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Biocides in hydraulic fracturing fluids: A critical review of their usage, mobility, degradation, and toxicity

Genevieve A. Kahrilas,[1] Jens Blotevogel,[2] Philip S. Stewart,[3] and Thomas Borch*[,1,4]

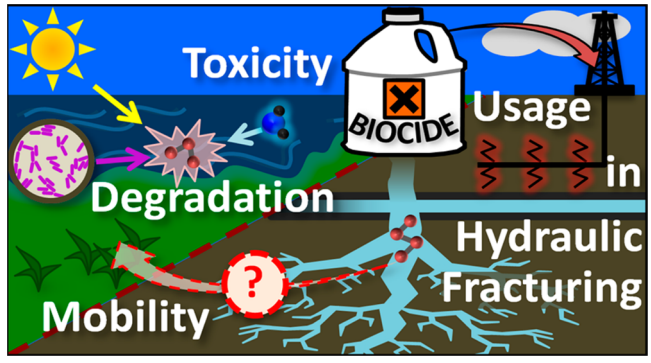
[1]Department of Chemistry, Colorado State University, 1872 Campus Delivery, Fort Collins, Colorado 80523, United States

[2]Department of Civil and Environmental Engineering, Colorado State University, 1320 Campus Delivery, Fort Collins, Colorado 80523, United States

[3]Department of Chemical and Biological Engineering & Center for Biofilm Engineering, Montana State University, 366 EPS Building, Bozeman, Montana 59717, United States

[4]Department of Soil and Crop Sciences, Colorado State University, 1170 Campus Delivery, Fort Collins, Colorado 80523, United States

ABSTRACT: Biocides are critical components of hydraulic fracturing ("fracking") fluids used for unconventional shale gas development. Bacteria may cause bioclogging and inhibit gas extraction, produce toxic hydrogen sulfide, and induce corrosion leading to downhole equipment failure. The use of biocides such as glutaraldehyde and quaternary ammonium compounds has spurred a public concern and debate among regulators regarding the impact of inadvertent releases into the environment on ecosystem and human health. This work provides a critical review of the potential fate and toxicity of biocides used in hydraulic fracturing operations. We identified the following physicochemical and toxicological aspects as well as knowledge gaps that should be considered when selecting biocides: (1) uncharged species will dominate in the aqueous phase and be subject to degradation and transport whereas charged species will sorb to soils and be less bioavailable; (2) many biocides are short-lived or degradable through abiotic and biotic processes, but some may transform into more toxic or persistent compounds; (3) understanding of biocides' fate under downhole conditions (high pressure, temperature, and salt and organic matter concentrations) is limited; (4) several biocidal alternatives exist, but high cost, high energy demands, and/or formation of disinfection byproducts limits their use. This review may serve as a guide for environmental risk assessment and identification of microbial control strategies to help develop a sustainable path for managing hydraulic fracturing fluids.



INTRODUCTION

Biocides are widely used in food preservation, water treatment, healthcare sanitation, textile, and other industries.[1−4] During past decades, a wide variety of bioactive organic chemicals have been developed for disinfection, sterilization, and preservation purposes, including quaternary ammonium compounds, alco-holic and phenolic compounds, aldehydes, halogen-containing compounds, quinoline and isoquinoline derivatives, hetero-cyclic compounds, and peroxygens.[5,6] Biocides have also been applied in oil reservoirs for many decades, particularly in water flooding operations during secondary oil recovery.[7] Likewise, biocides are among the most common chemical additives used for hydraulic fracturing ("fracking" or "fraccing"), a process in which a water-based fluid is used to help induce cracks in oil-and/or natural gas-containing unconventional formations such as shale rock. At total concentrations of up to >500 mg/L[8] and total fluid volumes surpassing 10 million L per horizontal well,[9] total amounts of biocide(s) used per hydraulic fracturing event can exceed 1,000 gallons.[10]

Bacterial control is necessary in hydraulic fracturing opera-tions to prevent excessive biofilm formation downhole that may lead to clogging, consequently inhibiting gas extraction.[11] Biocides inhibit growth of sulfate-reducing bacteria (SRB),[12−14] which anaerobically generate sulfide during the organisms' respiration process. Sulfide species created in the subsurface may pose a risk regarding occupational safety and health when the fluid returns along with produced H_2S gas. Furthermore, SRB and acid-producing bacteria (APB) may induce corrosion of the production casing/tubing underground, potentially leading to casing failure and environmental contamination by petroleum products.[7,12,14−18]

Hydraulic fracturing operations provide bacterial species with many habitats favorable to their (unwanted) growth and

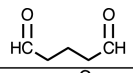
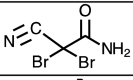
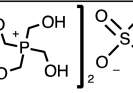
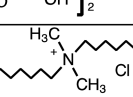
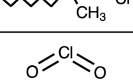
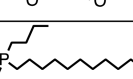
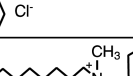
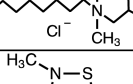
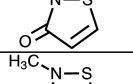
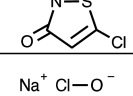
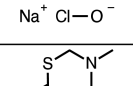
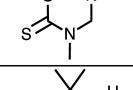
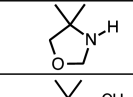
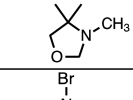
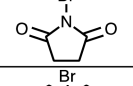
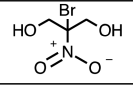
proliferation. The major sources of bacterial contamination are (1) drilling mud, (2) water, (3) proppants, and (4) storage tanks. Prolonged storage of water prior to use, typically in lined or unlined earthen pits,[12,14] can lead to mass proliferation of microorganisms. Likewise, bacteria can thrive in stored produced water that was recycled for use in future fracturing operations.[19,20] The increased temperatures fracturing fluids are exposed to underground may also favor microbial growth,[21] and therefore many bacterial species (including anaerobic species that are native to shale formations)[16,22−25] may proliferate underground during hydraulic fracturing. A diverse array of bacteria including those within the taxa *γ*-proteobacteria, *α*-proteobacteria, *δ*-proteobacteria, *Clostridia*, *Synergistetes*, *Thermotogae*, *Spirochetes*, *Bacteroidetes*, and *Archaea* have all been found in untreated flowback water samples.[25] Sulfate reduction by piezophilic bacteria coupled to oxidation of methane or organic matter is stimulated at high pressure;[26−30] pressure increases naturally underground but is also artificially increased during the process of hydraulic fracturing, matching values relevant to the referenced studies. Similar pressure-stimulation effects have also been observed in iron-reducing bacteria.[26,31,32] In fact, reduction in viability of bacteria due to high pressure does not occur until 100−150 MPa (~15,000−22,000 psi),[26] which exceed most formation pressures.

