Analysis of Elevated Health Risks for South Granville Water and Sewer Authority System and Potential Association with Drinking Water Disinfection By-Products

Report

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Executive Summary

The South Granville Water and Sewer Authority (SGWASA) serves a population of approximately 19,216 consumers located in the southern part of Granville County, NC, including the Town of Butner, the City of Creedmoor, the Town of Stem, and part of the unincorporated areas of southern Granville County. Over past years, SGWASA was cited for non-compliance of the Stage 2 Disinfectants/Disinfection By-Product (DBP) Rule by having periodic exceedances of the limits established in the DBP rule for total trihalomethane (TTHM) and haloacetic acid (HAA5) levels in finished drinking water within their distribution network. These D/DBP Rule violations were based on locational running annual averages. We investigated these exceedances, along with all of the other DBP data from 2005-2017, to determine whether there was a significant risk for cancer for consumers receiving this tap water.

Our findings include the following: Episodes of noncompliance were minor and sporadic and involved dispersed locations within the distribution network. For HAA5 violations, the predominant HAAs present were dichloroacetic acid and trichloroacetic acid, which are the least cytotoxic HAAs in mammalian cells, and neither is genotoxic.

Chronic diseases such as cancer usually are the result of long-term exposure to causative factors. To accommodate a long-term perspective of the SGWASA *system-wide release* of TTHMs and HAAs, we generated a yearly overview of the levels of these DBPs. We calculated the yearly averages of the TTHMs and HAAs across all plant and distribution system samples during the 2005-2017 period. Under this metric, we found that SGWASA did not exceed the regulatory limit for TTHMs, and there was only one year (2013) where the HAA limit was exceeded (by ~20%). Further, based on this extended time period, the vast majority of the THM and HAA data were well below the compliance levels, and were not significantly higher than the maximum contaminant levels (MCLs) when there were exceedances.

We also considered the reported cancer rates of Granville County, as compared to the State of North Carolina and the United States. The area served by the SGWASA drinking water distribution network is a small fraction of the area of Granville County. While it is true that Granville County has a higher overall cancer rate than the State of North Carolina, the type of cancer that is associated with DBPs − bladder cancer − was not statistically higher in Granville County versus the State of North Carolina or the United States. However, tobacco use and obesity, which are significant drivers of many types of cancer, were elevated in Granville County, exceeding the North Carolina statewide rates by 32% and 11%, respectively. These data strongly suggest that increased cancer risk observed in Granville County is more likely due to the use of tobacco products and to obesity. Our conclusions are also consistent with an earlier report from the Department of Health and Human Services, which concluded that the elevated cancer rates in Granville County and the Town of Butner were not associated with environmental contamination such as drinking water.

Definition of Abbreviations and Terms

List and definition of abbreviations and terms used in this report	
adipokines	Cell cytokines (cell signaling proteins) secreted by adipose tissue.
chromosome aberrations	Any irregularity or abnormality of chromosome distribution, number, structure, or arrangement.
cytotoxic	Physical or chemical agents that are directly toxic to cells, preventing their reproduction or growth and can induce cellular death.
DBP	Disinfection by-product usually formed by the reaction between a disinfectant and organic material, bromide, and iodide in source waters.
EPA	Environmental Protection Agency
epigenetic	The study of the mechanisms of temporal and spatial control of gene activity during the development of complex organisms. The term epigenetic can be used to describe anything other than DNA sequence that influences the development of an organism.
genetic	The study of how the characteristics of living things are transmitted from one generation to the next. Every living thing contains the genetic material that makes up DNA molecules. This material is passed on when organisms or cells reproduce. The basic unit of heredity is the gene.
genotoxic	The property of chemical or physical agents that damages the genetic information within a cell causing mutations, which may lead to cancer. While genotoxicity is often confused with mutagenicity, all mutagens are genotoxic, whereas not all genotoxic substances are mutagenic.
HAA	Haloacetic acid disinfection by-products
MCL	Maximum contaminant level (regulatory limit)
monoclonal	Monoclonal cells are defined as a group of cells produced from a single ancestral cell by repeated cellular replication.
neoplasia	A new, often uncontrolled growth of abnormal tissue; tumor.
NOM	Natural organic matter
oncogenes	A gene that played a normal role in the cell as a proto-oncogene and that has been altered by mutation and now may contribute to the growth of a tumor.
oxidative stress	An imbalance between the production of free radicals and the ability of the body to counteract or detoxify their harmful effects through neutralization by antioxidants.
pathogens	An agent that causes infection or disease, especially a microorganism, such as a bacterium, protozoan, or virus.
SGWASA	South Granville Water and Sewer Authority
somatic mutations	An alteration in DNA that occurs after conception. Somatic mutations can occur in any of the cells of the body except germ cells, and therefore, are not passed on to children. These alterations can (but do not always) cause cancer or other diseases.
THM	Trihalomethane disinfection by-products

