TURI TOXICS USE REDUCTION INSTITUTE UMASS LOWELL

Quaternary Ammonium Compounds (QACs)

The TURA Science Advisory Board (SAB) has recommended that certain Didecyl Dimethyl Ammonium Chloride (DDAC) and Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) chemicals be added to the TURA list of Toxic or Hazardous Substances. In reviewing the science about DDAC and ADBAC, the SAB had concerns related to these substances, including respiratory system irritation and inflammation including outcomes consistent with occupational asthma and work-exacerbated asthma; corrosive effects; hazard for aquatic life; and environmental fate and persistence. The SAB had additional concerns for reproductive effects and neural tube development.

This policy analysis summarizes key scientific information on DDAC and ADBAC; estimates the number of facilities that are likely to enter the program as a result of the proposed listing; analyzes opportunities and challenges new filers are likely to face; and discusses the implications of this policy measure for the TURA program. Based on this analysis, the Toxics Use Reduction Institute supports the SAB's recommendation that DDAC and ADBAC be added to the TURA list of Toxic or Hazardous Substances.

OVERVIEW

Quaternary ammonium compounds ("QACs" or "quats") are a broad class of several hundred chemicals. QACs were first discovered in the early 1940s and used mainly as active ingredients in antimicrobials, disinfectants, sanitizers, and surfactants. QACs are used in many products, including wood preservatives, herbicides, eye drops, mouthwashes, nasal sprays, detergents and shampoos, dryer sheets and fabric softeners.

DDAC and ADBAC QACs remain largely used in the United States as ingredients in antimicrobial products for use in consumer and institutional cleaning and disinfecting. Applications range from domestic to agricultural, industrial, and clinical. These products can be found in restaurants, medical settings, food production facilities, and households. They are considered to be effective against most vegetative bacteria, enveloped viruses, and some fungi. Ready-to-use products may contain 0.08-20% active QAC ingredients, and industrial concentrates can contain 20-80% active QAC ingredients. ADBAC and DDAC can be used in acid, neutral and alkaline formulations and is available in a dilutable concentrate that reduces shipping weight.

Although QACs have been used for over 80 years, they have had a recent increase in use. The demand for QAC-based disinfectants rose significantly as a result of the global SARS-CoV-2 pandemic. More than half of the products listed on the U.S. EPA's "List N: Disinfectants for Coronavirus" are QAC based.[1] As new QAC-based coatings and disinfectant formulations are introduced and overall use increases, environmental health and safety concerns about QAC exposure are also increasing. In 2020 alone, more than 700 hundred papers were published related to QAC research.[2]

Recommendation

After reviewing the science and the hazards of QACs, the TURA Science Advisory Board recommended in May 2021 that certain DDAC and ADBAC chemicals be added to the TURA list of Toxic or Hazardous Substances. The Toxics Use Reduction Institute considered the policy implications, and based on this analysis supports the SAB's recommendation that DDAC and ADBAC quaternary ammonium compounds be added to the TURA list of Toxic or Hazardous Substances.

BACKGROUND ON QACS

In the early years, EPA required all QACs to be individually registered as a new chemical under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), but in 1988 EPA issued a notice in which structurally similar QACs were clustered into the 4 groups listed below:

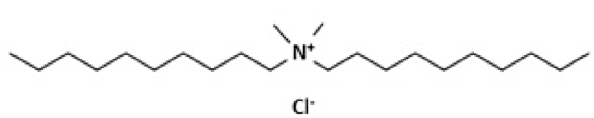
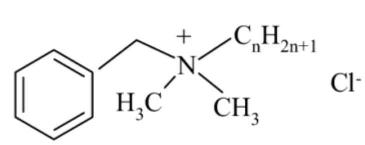
- ***Group I:*** The alkyl or hydroxyalkyl (straight chain) substituted Quats
- ***Group II:*** The non-halogenated benzyl substituted Quats (includes hydroxybenzyl, ethyl benzyl, hydroxyethybenzyl, napthylmethyl, dodecyl benzyl, and alkyl benzyl)
- ***Group III:*** The di- and tri-chlorobenzyl substituted
- ***Group IV:*** Quats with unusual substituents (charged heterocyclic ammonium compounds)

This policy analysis will focus on the commonly used disinfectants in Group I - Didecyl Dimethyl Ammonium Chloride (DDAC) and - Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) in Group II. Multiple individual substances with unique CAS numbers fall within these subclasses.

