BY JENNIFER CALLES,
RANDY GOTTLER,
MATTHEW EVANS,
AND JACK SYAGE

Increased terrorist activity is raising concerns about the safety of water supplies. Early warning systems that are accurate and fast are needed to deploy effective strategies for rapid response. A new analyzer based on photoionization (PI) and quadrupole ion trap, time-of-flight (QitTof) mass spectrometry (MS) offers high-speed, high-throughput screening and molecular identification of chemical weapons threats and other hazardous compounds. A growing number of municipalities and government facilities are adopting this new screening instrumentation to help safeguard public drinking water. This article reviews the strategy being taken by cities such as Phoenix, Ariz., to develop an early warning capability based on the PI/QitTof MS screening technology. The screening technology can detect a wide range of compounds at subacute concentrations with no sample preparation and a sampling cycle time of about 45 s.

Early warning surveillance of drinking water

by photoionization/mass spectrometry

Water utilities across the United States have developed effective treatment methods and analytical capabilities to ensure the quality of drinking water. Yet many sources of water are vulnerable to tampering and abuse because of their accessibility and diverse size. The potential for contamination has always existed from inadvertent, intentional, and natural causes, and water authorities currently handle these potential scenarios with varying degrees of preparedness. Recent papers by Gullick et al (2003 and 2004) have reviewed progress toward developing early warning systems for source water supplies. Another useful reference is a collection of monographs edited by Mays (2004a). The potential for terrorist contamination using illicit compounds, such as chemical weapons (CWs), represents a threat scenario for which water utilities are not adequately prepared. Since 9/11 there has been considerable activity focused on vulnerability assessments (ASDWA, 2002; USEPA, 2002) and preparedness planning. However, there is still no widely accepted early warning system (EWS) for CWs and other threat compounds that meets the standards required for public safety.

REQUIREMENTS FOR EWSs

Because of the lethal nature of CWs, rapid detection is imperative. Standard methods of analysis generally take considerable time and effort as a result of laborious sample preparation, development of standard calibration curves, and long run times. They are also not amenable to rapidly analyzing large numbers

The chemical weapons analyzer is based on photoionization and quadrupole ion trap, time-of-flight mass spectrometry technology. An integrated autosampler injects samples from a vial tray or microtiter plate. This instrument is in a hood, although this is not necessary for most applications.

of samples. Online monitors that can give more rapid indications of changing conditions generally measure nonspecific properties such as pH, conductivity, or total organic compounds.

An effective EWS must satisfy several requirements. The International Life Sciences Institute has published guidelines for EWS monitoring equipment (1999), and these are summarized in the sidebar on page 66. The most basic functionalities required of an effective rapid-screening device are described in the following sections:

High-speed, high-throughput analysis. High-speed analysis does not necessarily equate to high-throughput capability, though it is a prerequisite. An effective screening system must provide short response time and repeatable sampling. High-throughput capability does equate with the requirement for high-speed analysis. For example, a 1-h response time does not necessarily require a high-speed instrument; however, screening for 80 samples with a 1-h response time does require a high-speed instrument.

Low false-positive/false-negative rates. Because an early warning system is a prelude to some type of rapid response, it is essential that the screening method reliably detect suspect compounds at concentrations corresponding to a predetermined acute level (high detection probability = minimal false-negatives [FN]) and not exceed some acceptable level of false-positive (FP) events. If a positive result occurs, there needs to be a second level of analysis to confirm the event. Development of new, powerful detection technologies is often driven by military requirements because of the large costs involved. However, military personnel are trained to respond to various threats, thus the acceptable FP rates are significantly higher than for the civilian sector. Civilian security imposes added requirements on screening systems.

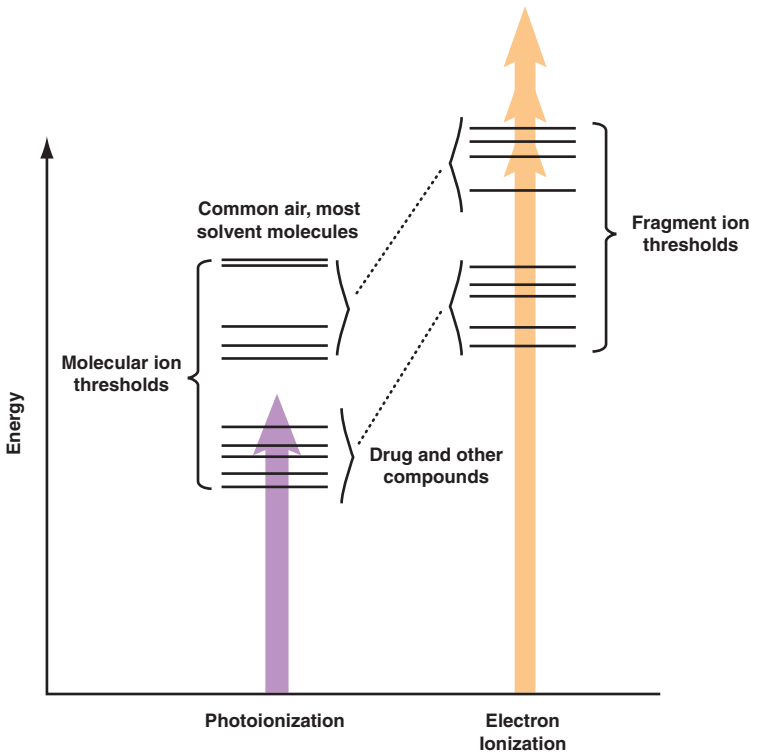
Minimal sample preparation. Early warning monitoring means collecting many samples from many locations at regular intervals. If sample preparation is needed or reagents need to be used, the overall throughput for screening will be negatively affected.

Automation/ease of operation. The large number of samples that must be analyzed requires a system that is easy to operate by nontechnical personnel. One of the commonly expressed concerns of water quality labs is whether the acquisition of new instrumentation will require added personnel. These resources may be difficult to fulfill and add a high recurring operating cost.