Introduction: Regulated Drinking Water Disinfection By-Products

The disinfection of drinking water to reduce the incidence of waterborne disease was arguably the greatest public health achievement of the 20th century (Calderon, 2000). Chemical disinfectants inactivate pathogens in source waters; however, an unintended consequence is their reaction with natural organic matter (NOM), anthropogenic contaminants, and bromide/iodide to form disinfection by-products (DBPs) (Richardson et al., 2007; Richardson and Postigo, 2015; Yang et al., 2014). Factors including the concentration and type of organic matter, pH, temperature, disinfectant type and concentration, and contact time affect the formation of DBPs (Hong et al., 2013; Singer, 1994). The most widely employed disinfectants include chlorine, chloramines, chlorine dioxide, and ozone; each disinfectant generates DBPs with a different spectra of chemical classes (Hua and Reckhow, 2007; Zhang et al., 2000). Since their discovery in 1974 (Bellar et al., 1974; Rook, 1974), more than 700 DBPs have been reported (Richardson and Postigo, 2015) and more than 100 have been analyzed for their quantitative, comparative mammalian cell toxicity (Wagner and Plewa, 2017). This number of DBPs represents only a fraction of the total halogenated DBPs generated in disinfected water (Krasner et al., 2006).

In 1979, the U.S. Environmental Protection Agency (EPA) issued the first DBP regulations under the Safe Drinking Water Act, which set maximum contaminant limits (MCLs) for total trihalomethanes (THMs) at an annual average of 0.100 mg/L in drinking water (U. S. Environmental Protection Agency, 1979). In 1998, the U.S. EPA issued the Stage 1 Disinfectants (D)/DBP Rule, which lowered permissible levels of total THMs to 0.080 mg/L and regulated for the first time five haloacetic acids (HAA5) at 0.060 mg/L, bromate at 0.010 mg/L, and chlorite at 1.0 mg/L (U. S. Environmental Protection Agency, 1998). Stage 1 regulations required monitoring based on running annual averages, which represented averages of all samples collected in a utility's distribution system over a one-year period. This Rule became effective on January 1, 2002. The current U.S. EPA regulation is the Stage 2 D/DBP Rule (published in January 2006) (Table 1) (U. S. Environmental Protection Agency, 2006). The Stage 2 Rule maintains the Stage 1 Rule MCLs for total trihalomethanes (TTHMs) as 0.080 mg/L and 0.060 mg/L for HAA5. In addition, the Stage 2 Rule required that MCLs be based on locational running annual averages; that is, each location in the distribution system needs to comply on a running annual average basis (U. S. Environmental Protection Agency, 2006). Although these DBPs have toxic characteristics (Table 2), the EPA regulations were not based primarily on health risk calculations, but were meant as a metric to ensure that water treatment plants provided high quality potable drinking water to their customers.

Table 1. U.S. regulations for disinfection by-products.

