Detection of Toxic Industrial Compounds: A Guide to Analytical Techniques

Application

Homeland Security

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Abstract

With an estimated 800,000 shipments of hazardous materials [1] transported throughout the U.S. each day, the threat of an accidental or intentional release of a toxic industrial compound is viewed as a serious one. Chemical plants, pipelines, storage facilities, railroads, and trucks are all possible sources from which toxic industrial compounds could be released. Should such an incident occur, there would be an immediate analytical need to determine the nature of the release, establish perimeters to ensure public safety, monitor decontamination efforts, and confirm effective remediation of the chemical agent. This application note describes the analytical tools required to address these chemical measurement needs.

Introduction

One of the most challenging aspects of planning the analytical response to the release of a toxic industrial compound is the vast number of potential target compounds. In order to decide what analytical methods and instrumentation would be required to respond to toxic industial compound incidents, it would be useful to identify a list of highly toxic compounds which might be encountered. This list would help in the selection of analytical techniques. A useful starting point is the list of toxic compounds available from the U.S. Environmental Protection Agency (EPA). The list, entitled "Alphabetical Order List of Extremely Hazardous Substances (Section 302 of EPCRA)", is maintain by the Chemical Emergency Preparedness and Prevention Office (CEPPO), Office of Solid Waste and Emergency Response (OSWER), U.S. EPA. The URL for the list is http://www.epa.gov/swercepp/ehs/ehsalpha.html. The list contains the name, Chemical Abstract Service (CAS) Number, chemical profile, and emergency treatment and first aid guide for each of the 356 compounds listed.

Table 1 summarizes the different classifications of compounds posted on the EPA Hazardous Substances List along with examples of each. The numbers in parentheses following some of the compound names are the estimated U.S. annual production in millions of pounds for 2001.

Table 1. General Classification and Examples from the EPA List of Extremely Hazardous Substances

Classification	Examples
Organic compounds (50%)*	Acrolein, Acrylamide, Acrylonitrile (**2961**) [2], Aniline (**1907**), Bis(chloromethyl) ketone, Chloroform, Colchicine, Cyclohexylamine, Ergotamine tartrate, Ethylthiocyanate, Hydroquinone, Mitomycin C, Propionitrile, Vinyl acetate (**2784**)
Pesticides (30%)	Aldrin, Chlordane, Endosulfan, Ethion, Methidathion, Parathion, Phosmet
Inorganic compounds (10%)	Chromic chloride, Gallium trichloride, Sodium selenite, Tellurium hexafluoride, Thallium sulfate, Aluminum phosphide, Potassium cyanide
Gases (5%)	Ammonia (13046), Chlorine (**12019**), Ethylene oxide (**7370**), Hydrogen cyanide, Phosphine, Hydrogen sulfide, Boron trifluoride, Arsine, Sulfur dioxide
Organometallic compounds (5%)	Cobalt carbonyl, Methylcyclopentadienylmanganese tricarbonyl, Nickel carbonyl, Phenylmercury acetate, Tetraethyl lead

*Approximate percentage of total compounds on list. Annual production in millions of pounds for year 2001[2]

Inspection of the complete EPA list and the summary given in Table 1 demonstrates the broad range of possible target compounds making the analytical task a formidable one. The ideal measurement technique for this application would be highly sensitive, selective, capable of resolving potentially complex mixtures of chemicals, and able to identify complete unknowns. Mass spectrometric detection is highly suited to this task given its selectivity and mass specificity.

In mass spectrometry, the sample components are ionized by chemical, electrical, or thermal means. The resulting ions are then separated in a mass filter by their mass to charge ratio, and detected. The mass spectrum, which is a plot of the number of ions detected (abundance) vs. the mass of the ion, forms a unique fingerprint which identifies each individual chemical component. Although no single MS instrument would be able to analyze for the presence of all the compounds listed, several different complimentary mass spectrometric techniques could be used in tandem to provide near comprehensive analytical capability.

