Updated EHS Summary of Didecyl Dimethyl Ammonium Chloride (DDAC) for the MA TURA Science Advisory Board Meeting – March 11, 2021

CAS #: 7173-51-5	**NAME:** Didecyl Dimethyl Ammonium Chloride **Synonym[1]s:** DDAC, Didecyldimethylammonium chloride, N-decyl-N,N-dimethyldecan-1-aminium chloride **RTECS #[2]:** **EINECS #[3]:** 230-525-2 **Molecular Weight[4]**: 362.1 g/mol **Molecular Formula[5]:** $C_{22}H_{48}ClN$ **Pesticide Code:** 69149 **Chemical Family:** Quaternary amines **Related CAS #'s:** 20256-56-8 (Parent) (see list at end of summary) **EPA Group 1 Quat Cluster:** The alkyl or hydroxyalkyl (straight chain) substituted Quats
PHYSICAL CHARACTERISTICS	
Primary Use	Cleaning products, disinfectants, bactericidal and fungicidal biocide. Several applications including, swimming pools and aquatic areas, industrial processes, wood treatment, healthcare and food handling and storage. ***Comment:*** The first sentence in the following paragraph is inaccurate, as the concentrate is not a "ready-to-use" product. Therefore the following edits are suggested: Products containing DDAC are diluted from concentrates into liquid ready-to-use formulations with the active ingredient typically ranging from 0.08 to 0.5% DDAC. ~~formulated as liquid ready-to-use soluble concentrates and the ratio of DDAC in various end-use products can range anywhere from 0.08% to 80% DDAC~~. 279 registered products contain DDAC, but 5 main structurally similar quaternary ammonium compounds. Production volume data from 2011 through 2014 indicate that approximately 99 million pounds of DDAC are sold per year in the United States[1]. "Due to their amphiphilic nature, QACs act as detergents or surface-active agents against microorganisms. QACs target bacterial cell membranes through electrostatic interactions between the positively charged head group and negatively charged cytoplasmic membrane, adsorption, and then permeation of side chains into the intramembrane region. The lipid layer of enveloped viruses makes them sensitive to the hydrophobic activity of QACs" (Hora, 2020).

Physical state, odor at room temperature & pressure	Clear yellow liquid with an ethanolic or mushroom-like odor [in aqueous solution][1] White slight yellowish solid powder with a mushroom-like odor[6]
Melting point; Boiling point	**MP:** 228.81˚C[1] **BP:** >180 °C; decomposes before boiling at 1 atm /OECD Guideline 103[7]
Solubility	Completely soluble in water[1]
Specific Gravity	

SAFETY/PHYSICAL HAZARDS	
Vapor Pressure	2.33 x 10^{-11} mm Hg[1] <4.3X10-5 mm Hg at 25 °C, <1.1X10-5 mm Hg at 20 °C /OECD Guideline 104[6]
Flammability	
Flashpoint	A study was conducted to determine the flash point of the test substance 'didecyldimethylammonium chloride' (DDAC), using a closed crucible according to DIN ISO 2719, EU Method A.9 (Flash-Point). The test substance was been determined to have a flash point of 26.4°C at 103.6 kPa[6].
Flammability Rating	
Auto Ignition Point	
Combustion products	
Explosivity (UEL, LEL, shock sensitive)	
Oxidizer	
Corrosivity	**Industrial Concentrates:** 50-80% of active QAC ingredient. Acute Tox, Inhalation – Category 2 Skin Corrosion/Irritation – Category 1 Serious eye damage/eye irritation – Category 1 Hazardous to the aquatic environment, acute & chronic hazard – Cat 1 **Ready-to-use Products:** .08-0.5% of active QAC ingredient. Skin corrosion/irritation – Category 2 Serious eye damage/eye irritation – Category 1 ***Comment***: Previous version reflected a Ready-to-use product concentration of up to 20%; this in inaccurate. As revised above, typically Ready-to-use products do not exceed 0.5%. Additionally, these products, at concentrations below 0.5% **are rarely if ever,** classified as Toxicity Category 1, "Serious Eye Damage." Category 2 is more common for dilute products.
pH	pH = 6.8 to 6.9 at 25 °C in a 29.5% water solution[6]
Reactivity	
Viscosity	
Odor Threshold	
Particle size, shape, respirable fraction	
Other physical hazards associated with process: Heat, gases under	When heated to decomposition it emits very toxic fumes of nitrogen oxides, ammonia, and hydrogen chloride[8]

pressure, noise, vibration, ergonomic hazard	
HEALTH HAZARDS	
Acute Toxicity	

Oral LD_{50}	**EPA Toxicity Category II**[1] LD_{50} (combined) = 238 mg/kg[1] LD_{50} (combined) = 262 mg/kg[1]
Dermal LD_{50}	**EPA Toxicity Category III**[1] LD_{50} (male) = 3140 mg/kg[1] LD_{50} (female) = 2730 mg/kg[1] LD_{50} (combined) = 2930 mg/kg[1]
Inhalation LC_{50}	**EPA Toxicity Category II**[1] LC_{50} = 0.07 mg/L[1] ECHA (2015a,b) did not classify either DDAC or C12 – C16 ADBAC as acutely toxic via the inhalation route, as inhalation of DDAC or C12–C16 ADBAC was not considered a potential exposure pathway because both DDAC and C12 – C16 ADBAC have low volatility and manufacturers recommend only spraying with large, non-inhalable, droplets (i.e., MMAD > 40 µM). (Luz et al., 2020)
Intraperitoneal LD_{50}	
Chronic or Sub-chronic Toxicity	
IARC rating	Not classified by IARC Monographs, Volumes 1-123
Carcinogenicity	The carcinogenic effects of DDAC and C12–C16 ADBAC have been investigated in multiple chronic oral toxicity studies conducted with mice and rats. All available studies indicate that neither DDAC nor ADBAC are carcinogenic via the oral exposure route, which is consistent with the conclusions of both EPA (2006a,b) and ECHA (2015a,b). Furthermore, EPA's Cancer Assessment Review Committee classified C12–C16 ADBAC and DDAC as "not likely to be carcinogenic to humans" and "Group E – evidence of non-carcinogenicity for humans," respectively (EPA, 2018). (Luz et al., 2020) In a GLP-compliant OECD TG 453 study, male and female Sprague Dawley rats were administered 0, 700, 1500, or 3000 ppm DDAC (40% a.i.) chronically via a feed admixture for 104 weeks (CIT, 2008a, as cited in ECHA, 2015a). Based on body weight and feed consumption, the received doses of DDAC were calculated to be 12.6, 27.3, and 55.4 mg a.i./kg-day for males, and 15.7, 33.8, and 69.5 mg a.i./kg-day for females. No DDAC-related mortality, clinical signs of toxicity, macroscopic observations, or alterations in any hematological, biochemical, or urinalysis parameters were reported for either sex at any dose. During the first 13 weeks of the study, average body weight and weight gain were slightly lower in the highest exposure group