DBPs	MCL (mg/L)
Total THMs	0.080
5 Haloacetic acids	0.060
Bromate	0.010
Chlorite	1.0

Table 2. Summary of occurrence, genotoxicity, and carcinogenicity of regulated THMs and HAAs			
DBP	**Occurrence [a]**	**Genotoxicity [b]**	**Carcinogenicity**
THMs			
Chloroform	*****	–	+
Bromodichloromethane	****	+	+
Chlorodibromomethane	****	+	+
Bromoform	****	+	+
HAAs			
Chloroacetic acid	***	+	–
Bromoacetic acid	***	+	
Dichloroacetic acid	*****	+	+
Dibromoacetic acid	*****	+	+
Trichloroacetic acid	*****	–	+

[a]Key to occurrence symbols: *low ng/L levels, **ng/L to sub-µg/L levels, ***sub to low µg/L levels, ****low µg/L levels, *****low-mid µg/L levels, ******high µg/L levels.
[b] Symbols represent weight of evidence for the genotoxicity data. In general, where a compound was genotoxic in several studies in the same assay or was genotoxic in several different assays, it was declared "+" in the table even if the compound was negative in other assays.

SGWASA System Distribution

The South Granville Water and Sewer Authority serves a population of approximately 19,216 consumers located in the southern part of Granville County, NC, including the Town of Butner, the City of Creedmoor, the Town of Stem, and part of the unincorporated areas of southern Granville County (SGWASA, 2017). SGWASA's water source is the R.D. Holt Reservoir located near Butner, NC. It is part of the Upper Neuse River Basin, in a heavily forested watershed (75%), and it contains approximately 2.2 billion gallons of water, with the possibility of providing > 13 million gallons of water for treatment per day. Raw water from the R.D. Holt Reservoir is treated at the SGWASA Water Plant and involves the following treatment steps: coagulation, flocculation, sedimentation, disinfection, and filtration. Chlorine is added for disinfection to the coagulated/settled water (immediately after the sedimentation process), just prior to filtration. Following filtration, chloramines are added as the disinfectant residual for the distribution system (from the plant to the consumers' tap).

Over past years, SGWASA was cited for non-compliance of the Stage 2 Rule by having periodic, excessive TTHM and HAA5 levels in finished drinking water within its distribution network. There were eight quarters with exceedances that occurred in 2013-2017; two of these were for TTHM violations (levels ranged from 0.086-0.102 mg/L), and eight were for HAA5 violations

(0.062-0.076 mg/L). These episodes of noncompliance were minor and sporadic and involved dispersed locations within the distribution network. For HAA5 violations, the predominant HAAs present were dichloroacetic acid and trichloroacetic acid. Dichloroacetic acid and trichloroacetic acid are the least two cytotoxic HAA in mammalian cells and neither of these two HAAs is genotoxic (Plewa et al., 2010).

These episodic non-compliance incidences were the foundation of a formal complaint on the quality of finished drinking water registered by a customer in the Town of Butner, NC. The complainant argued that the poor quality of drinking water provided by SGWASA was associated with elevated cancer rates in Granville County and the Town of Butner NC (Arias, 2017). A petition was submitted by the complainant in July 2016 to the Agency for Toxic Substances and Disease Registry (ATSDR) questioning the quality of drinking water being provided by SGWASA (Arias, 2017). In the petition, the complainant indicated that higher cancer incidence in Granville County may be associated with the poor drinking water quality (Camp, 2017).

We prepared an overview regarding the quality of drinking water generated by SGWASA during the period from 2005 to 2017. The individual laboratory quarterly reports for the TTHMs and the HAA5 for water samples from the drinking water facility, as well as the samples taken from the distribution network, were averaged and the standard error of the mean was calculated. For 2005, the averaged TTHMs and HAA5 were derived from 20 water samples, from 2006-2012 the average yearly values were based on 24 water samples, and from 2013-2017, 32 yearly water samples were analyzed for each DBP. This approach provides an overall metric on the quality of SGWASA drinking water based on the MCLs listed in the Stage 2 Rule.

The results from this analysis are presented in Figure 1 for the TTHMs and in Figure 2 for the HAA5 DBPs.

Section Conclusion

Using the yearly averages for 2005 to 2017 across all plant and distribution system samples, SGWASA did not exceed the MCL for the TTHMs. During the same time period, SGWASA exceeded the MCL for the HAA5s for only one year (2013). From the results presented in Figures 1-2, we conclude that SGWASA produced high quality drinking water to the Town of Butner and to Granville County, NC.

