Australian Government
Department of Health and Aged Care
Australian Industrial Chemicals Introduction Scheme

Hexamine and related chemicals

Evaluation statement

15 April 2024

Draft

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AICIS evaluation statement

Subject of the evaluation

Hexamine and related chemicals

Chemicals in this evaluation

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3,5,7-Triaza-1-azoniatricyclo[3.3.1.1^{3,7}]decane, 1-(3-chloro-2-propenyl)-, chloride	4080-31-3
3,5,7-Triaza-1-azoniatricyclo[3.3.1.1^{3,7}]decane, 1-(3-chloro-2-propenyl)-, chloride, (Z)-	51229-78-8
1,3,5,7-Tetraazatricyclo[3.3.1.1^{3,7}]decane, hydrochloride	58713-21-6
3,5,7-Triaza-1-azoniatricyclo[3.3.1.1^{3,7}]decane, 1-methyl-, chloride (1:1)	76902-90-4

Reason for the evaluation

Evaluation Selection Analysis indicated a potential environmental risk.

Parameters of evaluation

These chemicals are a group of structurally related chemicals with a hexamine moiety that are listed on the Australian Inventory of Industrial Chemicals (the Inventory). This evaluation considers the environmental risks associated with the identified industrial uses of these chemicals. These chemicals have been assessed for:

- default Australian introduction volume of 100 tonnes/year, except for methenamine, which considers a volume of 1,000 tonnes/year
- industrial uses listed in the ‘Summary of Use’ section
- expected emission into sewage treatment plants from consumer and commercial uses.

Uses of hexamines in oil extraction and processing have not been assessed in this evaluation.

Summary of evaluation

Summary of introduction, use and end use

These chemicals may be used to manufacture, or be found in, a variety of consumer, household and industrial products, including:

- adhesives and sealants
- construction products (resins)
- plastic and polymer products
- lubricants and hydraulic fluids
- paints and coatings
- laundry washing and cleaning products
- leather treatment and dyes
- metalworking fluids
- personal care and cosmetics
- pulp and paper products
- toners.

Available information indicates that methenamine (CAS RN 100-97-0) may be used in volumes up to 1,000 tonnes/year in Australia. No other Australian use volume information is available for these chemicals in this evaluation.

Limited international use volume information is available for Quaternium-15 (CAS RNs 4080-31-3 and 51229-78-8). Previous maximum use volumes for Quaternium-15 ranged from 100–227 tonnes/year in the United States and Canada. No volume information is available for other chemicals in this evaluation.

Environment

Summary of environmental hazard characteristics

According to domestic environmental hazard thresholds and based on the available data these chemicals are:

- not Persistent (not P)
- not Bioaccumulative (not B)
- not Toxic (not T).

Environmental hazard classification

Sufficient ecotoxicity information is available to classify the hazards of some chemicals in this evaluation according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) (UNECE 2017). Physical hazards and health hazards have not been considered in this evaluation.

Isomers of Quaternium-15 (CAS RNs 4080-31-3 and 51229-78-8) satisfy the GHS criteria as follows:

Environmental Hazard	Hazard Category	Hazard Statement
Hazardous to the aquatic environment (acute/short-term)	Aquatic Acute 2	H401: Toxic to aquatic life
Hazardous to the aquatic environment (long-term)	Aquatic Chronic 3	H412: Harmful to aquatic life with long lasting effects

Methenamine (CAS RN 100-87-0) and methenamine hydrochloride (CAS RN 58713-21-6) do not satisfy the classification criteria for aquatic hazards. No adequate ecotoxicity information

is available for methenammonium chloride (CAS RN 76902-90-4) and so no classification has been made.

Summary of environmental risk

These chemicals are expected to be released into wastewaters through the use of industrial and commercial products. Ultimately, these chemicals are released to the aquatic environment after treatment in sewage treatment plants (STP).

These chemicals are not persistent in the environment and have a low potential for bioaccumulation. These chemicals and their hydrolysis products are not toxic according to domestic threshold values.

