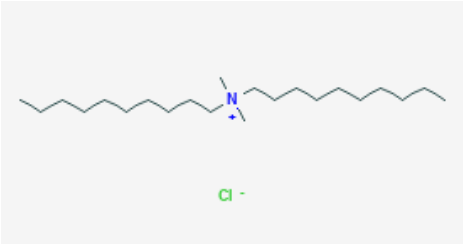
Updated EHS Summary of Didecyl Dimethyl Ammonium Chloride (DDAC) for the MA TURA Science Advisory Board Meeting – September 30, 2020

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) **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. Products containing DDAC are formulated as liquid ready-to-use soluble concentrates and the content ratio of DDAC in various end use products ranges from 0.08% to 80% DDAC.
Physical state, odor at room temperature & pressure	Clear yellow liquid with an ethanolic or mushroom-like odor[1]
Melting point; Boiling point	MP: 228.81˚C[1] BP: >180 °C; decomposes before boiling at 1 atm /OECD Guideline 103[6]
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	
Flammability Rating	
Auto Ignition Point	
Combustion products	
Explosivity (UEL, LEL, shock sensitive)	
Oxidizer	

Corrosivity	
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 pressure, noise, vibration, ergonomic hazard	When heated to decomposition it emits very toxic fumes of /nitrogen oxides, ammonia, and hydrogen chloride[7]
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]
Intraperitoneal LD_{50}	
Chronic or Sub-chronic Toxicity	
IARC rating	
Carcinogenicity	
Neurotoxicity	
Developmental/Reproductive Toxicity	"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.[8] 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 and gavage groups exhibited significantly increased levels of NTDs compared with unexposed controls.[9]
Genotoxicity/Mutagenicity	
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. It is, therefore, conceivable that ADBAC + DDAC 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.[10]
Thyroid	
Immunotoxicity	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.[11]

Liver	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.[11]
Other organ toxicity	
Skin, Eye and Respiratory Effects	
*Irritant – **S**kin, **E**ye, or **R**espiratory*	EPA Toxicity Category I: highly irritating to the skin and eyes[1]
*Corrosive – **S**, **E**, or **R***	
*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.[12]
*Sensitizer– **S** & **R***	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.[13]
Asthmagen – Initiator or Exacerbator	AOEC listed as an asthmagen and sensitizer[14]
Skin Absorption, Kp	
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	

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]
ATSDR-MRL	MRL of 0.1 mg/kg for all food commodities covered by the EU MRL legislation for DDAC[15]
Adverse Effect Levels: DNEL, PNEC, PNEL	PNEC (ug/L) = 2.8[16]
Health Based Exposure Limits	
NIOSH-REL/IDLH/Ceiling Limits	
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.[17] 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]
ENVIRONMENTAL & ECO-SYSTEM HAZARDS	
PBT	
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	LC50; Species: Anas platyrhynchos (Mallard duck) age 10 days; diet >5620 ppm for 8 days[18] LC50; Species: Anas platyrhynchos (Mallard duck) diet >3500 ppm for 8 days[15]
Mammalian Toxicity: LC_{50}, EC_{50}, ErC_{50}, NOAEC/NOEC	
Wildlife Toxicity: LC_{50}, EC_{50}, ErC_{50}, NOAEC/NOEC	
Breakdown/degradation /combustion products	log Kow = 2.59 at 20 °C, pH 7[6] The available data indicates that DDAC is hydrolytically stable under abiotic and buffered conditions over the pH 5-9 range.[1]
Anaerobic degradation	
Aerobic degradation	DDAC was found to be stable with very little degradation in aerobic soils during a year-long metabolism study. 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	
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.[7]
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	

