Chemical mixtures in untreated water from public-supply wells in the U.S. — Occurrence, composition, and potential toxicity

Patricia L. Toccalino [a,*], Julia E. Norman [b], Jonathon C. Scott [c]

[a] U.S. Geological Survey (USGS), 6000 J Street, Placer Hall, Sacramento, California 95819, United States
[b] USGS, 2130 SW 5th Avenue, Portland, Oregon 97201, United States
[c] USGS, 202 NW 66th Street, Oklahoma City, Oklahoma 73116, United States

ABSTRACT

Chemical mixtures are prevalent in groundwater used for public water supply, but little is known about their potential health effects. As part of a large-scale ambient groundwater study, we evaluated chemical mixtures across multiple chemical classes, and included more chemical contaminants than in previous studies of mixtures in public-supply wells. We (1) assessed the occurrence of chemical mixtures in untreated source-water samples from public-supply wells, (2) determined the composition of the most frequently occurring mixtures, and (3) characterized the potential toxicity of mixtures using a new screening approach. The U.S. Geological Survey collected one untreated water sample from each of 383 public wells distributed across 35 states, and analyzed the samples for as many as 91 chemical contaminants. Concentrations of mixture components were compared to individual human-health benchmarks; the potential toxicity of mixtures was characterized by addition of benchmark-normalized component concentrations. Most samples (84%) contained mixtures of two or more contaminants, each at concentrations greater than one-tenth of individual benchmarks. The chemical mixtures that most frequently occurred and had the greatest potential toxicity primarily were composed of trace elements (including arsenic, strontium, or uranium), radon, or nitrate. Herbicides, disinfection by-products, and solvents were the most common organic contaminants in mixtures. The sum of benchmark-normalized concentrations was greater than 1 for 58% of samples, suggesting that there could be potential for mixtures toxicity in more than half of the public-well samples. Our findings can be used to help set priorities for groundwater monitoring and suggest future research directions for drinking-water treatment studies and for toxicity assessments of chemical mixtures in water resources.

Published by Elsevier B.V.

1. Introduction

In 2009, about 104 million people in the U.S.—more than one-third of the population—received their drinking water from about 139,000 public water systems that use groundwater as their source (U.S. Environmental Protection Agency, 2009). Analysis of individual contaminants in groundwater used for public water supply serves to identify contaminants that occur at concentrations of potential human-health concern, and to assess where and why they occur. Most people, however, are exposed to mixtures of organic and inorganic contaminants, rather than to individual contaminants (Carpenter et al., 2002; Hertzberg et al., 2008). Most mixtures, and many contaminants in mixtures, are not regulated in drinking water by the U.S. Environmental Protection

Agency (USEPA) under the Safe Drinking Water Act. Disinfection by-products (DBPs) are examples of contaminants regulated in drinking water as mixtures (U.S. Environmental Protection Agency, 2011).

Little is known about the potential health effects associated with exposure to multiple contaminants at the low concentrations typically detected in the environment, yet toxicologic actions that can result in adverse effects are possible at these concentrations (Sexton et al., 1995; Yang, 1994). Identifying all possible chemical mixtures in drinking water and assessing their toxicity is not practical (Ryker and Small, 2008; Squillace et al., 2002); often we do not know which mixtures are most important to assess, or which biologic end points should be studied (Carpenter et al., 2002).

Many investigators have stressed the importance of conducting toxicologic research on chemical mixtures actually identified in environmental media and at environmentally relevant concentrations (Carpenter et al., 2002; Hertzberg et al., 2008; Johnson and De Rosa, 1995; Sexton et al., 1995; Suk et al., 2002), but relatively few animal toxicity studies of chemical mixtures have been conducted at such concentrations. Some studies have used groundwater data from hazardous waste sites to inform chemical mixtures research (Fay and Mumtaz,

1996; Johnson and De Rosa, 1995; Simmons, 1995), but there are few examples of ambient groundwater data that have been used in chemical mixtures research (Teuschler and Simmons, 2003; Yang, 1992). This study evaluates chemical mixtures in a large-scale real-world ambient groundwater dataset. Examples of toxicologic studies of chemical mixtures that have used groundwater data are summarized in the Supplementary Data.

Previous U.S. Geological Survey (USGS) investigations have assessed the occurrence, distribution, and benchmark exceedances of individual contaminants in ambient water from public wells (Gilliom et al., 2006; Toccalino et al., 2010; Zogorski et al., 2006). Gilliom et al. (2006) reported the frequency that pesticide mixtures were detected in major aquifers, but did not specifically describe mixtures findings for public wells. Zogorski et al. (2006) examined the detection frequency and composition of mixtures of volatile organic compounds (VOCs) in public and domestic wells, but only individual concentrations greater than 0.2 μg/L were considered. Other USGS studies included mixtures findings primarily from domestic wells (Squillace et al., 2002; DeSimone, 2009).

In this study, we assessed chemical mixtures in a subset of untreated groundwater samples from public wells from recent USGS ambient water-quality studies (Toccalino et al., 2010). This study differs from previous studies; we examined more chemical contaminants (91 organic and inorganic contaminants), across more chemical classes, than in any previous study of mixtures in public-supply wells. We (1) assessed the occurrence of chemical mixtures in source-water samples from public-supply wells, (2) determined the composition of the most frequently occurring mixtures, and (3) characterized the potential toxicity of mixtures using a new screening approach.

By identifying chemical mixtures that most frequently occur and have the greatest potential toxicity in groundwater, results from this study can be used to help set priorities for monitoring, such as for the USEPA Unregulated Contaminant Monitoring Program and the drinking water Contaminant Candidate List (Ryker and Small, 2008). Our findings also could suggest future research directions for engineers and scientists who study drinking-water treatment technologies and for human-health researchers who conduct toxicity assessments of chemical mixtures in water resources. For example, the Agency for Toxic Substances and Disease Registry (ATSDR) has evaluated the toxicity of the mixture of atrazine, deethylatrazine, diazinon, nitrate, and simazine (Agency for Toxic Substances and Disease Registry, 2006) because of the frequency of its occurrence in public and domestic wells sampled by USGS (Squillace et al., 2002). Given the vast number of potential chemical mixtures in groundwater, and the need to study mixtures based on human exposures, it is important to focus toxicologic studies on those mixtures that have the greatest potential to impact human health (Johnson and De Rosa, 1995; Ryker and Small, 2008; Simmons, 1995; Suk et al., 2002).

2. Methods

2.1. Selection of public wells and contaminants

The data used in this study are a subset of data collected by the USGS for the National Water Quality Assessment (NAWQA) Program. One untreated source-water sample was collected from each of 383 public wells during 1993–2007. The wells were part of groundwater assessment studies which typically were designed to describe the water quality of major aquifers used for drinking water within study areas throughout the U.S. To characterize large aquifer areas, wells selected for sampling were randomly located, but were distributed approximately equally across the USGS study areas to represent typical aquifer conditions in these hydrogeologic settings.

