SANJIB BHATTACHARYYA, JACK BENNETT, LUKE C. SHORT,
TAMARA S. THEISEN, MICHAEL D. WICHMAN,
JASON C. WHITE, AND SARAH WRIGHT

Nanotechnology in the Water Industry, Part 2: Toxicology and Analysis

NANOTECHNOLOGY AND WATER TREATMENT IS A NEW, EMERGING PAIRING THAT REQUIRES EXAMINING THE OPPORTUNITIES AS WELL AS THE RISKS.

As stated in Part 1 of this article (Bhattacharyya et al. 2017), nanotechnology has been applied in the last 10 to 15 years across a wide and increasing range of sectors including healthcare, electronics, food production, and cosmetics. Nanotechnology could also improve water and wastewater treatment and use, including enabling use of traditionally unconventional water sources. Just as with any new technology, there are risks associated with nanotechnology use and as such, strategic and wise application is necessary.

This two-part article is an overview of nanotechnology applications and implications within the water industry. Part 1 provided a basic background on nanotechnology and literature survey on nanoparticle use, fate, and effects in various types of water systems. Part 2 describes the toxicological and ecological impacts of nanoparticles (NPs), reviews analytical measurement techniques, and assesses where novel platforms would be most beneficial.

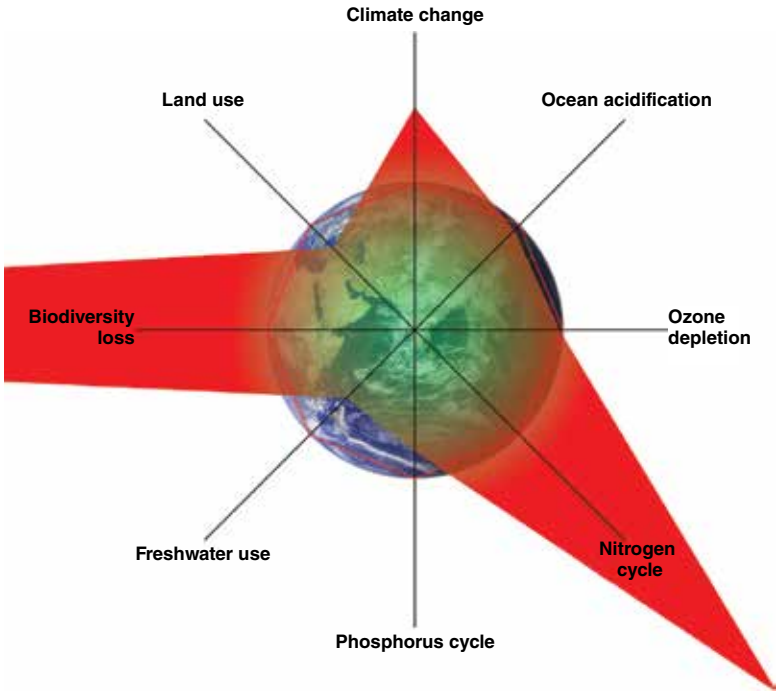
TOXICOLOGY/ECOLOGY IMPACTS

With rapidly increasing use of engineered nanomaterials, environmental release of these contaminants is likely already occurring, perhaps on a significant scale. Approximately 6–8% of annual funding from the National Nanotechnology Initiative is for assessing environmental health and safety of nanomaterials (NNI n.d.). A significant amount of those resources are by necessity concerned with occupational human exposure and many ecological

Layout imagery by Shutterstock.com artist: Macrovector

2017 © American Water Works Association

FIGURE 1 Schematic of generation of nanoparticles and environmental impact



Source: Christian Leichsenring, CC BY-SA 3.0

questions are unaddressed (Servin & White 2016). For both terrestrial and aquatic systems, there are numerous potential release and exposure pathways (Gottschalk & Nowack 2011), including intentional release of nano-enabled agrichemicals and agents/substances for soil remediation (Servin et al. 2015). Given the widespread use of NPs in consumer products, presence of engineered nanoparticles (ENPs) in the waste stream is anticipated (Peijnenburg et al. 2015), and land application of resulting biosolids represents an indirect but potentially significant pathway for ENP introduction into agriculture. Ecotoxicological impacts of NPs and the potential for bioaccumulation in plants and microorganisms is a subject of current research, as NPs are considered to be generated as a result of enviornmental effects and thus have novel impacts (Figure 1). There is consensus in the scientific community that understanding nanomaterial fate and effects in the environment is insufficient. Given the size-specific toxicity/risk concerns and the lack of a robust nano-specific regulatory framework for ENP-containing consumer products, the discipline of nanotoxicology has developed to address these critical knowledge gaps.

There has been incremental progress in this area recently, including some comprehensive literature reviews that also highlight major topics of concern (Schwab et al. 2016, Gardea-Torresdey et al. 2014, Garner & Keller 2014, Batley et al. 2013, Gottschalk et al. 2013). Most research in nanotoxicology has focused on detrimental effects of the NPs themselves, with the vast majority of work focusing on short-term, high-dose assays in model systems. Consideration of chronic, low, or environmentally realistic dose scenarios in more complex systems is widely recognized as a more likely exposure pathway for sensitive receptors, but to date, these scenarios have remained largely unexplored (Servin & White 2016). Only after these types of investigations have been completed can true exposure to human and nonhuman receptors be determined for an accurate risk assessment (Holden et al. 2016).

Some early reviews were published in an attempt to evaluate nanomaterial effects in terrestrial systems (Handy et al. 2008, Klaine et al. 2008). Much of the focus was on identifying strengths and weaknesses of published studies and, more importantly, on highlighting the many areas in need of study. Inclusion of appropriate controls, such as bulk and ionic treatments, is needed for robust experimental design and meaningful analysis of the results (Bar-Ilan et al. 2012). Studies have been published that address most aspects of the biotic community; however, because many of the exposure concentrations are quite (likely unrealistically) high, the literature is dominated by reports of toxicity. The measured parameters as a function of exposure range from basic physiological assays, such as growth or oxidative stress response, to highly sensitive molecular and "omic" endpoints. For example, Jiang et al. (2009) examined the toxicity of bulk and NP aluminum, silicon, titanium dioxide (TiO_2), and zinc oxide (ZnO) to three bacterial species; with the exception of TiO_2, NPs were significantly more toxic than their bulk counterparts. Gong et al. (2011) reported that NP nickel oxide was severely toxic to *Chlorella vulgaris*, causing thylakoid dysfunction and membrane breakage. With regard to animal species, Zhang et al. (2011) noted that at relatively low concentrations (1–100 nM), exposure to NP cerium oxide (CeO_2) induced oxidative damage in *C. elegans* and reduced overall life span by 12%. Hu et al. (2010) observed that exposure to NP TiO_2 and ZnO caused significant toxicity to the redworm