[1] USEPA/Office of Pesticide Programs; Reregistration Eligibility Decision Document - Aliphatic Alkyl Quaternaries (DDAC) p.4 EPA739-R-06-008 (August 2006).
[2] www.toxplanet.com; RTECS for Didecyldimethylammonium chloride (7173-51-5).
[3] www.toxplanet.com; Chemical Identity Page for Didecyldimethylammonium chloride (7173-51-5).
[4] www.toxplanet.com; Chemical Identity Page for Didecyldimethylammonium chloride (7173-51-5).
[5] www.toxplanet.com; Chemical Identity Page for Didecyldimethylammonium chloride (7173-51-5).
[6] ECHA; Didecyldimethylammonium chloride (7173-51-5). Registered Data Dossier. Helsinki, Finland: European Chemicals Agency.
[7] Lewis, R.J. Sr. (ed) Sax's Dangerous Properties of Industrial Materials. 11th Edition. Wiley-Interscience, Wiley & Sons, Inc. Hoboken, NJ. 2004., p. 1230
[8] Melin, V. E., Potineni, H., Hunt, P., Griswold, J., Siems, B., Werre, S. R., & Hrubec, T. C. (2014). Exposure to common quaternary ammonium disinfectants decreases fertility in mice. *Reproductive Toxicology*, *50*, 163–170. https://doi-org.umasslowell.idm.oclc.org/10.1016/j.reprotox.2014.07.071
[9] Hrubec TC, Melin VE, Shea CS, et al. Ambient and Dosed Exposure to Quaternary Ammonium Disinfectants Causes Neural Tube Defects in Rodents. *Birth Defects Res*. 2017;109(14):1166-1178. doi:10.1002/bdr2.1064
[10] Melin, V. E., Melin, T. E., Dessify, B. J., Nguyen, C. T., Shea, C. S., & Hrubec, T. C. (2016). Quaternary ammonium disinfectants cause subfertility in mice by targeting both male and female reproductive processes. *Reproductive Toxicology (Elmsford, N.Y.)*, *59*, 159–166. https://doi-org.umasslowell.idm.oclc.org/10.1016/j.reprotox.2015.10.006
[11] Anderson, S. E., Shane, H., Long, C., Lukomska, E., Meade, B. J., & Marshall, N. B. (2016). Evaluation of the irritancy and hypersensitivity potential following topical application of didecyldimethylammonium chloride. Journal of Immunotoxicology, 13(4), 557–566.https://doi-org.umasslowell.idm.oclc.org/10.3109/1547691X.2016.1140854
[12] Ohnuma A, Yoshida T, Horiuchi H, Fukumori J, Tomita M, Kojima S, Takahashi N, Fukuyama T, Hayashi K, Yamaguchi S, et al. 2011. Altered pulmonary defense system in lung injury induced by didecyldimethylammonium chloride in mice. Inhal Toxicol. 23:476–485.
[13] Anderson, S. E., Shane, H., Long, C., Lukomska, E., Meade, B. J., & Marshall, N. B. (2016). Evaluation of the irritancy and hypersensitivity potential following topical application of didecyldimethylammonium chloride. *Journal of Immunotoxicology*, *13*(4), 557–566. https://doi-org.umasslowell.idm.oclc.org/10.3109/1547691X.2016.1140854
[14] Association of Occupational and Environmental Clinics (AOEC) Exposure code lookup for Didecyl Dimethyl Ammonium Chloride (CAS 7173-51-5) accessed on 8/17/20: http://www.aoecdata.org/ExpCodeLookup.aspx

[15] EFSA (2014) European Food Safety Authority, Reasoned opinion on the dietary risk assessment for proposed temporary maximum residue levels (MRLs) of didecyldimethylammonium chloride (DDAC) and benzalkonium chloride (BAC). Parma, Italy

[16] NICNAS (2015). National Industrial Chemicals Notification and Assessment Scheme (NICNAS) Inventory Multi-tiered Assessment and Prioritisation (IMAP) framework, Mono-and di-alkyl quaternary ammonium surfactants: Environmental tier II assessment

[17] 40 CFR 180.940(c) (USEPA); U.S. National Archives and Records Administration's Electronic Code of Federal Regulations.

[18] USEPA, Office of Pesticide Programs; Pesticide Ecotoxicity Database (2000) on N-Decyl-N,N'-dimethyl-1-decanaminium chloride (7173-51-5).