The NAWQA Program's nationally consistent sampling and analysis design, along with criteria for well selection, are described elsewhere (Gilliom et al., 1995; Lapham et al., 1995; Scott, 1990). Well selection criteria included the availability of well-construction and aquifer information. We did not target areas of known contamination

and excluded wells that were less than 1000 m apart. The quality of the sampled source water does not necessarily reflect the quality of finished water ingested by the people served by these wells because the samples were collected prior to any treatment or blending.

This study, using a subset of NAWQA data, is not intended to represent a statistical sampling of all public wells, populations served, or groundwater withdrawals nationwide. The 383 wells, however, are widely distributed nationally, include wells in selected parts of 35 states, and withdraw water from parts of nearly one-half of the regionally extensive aquifers used for public water supply in the U.S. The wells are distributed among 291 unique public water systems—less than 1% of all groundwater-supplied water systems in the U.S. Our study, however, was not designed to assess water quality in specific public water systems, some of which are comprised of tens or hundreds of individual public wells.

The USGS has analyzed more than 200 chemical contaminants in water samples from public wells (Toccalino et al., 2010), but not all contaminants were analyzed in all samples. Each contaminant included in this study was analyzed in most of the 383 samples. Concentrations of inorganic contaminants were greater than one-tenth of human-health benchmarks in at least 1 sample, and organic contaminants were detected in at least one sample. Using these criteria, water-quality data for 91 contaminants (19 inorganic and 72 organic) were included in this study (Table 1).

DeSimone (2009) summarized quality-control data for these contaminants. Toccalino et al. (2010) showed that analytical method detection levels were less than human-health benchmarks for all but two of the contaminants included in this study—dieldrin and dibromochloropropane—indicating that the analytical methods were adequate for detecting concentrations of potential human-health concern for most contaminants. The analytical method detection level was at least 10-fold less than the MCL or HBSL for 69 of the 78 contaminants with benchmarks.

2.2. Mixtures datasets

Because few human-health benchmarks have been established for chemical mixtures, mixtures in the 383 public-well samples were assessed relative to benchmarks for individual contaminants. Specifically, concentrations of contaminants that are regulated by USEPA in drinking water under the Safe Drinking Water Act were compared to Maximum Contaminant Levels (MCLs), and concentrations of unregulated contaminants were compared to Health-Based Screening Levels (HBSLs). MCLs are legally enforceable USEPA drinking-water standards (U.S. Environmental Protection Agency, 2011). HBSLs are non-enforceable benchmark concentrations of contaminants in water that were developed by the USGS in collaboration with the USEPA and others (Toccalino, 2007).

Contaminant concentrations were normalized to human-health benchmarks by computing Benchmark Quotient (BQ) values, which are ratios of contaminant concentrations to MCLs or HBSLs (Toccalino, 2007). BQ values were not computed for contaminants for which MCLs or HBSLs were not available. Contaminant concentrations were assumed to be zero for contaminants that were analyzed but not detected.

BQ values are conceptually similar to Hazard Quotient (HQ) values defined by the USEPA and the ATSDR as the exposure level divided by an "acceptable" or "safe" level of exposure (Agency for Toxic Substances and Disease Registry, 2004; U.S. Environmental Protection Agency, 2000). When an HQ value is greater than 1, concern increases for the potential hazard associated with an individual chemical (Agency for Toxic Substances and Disease Registry, 2004).

Similarly, a BQ value greater than 1 (BQ > 1) indicates that a concentration is greater than a benchmark and is of potential human-health concern. A BQ > 0.1 indicates that a concentration is greater than one-tenth of a benchmark. Including contaminants with BQ > 0.1 in a mixtures analysis is consistent with ATSDR guidance, which

Table 1
Contaminants and human-health benchmarks included in this study.

Contaminant	Benchmark value[a]	Benchmark type[a]	Mixtures categories[b]
Major ions (mg/L)			
Fluoride	4	MCL	1[c]
Trace elements (µg/L)			
Antimony	6	MCL	2,3
Arsenic	10	MCL	1,2,3
Barium	2000	MCL	1,2,3
Beryllium	4	MCL	2,3
Boron	1000	HBSL	1,2,3
Cadmium	5	MCL	2,3
Chromium	100	MCL	2,3
Lead	15	MCL[d]	1,2,3
Manganese	300	HBSL	1,2,3
Molybdenum	40	HBSL	1,2,3
Nickel	100	HBSL	2,3
Selenium	50	MCL	2,3
Strontium	4000	HBSL	1,2,3
Thallium	2	MCL	2,3
Uranium	30	MCL	1,2,3
Zinc	2000	HBSL	1,2,3
Nutrients (mg/L as nitrogen)			
Nitrate	10	MCL	1,2,3
Radionuclides (pCi/L)			
Radon-222	300 (4000) Proposed MCL (AMCL)		1,2,3
Pesticide compounds (µg/L)			
Acetochlor	1	HBSL[e]	2,3
Alachlor	2	MCL	3
Atrazine	3	MCL	2,3
Carbaryl	40	HBSL[e]	3
Carbofuran	40	MCL	3
Chlorpyrifos	2	HBSL	3
Cyanazine	1	HBSL	3
p,p'-DDE	0.1	HBSL[e]	3
Deethylatrazine	–	–	3
Dieldrin	0.002	HBSL[e]	1,2,3
Ethoprop	1	HBSL[e]	3
alpha-HCH	0.006	HBSL[e]	1,2,3
gamma-HCH	0.2	MCL	2,3
Metolachlor	700	HBSL	3
Metribuzin	90	HBSL	3
Molinate	0.7	HBSL	3
Parathion-methyl	1	HBSL	3
Prometon	400	HBSL	3
Simazine	4	MCL	3
Tebuthiuron	1000	HBSL	3
Terbacil	90	HBSL	3
Volatile organic compounds (µg/L)			
Acetone	6000	HBSL	3
tert-Amyl methyl ether	–	–	3
Benzene	5	MCL	3
Bromobenzene	–	–	3
Bromochloromethane	90	HBSL	3
Bromodichloromethane	80	MCL[f]	2,3
Bromoform	80	MCL[f]	3
Carbon disulfide	700	HBSL	3
Carbon tetrachloride	5	MCL	3
Chlorobenzene	100	MCL	3
Chloroform	80	MCL[f]	2,3
Chloromethane	30	HBSL	3
Dibromochloromethane	80	MCL[f]	3
Dibromochloropropane	0.2	MCL	1,2,3
Dibromomethane	–	–	3
1,2-Dichlorobenzene	600	MCL	3
1,4-Dichlorobenzene	75	MCL	3
Dichlorodifluoromethane	1000	HBSL	3
1,1-Dichloroethane	–	–	3
1,2-Dichloroethane	5	MCL	2,3
1,1-Dichloroethene	7	MCL	2,3
cis-1,2-Dichloroethene	70	MCL	3