Based on the worst-case exposure scenarios, the concentrations of these chemicals in STP effluent are expected to be below levels of concern. The calculated risk quotient values (RQ) for these chemicals are less than 1. Therefore, the current use of these chemicals is not expected to pose a significant risk to the environment.

Conclusions

The Executive Director proposes to be satisfied that the identified risks to the environment from the introduction and use of the industrial chemicals can be managed.

Note:

1. Obligations to report additional information about hazards under *Section 100* of the *Industrial Chemicals Act 2019* apply.
2. You should be aware of your obligations under environmental, workplace health and safety and poisons legislation as adopted by the relevant state or territory.

Supporting information

Grouping rationale

This evaluation considers the environmental risks of five chemicals that contain the hexamine moiety. This tetrahedral cage-like structure of four nitrogen atoms linked by methylene groups is also known as hexamethylenetetramine.

The evaluation has been performed as a group, as these chemicals are structurally similar and are all expected to be susceptible to hydrolysis to produce formaldehyde (CAS RN 50-00-0), a reactive chemical with biocidal activity.

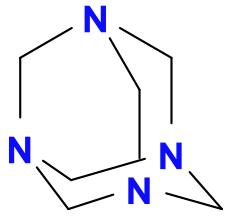
The Evaluation Selection Analysis for this chemical group indicated a potential risk to aquatic organisms for some group members.

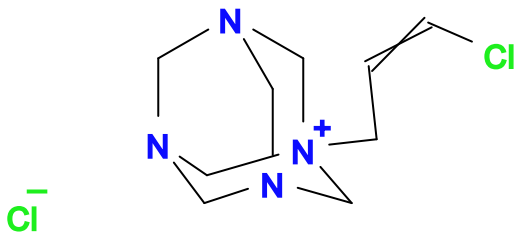
Chemical identity

All five chemicals included in this evaluation contain the hexamine moiety, a tetrahedral cage molecular structure where the four vertices are occupied by nitrogen atoms linked by methylene groups:

Chemical name	1,3,5,7-Tetraazatricyclo[3.3.1.1^{3},^{7}]decane
CAS RN	100-97-0
Synonyms	Hexamine Hexamethylenetetramine Methenamine (INCI) Urotropine
Molecular formula	C6H12N4
Molecular weight (g/mol)	140.19
SMILES (canonical)	N12CN3CN(C1)CN(C2)C3
Chemical description	-

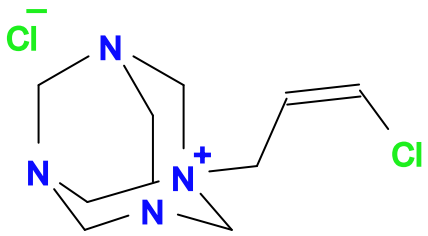
Structural formula:

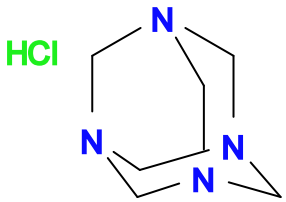


Chemical name	3,5,7-Triaza-1-azoniatricyclo[3.3.1.1^{3,7}]decane, 1-(3-chloro-2-propenyl)-, chloride
CAS RN	4080-31-3
Synonyms	1-(3-Chloroallyl)-3,5,7-triaza-1-azoniaadamantane chloride 1-(3-chloroallyl)-hexaminium chloride Methenamine 3-chloroallylochloride N-(3-Chloroallyl)hexaminium chloride Quaternium-15 (INCI)
Molecular formula	C9H16ClN4.Cl
Molecular weight (g/mol)	251.15
SMILES (canonical)	[Cl-].ClC=CC[N+]12CN3CN(CN(C3)C1)C2
Chemical description	This CAS RN is a mixture of cis- and trans- isomers.
Structural formula:	

