

Increased Use of Quaternary Ammonium Compounds during the SARS-CoV-2 Pandemic and Beyond: Consideration of Environmental Implications

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ABSTRACT: Quaternary ammonium compounds (QACs) are active ingredients in over 200 disinfectants currently recommended by the U.S. EPA for use to inactivate the SARS-CoV-2 (COVID-19) virus. The amounts of these compounds used in household, workplace, and industry settings has very likely increased, and usage will continue to be elevated given the scope of the pandemic. QACs have been previously detected in wastewater, surface waters, and sediments, and effects on antibiotic resistance have been explored. Thus, it is important to assess potential environmental and engineering impacts of elevated QAC usage, which may include disruption of wastewater treatment unit operations, proliferation of antibiotic resistance, formation of nitrosamine disinfection byproducts, and impacts on biota in surface waters. The threat caused by COVID-19 is clear, and a reasonable response is elevated use of QACs to mitigate spread of infection. Exploration of potential effects, environmental fate, and technologies to minimize environmental releases of QACs, however, is warranted.



INTRODUCTION

During the SARS-CoV-2 (COVID-19) pandemic, many disinfection practices, including hand washing and surface cleaning, have changed to limit disease transmission. These practices will continue to evolve as people return to work and resume other activities, leading to more routine and thorough disinfection to minimize virus transmission. These new cleaning routines and habits may continue past the time when SARS-CoV-2 is an urgent threat. Quaternary ammonium compounds (QACs) are known to be effective at inactivating enveloped viruses,^{1,2} such as SARS-CoV-2, and the U.S. Environmental Protection Agency's (EPA) *List N: Disinfectants for Use Against SARS-CoV-2* has 430 products, of which 216 contain QACs as the active ingredient,³ with specifics shown in [Figure 1](#). Of the 18 virucidal products for surface disinfection listed by the Association for Applied Hygiene in Germany, three contain QACs.⁴ It has been recently noted, however, that additional evaluation of the effectiveness of QACs against coronaviruses is needed.⁵

Before the pandemic, QACs, including benzalkyl dimethylammonium compounds (BACs or benzalkonium compounds), alkytrimethylammonium compounds (ATMACs), and dialkyldimethylammonium compounds (DADMACs) were already widely used in the U.S.; i.e., all of these were designated high production volume chemicals by the EPA and the Organization for Economic Cooperation and Development

with over 1 million pounds per year manufactured or imported. In Europe, however, uses of QACs have recently been limited in food products and consumer hand and body washes.⁶ Past reviews have focused on the detection, fate, impacts, and regulation of QACs,^{6–9} but usage has likely increased in various settings during the pandemic, including hospitals, long-term care facilities, households, and workplaces considered essential (like grocery stores and food processing plants). Increased handwashing with antibacterial soaps will also lead to more use. After the ban on triclosan, BACs are used as replacements in many over-the-counter antibacterial hand soaps, particularly because BACs were not disallowed ingredients by the U.S. Food and Drug Administration.^{10,11} As economies begin to open, and disinfection protocols for office, retail, manufacturing, and other industrial workspaces are required, usage of products containing QACs will likely continue to increase. There may also be usage in heavily trafficked areas such as outdoor common spaces and public transit systems. This usage is understandable given the ubiquity

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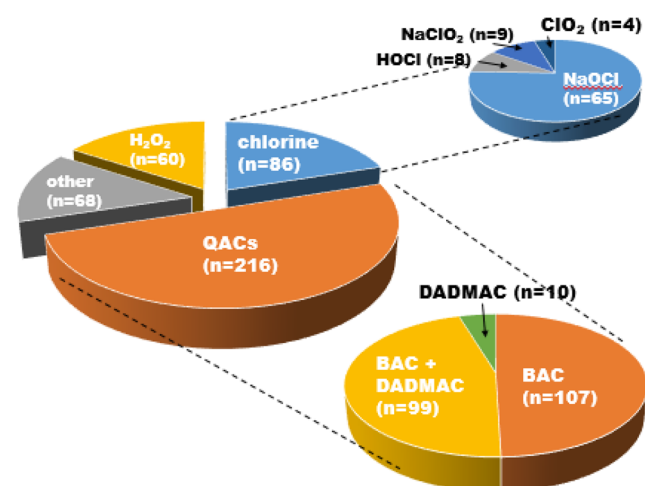