Biocides are often (but not always) used in hydraulic fracturing fluid formulations. While their application is often mandatory in aboveground oil−water separation units, water storage tanks, and pipelines used to transport these fluids, it is believed that the extremely high temperatures inherent to some shale formations may naturally impede microbial growth.[7] The temperature of shale plays in the continental U.S. varies greatly, even within a single formation. The gas-bearing shales of the Marcellus formation, which exist from 1,200 to 2,600 m underground,[33,34] typically fall within a temperature range of 40−100 °C, but can reach temperatures of 100−125 °C in the southwestern region.[20] In deeper shales such as the Haynesville in Texas/Louisiana (3,200 to 4,100 m underground[34]), the downhole temperature can reach almost 200 °C.[34,35] However, a few studies have suggested that some bacteria are very persistent and may not be completely killed by the extreme underground conditions[23,35,36] or that higher pressures may prevent bacterial death at higher temperatures.[29,37] Furthermore, injection of colder fracturing fluids may lead to considerable cooling of the casing and target formation. Thus, biocides are sometimes added to fracturing fluids even in formations with temperatures exceeding 122 °C, the highest recorded temperature at which aerobic bacteria reproduction has been observed.[38]

To achieve downhole bacterial control, a variety of biocides are currently being added to hydraulic fracturing fluids (Table 1, Supporting Information (SI) Figure S1). Selection of the biocide(s) used is highly dependent on the geology and biogeochemistry of the respective shale formation, and packages are individually tailored depending on their efficacy in bacterial control, compatibility with the respective environment, and cost efficiency.[6,39−43] Combinations of certain biocides may create synergistic effects, thereby decreasing the doses needed for sufficient treatment.[44,45] Furthermore, the reactivity toward other fluid additives must be considered, as many biocides are inherently reactive molecules and side reactions are undesirable.[15]

Unlike water flooding, in which there are continuous inflows and, thus, there is a need for long-term suppression of microbial activity, the goal of biocide application in hydraulic fracturing is to reduce the deleterious microbial populations up-front to the lowest levels possible, in order to mitigate the risk of their colonization of the reservoir and well system long after the fracturing operation has been completed. This is due to the fact that reservoir souring in the fractures downhole cannot be cured after hydraulic fracturing is complete.[46] While sterilization is unlikely, targeting deleterious bacteria with biocides that have been efficacy-tested for performance against those specific species can lead to long-term protection for months or longer, mitigating the risk for souring and microbially induced corrosion (MIC). Thus, it is critical to understand microbial dynamics in this context, i.e., types and concentrations of

Table 1. Chemical Identification Information on Hydraulic Fracturing Biocides[a]

Trade Name & CAS No.	Chemical Structure	Chemical Formula	MOA	Freq. of Use
Glutaraldehyde 111-30-8		$C_5H_8O_2$	E	27%
Dibromo-nitrilopropionamide 10222-01-2		$C_3H_2Br_2N_2O$	E	24%
Tetrakis hydroxymethyl phosphonium sulfate 55566-30-8		$[(HOCH_2)_4P]_2SO_4$	E	9%
Didecyl dimethyl ammonium chloride 7173-51-5		$C_{22}H_{48}NCl$	L	8%
Chlorine dioxide 10049-04-4		ClO_2	O	8%
Tributyl tetradecyl phosphonium chloride 81741-28-8		$C_{26}H_{56}PCl$	L	4%
Alkyl dimethyl benzyl ammonium chloride 68424-85-1		$C_{19}H_{34}NCl$	L	3%
Methylisothiazolinone 2682-20-4		C_4H_5NOS	E	3%
Chloro-methylisothiazolinone 26172-55-4		C_4H_4NOSCl	E	3%
Sodium Hypochlorite 7681-52-9		NaClO	O	3%
Dazomet 533-74-4		$C_5H_{10}N_2S_2$	E	2%
Dimethyloxazolidine 51200-87-4		$C_5H_{11}NO$	E	2%
Trimethyloxazolidine 75673-43-7		$C_6H_{14}NO$	E	2%
N-Bromosuccinimide 128-08-5		$C_4H_4BrNO_2$	E	1%
Bronopol 52-51-7		$C_3H_6BrNO_4$	E	<1%
Peracetic acid 79-21-0		$C_2H_4O_3$	O	<1%

[a]Mode of action (MOA) listed is electrophilic (E), lytic (L), or oxidizing (O). Frequency of use is normalized to only those wells reported on FracFocus[48] in which biocides were used.

microorganisms, carbon sources, nitrogen sources, and electron acceptors present, as well as growth-limiting factors. Furthermore, potential growth rates of microorganisms in fracturing fluids under subsurface conditions need to be considered, which are not yet fully understood.[23−25] To determine a suitable site-specific biocide (combination), 6-log reductions or greater in SRB, APB, or other deleterious bacterial populations are typically aimed for in preliminary laboratory testing according to NACE Standard TM0194.[47] When choosing suitable biocide(s), typical specific parameters of the fracturing operation that can affect biocide performance are taken into account. Some of these parameters include compatibility with the other fracturing chemicals being used, flow rates of the fracture fluids, and the chemistry of the water used. Reservoir conditions such as temperature and formation geology may also be considered. However, selection of biocides is often done based on historical precedence and currently is not optimized on a well-by-well basis.

The following sections of this review will focus on the most common hydraulic fracturing biocides by frequency of application (Table 1) according to the national hydraulic fracturing chemical registry FracFocus.[48] FracFocus is managed by the Ground Water Protection Council and the Interstate Oil and Gas Compact Commission and is currently used as the official state chemical disclosure system in 10 U.S. states (CO, OK, LA, TX, ND, MT, MS, UT, OH, PA). While the registry is not inclusive of wells outside the listed states and is dependent on company-volunteered information in states that do not mandate reporting of injected chemicals, it is the largest registry of its type and allows an approximate estimation of national chemical use trends. Additionally, not all compounds listed as biocides on FracFocus are active ingredients with biocidal activity (i.e., ethylene glycol); regardless, these compounds are registered as biocides because they are components in commercial biocide product mixtures. To enable assessment of the potential environmental and health impacts of the biocides used in hydraulic fracturing fluids, we review their relevant pathways of environmental contamination, environmental mobility, stability and chemical behavior in a variety of natural environments, and toxicity. Alternatives to traditional chemical biocides will be highlighted as methods of achieving the necessary bacterial control in hydraulic fracturing operations while lowering environmental risks. Finally, areas in need of research are revealed as current knowledge gaps impede full understanding of environmental fate and transport of biocides.

HYDRAULIC FRACTURING BIOCIDES AND THEIR MODES OF ACTION

Biocides function by various modes of action to control bacteria—they are generally divided into oxidizing and nonoxidizing compounds.[49] Oxidizing biocides such as bromine- (e.g., *N*-bromosuccinimide, NBS) and chlorine-based (e.g., chlorine dioxide and sodium hypochlorite) species rely on the action of released free radical species that attack cellular components.[50,51] Peroxides are often used in pretreatment of obtained natural water sources due to the fact that they are extremely nonspecific and work efficiently on a wide range of bacteria.[51,52] However, oxidizing biocides pose the risk of equipment corrosion as well as unwanted reactions with other hydraulic fracturing chemicals. Furthermore, their reaction may produce halogenated hydrocarbons and other unwanted disinfection byproducts (DBPs).[15,53] Oxidizing biocides are too short-lived to control microbial growth for long periods of time during fluid storage and to control growth of bacteria that may already be present in the well bore area from the drilling operation, making this class of biocide poorly suited for injection.[54] For these reasons, oxidizing biocides are more commonly used for on-site treatment of stored fresh and wastewater, and less often in hydraulic fracturing fluids (Table 1, SI Figure S2) (though their use is increasing in some areas based on recent trial-and-error successes). However, oxidizing biocides are well-reviewed in the existing literature and therefore will not be emphasized in this critical review.

The most common biocides used in hydraulic fracturing fluids used are nonoxidizing organic chemicals, which will therefore be focused on. These biocides are split into two groups according to their respective modes of action: electrophilic and lytic (often used in conjuncture in fracturing fluids). Many of these biocides are not exclusive to hydraulic fracturing and are used by many other industries and products (SI Table S1).

Lytic Biocides. Lytic (also known as membrane-active) biocides are amphiphilic surfactants, and their activity is generally based on dissolution into the bacterial cell wall and its subsequent disruption.[52] Specifically, their known mode of action involves binding to anionic functional groups on the membrane surface and subsequent perturbation and dissolution of the lipid bilayer, resulting in loss of osmotic regulation capacity and eventual lysis of the cells.[55]

The two main lytic biocides used for hydraulic fracturing are the cationic quaternary ammonium/amine compounds ("QACs" or "quats") didecyl dimethylammonium chloride (DDAC or decanaminium; Table 1), and alkyldimethylbenzylammonium chloride (ADBAC, benzalkonium chloride, BAC, BC, or benzenemethanaminium), although they are often not distinguished specifically on disclosure forms. These biocides are characterized by a central quaternary nitrogen atom that carries a permanent positive charge and is bonded to four carbon-containing "R"-substituents.