	(3000 ppm) compared to the control, which correlated with reduced food consumption in female rats. Non-neoplastic lesions were observed in the mesenteric lymph nodes and Peyer's patches; however, the study author concluded that these findings are consistent with continued exposure to an irritant. No neoplastic lesions were observed in any examined tissue, indicating a lack of carcinogenicity (Luz, et al., 2020). In a second chronic oral toxicity study that adhered to OCSPP 870.4300, male and female Sprague Dawley rats (60/sex/dose) were exposed to 0, 300, 750, or 1500 ppm DDAC (80.8% purity) in a feed admixture for 2 years (BRRC, 1991b, as cited in EPA, 2006c & ECHA, 2015a, 2019a). Equivalent doses were calculated to be 13, 32, and 64 mg a.i./kg-day for males, and 16, 41, and 83 mg a.i./kg-day for females. Mean body weight was significantly reduced (<10%) in male and female rats in the highest treatment group. Additional treatment-related effects, all occurring in the highest exposure group, included increased incidence of hemosiderosis, sinusoidal blood, and histiocytosis in the mesenteric lymph nodes. A slight increase in the incidence of interstitial cell adenomas in testes was observed in the mid-dose (17.9% vs. 5% in controls) and high-dose (11.7% vs. 5% in controls) groups. However, this effect did not display strong dose dependency and was within the range of historical control data for the laboratory; thus, the effect was not considered DDAC-related by EPA (2006c). (Luz et al., 2020) In a third chronic oral feed study adhering to OCSPP 870.4300, male and female CD-1 mice (60/sex/dose) were exposed to 0, 100, 500, or 1000 ppm DDAC (purity 80.8%; BRRC, 1991c, as cited in EPA, 2006c & ECHA, 2015a, 2019a) for 78 weeks. Equivalent doses were calculated to be 15.0, 76.3, and 155.5 mg/kg-day for males, and 18.6, 93.1, and 193.1 mg/kg-day for females. No DDAC-related mortality, clinical signs of toxicity, alterations in hematology, gross pathological findings, or incidence of non-neoplastic or neoplastic lesions were observed in either sex at any dose. The only reported treatment-related effect was a decrease in mean body weight in high-dose (1000 ppm) male and female mice (Luz et al., 2020).
Neurotoxicity	The EPA's Hazard and Science Policy Council (HASPOC) reviewed the toxicology database for DDAC and ADBAC and waived the requirements for immunotoxicity and acute and subchronic neurotoxicity testing based on the weight of evidence that strongly suggests that these studies would not result in a lower point of departure for use in risk assessment (EPA, 2016a,b). (Luz et al., 2020)

	Neurotoxicity studies were waived because no clinical signs or evidence of neurotoxicity have been reported in the toxicology databases for DDAC or C12–C16 ADBAC (EPA, 2016b). (Luz et al., 2020)
Developmental/Reproductive Toxicity	In a two-generation reproductive toxicity study that adhered to OCSPP 870.3800, rats were continuously dosed with a feed admixture of 0, 300, 750, or 1500 ppm DDAC (purity 80.8%) starting during the premating period and continuing through the F2 generation (BRRC, 1991g, as cited in EPA, 2006c & ECHA, 2015a, 2019a). Equivalent received doses were reported to be 20, 50, and 103 mg/kg-day for males, and 24, 61, and 122 mg/kg-day for females. No mortality or clinical signs of toxicity were reported for either sex at any dose or in any generation. The parental NOAELs for DDAC were reported to be 50 mg/kg-day for males and 61 mg/kg-day for females based upon a reduction in mean body weight, weight gain, and food consumption in both sexes in the highest exposure group (1500 ppm). No specific reproductive toxicity was observed. NOAELs for developmental effects were 50 mg/kg-day (male) and 61 mg/kg-day (female) DDAC, based upon decreased mean pup body weight and decreased weight gain in the highest exposure group (1500 ppm). (Luz, et al., 2020) In a second GLP-compliant OECD TG 416 study (CIT, 2008b, as cited in ECHA, 2015a), Sprague Dawley rats (25/sex/dose) were continuously fed 0, 500, 1500, or 4000 ppm DDAC (40% a.i.). Equivalent received doses were 14, 39, and 109 mg a.i./kg-day for males, and 18, 51, and 137 mg a.i./kg-day for females. Dosing started 10 weeks prior to mating and ended upon weaning of the F2 generation. Exposure to 4000 ppm DDAC reduced body weight gain and food consumption in both the P0 and P1 parents, while no DDAC-related effects were observed at lower doses. No DDAC-related effects on mating, fertility, gestation, fecundity, delivery, or pre- or post-natal pup development were reported at any concentration for either generation. An increased incidence of adrenal gland hypertrophy was noted in high-dose (4000 ppm) P0 females, and a reduction in spleen weight was noted in high-dose F1 pups (but not in F2 pups). This study supports a parental NOAEL of 39 mg/kg-day for males and 51 mg/kg-day for females, and an unbounded NOAEL of 109 mg/kg-day for males and 137 mg/kg-day for females for reproductive toxicity. (Luz, et al., 2020) "Decreased reproductive performance in laboratory mice coincided with the introduction of a disinfectant containing both ADBAC and

DDAC. QACs were detected in caging material over a period of several months following cessation of disinfectant use. Breeding pairs exposed for six months to a QAC disinfectant exhibited decreases in fertility and fecundity: increased time to first litter, longer pregnancy intervals, fewer pups per litter and fewer pregnancies. Significant morbidity in near term dams was also observed. In summary, exposure to a common QAC disinfectant mixture significantly impaired reproductive health in mice."[9]

Comment: It is noteworthy that this is a non-guideline study and has not been subjected to assessment for data quality or reliability. The study evaluated doses without justification and with questionable relevance to human exposures.

"Breeding pairs exposed for six months to a QAC disinfectant exhibited decreases in fertility and fecundity: increased time to first litter, longer pregnancy intervals, fewer pups per litter and fewer pregnancies. Significant morbidity in near term dams was also observed. Exposure to a common QAC disinfectant mixture significantly impaired reproductive health in mice. The study demonstrated that ADBAC + DDAC exposure is toxic to both male and female fertility. Female mice exposed to ADBAC + DDAC exhibited decreased reproductive capacity with reduced ovulation and fewer estrus cycles. Male mice exposed to ADBAC + DDAC exhibited significantly decreased sperm concentration and motility."[10]

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"Neural tube defects (NTD) were seen in both rats and mice following ambient exposure to the QAC's containing disinfectant in the mouse room. NTDs were also observed in mice dosed with the disinfectant at 60 or 120 mg/kg/day in feed, or with ADBAC+DDAC chemical by gavage at 7.5, 15, or 30 mg/kg/day. Mice received ambient exposure for 2 weeks or ambient and gavage. NTDs were seen with ADBAC and DDAC dosed acutely by oral gavage, chronically in feed, and ambiently through the use of disinfectant in the mouse room. Both ambient and ambient plus gavage groups exhibited significantly increased levels of

NTDs compared with unexposed controls" (Hrubec, 2017).[11]

Comment: It is noteworthy that the above **authors misused the term "neural tube defect."** This term is applied to structural malformations observed at the end of gestation. The above study evaluated mouse fetuses at approximately gestation day 10.5. When pregnancy was allowed to continue to term, **there were no cases of neural tube defects.** The authors would have been correct to term their observations "apparent developmental delays."