Figure 1. Active ingredients in products on the EPA List N as of June 21, 2020. The benzalkyl dimethylammonium compounds (BACs) are benzalkyl dimethyl or ethylbenzalkyl dimethyl ammonium compounds or a combination of the two. The dialkyldimethylammonium compounds (DADMACs) are predominantly dioctyl, octyl decyl, or didecyl dimethylammonium chloride or a combination of these. Eight of the products containing only DADMAC, 14 containing only BACs, and four with both also contain ethanol or isopropanol. A peroxy acid is present for 25% of the products containing hydrogen peroxide. Other disinfectants include citric acid (10), dodecylbenzenesulfonic acid + lactic acid (2), ethanol (5), glycolic acid (3), 1,2-hexandiol (1), hydrochloric acid (5), isopropanol (1), lactic acid (6), octanoic acid (1), peroxyacetic acid (8), phenolic compounds (11), potassium peroxymonosulfate (3), silver ion (2), sodium dichloroisocyanurate (4), sodium dichloro-S-triazinetriene (2), and thymol (4).

of QACs in disinfectant wipes and surface spray cleaners and the current recommendations to use these compounds to limit virus transmission. The increased consumption of QACs, however, will lead to increased loads to wastewater treatment systems and to the environment. Thus, it is important to identify (i) resulting concentrations from elevated loads and their environmental fate, (ii) potential impacts to wastewater treatment infrastructure and aquatic systems, and (iii) the processes that lead to degradation/removal. This is *not* to say that use should be restricted at this time; rather we are noting that, in addition to more data regarding effectiveness, ancillary environmental impacts need exploration along with means to ameliorate identified risks. Coupled with effectiveness data, evaluation of environmental risks is important information for developing a hierarchy for disinfectant product usage recommendations that maximize efficacy and minimize environmental and other risks.

The majority of QACs used ultimately enter wastewater treatment plants (WWTPs) indicating this is one location where effects could manifest. QACs are present in the effluent water and sorbed to sludge, which provides two pathways to the environment if biosolids are used as a soil amendment.⁷ If use increases in outdoor spaces or in transit systems, stormwater runoff could also carry QACs.¹² Therefore, loadings to WWTPs, discharges to surface waters receiving effluent, and direct inputs into the environment are likely to increase in the immediate and foreseeable future. Potential concerns regarding increased usage include disruption of treatment plant operation and impacts on the spread of antibiotic resistance.^{13–16} Toxicity to aquatic organisms is of concern, as is the formation of *N*-nitrosamines via reaction

with chloramines. The following sections provide an overview of QAC history and environmental fate and explore potential impacts of increased QAC loadings to both wastewater treatment systems and aquatic environments, identify situations where increased monitoring of QAC levels may be needed, and propose potential ways to reduce these impacts.

HISTORY AND USAGE

QACs were first introduced as derivatives of hexamethylene tetramine, and the bactericidal properties of these salts were explored in several publications from 1915 to 1916.^{17–20} It was not until 1935 that the broader use of QACs began with the development of benzalkyl dimethylammonium chloride (ADBAC or benzalkonium chloride or BAC), in which the alkyl group can be a chain containing eight to 18 carbon atoms.²¹ The new surface disinfectant was marketed as Zephrol (sold in the U.S. as Zephiran, Roccal, or BTC).²² By the 1940s, QACs were increasingly used as surface-active agents and detergent disinfectants. Proposed and actual applications ranged from disinfection of utensils and glassware to prevent disease transmission in public eateries and military mess halls; to curbing infection in military settings and hospitals, in particular to combat drug resistant strains of bacteria; to the dairy industry to wash udders and to disinfect milking machines, processing and pasteurization equipment, and dairy tanks and cans used to transport milk.²³ In addition to BACs, the other major classes of QACs are the ATMACs and DADMACs. Other historically commonly used QACs include Cetavlon or CTAB (cetyltrimethylammonium bromide) and DTDMAC (ditallow dimethylammonium chloride), which was a common fabric softener ingredient until voluntary phase-out and replacement by a less hydrophobic, more readily biodegradable surfactant.^{9,22}

Demand for QACs has increased over the decades, and they continue to be widely used chemicals, chemical mixtures, and additives in a variety of industrial, agricultural, clinical, and consumer products and applications.^{7,9,24} In 1945, the U.S. produced 3 million pounds of surface-active agents; by 1993, that number reached 7787 million pounds.²³ U.S. production of QACs was estimated to be approximately 100 million pounds in 1979 with DADMACs accounting for the largest production volume due to use in fabric softeners and oil-based drilling muds. The estimated consumption of the other major class of QACs, BACs, was 20–25 million pounds. Approximately 80% of the market for BACs was in biocides, sanitizers, and disinfectants, with the remainder being in hair conditioners in shampoos and cream rinses, emulsifying agents, and constituents in deodorizers.²⁵ On the basis of U.S. EPA Chemical Data Reporting in 2015, national aggregate production volumes ranged from 10 to 50 million pounds each for several BAC, ATMAC, and DADMAC mixtures.²⁶