QACs are injected into 22% of all wells registered on FracFocus and used in nearly every shale formation in the U.S.,[48] though not solely as biocides since QACs also serve as cationic surfactants, corrosion inhibitors, and clay stabilizers.[56] The QACs used for biocidal purposes, DDAC (comprising 8% of all biocide use, Table 1), and ADBAC (3% of all use, Table 1) are often combined with electrophilic biocides such as glutaraldehyde to increase their efficiency through synergistic effects, thus lowering the total amounts of biocide needed for appropriate bacterial control.[48,57] The only other commonly used lytic biocide is tributyltetradecylphosphonium chloride (TTPC), whose U.S. EPA registration review is scheduled to be completed in 2017.[58] Therefore, information on this substance is limited.

Electrophilic Biocides. Electrophilic biocides typically have reactive electron-accepting functional groups (i.e., aldehydes) that react with electron-rich chemical groups such as exposed -SH (thiol) and -NH (secondary amine) groups in membrane proteins on bacterial cell walls.[52] Glutaraldehyde ("glut") is the most commonly used electrophilic biocide in hydraulic fracturing operations (Table 1). Similar to formaldehyde and other aldehydes, it is a potent cross-linker for amino and nucleic acids (SI Scheme S1), leading to cell wall damage and cytoplasmic coagulation.[59] Glutaraldehyde is one of the main biocides being used in off-shore hydraulic fracturing operations internationally.[60]

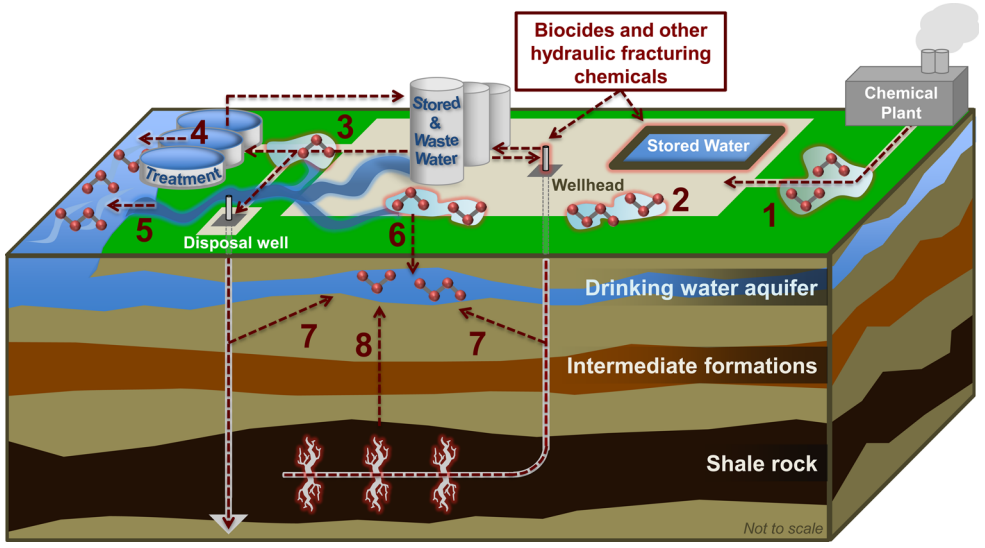


Figure 1. Modes of potential environmental exposure: (1−3) surface spills resulting in contamination of soil; (4) incomplete removal in treatment plants; (5) surface spill runoff into surface water; (6) surface spills leaching into shallow aquifer; (7) contamination of shallow groundwater via borehole leakage, fault lines, and abandoned wells; (8) contamination of shallow groundwater via induced fractures. Artwork is conceptual and not drawn to scale.

Both 2,2-dibromo-2-nitrilopropionamide (DBNPA, 2,2-dibromo-2-cyanoacetamide) and 2-bromo-2-nitropropane-1,3-diol (bronopol) are not considered oxidizing biocides despite small releases of bromine[61] which are assumed to enhance their biocidal activity.[49,62] Both rapidly react with sulfur-containing nucleophiles such as glutathione or cysteine, thereby disrupting key cell components and biological functions.[63]

Another quaternary phosphonium compound currently registered for use as a biocide in hydraulic fracturing fluid is tetrakis(hydroxymethyl)phosphonium sulfate (THPS). Under alkaline conditions, it deformylates and releases tris(hydroxymethyl)phosphine (THP), which cleaves sulfur−sulfur bonds in the disulfide amino acids of the microbial cell wall (SI Scheme S2).[63] Dazomet (3,5-dimethyl-1,3,5-thiadiazinane-2-thione or "mylon") is often combined with THPS in fracturing fluids.[12]

Finally, although rare, use of sulfur-containing biocides is still reported (i.e., California and Texas, Table 1 and SI Figure S1). The most commonly used sulfur-containing biocide treatment is comprised of two chemicals, chloromethylisothiazolinone (CMIT, or MCI, 5-chloro-2-methyl-3(2*H*)-isothiazolinone) and methylisothiazolinone (MIT, or MI, 2-methyl-3(2*H*)-isothiazolinone). They react with a wide range of amino acids, inhibiting critical metabolic processes.

MODES OF ACCIDENTAL ENVIRONMENTAL CONTAMINATION

Environmental exposure to biocides after an inadvertent release may occur during (1) transportation of chemicals to well pads (Figure 1, pathway 1); (2) mixing of chemical additives with the bulk of the fracturing fluid (pathway 2); (3) injection of the mixed fluid into the borehole (often occurs simultaneously with in-line mixing; pathway 2); (4) handling, collection, and storage of chemical-containing produced water (pathways 5 and 6); and (5) reuse, treatment, recycling, and/or disposal of the produced water (pathways 3, 4, 5, and 7).[64] The hydraulic fracturing event itself may have a considerable impact on the chemical stability of the organic additives and thus on the composition of the produced water. As the fluids are exposed to the high pressures, temperatures, salt concentrations, and organic matter contents of the oil- and gas-bearing formations, abiotic transformation and sorption reactions may greatly accelerate the chemicals' depletion (Figure 2). To our knowledge, there is currently only one study that directly addresses this critical effect.[65] For the biocide glutaraldehyde, it was shown that transformation increases with increasing temperature and pH and may be substantial under conditions encountered downhole.[66] Consequently, it can be expected that a portion of the injected biocides will not resurface or may resurface as transformation product(s). Thus, the potential risks associated with biocide exposure may differ substantially before and after hydraulic fracturing.