Table 1 (*continued*)

Contaminant	Benchmark value[a]	Benchmark type[a]	Mixtures categories[b]
Volatile organic compounds (µg/L)			
trans-1,2-Dichloroethene	100	MCL	3
1,2-Dichloropropane	5	MCL	3
1,1-Dichloropropene	–	–	3
Diethyl ether	1000	HBSL	3
Diisopropyl ether	–	–	3
Ethylbenzene	700	MCL	3
Hexachlorobutadiene	0.9	HBSL[e]	3
Iodomethane	–	–	3
Isopropylbenzene	700	HBSL	3
Methyl ethyl ketone	4000	HBSL	3
Methyl isobutyl ketone	–	–	3
Methyl tert-butyl ether	–	–	3
Methylene chloride	5	MCL	3
Perchloroethene	5	MCL	1,2,3
Styrene	100	MCL	3
1,1,1,2-Tetrachloroethane	70	HBSL	3
Tetrahydrofuran	–	–	3
Toluene	1000	MCL	3
1,2,3-Trichlorobenzene	–	–	3
1,2,4-Trichlorobenzene	70	MCL	3
1,1,1-Trichloroethane	200	MCL	3
1,1,2-Trichloroethane	5	MCL	3
Trichloroethene	5	MCL	1,2,3
Trichlorofluoromethane	2000	HBSL	3
1,2,3-Trichloropropane	40	HBSL	3
Trichlorotrifluoroethane	200,000	HBSL	3
1,2,4-Trimethylbenzene	–	–	3
o-Xylene	10,000	MCL[g]	3
m- and p- Xylenes	10,000	MCL[g]	3

[mg/L, milligrams per liter; MCL, Maximum Contaminant Level; µg/L, micrograms per liter; HBSL, Health-Based Screening Level; pCi/L, picocuries per liter; –, not available or not applicable; AMCL, Alternative Maximum Contaminant Level].

[a] Human-health benchmark values are listed in the units shown and were current as of March 2011. MCL values were obtained from the U.S. Environmental Protection Agency (2011) and HBSL values were obtained from the HBSL website (Toccalino et al., 2008).

[b] Each contaminant was evaluated in the mixtures categories shown. Category 1 = BQ > 1; Category 2 = BQ > 0.1; Category 3 = BQ > 0.1 plus any detected pesticide compound or VOC (Table 2 describes the mixtures categories). As an example, antimony was not evaluated in Category 1 because antimony was not detected at a concentration greater than its benchmark in any of the samples.

[c] Fluoride was not included in Categories 2 or 3 because fluoride at this concentration (0.4 mg/L) is less than the range of concentrations in drinking water recommended for the prevention of tooth decay (U.S. Centers for Disease Control and Prevention, 2001).

[d] MCL is a treatment technique. Lead action level = 15 µg/L (at tap).

[e] Low end of HBSL range corresponding to a 10^{-6} (1 in 1 million) cancer risk.

[f] The MCL is for total trihalomethanes.

[g] The MCL is for total xylenes (o-, m-, and p-xylene).

suggests evaluating mixtures when at least two mixture components have HQ ≥ 0.1 (Agency for Toxic Substances and Disease Registry, 2004).

Mixtures in the 383 public-well samples were examined in three categories: (1) mixtures of two or more contaminants with BQ > 1, (2) mixtures of two or more contaminants with BQ > 0.1, and (3) mixtures of two or more contaminants with BQ > 0.1 plus any detected pesticide compound or VOC (Table 2). The third category included any detected pesticide compound or VOC because some of these contaminants are frequently detected but do not have benchmarks. Each mixtures category builds upon the previous category such that the datasets are layered and become progressively more inclusive. Because large numbers of mixtures were identified in the second and third categories, only unique mixtures that were detected in at least 10% of samples in those categories were examined.

2.3. Occurrence and composition of mixtures

We determined the number, composition, and frequency of occurrence of unique mixtures in each mixtures category using the methods

Table 2
Description of three chemical mixtures categories examined in 383 public-well samples.

Mixtures category	Number of contaminants evaluated in category[a]	Total number of unique mixtures detected	Criteria for examination of unique mixtures	Number of unique mixtures meeting criteria
BQ>1. Mixtures of two or more contaminants, each with concentrations greater than individual human-health benchmarks[b,c].	17	21	All mixtures	21
BQ>0.1. Mixtures of two or more contaminants, each with concentrations greater than one-tenth of individual benchmarks[b,d,e]. Includes all mixtures in the BQ>1 category.	30	3,704	Each mixture detected in at least 10% of samples	24
BQ>0.1 plus any detected pesticide compound or VOC. All mixtures in the BQ>0.1 category, plus any detected pesticide compound or VOC[e,f].	90	24,633,995[g]	Each mixture detected in at least 10% of samples	125

BQ, Benchmark Quotient (ratio of concentration to human-health benchmark); VOC, volatile organic compound.

[a] Table 1 lists these contaminants.
[b] Only contaminants with benchmarks are considered.
[c] Radon activities were compared to the proposed Alternative Maximum Contaminant Level (AMCL) of 4000 picocuries per liter (pCi/L).
[d] Radon activities were compared to the proposed Maximum Contaminant Level of 300 pCi/L, which is about one-tenth of the proposed AMCL.
[e] Fluoride was not included in these categories (see Table 1 for an explanation).
[f] Pesticide compounds and VOCs were assessed regardless of the availability of human-health benchmarks or the concentrations relative to individual benchmarks.
[g] Most of these unique mixtures occurred in relatively few samples.

of Squillace et al. (2002) and Scott et al. (2007). Unique mixtures are specific combinations of any two, three, or more contaminants in a given sample, regardless of the presence of additional contaminants in the same sample (Squillace et al., 2002). A single sample can contain many unique mixtures. For example, a water sample in which three contaminants are detected (A, B, and C) contains four unique mixtures (AB, AC, BC, and ABC). Samples with the largest numbers of detected contaminants contribute most of the unique mixtures.

For each mixtures category, the number of contaminants detected (d) that meet the mixtures criteria (e.g., BQ>1, BQ>0.1, etc.) in each sample was counted. The number of mixtures composed of n contaminants is $d!/n!(d-n)!$, where n ranges from 2 to d. The total number of unique mixtures in a sample is the sum of the numbers of unique mixtures calculated for each n from 2 through d. A computer program (Scott et al., 2007) was used to identify the specific contaminants that compose each unique mixture in the sample. The detection frequency of each unique mixture was determined by dividing the number of samples in which all mixture components were detected by the total number of samples in which all mixture components were analyzed.