DDAC AND ADBAC

The DDAC subclass in Group I consists of five individually registered compounds[3] and the ADBAC subclass in Group II consists of 19 compounds;[4] see Table 1 and Table 2 in the Regulation of QACs section for complete lists of individual compounds. Within these groups, the Toxics Use Reduction Act (TURA) Science Advisory Board (SAB) looked in detail at common DDAC and ADBAC chemicals as the representative compounds of each group. Both of these example compounds were selected because they are among the most commonly used in disinfecting products, have the highest number of active registrations, and are often found together in mixtures. The table below summarizes key properties for each of the representative substances.

Properties of DDAC and ADBAC*

Property	DDAC	ADBAC
CAS Number	7173-51-5	68424-85-1
Melting Point	228.81˚C	241.02˚C
Boiling Point	>180 °C[5]	>560.84 °C
Vapor Pressure	2.33×10^{-11} mm Hg	3.53×10^{-12} mm Hg
Flash Point	26.4°C[6]	32°C[7]
pH	6.8 - 6.9	7.59
Log K_{ow}	4.66	3.91
Structure		

*Properties sourced from EPA Registration Documents and Final Work Plans unless otherwise noted.

SUMMARY OF SCIENTIFIC INFORMATION

The TURA SAB makes recommendations about chemical listings based on hazard. In reviewing the science about DDAC and ADBAC, the SAB noted respiratory system irritation and inflammation including outcomes consistent with occupational asthma and work-exacerbated asthma; corrosive effects; aquatic life hazards; and environmental fate and persistence as the basis for listing. The SAB had additional concerns for reproductive effects and neural tube development.

QACs are associated with both acute (short-term) and chronic (long-term) health effects. Exposure can occur by inhalation, dermal, and oral routes. QACs pose concerns for people using them for cleaning both in the home and in the workplace. In addition, the residues from treated surfaces, including utensils, countertops, equipment, and appliances, can migrate to food, resulting in ingestion by humans.

The majority of data that regulatory agencies have used to make determinations on use as antimicrobials, are based on an individual chemical. However, many of the product formulations on the market contain several different QAC substances, in addition to other ingredients that may be irritating or sensitizing.[8]

Acute Health Effects

EPA classifies five types of acute exposures to pesticides (oral, dermal, inhalation, skin and eye irritation) into four Toxicity Categories, with Category I being the highest hazard. ADBAC and DDAC are acutely toxic through the oral, dermal, and inhalation exposure routes. EPA classifies both substances in Toxicity Category II for the oral and inhalation route, and Toxicity Category III for the dermal route.

Irritant: Eyes, nose, throat, or lung irritation have all been reported among workers exposed to QACs. For skin and eye irritation EPA has categorized DDAC and ADBAC as Toxicity Category I: Corrosive. According to the European Union's harmonized classification they are considered irritants and corrosive to the skin and eyes.

Chronic Health Effects

Chronic occupational health hazards associated with using QACs include dermal irritation that may lead to skin sensitization, and an increased risk of asthma.[9,10,11,12] The Association of Occupation and Environmental Clinics (AOEC) lists both DDAC and ADBAC as asthmagens and respiratory sensitizers.[13,14]

Respiratory Effects/Asthma: Surveillance studies, case reports, and animal studies indicate that DDAC and ADBAC are associated with respiratory system irritation and inflammation including outcomes consistent with occupational asthma and work-exacerbated asthma. Recent studies have suggested that occupational exposure to cleaning agents and disinfectants containing DDAC and ADBAC may cause work-related asthma, chronic obstructive pulmonary disease, and other respiratory illnesses in occupations such as laundry workers, pharmacists, janitors, nursing/medical assistants, health technicians, and housekeepers.[15,16] Exposure to QACs was found to significantly increase the risk of nasal symptoms and physician diagnosed asthma at work more than any other potentially hazardous exposures including glutaraldehyde, latex gloves, or chlorinated/bleach products.[17]

Dermal Effects: ADBAC and DDAC are highly irritating to the skin, and long-term exposure may result in skin sensitization or allergic dermatitis. There have been several cases in which workers reported symptoms of skin sensitization. More recent animal studies have documented that mice dermally exposed to these substances developed not only irritation but also allergic sensitization.[18]