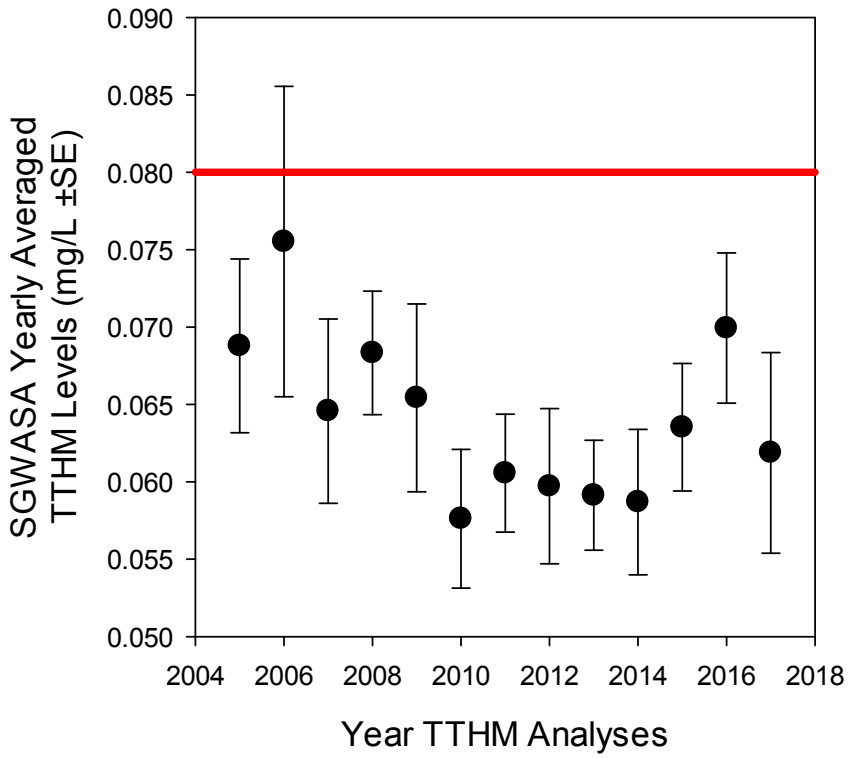

Figure 1. The average ± standard error (SE) yearly TTHM concentration (mg/L) in SGWASA drinking water. The horizontal red line represents the TTHM MCL.

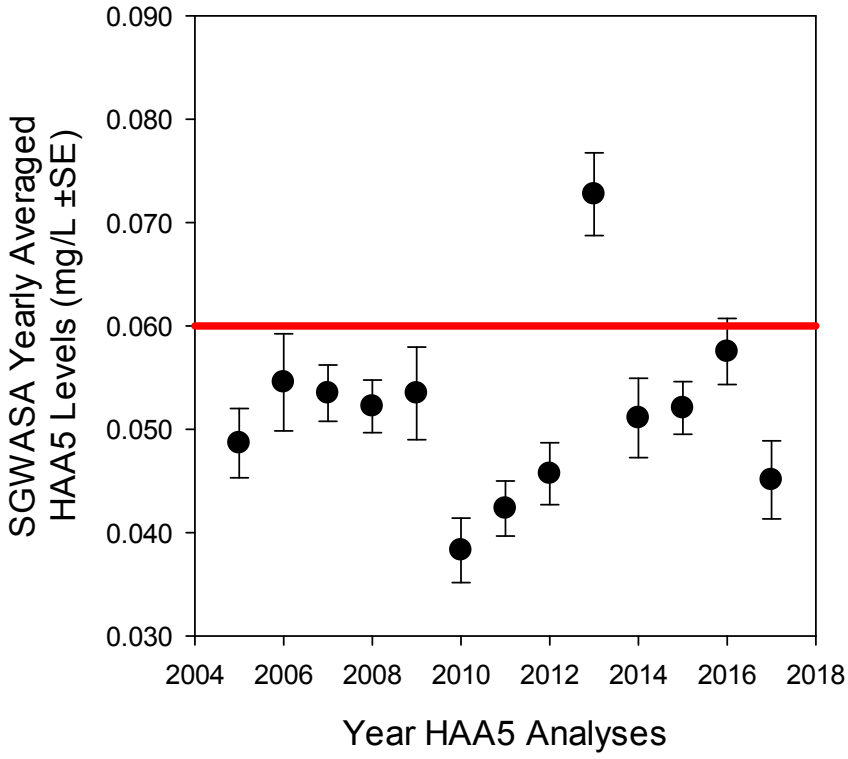

Figure 2. The average ± standard error (SE) yearly HAA5 concentration (mg/L) in SGWASA drinking water. The horizontal red line represents the HAA5 MCL.