2017 © American Water Works Association

Eisenia fetida. Many reports investigating NP toxicity to plants as measured by germination, growth, or other physiological parameters have been published (Schwab et al. 2016, Ma et al. 2015, Yin et al. 2012). Atha et al. (2012) used mass spectrometry to show that 1,000 mg/L CuO (copper oxide) NP increased oxidative modification of DNA bases in radish relative to corresponding bulk particles. Marmiroli et al. (2014) used a genome-wide transcriptomic approach to characterize *Arabidopsis thaliana* toxicity from and tolerance to cadmium sulfide quantum dots. Majumdar et al. (2015) used a proteomic analysis to show that NP CeO_2 exposure caused significant alterations in the protein profile of exposed kidney beans, potentially compromising nutritional quality and raising significant food safety concerns. Pagano et al. (2016) used a transcriptomic approach to evaluate the response of three crop species to NP (bulk, ion) CeO_2, lanthanum oxide, and CuO; the authors report NP-specific effects in both molecular and physiological response to exposure.

Similar to terrestrial environments, a number of reviews have sought to describe the current literature on nanomaterial fate and effects in aquatic systems (Peijnenburg et al. 2015, Quik et al. 2014, Schultz et al. 2014). The literature contains a relatively large number of studies looking at NP toxicity to a range of species under varying conditions (Binh et al. 2014, Garcia-Gomez et al. 2014, Lopez-Serrano et al. 2014, Angel et al. 2013, Pang et al. 2013), and although little consensus is available, it is notable and not surprising that most materials are more toxic in aquatic systems than in terrestrial environments. Dale et al. (2015) and Koelmans et al. (2015) both offer perspectives and recommendations on modeling NP fate in aquatic media. Similarly, Petersen et al. (2015) and Schultz et al. (2014) offer thorough evaluations of current toxicity testing regimes for NPs in aquatic environments.

Several difficulties are apparent when reviewing literature on nanomaterial effects in the environment. Particle type-specific and species-specific response is common. In addition, growth/exposure conditions and overall system complexity dramatically impact observed effects. Many published studies involve short-term, high-dose exposures in media that may have little environmental relevance (Servin & White 2016). Although this experimental approach was a valid and necessary first step in addressing NP toxicity, the data generated are not sufficient for determining true risk to sensitive receptors in the environment. Lastly, the lack of robust detection platforms for NPs in complex environmental media (soils, sediments, biotic tissues) remains a major hurdle. Although techniques to determine effects are mature and range from the biochemical to the molecular (the various "omics"), thoroughly characterizing the nature of the toxicant at the time of exposure remains problematic.

> With rapidly increasing use of engineered nanomaterials, environmental release of these contaminants is likely already occurring, perhaps on a significant scale.

LABORATORY METHODS FOR NP DETECTION

A variety of analytical techniques are used for detecting nanomaterials, depending upon type of physiochemical property or other information sought. Several technologies have been developed to characterize either bulk nanomaterials or individual NPs (including the subset of materials termed "quantum dots"). While the list of potential physical and chemical properties is expansive, a short list of most commonly sought properties includes (1) size distribution, (2) shape, (3) composition, (4) physiochemical structure, and (5) agglomeration state. For a more complete list, including analytical techniques for measuring properties, see Table 1.

Recently nanomaterial characterization has seen considerable growth by application of inductively coupled plasma–mass spectrometry (ICP–MS) to analyze single particles (sp–ICP–MS) (Lee & Chan 2015). The benefit of this approach is a simplified sample preparation or even a direct, dilute-and-shoot approach. After in-line dilution, sp–ICP–MS can be used to analyze each separate NP as it is aerosolized and ionized in the plasma, resulting in a signal intensity that is directly proportional to particle size. The mass-to-charge ratio of resulting ions can subsequently be used to provide elemental analysis. Taken together, the analysis from an sp–ICP–MS can therefore provide elemental composition of most nanomaterials (although only a single isotope can be determined at a time), size distribution, and concentration of the nanomaterial in the test solution. The typical lower size limit of detection for sp–ICP–MS is 20 nm. This technique may be applied to complex or biological matrixes, such as processing of organic material via enzymatic digestion (Linsinger et al. 2013, Loeschner et al. 2013) or acidic digestion (Loeschner et al. 2011).

This application of ICP–MS to the characterization of nanomaterial fate began in the early 2000s, with initial focus on leaching silver (Ag) NPs from implanted medical devices (Furno et al. 2004). Concern has also been raised about the increased