QACs are some of the most extensively used classes of biocides, disinfectants, sanitizers, antimicrobials, and cleaners.^{7,9,24,27} Because of their broad-spectrum antimicrobial properties against bacteria, fungi, and viruses, QACs are applied in household, food-processing, agriculture, and clinical settings to control the spread of environmentally transmitted pathogens.^{6,27} Many commercial cleaning products marketed as antibacterial and personal care products including antibacterial soaps and alcohol-free hand sanitizers contain QACs as active ingredients. The carbon chain influences the antimicrobial activity of QACs. Generally, alkyl chain lengths from C₁₂ to C₁₆ exhibit greater antimicrobial activity, and twin-

chained compounds such as DADMACs demonstrate better bioactivity toward some Gram-positive bacteria compared to BACs.^{27,28} 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 headgroup and negatively charged cytoplasmic membrane, adsorption, and then permeation of side chains into the intramembrane region.²⁸ The lipid layer of enveloped viruses makes them sensitive to the hydrophobic activity of QACs.^{5,27}

ENVIRONMENTAL INPUTS AND FATE

QACs have been detected worldwide not just in domestic wastewater and sludge but also in treated effluent, surface water, and sediment.^{29–32} It is anticipated that the majority of QAC applications leads to their eventual release (~75%) into sewers and WWTPs.^{24,25} Though QACs are removed from the liquid stream during conventional wastewater treatment via a combination of sorption to biosolids and biodegradation, these compounds are still detected in aquatic environments, especially at higher concentrations in locations downstream of the discharge of municipal WWTP effluents and hospital and industrial (e.g., laundry and food processing) effluents.^{32,33} The reason elevated environmental concentrations are found despite ~90% removal from the liquid stream in wastewater treatment is because QACs are high production volume chemicals; consequently, as the global appetite for QACs grows,³⁴ these compounds will increasingly enter the environment through point source pollution, land application of biosolids, or treated municipal and industrial effluent discharges. Concentrations of QACs detected worldwide in surface water and wastewater effluent range from less than 1 $\mu\text{g/L}$ to approximately 60 $\mu\text{g/L}$, and QACs have been found to be up to 10 times these levels in influent wastewater.^{7,24,32,35–39} A study in Germany detected average total C_{12} -BAC concentrations of 4.7 and 7.7 $\mu\text{g/L}$ in wastewater samples collected directly from two neighborhood street sanitary sewers.⁴⁰ On the basis of product surveys in households, the researchers tentatively linked BAC detection to use in surface disinfectants, soaps, and/or washing and cleaning agents. BACs are the most frequently found QAC group worldwide in municipal or industrial wastewater effluents at levels up to the mg/L range in indirect discharge wastewater and effluent from hospitals.^{32,33,37,41} Ruan et al. detected total concentrations of homologues of ATMAC, BAC, and DADMAC ranging from 1.12 to 505 mg/kg dry weight in municipal biosolids throughout China.²⁹ Of the different homologues, C_8 - to C_{18} -DADMACs, C_{12} - to C_{18} -ATMACs, and C_{12} - to C_{18} -BACs are identified as the most frequently detected in the environment.^{8,42–44} We note that while there are many reports of BAC detection there is minimal information on the ethylbenzalkyl dimethylammonium compounds that are components of many of the BAC-containing products in Figure 1, and the environmental levels of these compounds merit study. Benzethonium chloride is another QAC active ingredient in a few of the hard-surface disinfectant products on the EPA list, which has a paucity of environmental data and might warrant further study.

There are three main attenuation mechanisms for QACs in the aquatic environment: photolysis, biodegradation, and sorption to suspended particles followed by sedimentation. Generally, QACs have been considered stable or relatively slow to degrade by hydrolysis, photolysis, or microbial activity.