Chemical name	3,5,7-Triaza-1-azoniatricyclo[3.3.1.1^{3,7}]decane, 1-(3-chloro-2-propenyl)-, chloride, (Z)-
CAS RN	51229-78-8
Synonyms	1-[(2Z)-3-chloroprop-2-en-1-yl]-1,3,5,7-tetraazatricyclo[3.3.1.1^{3,7}]decan-1-ium chloride 1-((Z)-3-Chloroallyl)-1,3,5,7-tetraazaadamantan-1-ium chloride 1-(3-Chloroallyl)-3,5,7-triaza-1-azoiaadamantane chloride, cis- (cis-CTAC) Chloroallyl methenamine chloride Hexamethylenetetramine chloroallyl chloride
Molecular formula	C9H16ClN4.Cl
Molecular weight (g/mol)	251.15
SMILES (canonical)	C(/C=C\Cl)[N+]12CN3CN(C1)CN(C2)C3.[Cl-]
Chemical description	The cis-isomer of Quaternium-15.

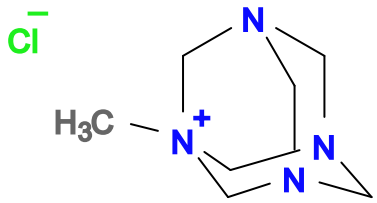
Structural formula:



Chemical name	1,3,5,7-Tetraazatricyclo[3.3.1.1^{3,7}]decane, hydrochloride
CAS RN	58713-21-6
Synonyms	Methenamine hydrochloride
	Hexamethylenetetramine hydrochloride
	Pellurin
	Urotropine hydrochloride
Molecular formula	C6H12N4.xClH
Molecular weight (g/mol)	176.65
SMILES (canonical)	C1N2CN3CN1CN(C2)C3.Cl
Chemical description	-
Structural formula:	

Chemical name	3,5,7-Triaza-1-azoniatricyclo[3.3.1.1^{3,7}]decane, 1-methyl-, chloride (1:1)
CAS RN	76902-90-4
Synonyms	1-Methyl-3,5,7-triaza-1-azoniaadamantane chloride
	1-methyl-3,5,7-triaza-1-azoniatricyclo[3.3.1.1^{3,7}]decane;chloride
	3,5,7-triaza-1-azoniatricyclo[3.3.1.1^{3,7}]decane deriv.
	Methenammonium chloride
Molecular formula	C7H15N4.Cl
Molecular weight (g/mol)	190.67
SMILES (canonical)	[Cl-].N12CN3CN(C1)C[N+](C)(C2)C3
Chemical description	-

Structural formula:



Relevant physical and chemical properties

Information on methenamine properties was retrieved from the European Union (EU) Risk Assessment Report for methenamine (ECB 2008) and the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) registration dossier for methenamine (REACH n.d.-a). Information on Quaternium-15 was retrieved from the United States Environmental Protection Agency (US EPA) reregistration eligibility decision report on "Dowicil®CTAC" (trade name) (US EPA 1995). Information for methenammonium chloride was calculated using EPI Suite (US EPA 2017a). Henry's Law constants were calculated using EPISUITE or from experimental water solubility and vapour pressure data, where available (US EPA 2017a):

Chemical	Methenamine	Quaternium-15	Methenammonium chloride
Physical form	solid	solid	solid
Melting point (in ºC)	>270 (sublimes at 230) (exp.)	178–210 (exp.)	174 (calc.)
Boiling point (in ºC)	N/A	N/A	417 (calc.)
Vapour pressure (Pa)	0.05 @ 20°C (exp.)	<1.0 x 10^{-5} (calc.)	1.2 x 10^{-5} (calc.)
Water solubility (g/L)	667 (exp.)	1272 (exp.)	≥1,000 (calc.)
Henry's law constant (Pa·m^3/mol at 25 ºC)	1.05 x 10^{-5} (calc.)	<1.97 x 10^{-9} (calc.)	2.29 x 10^{-9} (calc.)
Ionisable in the environment?	Yes	Yes	Yes
pKa	Various	N/A	N/A
log K_{ow}	-2.18 (exp.)	-0.1 (exp.)	<-4.0 (calc.)

Chemicals in this evaluation are readily soluble in water. Based on their Henry's law constants these chemicals are unlikely to volatilise from water.