Emerging Evidence

Reproductive/Developmental Effects: Some emerging evidence has suggested that exposure to QACs such as DDAC and ADBAC may affect reproduction and development in animals.[19] The SAB noted during their review that these early studies are concerning and warrant follow-up, but that the evidence was not yet conclusive and there is mixed evidence for frank birth defects. Mice experienced adverse effects after exposure to a ready-to-use product that contained both ADBAC and DDAC, including decreased fertility, fewer pregnancies, reduced number of offspring, disruption of hormone-regulated processes such as ovulation, and birth defects.[20,21,22,23] Exposure to a disinfectant containing both ADBAC and DDAC was associated with delayed neural tube closing in both mice and rats.[24] Some of these effects may relate to potential endocrine activity.

Other Human Health Effects: A human biomonitoring study of 43 random volunteers detected measurable concentrations of QACs in the blood of 80% of participants and identified correlations between levels of QACs, cellular disruption and specific biomarkers related to human health.[25] This was the first study to measure QACs in human blood and to find evidence that QAC concentrations may influence important biomarkers. Some recent studies have shown that QACs can worsen inflammation and disrupt overall cellular function and regulation.[26,27]

Environmental Fate

QACs usually go down the drain and to wastewater treatment plants, which remove some but not all of the QACs prior to discharge to the environment. QACs have been found in surface waters, soil, sediments, and wastewater sludge. Researchers have raised concerns for microorganisms and aquatic organisms as well as the impact of QACs on wastewater treatment plants. DDAC and ADBAC are recognized as toxic to aquatic life. They are considered immobile in soil by both EPA and ECHA. Due to their low volatility, they are expected to bind to sediments and soils. There are also concerns that the overuse of DDAC, ADBAC, and other QACs could lead to development of antibiotic-resistant bacteria.

QACs have also been detected on surfaces long after being used, and in household dust, meaning they may have the potential to persist in the environment, our workplaces, and our homes. A recent study detected 19 different QAC substances in residential dust samples. QACs, the majority of which were ADBAC substances, were found in over 90% of samples taken. When compared to pre-COVID dust samples, the level of QAC concentrations had nearly doubled.[28]

Chemicals Included in SAB Recommendation

Table 1: Individual DDAC Chemicals

CAS Number	Ingredient Name
7173-51-5	Didecyl dimethyl ammonium chloride
32426-11-2	1-Decanaminium, N,N-dimethyl-N-octyl-, chloride
5538-94-3	1-Octanaminium, N,N-dimethyl-N-octyl-, chloride
68607-28-3	Oxydiethylenebis(alkyl*dimethyl ammonium chloride) *(as in fatty acids of coconut oil)
61789-18-2	Alkyl* trimethyl ammonium chloride*(as in fatty acids of coconut oil)