While the ethylbenzalkyl dimethylammonium compounds have not received specific attention, it is expected that their fate would be similar to other QACs. The photochemical processing of QACs in the environment has been explored in a limited capacity. Although some QACs contain chromophoric functional groups that would make them susceptible to direct photodegradation, many lack these groups or weakly absorb light in the solar spectrum. QACs like BACs and DADMACs have previously exhibited relatively long photolysis half-lives in aqueous and soil environments.^{45,46} Recent work exploring indirect photolysis of QACs including two BAC homologues, a DADMAC, an ATMAC, and benzethonium chloride in surface waters estimated half-lives from 12 to 94 days.⁴⁷

Most studies of biodegradation of QACs have been performed using activated sludge or enrichment cultures, but there is some evidence for degradation over a period of 5–10 days of ATMACs and BACs by marine bacteria.^{48–54} From previous studies relying on enrichment and isolation of QAC-resistant bacteria, species that degrade and even mineralize QACs to carbon dioxide have been identified.^{24,28,55–57} These include strains of *Pseudomonas*, *Xanthomonas*, *Aeromonas*, *Stenotrophomonas*, and *Achromobacter*.^{48,57–60} Biotransformation pathways have also been elucidated for several QACs by bacterial isolates. A few studies have reported the microbial degradation of BAC by several pure cultures (*Pseudomonas nitroreducens*, *Aeromonas hydrophila*, and *Bacillus niabensis*) to benzyldimethylamine by dealkylating amine oxidase and related enzymes.²⁸ Other identified enzymes include tetradecyl trimethylammonium bromide monooxygenase, a Rieske-type oxygenase oxyBAC, as well as three genes encoding oxygenases that metabolize naturally occurring QACs.⁴⁸ Work is needed, however, to assess if such degradation occurs in aquatic systems by complex microbial communities.

Due to their strong affinity to organic and inorganic particles, a large fraction of QACs is removed from surface waters by sedimentation. Consequently, QACs have been identified in surface sediment samples from rivers in Austria, WWTP effluent-impacted estuaries in New York City, and sewage-impacted lakes in Minnesota with total QAC concentrations between 1 ng/g ($\mu\text{g/kg}$) and 74 $\mu\text{g/g}$ (mg/kg).^{30,39,41,61,62} Concentrations of BACs and DADMACs are typically much higher than concentrations of ATMACs with C_{12} -BAC (3.6 $\mu\text{g/g}$), C_{14} -BAC (7.2 $\mu\text{g/g}$), C_{18} -DADMAC (26 $\mu\text{g/g}$), and C_{22} -ATMAC (6.8 $\mu\text{g/g}$) reaching the highest recorded levels of individual QACs. Surface sediment samples from effluent-impacted estuaries in New York City were found to contain especially high QAC concentrations, with median total QAC concentration about 25 times higher than the median sum of polycyclic aromatic hydrocarbons at the same location.³⁰ QACs have also been quantified in dated sediment cores from lakes in Minnesota and from urban estuaries near New York City, Hong Kong, and Tokyo.^{39,62–64} A common pattern to all these sediment cores, which represent a temporal archive of contaminant input into aquatic environments, is positive detection of QACs since the 1950s and peak concentrations (0.7–400 $\mu\text{g/g}$ total QAC) corresponding to depositions between the 1960s and the 1980s. Sediment concentrations decrease afterward, likely due to implementations of improved domestic and industrial wastewater treatment, for most QACs and locations, except for certain short-chain DADMACs and long-chain ATMACs. Increased current and future usage in response to the COVID-19 pandemic,

however, could lead to increasing levels in sediments. Despite being detected worldwide at high levels in sediments, conclusive data about the bioavailability of QACs once sorbed are scarce. So far only Li et al. were able to show that total masses of BACs and ATMACs were reduced by 39%–55% in two dated sediment cores from the same location taken 12 years apart, indicating *in situ* degradation of ATMACs and BACs (particularly those with short chains), while DADMACs were concluded to be recalcitrant.⁶³

Another route of QACs to the environment is inputs to soils via amendments of biosolids. Mulder et al. predict environmental concentrations of QACs in biosolids-amended soil ranging from high $\mu\text{g}/\text{kg}$ to mg/kg , but this may arise from animal manure instead of municipal biosolids.⁶⁵ While biodegradation in soil is possible, it has not been specifically studied and will be a function of bioavailability, and QACs are known to sorb to clays.⁶⁵ Because biosolids retain QACs, potential effects of land application of biosolids with QAC levels higher than those previously used need attention.

■ POTENTIAL IMPACTS

Effects on Wastewater Treatment Plant Operations.

During activated sludge treatment, QACs are removed by sorption to organic-rich substrates and biomass and/or biodegradation. Several QAC classes, particularly BACs and ATMACs, are known to be degraded by certain microorganisms during aerobic biological wastewater treatment.^{37,49,66–68} The process, however, is dependent on QAC concentration, structure, microbial consortia, and treatment conditions. If the concentration of QACs is too high, the presence of QACs proves inhibitory to microbial activity and even detrimental to the microorganisms.^{50,56,57,69} If the concentration of QACs is too low, the QAC may no longer serve as an attractive carbon source for the microorganisms.