The potential for terrorist contamination using illicit compounds, such as chemical weapons, represents a threat scenario for which water utilities are currently unprepared.

This article expands on information published in the December 2004 issue of JOURNAL AWWA (Wu et al, 2004) and describes a new and highly effective screening technology for monitoring CWs, related compounds (e.g., precursors and decomposition products), and other suspect compounds (e.g., pesticides, drugs) that meets essentially all of the requirements shown in the sidebar on page 66. This is made possible by a combination of tech-

FIGURE 1 Schematic showing the principle of photoionization



Photoionization provides threshold ionization of target compounds in order to minimize fragmentation and minimize ionization of smaller molecules such as the constituents of air and common solvents. Electron ionization, on the other hand, provides excessive energy, which leads to significant fragmentation

nologies that enables the rapid and high-throughput screening of samples without the need for laborious sample preparation and detailed analytical methods, as well as the extensive development of a CWs database and spectral library. The key advance is the ability to conduct accurate measurements of trace constituents in complex mixtures without the use of a chromatographic front-end separation stage. Generally, quantitative analysis is conducted by gas chromatography or liquid chromatography mass spectrometry (GC/MS and LC/MS) by specific and detailed methods that usually involve sample preparation and concentration to achieve the ultimate levels of accuracy and detection limits. For early warning systems, the critical measure is not a precise value of absolute concentration but rather a fast and definitive detection of a suspect compound at less than acute concentrations and "flagging" that sample for confirmatory analysis that would be used to alert the public expeditiously and mitigate the contamination.

The screening method described here is based on a new MS and ionization technology that has been integrated into an automated instrument capable of screening water samples on a 45-s cycle time. This screening technology is being adopted by major municipal water utilities and government facilities. This article describes the strategy and mode of operation of these facilities and highlights the progressive steps being taken by the city of Phoenix, Ariz., to implement early warning capabilities for new threat scenarios. The photograph on page 63 shows a picture of the instrument,[1] which has a sufficiently small footprint to be placed in a specially designed laboratory hood in the City of Phoenix Water Services Department. Other municipalities are using this instrument without placement in a hood. The use of the hood is for a specific threat scenario described later in this article. The following text describes the technical attributes of the analyzer.

COMPETING INSTRUMENTATION FOR CWs DETECTION

The development of CW detection technology has been driven primarily by Department of Defense (DOD) requirements for battlefield and base protection. The level of accuracy is somewhat a function of size, weight, and power requirements. Fixed-location applications can use more sophisticated technology, whereas human-portability imposes compromises in performance by comparison. The following summarizes CWs detection technology (CBD, 2004):

Mass spectrometry. It is generally accepted that MS offers the highest levels of accuracy compared with other technologies for chemical detection. Its traditional disadvantages have been its high cost and complexity. Over the past few years, however, the economics have greatly improved, and certain models are leading the way toward routine, automated operation.

Ion mobility spectrometry (IMS). IMS is similar in concept to MS except that the ions are dispersed by gas-phase viscosity and not by molecular weight. The main advantage of IMS is that it does not use a vacuum system, which greatly reduces the size, cost, and complexity relative to MS. However, the tradeoff is that the measurement accuracy is considerably less than MS. This is especially true for complex samples or when screening for a large number of target compounds simultaneously.

GC. This method provides high-resolution separation of compounds that are then detected by a variety of means. The highest accuracy is obtained using an MS detector. For other nonspecific detectors, identification

is dependent on accurate and reproducible retention times, which can introduce uncertainty in making definitive identifications.

Chemical sensors. This approach is attractive for applications that require a hand-held device and generally relies on an array of detectors, each of which responds differently to different compounds. The principle is for each target compound to give a different pattern of responses on the detector array. The detectors can respond to conductivity, wave propagation, fluorescence, or other indications. Chemical sensors are not very specific or sensitive for complex mixtures, and the devices can be prone to high FP rates.

Optical spectroscopy. Infrared and Raman spectroscopy can be used to make positive identifications; however, they are not well-suited to complex mixtures or detecting compounds at very low concentrations.

New technologies. The quest for a broad-based CWs agent detector that is fast, sensitive, specific, small, and inexpensive continues. Promising technologies include molecularly imprinted polymer (MIP) sensors. It will take considerable time and work to develop MIPs for a wide range of compounds; however, results on selected test compounds showed mid parts-per-billion detection limits with a response time of 10–15 min (Jenkins et al, 2004).

MS is still the leading technology for CWs agent detection in terms of speed and accuracy. The other methods are used where field- or human-portability is needed.

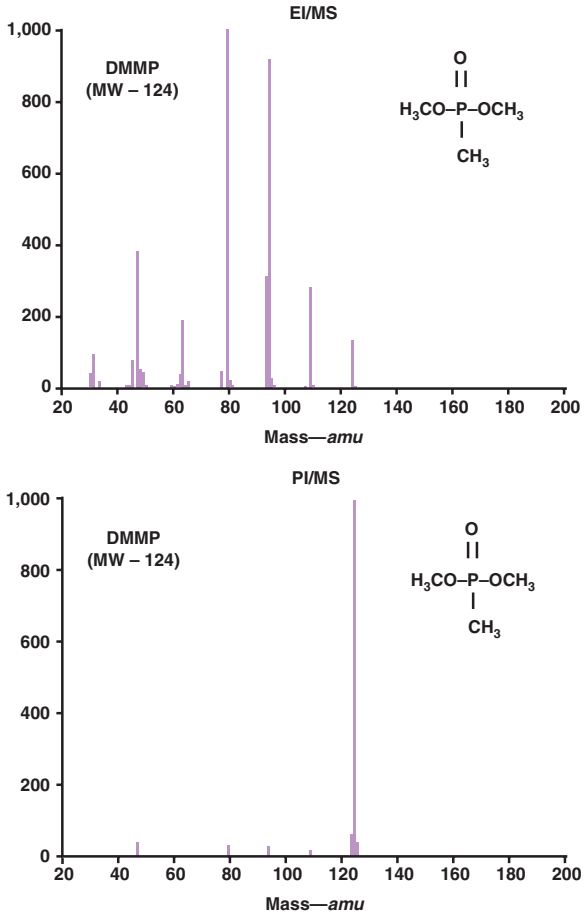
PHOTOIONIZATION/MASS SPECTROMETRY

The merits of photoionization/mass spectrometry (PI/MS) have been reviewed in previous articles (Syage & Evans, 2001; Syage et al, 2000). The main characteristics that differentiate PI from other ionizers and make it uniquely suitable for rapid and accurate analyses of mixtures are:

- ionization of a wide range of compounds,
- predominant parent ion signal with minimal fragmentation,
- minimal susceptibility to ion suppression, and
- minimal ionization of common matrixes, such as air and most solvents.