Few studies have been conducted on the presence of organics in produced water from shales which had undergone hydraulic fracturing.[42,67,68] The compounds detected included polyaromatic hydrocarbons (PAHs), aliphatic hydrocarbons, and long-chain fatty acids.[67] Certain chemicals unique to hydraulic fracturing, including ethoxylated surfactants[68] and the biocide 1,3,5-trimethylhexahydro-1,3,5-triazin-2-thione (a dazomet derivative),[67] were also detected in produced water. Levels of dissolved organics in the produced water as measured directly from active wellheads decreased sharply after the first 20 days; concentration of the biocide dropped from 1.5 mg/L on day 1 to 0.01 mg/L on day 8.[67]

The most commonly reported accidents leading to environmental contamination are surface spills (pathways 1−3 in Figure 1), which can happen on-site (including well blowouts and casing failures)[10,69,70] or during transportation to or off the site via pipelines, trains, or trucks.[71−73] On-site spills, which may result in surface water, soil, or shallow groundwater contamination (pathways 5 and 6 in Figure 1),[53] are often a result of use of lined pits to temporarily store and evaporate flowback brine in order to reduce the volume of waste.[10,69] More recently, storage tanks have replaced these pits in an attempt to reduce the potential for unintentional spills.[74]

While comprehensive and complete data on surface spills for most shale plays are still lacking or are otherwise difficult to access, the Colorado Oil and Gas Conservation Commission

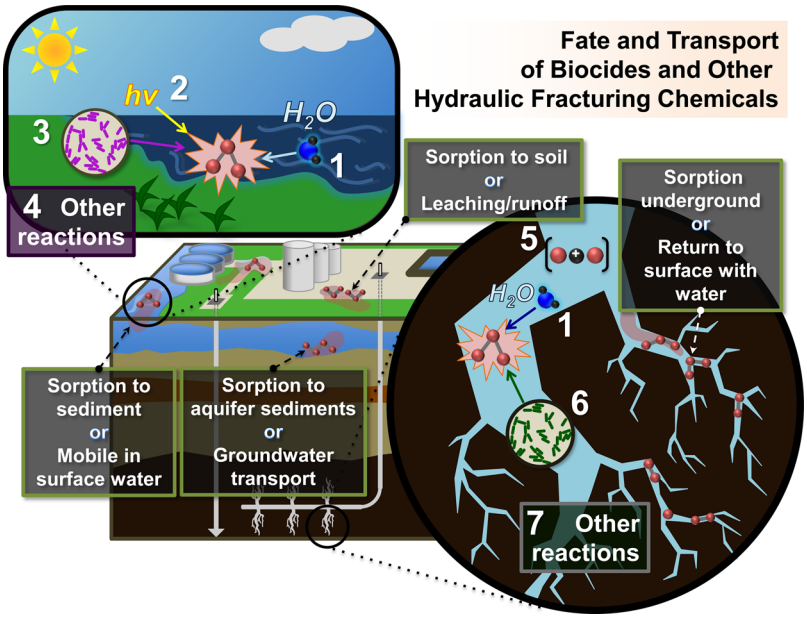


Figure 2. Fate and transport of hydraulic fracturing chemicals (including biocides) in different environments. Possible degradation pathways are numbered as follows: (1) hydrolysis; (2) direct or indirect photolysis; (3) aerobic biodegradation in the water or soil; (4) other chemical reaction with oxygen present; (5) complexation underground with dissolved inorganic species; (6) anaerobic biodegradation; (7) other chemical reaction (e.g., nucleophilic substitution or polymerization) under anoxic conditions, high pressure, and elevated temperature. Artwork is conceptual and not drawn to scale.

(COGCC) offers a robust database that includes any spill or release of exploration and production waste within the State of Colorado of one barrel or more outside and of five barrels or more inside of berms or other secondary containment.[75] In 2013, there were 591 reported spills, which released a total of 14,067 barrels (i.e., ~2,200,000 L), or 0.004% of all produced water. This relates to a total of 50,067 active oil and gas wells in Colorado, including 4,025 new wells that had been drilled in 2013.

To minimize wastewater volumes and thus potential environmental impacts, wastewater can be reused in subsequent hydraulic fracturing events, which is the dominant management practice in the Marcellus shale region.[76] Of the 12,604 instances of unconventional waste disposal (which includes all fluid and solid waste generated from unconventional resource extraction) reported in Pennsylvania from January to June in 2013, 33.4% indicated treatment by a centralized plant and then recycling in another hydraulic fracturing operation, 30.3% indicated direct reuse of the wastewater in other drilling operations, 26.0% indicated disposal via injection in disposal wells, 9.5% indicated disposal via landfills, and only 0.3% indicated treatment for eventual discharge into surface waters.[77] It is important to note that wastewater treatment strategies vary between states and these statistics may not necessarily be representative of those nationwide.

While injection into deep underground reservoirs is currently the most common method of unconventional waste disposal,[78−80] little is known about the long-term impact and risk of this technique.[78,81] However, depending on exposure times of the organic chemical additives to the increased pressures and temperatures of these deep formations, (further) chemical transformation is conceivable.[65] Environmental exposure to the injected solution may occur if the cement or casing is faulty (pathway 7, Figure 1); however, this has yet to be documented.

In the minority of instances where wastewater is treated for discharge, publicly owned treatment works (POTWs), municipal wastewater treatment plants (WWTPs), or commercially operated industrial wastewater treatment plants are used to treat hydraulic fracturing wastewater.[77,82] However, most of the municipal treatment plants are designed for common compounds (nutrients and organic matter) and were not intended to treat the multitude and amounts of chemical species that resurface with flowback brine. Furthermore, assuming the presence of biocides in wastewater at sublethal concentrations, adaptation of surviving microorganisms to biocides becomes possible—a process that is well-documented for ADBAC[83,84] and other biocides.[45,85] This biocidal resistance is sometimes accompanied by low-level increases in antibiotic resistance,[86] which is already an existing problem in WWTPs.[87] Fortunately, dilution below the minimum inhibitory concentration also enables the majority of these chemicals to undergo biodegradation in WWTPs and in natural waters, which will be discussed in more detail later. In hypothetical cases where biocides persist through WWTP treatment, however, contamination of water and soil may occur (pathway 4 in Figure 1).

Although WWTP effluent is typically released into natural streams and waterways, there are rare documented cases of its reuse for other purposes such as to irrigate crops[73,88] or to spread on roads to reduce dust and/or deice.[53,77,89,90] Finally, wastewater from hydraulic fracturing operations off the coast of southern California is sometimes discharged directly into the ocean; as of recently, the EPA is requiring full disclosure of all chemicals meant for direct discharge into the Pacific Ocean.[91]

In contrast to accidents occurring at the surface, underground contamination phenomena may go unreported and undetected for years before any negative consequences are observed. As such, though not considered a dominant exposure pathway in hydraulic fracturing operations, underground exposure pathways are the focus of much peer-reviewed literature. The majority of research available suggests that natural upward migration of chemicals such as biocides from hydraulically induced fractures to aquifers (Figure 1, pathway 8) is unlikely.[92,93] Usually, hydraulic fracturing is performed >1,000 m

Table 2. Physicochemical Properties, Reaction Half-Lives, and Biodegradability of Biocides Used in Hydraulic Fracturing Operations[a]