Cancer Incidence and Causation

Cancer is a disease that is usually classified by the organ system that is damaged by a tumor (e.g. bladder cancer, liver cancer, or skin cancer). All types of cancer are related, due to the monoclonal nature of the cells within initiating tumor. Cancer is a genetic (or epigenetic) disease that begins with a neoplastic mother cell that arises due to mutant oncogenes, genome instability, or chromosome aberrations that adversely affect cellular homeostasis (National Cancer Institute, 2017a; Vaux, 2011). The neoplastic mother cell replicates its DNA and undergoes unrestricted cell division. The resulting clonal neoplastic daughter cells also uncontrollably divide and spread into surrounding tissues. Cancer cells differ from normal cells in many ways that allow them to grow out of control and become malignant tumors (Greaves and Maley, 2012). By definition, cancer is a genetic disease. It is caused by somatic mutations, chromosome aberrations, or epigenetic aberrant expression of genes that control the way our cells grow and divide. Mutant oncogenes or other genetic changes that cause cancer can be inherited (National Cancer Institute, 2017c; National Cancer Institute, 2013). A principal cause of cancer is the induction of somatic cell mutations generated during a person's lifetime as a result of genetic errors that occur as cells divide or because of damage to genomic DNA caused by genotoxic agents either through environmental exposures (tobacco smoking) (National Cancer Institute, 2017d; Shah and Karnes, 2010) or by poor life habits (obesity) (National Cancer Institute, 2015). Cancer-causing environmental exposures include substances, such as the chemicals in tobacco smoke, radiation, and to a lesser extent, drinking water DBPs (Bove et al., 2007b, 2007a; Cantor et al., 2006; Villanueva et al., 2004). The concern for drinking water DBPs is that many are toxic agents (Plewa and Wagner, 2015; Richardson and Postigo, 2015; Wagner and Plewa, 2017).

Risk Factors Associated with Cancer

For 2016 in the United States, 1,685,210 new cases of cancer were diagnosed and 595,690 people perished from the disease. Based on the 2008-2012 reporting period, the cancer incidence rate was 454.8 per 100,000 men and women per year while cancer mortality was 171.2 per 100,000 men and women per year (National Cancer Institute, 2017f). As illustrated in Figure 3, among the primary factors associated with cancer, tobacco use and obesity rank high. Tobacco use, as well as second hand smoke, cause approximately 40% of the yearly cancer incidence (Centers for Disease Control and Prevention, 2016). The genotoxic and carcinogenic chemicals in tobacco products are the primary causal agents for cancer induction (Hecht, 1999). Likewise, the poor health habits that lead to obesity are also associated with 40% of the cancer incidence in the United States (Centers for Disease Control and Prevention, 2017; National Cancer Institute, 2015). The mechanisms that drive this high level of cancer association with obesity involve increased lipid and lipid signaling within the body, inflammatory responses that generate reactive oxidative stress, insulin resistance, and adipokines (cell signaling proteins secreted by adipose tissue) (Louie et al., 2013; National Cancer Institute, 2015). Predisposition to acquiring cancer by hereditary factors accounts for about 10% of cancer incidence (Evans, 2015; National Cancer Institute, 2017c; National Cancer Institute, 2013). Other factors, both environmental and personal care, account for approximately 9.2% cancer incidence. The Centers for Disease Control and Prevention, as well as the National Cancer

Institute, do not carry statistics for cancer induction by disinfected drinking water or drinking water DBPs. However, disinfected drinking water is most associated with bladder cancer (Bove et al., 2007b; Villanueva et al., 2004). The U.S. EPA estimated that between 2% and 17% of the observed bladder cancer incidence is caused by consuming disinfected drinking water (U.S. Environmental Protection Agency, 1998). Bladder cancer accounts for approximately 4.7% cancer incidence (National Cancer Institute, 2017e). We took the highest estimate for bladder cancer induction by the U.S. EPA (17%) times the bladder cancer incidence rate (4.7%), and the product was 0.80% (Figure 3).