The most widely used ionizers on today's MS systems are not suitable for analyzing mixtures, which largely explains the use of online chromatographic separation of samples before entering the ionizer and MS. These ionizers include electron ionization (EI), electrospray ionization (ESI), and chemical ionization (CI) including atmospheric pressure CI (APCI). EI and CI are low-pressure methods used primarily with GC/MS. ESI and APCI are atmospheric-pressure methods used primarily with LC/MS. The reason these ionizers are not suitable for direct analysis of mixtures has to do with their susceptibility to either extensive ion fragmentation or ion suppression. PI, on the other hand, greatly minimizes these deficiencies, yet ionizes a broad range of compounds including nearly all major CWs compounds and other hazardous threats.

FIGURE 2 Comparison of PI/MS and EI/MS spectra for the CW surrogate molecule DMMP



CW—chemical weapon, DMMP—dimethyl methylphosphonate, EI—electron ionization, MS—mass spectrometry, MW—molecular weight, PI—photoionization

EI is a process that leads to significant fragmentation, which is desirable for analysis of single compounds because it provides fragment ion signatures or "fingerprints" with which to identify and confirm compounds. It is widely used for GC/MS when the sample constituents are separated chromatographically. However, if multiple compounds co-elute, the superposition of highly fragmented mass spectra can be very difficult to decipher. This problem is further aggravated if the sample is not separated by GC or by other means. Moreover, the signal for a low abundant target compound can easily be swamped by the strong signal of common compounds present in high abundance.

ESI and APCI (and also CI) are based on the production of charges (e.g., protons) that attach to molecules

Characteristics of Early Warning Systems*

- Rapid response time
- Fully automated
- Screens for a range of contaminants
- Specific for the contaminants of concern
- Sufficient sensitivity
- Low occurrence of false positives and false negatives
- High rate of sampling
- Reliable and rugged
- Requires minimal skill and training
- Affordable cost

*ILSI, 1999; as summarized by Clark et al, 2004

with an affinity for that charge. If more than one compound is present, then those with the highest charge affinity will receive a disproportionate share of the charge. This can lead to ion suppression of compounds with low charge affinity. The mechanism of PI, however, is based on the absorption of a photon by a molecule. Because a molecule cannot "steal" a photon from another molecule, the only condition that is important for ionization is whether the photon energy exceeds the ionization energy (IE) of the molecule. Unlike ESI and APCI, PI is not as susceptible to ion suppression. Atmospheric pressure photoionization (APPI) has recently been developed for LC/MS and is the fastest growing new ionization technology today (Hanold et al, 2004; Robb et al, 2000).

Although APPI minimizes ion suppression and expands on the range of compounds that can be ionized relative to ESI and APCI, the ions are formed at atmospheric pressure and are susceptible (as is ESI and APCI) to subsequent ion-molecule chemistry that can deplete the target ion of interest. For this reason a low-pressure PI (LPPI) source has been developed for the CWs high-speed analyzer[1] to minimize the potential for undesirable ion–molecule reactions.

Figure 1 on page 64 illustrates the advantages of PI. The CW analyzer[1] uses a light source that emits photons with an energy of 10 eV. This energy exceeds the IE of almost all compounds of environmental significance including CWs and related compounds (e.g., precursors and decomposition products), aromatics, drugs, and many other classes of compounds. Smaller molecules tend to have higher IEs and are not as efficiently ionized. This is actually an important advantage for trace detection because all major constituents of air (e.g., nitrogen gas, free oxygen, water, carbon dioxide, carbon monoxide, argon) and most common solvents (e.g., methanol, acetonitrile, halogenated solvents) have IEs higher than the photon energy and are not ionized. This makes possible the proverbial "detecting the needle in the haystack," in this case by making the haystack invisible.

Figure 2 compares the PI/MS and EI/MS spectra for the CW surrogate dimethyl methylphosphonate (DMMP). PI leads to a dominant parent ion spectrum with minimal fragmentation, whereas EI leads to a highly fragmented ion spectrum.

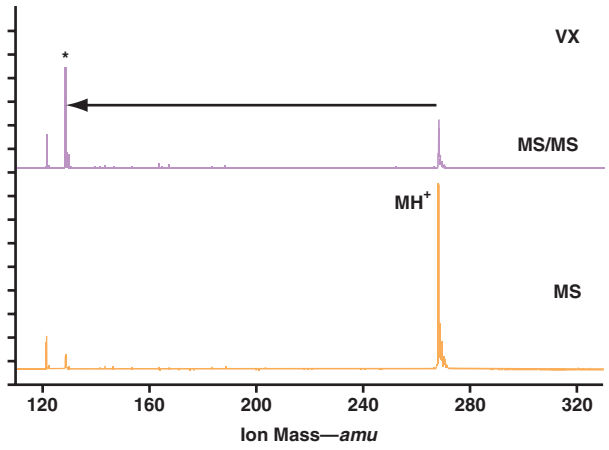
QitTof MS ANALYZER

Rapid screening also needs an analyzer that is fast and accurate. One company has developed the quadrupole ion trap, time-of-flight (QitTof) MS analyzer, and technical details are given by Syage (2004). QitTof MS is a powerful analyzer, yet surprisingly simple in electronic and mechanical construction. The main characteristics that differentiate it from other MS systems include:

- the Tof MS analyzer records all ions simultaneously.
- full mass spectral acquisitions are recorded at high speed (60 Hz).
- The Qit stage enables sophisticated multiple mass spectral analysis (e.g., MS/MS), whereby parent ions can be selectively fragmented to deduce the chemical structure and make a definitive identification.