2017 © American Water Works Association

TABLE 1 Nanomaterial characteristics and applicable analytical techniques

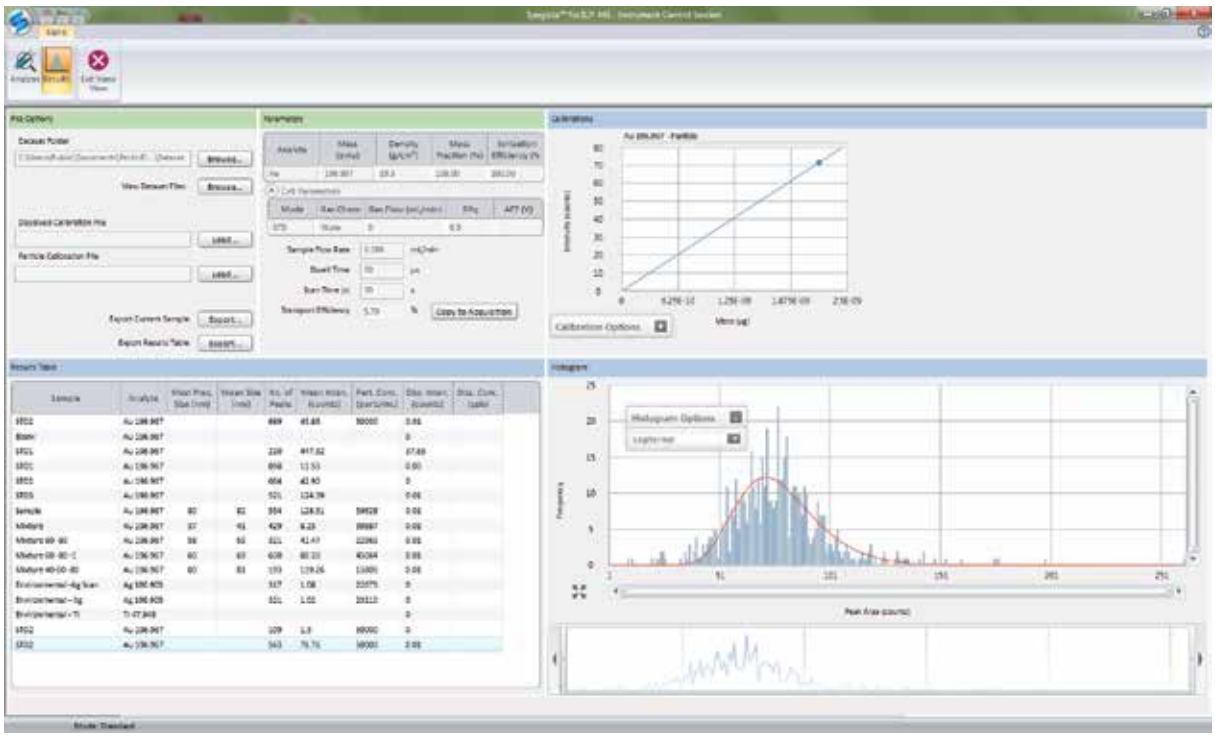
Technique	Nano-object Parameter												
	Abbreviation	Concentration	Size	Size Distribution	Surface Charge	Surface Area	Shape	Agglomeration	Crystallinity	Chemical Properties	Mechanical Properties	Thermal Properties	Electrical Properties
Acoustic spectroscopy	—	✓	✓	✓									✓
Atomic force microscopy	AFM		✓	✓		✓	✓	✓			✓		
Aerosol particle mass analyzer	AMS	✓											
Brunauer–Emmett–Teller	BET					✓							
Condensenation particle counter	CPC	✓											
Differential electric mobility analyzing system	DMAS	✓	✓	✓									
Differential scanning calorimetry	DSC											✓	
Dynamic light scattering	DLS	✓	✓	✓									
Electron back-scatter diffraction	EBSD								✓				
Electron energy loss spectroscopy	EELS									✓			
Energy dispersive X-ray spectrometry	EDX/EDS	✓											
Fluorescence spectroscopy	FL	✓	✓					✓		✓			
Fourier transform infrared spectroscopy/imaging	FTIR									✓			
Induced grating method	IG		✓	✓				✓					
Inductively coupled plasma–mass spectrometry and single particle ICP–MS	ICP–MS	✓	✓	✓				✓		✓			
Laser diffraction	—		✓	✓				✓					
Liquid chromatography–mass spectrometry	LC–MS												
Particle tracking analysis	PTA	✓	✓	✓	✓			✓					
Optical absorption spectroscopy	UV-Vis-NIR	✓	✓					✓		✓			
Quartz microbalances	QCM		✓							✓			
Raman spectroscopy/imaging	—		✓						✓	✓			
Scanning electron microscopy	SEM		✓	✓			✓	✓					
Secondary ion mass spectrometry	SIMS	✓	✓	✓			✓	✓	✓				
Selected area electron diffraction	SAED								✓				
Small angle X-ray scattering	SAXS		✓	✓			✓	✓					
Static light scattering photometer	SLS	✓	✓	✓									
Thermogravimetric analysis	TGA		✓							✓		✓	
Transmission electron microscopy	TEM		✓	✓			✓	✓	✓				
X-ray diffraction	XRD			✓					✓				
X-ray photoelectron spectroscopy	XPS				✓	✓				✓			

Adapted from Salmon et al. 2010

Checkmarks indicate parameters that can be measured by each technique.

2017 © American Water Works Association

FIGURE 2 Screenshot from an ICP–MS for nanoparticle analysis



Source: DC Public Health Laboratory

ICP–MS—inductively coupled plasma–mass spectroscopy

prevalence of Ag NP suspensions used in hospitals for their bactericidal properties (Chen & Schluesener 2008), as well as often incorporated into other surgical materials for slow release (Nangmenyi et al. 2009). Long-term exposure to these Ag NPs has been shown to result in bioaccumulation in the environment (Judy et al. 2011), and accumulation in rats has been linked to neurological lesions (Tang et al. 2009). Once exposed to such nanomaterials, rats can retain the particles for up to six months, during which time they are slowly excreted (e.g., via urine) (Sadauskas et al. 2009). The US Environmental Protection Agency has led research on the environmental transformation and fate of several types of nanomaterials, and has concluded that common disinfectants are a significant source of potentially toxic nanomaterials in the environment. The rise in use of nanomaterials and their potential toxic effects stresses the urgency for a nanomaterial biomonitoring effort.

Another useful technique for the characterization of nanomaterials at low concentrations and for simultaneous, multiple NP composition analysis is the field-flow fractionation, or FFF, to ICP–MS (Meermann & Laborda 2015). The size of the nanomaterial is characterized according to its size-specific mobility within a channel, resulting in a distribution of particles, called a fractogram. Figure 2 shows a screenshot from an ICP–MS run for nanoparticles. The benefit of this added separatory technique is that many particles may be measured at the same time, including different isotopes, although the throughput is more restrictive than sp–ICP–MS. The typical lower size limit of detection of FFF is 1 nm.

Scanning electron microscopy (SEM) is another well-established method for assessing individual NP size. A finely focused electron beam is used to scan the surface of a material in a vacuum chamber, characterizing the surface (or material on the surface) according to shape and structure, with a resolution of tens of nanometers. The addition of an energy dispersive spectrometer can further permit characterization of larger NPs, useful for measuring the spectroscopy of backscatter X-rays from the initial electron beam scan (thus providing compositional analysis).

With the advent of transmission electron microscopy (TEM), the minimum size resolved can be <10 nm, and is often coupled to X-ray spectroscopy techniques to further characterize NP composition (X-ray energy dispersive spectrometer) (Pyrz & Buttrey 2008). Additionally, the TEM penetrates the sample, providing additional material characteristics. Information for an individual or bulk nanomaterial using a TEM can

2017 © American Water Works Association

include structure, crystallography, and chemical composition of the material. Recent work has compared TEM with other methods for NP characterization, including dynamic light scattering, sedimentation flow-field fractionation, asymmetrical flow-field flow fractionation, and centrifugal liquid sedimentation (Cascio et al. 2014).