The occurrence of the most common unique mixtures was examined as a function of aquifer type and region of the U.S. as defined by the U.S. Census Bureau (U.S. Census Bureau, 2010). Of the 383 public wells in this study, 172 (45%) were in confined aquifers, 198 (52%) were in unconfined aquifers, and the remainder were in mixed or unknown aquifer types. By region, 38 public wells (10%) were in the Northeastern U.S., 85 (22%) were in the Midwest, 83 (22%) were in the South, and 177 (46%) were in the West.

2.4. Characterizing potential toxicity of mixtures

For the 30 contaminants in the BQ>0.1 category (Tables 1 and 2), we characterized the potential for mixtures toxicity in each public-well sample using a screening approach. First we computed BQ values for every detected contaminant in each sample, then summed the component BQ values (BQSiteSum):

$$\text{BQSiteSum} = \sum_{i=1}^{n} \frac{C_i}{\text{MCL}_i \text{ or HBSL}_i} = \sum \text{BQ}$$

where n is the number of contaminants, C_i is the concentration of contaminant i, and MCL_i or HBSL_i is the MCL or HBSL value for contaminant i; C and MCL or HBSL are expressed in the same units.

The BQSiteSum value can be used to screen for the potential for mixtures toxicity. The BQSiteSum is conceptually similar to the Hazard Index (HI) in that it is motivated by dose additivity; $\text{HI} = \sum \text{HQ}$.

HI>1 indicates concern for the potential health hazard associated with a chemical mixture (Agency for Toxic Substances and Disease Registry, 2004; U.S. Environmental Protection Agency, 2000), as does BQSiteSum>1. Conversely, BQSiteSum<1 suggests that the potential for mixtures toxicity is low.

Maximum BQ values (BQSiteMax) were compared to BQSiteSum values to determine how much of the potential toxicity results from a single contaminant. For example, a BQSiteMax to BQSiteSum ratio of 0.6 indicates that one contaminant (the one with BQSiteMax) accounts for 60% of the potential toxicity, and that other contaminants account for 40% of the potential toxicity. The ratio of the BQSiteMax to the BQSiteSum is similar to the Maximum Cumulative Ratio concept, which is the ratio of the cumulative toxicity to the maximum chemical toxicity (Price and Han, 2011). Additionally, the sums of the two, three, and four highest BQ values in each sample were compared to the BQSiteSum to determine how much of the BQSiteSum was accounted for by unique mixtures of two to four contaminants.

To determine which mixtures contributed the most to BQSiteSum>1, summed BQs were calculated for each unique mixture. For each sample, the summed BQ for mixture XY was $\text{BQ}_X + \text{BQ}_Y$. If X or Y was not detected in a given sample, then the summed BQ was zero. If X or Y was not analyzed in a given sample, then that sample was removed in the BQSiteSum analysis.

2.5. Limitations and assumptions

Characterizing chemical mixtures is limited by the availability of occurrence data and toxicity data. There are thousands of contaminants beyond the 91 included in this study that could be present in source water, including additional pesticides and industrial and pharmaceutical chemicals. Human-health benchmarks were not available for 13 of the 91 contaminants in this study (Table 1) because of insufficient toxicity data, so BQ values could not be computed for those contaminants. As more contaminants are measured and more benchmarks are established using new toxicity data, more mixtures of potential concern could be identified.

For exposures to chemical mixtures at low doses where toxicological interactions are not expected to occur, methods based on additivity concepts often are used as default procedures to estimate risk or hazard (Hertzberg et al., 2008). This default assumption of noninteraction is probably applicable to many mixtures found in drinking water (Ryker and Small, 2008). The default additivity approach for mixtures assessment also has the advantage of being conservative and consistent with the precautionary principle (Kortenkamp et al., 2007; Meek et al., 2011). In addition, several studies have demonstrated that dose
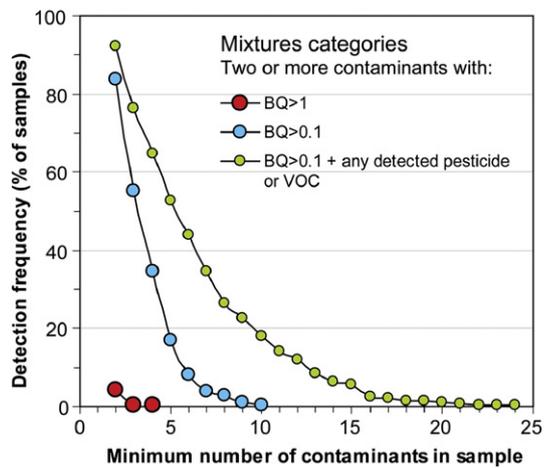
Fig. 1. Detection frequency of mixtures of two or more contaminants for 383 public-well samples.

(or concentration) addition often approximates the toxicities of mixtures composed of both similar and dissimilar compounds (Hertzberg et al., 2008; Kortenkamp et al., 2009, 2007). Although simple dose additivity may not strictly apply for complex mixtures of chemicals with different effects and toxic modes of action, the BQSiteSum screening approach is useful as a relative index. BQSiteSum values can indicate that one sample may be more or less toxic relative to another sample, but does not indicate actual toxicity nor probability of harm.

3. Results and discussion

3.1. Occurrence of mixtures

Contaminants in untreated source-water samples from public wells frequently co-occurred with other contaminants as mixtures, often with concentrations of individual contaminants approaching their human-health benchmarks. Sixteen (4%) of 383 source-water samples contained mixtures of two or more contaminants in which each contaminant had BQ>1. A total of 321 (84%) of the samples, however, contained two or more contaminants in which each contaminant had BQ>0.1. Mixtures of BQ>0.1 that also included detections of any pesticide compound or VOC (without regard to the availability of benchmarks or concentrations relative to individual benchmarks) were detected in 353 (92%) of the samples (Fig. 1). The remaining 30 samples did not meet the criteria for inclusion in any of the three mixtures categories.

DeSimone (2009), observed similar results in untreated water from domestic wells where mixtures of two or more contaminants with BQ>1 occurred in about 4% of samples, and mixtures of two or more contaminants with BQ>0.1 occurred in 73% of samples. This similarity likely results from the fact that groundwater samples used in this study and the domestic-well study both were collected from many of the same principal aquifers in the U.S., using USGS sampling protocols and laboratory methods for the same suite of contaminants (Toccalino et al., 2010).

The complexity of the mixtures and the number of unique mixtures increased as the mixtures categories were made more inclusive (Table 2). For example, mixtures of five or more contaminants were not detected in any of the samples in the BQ>1 category, but were detected in about 17% of samples in the BQ>0.1 category, and in about 53% of samples in the BQ>0.1 plus any detected pesticide compound or VOC category (Fig. 1).