In general, QACs are inhibitory to activated sludge at levels (e.g., 10–40 mg/L) higher than currently found in treatment plants.⁷⁰ Nitrification processes, however, are more susceptible to inhibition than carbonaceous biochemical oxygen demand removal.⁷¹ The noncompetitive nitrification inhibition coefficient was reported to be 1.5 mg/L for BAC,⁷² which is only about a factor of 3 higher than average wastewater influent concentration.^{7,24,32,37} In full-scale systems, the majority of QACs are either biodegraded or sorbed during the activated sludge process prior to the nitrification step.³⁷ QACs are thought to sorb first to solids, and then, after readily available substrates are utilized, QACs are biodegraded. Using longer retention times via extended aeration or attached growth systems has been recommended to increase BAC removal,⁷¹ but levels higher than 2 mg/L have been shown to affect performance and increase biofouling in membrane bioreactors.⁷³ If given sufficient time to adapt, biological nitrogen removal systems can adjust to increasing QAC loadings,⁷⁴ but sudden increases in QAC inputs could cause operational problems.

BAC can be transformed under nitrate reducing (denitrification) conditions,⁷⁵ and nitrate was still reduced to dinitrogen at BAC concentrations up to 25 mg/L . At higher BAC concentrations nitrous oxide was formed. Specifically, nitrite reduction is the step most inhibited by BAC during denitrification.⁷⁶ Lower temperatures lead to increased inhibition by BAC. Overall, increased monitoring of QACs in WWTPs performing nitrification/denitrification may be required if system operations appear to be affected.

While degradation of QACs occurs in aerated activated sludge systems, a major removal mechanism is sorption to biosolids with 38%–96% of the QACs mass ultimately residing in the digester solids.⁷⁷ Sorption of QACs occurs faster than aerobic biodegradation, which means that QACs end up being transferred to biosolids handling treatment processes, often anaerobic digestion.^{7,9,25,29,41,65,78} This is particularly an issue for longer chained compounds. While biodegradation has been identified as a potential sink for QACs during wastewater treatment, sorption could reduce QAC availability to microorganisms that might degrade them. Moreover, there has been little experimental evidence that QACs containing alkyl and benzyl groups are mineralized under anaerobic treatment conditions, and research has suggested that biodegradation of QACs under anaerobic conditions is limited.^{7,79} Inhibitory impacts to digester functioning (as measured by biogas production) can vary by compound and concentration.^{79,80}

Tezel et al. reported that QACs were more inhibitory to methanogenesis (a process carried out by Archaea) than to acidogenesis (a process carried out by Bacteria).⁸¹ It was postulated that this finding could be due to the makeup of the cell wall in methanogens or due to their reliance on the proton motive force instead of substrate level phosphorylation for ATP generation. The authors tested benzalkyl, dodecyl, dioctyl, and octyldecyl dimethylammonium compounds and found that the QACs with shorter alkyl chain lengths, i.e., the more hydrophilic compounds, were more inhibitory. The IC50 values were approximately 25 mg/L or greater (equivalent to 833 mg/kg assuming 3% solids in a digester). Longer-term batch-fed studies revealed that initial methanogenesis inhibition by a QAC mixture was eventually overcome, suggesting that microbial communities can adapt and/or QACs become less bioavailable over time. The QACs were not biodegraded under anaerobic conditions indicating that QACs present in anaerobic digesters will remain with biosolids that are land applied.

The type and source of sludge will likely affect how inhibitory QACs are to anaerobic digestion. Flores et al. reported an IC50 value of BAC in digester sludge closer to 13 mg/L .⁸² As opposed to Tezel et al., who used municipal anaerobic digester sludge, the inoculum sludge was granular sludge taken from an upflow anaerobic sludge blanket (UASB) reactor treating pharmaceutical wastewater. They also operated a lab-scale UASB reactor fed BAC at the IC50 dose, and it failed. However, they noted concentrations of BAC in full-scale digesters have been found above this level. Thus, real-world digesters with high levels must have acclimated over time. A wide range of sludge concentrations have been reported (0.1–300 mg/kg total suspended solids), with up to 25 mg/kg for individual compounds at the highest reported levels.⁷ Thus, increasing QAC concentrations could lead to one of two results: digester failure or further acclimation via changes in microbial community structure, potentially to communities that harbor more antibiotic resistance (see below). He et al. confirmed that BAC altered the diversity and microbial community composition of both Bacteria and Archaea in anaerobic digesters.⁸³ Monitoring of QACs and associated resistance genes in anaerobic digester systems may be warranted.