biocide	log K_{ow}	water sol. at 25 °C (mg/L)	log K_H[b]	log K_{oc}	hydrolysis half-life (25 °C)			photolysis half-life (12 h day)	readily biodegradable (half-life < 30 days)
					pH 5	pH 7	pH 9		
ADBAC	no data	>350,000[103]	*−10.87*	5.810[103]	stable[133]	stable[133]	stable[133]	stable (aq)[133]	no[133]
bronopol	*−0.64*	200,000[219]	−10.88[218]	*−0.033*	1.5 (pH 6, 20 °C) to 2 years[137]	1.5 (pH 6, 20 °C) to 2 years[137]	1.5 (pH 6, 20 °C) to 2 years[137]	2 days (aq, pH 4)[137]	no data
chlorine dioxide	−3.22[221]	3.01 × 10[03220]	−1.40[220]	no data	<25 min[221]	<25 min[221]	<25 min[221]	no data	no data
CMIT	*−0.34*	*149,000*	*−7.45*	*0.711*	stable	stable	22 days[223]	no data	aq (aer)[223]
dazomet	0.63[218]	3,000[218]	−9.30[218]	1.000[218]	23.8 h	180 h	45.6 h[147]	1.6 h (aq, pH 7)[147]	no data
DBNPA	0.82[218]	15,000[218]	−7.72[218]	*1.767*	67 days	63 h	73 min[62]	14.8 h (aq, pH 5); 6.9 h (aq, pH 7)[62]	aq (aer, anaer)[62]
DDAC	≈0[134]	700[225]	*−9.16*	5.64−6.20[104]	368 days	184.5 days	506 days[132]	132 days (soil)[132]	no[132]
DMO	0.73[227]	miscible[226]	*−5.52*	*0.747*	<5 min[227]	<5 min[227]	<5 min[227]	no data	no data
glutaraldehyde	−0.33[102]	miscible[228]	−4.48[102]	2.07−2.70[102]	628 days	394 days	63.8 days[102]	196 days (aq, pH 5)[102]	aq (aer, anaer)[102]
hypochlorite	−3.42[221]	miscible[229]	nonvolatile[221]	no data	<25 min[221]	<25 min[221]	<25 min[221]	no data	no data
MIT	*−0.83*	*536,700*	*−7.30*	*0.440*	stable	stable	22 days[223]	no data	aq (aer)[223]
N-bromo	*−1.19*	14,700[218]	*−6.41*	*0.259*	unstable, no data	unstable, no data	unstable, no data	no data	no data
peracetic acid	*−1.07*	miscible[231]	−5.67[218]	*0.104*		8.295 h[232]		8.3 days[233]	aq (aer, anaer)[233]
THPS	*−9.77*	400,000[218]	*−12.64*	*−5.302*	131 days	72 days	7 days[142]	<2 h (aq, pH 7)[169]	aq (aer, anaer), soil (aer)[169]
TMO	(≈DMO)	miscible[226]	*−5.18*	*0.841*	<5 min[227]	<5 min[227]	<5 min[227]	no data	no data
TTPC	no data	miscible[234]	3.75 × 10^{-8} mmHg, 39 °C[145]	*7.66*[c]	unknown	unknown	unknown	no data	no data

[a]Values in italics are calculated using EPI Suite v4.11.[101] Biodegradation reported in aqueous phase (aq) or soil under aerobic (aer) or anaerobic (anaer) conditions. [b]log K_H, Henry's law coefficient. [c]Estimation uses MCI method (otherwise K_{OW} is used in K_{OC} predictions).

below a shallow aquifer used for drinking or irrigation water extraction. Even though some fractures have been documented to grow upward by as much as 450 m, their tops were still almost 1,500 m below the aquifer.[94]

Underground contamination via borehole leakage, preexisting vertical cracks, fault lines, or uncharted boreholes (Figure 1, pathway 7) remains a possibility. Several studies using isotopic analysis have traced methane found in groundwater back to natural gas wells nearby.[95−98] Darrah and co-workers (2014)[93] demonstrated that fugitive gas contamination was due to (1) release of intermediate-depth gas along the well annulus, likely due to cement failure; (2) release of target formation gas implicating improper, faulty, or failing production casings; and (3) underground well failure. While upward flow of leaking hydraulic fracturing fluids would be substantially slower than that of buoyant natural gas,[53] production well failure in the proximity or above an aquifer is a more likely potential pathway for groundwater contamination by fracturing fluid components. However, due to the lack of solid (baseline) data, further research is needed to address this question.

In conclusion, while a realistic potential for groundwater contamination via natural upward migration of deep-injected biocides may exist if the fractured formation is very shallow, it appears unlikely.[76,93] However, several other scenarios exist which may result in unintentional environmental contamination with biocides, including surface spills and well integrity issues associated with casing or cement failure.[53,64,76,93,98−100]

MOBILITY

Table 2 summarizes the key physicochemical properties that can be used to predict the mobility of the hydraulic fracturing biocides. The property estimation software EPI Suite v4.11[101] was chosen after statistical comparison of the performance of different estimation methods (SI Tables S2 and S3) to close the large existing experimental data gaps regarding their water solubilities, Henry's law constants (K_H), soil organic carbon−water partition constants (K_{OC}), and octanol−water partition constants (K_{OW}).

In general, it can be seen that the organic-based hydraulic fracturing biocides considered here possess low K_H values and are thus not very volatile. Consequently, partitioning into the air phase is not considered a major pathway. However, biocides tend to be water-soluble or miscible, enabling their transport via surface water or groundwater depending on their affinity for sorption to natural solid phases (Table 2, Figure 2).

With the exception of glutaraldehyde (log K_{OC} = 2.07−2.70),[102] the K_{OC} values of the uncharged biocides lie predominantly below 100 (i.e., log K_{OC} < 2), indicating comparably low retardation during aqueous transport through the soil, especially soils which are low in organic matter content. Glutaraldehyde's mobility is reported to be moderate in soils and high in sediments,[102] and due to its rapid aerobic degradation in soil and water (see below), its potential for soil contamination may only be relevant under anaerobic conditions.

In contrast, ADBAC, DDAC, and TTPC possess substantially higher log K_{OC} values between 5.6 and 7.7,[101,103,104] which is due in part to their large hydrophobic moieties.[105] In addition to hydrophobic interactions with soil organic matter, these cationic biocides can adsorb to permanent negatively charged clay surfaces, an effect which enables the use of these compounds as shale inhibitors/clay stabilizers (only quaternary ammonium/amine polyelectrolytes called "polyquats" with multiple charges are used for this purpose).[56] Despite being sorbed, these biocides potentially remain bioactive.[106] Several studies reported strong sorption of cationic organic amines to the surfaces and interlayers of clay beyond its cation exchange capacity, causing extensive clay aggregation.[107−109]

Experiments simulating river water contamination revealed that the quaternary ammonium compound paraquat (*N*,*N*′-dimethyl-4,4′-bipyridinium dichloride) becomes almost completely sorbed onto sediments (≥97%).[110] Similar findings were reported from leaching studies with CTAB (cetyltrimethylammonium bromide), which showed strong sorption to silica and soil.[111−114] Moreover, it was observed that adsorption of CTAB to silica surfaces occurs within minutes, indicating that QACs will quickly sorb to soils and sediments upon accidental release.[111] This may result in the accumulation of chemical in soil or sediments affected by a spill.[53]

Studies investigating QACs in municipal sludge observed a substantial extent of sorption.[115,116] Since about 50% of the municipal biosolids in the U.S. are land-applied,[115] an accumulation of QACs in agricultural soils over time may result, potentially leading to plant uptake as is seen with other pollutants such as organophosphates[117] or to contamination of water resources through leaching and runoff.

Sorption of hydraulic fracturing biocides (and other organic additives) may also occur downhole in the resource-bearing fractured formations. Though unconventional formations such as shale are typically nonpermeable, the process of hydraulic fracturing induces many microfractures, which drastically increases the number of available sorption sites. Negatively charged sorption sites, to which cationic species such as DDAC and ADBAC are strongly attracted, are abundant in shale rock due to the presence of clays.[118] Furthermore, the total organic carbon content in unconventional shale formations can exceed 10%.[119] Thus, partitioning into organic carbon-dominated phases (e.g., kerogen) even for biocides with a rather low log K_{oc} < 2 may become a major pathway for their removal under downhole conditions.[105] It has also been shown that elevated temperature increases the rate of chemical sorption of organics to soils, sediments, and clays[118] within time scales relevant for hydraulic fracturing operations. When further considering the high pressures (known to enhance adsorption processes[105,120]) under downhole conditions, substantial sorption of hydrophobic biocides underground can be expected.