Public wells yielding water containing chemical mixtures with BQ>1 and BQ>0.1 were distributed throughout the U.S. with no strong geographic pattern (data not shown). Mixtures with the largest number of contaminants (5 to 10) with BQ>0.1 also were distributed among a number of sampled areas throughout the U.S., but were most common in public wells located in parts of the western U.S. About three-quarters of the public wells with five or more contaminants with BQ>0.1 withdraw water from aquifers in the western U.S., mostly in California, Utah, Nevada, and Arizona (Fig. 2).

3.2. Composition of mixtures

Tables 3–5 summarize the composition of the most commonly occurring unique mixtures in each mixtures category. The most common contaminants in unique mixtures were those that were most frequently detected individually, and relatively few contaminants contributed to most detections.

3.2.1. BQ>1
The 21 unique mixtures for which each individual contaminant had BQ>1 were detected in less than 1% of the 383 source-water samples (most of these mixtures were detected in only one sample at these concentrations). These 21 mixtures were composed of combinations of 12 individual contaminants including solvents (perchloroethene (PCE) or trichloroethene (TCE)), trace elements (arsenic or strontium were most common), and nitrate—representing a combination of naturally occurring and man-made contaminants (Table 3).

3.2.2. BQ>0.1
The 24 most frequently detected unique mixtures for which each contaminant had BQ>0.1 (those detected in at least 10% of samples) were composed of combinations of eight individual inorganic contaminants including radon, nitrate, and six trace elements (arsenic, strontium, or uranium were most common, followed by boron, molybdenum, and
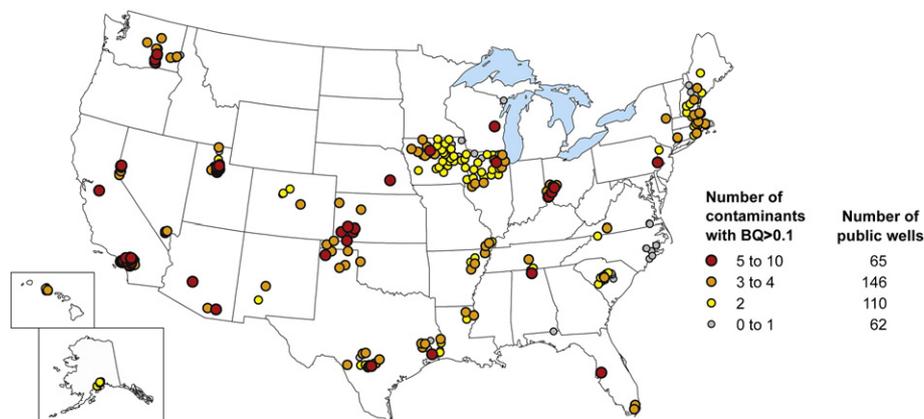

Fig. 2. Geographic distribution of the numbers of contaminants in mixtures with BQ>0.1 in 383 public-well samples.

Table 3
Composition and detection frequency of the 21 unique mixtures for which every component had BQ > 1 in 383 public-well samples.

Chemical mixture	Detection frequency (% of samples)
B + Sr	0.8
As + Mn	0.8
Nitrate + PCE	0.5
As + Mo	0.5
B + Rn	0.4
Nitrate + Sr	0.4
As + Sr	0.4
PCE + Dieldrin	0.3
Nitrate + PCE + TCE	0.3
Nitrate + PCE + TCE + DBCP	0.3
Nitrate + PCE + DBCP	0.3
As + Dieldrin	0.3
PCE + TCE	0.3
PCE + TCE + DBCP	0.3
PCE + DBCP	0.3
Nitrate + TCE	0.3
Nitrate + TCE + DBCP	0.3
Nitrate + DBCP	0.3
Mn + U	0.3
U + TCE	0.3
TCE + DBCP	0.3

B, boron; Sr, strontium; As, arsenic; Mn, manganese; PCE, perchloroethene; Mo, molybdenum; Rn, radon; TCE, trichloroethene; DBCP, dibromochloropropane; U, uranium.

Table 5
Composition and detection frequency of the 25 most frequently detected unique mixtures of contaminants with BQ > 0.1 plus any detected pesticide compound or VOC in 383 public-well samples.

Chemical mixture	Detection frequency (% of samples)
Nitrate + Chloroform	34.4
Chloroform + Rn	33.5
Nitrate + Rn	32.5
As + Rn	28.5
Nitrate + Deethylatrazine	27.1
B + Sr	26.5
Deethylatrazine + Atrazine	25.7
Nitrate + Atrazine	23.9
Nitrate + Chloroform + Rn	23.9
Nitrate + Deethylatrazine + Atrazine	23.4
Deethylatrazine + Chloroform	23.0
Sr + Rn	22.0
Nitrate + Deethylatrazine + Chloroform	21.9
Chloroform + Atrazine	20.9
Deethylatrazine + Chloroform + Atrazine	20.1
U + Rn	19.8
Deethylatrazine + Rn	19.7
Nitrate + Sr	19.5
Nitrate + As	19.4
Nitrate + Chloroform + Atrazine	19.2
Sr + Chloroform	19.0
Nitrate + Deethylatrazine + Chloroform + Atrazine	19.0
Nitrate + Deethylatrazine + Rn	18.6
Chloroform + PCE	18.4
Atrazine + Rn	17.9

Rn, radon; As, arsenic; B, boron; Sr, strontium; U, uranium; PCE, perchloroethene.

manganese). These 24 mixtures did not include any organic contaminants because organic contaminants typically were infrequently detected at concentrations greater than one-tenth of benchmarks (e.g., chloroform) or lacked benchmarks (e.g., deethylatrazine or methyl *tert*-butyl ether). Nitrate plus radon was the most common unique mixture in the BQ > 0.1 category (Table 4).

The most common mixtures of contaminants with BQ > 0.1 were composed of inorganic contaminants because individual inorganic contaminants were frequently detected at concentrations approaching human-health benchmarks in samples from public wells (Toccalino

Table 4
Composition and detection frequency of the 24 unique mixtures for which every component had BQ > 0.1 in at least 10% of 383 public-well samples.

Chemical mixture	Detection frequency (% of samples)
Nitrate + Rn	32.5
As + Rn	28.5
B + Sr	26.5
Sr + Rn	22.0
U + Rn	19.8
Nitrate + Sr	19.5
Nitrate + As	19.4
Nitrate + U	17.8
Nitrate + As + Rn	16.3
As + U	16.0
As + Sr	15.8
Nitrate + U + Rn	15.2
B + Rn	13.7
Mo + Rn	13.6
As + U + Rn	13.6
Nitrate + Sr + Rn	13.6
As + Sr + Rn	12.8
As + Mo	12.1
Nitrate + As + U	11.8
Sr + U	11.7
Nitrate + Mo	11.6
Mn + Rn	10.5
Nitrate + As + U + Rn	10.2
As + B	10.0

Rn, radon; As, arsenic; B, boron; Sr, strontium; U, uranium; Mo, molybdenum; Mn, manganese.

et al., 2010). The frequent detections of naturally occurring trace elements and radon with BQ > 0.1 reflect, in large part, their abundance in aquifer materials and the length of time that the water is in contact with aquifer materials. Nitrate occurs naturally, but also has several man-made sources, including fertilizers, livestock, and wastewater.