Antibiotic Resistance. QACs kill bacteria by gross membrane disruption, and the impacts of QACs on selecting for antibiotic resistance in pure cultures has been well documented and reviewed in detail elsewhere.^{6,24,84} This

selection is not of concern for chlorine-based disinfectants or hydrogen peroxide, which decompose more rapidly. Perhaps of greatest concern is the proliferation of pathogenic multidrug resistant bacteria (“superbugs”), following exposure to QACs. Indeed, methicillin-resistant *Staphylococcus aureus* (MRSA) strains exposed to BAC as well as benzethonium chloride had increased resistance to oxacillin and β -lactam antibiotics.⁸⁵ *Salmonella enterica* and *Escherichia coli* O157 exposed to BAC also developed cross-resistance to antibiotics.⁸⁶

Of great interest following the heightened use of QACs during the COVID-19 pandemic will be what effects QACs have on antibiotic resistance in mixed microbial communities, i.e., the microbial communities present in natural and engineered environments. Exposure to BAC at subinhibitory levels in an aerobic sediment microbial community altered microbial community composition and increased resistance to BAC as well as penicillin G, tetracycline, and ciprofloxacin.⁵⁷ The increased resistance was attributed to the selection for bacteria that harbored efflux pumps and other resistance mechanisms. Follow-up research on the aerobic sediment communities revealed that BAC selected for BAC resistance and antibiotic resistance in multiple sediment strains, including *Achromobacter* sp., *Citrobacter freundii* sp., *Klebsiella michiganensis* sp., and *Pseudomonas aeruginosa* sp.⁸⁷ Resistance was due to multiple mechanisms, including mutations and overexpression of multidrug efflux pumps. Another key finding was that antibiotic resistance can arise due to coresistance, i.e., acquisition of two collocated genes, one that confers resistance to BAC and one that confers resistance to an antibiotic. Of note, though, is that increased resistance was not universal. Of the seven antibiotics tested, resistance increased to three antibiotics. A similar finding was observed in a study on a mixed microbial community taken from a freshwater lake used for drinking water.⁸⁸ BAC selected for resistance to the fluoroquinolone antibiotic ciprofloxacin at only 0.1 $\mu\text{g/L}$ and also selected for resistance to sulfamethoxazole. The resistance of the community to other antibiotics, though, declined after exposure to BAC. Collectively, these studies indicate that BAC is not a universal selective agent for antibiotic resistance, but rather it will alter the antibiotic resistance profiles of microbial communities. If this effect will be better or worse from a public health standpoint depends on the clinical need for the particular antibiotics that are less effective after BAC exposure. Multiple studies revealed that BAC increased resistance to ciprofloxacin, which is currently a top 5 prescribed antibiotic, and was the most abundant antibiotic found in biosolids in the U.S., an indication of its high usage.⁸⁹ As concentrations of BAC increase, it is possible that BAC will promote more clinically relevant antibiotic resistance. As noted in the above sections, a majority of BAC passes through anaerobic digesters. Yet, to the best of our knowledge, no research has been conducted to elucidate the impacts of BAC on selection of antibiotic resistance in anaerobic digesters. Previous work on the broad-spectrum antimicrobials triclosan and triclocarban revealed their selection for antibiotic resistance genes as well as functional cross-resistance to antibiotics in anaerobic digestion.^{90–92} The QACs DTDMAC and CTAB were also found to correlate with higher frequencies of *intI1* and antibiotic resistance genes.⁹³ Class 1 integrons often contain *qac* genes which confer resistance to QACs via efflux.^{13–16} This is an especially interesting phenomenon because integrons allow bacteria to acquire other antibiotic resistance genes via horizontal gene transfer.¹⁵ Thus, increased QAC concen-

trations could select for bacteria that harbor *qac* genes and integrons/antibiotic resistance genes, ultimately leading to more multidrug resistant bacteria. Another unintended consequence of more frequent QAC usage, especially in food preparation and clinical settings, is increasing tolerance or resistance to a particular QAC and development of cross-tolerance to other QAC formulations among pathogenic bacteria.⁹⁴ The impact of QACs on antibiotic resistance, including impacts on horizontal gene transfer rates and multidrug resistance, in environments that will be exposed to higher QAC concentrations should be further researched, including anaerobic digestion and soils amended with municipal biosolids.