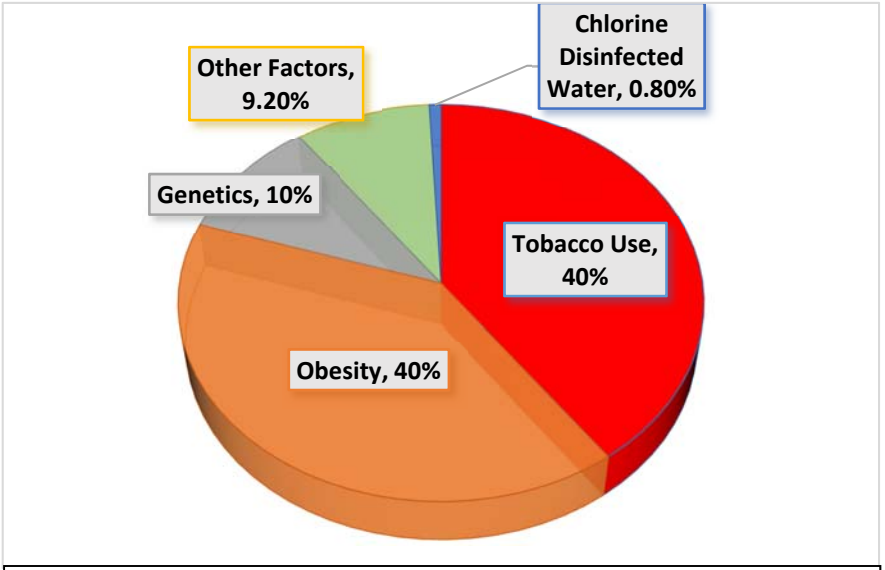

Figure 3. Major inducers of cancer in the United States. The data were derived from the Department of Health and Human Services, National Cancer Institute, and the Centers for Disease Control and Prevention. All of the factors were based on overall cancer causation except for disinfected drinking water, which was an estimate based on the induction of bladder cancer.

Section Conclusion

As illustrated in Figure 3, the cancer incidence associated with drinking water DBPs was by far the lowest of the accepted causative factors for cancer in the United States.

Complainant Issues

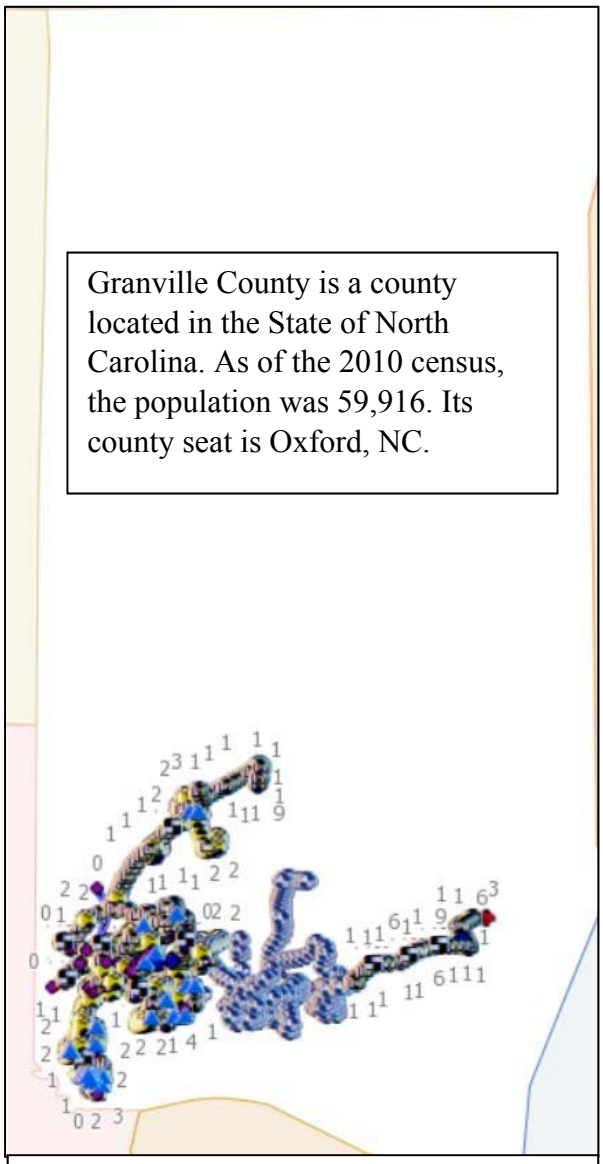

Figure 4. The disinfected drinking water distribution network of the South Granville Water and Sewer Authority, North Carolina.