Table 2: Individual ADBAC Chemicals

CAS Number	Ingredient Name

53516-76-0	Alkyl (60%C_{14}, 30%C_{16}, 5%C_{18}, 5%C_{12}) dimethyl benzyl ammonium chloride
68424-85-1	Alkyl (50%C_{14}, 40%C_{12}, 10%C_{16}) dimethyl benzyl ammonium chloride
8001-54-5	Alkyl (50%C_{12}, 30%C_{14}, 17%C_{16}, 3%C_{18}) dimethyl benzyl ammonium chloride
139-08-2	Alkyl (100% C_{14}) dimethyl benzyl ammonium chloride
8045-21-4	Alkyl (50%C_{12}, 30%C_{14}, 17%C_{16}, 3%C_{18}) dimethyl ethylbenzyl ammonium chloride
73049-75-9	Dialkyl (60% C_{14}, 30% C_{16}, 5% C_{18}, 5% C_{12}) methyl benzyl ammonium chloride
121-54-0	Benzenemethanaminium, N,N-dimethyl-N-(2-(2-(4 (1,1,3,3tetramethylbutyl)phenoxy)ethoxy)ethyl)-, chloride
1330-85-4	Dodecylbenzyl trimethyl ammonium chloride
68424-85-1	Alkyl (60%C_{14}, 25%C_{12}, 15%C_{16}) dimethyl benzyl ammonium chloride
61789-71-7	Alkyl (61% C_{12}, 23% C_{14}, 11% C_{16}, 2.5% C_{18}, 2.5% C_{10}, traceC_8) dimethyl benzyl ammonium chloride
68424-85-1	Alkyl (58%C_{14}, 28%C_{16}, 14%C_{12}) dimethyl benzyl ammonium chloride
85409-23-0	Alkyl (68%C_{12}, 32%C_{14}) dimethyl ethylbenzyl ammonium chloride
68956-79-6	Alkyl (60%C_{14}, 30%C_{16}, 5%C_{12}, 5%C_{18}) dimethyl ethylbenzyl ammonium chloride
68989-01-5	Alkyl (50% C_{14}, 40% C_{12}, 10% C_{16}) dimethyl benzyl ammonium saccharinate
68391-01-5	Alkyl (67%C12, 25%C14, 7%C16, 1%C18) dimethyl benzyl ammonium chloride
68424-85-1	Alkyl (95%C14, 3%C12, 2%C16) dimethyl benzyl ammonium chloride
68391-01-5	Alkyl (41%C14, 28%C12, 19%C18, 12%C16) dimethyl benzyl ammonium chloride
63449-41-2	Alkyl (67%C12, 25%C14, 7%C16, 1%C8, C10, and C18) dimethyl benzyl ammonium chloride
61789-18-2	Alkyl (as in fatty acids of coconut oil) trimethyl ammonium chloride

* Table 1 and 2 list the active ingredients listed for Group 1 and Group 2 in EPA 2017 Final Work Plans

USE INFORMATION

In the US, ADBAC and DDAC were some of the first QACs to be used as antimicrobials, registering as active ingredients under EPA's Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) in 1947 and 1962 respectively. ADBAC and DDAC are considered High Production Volume chemicals, which means more than one million pounds are manufactured or imported into the US each year. Data for the years 2011 through 2014 indicate that approximately 198 million pounds of ADBAC and 99 million pounds of DDAC are sold per year in the US.[3] QAC use increased dramatically during the pandemic, accounting for the highest revenue share of the U.S. antiseptics and disinfectants market in 2020.[29]

There are over 600 EPA-registered products that contain ADBAC as an active ingredient. DDAC is registered as the active ingredient in almost 300 antimicrobial EPA-registered products. Many DDAC and ADBAC products contain several ingredients, including other DDAC- and ADBAC-related compounds, isopropyl alcohol, glutaraldehyde, chlorine dioxide, and fragrances.

EPCRA Tier II Data

EPCRA Tier II requires reporting of any chemical with a Safety Data Sheet if it is stored at 10,000 pounds or more at a facility (or at 500 pounds or more if the chemical is designated as an extremely hazardous substance). A review of the 2017 Tier II data shows 42 records for QAC chemicals, and 25 of which fall within the category of DDAC or ADBAC. Only three of these filers are in TURA Covered SIC codes, have 10 or more employees and appear to be using over 10,000 pounds of QAC. Given this information, and the known limitations of Tier II data, the program estimates between 3 and 6 filers.

OPPORTUNITIES FOR TUR

There are numerous alternatives to QACs for disinfecting applications, including against SARS-CoV-2 (COVID-19). These include chemical alternatives as well as non-chemical disinfecting technologies. Safer active disinfectant ingredients include hydrogen peroxide, alcohol (isopropyl alcohol or ethanol), caprylic acid, citric acid, and lactic acid. Hydrogen peroxide, ethanol, citric acid, and L-lactic acid have been evaluated by EPA's Design for the Environment (DfE) program and are considered safer active ingredients.[30] The TURI Laboratory has investigated the performance of many of these products in addition to other safer alternative disinfectants. Listed below are some of the safer active ingredients and disinfecting technologies available as alternatives to QACs. All products must be used in accordance with the manufacturer's label directions, including dilution rates and dwell time on surfaces, in order to ensure proper disinfection.

Caprylic Acid: Caprylic or octanoic acid is a natural agent produced by the distillation of coconut or palm kernel oils. In its pure form it is a colorless and corrosive liquid with a relative shelf life of two years. Caprylic acid is used in small percentages as the active ingredient in ready to use disinfecting products. Caprylic acid is biodegradable and considered to have low toxicity.