One of the key benefits of the QitTof MS analyzer is the MS/MS capability, which may be used to characterize the identity of a compound. For screening of targeted compounds, only one level of dissociation is needed for compound characterization. An MS analysis of the primary ions constitutes the detection phase of the screen.

FIGURE 3 PI/MS spectrum of VX nerve agent and the resulting MS/MS spectrum from selective fragmentation of the VX parent ion



MS—mass spectrometry, PI—photoionization, MH^+—protonated molecule M, M^+—molecular ion

The parent ion is MH^+, which results when the initially formed molecular photoion M^+ reacts with the surrounding solvent (typically either nascent water or an organic solvent such as methanol).

TABLE 1 Comparison of operational characteristics of PI/MS versus other analytical methods*

Characteristic	PI/MS	GC/MS or LC/MS	Benefits of PI/MS
Speed	Yes	No	Can analyze more than 1,000 samples/day by direct injection
Accuracy	Yes	Yes	Can analyze compounds that are missed by LC/MS using APCI and ESI
Minimal sample preparation	Yes	Sometimes	No sample preparation is needed (i.e., no need for additives or derivation)
Minimal consumables	Yes	No	Minimal solvent waste and no consumable gases used
Simple operation	Yes	Sometimes	Intuitive software and automated data analysis and archiving

*APCI—atmospheric pressure chemical ionization, ESI—electrospray ionization, GC/MS—gas chromatography/mass spectrometry, LC/MS—liquid chromatography/mass spectrometry, PI/MS—photoionization/mass spectrometry

The detected ions are compared with a library of MS signatures of suspect compounds (e.g., CWs agents). If the signal level exceeds a detection threshold, then the MS/MS capability is invoked to determine if the parent ion dissociates to the known fragment ions of the suspect compound. This is the characterization phase of screening.

There are two programmable modes for the MS/MS characterization. For ultimate speed, the MS/MS can be set to automatically dissociate a suspect ion if the signal intensity exceeds a preset threshold value. A disadvantage of this mode is that the integrated MS ion signal may not exceed the threshold until near the end of the sample injection, and thus the MS/MS signal may be too weak to give a meaningful characterization. Therefore, this MS/MS "on-the-fly" is not the optimum method for best sensitivity. When >1-min response time is tolerable for characterization (detection remains at 45 s), then it is preferable to conduct an MS detection on a single sample injection and if a suspect ion is detected, to repeat a sample injection in MS/MS mode for characterization.

AUTOMATED SAMPLING AND ANALYSIS

The CW analyzer encompassing the PI/QitTof MS technology has an integrated autosampler that can inject sample for analysis on a 45-s cycle time. There are several key benefits to this configuration versus more conventional analytical methods such as GC/MS and LC/MS. Table 1 summarizes some of these key benefits. It should be evident that the CW analyzer is much more suited to the requirements of an EWS than other analytical methods, as shown in the sidebar on page 66.

Though MS instrumentation is not inexpensive, this particular technology has a low operating cost for the following reasons: (1) a relatively nontechnical person can operate it, (2) sample preparation is minimal, (3) the analysis times are short, reducing the labor burden on a per-sample basis, and (4) there are minimal consumables (no gases or solvent flows) that may otherwise add recurring costs.

The CWs analyzer is capable of screening and confirming the presence of CWs and other suspect compounds. The instrument is first calibrated with a standard, uncontaminated water sample to measure the natural levels. Generally, eight measurements are made (about 6 min). The next step is to analyze a collection of samples by measuring the MS spectrum and comparing it with the CW library (and/or other compound library) for the initial screen. As described previously, if a target compound registers a positive signal, then the MS/MS routine is implemented to characterize the positive signal to determine whether it is a real event. An example of MS/MS characterization is given in Figure 3 for the nerve agent compound VX. The primary parent ion signal is at a mass-to-charge ratio (m/z) of 268, and the characteristic fragment ion that is used to confirm the detected compound is at m/z 128.

The instrument has been tested with a multitude of CWs agents and related compounds. For example, the Defense Threat Reduction Agency (DTRA) partially funded the development of the PI/QitTof MS technology for compliance monitoring of the Chemical Weapons Convention Treaty. This was a challenging requirement because inspection teams have limited time to conduct on-site analyses and the only certified technique for confirmation is GC/MS by a method that takes about 60 min per analysis. The PI/QitTof MS was developed to provide fast screens to reduce the sample load on the GC/MS to only those that tested "hot" in the screening stage. The PI/QitTof MS proved capable of providing the required sensitivity in complex matrixes. An example is given in Figure 4 for detection of VX in dirty soil extracts.

A list of compounds, tabulated in Table 2, was provided to the instrument's manufacturer by DTRA to test the screening capabilities for targeted compounds of interest. The PI/QitTof MS instrument successfully detected and registered distinct signatures for about 95% of the compounds. The misses included phosgene and chloropicrin. Further study showed that the instrument is insensitive to the detection of Lewisite. These negatives are presumed the result of high IE values for these compounds. However, Lewisite is an arsenic (As) compound, and would be detectable by standard methods for detecting As in water.

