxidising.

4.5.2. Risk characterisation

Not relevant.

5. RESULTS [2]

5.1. 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 for four sites with wet process (Industrial use 1) at the local scale (i.e. sites B9, B10, B23 and B25).

From these four starch cationisation sites, which have risk ratio higher than one, only one site (B25) has monitoring data on CHPTAC releases to waste water. However, the detection limit of CHPTAC from waste water effluent (2 mg/l) has been rather high compared to PNEC (0.051 mg/l l). Use of lower detection limit might decrease risks from this site. For those three sites where no monitoring data is available (B9, B10 and B23), releases have been calculated with an emission factor from a starch cationisation site with highest release factor (2.2 %). 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, cationisation of starch for seven sites with dry process (B6, B11, B12, B13, B15, B22 and B28) and for eight sites with wet process (B3, B4, B5, B14, B16, B17, B18, B21) (Industrial use 1), 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 (ii) 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.

5.2. 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 to all use scenarios because of concerns for mutagenicity, carcinogenicity and sensitisation.due to the intentional conversion of CHPTAC to EPTAC.

Conclusion ii is drawn in the CHPTAC production scenario. In CHPTAC production phase, a category 2 carcinogen, namely epichlorohydrin, is used in the synthesis. Due to the presence of epichlorohydrin, sufficient risk reduction measures need to be in place already during synthesis. These are considered sufficient also for limiting the theoretical risk from CHPTAC exposure during manufacturing phase. In the end product, formation of EPTAC is controlled by pH. Therefore, due to current risk reduction measures in the production phase the risk is foreseen as minor and thus, conclusion ii is drawn.

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 (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.

Combined exposure
This section was not separately assessed due to negligible additive significance from consumer exposure.

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 th comprehensive risk assessment of the substance (3-Chloro-2-hydroxypropyl)trimethylammonium chloride (CHPTAC) 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 four 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 for all use scenarios as a consequence of exposure to EPTAC due to the intentional conversion of CHPTAC to EPTAC during use. For consumers, for humans exposed via the environment 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.