The occurrence patterns of the most common mixtures in the BQ > 0.1 category roughly followed the occurrence patterns of individual contaminants as described by Toccalino et al. (2010). For example, the highest individual concentrations of nitrate and of arsenic were observed in the western U.S. Similarly, the most common mixtures that contained nitrate or arsenic—such as nitrate plus radon, arsenic plus radon, and nitrate plus arsenic—were detected mostly in unconfined aquifers (62 to 73% of samples) and primarily in the West (65 to 78% of samples). Samples with radon activities with BQ > 0.1 were geographically distributed across the U.S., so the presence of radon in mixtures did not strongly affect geographic distribution patterns. By contrast, 75% of the samples containing the mixture of boron plus strontium were detected in confined aquifers, primarily in the Midwest (79% of samples), which is consistent with the occurrence of the highest individual concentrations of boron and of strontium.

3.2.3. BQ > 0.1 plus any detected pesticide compound or VOC

The 125 most frequently detected unique mixtures in the BQ > 0.1 plus any detected pesticide compound or VOC category (those detected in at least 10% of samples), were composed of combinations of 15 individual chemicals representing both man-made and naturally occurring contaminants. These 125 unique mixtures primarily were composed of combinations of herbicides or herbicide degradates such as atrazine and deethylatrazine, trace elements such as strontium, arsenic, and uranium, nitrate, DBPs such as chloroform, radon, and solvents such as PCE. Table 5 shows the 25 most common mixtures in this category; the mixture of nitrate plus chloroform was most frequently detected.

The frequent detection of some herbicides, DBPs, and solvents in mixtures was consistent with national-scale studies that examined the occurrence of pesticide and/or VOC mixtures in groundwater
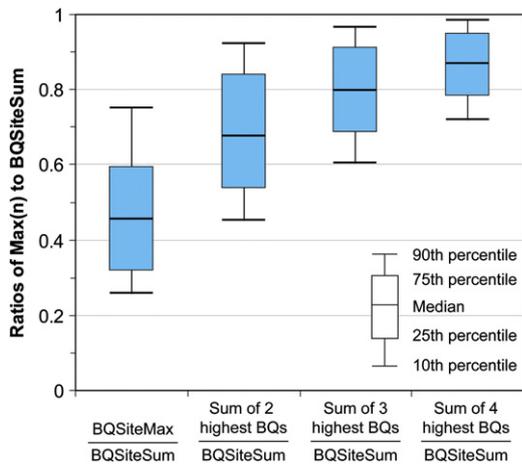
Fig. 3. Distribution of ratios of maximum to summed BQ values for 383 public-well samples in the BQ>0.1 mixtures category. Max(n) indicates the maximum BQ, or the sum of the two, three, or four highest BQ values in each sample.

from public and domestic wells (DeSimone, 2009; Gilliom et al., 2006; Squillace et al., 2002; Zogorski et al., 2006). Organic contaminants, however, were much more prevalent in mixtures in public-well samples than in domestic-well samples, likely because of the proximity of public wells to developed areas and high pumping rates (Toccalino et al., 2010).
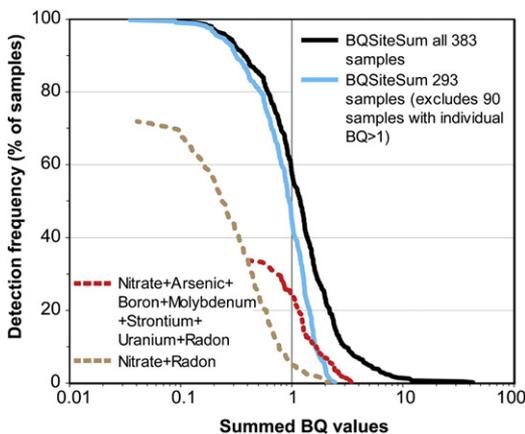

Fig. 4. Comparison between cumulative distributions of BQSiteSum values for all 383 public-well samples, 293 samples for which individual BQ>1 were excluded, and selected unique mixtures.

The most common mixtures that contained atrazine and deethylatrazine—such as nitrate plus deethylatrazine, deethylatrazine plus atrazine, and nitrate plus deethylatrazine plus atrazine—primarily were detected in unconfined aquifers (in 73 to 79% of the samples). These mixtures mainly were detected in the western U.S. (about 60% of the samples) and in the South (about 25% of the samples).

3.3. Potential toxicity of mixtures

In the BQ>0.1 category, the median ratio of BQSiteMax to BQSiteSum was 0.45, indicating that for one-half of the samples, a single contaminant (the one with BQSiteMax) accounted for 45% of the potential toxicity (Fig. 3). Stated another way, for one-half of the samples, 55% of the potential toxicity was accounted for by other contaminants. For mixtures of two to four contaminants, we found that for one-half of the samples, the sum of the two highest BQ values accounted for 68% or more of the BQSiteSum, the sum of the three highest BQ values accounted for 80% or more of the BQSiteSum, and the sum of the four highest BQ values accounted for 87% or more of the BQSiteSum (Fig. 3). In other words, a larger percentage of the BQSiteSum was accounted for as the number of mixture components increased, as might be expected.

All together, BQSiteSum values were >1 for 222 of the 383 (58%) samples (Fig. 4), which was not entirely surprising because 90 (23%) of the untreated water samples had one or more individual contaminants with concentrations greater than MCLs or HBSLs. When the 90 samples with one or more individual contaminants with BQ>1 were excluded from the dataset, however, BQSiteSum values remained >1 for 132 of the remaining 293 (45%) samples (Fig. 4). All except one of these 132 samples contained two to eight contaminants with BQ>0.1, suggesting that multiple contaminants contribute similarly to the BQSiteSum (roughly equitoxic mixtures). The highest BQSiteSum values (>3), however, were driven by individual contaminants.