Citric Acid: Citric acid is a naturally occurring substance that can be extracted from pineapple waste and citrus fruits. It is used as an active ingredient ranging anywhere from 0.7-6% in ready to use antimicrobial products but can be corrosive in its concentrated form. It is always important to read specific product labels for effectiveness claims but many of these products are effective against a variety of microbes including H1N1, MRSA, HBV, HIV, and COVID-19.[31]

Hydrogen Peroxide: Hydrogen peroxide is a clear liquid that is fairly inexpensive and is easily accessible at most stores as a dilute 3% formulation. Many of these products can have a shelf life up to two years and are effective against a broad spectrum of microbes such as H1N1, norovirus, MRSA, and the virus causing COVID-19.[32] Products that contain hydrogen peroxide as the only active ingredient are generally considered safer alternatives. However, there is evidence that hydrogen peroxide and peroxyacetic acid together are respiratory sensitizers and may cause asthma, therefore they are **not** considered safer alternatives.[33]

L-Lactic Acid: L-Lactic acid is a naturally occurring organic acid that can be used in a variety of applications and on various surfaces as an antimicrobial solution. At the highest level of purification, lactic acid is a colorless and odorless liquid. Concentrated L-Lactic Acid is corrosive and a severe skin and eye irritant. Lactic acid is used as the active ingredient in ready to use disinfecting products ranging anywhere from 0.5-5%.

Additional alternative chemicals

In addition, other active ingredients and disinfecting technologies are useful in some circumstances.

Alcohols: Alcohols such as isopropanol (IPA) and ethanol (ethyl alcohol) are clear colorless liquids in their pure form; they evaporate quickly and are best used for spot cleaning. 70% IPA is also commonly referred to as rubbing alcohol. Concentrated alcohols are flammable and exposure may cause nausea, dizziness, headache, and irritating effects to the skin, eyes, and throat. IPA and ethanol have a shelf life of roughly 2-3 years and are effective against a broad spectrum of microbes such as MRSA, HBV, HIV, H1N1, and the virus causing COVID-19.[34]

Aqueous Ozone: Aqueous ozone is a water-based sanitizer that has been used for years primarily for drinking water disinfection. Only requiring water and electricity, the solution is produced at the point of use in an ozone generator. The technology can be hard piped for large production facilities, smaller portable equipment, and handheld spray bottle devices. Aqueous ozone has a short shelf life as the ozone readily reverts back to oxygen. Ozone gas is on the TURA list of Toxic or Hazardous Substances, and chemical and inhalation exposure at high concentrations can cause respiratory irritation and exacerbate asthma.

HYPOCHLOROUS ACID: Hypochlorous acid is a chlorine solution that can be generated by dissolving concentrated sodium dichloroisocyanurate (NaDCC) tablets in water, or by using electrolyzed water systems, which use salt and, in some instances, vinegar, in water that is electrolyzed in small units. Hypochlorous acid has a short shelf life and a slightly acidic pH between 4.5 and 6.0. Chlorine solutions have inherent hazards, but TURI lab testing has found that airborne chlorine is lower for hypochlorous acid solutions than for bleach (sodium hypochlorite) solutions. For more information on hypochlorous acid, see TURI's fact sheet.

Non-chemical alternatives

Non-chemical technologies for disinfection include UV light and steam.

STEAM: High temperature, low-moisture or dry steam does not leave a residue or chemical film and is effective and suitable for many surfaces. The use of a pressurized system to generate steam at a high temperature creates a risk of burns.

UV LIGHT: UVC light may be appropriate for specific disinfecting applications. For example, it can be used to disinfect unoccupied medical rooms and high-tech electronic devices and can be used inside air ducts to disinfect the air. UV light exposure can be hazardous for the eyes and skin.

REGULATORY CONTEXT

ADBAC and DDAC are active ingredients for use in antimicrobial products registered with the U.S. EPA and other agencies around the world. These QACs are regulated under the U.S. EPA FIFRA, the European Biocidal Products Regulation (BPR), Health Canada (HC), and the California Department of Pesticide Regulation (CA DPR). California's Scientific Guidance Panel recently listed QACs as Priority Chemicals under its Biomonitoring Program.