Disinfection Byproducts: N-Nitrosamines. The last treatment step in wastewater treatment is often disinfection. Even when disinfection is performed with chlorine, there are still chloramines formed from reaction with ammonia present, even in nitrified effluents. Chloramines are known to react with organic amines to form nitrosamines.⁹⁵ N-Nitrosodimethylamine (NDMA), a known carcinogen, receives the most attention. Gray and black waters containing various cleaning and bathing products have been shown to produce N-nitrosamines upon exposure to chloramine.⁹⁶ While likely responsible for only a fraction of the production, QACs do form NDMA with low molar yields ($\sim 0.03\%–0.3\%$).⁹⁷ The yield is not reduced upon purification, indicating that trace tertiary amines are likely not the precursors, as seen for polymers treated to remove tertiary amines.⁹⁸ NDMA, however, is only a small fraction of the total production of N-nitrosamines.⁹⁹ Recent work has demonstrated that while NDMA yield for a BAC and an ATMAC are minimal, total N-nitrosamine molar yields range from 0.7% (pH 6) to 5% (pH 8) upon treatment with chloramine.¹⁰⁰ While release of N-nitrosamines into the environment is undesirable, they are subject to decay processes. The production of elevated levels of N-nitrosamines from increased levels of QACs upon chlor(am)ination of wastewater is likely to be of greatest concern for direct or indirect potable reuse scenarios, where there is potential for human exposure to the N-nitrosamines. In these situations, increased monitoring of QAC levels and N-nitrosamine formation is likely needed.

Toxicity to Aquatic and Soil Organisms. A more in-depth overview of the toxicity of QACs on aquatic organisms can be found in recently published reviews.^{7,101} QACs are algistatic and bacteriostatic at concentrations ranging from 0.5 to 5 mg L^{-1} and microbiocidal at concentrations from 10 to 50 mg/L .²⁷ Acute toxic effects on marine bacteria of the *Vibrionaceae* family, however, have already been observed at high $\mu\text{g/L}$ concentrations ($\text{EC}_{50} = 57–630 \mu\text{g/L}$).^{54,102} The largest number of toxicity studies with QACs over the past 20 years were performed with various algae species. Typical acute toxicity thresholds (EC_{50} –96h) were between 0.1 and 1.8 mg/L .^{33,103–109} Large variations were observed between different algae species, as well as for different endpoints and QAC structures. Overall, the toxicity of QACs toward algae increased with exposure time and with chain lengths of ATMACs and BACs but not with chain lengths of DADMACs.^{103,105} Aquatic organisms also frequently studied are protozoa, daphnids, and fish. Protozoa (*Tetrahymena thermophila* and *Spirostomum ambiguum*) appear less sensitive than algae with EC_{50} –24h of 1.5–10 mg/L and LC_{50} –24h of 0.2–0.9 mg/L , while *Daphnia magna* are especially sensitive to QACs with average EC_{50} –24h of 0.18 mg/L and EC_{50} –48h of

0.03 mg/L.^{33,54,102,104,110,111} Chronic toxicity thresholds for aquatic species were only reported for the green algae *Dunaliella bardawil* (IC50-10d = 0.78 mg/L), *Daphnia magna* (EC50-21d = 1.0 µg/L), and *Ceriodaphnia dubia* (EC50-7d = 0.04 mg/L).^{107,111} Lethal toxicity of ATMACs toward rainbow trout increased with chain length, and LC50-24h of 0.6–41 mg/L were reported.¹¹⁰ Interestingly, chronic effects on cell lines from rainbow trout appear to be in the same range with EC50 or IC50 values of 0.3–2.7 mg/L.^{104,112} Chen et al. as well as van Wijk et al. studied the effects of adding sediments, clays, or dissolved organic matter to their toxicity tests and found that the freely dissolved fraction of QACs is predominantly responsible for causing toxic effects, likely because sorbed QACs are not as bioavailable.^{104,109} For similar reasons, toxicity thresholds are substantially higher for benthic organisms and terrestrial and aquatic plants.^{104,113–116} It is assumed that QACs sorbed to sediments or soils are not bioavailable, and thus, only the freely dissolved fraction in pore water causes toxic effects in benthic organisms and plants.