Note also QAC industry critique of Hrubec 2017 study[12]

"Some QACs have historically been used in the US as the active compound in fertility control. In an in vitro screening of organic compounds, Holzaepfel et al. (1959) identified some QA salts as having high spermicidal activity, including benzylhexadecyldimethyl ammonium chloride, n-octadecyldimethylbenzyl ammonium chloride (C18), and alkyldimethylbenzyl ammonium chloride. A US patent from the 1970s describes QACs (including BACs, DADMACs, ATMACs, and QAC mixtures) as having the capability of controlling fertility if administered at the time of mating or within an effective period after mating (Dalgard and Coval, 1975). This patent described dog and rat studies that indicated QACs administered via the diet may be embryocidal, ovicidal, and/or spermicidal. Benzalkonium chloride is used as the active spermicidal ingredient in some sponges and vaginal creams and capsules currently sold in Europe (Aubeny et al., 2000; Creatsas et al., 2001; Pharma GDD website, accessed 2020). Its spermicidal mechanism of action occurs through destruction of the sperm cell plasma membrane (Creatsas et al., 2001). Plasma membrane disruption is also the general mechanism of action by which QACs, including benzalkonium chloride, are effective as preservatives, disinfectants, and biocides (Gilbert and Moore, 2005; Wessels and Ingmer, 2013)."[13]

Comment: It is noteworthy that these are all a non-guideline studies that have not been subjected to assessment for data quality or reliability. Their relevance in the evaluation of DDAC is questionable.

"The prenatal developmental toxicity potential of ADBAC and DDAC was evaluated in regulatory compliant studies. Pregnant female CD® rats (25/group) and New Zealand White rabbits (16/group) were administered ADBAC (0, 10, 30 or 100 mg/kg/day and 0, 1, 3 or 9 mg/kg/day, respectively), or DDAC (0, 1, 10 or 20 mg/kg/day and 0, 1, 3 or 10 mg/kg/day, respectively), by oral gavage on gestation days

	(GD) 6-15 for rats and GD 6-18 for rabbits. At scheduled termination (GD 21 for rats; GD 29 for rabbits), maternal necropsies were conducted and live fetuses were weighed and examined for external, visceral, and skeletal malformations and variations. Clinical signs of maternal toxicity were observed in rats and rabbits dosed with ADBAC, resulting in no- observed-adverse-effect levels (NOAELs) of 10 and 3 mg/kg/day, respectively. Despite the treatment-related maternal toxicity of ADBAC, the NOAEL for prenatal developmental toxicity was 100 and 9 mg/kg/day for rats and rabbits, respectively, the highest doses evaluated. Repeated oral doses of DDAC resulted in maternal toxicity in both species at the top two doses, with 25% mortality noted in rabbits at 10 mg/kg/day. No teratogenic effects were observed at any dose for either species. However, increased incidence of dead fetuses per litter and decreased fetal body weights were observed in rabbits at the maternally lethal dose of 10 mg/kg/day. The NOAEL for maternal toxicity of DDAC was 1 mg/kg/day for both species and the NOAEL for prenatal developmental toxicity was 20 and 3 mg/kg/day, for rats and rabbits, respectively." [14]
Genotoxicity/Mutagenicity	The genotoxicity and mutagenicity of DDAC and C12–C16 ADBAC has been investigated in a number of *in vitro* and *in vivo* test systems (Bacterial Reverse Mutation Test, Mammalian Cell Gene Mutation Test, Mammalian Chromosome Aberration Test, Unscheduled DNA Synthesis Assay, In Vivo Mammalian Bone Marrow Chromosome Aberration Test) that adhere to current OECD and OCSPP test guidelines. Collectively, available studies indicate that DDAC and C12–C16 ADBAC are non-mutagenic and non-clastogenic, and do not cause unscheduled DNA synthesis. The following table includes the genotoxicity study results for DDAC. (Luz, et al., 2020)

Genotoxicity/Mutagenicity (continued)

Test Substance (% a.i.)	Guideline/Test System	Tested Doses	Result	Reference
DDAC (50%)	OCSPP 870.5100 (Bacterial Reverse Mutation Test) *S. typhimurium* TA98, TA100, TA1535, TA1537, TA1538	3.9–1000 µg/plate (±S9 activation)	Negative	Institute of Toxicology (1982), as cited in EPA 2006c
DDAC (50%)	OECD 471 (Bacterial Reverse Mutation Test) *S. typhimurium* TA98, TA100, TA1535, TA1537	0.03–3.3 µg/plate (-S9 activation) 0.03–10 µg/plate (+S9 activation)	Negative	Notox (1990b), as cited in ECHA 2015a
DDAC (40%)	OECD 476 (In Vitro Mammalian Cell Gene Mutation Test) Mouse lymphoma L5178Y cells (thymidine kinase gene)	0.06–5 µg/mL (-S9 activation) 0.19–10 µg/mL (+S9 activation)	Negative	CIT 2002b, as cited in ECHA 2015a
DDAC (80.8%)	OCSPP 870.5300 (Mammalian Cell Forward Gene Mutation Assay) CHO cells	1.0–13.0 µg/mL (-S9 activation) 1.0–40.0 µg/mL (+S9 activation)	Negative	Hazleton Laboratories (1990a), as cited in EPA 2006c & ECHA 2015a
DDAC (80%)	OCSPP 870.5375 (In Vitro Mammalian Chromosome Aberration Test) CHO cells	2–16 µg/mL (-S9 activation) 1–8 µg/mL (+S9 activation)	Negative	Lonza Inc. (1986), as cited in EPA 2006c
DDAC (80.8%)	OCSPP 870.5550 (Unscheduled DNA Synthesis Assay) Rat hepatocytes	0.05–10 µg/mL	Negative	Hazleton Laboratories (1990b), as cited in EPA 2006c & ECHA 2015a

Abbreviations: a.i. = active ingredient; CHO = Chinese hamster ovary;