A limitation of both SEM and TEM has been the requirement of placing samples in a vacuum for analysis. This limitation has recently been addressed by the emerging technique called environmental transmission electron microscopy, whereby a thin, electron-transparent window separates the beam and the sample (Takeda & Yoshida 2013).

There have been recent advances in the use of surface enhanced Raman spectroscopy (SERS) to detect Ag NPs in complex matrixes, including consumer products and food (Guo et al. 2016, 2015; Zhang et al. 2016). Here the approach is to use indicator molecules (ferbam, 4-mercapto-benzoic acid) that bind specifically to the Ag NP (not ion or bulk), resulting in a complex that generates a unique SERS signal that can be readily detected. Current efforts are focused on expanding the list of various engineered NPs detectable by this procedure as well as lowering detection limits in a range of additional complex matrixes.

Common environmental and industrial nanomaterials that may accumulate in humans include TiO_2, associated with neurological lesions (Wang et al. 2008a, 2008b), CuO, associated with kidney and liver lesions (Liu et al. 2009), TiO_2/ZnO/CeO_2, associated with oxidative stress (Xia et al. 2008), and cadmium selenide/zinc sulfide, associated with acute toxicity (Pace et al. 2010). In the latter case, not only is the nanomaterial itself toxic, but any solubilized cadmium that leaches from the nanomaterial is also toxic.

Morphology of the nanomaterial is also a significant characteristic—smaller NPs are generally more toxic than larger ones (Liu et al. 2010), and the more aspherical NPs are more toxic than spherical (Stoehr et al. 2011, Sun et al. 2011). Thus, in developing a clinical assessment for nanomaterials in specimens, one needs to focus on composition and morphology as well as the presence of dissolved toxic elements.

ICP–MS technology has been specifically used to detect the presence of suspect toxic elements (not specifically NPs) in biological specimens, including TiO_2 (Schmidt & Vogelsberger 2006), CeO_2 (Patil et al. 2007), beryllium (Huang et al. 2011), gold (Scheffer et al. 2008, Kerr & Sharp 2007), platinum (Gehrke et al. 2011), and silicon dioxide (Gonzalez et al. 2010). Use of ICP–MS with SEM or TEM orthogonally has been beneficial in demonstrating that composition, concentration, and morphology all play roles in assessing overall NP toxicity (Beltrami et al. 2011, Chen et al. 2010, Sonavane et al. 2008).

CONCLUSION

Assessment of future use of nanotechnology-based water treatment must take account of both the risks and opportunities. The regulatory, ethical, legal, and social implications of nanotechnology require additional research in developed as well as developing counties. There are reports on the potential health and environmental risks of using nanotechnology for water treatment (Kumar et al. 2014), but the full effects of exposure to nanomaterials at water treatment plants or in drinking water are yet to be determined. While nanotechnologies have tremendous potential to address global water problems, water professionals and scientists need to work constructively to discuss and engage in dialogues with industries and local communities to understand the problems and opportunities for applying nanotechnology to water improvements. The lack of regulatory aspects for the of use of nanotechnology demands partnering among researchers, communities, and industry in public and private sectors to encourage and support novel research and innovative applications, develop positions for related policies, and develop appropriate business models to sustainably exploit the potential in field of nanotechnology.

ACKNOWLEDGMENT

This article was developed under Assistance Agreement No. 83483301 awarded by the US Environmental Protection Agency (USEPA); it has not been formally reviewed by the agency. The views expressed in this article are solely those of the Association of Public Health Laboratories (APHL) and/or the authors and USEPA does not endorse any products or commercial services mentioned in this publication. This project was entirely funded with funds from a federal program of $1,400,000. We thank Julianne Nassif at APHL for her valuable comments on the manuscript.

ABOUT THE AUTHORS

Sanjib Bhattacharyya *(to whom correspondence may be addressed) is laboratory director of the City of Milwaukee Health Department, 841 N. Broadway, Rm. 205, Milwaukee, WI 53202 USA; sbhatt@milwaukee.gov. He is an adjunct faculty member at the University of Wisconsin–Milwaukee Zilber School of Public Health and clinical associate professor, College of Health Sciences. He has a PhD in medical microbiology and postdoctorate from the Medical College of Wisconsin, Milwaukee. He also has BS, MS, and PhD degrees from the University of Kolkata, Kolkata, West Bengal, India. Bhattacharyya has more than 20 years of relevant experience in the fields of chemistry, microbiology, molecular biology, and laboratory management in the areas of clinical and environmental health science.* ***Jack Bennett*** *is section chief of environmental chemistry at the Connecticut Department of Public*

2017 © American Water Works Association

Health Laboratory, Rocky Hill, Conn. ***Luke C. Short*** *is unit manager at the DC Public Health Laboratory, Department of Forensic Sciences, Washington, D.C.* ***Tamara S. Theisen*** *is laboratory director at the Saginaw County Department of Public Health, Saginaw, Mich.* ***Michael D. Wichman*** *is an adjunct assistant professor at the University of Iowa, Coralville, Iowa.* ***Jason C. White*** *is vice-director at the CT Agricultural Experiment Station, New Haven, Conn.* ***Sarah Wright*** *is environmental laboratories senior specialist at the Association of Public Health Laboratories, Silver Spring, Md.*

https://doi.org/10.5942/jawwa.2017.109.0154

REFERENCES

Angel, B.M.; Batley, G.E.; Jarolimek, C.V.; & Rogers, N.J., 2013. The Impact of Size on the Fate and Toxicity of Nanoparticulate Silver in Aquatic Systems. *Chemosphere*, 93:2:359.

Atha, D.H.; Wang, H.; Petersen, E.J.; Cleveland, D.; Holbrook, R.D.; Jaruga, P.; Dizdarolglu, M.; Xing, B.; & Nelson, B.C., 2012. Copper Oxide Nanoparticle Mediated DNA Damage in Terrestrial Plant Models. *Environmental Science & Technology*, 46:3:1819. https://doi.org/10.1021/es202660k.

Bar-Ilan, O.; Louis, K.M.; Yang, S.P.; Pedersen, J.A.; Hamers, R.J.; Peterson, R.E.; & Heideman, W., 2012. Titanium Dioxide Nanoparticles Produce Phototoxicity in the Developing Zebrafish. *Nanotoxicology*, 6:6:670.