Gas Chromatography/Mass Spectrometry (GC/MS)

Gas chromatography interfaced to MS (GC/MS) is the method of choice when dealing with completely unknown compounds. In GC/MS, the sample is introduced to a gas chromatograph as a liquid or a gas, where it is vaporized and its components separated. The sample components are then introduced to the mass spectrometer while in the gas phase. Consequently, for a compound to be amenable to analysis by GC/MS, it must be possible to vaporize the compound in an inert atmosphere at temperatures below 350 °C. Approximately half of the compounds in the EPA list would fall into this category. The majority of the pesticides listed, the gases and a substantial percentage of the organic compounds have all been analyzed by GC/MS. Even many of the metal containing compounds such as tetraethyllead and arsine are sufficiently volatile to be analyzed using this technique. The technique is applicable to compounds ranging from permanent gases up through hydrocarbons as large as 100 carbons. Modern GC methods can separate as many as 200 compounds in complex samples.

Figure 1 shows the mass spectra of three toxic gases from the EPA Hazardous Substances list. The spectrum of each gas is significantly different and easy to interpret. However, interpretation of the spectra of complex molecules like pesticides are much more challenging. In order to facilitate data interpretation, the National Institute of Standards and Technology (NIST) mass spectral library is available on Agilent GC/MS systems. This library contains over 143,000 spectra. Since the electron impact ionization (EI) spectra obtained from the GC/MS are the same type as those in the NIST library, automated searching for compound identification is enabled.

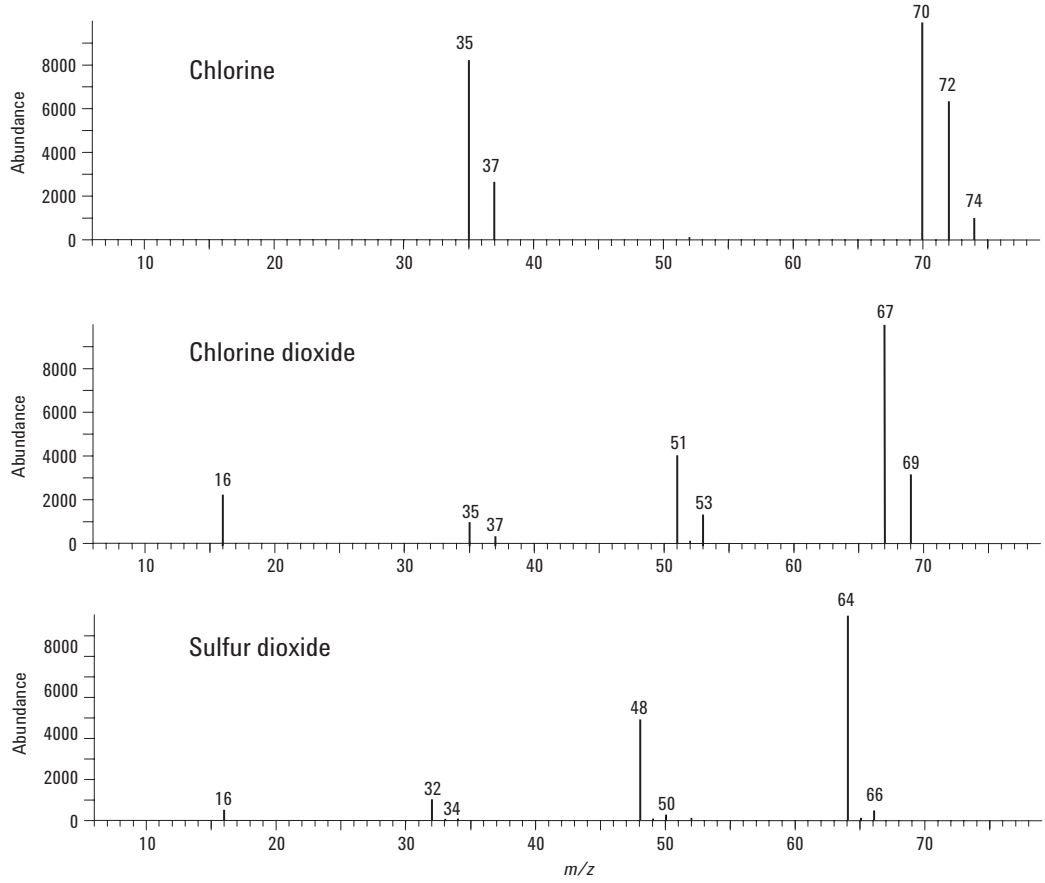

Figure 1. Mass spectra of three toxic gases contained in the EPA list.