Endocrine Disruption	Females exposed to ADBAC + DDAC demonstrated significantly decreased ovulatory capacity, spent less time in estrus, and progressed through fewer estrus cycles compared to controls. ADBAC + DDAC may have reduced estrus length and frequency through disruption of estrogen-regulated processes. ADBAC + DDAC treated mice had significantly fewer estrus cycles over the evaluation period. This correlates directly with our 6 month breeding trial which observed significantly fewer litters produced in ADBAC + DDAC treated mice. These two findings reinforce that ADBAC + DDAC disrupt reproductive function in female mice (Melin, 2016).[15] ***Comment:*** It is noteworthy that this is a non-guideline study and has not been subjected to assessment for data quality or reliability. The study evaluated doses without justification and with questionable relevance to human exposures. "Based on a thorough review of all identified data pertinent to the potential endocrine activity and ED–mediated adversity of DDAC, it is concluded that the substance is not an endocrine disruptor according to the criteria laid down in Regulation (EU) 2018/605. There is no evidence for DDAC to cause adverse effects as a consequence of an endocrine mode of action."[16] See Excel download of EPA Comp Tox Data with active endocrine disruption assays listed.
Thyroid	
Immunotoxicity	Immunotoxicity study requirements were waived by HASPOC based on the fact that no hematology, clinical chemistry, organ weight, or histopathology indicators are present in the toxicology database for ADBAC to suggest ADBAC can cause immunotoxicity, while reductions in spleen weight and increased incidence of non-neoplastic lesions in the mesenteric lymph following exposure to DDAC occur secondary to irritation (Luz, et al., 2020). "DDAC induced significant irritancy (0.5 and 1%), evaluated by ear swelling in female Balb/c mice. Initial evaluation of the sensitization potential was conducted using the local lymph node assay (LLNA) at concentrations ranging from 0.0625–1%. A concentration dependent increase in lymphocyte proliferation was observed with a calculated EC3 value of 0.17%. Dermal exposure to DDAC did not induce increased production of IgE as evaluated by phenotypic analysis of draining lymph node B-cells (IgE + B220+) and measurement of total serum IgE levels.

	Additional phenotypic analyses revealed significant and dose-responsive increases in the absolute number of B-cells, CD4 + T-cells, CD8 + T-cells and dendritic cells in the draining lymph nodes, along with significant increases in the percentage of B-cells (0.25% and 1% DDAC) at Day 10 following 4 days of dermal exposure. There was also a significant and dose-responsive increase in the number of activated CD44 + CD4 + and CD8 + T-cells and CD86 + B-cells and dendritic cells following exposure to all concentrations of DDAC." "There was a significant increase in the percentage of B-cells in the absence of increasing IgE+ B-cells in the DLN and total IgE in the serum. TDI was included in these experiments as a chemical that induces a prototypical TH2 (IgE-mediated) hypersensitivity response. Although only a single concentration of TDI (1%) was included, it fell into the concentration range that was examined for DDAC, specifically activation percentages of the immune cell subsets examined. The percentage of activated CD8+ T cells in the DLN was higher for DDAC compared to TDI for all concentrations tested. In contrast, the percentage of activated B-cells in the DLN was strikingly higher for TDI than for any concentration of DDAC. These findings demonstrate a lack of increase in both local and total IgE, along with an increased percentage of activated CD8+ T-cells in the DLN following exposure; this data suggests that DDAC may induce a T-cell or TH1-mediated hypersensitivity response. Due to the emergence of a ''new generation'' of QAC that are structurally heterogeneous and potentially exhibit increased immunogenicity compared to their predecessors, it is imperative to analyze the immunotoxicological effects of these compounds. The immunological consequences of these types of mixed exposures has not thoroughly been studied" (Anderson, 2016).[11]
Liver	Systemic toxicity following repeated oral exposure to DDAC has been investigated in four subchronic 90-day studies conducted with beagles and rats, and in four chronic toxicity studies conducted with beagles, mice, and rats. Reported no-observed-adverse-effect levels (NOAELs) range from 10 to 93.1 mg/kg-day DDAC, with toxicological effects consistently characterized by reduced food consumption, reduced mean body weight, and reduced weight gain, which is consistent with the mode of action (MoA) of an irritating/corrosive chemical (EPA, 2006a,b,c,d; ECHA, 2015a,b). (Luz, et al., 2020) Significant decreases in percentage body weight (11% at 0.5% and 14% at 1%) were observed at Day 10 following a 4-day DDAC exposure

	regimen. Although no statistically significant changes in organ weight were observed following exposure to any tested concentrations of DDAC, a decreasing trend (Linear Trend Test, p50.01 and p50.05, respectively) in thymus and liver weight (but not percentage of body weight) was observed at Day 10 following a 4-day exposure (Anderson, 2016).[17]
Other organ toxicity	Low dermal and oral absorption of DDAC and C12–C16 ADBAC is consistent with the lack of systemic toxicity observed across available repeated dose oral and dermal toxicology studies conducted with beagles, mice, and rats. Toxicological findings from acute, subchronic, and chronic oral toxicity studies are consistently characterized by local stomach irritation, reduced food consumption, reduced body weight, and reduced weight gain. This pattern of effects supports the MoA for irritating/corrosive substances. Therefore, sporadic and inconsistent effects on organ weight (i.e., reduced spleen weight, an organ that is highly sensitive to body weight changes), hematology, and clinical chemistry that have been reported in a few repeat-dose toxicity studies should be considered secondary to local irritation and subsequent changes in food consumption and body weight. Importantly, both ECHA (2015a,b) and EPA (2006a,b) drew similar conclusions regarding the MoA of DDAC and C12–C16 ADBAC in their assessments (Luz et al., 2020).
Skin, Eye and Respiratory Effects	

*Irritant – **S**kin, **E**ye, or **R**espiratory*	In an OCSPP 870.2500 guideline study, 0.5 mL of a formulation containing 80% DDAC was applied to the skin of one male rabbit for 4 h (Hill Top Biolabs, Inc. 1991a, as cited in EPA, 2006c & ECHA, 2015a, 2019a). Dermal application of DDAC resulted in severe skin irritation, including changes in skin texture and coloration, and necrosis, which led study authors to conclude that DDAC is corrosive to skin. In support of this conclusion, severe skin irritation/corrosion has also been reported in two additional OECD TG 404 (Acute Dermal Irritation/Corrosion) studies conducted with rabbits (Safepharm Laboratories, 1995, 1986, as cited in ECHA, 2015a, 2019a). However, skin irritation is a threshold effect, and a 2-week skin irritation study in rats indicates that the 5-day and 14-day no-observed-adverse-effects concentrations (NOAECs) for the skin-irritating properties of DDAC are 0.6% and 0.3%, respectively (ECHA, 2015a). (Luz, et al., 2020) Two OCSPP 870.2400 guideline studies have been conducted to investigate primary eye irritation following ocular DDAC exposure (EPA, 2006c; Hill Top Biolabs, Inc. 1991b, as cited in EPA, 2006c; ECHA, 2015a). In the first study, 0.1 mL of a formulation containing 80% DDAC was instilled into one eye of two separate rabbits. After 1 h, severe corneal opacity, redness, and chemosis of the conjunctiva were observed, and persisted until 48 h post-dosing when the animals were sacrificed due to welfare concerns. In a second study, 0.1 mL of a formulation containing 80% DDAC was instilled into the eye of one male rabbit. One hour after dosing, severe eye irritation was evident and was characterized by corneal opacity, redness, and a misshapen eye, which led the study authors to terminate the study. In addition, results from a Draize test for determining the threshold irritant concentration (TIC) of DDAC in rabbits are reported in the REACH Registration Dossier for DDAC (ECHA, 2019a). The registrant-provided study summary indicates that concentrations of DDAC as low as 0.1%–0.5% are irritating to the eye (Luz, et al., 2020). No guideline studies were identified that investigated respiratory irritation following inhalation exposure to DDAC. Ohnuma et al. (2010, 2011, 2013) conducted a serious of non-guideline/non-GLP studies in which male C57BL/6J mice were instilled within the trachea with low doses (15–1500 µg/kg) of DDAC dissolved in phosphate-buffered saline and reported signs of inflammation and pulmonary fibrosis, which is consistent with respiratory system irritation (Luz, et al., 2020). **EPA Toxicity Category I**: highly irritating to the skin and eyes[1]