Batley, G.E.; Halliburton, B.; Kirby, J.K.; Doolette, C.L.; Navarro, D.; McLaughlin, M.J.; & Veitch, C., 2013. Characterization and Ecological Risk Assessment of Nanoparticulate CeO_2 as a Diesel Fuel Catalyst. *Environmental Toxicology and Chemistry*, 32:8:1896. https://doi.org/10.1002/etc.2246.

Beltrami, D.; Calestani, D.; Maffini, M.; Suman, M.; Melegari, B.; Zappettini, A.; Zanotti, L.; Casellato, U.; Careri, M.; & Mangia, A., 2011. Development of a Combined SEM and ICP-MS Approach for the Qualitative and Quantitative Analyses of Metal Nano and Microparticles in Food Products [corrected]. *Analytical and Bioanalytical Chemistry*, 401:4:1401. https://doi.org/10.1007/s00216-011-5149-2.

Bhattacharyya, S.; Bennett, J.; Short, L.C.; Theisen, T.S.; Wichman, M.D.; White, J.C.; & Wright, S., 2017. Nanotechnology in the Water Industry, Part 1: Occurrence and Risks. *Journal AWWA*, 109:11:30. https://doi.org/10.5942/jawwa.2017.109.0142.

Binh, C.T.T.; Tong, T.; Gaillard, J.F.; Gray; K.A., & Kelly, J.J., 2014. Common Freshwater Bacteria Vary in Their Responses to Short Term Exposure to Nano TiO_2. *Environmental Toxicology and Chemistry*, 33:2:317.

Cascio, C.; Gilliland, D.; Rossi, F.; Calzolai, L.; & Contado, C., 2014. Critical Experimental Evaluation of Key Methods to Detect, Size and Quantify Nanoparticulate Silver. *Analytical Chemistry*, 86:24:12143. https://doi.org/10.1021/ac503307r.

Chen, X. & Schluesener, H.J., 2008. Nanosilver: A Nanoproduct in Medical Application. *Toxicology Letters*, 176:1:1. https://doi.org/10.1016/j.toxlet.2007.10.004.

Chen, Y.S.; Hung, Y.-C.; Lin, L.-W.; Liau, I.; Hong, M.-Y.; & Huang, G.S., 2010. Size-Dependent Impairment of Cognition in Mice Caused by the Injection of Gold Nanoparticles. *Nanotechnology*, 21:48:485102. https://doi.org/10.1088/0957-4484/21/48/485102.

Dale, A.L.; Lowry, G.V.; & Casman, E.A., 2015. Stream Dynamics and Chemical Transformations Control the Environmental Fate of Silver and Zinc Oxide Nanoparticles in a Watershed-Scale Model. *Environmental Science & Technology*, 49:12:7285.

Furno, F.; Morley, K.S.; Wong, B.; Sharp, B.L.; Arnold, P.L.; Howdle, S.M.; Bayston, R.; Brown, P.D.; Winship, P.D.; & Reid, H.J., 2004. Silver Nanoparticles and Polymeric Medical Devices: A New Approach to Prevention of Infection? *Journal of Antimicrobial Chemotherapy*, 54:6:1019. https://doi.org/10.1093/jac/dkh478.

Garcia-Gomez, C.; Babin, M.; Obrador, A.; Alvarez, J.M.; & Fernandez, M.D., 2014. Toxicity of ZnO Nanoparticles, ZnO Bulk, and $ZnCl_2$ on Earthworms in a Spiked Natural Soil and Toxicological Effects of Leachates on Aquatic Organisms. *Archives of Environmental Contamination and Toxicology*, 67:4:465.

Gardea-Torresdey, J.L.; Rico, C.M.; & White, J.C., 2014. Trophic Transfer, Transformation, and Impact of Engineered Nanomaterials in Terrestrial Environments. *Environmental Science & Technology*, 48:4:2526. https://doi.org/10.1021/es4050665.

Garner, K.L. & Keller, A.A., 2014. Emerging Patterns for Engineered Nanomaterials in the Environment: A Review of Fate and Toxicity Studies. *Journal of Nanoparticle Research*, 16:8:1.

Gehrke, H.; Pelka, J.; Hartinger, C.G.; Blank, H.; Bleimund, F.; Schneider, R.; Gerthsen, D.; Bräse, S.; Crone, M.; Türk, M.; & Marko, D., 2011. Platinum Nanoparticles and Their Cellular Uptake and DNA Platination at Non-cytotoxic Concentrations. *Archives of Toxicology*, 85:7:799. https://doi.org/10.1007/s00204-010-0636-3.

Gong, N.; Shao, K.; Feng, W.; Lin, Z.; Liang, C.; & Sun, Y., 2011. Biotoxicity of Nickel Oxide Nanoparticles and Bio-remediation by Microalgae *Chlorella vulgaris*. *Chemosphere*, 83:4:510. https://doi.org/10.1016/j.chemosphere.2010.12.059.

Gonzalez, L.; Thomassen Center for Surface Chemistry and Catalysis, Katholieke Universiteit Leuven, Heverlee, L.C.J.; Plas Laboratory of Cell Genetics, Department of Biology, Vrije Universiteit Brussel, Brussels, G.; Rabolli Louvain Center for Toxicology and Applied Pharmacology, Université catholique de Louvain, Brussels, V.; Napierska Laboratory of Lung Toxicology, Katholieke Universiteit Leuven, D.; Decordier Laboratory of Cell Genetics, Department of Biology, Vrije Universiteit Brussel, Brussels, I.; Roelants, M.; et al., 2010. Exploring the Aneugenic and Clastogenic Potential in the Nanosize Range: A549 Human Lung Carcinoma Cells and Amorphous Monodisperse Silica Nanoparticles as Models. Nanotoxicology, 4:4:382. https://doi.org/10.3109/17435390.2010.501913.

Gottschalk, F.; Sun, T.; & Nowack, B., 2013. Environmental Concentrations of Engineered Nanomaterials: Review of Modeling and Analytical Studies. *Environmental Pollution*, 181:287. https://doi.org/10.1016/j.envpol.2013.06.003.

Gottschalk, F. & Nowack, B., 2011. The Release of Engineered Nanomaterials to the Environment. *Journal of Environmental Monitoring*, 13:5:1145. https://doi.org/10.1039/c0em00547a.