In contrast to this study where chemical mixtures contributed considerably more to BQSiteSum values >1 than individual contaminants, Toccalino et al. (2004) reported that a single contaminant accounted for about 85% or more of the potential toxicity in one-half of the public-well samples analyzed for 97 pesticides and 85 VOCs in a state-scale USGS groundwater study. Similarly, Price and Han (2011) found that one or two pesticides tended to dominate the potential toxicity of mixtures in surface-water samples analyzed for 81 pesticide compounds by the USGS. The findings from these previous studies differed from the results of this study because of the diversity of contaminants analyzed. When the mixtures analysis included trace elements, radon, and nitrate, along with pesticides and VOCs, multiple inorganic contaminants tended to contribute similarly to the potential toxicity, highlighting the importance of evaluating mixtures across different chemical classes.
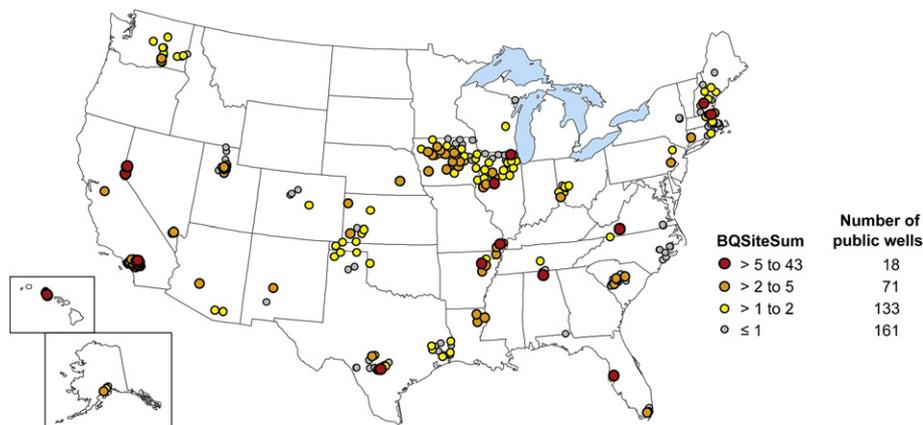

Fig. 5. Geographic distribution of BQSiteSum values for 383 public-well samples.

Table 6
Composition of the 25 unique chemical mixtures with the greatest percentage of samples with BQSiteSum values > 1.

Chemical mixture	Frequency that BQSiteSum > 1 (% of samples)
Nitrate + As + B + Mo + Sr + U + Rn	24.4
Nitrate + As + Ba + B + Mo + Sr + U + Rn	23.1
Nitrate + As + Ba + B + Mo + U + Rn	22.6
Nitrate + As + Mo + Sr + U + Rn	22.6
Nitrate + As + B + Mo + U + Rn	22.2
Nitrate + As + B + Sr + U + Rn	21.7
Nitrate + As + Ba + Mo + Sr + U + Rn	21.5
Nitrate + As + Ba + B + Sr + U + Rn	21.3
Nitrate + As + Ba + B + Mo + Sr + Rn	21.1
Nitrate + As + Sr + U + Rn	20.6
Nitrate + As + B + Mo + Sr + Rn	19.8
Nitrate + As + Ba + Sr + U + Rn	19.5
As + B + Sr + Rn	19.2
As + B + Sr + U + Rn	18.8
Nitrate + As + Ba + B + U + Rn	18.7
Nitrate + As + Ba + B + Pb + Mo + Sr + U + Rn	18.6
Nitrate + As + Ba + B + Mo + Sr + U	18.6
Nitrate + As + B + Pb + Mo + Sr + U + Rn	18.6
Nitrate + B + Mo + Sr + U + Rn	18.6
Nitrate + As + B + Mo + Sr + U	18.2
Nitrate + As + Ba + B + Mo + Sr + U + Rn	18.2
Nitrate + As + Ba + B + Pb + Sr + U + Rn	18.1
Nitrate + As + Ba + Mo + Sr + Rn	18.1
As + B + Mo + Sr + U + Rn	18.1
Nitrate + As + B + U + Rn	17.9

As, arsenic; B, boron; Mo, molybdenum; Sr, strontium; U, uranium; Rn, radon; Ba, barium; Pb, lead.

The 222 samples with BQSiteSum > 1 were widely distributed throughout the U.S. with no strong geographic pattern (Fig. 5). For example, the 18 public wells associated with samples with BQSiteSum > 5 were located in 12 different states. However, although the 89 wells associated with samples with BQSiteSum > 2 were widely distributed, 42 (47%) of these wells were located in the western U.S., and 25 (28%) were located in the Midwest (Fig. 5).

The composition of the 25 chemical mixtures with the greatest percentage of samples with summed BQ values > 1 is provided in Table 6; these 25 mixtures contained four to nine components. The 7-component mixture of nitrate, arsenic, boron, molybdenum, strontium, uranium, and radon had summed BQ values > 1 in nearly one-quarter of the samples. Further, this 7-component mixture was detected in 34% of samples, which means that about three-quarters of the time that this mixture was detected, its summed BQ was > 1 (Fig. 4 and Table 6). By contrast, the mixture of nitrate and radon (the most common unique mixture for which every component had BQ > 0.1, Table 4) was detected in 72% of samples, and the summed BQ for nitrate plus radon was > 1 in about 5% of samples (Fig. 4). Similar to mixtures with two or three constituents, the 7-component mixture primarily was detected in unconfined aquifers (70% of samples). However, nearly all samples (93%) in which the 7-component mixture was detected were located in the western U.S.

4. Conclusions

Chemical mixtures were frequently detected in untreated source-water samples from public wells, often with concentrations of individual contaminants approaching human-health benchmarks. Chemical mixtures that most frequently occurred and had the greatest potential toxicity primarily were composed of various combinations of nine or fewer inorganic contaminants including trace elements (arsenic, strontium, or uranium were most common), radon, and nitrate. Our results suggest that combined contaminant concentrations could be of potential concern in nearly half of the samples, even when no individual contaminant is detected at a concentration greater than a human-health benchmark. The implication is that source water that is treated to reduce the concentrations of individual contaminants in order to satisfy drinking-water regulations could still contain mixtures at concentrations of potential concern.

Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.scitotenv.2012.05.044.

References

Agency for Toxic Substances and Disease Registry. Guidance manual for the assessment of joint toxic action of chemical mixtures. Atlanta (GA): U.S. Department of Health and Human Services, Agency for Toxic Substances and Disease Registry; 2004. 107 pp.

Agency for Toxic Substances and Disease Registry. Interaction profile for: atrazine, deethylatrazine, diazinon, nitrate, and simazine. Atlanta (GA): U.S. Department of Health and Human Services, Agency for Toxic Substances and Disease Registry; 2006. 68 pp.

Carpenter DO, Arcaro K, Spink DC. Understanding the human health effects of chemical mixtures. Environ Health Perspect 2002;110(Suppl. 1):25–42.

DeSimone LA. Quality of water from domestic wells in principal aquifers of the United States, 1991–2004. Scientific Investigations Report 2008-5227. Reston (VA): U.S. Geological Survey; 2009. 139 pp.