All chemicals in this evaluation are expected to be protonated or positively charged in the environmental pH range (pH 4–9). For methenamine, QSAR Toolbox contains experimental pKa endpoints of 4.85, 5.13, and 8.87 (LMC 2020). Different pKa values for the protonation of methenamine have also been reported based on different calculation methods. Chemaxon estimates a basic pKa = 5.88, while the OASIS regression method estimates a basic

pKa = 9.18 (LMC 2020). A pKa value of 8.4 was reported in the EU Risk Assessment Report for methenamine (ECB 2008).

Introduction and use

Australia

Methenamine was reported to have a total volume of 100–1,000 tonnes, based on information provided to the former National Industrial Chemicals Notification and Assessment Scheme (NICNAS 2013). A conservative introduction volume of 1,000 tonnes of methenamine is used in this evaluation.

No Australian volume data are available for other chemicals in this evaluation. The default introduction volume of 100 tonnes/year has been used for these chemicals.

No information about specific uses of these chemicals has been identified in Australia.

International

Methenamine is predominantly used as a hardener in the production of phenolic resins and as a curing or vulcanisation agent in the manufacture of rubber and other polymers (ECB 2008; US EPA 2020a). Minor industrial uses are in fuel tablets for camping stoves and as intermediate for the production of explosives (ECB 2008). Methenamine may have limited use in personal care products as a preservative (Personal Care Products Council n.d.). Products that methenamine may be involved in the production of include:

- adhesives and sealants
- construction products (particle board)
- plastic and polymer products
- lubricants and hydraulic fluids
- paints and coatings.

Non-industrial uses of methenamine in pharmaceuticals, registered pesticides or as a food additive (ECB 2008; NCBI n.d.-b) are not considered in this evaluation.

Quaternium-15 (as cis-isomer or as isomer mixture) has reported use as a preservative in a wide variety of household and industrial products (NCBI n.d.-a; n.d.-c), including:

- adhesives and sealants
- construction products
- laundry washing and cleaning products
- leather treatment and dyes
- lubricants and hydraulic fluids
- metalworking fluids
- paints and coatings
- personal care products (including cosmetics)
- pulp and paper
- toners.

Methenammonium chloride has limited uses as antistatic agent in cosmetics (EC n.d.), in anti-viral paints, coatings and food packaging products (NCBI n.d.-d).

Methenamine hydrochloride has reported uses in hobby and craft products (NCBI n.d.-e). It is also an impurity in the Quaternium-15 mixture, where it can reach concentrations up to 7% (SCCS 2011).

Methenamine is used at very high volumes. The reported use volume of methenamine in the USA was 22,700–45,400 tonnes/year over the years 2016–2019 (US EPA 2020a). Production of methenamine in Europe was estimated at 30,000 tonnes/year in 2008, and the current (year 2024) REACH registration volume is 10,000–100,000 tonnes/year (ECB 2008; REACH n.d.-a). Use volumes of methenamine in Japan varied between 1,000–10,000 tonnes/year over the years 2019–2021 (NITE n.d.).

Production volumes of Quaternium-15 were reported as 4.54–227 tonnes/year in the USA in 1998 (NCBI n.d.-a; n.d.-c). Canadian import volumes of Quaternium-15 in 2011 were reported to be 10–100 tonnes/year for the isomer mixture and 1–10 tonnes/year for the cis isomer (ECCC 2021).

No use volume information for methenammonium chloride or methenamine hydrochloride has been identified.

Uses of chemicals in this evaluation in resource extraction (including oil drilling and processing) have not been evaluated in this evaluation.

Existing Australian regulatory controls

Environment

Use of these chemicals in this group is not subject to any specific national environmental regulations.

International regulatory status

Industrial chemicals that have uses as preservatives are commonly regulated under specific pesticide or biocide legislation in other international jurisdictions.

United Nations

Chemicals in this group are not listed as Persistent Organic Pollutants (UNEP 2001), ozone depleting substances (UNEP 1987), or hazardous substance for the purpose of international trade (UNEP & FAO 1998).