The instrument is preloaded with a CW database that includes the agent compounds VX, Tabun (GA), Sarin (GB), Soman (GD), GF nerve agent, sulfur mustard (HD),

TABLE 2 CWC treaty compounds detected by PI/QitTof MS analyzer

Schedule–1 Compounds	Schedule–2 Compounds	Schedule–3 Compounds
Toxic	Toxic	Precursors
VX	BZ	Phosphorus oxychloride
GA (Tabun)	Precursors	Dimethyl phosphite
GB (Sarin)	Diisopropyl methylphosphonate	Trimethyl phosphite
GD (Soman)	Diethyl methylphosphonate	Diethyl phosphite
GF	Dimethyl methylphosphonate	Triethyl phosphite
HD (sulfur mustard)	Diethyl ethylphosphonate	Triethanolamine
HN—1 (nitrogen mustard)	Diethyl methylphosphonothioate	N-ethyldiethanolamine
HN—3	Isopropyl methylphosphonic acid	N-methyldiethanolamine
CR	Cyclohexyl methylphosphonic acid	Decomposition products
CS	Pinacolyl methylphosphonic acid	Methylphosphonic acid
Precursors (binary)	Methyl phosphonyl dichloride	Ethylmethylphosphonic acid
QL	3-quinuclidinol	EMPTA
DF	Benzilic acid	2-Chlorodiethylsulfide
	Pinacolyl alcohol	Other relevant compounds
	Thiodiglycol	VX disulfide
	N,N-diethylethanolamine	YL
	1,4-Dithiane	
	Thiodiglycol sulfoxide	
	Methylamine	
	Isopropylamine	
	Thioxane	

Not detected: phosgene, chloropicrin, Lewisite
CWC—Chemical Weapons Convention, PI/QitTof MS—photoionization and quadrupole ion trap, time-of-flight mass spectrometry

and nitrogen mustards (HN-1, HN-3). Many other compounds have been shown to be detectable and can be added to the database, such as the riot agents dibenzoxazepine (CR) and alononitrile (CS), the hallucinogen 3-quinuclidinyl benzilate (BZ), CWs starting materials such as methylphosphonic difluoride (DF) and *o*-ethyl-diisopropylaminoethyl methylphosphonite (QL), and CWs decomposition products such as VX-disulfide. The screening results are recorded in a spreadsheet-compatible file for quick review. A visual indicator of the results of each sample is also available as shown in Figure 5. If desired, the instrument software allows users to adjust a wide range of instrument parameters.

STRATEGY FOR EWSs

A desirable strategy for an EWS is online, continuous monitoring at various sites in the water supply and distribution network with remote data communication. However, because of the breadth of possible threats (e.g., chemical, biological, particulate), a battery of different instruments is generally required, which can place a financial burden on a utility. Another approach is to have a central laboratory that houses the instrumentation and to collect samples sufficiently often (e.g., daily) to maintain an effective real-time capability. This approach enables collection in many locations. The most serious threat scenario for deliberate chemical contamination is after the treatment facility or within the distribution system where high concentrations with minimal degradation can reach end users.

At the City of Phoenix Water Services Department, the grab-sample approach was adopted because of the limited number of online instruments available to detect specific categories or classes of samples that had been identified as having the potential for use in an act of terrorism. There was also concern with the limited information available on operating and maintaining these instruments in a continuous mode under field conditions, as well as the costs of those instruments. Using grab sampling also made it possible to take advantage of current laboratory instruments and facilities.

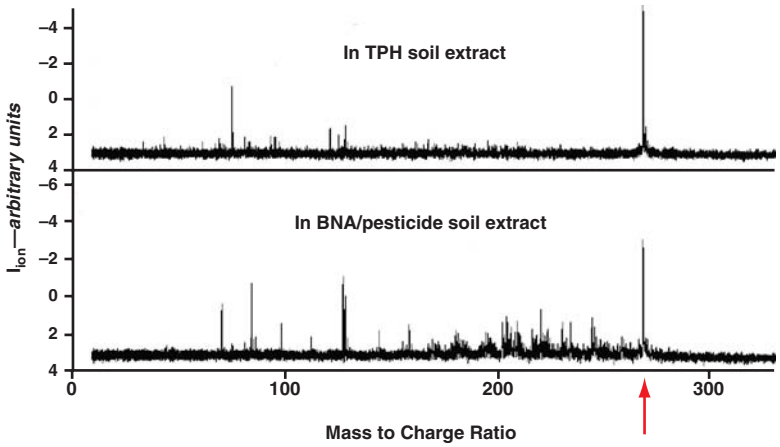
Potential agents of intentional contamination. Through an extensive literature search and contact with several experts in the field of chemical and biological terrorism, a number of potential agents were identified that might effectively be used to intentionally contaminate drinking water and/or drinking water systems. These agents can be summarized by grouping them into the following categories: chemical warfare agents, toxins, microbiologicals, and toxic industrial chemicals. It is important to remember that although the list is extensive, the agents appearing on it have varying degrees of application to intentional acts of water con-

tamination because of routine disinfection practices, more effective modes of agent dispersal, and chemical attributes that limit mixing with water or impart strong tastes and odors to the water. In addition, it is important to understand that the list of agents is dynamic. As new information is received, items may be added or dropped and changes made as necessary.

Sampling program. Before this program was implemented, the established practice was to sample and monitor points of entry and distribution system sampling points as required under the Safe Drinking Water Act (USEPA, 1976). Monitoring frequencies ranged from monthly to every fifth year. Events that caused concern over the possibility of drinking water contamination (i.e., break-ins at storage or treatment facilities) and events that were known to have compromised drinking water quality prompted sampling and monitoring on an as-needed basis.

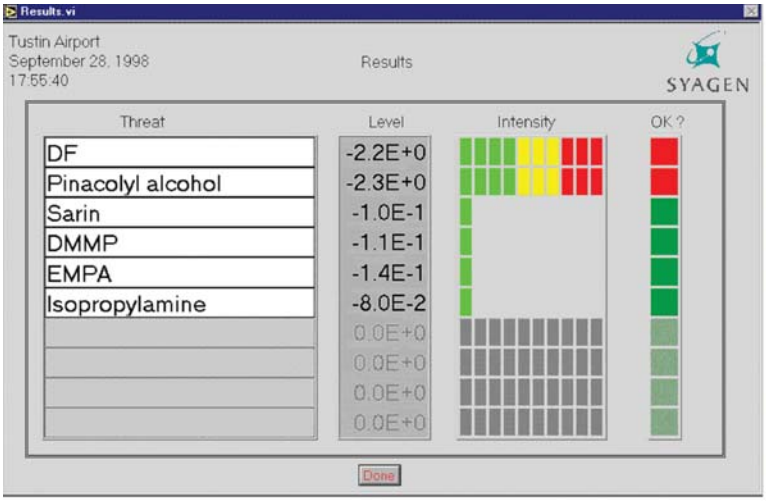
Of the agents identified that might be used to contaminate drinking water, 12 were already being monitored on a routine basis and consequently were included in previously established sampling programs. Sampling and analytical practices and capabilities were expanded to include more frequent monitoring as well as monitoring for some of the remaining identified contaminants. These practices and capabilities were added through minor changes to sampling schedules, minor changes to analytical technologies already in place, and the acquisition of several new analytical technologies including the PI/QitTof MS CW analyzer.