To illustrate the use of GC/MS and the mass spectral library, consider a sample containing 16 pesticides. Figure 2 shows the Total Ion Chromatogram (TIC) for the mixture. The TIC is a chromatogram constructed by taking the sum of the ion abundances over the scanned mass range for each MS scan and plotting it vs. time. The MS is scanned every 0.33 sec in this example. A response on the TIC indicates the presence of a compound eluting from the GC.

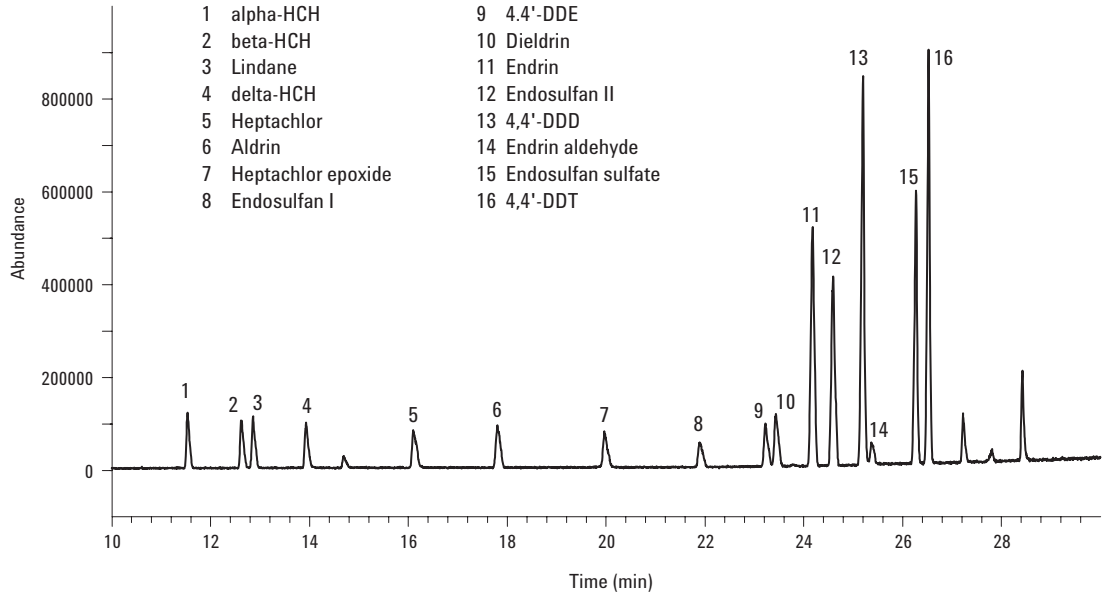

Figure 2. Total ion GC chromatogram of a pesticide mixture. Compounds are 12 ppm in methanol except for numbers 11, 12, 13, 15, and 16, which are 63 ppm.

To identify a compound that produced one of the peaks in the TIC, the spectrum corresponding to the apex of the peak is searched against the library. The upper plot in Figure 3, for example, is the mass spectrum for peak number six. Note the complexity of the spectrum. Manual interpretation of this data would be formidable, however, when searched against the NIST library, the database correctly identifies the compound to be Aldrin (bottom plot of Figure 3).

Comparison of the complete spectrum of an unknown with the library is the best approach for identification and/or confirmation of unknowns. Some samples are so complex, however, that it is not possible to completely separate the toxic compound from the rest of the compounds in the matrix. A commonly used alternative is target compound analysis, which recognizes the value of the GC retention time as part of the identification process. This approach works very well but requires that the retention time and ion ratio information be collected for every compound that is to be searched for. If this information is not collected for a compound, then that compound will not be identified by this technique.