OECD

Methenamine was sponsored by Germany under the Cooperative Chemicals Assessment Programme (CoCAP). The 24th SIDS Initial Assessment Meeting (SIAM 24) in 2007 concluded that methenamine presents a low potential for risk to the environment (OECD 2007).

European Union

Quaternium-15 (cis-isomer; CAS RN 51229-76-8) is listed under Annex II of the European Cosmetic products regulation and is prohibited for use in cosmetics (EC 2019; 2023b).

Biocidal use of Quaternium-15 (as cis-isomer or as isomer mixture) is no longer supported under the European Biocidal Products Regulation (EC 2023a). Previously the registrations covered the categories “preservatives for products during storage”, “slimicides”, and “working or cutting fluid preservatives”.

United States of America

There are no active pesticide registrations for Quaternium-15 in the United States of America (US EPA n.d.). The most recent pesticide registrations for Quaternium-15 were voluntarily cancelled in 2019 (US EPA 2019; 2020b).

Environmental exposure

Chemicals in this evaluation will be released into the environment when products containing these chemicals are used. Main emissions to the environment are through wastewater that will be treated in STPs.

Chemicals in this evaluation may be found in household and commercial products available for use in Australia. Formulated products on the Australian market are assumed not to differ significantly from those available internationally.

The dominant use of methenamine is in the production of resins, polymers and adhesives. Most of the methenamine is expected to either be consumed during these processes or captured in the final product. Some fraction of methenamine may also be released to wastewaters. During resin production, the final resin does not contain methenamine but rather its breakdown products ammonia and formaldehyde, which are produced during the thermal polymerization process and remain embedded in the final product (ECB 2008). Resin and polymer production using methenamine may release the formaldehyde product directly to air. However, the short atmospheric lifetime of formaldehyde suggests that this route of exposure will not result in significant risk to the environment (NICNAS 2006).

For Quaternium-15 and other chemicals reported in this evaluation, the amount of chemical released to wastewater depends on the specific end use of products. Use in products such as paper and pulp processing and personal care products and cleaning products would result in full release of the chemical to wastewater. Comparatively, use in hydraulic fluids, cutting fluids, adhesives, sealants, paints and coatings are expected to result in low releases of this chemical to wastewater.

Environmental fate

Dissolution, speciation and partitioning

These chemicals will mainly partition to soil and water, with negligible amounts going to air or sediments.

Chemicals in this group are readily soluble in water, with solubilities ranging from 667 g/L to being miscible in water. All chemicals in this evaluation are expected to be protonated or positively charged in the environmental pH range (pH 4–9). Values of Henry’s law constant for all chemicals are $<1.0 \times 10^{-4}$ Pa m^3/mol, which indicates very low potential for volatilisation from surface waters.

These chemicals are very mobile in soil, as they exhibit low potential for adsorption to organic matter. Estimated K_{OC} values range from 10 L/kg for methenamine to 34.05 L/kg for Quaternium-15 isomers (US EPA 2017a). These values suggest that these chemicals have little potential for partitioning to sediments in aquatic environments. This estimate does not consider charge effects on adsorption, so the actual adsorption of Quaternium-15 to soils and sediments may be underestimated (Sigmund et al. 2022).

Fugacity modelling (level III) using direct emissions to water suggests when chemicals in this evaluation are released directly into waters, they will predominantly stay in water (>99%), with minimal partitioning to sediment (0.24–0.37%) and negligible partitioning to air (US EPA 2017).

All chemicals in this evaluation will release formaldehyde and ammonium cations through hydrolysis in aquatic media and acidic soils. Formaldehyde is readily water soluble and highly volatile, although its volatility from water is considered moderate (Henry's Law constant 0.022–0.034 Pa m^3 /mol). Most of the formaldehyde released into water is expected to stay dissolved in water. Formaldehyde that is released to air is expected to stay in the air (NICNAS 2006). Ammonium cations are ubiquitous in the environment and are expected to stay in water.

Degradation

These chemicals are not persistent in the environment and are inherently biodegradable. All chemicals in this group hydrolyse in water to produce formaldehyde, ammonium cations and other degradation products.