The South Granville Water and Sewer Authority provides water and sewer service to south Granville County, including the communities of Stem, Butner, and Creedmoor, NC. In 2012, SGWASA served a population of approximately 19,000 with an average tap water use of 1.9 million gallons per day. The maximum use was recorded in 2012 as 4.3 million gallons per day (Figure 4) (SGWASA, 2017). The area served by the SGWASA drinking water distribution network is a small fraction of the area of Granville County. Until recently the SGWASA service area used different source waters. Stem, from wells until 2004, Creedmoor from Lake Rogers until 2012 and Butner from the water treatment plant now controlled by SGWASA since 1942.

A petition was submitted from a Butner, NC resident in July 2016 to the Agency for Toxic Substances and Disease Registry (ATSDR) questioning the quality of drinking water being provided by SGWASA. In the petition, the complaint indicated that some community members believed the alleged higher cancer incidence may be associated with the poor drinking water quality (Arias, 2017).

Drinking water quality and the MCLs for the drinking water DBPs are regulated by the U.S. EPA (U. S. Environmental Protection Agency, 2006). When the U.S. EPA established the drinking water DBP MCLs, it published the following statement:

"In part, both the TTHM and HAA classes are regulated because they occur at high levels and represent chlorination byproducts that are produced from source waters with a wide range of water quality. The combination of TTHM and HAAs represent a wide variety of compounds resulting from bromine substitution and chlorine substitution reactions (i.e., bromoform has 3 bromines, TCAA has 3 chlorines, BDCM has one bromine and two chlorines, etc.). EPA believes that the TTHM and HAAS classes serve

as an indicator for unidentified and unregulated DBPs. EPA believes that controlling the occurrence levels of TTHM and HAAS will control the levels of all chlorination DBPs to some extent."

As stated by Dr. Arias, the MCL for these DBPs "… is not a health-based standard but rather an operational quality control indicator that was established to help assure that high quality drinking water is provided to consumers."

Since chronic diseases such as cancer usually are the result of long-term exposure to causative factors, a yearly averaged DBP metric may better reflect a public health hazard due to these agents. As illustrated in Figures 1-2, the yearly averaged TTHM and HAA5 do not show a constant yearly level above the MCLs for these drinking water DBPs established by the U.S. EPA. Based on this analysis, we conclude that SGWASA has provided its customers with quality, safe potable tap water.

The complainant stated that Granville County had a higher cancer rate than that of North Carolina. This is indeed true. The overall cancer mortality rate for North Carolina is 196.2/100,000 population (America's Health Rankings, 2017) versus 171.2 cancer deaths per 100,000 population in the United States (National Cancer Institute, 2017f). However, this enhanced cancer mortality rate is likely due to factors other than the consumption of SGWASA tap water. As illustrated in Figure 3, the primary causes of cancer in the United States are tobacco use and obesity. The genotoxic agents in tobacco products induce neoplasia, and regions with higher tobacco use by the residents express higher cancer rates. Using the Granville-Vance Public Health Department report for 2015, the rate of use of tobacco products by residents in Granville County exceeded the North Carolina statewide rates by 32% (Arias, 2017). Obesity is also a lifestyle factor that is highly associated with increased levels of cancer (National Cancer Institute, 2017b). In Granville County, the population has approximately 11% higher obesity rates as compared to North Carolina state-wide (Open Data Network: Granville County, NC, 2015). Cancer is a disease related to an aging population (National Cancer Institute, 2017a), and the median age for Granville County is 41.4 years as compared to the statewide age of 37.8 for North Carolina. The population residing in Granville County is 9.5% older than the population of the state as a whole. These health and demographic data strongly suggest that increased cancer risk observed in Granville County is more likely to be associated with the use of tobacco products and obesity and an aging population.