Several of these QAC are chemicals approved for use in food contact surface sanitizing solutions under 40 CFR 180.940. [35]

IMPLICATIONS FOR THE TURA PROGRAM

This section presents the expected implications for the TURA program of adding a QAC category to the TURA list. This includes implications of category designation; implications for compliance and reporting; implications for and applicability of TURA program services; and implications for fees and costs.

IMPLICATIONS OF CATEGORY DESIGNATION

Chemical categories are used in the TURA list in a number of cases. The TURA program's approach to categories has generally been based on the approach used under the federal Emergency Planning and Community Right-to-Know Act (EPCRA). The most recent case in which the TURA program created a category designation was for the PFAS category. In this case, as in some others, the category is defined using a delimited list of CAS numbers to assist the regulated community.

Defining a chemical category is appropriate in a number of circumstances, and can provide several advantages compared with listing chemicals individually. Advantages to use of categories include avoiding adverse substitutions; providing clear information to users in the absence of a defined list of CAS numbers; and addressing a set of chemicals with similar health or environmental effects together.

- **Adverse substitutions:** One important reason to create a chemical category is to address concerns related to adverse, or "regrettable," substitutions. If a large group of chemicals that are structurally similar may potentially be used as substitutes for one another, regulating them one at a time can create unintended consequences, in which a more-regulated chemical may be replaced by an equally hazardous, less-regulated chemical. Creating a category provides clear guidance to chemical users, and helps to avoid such adverse substitutions.

- **Incomplete set of CAS numbers:** A chemical category is also helpful when specific CAS numbers do not adequately capture the chemicals of concern. For example, if there are a number of theoretical compounds in a category, and many of them do not yet have CAS numbers, then a category defined through chemical structure and descriptive text is more informative than a list of specific chemicals. For the proposed ADBAC and DDAC category the list of CAS numbers is defined.
- **Similar hazards across a group:** A category is also useful when a number of structurally similar chemicals have, or are reasonably anticipated to have, similar health or environmental impacts. This makes it possible to address these hazards proactively by addressing the group of chemicals together.
- **Confidential Business Information (CBI):** A category approach is useful when the specific identity of many chemicals in the category are claimed by the manufacturers as CBI. Reporting under TURA would not require a user to obtain and report that specific chemical identity.

The proposed QAC category meets two of the criteria described above. A number of the chemicals may be reasonably anticipated to be used as substitutes for one another. Across the group of chemicals, specific health and environmental impacts (e.g., respiratory effects) appear frequently.

By defining and listing a QAC category, the TURA program can efficiently address this group of chemicals. The TURA program can provide clear, proactive guidance to businesses to assist them in addressing all chemicals in the category.

TURA PROGRAM SERVICES

Both the Office of Technical Assistance (OTA) and TURI are available as a resource for new filers entering the program.

The TURI Lab has significant experience helping large and small users identify safer cleaning and disinfecting alternatives. The TURI Lab has conducted cleaning alternative testing since 1993, assisting businesses in making the transition to less toxic alternatives without compromising performance. In addition, the TURI lab has recently focused on safer alternatives for janitorial and disinfection chemicals.

TURI has an academic research grant program that can target seed funding to researchers who are developing safer alternatives to toxic chemicals for specific applications. When specific industry needs are identified, along with companies willing to share performance criteria, materials and/or other forms of expertise, TURI can identify university researchers interested in focusing their R&D efforts for solutions. If a specific application of the use of chemicals in the QAC category presents an ongoing challenge for companies with respect to shifting to safer alternatives, TURI could support R&D to find feasible solutions. An example could be additional research on alternative fume suppressant options.

TURI's incentive grants for businesses can support businesses as they test and implement innovative safer technologies. TURI's demonstration site grants can help businesses that have already made a change to showcase their innovations to other businesses in related sectors. Both of these categories of grants can be used as a resource in helping Massachusetts businesses and communities adopt safer alternatives to chemicals in the QAC category.

In addition to the TURA program's ongoing trainings for businesses, OTA provides free, confidential, onsite technical assistance to Massachusetts manufacturers, businesses, and institutions.

FEES AND PLANNING-RELATED COSTS

There would be some additional cost to companies that would begin reporting the QAC Category, including preparing annual toxics use reports and biennial toxics use reduction plans, and paying toxics use fees. All facilities currently reporting QAC under Tier II are already filing under TURA for other chemicals, so these facilities would not incur a base fee due to this listing. If they are not already paying the maximum fee, they would begin to pay an additional per-chemical fee of $1,100.