Hydrolysis is expected to be the main degradation pathway of these chemicals. Breakdown of the hexamine moiety is fast in acidic media. However, unsubstituted hexamines may be slow to hydrolyse at pH 7 and above. The hydrolysis half-lives of methenamine were observed to be 1.6 hours at pH 2.0 and 13.8 hours at pH 5.8 and 37.5°C. No hydrolysis was observed at pH 7.4 (REACH n.d.-a). In comparison, Quaternium-15 hydrolysis half-lives of 1.1–2.7 days were reported for pH values ranging from pH 5 to pH 9 (US EPA 1995).

Hydrolysis of these chemicals will primarily produce formaldehyde and ammonium cations. Formaldehyde is not persistent in water, air, soils or sediments (NICNAS 2006). Ammonium cations are ubiquitous in the environment and are not considered further.

Substituted hexamines may produce other hydrolysis products such as:

- methylamine (CAS RN 74-89-5), a chemical previously assessed as having a low risk to the environment (NICNAS 2020)
- cis- and trans-3-chloroallylamine (CAS RN 4152 99 2) (US EPA 1995). These chemicals are predicted to be moderately volatile from water, and short lived in the atmosphere (US EPA 2017b).

Biodegradation screening tests indicate that these chemicals are inherently biodegradable. The mean degradation of methenamine after 28 days in a 24-lab ring test was 29% according to oxygen consumption (ThOD) and 39% according to dissolved organic carbon (DOC) removal (EC 1985). Other methenamine degradation results range from 27–87% according to ThOD and 54–98% according to DOC removal (Painter and King 1986). Unspecified tests with cis-Quaternium-15 indicate 38–60% degradation of this chemical after 28 days (REACH n.d.-c).

Bioaccumulation

These chemicals are not expected to bioaccumulate in organisms. Chemicals in this evaluation all have experimental or estimated log K_{OW} values <0, which is below the domestic threshold for bioaccumulation (DCCEEW 2022).

Environmental transport

These chemicals are unlikely to undergo long range environmental transport as they are not persistent in the aquatic environment. Transport of these chemicals through the air is not expected based on their low Henry's Law Constant values.

Predicted environmental concentration (PEC)

The PECs for chemicals in the evaluation are estimated at 63.6 µg/L for methenamine and 31.8 µg/L for all others. These PECs are derived from available use volumes for these chemicals and conservative worst case assumptions.

Monitoring data have not been found for any chemicals in this group. Therefore, environmental concentrations in surface waters were calculated based on estimated discharges from sewage treatment plants according to the various uses and volumes of products.

The emission scenario for methenamine considers an annual volume of 1,000 tonnes used in particle board and other construction products (release factor = 0.2). Other potential uses of methenamine such as paints and coatings are expected to have lower release factors and have not been included. The total volume of methenamine predicted to go into wastewaters is 200 tonnes/year.

The emission scenario for Quaternium-15 isomers considers a default volume of 100 tonnes/year. High release uses, such as paper and pulp processing (release factor = 1) are possible for this chemical. The total volume of Quaternium-15 expected to go into wastewaters is conservatively 100 tonnes/year.

Using SimpleTreat 3.1 and inherent biodegradability for removal of these chemicals in sewage treatment plants (Struijs 1996), the highest predicted concentrations in effluents of STPs are:

- 63.6 µg/L for methenamine
- 31.8 µg/L for Quaternium-15 isomers

The above concentrations are worst case predicted values since they do not consider any hydrolysis occurring before these chemicals enter the water treatment facilities. They also do not consider any increased removal due to cationic charges on these chemicals.

As a worst case, the exposure scenarios for methenamine hydrochloride and methenammonium chloride are assumed to be the same as Quaternium-15.

Environmental effects

Effects on aquatic life

Chemicals in this evaluation undergo hydrolysis to form formaldehyde, ammonium cations and other products. Organisms in the aquatic environment will be exposed to a combination of these chemicals and their breakdown products.