Guo, H.; Baoshan Xing, B.; White, J.D.; Mukherjee, A.; & He, L., 2016. Ultra-sensitive Determination of Silver Nanoparticles by Surface-Enhanced Raman Spectroscopy (SERS) After Hydrophobization-Mediated Extraction. *Analyst*, 141:5261. https://doi.org/10.1039/C6AN01186A.

Guo, H.; Zhang, Z.; Xing, B.; Mukherjee, A.; Musante, C.; White, J.C.; & He, L., 2015. Analysis of Silver Nanoparticles in Antimicrobial Products Using Surface Enhanced Raman Spectroscopy (SERS). *Environmental Science & Technology*, 49:7:4317. https://doi.org/10.1021/acs.est.5b00370.

Handy, R.D.; Owen, R.; & Valsami-Jones, E., 2008. The Ecotoxicology of Nanoparticles and Nanomaterials: Current Status, Knowledge Gaps, Challenges, and Future Needs.

2017 © American Water Works Association

Ecotoxicology, 17:315. https://doi.org/10.1007/s10646-008-0206-0.

Holden, P.A.; Gardea-Torresdey, J.L.; Klaessig, F.; Turco, R.F.; Mortimer, M.; Hund-Rinke, K.; Cohen Hubal, E.A.; et al., 2016. Considerations of Environmentally-relevant Test Conditions for Improved Evaluation of Ecological Hazards of Engineered Nanomaterials. *Environmental Science & Technology*, 50:12:6124. https://doi.org/10.1021/acs.est.6b00608.

Hu, C.W.; Li, M.; Cui, Y.B.; Li, D.S.; Chen, J.; & Yang, L.Y., 2010. Toxicological Effects of TiO_2 and ZnO Nanoparticles in Soil on Earthworm *Eisenia fetida*. *Soil Biology and Biochemistry*, 42:586. https://doi.org/10.1016/j.soilbio.2009.12.007.

Huang, W.; Fernandez, D.; Rudd, A.; Johnson, W.P.; Deubner, D.; Sabey, P.; Storrs, J.; & Larsen, R., 2011. Dissolution and Nanoparticle Generation Behavior of Be-associated Materials in Synthetic Lung Fluid Using Inductively Coupled Plasma Mass Spectroscopy and Flow Field-Flow Fractionation. *Journal of Chromatography A*, 1218:27:4149. https://doi.org/10.1016/j.chroma.2010.11.070.

Jiang, W.; Mashayekhi, H.; & Xing, B., 2009. Bacterial Toxicity Comparison Between Nano- and Micro-scaled Oxide Particles. *Environmental Pollution*, 157:1619. https://doi.org/10.1016/j.envpol.2008.12.025.

Judy, J.D.; Unrine, J.M.; & Bertsch, P.M., 2011. Evidence for Biomagnification of Gold Nanoparticles Within a Terrestrial Food Chain. *Environmental Science & Technology*, 45:2:776. https://doi.org/10.1021/es103031a.

Kerr, S.L. & Sharp, B., 2007. Nano-particle Labelling of Nucleic Acids for Enhanced Detection by Inductively-Coupled Plasma Mass Spectrometry (ICP-MS). *Chemical Communications*, 43:4537. https://doi.org/10.1039/b709466c.

Klaine, S.J.; Alvarez, P.J.J.; Batley, G.E.; Fernandes, T.F.; Handy, R.D.; Lyon, D.Y.; Mahendra, S.; McLaughlin, M.J.; & Lead, J.R., 2008. Critical Review—Nanomaterials in the Environment: Behavior, Fate, Bioavailability, and Effects. *Environmental Toxicology and Chemistry*, 27:1825. https://doi.org/10.1897/08-090.1.

Koelmans, A.A.; Diepens, N.J.; Velzeboer, I.; Besseling, E.; Quik, J.T.K.; & Van de Meent, D., 2015. Guidance for the Prognostic Risk Assessment of Nanomaterials in Aquatic Ecosystems. *Science of the Total Environment*, 535:141. https://doi.org/10.1016/j.scitotenv.2015.02.032.

Kumar, S.; Ahlawat, W.; Bhanjana, G.; Heydarifard, S.; Nazhad, M.M.; & Dilbaghi, N., 2014. Nanotechnology-Based Water Treatment Strategies. *Nanoscience and Nanotechnology*, 14:2:1838. https://doi.org/10.1166/jnn.2014.9050.

Lee, W.-W. & Chan, W.-T., 2015. Calibration of Single-Particle Inductively Coupled Plasma-Mass Spectrometry (SP-ICP-MS). *Journal of Analytical Atomic Spectrometry*, 30:6:1245. https://doi.org/10.1039/C4JA00408F.

Linsinger, T.P.J.; Chaudhry, Q.; Dehalu, V.; Delahaut, P.; Dudkiewicz, A.; Grombe, R.; von der Kammer, F.; et al., 2013. Validation of Methods for the Detection and Quantification of Engineered Nanoparticles in Food. *Food Chemistry*, 138:2–3:1959. https://doi.org/10.1016/j.foodchem.2012.11.074.

Liu, W.; Wu, Y.; Wang, C.; Li, H.C.; Wang, T.; Liao, C.Y.; Cui, L.; Zhou, Q.F.; Yan, B.; & Jiang, G.B., 2010. Impact of Silver Nanoparticles on Human Cells: Effect of Particle Size. *Nanotoxicology*, 4:3:319. https://doi.org/10.3109/17435390.2010.483745.

Liu, Y.; Gao, Y.; Zhang, L.; Wang, T.; Wang, J.; Jiao, F.; Li, W.; et al., 2009. Potential Health Impact on Mice After Nasal Instillation of Nano-sized Copper Particles and Their Translocation in Mice. *Journal of Nanoscience and Nanotechnology*, 9:11:6335. https://doi.org/10.1166/jnn.2009.1320.

Loeschner, K.; Navratilova, J.; Købler, C.; Mølhave, K.; Wagner, S.; von der Kammer, F.; & Larsen, E.H., 2013. Detection and Characterization of Silver Nanoparticles in Chicken Meat by Asymmetric Flow Field Flow Fractionation With Detection by Conventional or Single Particle ICP-MS. *Analytical and Bioanalytical Chemistry*, 405:25:8185. https://doi.org/10.1007/s00216-013-7228-z.