FIGURE 4 PI/MS spectrum of VX at 12 mg/L (0.83 ppm molar ratio) spiked in TPH and BNA soil extracts



BNA—base/neutral/acid extractable compounds, MS—mass spectrometry, PI—photoionization, TPH—total petroleum hydrocarbons

FIGURE 5 Software window showing visual indications for the presence of target compounds

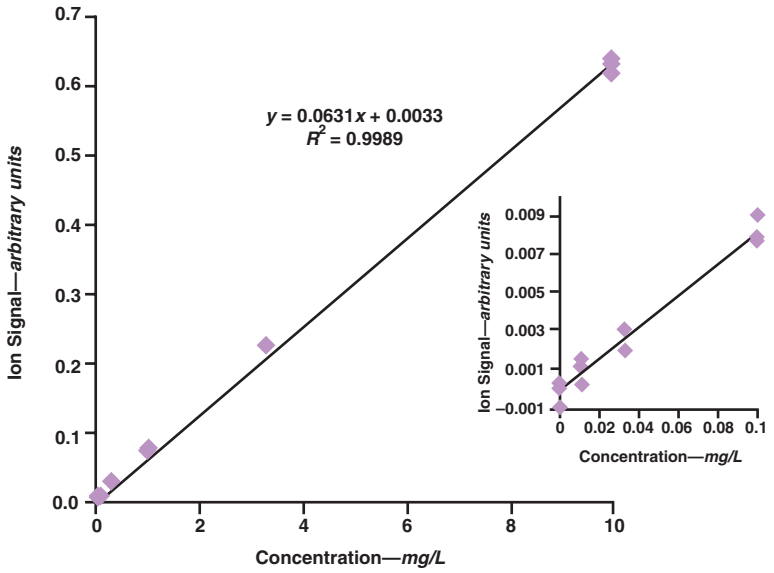


DF—methylphosphonic difluoride, DMMP—dimethyl methylphosphonate, EMPA—ethylmethylphosphonic acid

Several factors were considered in the development of the monitoring plan to detect or identify these fugitive agents. Among these were criteria for establishing representative sampling points and staff availability. In this case, initial efforts to expand the routine monitoring program were most easily accommodated by choosing sampling points and frequencies that were incorporated into the monitoring routines already in use. However, it was equally important to give consideration to having samples collected on a schedule that was somewhat unpredictable. The use of established sampling points also provided immediate baseline information for several of the agents under consideration.

Sampling point selection was also based on potential vulnerabilities to contamination and the consequences of contamination. Points selected on this basis include source waters, treatment facilities, storage, and maximum retention sites in the distribution system. Consideration was also given to pressure zones, population served, and assessed vulnerability. As a consequence of this effort, 13 maximum retention sites were identified and 41 sites were included in the sampling program. Because of the rate of population growth in the service area, the sampling sites are reviewed and revised on a regular basis.

FIGURE 6 Serial dilutions of DMMP in methanol



DMMP—dimethyl methylphosphonate

Triplicate measurements over a three-decade range; the lowest level of 0.01 mg/L corresponds to 10 ppb (mass ratio) and 2.5 ppb (molar ratio); similar results were obtained for DMMP in water.

Sampling frequencies were determined based on a number of criteria. Because several of the monitored compounds (other than the CWs agents) either occur naturally or are frequently used in industrial settings, it was important that baseline monitoring occur to avoid unnecessary reaction to the detection of any given compound. The data accumulated would form the basis for identifying anomalies in the occurrence or levels of contaminants in the distribution and storage systems. Consequently, initial sampling frequencies were set to take place on a monthly basis. However, should national alert levels be raised under conditions defined by the Department of Homeland Security (DHS, 2002), sampling would be conducted on a more frequent basis. For example, under condition yellow or orange, sampling would be conducted five days a week, with the latter condition leading to more collected samples. A condition red would trigger sampling seven days a week.

Analytical program. Once the laboratory takes custody of the samples, they are distributed to the various analytical groups and analyzed using inductively coupled plasma MS, GC and GC/MS for volatile and synthetic organics, the PI/QitTof MS analyzer for CW agents, automated analysis for cyanide, and standard microbiological test procedures.

Development of methods for detection of other microbiologicals using polymerase chain reaction is under way. A priority list of microbiologicals has been determined, and method development is ongoing with work completed for one organism and work to detect several other organisms currently under way.

PI/QitTof MS CW analyzer. Preloading of the CW mass spectral library is an important feature because CWs standards are generally unobtainable. The instrument's screening library can be expanded routinely for both nonstandard and standard compounds. This provides an additional tool for identifying compounds not regularly monitored in drinking water samples. In Phoenix the PI/QitTof MS analyzer is used more for its speed than for its high-throughput capability. Generally about 1–10 samples per day are analyzed on the instrument. However, the high-throughput capabilities are important in the event of an emergency or heightened security concern in which a greatly increased number of samples may need to be screened quickly. The short sampling times and automated analysis also help minimize needed labor. The labor expended on the instrument, including check-out and running blanks, averages about an hour a day.