Ecotoxicity information is available for formaldehyde (Eisentraeger et al. 2003; NICNAS 2006; OECD 2002; REACH n.d.-b). Ammonium cations are considered to be ubiquitous in the environment, although ammonia in solution can be harmful to fish at elevated pH > 8 (McCormick et al. 1984). Methylamine has previously been evaluated as low risk (NICNAS 2020), with acute aquatic ecotoxicity results >31 mg/L under buffered conditions (OECD 2011). Calculated acute endpoints for 3-chloroallylamine are all >15 mg/L (US EPA 2017b), which is above the pivotal endpoint for Quaternium-15.

Acute toxicity

Acute toxicity data are available for two chemicals in this group: methenamine and cis-Quaternium-15 (CAS RN 51229-78-8). The ecotoxicity of methenamine hydrochloride is expected to be similar to the ecotoxicity of methenamine. Quaternium-15 is expected to have higher ecotoxicity than methenammonium chloride due to its chlorallyl functional group.

The following acute endpoints are sourced from the REACH registration dossiers for the respective compounds (REACH n.d.-a; n.d.-c). Endpoints for the hydrolysis product formaldehyde (CAS RN 50 00 0) are also shown for comparison (Eisentraeger et al. 2003; NICNAS 2006; OECD 2002):

Taxon	Chemical	Endpoint	Method
Fish	Methenamine	96 h LC50 = 41,000 mg/L	*Lepomis macrochirus* (bluegill) Nominal concentrations US EPA 660
Fish	Quaternium-15 (cis-isomer)	96 h LC50 = 26 mg/L	*Unknown species* Semi-static OECD TG 203
Fish	Formaldehyde	96 h LC50 = 6.7 mg/L	*Morone saxatilis* (striped bass) Semi-static, nominal concentrations
Invertebrate	Methenamine	48 h EC50 = 36,000 mg/L	*Daphnia magna* (Water flea) Immobilisation Nominal concentrations ATSM
Invertebrate	Quaternium-15 (cis-isomer)	48 h EC50 = 25.8 mg/L	*Daphnia magna* (water flea) Immobilisation OECD TG 202
Invertebrate	Formaldehyde	48 h EC50 = 5.8 mg/L	*Daphnia pulex* (water flea) Immobilisation Static, nominal concentrations OECD TG 202
Algae	Methenamine	14 d EC50 = 3,000 mg/L	*Raphidocelis subcapitata* (green algae) Growth rate Nominal concentrations US EPA
Algae	Quaternium-15 (cis-isomer)	72 h EC50 = 1.5 mg/L	*Raphidocelis subcapitata* (green algae) Growth rate OECD TG 201
Algae	Formaldehyde	72 h EC50 = 4.89 mg/L	*Desmodesmus subspicatus* (green algae) Growth rate Static, nominal concentrations OECD TG 201

Chronic toxicity

Chronic endpoints for fish are not available for any chemical in this group. The only chronic toxicity available is a 21-d reproduction test for Quaternium-15 (cis-isomer) on an unspecified invertebrate species (REACH n.d.-c) and the no observed effect concentration (NOEC) values from the algae tests for methenamine and Quaternium-15 (cis-isomer), which can be used to evaluate the chronic toxicity to this taxon (EPHC 2009). Chronic toxicity data for formaldehyde are also shown for a comparison (OECD 2002; REACH n.d.-b):

Taxon	Chemical	Endpoint	Method
Invertebrates	Quaternium-15 (cis-isomer)	21 d NOEC = 19.8 mg/L	*Unknown sp.,* Reproduction Semi-static OECD TG 211
Invertebrates	Formaldehyde	21 d NOEC = 6.4 mg/L	*Daphnia magna* (water flea) Reproduction Semi-static, nominal concentrations OECD TG 211
Algae	Methenamine	14 d NOEC = 1,500 mg/L	*Raphidocelis subcapitata* (green algae) Growth rate, nominal concentrations US EPA
Algae	Quaternium-15 (cis-isomer)	72 h NOEC = 0.35 mg/L	*Raphidocelis subcapitata* (green algae) Growth rate OECD TG 201

Effects on terrestrial life

Information about the toxicity of Quaternium-15 to birds is available. Quaternium-15 (mixed isomer) is slightly toxic to bird via oral exposures. Median lethal dose (LD50) values for acute oral toxicity were ≥1440 mg/kg for mallard duck (US EPA 1995). LD50 values for subacute dietary toxicity were ≥2,645 ppm for bobwhite quail and mallard duck (US EPA 1995).