Fay RM, Mumtaz MM. Development of a priority list of chemical mixtures occurring at 1188 hazardous waste sites, using the HazDat database. Food Chem Toxicol 1996;34: 1163–5.

Gilliom RJ, Alley WM, Gurtz ME. Design of the National Water-Quality Assessment Program: occurrence and distribution of water-quality conditions. Circular 1112. U.S. Geological Survey; 1995. 33 pp.

Gilliom RJ, Barbash JE, Crawford CG, Hamilton PA, Martin JD, Nakagaki N, et al. The quality of our Nation's waters—pesticides in the Nation's streams and ground water, 1992–2001. Circular 1291. Reston (VA): U.S. Geological Survey; 2006. 172 pp.

Hertzberg RC, Rice GE, Teuschler LK, Wright JM, Simmons JE. Health risk assessment of chemical mixtures in drinking water. In: Howd RA, Fan AM, editors. Risk assessment for chemicals in drinking water. Hoboken (NJ): John Wiley & Sons, Inc.; 2008. p. 123–70.

Johnson BL, De Rosa CT. Chemical mixtures released from hazardous waste sites: implications for health risk assessment. Toxicology 1995;105:145–56.

Kortenkamp A, Faust M, Scholze M, Backhaus T. Low-level exposure to multiple chemicals: reason for human health concerns? Environ Health Perspect 2007;115(Suppl. 1): 106–14.

Kortenkamp A, Backhaus T, Faust M. State of the art report on mixture toxicity final report. Report to the Commission of the European Union. Brussels, Belgium: European Commission, Directorate General for the Environment; 2009, 391 pp.

Lapham WW, Wilde FD, Koterba MT. Ground-water data-collection protocols and procedures for the National Water-Quality Assessment Program: selection, installation, and documentation of wells, and collection of related data. Open-File Report 95-398. U.S. Geological Survey; 1995. 71 pp.

Meek ME, Boobis AR, Crofton KM, Heinemeyer G, Van Raaij M, Vickers C. Risk assessment of combined exposure to multiple chemicals: a WHO/IPCS framework. Regul Toxicol Pharmacol 2011;60:S1-S14.

Price PS, Han X. Maximum Cumulative Ratio (MCR) as a tool for assessing the value of performing a cumulative risk assessment. Int J Environ Res Public Health 2011;8: 2212–25.

Ryker SJ, Small MJ. Combining occurrence and toxicity information to identify priorities for drinking-water mixture research. Risk Anal 2008;28:653–66.

Scott JC. Computerized stratified random site-selection approaches for design of a ground-water-quality sampling network. Water-Resources Investigations Report 90-4101. U.S. Geological Survey; 1990.109 pp.

Scott JC, Martin JD, Stackelberg PE. The quality of our Nation's waters—pesticides in the Nation's streams and ground water, 1992–2001; supplemental technical information for table 5-1. Circular 1291. U.S. Geological Survey; 2007. Updated November 23, 2007. Accessed August 13, 2010, at http://water.usgs.gov/nawqa/pnsp/pubs/circ1291/table_5_01.html.

Sexton K, Beck BD, Bingham E, Brain JD, DeMarini DM, Hertzberg RC, et al. Chemical mixtures from a public health perspective: the importance of research for informed decision making. Toxicology 1995;105:429–41.

Simmons JE. Chemical mixtures: challenge for toxicology and risk assessment. Toxicology 1995;105:111–9.

Squillace PJ, Scott JC, Moran MJ, Nolan BT, Kolpin DW. VOCs, pesticides, nitrate, and their mixtures in groundwater used for drinking water in the United States. Environ Sci Technol 2002;36:1923–30.

Suk WA, Olden K, Yang RSH. Chemical mixtures research: significance and future perspectives. Environ Health Perspect 2002;110(Suppl. 6):891–2.

Teuschler LK, Simmons JE. Approaching DBP toxicity as a mixtures problem. J Am Water Works Assoc 2003;95:131–8.

Toccalino PL. Development and application of health-based screening levels for use in water-quality assessments. Scientific Investigations Report 2007-5106. Reston (VA): U.S. Geological Survey; 2007. 12 pp.

Toccalino PL, Norman JE, Phillips RH, Kauffman LJ, Stackelberg PE, Nowell LH, et al. Application of health-based screening levels to ground-water quality data in a state-scale pilot effort. Scientific Investigations Report 2004-5174. Reston (VA): U.S. Geological Survey; 2004. 64 pp.

Toccalino PL, Norman JE, Hitt KJ. Quality of source water from public-supply wells in the United States, 1993–2007. Scientific Investigations Report 2010-5024. Reston (VA): U.S. Geological Survey; 2010. 206 pp.

Toccalino PL, Norman JE, Booth NL, Zogorski JS. Health-based screening levels: a tool for evaluating what water-quality data may mean to human health. U.S. Geological Survey, National Water-Quality Assessment Program; 2008. Updated April 10, 2008. Accessed March 8, 2011, at http://water.usgs.gov/nawqa/HBSL.

U.S. Census Bureau. Census Bureau map products: census regions and divisions of the United States; 2010. Updated November 8, 2011. Accessed November 29, 2011, at http://www.census.gov/geo/www/maps/CP_MapProducts.htm.

U.S. Centers for Disease Control and Prevention. Recommendations for using fluoride to prevent and control dental caries in the United States. Morb Mortal Wkly Rep 2001;50:1–42.

U.S. Environmental Protection Agency. Supplementary guidance for conducting health risk assessment of chemical mixtures. Washington, DC: U.S. Environmental Protection Agency, Risk Assessment Forum; 2000. EPA/630/R-00/002. 143 pp.

U.S. Environmental Protection Agency. Factoids: drinking water and ground water statistics for 2009. Washington, DC: U.S. Environmental Protection Agency, Office of Water; 2009. EPA/816/K-09/004. 15 pp.

U.S. Environmental Protection Agency. Edition of the drinking water standards and health advisories. Washington, DC: U.S. Environmental Protection Agency, Office of Water; 2011. EPA 820-R-11-002. 18 pp.

Yang RSH. In: Ware GW, editor. Strategy for studying health effects of pesticides/fertilizer mixtures in groundwater. Reviews of Environmental Contamination and Toxicology. New York: Springer-Verlag; 1992. p. 1-22.

Yang RSH. Introduction to the toxicology of chemical mixtures. In: Yang RSH, editor. Toxicology of chemical mixtures. San Diego (CA): Academic Press; 1994. p. 1-10.

Zogorski JS, Carter JM, Ivahnenko T, Lapham WW, Moran MJ, Rowe BL, et al. The quality of our Nation's waters—volatile organic compounds in the Nation's ground water and drinking-water supply wells. Circular 1292. Reston (VA): U.S. Geological Survey; 2006. 101 pp.