*Corrosive – **S, E,** or **R***	See information added above for Irritant EU Harmonised classification: Skin Corr. 1B[18] Industrial concentrate (80-90%) DDAC:
	Skin corrosion/irritation Category 1 Serious eye damage/eye irritation Category 1[19] "Precautionary statement: Danger! Corrosive. Causes irreversible eye damage and skin burns. Do not get in eyes, on skin or on clothing. Wear goggles or face shield, protective clothing and rubber gloves. May be fatal if swallowed or inhaled. Do not breathe spray mist (or vapor)... Harmful if absorbed through the skin."[20]

Permanent Damage – ***S, E,*** *or* ***R***	A study examined the pulmonary defense system following a single intratracheal instillation of DDAC (60 and 150 mg/kg) in C57BL/6J mice. Those authors found that exposure to the high dose induced lung injury as early as 1-d post-exposure, as evidenced by increased lactate dehydrogenase (LDH) activity and protein concentrations in the bronchoalveolar (BAL) fluid. There was also an increase in total cells in the BAL (specifically macrophages, neutrophils and lymphocytes), along with increases in interleukin (IL)-6 production by 7-days post exposure. The authors also suggested that DDAC exposure altered oxidative stress and antimicrobial markers (evaluated by gene expression) in the lungs and systemic co-exposure with lipopolysaccharide (LPS) generated a further enhancement in pulmonary inflammation suggesting a potential increase in susceptibility to bacterial agents (Ohnuma, 2011).[21]
Sensitizer– ***S*** *&* ***R***	Four OCSPP 870.2600 guideline studies (Buehler Method) investigating skin sensitization in guinea pigs following dermal application of DDAC were identified, all of which concluded that DDAC is not a skin sensitizer (Hazleton-Institute Francais de Toxicologie, 1992, as cited in ECHA, 2015a; Tox Monitor Laboratories, Inc. 2003, as cited in ECHA, 2015a; Product Safety Laboratories, 2004, as cited in EPA, 2006c & ECHA, 2015a; Notox, 1996a, as cited in ECHA, 2015a, 2019a). DDAC has also been tested for skin sensitizing properties in a non-guideline combined irritancy and local lymph node assay (LLNA; Anderson et al., 2016). Dermal sensitization was observed in the LLNA at concentrations as low as 0.25% DDAC; however, the LLNA has a high false positive rate for chemicals that are strong dermal irritants, as irritants can induce non-specific lymphocyte proliferation (Anderson et al., 2011; Loveless et al., 1996). Finally, one study determined that DDAC is not a photosensitizer (Hill Top Biolabs, Inc. 1991c, as cited in EPA, 2006c; ECHA, 2015a). Although there are no direct data, the lack of dermal sensitization potential supports the notion that respiratory sensitization is also not anticipated (ECHA, 2015a). (Luz et al., 2020) DDAC was identified as an irritant and strong sensitizing chemical. The lowest concentrations that induced a significant increase in lymphocyte proliferation (0.25%) were below concentrations that resulted in significant increases in ear swelling (0.5%). In addition, there was a significant increase in the percentage of B-cells in the absence of increasing IgE+ B-cells in the DLN and total IgE in the serum. TDI was included in these experiments as a chemical that induces a prototypical

	TH2 (IgE-mediated) hypersensitivity response (Anderson, 2016).[22]
Asthmagen – Initiator or Exacerbator	AOEC listed as an asthmagen and sensitizer[23] "There are reports in the literature of work-related asthma associated with exposure to cleaning agents and disinfectants and some of these reports relate to the use of QUATS. The earliest reports include a case of a laundry worker who developed asthma after using a disinfectant containing QACs (Innocenti, 1978), a pharmacist who had asthma attacks when contacting a floor cleaning solution containing QACs (Burge, 1994) and a worker who had occupational asthma caused by prolonged exposure to cleaning agents containing QACs (Bernstein, 1994). Three more cases were reported in Purohit (2000) of nurses who experienced asthma symptoms when preparing a 10% solution of disinfectant containing QAC, cleaning surgical instruments in a tray with a QAC disinfectant, and entering a room where a solution of disinfectant containing 40% QAC was kept. In a multistate report of 401 cases of pesticide related illness of health care workers (Mehler et al, 2010), QACs were involved in the most cases (151) followed by glutaraldehyde (101) and sodium hypochlorite (71). In terms of occupation, janitors and housekeepers had the most cases (95), followed by nursing/medical assistants (64) and health technicians (59)"1. "Exposure to QACs increased significantly the risk of reported physician-diagnosed asthma and nasal symptoms at work (adjusted OR = 7.5 and 3.2, respectively). No significant association was found with other exposures such as latex glove use, chlorinated products/bleach or glutaraldehyde".24 "Challenge exposure to the suspected cleaning agents elicited a ≥20% fall in forced expiratory volume in 1 s (FEV1) in 17 (39%) participants. The cleaning products that induced a positive specific inhalation challenge (SIC) contained quaternary ammonium compounds (n=10), glutaraldehyde (n=3), both of these agents (n=1) and ethanolamines (n=2). Positive SICs were associated with a significant decrease in the median (IQR) value of the provocative concentration of histamine causing a 20% fall in FEV1 (PC20) from 1.4 (0.2–4.2) mg/mL at baseline to 0.5 (0.4–3.0) mg/mL after the challenge and a significant increase in sputum eosinophils from 1.8 (0.8–7.2)% at baseline to 10.0 (4.1–15.9)% 7 h after the challenge exposure while these parameters did not significantly change in participants with a negative SIC. Overall, 11 of 17 participants with positive SICs showed greater than threefold decrease in post challenge histamine PC20 value, a >2% increase in sputum

eosinophils, or both of these outcomes. Conclusions: **These data indicate that a substantial proportion of workers who experience asthma symptoms related to cleaning materials show a pattern of bronchial reaction consistent with sensitiser-induced occupational asthma. The results also suggest that quaternary ammonium compounds are the principal cause of sensitiser-induced occupational asthma among cleaners.**"[25]

"High-level exposure, evaluated by the JTEM, to several specific disinfectants (ie, glutaraldehyde, bleach, hydrogen peroxide, alcohol, and quaternary ammonium compounds) was significantly associated with COPD incidence, with adjusted hazard ratios ranging from 1.25 (95% CI, 1.04-1.51) to 1.36 (95% CI, 1.13-1.64). Associations were not modified by smoking or asthma status (P for interaction > .15)."[26]