Effects on sediment dwelling life

No ecotoxicity data are available for any of these chemicals in this group.

Endocrine effects/activity

No data were identified. Endocrine activity is not expected for any of these chemicals in this group, and none of their degradation products have known endocrine activity in aquatic organisms.

Predicted no-effect concentration (PNEC)

PNEC values have been calculated for methenamine and for the Quaternium-15 isomers.

The lowest chronic endpoints are for the algae *R. subcapitata* with endpoint values of 1,500 mg/L for methenamine and 0.35 mg/L for Quaternium-15.

Given that chronic ecotoxicity data for methenamine are available only for one trophic level, an assessment factor of 100 is used for this chemical. This results in a predicted no effect concentration (PNEC) of 15 mg/L for methenamine.

The toxicity of Quaternium-15 to algae is one order of magnitude lower than endpoints for other trophic levels. This suggests that algae are the most sensitive trophic level to Quaternium-15. As acute and chronic data are available for algae, an assessment factor of 10 has been used (EPHC 2009). This results in a PNEC of 0.035 mg/L (35 µg/L) for Quaternium-15.

Categorisation of environmental hazard

The categorisation of the environmental hazards of the assessed chemical according to domestic environmental hazard thresholds is presented below:

Persistence

Not Persistent (Not P). Based on measured hydrolysis and evidence of biodegradation, all chemicals in this group are categorised as Not Persistent.

Bioaccumulation

Not Bioaccumulative (Not B). Based on log K_{OW} values <4.2, all chemicals in this group are categorised as Not Bioaccumulative.

Toxicity

Not Toxic (Not T). Based on available aquatic toxicity endpoints above domestic threshold values for these chemicals and their degradation products, all chemicals in this group are categorised as Not Toxic.

Environmental risk characterisation

The environmental risk assessment of these chemicals in this evaluation considers releases from their industrial uses into wastewater as the main release pathway. After treatment in STPs, the remaining chemicals in the effluent may be released into the aquatic environment.

The concentrations of releases in effluents of STPs were determined according to the exposure scenarios identified in the exposure section above.

The following Risk Quotients (RQ = PEC ÷ PNEC) have been calculated for emissions of methenamine and Quaternium 15 isomers into the aquatic environment through STP effluents under these two scenarios:

Chemical	PEC	PNEC	RQ
Methenamine	63.6 µg/L	15,000 µg/L	<0.01
Quaternium-15 isomers	31.8 µg/L	35 µg/L	0.91

The RQs for methenamine hydrochloride and methenammonium chloride are expected to be lower than Quaternium-15 isomers.

Calculated RQ values less than 1 indicate that these chemicals in this evaluation are not expected to pose a significant risk to the aquatic environment. Environmental concentrations are expected to be below levels likely to cause harmful effects in typical environmental conditions.

Uncertainty

This evaluation was conducted based on a set of information that may be incomplete or limited in scope. Some relatively common data limitations can be addressed through use of conservative assumptions (OECD 2019) or quantitative adjustments such as assessment factors (OECD 1995). Others must be addressed qualitatively, or on a case-by-case basis (OECD 2019).

The most consequential areas of uncertainty for this evaluation are:

- The estimated RQ values are likely to be overestimates of risk. The PEC calculation did not consider the removal of these chemicals due to the hydrolytic breakdown of these chemicals or any removal to sludge, soil, or sediment through charge effects.
- Introduction volume data for all chemicals in this group except methenamine are unknown. The default introduction volume of 100 tonnes/year for the other chemicals could be an overestimate resulting in overestimated RQ values; and
- No environmental monitoring data for these chemicals or the non-formaldehyde degradants were identified. In their absence, standard exposure modelling was required to calculate a worst-case PEC.

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