The presence of high salt concentrations may have a considerable impact on biocide sorption to organic and inorganic surfaces. The presence of salt is partly a result of injection of acid into the well prior to injection of the organic fracturing additives. This acid, usually hydrochloric (HCl), is used in concentrations reaching 20% in the injected fluid[48] and induces dissolution from the shale, including iron, calcium, and radium.[121−124] For the uncharged biocides, increasing sorption with increasing salt concentration can be expected due to decreasing solubility as a result of salting out.[125] For cationic biocides, which may sorb via electrostatic interactions in addition to hydrophobic forces, the effect of salt concentration is more complex as the salts increasingly compete for ion exchange sites, thus counteracting the salting-out effect. Several studies observed that the sorption affinities of QACs to both clays and organic matter generally decreased with increasing salt concentration.[109,126,127]

The potential for bioaccumulation of the neutral organic biocides is predominantly low as their K_{OW} values consistently lie below 10 (i.e., log K_{OW} < 1; Table 2), for many even below 1

(i.e., log K_{OW} < 0), indicating a preference for the aqueous phase over the organic. However, as cationic surfactants typically accumulate at the interface between two phases and may be attracted to the negatively charged surface of cell membranes, the K_{OW} is not sufficient to predict bioaccumulation of ADBAC, DDAC, and TTCP. On the other hand, their potential to undergo strong ionic bonding may limit their mobility, and thus their potential for uptake by organisms: QACs have been found to be far less bioavailable (though potentially still bioactive) to organisms than other pollutants having similar K_{OW} values,[128,129] such as bisphenol A[130] and organophosphates.[117]

DEGRADATION

Lytic biocides have been reported to be relatively resistant to degradation in a wide range of environments. They are stable in the presence of strong oxidants,[131] under acidic and basic conditions,[131] and when exposed to heat,[54] and are not readily degraded by hydrolysis, photolysis, or bacteria.[132−134] On the other hand, electrophilic biocides are reactive chemicals and are therefore relatively short-lived in natural environments where reduced functional groups of proteins and organic matter are prevalent. None of the chemicals react with themselves with the exception of glutaraldehyde (SI Scheme S3): unique among biocides, glutaraldehyde undergoes autopolymerization via aldol condensation, especially at high pH values.[135] The resulting α,β-unsaturated polymer is not considered toxic, nor are the products of most known reactions between these biocides. Bronopol is an exception as it reacts with oxygen and thiols to produce superoxide, a reactive oxygen species.[61]

Hydrolysis. Hydrolysis is a major degradation pathway common to electrophilic biocides. Characterized by the addition of a water molecule resulting in two smaller fragment molecules, this process is strongly affected by the pH of the surrounding environment. In some cases, the hydrolysis products can be more toxic and/or persistent than their parent compounds, which is the case with the biocides DBNPA,[62,136] bronopol,[137−141] THPS,[12,142−144] and dazomet.[12,145−147] DBNPA's major products via hydrolysis (which occurs readily above pH 8.5[52]) are dibromoacetic acid and dibromoacetonitrile (DBA; SI Scheme S4).[62,136]

Bronopol hydrolyzes within 3 h at 60 °C and pH 8, producing formaldehyde, nitrosamines, and other molecules.[137−141] Although the parent compound (bronopol) is rather short-lived in the environment, its degradation products are toxic and more persistent.[138,148] The hydrolysis degradation products of THPS are THP molecules that subsequently degrade into tris(hydroxymethyl)phosphine oxide (THPO), accompanied by the release of two formaldehyde molecules.[12,142−144] Dazomet's hydrolysis half-life in water of pH 7 is 7.5 days (Table 2).[145] Its major products are methyl isothiocyanate, formaldehyde, monomethylamine, hydrogen sulfide, carbon disulfide (in acid soils), and nitrogen oxides.[12,145−147]

Another influence on chemical stability underground is the pH of the surrounding environment. Analysis of produced water revealed a pH range of 5−7, controlled mainly by bicarbonate species intrinsic to the shale formations.[122] Although the biocides used in hydraulic fracturing are relatively stable at near-neutral pH, small changes in pH can nonetheless have a large impact on any acid- or base-catalyzed reactions.[65,66]

Photodegradation. Some of the hydraulic fracturing biocides contain chromophores, such as MIT, CMIT, dazomet and *N*-bromo, and may thus undergo direct photolysis reactions when exposed to ultraviolet (UV) light. Experimentally, this has thus far only been tested for DBNPA and bronopol. Via direct photolysis, DBNPA yields dibromoacetic acid as the major degradation product (SI Scheme S5),[62] Bronopol was shown to produce tris(2-hydroxymethyl-2-nitropropane-1,3-diol).[137] In addition, all biocides can be degraded by the action of reactive species from indirect photodegradation. However, no experimental data are available for this process.

Biodegradation. Microbial degradation and mineralization of biocides become possible upon dilution or degradation to sublethal levels, and/or due to proliferation of biocide-adapted bacteria.[22,23,83] Minimum inhibitory concentrations not only depend on the type and mixture of biocide(s) but also on the type of organism and are typically lower for planktonic cells compared to biofilms.[16] For many hydraulic fracturing biocides, typical MICs are on the order of milligrams to hundreds of milligrams per liter.[16]

Below MICs, bacterially induced degradation of biocides can occur in soil or surface water in the event of a spill, underground as a result of ineffective bacterial control, or at WWTPs.[149,150] In soils, it is generally concluded that cationic surfactants such as DDAC, ADBAC, and TTPC exhibit such strong sorption to soil that their bioavailability and thus biodegradation rates are substantially reduced.[132,133,151,152] One strain of *Pseudomonas fluorescens* TN4, which had been isolated from activated sludge from a WWTP, was shown to be not only highly resistant to DDAC, ADBAC, and other QACs but also capable of aerobically degrading them at concentrations of 50 mg/L DDAC (MIC 250 mg/L) and 100 mg/L for ADBAC and all other QACs (MICs > 1,000 mg/L).[153] However, the study did not enable conclusions on whether complete mineralization occurred. In general, research pertaining to degradation of QACs in WWTPs is contradictory; most reports indicate that removal from wastewater is primarily based on sorption effects (not biodegradation) and that degradation of QACs by bacteria found in activated sludge is extremely limited.[152]

Aerobic bacteria rapidly mineralize glutaraldehyde with glutaric acid as an intermediate. In both wastewater and seawater, aerobic biodegradation has been reported at concentrations of up to 50 mg/L.[102] Under anaerobic conditions over a time period of 123 days, it was reported that glutaraldehyde biodegradation led to the accumulation of 1,5-pentanediol and 3-formyl-6-hydroxy-2-cyclohexene-1-propanal, but no mineralization to CO_2 was observed.[102]

For most of the other biocides, information on their biodegradation behavior is sparse and often only available through their reregistration eligibility decision reports without citation of peer-reviewed studies. DBNPA was reported to undergo aerobic and anaerobic biodegradation on the order of hours, yielding six different products: oxalic acid, 2-cyanoacetamide, bromoacetamide, dibromoacetic acid, bromoacetic acid, and dibromoacetonitrile.[62] No information on complete mineralization was given. Biodegradation studies also showed that THPS is completely converted into CO_2 by bacteria.[142]

Downhole Conditions. As stated previously, very little is known about the reactivity of chemicals under the high temperatures and pressures of downhole conditions. Previous research on produced water revealed that it did not contain all of the same organic compounds which had initially been injected into the well, suggesting that sorption and/or degradation had occurred underground.[42] As temperatures