Loeschner, K.; Hadrup, N.; Qvortrup, K.; Larsen, A.; Gao, X.; Vogel, U.; Mortensen, A.; Lam, H.R.; & Larsen, E.H., 2011. Distribution of Silver in Rats Following 28 Days of Repeated Oral Exposure to Silver Nanoparticles or Silver Acetate. *Particle and Fibre Toxicology*, 8:18. https://doi.org/10.1186/1743-8977-8-18.

Lopez-Serrano, A.; Munoz-Olivas, R.; Sanz-Landaluze, J.; Olasagasti, M.; Rainieri, S., & Camara, C., 2014. Comparison of Bioconcentration of Ionic Silver and Silver Nanoparticles in Zebrafish Eleutheroembryos. *Environmental Pollution*, 191:207. https://doi.org/10.1016/j.envpol.2014.04.020.

Ma, C.; White, J.C.; Parkash Dhanker, O.; & Xing, B., 2015. Metal-Based Nanotoxicity and Detoxification Pathways in Higher Plants. *Environmental Science & Technology*, 49:7109. https://doi.org/10.1021/acs.est.5b00685.

Majumdar, S.; Arigi, E.A.; Choi, H.; Trujillo-Reyes, J.; Margez, J.P.F.; Almeida, I.; White, J.C.; Peralta-Videa, J.R.; & Gardea-Torresey, J.L., 2015. Environmental Effects of Nanoceria on Seed Production of Common Bean (*Phaseolus vulgaris*): A Proteomic Analysis. *Environmental Science & Technology*, 49:13283. https://doi.org/10.1021/acs.est.5b03452.

Marmiroli, M.; Pagano, L.; Savo Sardaro, M.L.; Villani, M.; & Marmiroli, N., 2014. Genome-wide Approach in *Arabidopsis thaliana* to Assess the Toxicity of Cadmium Sulfide Quantum Dots. *Environmental Science & Technology*, 48:5902. https://doi.org/10.1021/es404958r.

Meermann, B. & Laborda, F., 2015. Analysis of Nanomaterials by Field-Flow Fractionation and Single Particle ICP-MS. *Journal of Analytical Atomic Spectrometry*, 30:1226.

Nangmenyi, G.; Yue, Z; Mehrabi, S.; Mintz, E.; & Economy, J., 2009. Synthesis and Characterization of Silver-Nanoparticle-Impregnated Fiberglass and Utility in Water Disinfection. *Nanotechnology*, 20:49:495705. https://doi.org/10.1088/0957-4484/20/49/495705.

NNI (National Nanotechnology Initiative), n.d. What Is Nanotechnology? http://www.nano.gov/nanotech-101/what/definition (accessed May 1, 2017).

Pace, H.E.; Lesher, E.K.; & Ranville, J.F., 2010. Influence of Stability on the Acute Toxicity of CdSe/ZnS Nanocrystals to *Daphnia magna*. *Environmental Toxicology and Chemistry*, 29:6:1338.

Pagano, L.; Servin, A.D.; De La Torre-Roche, R.; Mukherjee, A.; Majumdar, S.; Hawthorne, J.; Marmiroli, M.; et al., 2016. Molecular Response of Crop Plants to Engineered Nanomaterial Exposure. *Environmental Science & Technology*, 50:7198. https://doi.org/10.1021/acs.est.6b01816.

Pang, C.; Selck, H.; Banta, G.T.; Misra, S.K.; Berhanu, D.; Dybowska, A.; & Forbes, V.E., 2013. Bioaccumulation, Toxicokinetics, and Effects of Copper from Sediment Spiked With Aqueous Cu, Nano-CuO, or Micro-CuO in the Deposit feeding Snail, *Potamopyrgus antipodarum*. *Environmental Toxicology and Chemistry*, 32:7:1561.

Patil, S.; Sandberg, A.; Heckert, E.; Self, W.; & Seal, S. 2007. Protein Adsorption and Cellular Uptake of Cerium Oxide Nanoparticles as a Function of Zeta Potential. *Biomaterials*, 28:31:4600. https://doi.org/10.1016/j.biomaterials.2007.07.029.

2017 © American Water Works Association

Peijnenburg, W.J.G.M.; Baalousha, M.; Chen, J.; Chaudry, Q.; Von der Kammer, F.; Kuhlbusch, T.A.J.; Lead, J.; Nickel, C.; Quik, J.T.K.; Renker, M.; Wang, Z.; & Koelmans, A.A., 2015. A Review of the Properties and Processes Determining the Fate of Engineered Nanomaterials in the Aquatic Environment. *Critical Reviews in Environmental Science & Technology*, 45:2084. https://doi.org/10.1080/10643389.2015.1010430.

Petersen, E.J.; Diamond, S.A.; Kennedy, A.J.; Goss, G.G.; Ho, K.; Lead, J.; Hanna, S.K.; Hartmann, N.B.; Hund-Rinke, K.; Mader, B.; & Manier, N., 2015. Adapting OECD Aquatic Toxicity Tests for Use with Manufactured Nanomaterials: Key Issues and Consensus Recommendations. *Environmental Science & Technology*, 49:16:9532.

Pyrz, W. & Buttrey, D., 2008. Particle Size Determination Using TEM: A Discussion of Image Acquisition and Analysis for the Novice Microscopist. *Langmuir*, 24:20:11350. https://doi.org/10.1021/la801367j.

Quik, J.T.K.; Velzeboer, I.; Wouterse, M.; Koelmans, A.A.; & Van de Meent, D., 2014. Heteroaggregation and Sedimentation Rates for Nanomaterials in Natural Waters. *Water Research*, 48:269. https://doi.org/10.1016/j.watres.2013.09.036.

Sadauskas, E.; Danscher, G.; Stoltenberg, M.; Vogel, U.; Larsen, A.; & Wallin, H.; 2009. Protracted Elimination of Gold Nanoparticles From Mouse Liver. *Nanomedicine*, 5:2:162. https://doi.org/10.1016/j.nano.2008.11.002.

Salamon, A.; Courtney, P; & Shuttler, I., 2010. *Nanotechnology and Engineered Nanomaterials: A Primer*. PerkinElmer, Waltham, Mass. www.perkinelmer.com/Content/Manuals/GDE_Nanotechnology Primer.pdf (accessed May 1, 2017).

Scheffer, A.; Engelhard, C.; Sperling, M.; & Buscher, W., 2008. ICP-MS as a New Tool for the Determination of Gold Nanoparticles in Bioanalytical Applications. *Analytical and Bioanalytical Chemistry*, 390:1:249. https://doi.org/10.1007/s00216-007-1576-5.