The PI/QitTof MS analyzer shown on page 63 is placed in a hood as a precautionary measure to limit staff exposure in the event of a legitimate threat. The protocol for a suspect event is to unpack the collected samples in the fume hood and run them on the analyzer as the first screen performed by the lab. If the screen is negative, the remaining samples are distributed for screening in other areas of the laboratory.

A low FP rate is an important criterion for any screening system. This specific analyzer[1] has been operated for more than one year of regular use and has experienced only one FP event that was resolved by running replicate samples and by observing the absence of the expected ion fragment signatures for a true suspect compound.

Response. Protocol for the city of Phoenix is that results are reviewed and reported to the laboratory superintendent and/or the assistant superintendent who contacts the appropriate official(s). Which officials are contacted depends on the situation but will include the water services security manager, the pollution control superintendent or designee, and the water production superintendent or designee. Laboratory analysts are on call to respond to events or suspected events. Depending on the situation, the superintendent or the assistant superintendent determines which analysts are needed and contacts these individuals as deemed necessary. Process control chemists are assigned to each treatment facility and may be asked to respond by the respective treatment facility supervisor(s). The next

TABLE 3 Toxic and safe levels of compounds in drinking water

Compound	Recommended Guidelines 5 L/d (1.32 gpd)* *mg/L*	Tri-Services Water Quality Standards 5-L/d (1.32-gpd) Consumption, Seven-day Exposure† *mg/L*	Inhalation‡ Incapacitation, ICt_{50}—mg min/m³, I_{50}—mg *15 L/min*	Assumed Acute Concentrations for Short-term Exposure *mg/L*§
BZ	0.007			0.50
LSD				
GA (Tabun)	0.070	0.140		4.9
GB (Sarin)	0.014	0.028	35 (0.52)	0.98
GD (Soman)	0.006	0.012	35 (0.52)	0.42
VX	0.008	0.015	25 (0.38)	0.52
Sulfur mustard	0.140	0.140		4.9
Lewisite (arsenic fraction)	0.080	0.080		2.8

*Summary from Mays (2004b), footnotes and original source values provided in Table 1.2 including NRC (1995); listed doses are safe.
†Tri-Services, 1999
‡ICt_{50} is the concentration × duration of exposure that incapacitates 50% of people exposed, assuming normal breathing rate. I_{50} (which is also called the inhibitory dose) is the exposure level leading to 50% probability of incapacitation. The I_{50} is equal to the ICt_{50} × breathing rate, which for humans is 15 L/min (0.066 gps).
§Deleterious effects are assumed to occur at 5 times the recommended Tri-Services safe concentration guidelines adjusted for civilian consumption of 2.5 L/d (0.66 gpd) consumption and two-day exposure.

level of planning may include predictions about the transport of CWs within the distribution system in order to make more informed decisions for emergency response.

In the event of a credible CWs agent detection, the appropriate law enforcement and regulatory agencies would be notified. If the contamination was within the water system, the water department would take measures to isolate the CWs agent by shutting valves to and from reservoirs, closing valves in the distribution system, or shutting down treatment plants. Contamination of source waters would require working with the respective purveyor (in this case the Salt River Project and/or Central Arizona Project). Remediation would depend on the magnitude of the event.

TOXIC VERSUS DETECTION LEVELS

A rapid-screening capability must ensure low probability of FN at concentrations that pose a threat to individuals. Unlike the rigorous monthly or quarterly US Environmental Protection Agency (USEPA) methods used to monitor water for compliance with long-term safe drinking levels, an EWS instrument must be configured to provide an immediate alert to a more acute contamination that could impair individuals in a matter of days rather than years.

Table 3 tabulates ranges of concentrations from acute to safe drinking levels. Though extensive data exist for toxicity from vapor ingestion by inhalation or by absorption through the skin, much less information is available for toxicity in water assumed to derive from these data. However, the relationship between safe drinking levels and exposure levels is not stated in these reports. Moreover, the data reported are not always consistent. For example, the recommended guidelines (Mays, 2004b; NRC, 1995) do not quote an exposure level. The DOD Tri-Services guidelines for seven-day exposure (Tri-Services, 1999) are in most cases twice that of the National Research Council (NRC) guidelines (NRC, 1995) and are therefore assumed to be derived from these data; however, the relationship between safe levels of ingestion and safe levels of exposure is not stated in these reports.

From these considerations the acute concentration levels that must be detectable for an effective EWS system can be closely estimated. The starting point for this determination is the Tri-Services water quality standards (Tri-Services, 1999). The concentrations listed in Table 3 correspond to a total consumption of 35 L (9.3 gal) (i.e., 5 L/d × 7-day exposure [1.32 gpd × 7-day exposure]). The next assumption is that people will consume 2.5 L/d (0.66 gpd) of treated water and that a detector must be able to detect concentrations that are harmful for a two-day exposure (e.g., 5 L [1.32 gal] total consumption). Consumption of 5 L/d (1.32 gpd) reflects military water consumption under adverse conditions, for example heavy labor in desert conditions. The authors assume civilian consumption of 2.5 L/d (0.66 gpd), which is a conservatively high value. By assuming a linear relationship between safe concentrations and total consumption, the 5-L (1.3-gal) safe concentrations will be seven times greater than the 35-L (9.3-gal) safe concentrations reported by Tri-Services (1999). Finally, it is assumed that acute exposure leading to illness or impairment would occur at five times these safe concentration levels. On the basis of these assumptions, an acute dose of VX in water would equate to 2.6 mg (i.e., 0.52 mg/L × 5 L [1.97 mg/gal × 1.32 gal]).

As a consistency test, the incapacitation dose of 2.6 mg calculated for VX in water was compared with that derived from the inhalation data in Table 3 (FAS, 1998). The definition of ICt_{50} is the concentration × duration of

exposure that incapacitates 50% of people exposed, assuming normal breathing rate. ICt_{50} is measured in milligrams per minute per cubic metre. The definition of I_{50} (which is also called the inhibitory dose) is the exposure level leading to 50% probability of incapacitation. I_{50} is measured in milligrams. The I_{50} is equal to the ICt_{50} × breathing rate, which for humans is taken to be 15 L/min. For VX this leads to a value of I_{50} of about 0.4 mg (25 mg min/m^3 × 0.015 m^3/min). From these data it would appear that on a mass basis, inhalation is more debilitating than ingestion in water. This may not be surprising considering inhalation is about an order of magnitude more lethal than percutaneous exposure on a mass basis (Somani & Romano, 2001; Adler et al, 2000). Unfortunately, there is limited information on the physiology of CWs toxicity by water intake.