All potential filers are estimated to be current TURA filers, so additional planning costs would be modest. For companies that only need to report the QAC category, the cost of hiring a planner will likely be in the range of $1,000 - $3,000. Companies that want to have their own in-house TUR planner can qualify either by relying on past work experience in toxics use reduction or by having a staff member take the TUR Planners' training course. Those facilities with experienced staff can become certified for as little as $100. For those that want staff to take a course, the cost will be between $650 - $2000 depending on whether the company has previously filed a TURA report. Companies with in-house toxics use reduction planners are likely to reap ancillary benefits from having an employee on staff who is knowledgeable about methods for reducing the costs and liabilities of toxics use. Additionally, through the process of planning and reducing or eliminating use of chemicals in the category, facilities may be able to expand their markets, better comply with other regulations and reduce their overall regulatory burden.

The total additional cost in fees to filers (and revenue to the program) could be $3,300 to $6,600 in per-chemical fees (3-6 filers for QAC). No new base fees are estimated at this time.

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[1]United States Environmental Protection Agency, List N: Disinfectants for Use Against SARS-CoV-2 (COVID-19): https://cfpub.epa.gov/wizards/disinfectants/

[2] Vereshchagin, A.N.; Frolov, N.A.; Egorova, K.S.; Seitkalieva, M.M.; Ananikov, V.P. Quaternary Ammonium Compounds (QACs) and Ionic Liquids (ILs) as Biocides: From Simple Antiseptics to Tunable Antimicrobials. *Int. J. Mol. Sci.* **2021**, *22*, 6793. https://doi.org/10.3390/ijms22136793

[3] USEPA/Office of Pesticide Programs; Didecyl Dimethyl Ammonium Chloride (DDAC) Final Work Plan, Registration Review: Initial Docket Case Number 3003, March 2017. Docket Number EPA-HQ-OPP-2015-0740

[4] United States Environmental Protection Agency (2017) Alkyls Dimethyl Benzyl Ammonium Chloride (ADBAC) Final Work Plan, Registration Review: Initial Docket, Case Number 03050, Docket Number EPA-HQ-OPP-2015-0737.

[5] ECHA; Didecyldimethylammonium chloride (7173-51-5). Registered Data Dossier. Helsinki, Finland: European Chemicals Agency. Accessed at: https://echa.europa.eu/registration-dossier/-/registereddossier/5864/4/2

[6] ECHA; Didecyldimethylammonium chloride (7173-51-5). Registered Data Dossier. Helsinki, Finland: European Chemicals Agency. Accessed at: https://echa.europa.eu/registration-dossier/-/registereddossier/5864/4/2

[7] Stepan Company, Stepanquat 8358: https://zh.stepan.com/content/stepan-dot-com/en/products-markets/product/STEPANQUAT8358.html

[8] Quinn MM, Henneberger PK, Braun B, Delclos GL, Fagan K, Huang V, et al. Cleaning and disinfecting environmental surfaces in health care: toward an integrated framework for infection and occupational illness prevention. Am J Infect Control. 2015;43:424–34.

[9] Vandenplas, O., D'Alpaos, V., Evrard, G., Jamart, J.,Thimpont, J., Huaux, F., Renauld, J., (2013) Asthma related to cleaning agents: a clinical insight. *British Medical Journal* (http://dx.doi.org/10.1136/ bmjopen-2013-003568

[10] Preller L, Doekes G, Heederik D, Vermeulen R, Vogelzang PF, Boleij JS. Disinfectant use as a risk factor for atopic sensitization and symptoms consistent with asthma: an epidemiological study. Eur Respir J. 1996 Jul;9(7):1407-13. doi: 10.1183/09031936.96.09071407. PMID: 8836651.

[11] Dumas O, Boggs KM, Quinot C, Varraso R, Zock JP, Henneberger PK, Speizer FE, Le Moual N, Camargo CA Jr. Occupational exposure to disinfectants and asthma incidence in U.S. nurses: A prospective cohort study. Am J Ind Med. 2020 Jan;63(1):44-50. doi: 10.1002/ajim.23067. Epub 2019 Nov 6. PMID: 31692020; PMCID: PMC6891131.