"Weekly use of disinfectants to clean surfaces only (23% exposed) or to clean medical instruments (19% exposed) was not associated with incident asthma (adjusted hazard ratio [95%CI] for surfaces, 1.12 [0.87–1.43]; for instruments, 1.13 [0.87–1.48])."[27]

"Atopic sensitization (defined as increased production of IgE to common allergens) was found to occur more frequently in farmers who used disinfectants containing quaternary ammonium compounds (QACs) (odds ratio (OR) 7.4; 95% confidence interval (95% CI) 1.3–43.1)."[28]

"The onset or aggravation of asthma in this group could be related to an irritant-induced mechanism or to specific sensitization. The main sensitizers contained in cleaning products are disinfectants, quaternary ammonium compounds (such as benzalkonium chloride), amine compounds, and fragrances."[29]

Comment: MMWR published a surveillance report in 2010 (MMWR, 2010). From 2002–2007, 121 workers reported quat-based product respiratory exposures in healthcare facilities in four states. Of these, 11 were known asthmatics and another six experienced wheezing. What is unknown is what the other ingredients in these products were and what role other "triggers" may have been involved, or how the product exposures occurred. Most cases occurred among janitors/housekeepers and nursing/medical assistants. There were 2.8 million healthcare workers in these states. The percentage of reported incidence of respiratory issues was 0.014%. The authors, whom are all physicians, concluded that the solution to the issue was not to change products but to provide proper

	training to environmental health personnel.

Skin Absorption, Kp	In the dermal study, rats were exposed to a single, topical dose of 1.5 or 15 mg/kg ^{14}C-DDAC for 6 h, which was applied to clipped skin over the interscapular region of the upper back, compromising approximately 10% of the total body surface area (CIT, 2005a, as cited in ECHA, 2015a, 2019a). Of the administered dose, 1% and 50% were eliminated in urine and feces, respectively, over a 48-h period, which suggests a high dermal absorption rate. However, animals did not wear an Elizabeth collar to prevent unintentional oral ingestion via licking for the majority of the experiment (collar was only worn during 6-h exposure period), which compromises experimental results and led ECHA (2015a) to conclude that dermal absorption of DDAC could not be reliably quantified. Alternatively, results from an *in vitro* percutaneous absorption assay with ^{14}C-DDAC indicate that dermal absorption through human skin is negligible (Inveresk Research, 2001, as cited in ECHA, 2015a). Only 0.1% of the administered dose was found to fully penetrate human skin within a 24-h period, while 9.41% of radioactivity was detected in the dermis and epidermis, which led ECHA (2015a) to conclude that dermal absorption does not exceed 10% at non-corrosive doses (Luz, et al., 2020).
LOAEL	Incidental Oral (Short-Term) LOAEL (developmental) = 20 mg/kg/day based on increased incidence of skeletal variations.[1]
NOAEL	Incidental Oral (Short-Term) NOAEL (developmental) = 10/mg/kg/day[1]
Benchmark Dose Response (BMD)	
Toxicokinetics	The ADME properties of DDAC and C12–C16 ADBAC have been investigated in several studies conducted according to published guidelines (e.g., OCSPP and OECD). As discussed below, available studies indicate that DDAC and C12–C16 ADBAC are not readily absorbed through the skin or gastrointestinal tract, undergo limited oxidative metabolism, and are primarily eliminated in feces. Similarly, ECHA (2015a,b) concluded that oral and dermal absorption of DDAC and C12–C16 ADBAC is limited, and does not exceed 10% (Luz et al., 2020). In an OCSPP 870.7485 guideline study, male and female rats (5/sex/dose) were exposed to either (1) a single oral dose of 5 or 50 mg/kg ^{14}C-DDAC, or (2) 34 parts per million (ppm) DDAC in feed for 14 days followed by a single oral dose of 5 mg/kg ^{14}C-DDAC (Biological Test Center, 1989a, as cited in EPA, 2006c; ECHA, 2015a). The

	toxicokinetics of DDAC were not affected by dose or exposure duration. DDAC was found to be poorly absorbed via the oral route and was primarily excreted in feces as either the parent compound or as an oxidative metabolite within 3 days of the final dose for both sexes. Four oxidative metabolites of DDAC were identified, with oxidation being confined to the decyl side-chains of the parent compound. The study authors note that microbes in the intestinal tract are likely responsible for metabolism of DDAC; however, additional studies are required to substantiate this hypothesis (Luz, et al., 2020). In a second study, adhering to OECD TG 417, the oral and dermal toxicokinetics of DDAC were investigated with Sprague Dawley rats (CIT, 2005a, as cited in ECHA, 2015a, 2019a). In the oral study, male and female rats were dosed by gavage with single (50 or 200 mg/kg) or repeat (50 mg/kg-day DDAC for 7 days) doses of ^{14}C-DDAC. Radiolabeled DDAC was undetectable in blood in all exposure groups, with total oral absorption estimated to be between 3% and 7% based upon urinary (0.9–3.2%) and bile (1.8–4.0%) excretion. Quantifiable levels of radioactivity were detected in several organs in high-dose animals, including the liver, kidney, and intestines; however, exact levels of radioactivity were not reported in the study summary prepared by ECHA (2015a). The majority (86–96%) of DDAC was eliminated, unabsorbed, within 48 h in feces, and no DDAC or DDAC metabolites were detected in urine. Based upon low oral bioavailability, rapid excretion, and recovery of 90% radioactivity, the study indicates that DDAC lacks the potential to bioaccumulate (Luz, et al., 2020). In the dermal study, rats were exposed to a single, topical dose of 1.5 or 15 mg/kg ^{14}C-DDAC for 6 h, which was applied to clipped skin over the interscapular region of the upper back, compromising approximately 10% of the total body surface area (CIT, 2005a, as cited in ECHA, 2015a, 2019a). Of the administered dose, 1% and 50% were eliminated in urine and feces, respectively, over a 48-h period, which suggests a high dermal absorption rate. However, animals did not wear an Elizabeth collar to prevent unintentional oral ingestion via licking for the majority of the experiment (collar was only worn during 6-h exposure period), which compromises experimental results and led ECHA (2015a) to conclude that dermal absorption of DDAC could not be reliably quantified. Alternatively, results from an *in vitro* percutaneous absorption assay with ^{14}C-DDAC indicate that dermal absorption

through human skin is negligible (Inveresk Research, 2001, as cited in ECHA, 2015a). Only 0.1% of the administered dose was found to fully penetrate human skin within a 24-h period, while 9.41% of radioactivity was detected in the dermis and epidermis, which led ECHA (2015a) to conclude that dermal absorption does not exceed 10% at non-corrosive doses (Luz, et al., 2020).