An effective EWS system must be able to detect subacute concentrations in a response time much less than the relevant exposure time. The PI/QitTof MS instrumentation was tested at CWs surety labs on several occasions from which the MS and MS/MS spectral libraries were developed and the method detection limits (MDLs) determined. The MDLs are based on the USEPA method and are expressed as the concentration for which the signal level is 3σ above the background distribution. Essentially all of the CWs agents tested (Table 2) had MDL values in the 0.07–0.7 mg/L range, which meets the short-term acute concentration levels assumed in Table 3, and are VX—0.17 mg/L, GA—0.35 mg/L, GB—0.24 mg/L, GD—0.68 mg/L, GF—0.49 mg/L, HN-1—0.131 mg/L, HN-3—0.07 mg/L, as measured at the Edgewood Chemical and Biological Center in Edgewood, Md. Data for linearity and background signal for the CW surrogate DMMP are plotted in Figure 6. These results indicate a linear dynamic range of three decades. The quantitatable dynamic range using a binomial fit is about four decades. For screening applications, relevant performance includes low FP and FN rates at the required threshold levels for an alarm. For the measurements in Figure 6, the MDL was 0.02 mg/L. However, the data set in Figure 6 is not statistically large enough to derive a precise FN value. In a separate experiment containing four CWs surrogates—DMMP, diethyl methylphosphonate (DEMP), diethyl ethylphosphonate (DEEP), and diisopropyl methyl phosphonate (DIMP)—concentrations of 0, 0.03, and 0.10 mg/L in water were sampled 20 times each to determine FN and FP rates. From the blank measurements 3σ MDL values were determined, which ranged from 0.006 mg/L for DMMP to 0.033 mg/L for DIMP. The differences are mostly attributable to the size of the background signal. By definition, the 3σ MDL corresponds to an FP value of 0.15% (the fractional area of a Gaussian distribution 3σ removed from the mean). These low FP rates are consistent with findings of the City of Phoenix Water Services Department during its protocol development. At these levels the FN rate is 0% for DMMP and about 50% for DIMP at the lowest 0.03 mg/L measured (the latter being expected because the concentration is nearly exactly at the DIMP MDL level). However, the FN rate for DIMP is 0% for the 0.10 mg/L DIMP concentration, which is still below the acute concentrations of CWs agents in Table 3. On the basis of the MDLs for the live CWs agents noted earlier, the PI/QitTof MS analyzer meets the low FN and FP requirements for an effective screening technology for CWs in water.

An important question to consider is how viable a CWs threat is, given the sheer volume of water in which an agent is diluted. One way to assess this is to consider the daily consumption of potable water by a major population base. Using a value of 100 gpd/person (378.50 L/d/person), it follows that a population of 1 million people would consume 100 mgd (378.50 ML/d). Obviously most of this use is not for the purpose of consumption. The volume of a CW that must be added to this daily volume to reach the acute levels shown in Table 3 (about 0.5 mg/L) is then about 200 kg (441 lb). This is a plausible scenario with the potential to impair 1 million people after one or two days' exposure. Other threat scenarios include (1) contamination of source water (pretreated) for which a greater contamination volume would be required because of the greater source volume and (2) contamination in the distribution system where for more localized contamination less CW volume is needed to reach acute concentrations.

SUMMARY AND CONCLUSIONS

The risk of deliberate CWs contamination of water supplies to levels that can cause illness and impairment is plausible because of the high toxicity of these compounds and the relative accessibility of an extensive, delocalized, and unprotected water source and distribution system. Safeguarding the public against malicious activities requires an effective EWS that can rapidly detect and characterize illicit compounds with minimal FN and FP rates. A screening capability also must be integrated with a rapid response process to determine the best course of action and to trigger communication with the public. There are no magic bullets at this time, and new detection technologies should be viewed as improving the quality of information used to make decisions of public consequence.

The result of this research is the detailed description of a fast and accurate EWS screening system for CW compounds in water, based on the technology of PI and QitTof MS. The PI/QitTof MS was validated during several trials at DOD CWs surety labs. The instrument has been commercialized and consists of an integrated autosampler and user-friendly software. The result is a system that provides a fast and effective high-throughput monitor capable of analyzing samples every 45 s with automated operation. This advanced technology is being deployed in municipal water utilities such as the City of Phoenix

Water Services Department and government labs to test and develop EWS strategies and operations. This article discusses the strategy, sampling, analysis methods, and response protocols as well as how the PI/QitTof MS analyzer is used as a first-line screening method and for characterization in the event of positive detection.

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ABOUT THE AUTHORS

Jennifer Calles *is the assistant laboratory superintendent for the City of Phoenix Water Services Laboratory. For more than 17 years Calles has worked in the field of environmental laboratory analyses for water and wastewater and has worked for 10 years in laboratory management for the City of Phoenix. In 2002 she received the City of Phoenix Excellence Award for providing assistance with the Industrial Pretreatment Program. Calles also coordinated the Fugitive Agent Monitoring Program in 2002 for the City of Phoenix Water Services Department in conjunction with the city's Production/Distribution and Pollution Control Division. She is a member of AWWA. Randy Gottler is Laboratory Superintendent for the City of Phoenix Water Services Department. Matthew Evans is a senior scientist and Jack Syage (to whom correspondence should be addressed) is president of Syagen Technology Inc., 1411 Warner Ave., Tustin, CA 92780. Syage can be reached at jsyage@syagen.com.*

FOOTNOTES

[1]Radiance Pro™ chemical weapons high-speed analyzer, Syagen Technology Inc., Tustin, Calif.

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