[12] Bernstein, Jonathan, et al (1994) A combined respiratory and cutaneous hypersensitivity syndrome induced by work exposure to quaternary amines. Journal of Allergy and Clinical Immunology

[13] 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

[14] Association of Occupational and Environmental Clinics (AOEC) Exposure code lookup for Alkyl Dimethylbenzyl ammonium chloride (CAS #: 68424-85-1) accessed on 10/14/20: http://www.aoecdata.org/ExpCodeLookup.aspx
[15] Dumas O, Varraso R, Boggs KM, et al. Association of Occupational Exposure to Disinfectants With Incidence of Chronic Obstructive Pulmonary Disease Among US Female Nurses. JAMA Netw Open. 2019;2(10):e1913563. doi:10.1001/jamanetworkopen.2019.13563
[16] Dumas O, Boggs KM, Quinot C, Varraso R, Zock JP, Henneberger PK, Speizer FE, Le Moual N, Camargo CA Jr. Occupational exposure to disinfectants and asthma incidence in U.S. nurses: A prospective cohort study. Am J Ind Med. 2020 Jan;63(1):44-50. doi: 10.1002/ajim.23067. Epub 2019 Nov 6. PMID: 31692020; PMCID: PMC6891131.
[17] Gonzalez M, Jégu J, Kopferschmitt MC, Donnay C, Hedelin G, Matzinger F, Velten M, Guilloux L, Cantineau A, de Blay F. Asthma among workers in healthcare settings: role of disinfection with quaternary ammonium compounds. Clin Exp Allergy. 2014 Mar;44(3):393-406. doi: 10.1111/cea.12215. PMID: 24128009.
[18] 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
[19] 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
[20] 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
[21] 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
[22] 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
[23] Melin VE, Melin TE, Dessify BJ, Nguyen CT, Shea CS, Hrubec TC. Quaternary ammonium disinfectants cause subfertility in mice by targeting both male and female reproductive processes. Reprod Toxicol. 2016 Jan;59:159-66. doi: 10.1016/j.reprotox.2015.10.006. Epub 2015 Nov 12. PMID: 26582257
[24] 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
[25] Hrubec TC, et al. (2020) Altered Toxicological Endpoints in Humans with Quaternary Ammonium Compound Exposure doi: https://doi.org/10.1101/2020.07.15.20154963
[26] Herron, J.; Reese, R. C.; Tallman, K. A.; Narayanaswamy, R.; Porter, N. A.; Xu, L., Identification of environmental quaternary ammonium compounds as direct inhibitors of cholesterol biosynthesis. *Toxicol. Sci.* **2016,** *151*, 261-270.
[27] Datta, S.; He, G.; Tomilov, A.; Sahdeo, S.; Denison, M. S.; Cortopassi, G., In vitro evaluation of mitochondrial function and estrogen signaling in cell lines exposed to the antiseptic cetylpyridinium chloride. *Environ. Health Perspect.* **2017,** *125*, 087015-087015.
[28] Guomao Zheng, Gabriel M. Filippelli, and Amina Salamova Increased Indoor Exposure to Commonly Used Disinfectant during the COVID-19 Pandemic, *Environmental Science & Technology Letters* **2020** *7* (10), 760-765 DOI: 10.1021/acs.estlett.0c00587
[29] Global Antiseptics And Disinfectants Market Report, 2021-2028 (grandviewresearch.com)
[30] https://www.epa.gov/pesticide-labels/dfe-certified-disinfectants
[31] Rose, L., Westinghouse, C. (2020) Infection Control Handbook for Schools, Informed Green Solutions, Chapter 4
[32] Rose, L., Westinghouse, C. (2020) Infection Control Handbook for Schools, Informed Green Solutions, Chapter 4
[33] Association of Occupational and Environmental Clinics (AOEC) Exposure Code 050.480 "Mixture of Hydrogen Peroxide and Peroxyacetic Acid" Accessed 9/21/2021: http://www.aoecdata.org/ExpCodeLookup.aspx
[34] Rose, L., Westinghouse, C. (2020) Infection Control Handbook for Schools, Informed Green Solutions, Chapter 4
[35] eCFR :: 40 CFR 180.940 -- Tolerance exemptions for active and inert ingredients for use in antimicrobial formulations (Food-contact surface sanitizing solutions).