Table 3. Reported Toxicological Data of Biocides Used in Hydraulic Fracturing Operations[a]

	mammalian (rat)		
biocide	LD_{50}(oral) (mg/kg)	LC_{50}(inhaled) (4 h, mg/L)	chronic toxicity
ADBAC	305	0.054−0.51[133]	no evidence found[133]
bronopol	325	0.588[137]	reproductive toxicity; degradation products formaldehyde is known human carcinogen (IARC 1) and nitrosamines are likely human carcinogens (IARC 2A)[138]
chlorine dioxide	316	0.290[221]	developmental toxicity in lab animals[221]
CMIT	105	0.330[222,223]	*assumed to be same or similar to methylisothiazolinone (MIT)*[224]
dazomet	519	8.4[145]	developmental toxicity in lab animals (skeletal variations)[147]
DBNPA	207	0.320[172]	degradation product DBA is possible human carcinogen (IARC 2B) and developmentally toxic in lab animals[169,170]
DDAC	238	0.07[132]	developmental toxicity (skeletal abnormalities); no evidence of carcinogenicity[132]
DMO	1,173	1.10[227]	degradation product formaldehyde is known human carcinogen (IARC 1)[138]
glutaraldehyde	460[b]	>4.16[b,162]	no evidence found[162]
hypochlorite	5,800	no data[221]	mutagenic *in vitro*; may react to form trihalomethanes, possible human carcinogens (IARC 2B)[221]
MIT	105	0.330[223]	neurotoxic; no evidence of carcinogenicity[224]
N-bromo	1,170	no data[230]	no evidence found[147]
peracetic acid	1,540	0.450[232]	no evidence found[231]
THPS	290	0.591[142]	mutagenic *in vitro*; degradation product formaldehyde is known human carcinogen (IARC 1)[142]
TMO	1,173	1.10[227]	degradation product formaldehyde is known human carcinogen (IARC 1)[138]
TTPC	1,002	<0.9[168]	developmental toxicity in lab animals[168]

[a]Lowest reported value is displayed. Active ingredient (AI) concentration is 100% unless otherwise stated. [b]Values normalized to 100% AI from reported values which use 50% AI.

and pressures increase underground, chemical equilibrium will shift in accordance with Le Chatelier's principle, and reaction equilibrium will shift to favor endothermic products (negative $\Delta_r H$) and products with smaller volume (fewer molecules and liquid/solid phase) as compared to standard state conditions (25 °C at atmospheric pressure). The high downhole pressures and temperatures may not only lead to unexpected chemical reactions or degradation but may also alter the potential for biodegradation of organics (including biocides) underground.

The stability of aqueous organic chemicals at elevated temperatures is also highly influenced by the inorganic minerals present.[154−156] Therefore, it is important to attempt to understand the subsurface biogeochemistry that influences the fate of biocides[156] and other organic additives during hydraulic fracturing. Complete fracturing of a production well typically requires 3−5 days,[157] and during this time period the inorganics in solution may either complex with or catalyze degradation of the organic additives in fracturing fluids. Furthermore, the extreme pressures utilized in hydraulic fracturing may work in conjuncture with elevated temperatures underground to produce chemical reactions unexpected under normal surface conditions.[154,158−160] Although research is currently ongoing in this area,[65,66] the fate of biocides under these unique conditions is still unclear.

TOXICITY

Most of the biocides used in fracturing fluids are severe eye and skin irritants but have relatively low acute toxicity to mammals. Apart from a few exceptions, their oral median lethal dose (LD_{50}) values for rats range between 200 and >1,000 mg/kg (Table 3). However, the same biocides tend to be acutely toxic to aquatic life at low concentrations, especially to Mollusca such as oysters, which are highly sensitive to pollutants.[161] For example, glutaraldehyde displays only low to moderate toxicity toward aqueous organisms with the exception of oysters (LC_{50} = 0.78 mg/L in the Eastern Oyster, *Crassostrea virginica*).[162] DBNPA is quite toxic to all aquatic life; the lowest reported LC_{50} for *Daphnia magna* (*D. magna*) is 0.66 mg/L (48 h) and 1.0 mg/L for rainbow trout (96 h).[62,163] Shellfish such as the estuarine oyster are especially sensitive to the presence of DBNPA, showing acute toxicity at levels below 0.070 mg/L.[62] Additionally, DBNPA has been shown to affect the reproduction of *D. magna* at the subtoxic levels of 0.053 mg/L, and to negatively affect the growth of juvenile rainbow trout at concentrations as low as 0.019 mg/L[164] and fathead minnow at 1.8 mg/L.[165] DBA (breakdown product of DBNPA) also exhibits toxicity to aquatic life at very low concentrations[165] (fathead minnow LC_{50} is 0.55 mg/L within 96 h).[166] Bronopol is very toxic to marine invertebrates such as oysters—observed LC_{50} is 1.6 mg/L for *D. magna*[167] and 0.77 mg/L for the Eastern Oyster.[137] It can therefore be concluded that substantial spills into surface waters or streams may have noticeable ecotoxicological effects on aquatic species.

Despite not being highly acutely toxic, certain biocides are suspected to possess developmental toxicity, carcinogenicity, mutagenicity, genotoxicity, and/or chronic toxicity (Table 3). Only a few of the hydraulic fracturing biocides have thus far been evaluated by the International Agency for Research on Cancer (IARC) or the U.S. EPA. For the remaining biocides, the evidence that does exist is insufficient to draw any firm conclusions.

Though research is scarce, developmental toxicity (i.e., teratogenicity) has been observed from several of the lytic biocides used in fracturing fluids, such as DDAC and TTPC, as well as the conventional chlorine dioxide (Table 3). Observations of developmental toxicity associated with DDAC have led to a recommended daily intake limit of 0.1 (mg/kg)/day for females of reproductive age.[132] While preliminary EPA studies suggest TTPC exhibits some developmental toxicity,[168] the inclusive final report has yet to be published. Other biocides have shown developmental toxicity associated only with very high concentrations, such as bronopol[137] or THPS,[169] or *in vitro*, such as MIT.[170]

Carcinogenicity is rare among the biocides used for fracturing fluids (Table 3) and often is confirmed only *in vitro* at very high concentrations. Typically, any carcinogenicity is due to the

breakdown products of the biocides instead of the parent compound themselves, such as the possible human carcinogen DBA (IARC Group 2B), a breakdown product of DBNPA that has been shown to induce tumors in rat liver cells *in vitro*[171] and to have carcinogenic effects in laboratory animals when administered in concentrations over 100 mg/L.[172] Other examples include nitrosamines produced from hydrolysis of bronopol,[139−141] many of which are probably carcinogenic to humans (IARC Group 2A).[148,173] Also, several of the biocides used in hydraulic fracturing operations are known or suspected formaldehyde generators. Formaldehyde is a known human carcinogen (IARC Group 1) if inhaled.[137,138] However, when dissolved in aqueous media, formaldehyde exists predominantly in its less toxic hydrated form, methanediol ($CH_2(OH)_2$, methylene glycol), and its tendency to evaporate from aqueous solution is low.[174,175] Examples of formaldehyde generators include bronopol,[137] THPS,[12,144,176,177] and dazomet;[12,145−147] however, none of these have been found to be carcinogenic in laboratory tests.[178]

A few compounds (though not carcinogenic) have been found to mutate DNA *in vitro*. Examples of mutagenic biocides include THPS.[169] Other biocides, though not producing mutations, have been found to exert genotoxic effects *in vitro*, such as ADBAC in plant root tip cells and human lymphocytes at concentrations of 1.0 mg/L.[182] However, *in vitro* effects do not necessarily imply human effects. Genotoxic effects from ADBAC exposure have also been observed in human respiratory cells (study used 1,000 mg/L[183]) and fish cells at 0.12 mg/L.[184] This study also revealed that DDAC (or its bromide salt, respectively) exerted genotoxicity toward mammalian cells at 0.3 mg/L.[182] Finally, the electrophilic biocide THPS (or its chloride salt, respectively) was reported to be genotoxic to fish cells at concentrations of 0.2 μg/L.[184]

For a holistic risk assessment, the mobility and degradability of hydraulic fracturing biocides have to be included, which may limit their ability to exert toxicity on humans or other organisms. Attention must be paid, however, to transformation products that are known to be more toxic and/or more persistent than the parent biocide, such as DBNPA and its product DBA, further emphasizing the need for more detailed degradation studies. The charged, cationic biocides may be more resistant to breakdown, but their strong sorption to clay and organic matter is known to reduce their toxicity.[185]

ALTERNATIVE APPROACHES

Alternative products and technologies with biocidal activity exist or are currently being explored to enable a pathway to more sustainable bacterial control. However, none of them are without any environmental and/or human health impacts. One biocide that has been recognized for its relatively low environmental impact is THPS, which received the Presidential Green Chemistry Award in 1997 due to its low toxicity, low treatment levels, and rapid breakdown when used properly.[186] However, a surface spill may result in formaldehyde generation due to the evaporation-driven conversion from its hydrated form, methanediol, a breakdown product of THPS.