"This study tested whether QAC concentrations could be detected in the blood of 43 random volunteers, and whether QAC concentrations were associated with markers of inflammation, mitochondrial function, and cholesterol synthesis in a dose dependent manner. QAC concentrations were detected in 80% of study participants, and were associated with decreased mitochondrial function and an increase in inflammatory cytokines in a dose dependent manner. Cholesterol synthesis pathway intermediaries were generally increased, indicating disruption in cholesterol homeostasis. This is the first study to demonstrate that chronic exposure to QACs results in measurable concentrations in human blood, and to also demonstrate significant correlations between QAC level and meaningful biomarkers related to health."[30]

Comment: It is noteworthy that this is a non-guideline study that has not been subjected to assessment for data quality or reliability. The relevance in the evaluation of DDAC is questionable.

"QAC cytotoxicity to MDCK II cells *in vitro* is initiated by mitochondrial dysfunction at sub-lethal concentrations, followed by mitochondrial fragmentation and decreased cellular energy charge at slightly higher concentrations. In isolated mitochondria all of the QAC tested were shown to act via a common mechanism involving inhibition of NADH ubiquinone oxidoreductase (complex I) and of mitochondrial ADP-phosphorylation. QAC-induced mitochondrial dysfunction results in apoptosis (concentrations ≤ LD90), followed by a shift to necrotic cell death at concentrations above LD90."[31]

Comment: It is noteworthy that this is a non-guideline study that has not been subjected to assessment for data quality or reliability. The relevance in the evaluation of DDAC is questionable.

Metabolites	
Synergistic or Antagonistic Effects	
Environmental and Human Health Exposure and Risk Values	
RfC/RfD	"The acute RfD is **0.1 mg/kg/day** for females (13-50 years). This endpoint is based on a developmental toxicity study in rats with a reported NOAEL of 10 mg/kg/day. This study indicated increased incidence of skeletal variations at the LOAEL of 20 mg/kg/day. The chronic RfD is 0.1 mg/kg/day. This is based on increased incidence of clinical observation signs in males and females and decreased total cholesterol levels in females at 20 mg/kg/day in the chronic toxicity study in dogs. An uncertainty factor of 100 (10X for interspecies extrapolation and 10X for intraspecies variability) was applied to the NOAEL to obtain the acute and chronic RfDs."[1] ***Comment:*** The acute RfD of 0.1 mg/kg/day was determined from an acute oral toxicity study with DDAC (MRID 42296101), not from a developmental toxicity study as indicated above.[1]
ATSDR-MRL	MRL of 0.1 mg/kg for all food commodities covered by the EU MRL legislation for DDAC[32]
Adverse Effect Levels: DNEL, PNEC, PNEL	PNEC (ug/L) = 2.8[33]
Health Based Exposure Limits	
NIOSH-REL/IDLH/Ceiling Limits	Recently published Occupational Exposure Limit (OEL) for quats = 0.1 mg/m^3 (Dotson, et al., 2020).
OSHA-PEL	
ACGIH TLV-TWA	
TLV-STEL	
Biomonitoring Action Limits	
Drinking Water Standards	
Other	FIFRA Requirements (40 CFR 180.940): Residues of the following chemical substances are exempted from the requirement of a tolerance when used in accordance with good manufacturing practice as ingredients in an antimicrobial pesticide formulation, provided that the substance is applied on a semi-permanent or permanent food-contact surface (other than being applied on food packaging) with adequate draining before contact with food. ... (c) The following chemical substances when used as ingredients in an antimicrobial pesticide formulation may be applied to: Food-processing equipment

	and utensils. 1-Decanaminium, N-decyl-N,N-dimethyl-, chloride is included on this list. Limit: When ready for use, the end-use concentration is not to exceed 200 ppm of active quaternary compound.[34] Use data indicate that the general population may be exposed to DDAC via dermal contact with consumer products containing this compound. The use as an antimicrobial product on food contact surfaces, treatment of mushroom houses, and application to food-grade eggs may result in pesticide residues in human food. Residues from the use of DDAC for food contact sanitization on treated surfaces, such as food utensils, countertops, equipment, and appliances, can migrate to food coming into contact with the treated surfaces and can be ingested by humans.[1] Since the 2006 RED, 781 individual human health incidents have been reported for DDAC in OPP's Incident Data System (IDS) from August 1, 2006 to March 3, 2017. • A maintenance worker at a gas station used an ADBAC/DDAC disinfectant product. Another worker there was allegedly exposed to it and developed respiratory distress and ultimately died. She previously had chronic obstructive pulmonary disease. • An airline employee developed respiratory distress resulting in death. Chemical exposure to an ADBAC/DDAC product and three other cleaning products was the potential cause. No other details were provided. • A person deliberately inhaled a fabric and air deodorizer. This person had a history of inhalant abuse. • A 68-year dementia patient in a nursing home ingested an ABDAC/DDAC disinfectant product that was being used to clean wheelchairs during the overnight shift. • An individual ingested an ADBAC/DDAC powder product along with another nonpesticidal cleaning product in a correctional facility.
ENVIRONMENTAL & ECO-SYSTEM HAZARDS	
PBT	
Persistence	"We have determined the occurrence of 19 QACs in residential dust collected before and during the COVID-19 pandemic. QACs were detected in >90% of the samples collected during the pandemic at concentrations ranging from 1.95 to 531 µg/g (n = 40; median of 58.9 µg/g). The total QAC concentrations in these samples were significantly higher than in samples collected before the COVID-19 pandemic

	($p < 0.05$; n = 21; median of 36.3 µg/g). Higher QAC concentrations were found in households that generally disinfected more frequently ($p < 0.05$). Disinfecting products commonly used in these homes were analyzed, and the QAC profiles in dust and in products were similar, suggesting that these products can be a significant source of QACs. Our findings indicate that indoor exposure to QACs is widespread and has increased during the pandemic."[35]
Bioaccumulation	
BAF	
BCF	A measured BCF of 81 in fish suggests bioconcentration in aquatic organisms is moderate.[1]
BMF	
Ecological Toxicity	
Aquatic Toxicity: LC_{50}, EC_{50}, ErC_{50}, NOAEC/NOEC	Short term toxicity to fish was evaluated according to OECD Guideline 203 and EU Method C.1 under GLP conditions. Seven fish per concentration were exposed to 0.18, 0.32, 0.56, 1.0 or 1.8 mg/L of a commercial product containing 50% DDAC for 96 h. The test was conducted under semi-static conditions, with the test solution being renewed after 48 h. No analytical dose verification was performed and all values mentioned are nominal. The highest concentration causing no mortality (NOEC) after 96 h was 0.56 mg/L whereas 100% mortality occurred within 2 h at 1.8 mg/L. There were no effects on behavior during the exposure period, except for the fish at 1.0 mg/L which showed reduced activity after 6 h. The **96 h LC50** of the test substance was **0.49 mg a.i./L**[6]**.** A long-term toxicity study with aquatic invertebrates (*Daphnia magna*) was carried out according to OECD Guideline 211, in compliance with GLP. The following nominal concentrations were used: 0, 0.005, 0.0125, 0.032, 0.08 and 0.2 mg /L, corresponding to mean measured values of 0, 0.0031, 0.0078, 0.020, 0.047 and 0.124 mg/L. The test conditions were semi-static, with renewal every second day and over the weekend after three days. Animals were checked daily for immobilisation of parent daphnids by gently shaking the test vessel. From the day of the first brood, observations (aborted, living and dead progeny) were also made at each concentration. The day of brood release and the number of living and dead neonates per brood or abortions were noted. Any other abnormal observations were also recorded. Under the study conditions, results (based on mortality as well as reproduction, expressed as measured concentrations of active ingredient) were as