Another line of evidence that argues against the association of SGWASA disinfected drinking water and enhanced cancer risk involves the rates of bladder cancer in Granville County as compared to the levels seen in the United States and in North Carolina. Exposure to disinfected water is associated with the induction of *bladder cancer* (Costet et al., 2011; Regli et al., 2015; Villanueva et al., 2004). The rates of bladder cancer mortality for the United States, North Carolina, and Granville County are 19.8, 19.8, and 20.3 deaths per 100,000 population (America's Health Rankings, 2017; National Cancer Institute, 2017e, 2017f). As illustrated in Figure 5, there is no apparent difference in bladder cancer mortality among these three comparisons. If the consumption of SGWASA disinfected drinking water was associated with the enhanced levels of cancer observed in Granville County, the impact would be focused on *bladder cancer*.

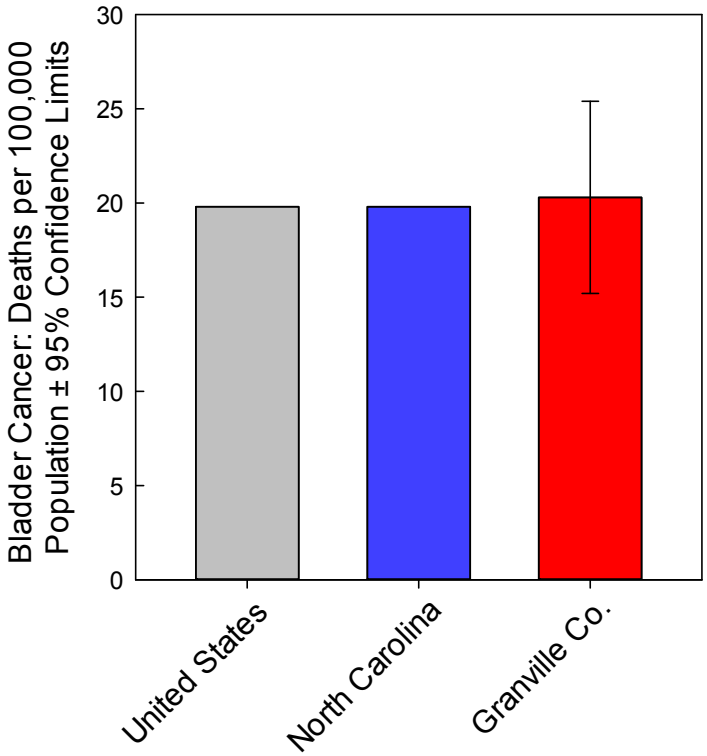

Figure 5. Comparison of the bladder cancer mortality rates in the United States, the State of North Carolina, and Granville County, NC.

After a review of the North Carolina Central Cancer Registry reports, the staff at the cancer registry, as well as the Department of Health and Human Services, Agency for Toxic Substances and Disease Registry, concluded that the elevated cancer rates in Granville County and the Town of Butner were not associated with environmental contamination such as drinking water (Arias, 2017). This is an important interpretation since it disagrees with the complainant's contention that a cancer cluster exists due to contaminated drinking water provided by SGWASA.

Overall Conclusions

In our opinion, it appears that the enhanced cancer rates recorded by the North Carolina Cancer Registry is due to enhanced tobacco product usage and a higher level of obesity found in the residents of Granville County. To be sure, DBPs generated in disinfected drinking water carries a chronic adverse health risk (Figure 3). This risk is overwhelmed by the substantial benefits of the

reduction of waterborne disease as a result of the disinfection of drinking water (Calderon, 2000). When compared to other factors involved in cancer risk, there are no redeeming benefits except for the regulated disinfection of water. Neither tobacco use nor obesity carry a redeeming health benefit to offset their cancer-causing risks. However, the disinfection of drinking water is considered a primary achievement in public health practice of the 20th century (Calderon, 2000). SGWASA continues its program of improving its facilities and water purification methods. The goal of all drinking water utilities and the goal of the U.S. EPA is to make good drinking water better.

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