Performing a systematic risk assessment for QACs is difficult due to the lack of chronic toxicity data and limited number of exposure measurements in surface waters. The available toxicity and exposure data, however, indicate that high ratios of predicted environmental concentrations (PEC) to predicted no-effect concentrations (PNEC) could be reached for aquatic systems, whereas PEC/PNEC ratios are unlikely to be elevated for sediments and soils. A similar conclusion has been reached previously by Kreuzinger et al.³³ A crude estimate of PNEC was made here based on acute toxicity data from studies with *Daphnia magna*, which appears to be the most sensitive aquatic organism toward adverse effects by QACs. Using the geometric mean of all EC50 values available and an assessment factor of 1000, a conservative PNEC estimate would amount to approximately 100 ng/L. Considering average reported surface water concentrations on the order of 70 ng/L for single QAC compounds and 280 ng/L for total QAC concentrations,^{32,33,117} PEC/PNEC ratio estimates range from 0.7 to 2.8 with a large degree of uncertainty. It is currently difficult to assess whether aquatic organisms are at risk by the levels of QACs seen today or expected in the future. Better chronic toxicity data, studies on mixture toxicity, and more comprehensive exposure measurements, especially for effluent dominated systems or those near chemical manufacturing and medical facilities, are needed.

■ IMPLICATIONS AND INTERVENTIONS

The amount of disinfectants being used has risen, with one manufacturer reporting production in May 2020 equivalent to the entire year of 2019,¹¹⁸ and U.S. sales of disinfectant wipes were 146% higher than the same period last spring.¹¹⁹ While it is unclear if this level will be sustained, some companies that produce hygiene and cleaning products anticipate lasting changes in consumer behavior and increased demand after the COVID-19 pandemic begins to wane.^{119,120} The global surface disinfectant market has a forecasted 9.1% compound annual growth rate from 2020 to 2027.¹²¹ Thus, it should be anticipated that the amounts of QACs used and released to the environment will increase. Because QACs are biologically active compounds, there are several potential environmental impacts that need to be considered due to elevated usage during the COVID-19 pandemic, and these need to be balanced with product efficiency for usage recommendations. Moreover, these unanticipated impacts could persist or

heighten if human behaviors (hand washing, surface disinfection) and product purchasing patterns are altered in the long term. With all biologically active compounds, there are both potential acute toxicity and chronic low-dose exposure issues. If there are short-term, high concentration doses sent to a WWTP, for example, from cleaning of a hospital or building, functional processes such as activated sludge basins or anaerobic digesters could be negatively impacted by the slug of QACs entering the treatment system. Because QACs are surfactants, an influx of the compounds could contribute to or exacerbate existing issues with foaming in WWTPs, which might temporarily disrupt or reduce treatment efficiency.¹²² More likely, increasing QAC concentrations steadily over time would lead to changes in microbial communities that may harbor more antibiotic resistance both in treatment systems and in the environment, especially downstream of WWTPs. Implications of elevated QAC levels in surface waters, sediments, and soils due to biosolids applications indicate a need for further testing of chronic toxicity for aquatic, benthic, and soil organisms to better evaluate potential impacts that may need to be addressed in the current unusual situation. Overall, increased monitoring of QAC levels in WWTP effluents and biosolids is indicated, and assessment of levels in surface waters (especially in cases of (in)direct potable reuse) and soils receiving these effluents and biosolids, respectively, should be considered as well. A better understanding of the ecologically relevant risks associated with low-level QAC exposure is required.

The processes that are known to facilitate degradation of QACs also indicate potential opportunities to improve treatment, limit environmental releases, and minimize environmental impacts. Extended aeration (longer SRT)⁷¹ or aeration with pure oxygen³⁹ or membrane systems could lead to better removal and degradation of the QACs. Treatment wetlands, which facilitate extended biodegradation, photolysis, and removal via particle settling would likely lead to QAC removal.^{123–125} Pyrolysis of biosolids to generate biochar would very likely lead to QAC removal from biosolids.^{126,127} Various advanced oxidation processes, including O₃/H₂O₂, UV/chlorine, and O₃/HOCl, have been shown to degrade QACs and eliminate the toxicity to bacteria or algae.^{128–131}

The threat posed by the COVID-19 pandemic is real and apparent, and priority needs to be given to protecting the health and safety of people in their homes and when in public. As part of the response to the pandemic, QAC usage will increase. Environmental engineers and scientists must be aware of and monitor the fate of QACs so that other aspects of society including wastewater treatment are not compromised. Ironically, fighting the virus could lead to increased infections from antibiotic resistant bacteria if elevated QAC exposure jolts the spread of antibiotic resistance. Fortunately, we cannot claim to be surprised by increases in QACs in our engineered and environmental systems, but we must now pay due diligence to monitor their presence, note concentrations of concern, and develop and implement technologies to remediate their presence when needed.

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Notes

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