	follows: **NOEC = 0.021 mg/L, LOEC = 0.047 mg/L, EC50 = 0.031 mg/L** (Thomas, 2004)[6]. **EPA Final Work Plan Data:** Freshwater fish: Acute LC_{50} = 190 ug ai/L (**highly toxic**) Freshwater fish: Chronic NOAEC =32 ai/L Freshwater invertebrates: Acute EC_{50} = 18 ug ai/L (**very highly toxic**) Freshwater invertebrates: Chronic NOAEC = 10 ug ai/L Marine fish: Acute LC_{50} = 960 ug ai/L (**highly toxic**) Marine invertebrates Acute EC_{50} = 69 ug ai/L (**very highly toxic**)
Mammalian Toxicity: LC_{50}, EC_{50}, ErC_{50}, NOAEC/NOEC	
Wildlife Toxicity: LC_{50}, EC_{50}, ErC_{50}, NOAEC/NOEC	LC50; Species: Anas platyrhynchos (Mallard duck) age 10 days; diet >5620 ppm for 8 days[36] LC50; Species: Anas platyrhynchos (Mallard duck) diet >3500 ppm for 8 days[15]
General degradation	log K_{ow} = 2.59 at 20 °C, pH 7[6]; log K_{ow} - 4.66 at 25°C (EpiSuite)[1] High log K_{ow} indicates DDAC is relatively hydrophobic and potential for sorption to soil and sediment, noting complicating factor of amphiphilic nature of surfactants. In aqueous media offering the potential for both sorption and biodegradation, there is conflicting information about which of these processes would be expected to predominate. In aerobic and anaerobic aquatic metabolism studies, DDAC was stable to microbial degradation under aerobic and anaerobic conditions in water and sediment, indicating that sorption would predominate, while other tests showed ready biodegradability in the absence of clay, indicating that biodegradation would predominate. There is also uncertainty about biodegradation during wastewater treatment, in terms of sorbing to sludge biomass and potential toxicity to activated sludge microorganisms. [1] The available data indicates that DDAC is hydrolytically stable under abiotic and buffered conditions over the pH 5-9 range; also stable to photodegradation in water at pH7 (calculated half life of 227 days). [1]
Breakdown/degradation /combustion products	Potential for QACs in wastewater to form n-nitrosamine disinfection byproducts (e.g., N-Nitrosodimethylamine or NDMA, a potent carcinogen), particularly if chloramine is used as the disinfecting agent. This is likely of greatest concern for direct or indirect potable reuse scenarios,[37] as most n-nitrosamines breakdown via photolysis in surface waters.

Anaerobic degradation	
Aerobic degradation	DDAC was found to be stable with very little degradation in aerobic soils during a year-long metabolism study using sandy loam soil. The calculated half-life for aerobic soil degradation was 1,048 days. DDAC is not considered to be degradable since it did not exhibit greater that 60% degradation within a 10-day window.[1]
Other observable ecological effects (e.g. BOD)	
Fate and Transport: Aquatic	QACs have been detected worldwide in domestic wastewater, sludge, treated effluent, surface water, and sediment. It is expected that the majority of QAC applications leads to their eventual release (~75%) into sewers and WWTPs. Though QACs are removed from the liquid stream during conventional wastewater treatment, these compounds are still detected in aquatic environments, and at higher concentrations in locations downstream of the discharge of municipal WWTP effluents, hospital, and industrial effluents (Hora, 2020).[38] "While biodegradation of QACs has been shown to occur in laboratory studies, their removal in wastewater treatment plants (WWTPs) is likely driven by sorption to activated sludge. Consequently, QACs have been detected world-wide in WWTP influent, effluent, and sludge samples with concentrations typically in the high and low µg L−1 range for influents and effluents, respectively, as well as in the mid-to-high µg g−1 range for sewage sludge. As evident from these results as well as detection of QACs in river water samples, QACs are not completely removed during wastewater treatment and are released into the natural environment. Concern about the presence of QACs in the environment arises from the potential of these compounds to promote antibiotic resistance and serve as precursors for disinfection by-products. In addition, the degradation of QACs in the natural environment by both microorganisms and photolysis is slow, resulting in accumulation of significant amounts of these compounds in sediments." [39] Presence in surface water and sediments upstream and downstream of WWTPs in Austria: Σ C10-C18 DDAC: Surface water ranged from 0.02- 0.32 µg/L; sediment ranged from 76 - 2712 µg/kg dm. Samples downstream of WWTP often were less than samples taken upstream - both for surface water and sediment, so presence was not

	heavily impacted by WWTP discharge. Study also sampled waste water from different businesses; hospitals and laundries had the highest values for C10-C18 DDAC (max 176 µg/L) and C12-C18 BAC (max 3929 µg/L)[40]
Fate and Transport: Terrestrial	
Fate and Transport: Atmospheric	Data from a random cage monitoring during QAC use and in the months after use of QAC disinfectants was discontinued, provided evidence that these chemicals may persist in the environment (Hrubec, 2017).
Transport Issues	Immobile in soil[1]
Factors affecting bioavailability	
Global Environmental Impacts	
Ozone Depletion Potential (ODP)	
Global Climate Change	
Greenhouse Gas Production	
Acid Rain Formation	
Special Reports	
EU/Other Countries	*Danger!* According to the **harmonised classification and labelling** (CLP00) approved by the European Union, this substance causes severe skin burns and eye damage and is harmful if swallowed. **Additionally**, the classification provided by companies to ECHA in **REACH registrations** identifies that this substance is toxic if swallowed, is very toxic to aquatic life, is toxic to aquatic life with long lasting effects, causes serious eye damage, is a flammable liquid and vapour and may cause drowsiness or dizziness[6].

PC code	CAS Number	Ingredient Name	Number of Active Antimicrobial Product Registrations as of 3/14/17 1	Number of Active Conventional Product Registrations as of 3/14/17 1
069149	7173-51-5	Didecyl dimethyl ammonium chloride	260	1
069165	32426-11-2	1-Decanaminium, N,N-dimethyl-N-octyl-, chloride	133	1
069166	5538-94-3	1-Octanaminium, N,N-dimethyl-N-octyl-, chloride	146	1
069173	68607-28-3	Oxydiethylenebis(alkyl* dimethyl ammonium chloride) *(as in fatty acids of coconut oil)	4	0
129012	61789-18-2	Alkyl* trimethyl ammonium chloride *(as in fatty acids of coconut oil)	1	0

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