Peracetic acid is a biocide already used in hydraulic fracturing operations, although thus far only in 0.01% of all wells registered on FracFocus (SI Figure S1). It is a stronger oxidizing agent than H_2O_2 but has not been found to produce harmful DBPs[187] and is not expected to have adverse health effects including carcinogenesis.[188]

Ozone has been widely used for drinking water and food disinfection.[189−191] It readily reacts with double bonds in critical cellular components but is known to generate some DBPs such as bromate.[192,193] Also, health effects such as various respiratory diseases, heart attack, and premature death are linked with ozone and its associated pollutants.[194] Furthermore, ozone's rapid reaction kinetics are disadvantageous for downhole applications, which usually take days to weeks to completion. As with other oxidizing agents including peracetic acid, it may induce metal corrosion and thus steel casing failure.

Chlorine dioxide has a longer lifetime than ozone and is thus already used in hydraulic fracturing fluids (Table 1). Its corrosion potential is comparably low, but it may produce carcinogenic DBPs.[195,196] Because total dissolved organic carbon in produced water has been measured as high as 5,500 mg/L,[53,67] formation of DBPs resulting from use of chlorine dioxide, chlorine (generated by sodium hypochlorite), and bromine (generated by *N*-bromo) must be considered.[197] A previous study correlated increased levels of THMs in WWTP effluent to Marcellus shale wastewater, especially brominated species, were observed.[198] Furthermore, chlorine dioxide gas is explosive when exceeding 10% (v/v) in air and must thus be produced on-site. Historical illnesses outside hydraulic fracturing activity including one fatality resulting from exposure to less than 19 ppm have been reported.[199]

The injection of nitrate or nitrite has been broadly used as an alternative electron acceptor for microbial respiration to avert unwanted sulfate reduction.[200−204] Especially in offshore water flooding operations, where seawater is continuously injected downhole, nitrate was proven to be very effective in reducing the amount and activity of SRB.[205]

There are other alternatives which circumvent the need for chemical addition altogether, such as use of ultrasonic radiation[206] or UV light.[207] These technologies have proven to be extremely effective for microbial control, but their high energy demands and lack of residual effect currently prevent them from widespread use. Furthermore, electrochemical approaches, such as generation of electrochemically activated solutions,[208] can be used to generate reactive oxygen species such as hydroxyl radicals. However, in the presence of high chloride concentrations, electrochemical techniques can also generate hypochlorous acid (HOCl), which, as stated previously, is known to produce DBPs. Due to their typically much lower energy consumption, electrochemical technologies are widely applied in drinking water and wastewater treatment plants.[209] Although their use for downhole applications is limited, they may be viable alternatives for hydraulic fracturing-related aboveground water operations.

DISCUSSION AND FUTURE WORK

Based on the currently available data regarding usage, mobility, degradation, and toxicity of the biocides used in hydraulic fracturing operations, the following conclusions can be drawn: (1) While the uncharged species can be mostly expected to be in the water phase where they are subject to biotic or abiotic degradation, the cationic quaternary ammonium and phosphonium compounds will strongly sorb to soil or sediments, where their (bio)availability to degrade may be limited and their toxicity attenuated. (2) In surface and shallow subsurface environments, many of the biocides are degradable through abiotic and biotic (especially aerobic) processes, but some can potentially transform into more toxic or persistent compounds, which may accumulate under certain conditions. (3) Although being a critical process, the understanding of the biocides' degradation and sorption under downhole conditions (high pressure, temperature, and salt

and organic matter concentrations) is extremely limited, currently not enabling reliable risk assessment. (4) Efforts in developing alternative biocides with lower human health risks are ongoing. Application of existing alternatives is currently limited by high cost, high energy demands, inapplicability under downhole conditions, or formation of DBPs.

Critical data regarding the fate and transport of hydraulic fracturing biocides are still missing despite the widespread and long-term use in other water-processing industries. This is especially true for biotic and abiotic (e.g., photolytic, hydrolytic) degradation processes, which are key to controlling organic contaminant removal from the environment. Future research addressing biocide degradation rates should thus focus on fundamental laboratory- and field-scale investigations under various environmental conditions as well as their runoff and leaching potential. Furthermore, as noted earlier, due to the unique exposure to deep geological formations either during hydraulic fracturing or after injection into deep disposal wells, their reactivity and sorption behavior downhole needs to be considered.

The biocides' susceptibility to various transformation[210] and degradation processes in combination with the fact that some degradation products have been reported to be more toxic and/or persistent than the parent compound highlights the need for appropriate analytical detection methods to more accurately assess their potential environmental impact. Excellent screening methods based on high-resolution mass spectrometry exist for polar organic molecules[211−213] and breakdown products,[210,213−215] which could theoretically be modified and applied toward detecting hydraulic fracturing chemicals. Modification (typically in sample preparation) is necessary to accommodate the high salinity and TDS commonly associated with fracturing wastewater or measurement accuracy may suffer due to matrix suppression effects, as was recently found responsible for underestimation of radium levels in produced water from the Marcellus shale.[216]

Furthermore, future environmental fate and transport studies need to address the complexity of hydraulic fracturing fluids. The presence of other organic additives, especially polymers that increase fluid viscosity such as gelling agents or the friction reducer polyacrylamide,[76] may have substantial impacts on their transport through soil. Vice versa, the presence of biocides above their minimum inhibitory concentrations may impact natural biodegradation processes of other organic fracturing fluid additives.

As of today, no groundwater contamination by hydraulic fracturing additives in the U.S. has been irrefutably documented in the peer-reviewed literature.[53,76,100] However, due to the fact that hydraulic fracturing fluid spills have been reported previously (e.g., there were 591 documented spills in 2013 in Colorado alone),[75] this scenario does not appear unlikely. Consequently, it appears mandatory to address this concern at a minimum through (1) adequate baseline monitoring in combination with (2) comprehensive chemical analyses beyond currently analyzed and suggested chemical reporting parameters (i.e., bulk water characteristics such as pH and TDS, and concentration of inorganics including chloride, sodium, calcium, barium, strontium, magnesium, radium, uranium, and iron).[217] In the case of inadvertent releases, these data will enable the development of appropriate cleanup strategies, allow for ecosystem and human health risk assessment, and thus pave the way for a more sustainable approach to natural resource extraction.

ASSOCIATED CONTENT

Supporting Information

Figure S1 showing use of biocides within U.S. shale plays, Figure S2 showing frequency of use and mode of action of biocides, Table S1 listing other uses of hydraulic fracturing biocides, Tables S2 and S3 providing data and statistical analyses of physicochemical property estimation, reaction schemes S1−S5 illustrating biocide transformation reactions, and text listing applicable references. This material is available free of charge via the Internet at http://pubs.acs.org.

Corresponding Author

*E-mail: thomas.borch@colostate.edu. Phone: +1-970-491-6235.

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