Schmidt, J. & Vogelsberger, W., 2006. Dissolution Kinetics of Titanium Dioxide Nanoparticles: The Observation of an Unusual Kinetic Size Effect. *Journal of Physical Chemistry B*, 110:9:3955. https://doi.org/10.1021/jp055361l.

Schultz, A.G.; Boyle, D.; Chamot, D.; Ong, K.J.; Wilkinson, K.J.; McGeer, J.C.; Sunahara, G.; & Goss, G.G., 2014. Aquatic Toxicity of Manufactured Nanomaterials: Challenges and Recommendations for Future Toxicity Testing. *Environmental Chemistry*, 11:3:207.

Schwab, F.; Zhai, G.; Kern, M.; Turner, A.; Schnoor, J.L.; & Wiesner, M.R., 2016. Barriers, Pathways and Processes for Uptake, Translocation and Accumulation of Nanomaterials in Plants—Critical Review. *Nanotoxicology*, 10:257.

Servin, A.D. & White, J.C., 2016. Nanotechnology and Agriculture: Next Steps for Understanding the Balance Between Applications and Implications. *NanoImpact*, 1:9. https://doi.org/10.1016/j.impact.2015.12.002.

Servin, A.; Elmer, W.; Mukherjee, A.; De la Torre-Roche, R.; Hamdi, H.; White, J.C.; Bindraban, P.; & Dimkpa, C., 2015. A Review of the Use of Engineered Nanomaterials to Suppress Plant Disease and Enhance Crop Yield. *Journal of Nanoparticle Research*, 17:92. https://doi.org/10.1007/s11051-015-2907-7.

Sonavane, G.; Tomoda, K.; & Makino, K., 2008. Biodistribution of Colloidal Gold Nanoparticles After Intravenous Administration: Effect of Particle Size. *Colloids and Surfaces B: Biointerfaces*, 66:2:274. https://doi.org/10.1016/j.colsurfb.2008.07.004.

Stoehr, L.C.; Gonzalez, E.; Stampfl, A.; Casals, E.; Duschl, A.; Puntes, V.; & Oostingh, G.J., 2011. Shape Matters: Effects of Silver Nanospheres and Wires on Human Alveolar Epithelial Cells. *Particle and Fibre Toxicology*, 8:36. https://doi.org/10.1186/1743-8977-8-36.

Sun, Y.N.; Wang, C.-D.; Zhang, X.-M.; Ren, L.; & Tian, X.-H., 2011. Shape Dependence of Gold Nanoparticles on In Vivo Acute Toxicological Effects and Biodistribution. *Journal of Nanoscience and Nanotechnology*, 11:2:1210. https://doi.org/10.1166/jnn.2011.3094.

Takeda, S. & Yoshida, H., 2013. Atomic-Resolution Environmental TEM for Quantitative In-Situ Microscopy in Materials Science. *Microscopy*, 62:1:193. https://doi.org/10.1093/jmicro/dfs096.

Tang, J.; Xiong, L.; Wang, S.; Wang, J.; Liu, L.; Li, J.; Yuan, F.; & Xi, T., 2009. Distribution, Translocation and Accumulation of Silver Nanoparticles in Rats. *Journal of Nanoscience and Nanotechnology*, 9:8:4924.

Wang, J.; Chen, C.; Liu, Y.; Jiao, F.; Li, W.; Lao, F.; Li, Y.; et al., 2008a. Potential Neurological Lesion After Nasal Instillation of TiO(2) Nanoparticles in the Anatase and Rutile Crystal Phases. *Toxicology Letters*, 183:1–3:72. https://doi.org/10.1016/j.toxlet.2008.10.001.

Wang, J.; Liu, Y.; Jiao, F.; Lao, F.; Li, W.; Gu, Y.; Li, Y.; et al., 2008b. Time-Dependent Translocation and Potential Impairment on Central Nervous System by Intranasally Instilled TiO(2) Nanoparticles. *Toxicology*, 254:1–2:82. https://doi.org/10.1016/j.tox.2008.09.014.

Xia, T.; Kovochich, M.; Liong, M.; Mädler, L.; Gilbert, B.; Shi, H.; Yeh, J.I.; Zink, J.I.; & Nel, A.E., 2008. Comparison of the Mechanism of Toxicity of Zinc Oxide and Cerium Oxide Nanoparticles Based on Dissolution and Oxidative Stress Properties. *ACS Nano*, 2:10: 2121. https://doi.org/10.1021/nn800511k.

Yin, L.; Colman, B.P.; McGill, B.M.; Wright, J.P.; & Bernhardt, E.S., 2012. Effects of Silver Nanoparticle Exposure on Germination and Early Growth of Eleven Wetland Plants. *PLoS ONE*, 7:10:e47674. https://doi.org/10.1371/journal.pone.0047674.

Zhang, Z.; Guo, H.; Carlisle, T.; Mukherjee, A.; Kinchla, A.; White, J.C.; Xing, B.; & He, L., 2016. Evaluation of Postharvest Washing on Removal of Silver Nanoparticles (AgNPs) from Spinach Leaves. *Journal of Agriculture and Food Chemistry*, 64:37:6916. https://doi.org/10.1021/acs.jafc.6b02705.

Zhang, H.; He, X.; Zhang, Z.; Zhang, P.; Li, Y.; Ma, Y.; Kuang, Y.; Zhao, Y.; & Chai, Z., 2011. Nano-CeO_2 Exhibits Adverse Effects at Environmental Relevant Concentrations. *Environmental Science & Technology*, 45:3725. https://doi.org/10.1021/es103309n.

AWWA RESOURCES

- Nanomaterials: Removal Processes and Beneficial Applications in Treatment. Boyd, G.R.; Tuccillo, M.E.; Sandvig, A.; Pelaez, M.; Han, C.; & Dionysiou, D.D., 2013. *Journal AWWA*, 105:12:E699 Product No. JAW_0078965.
- Current Issues—Understanding How Nanoparticles Behave in Natural and Engineered Waters. Lau, B.L.T., 2011. *Journal AWWA*, 103:11:20. Product No. JAW_0074802.
- Industry News—Study Examines Silver Nanoparticles' Effect on Wastewater Treatment. *Journal AWWA*, 2007, 99:9:106. Product No. JAW_0065065.

These resources have been supplied by *Journal AWWA* staff. For information on these and other AWWA resources, visit www.awwa.org.

2017 © American Water Works Association