In recent years this technique has been refined further by the use of Agilent's retention time locking (RTL) software [3]. RTL is a technique that precisely matches the retention times obtained on one GC or GC/MS system to those on other GC systems. This precise retention time matching makes comparison of results between laboratories much easier and more accurate. It also makes identification based on a retention time or retention time combined with ion ratios more reliable.

A good example of the power of using RTL in target compound screening is the Agilent Pesticide RTL Library [3]. This library contains the precise retention time and mass spectral data for 567 pesticides used worldwide. It allows the user to rapidly screen samples for the presence of any of these pesticides. Sixty-six of the compounds identified in the EPA Hazardous Substance list are currently catalogued in this library.

Once compound identification is complete, the next task is to determine the concentration of the target analyte. Given the very large number of potential target compounds, it is unlikely that a laboratory would maintain calibration standards

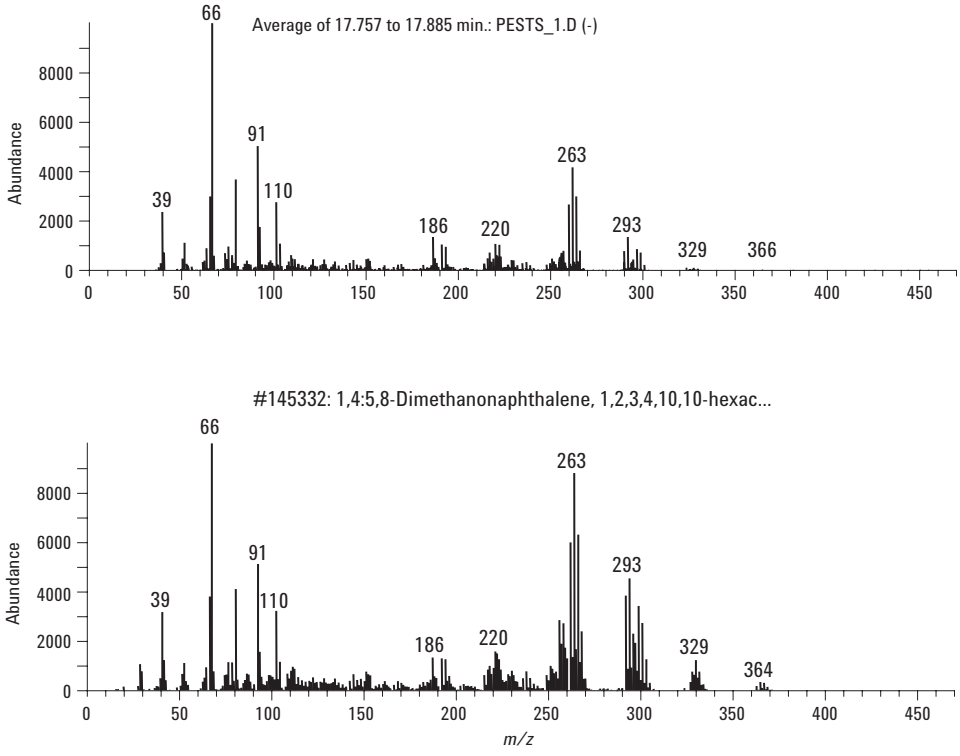

Figure 3. Mass spectrum from peak 6 in Figure 2 (top). Spectrum of best match from NIST library, Aldrin, (bottom). The name listed above the spectra is the International Union of Pure and Applied Chemistry (IUPAC) name for Aldrin.

for all of them. If a compound is identified for which a standard is not available, its concentration can be estimated by using the response factor from a different known compound, for example, as specified in US EPA method 8270D. Since response factors in GC/MS rarely differ by more than a factor of 20, this technique can give a reasonable estimate of the compound's concentration.

Enhancing Sensitivity in GC/MS

One useful means of improving the detection limits of the GC/MS is to use chemical ionization [4]. In this technique, a reagent gas is added to the ion source. The addition of the reagent gas provides a “softer” ionization mechanism for sample molecules. Using methane or ammonia in positive chemical ionization mode (PCI) produces less fragmentation of the molecule and thus a much simpler spectrum (Figure 4). This allows the molecular weight of the compound to be determined more reliably and aids in confirming the identity of the compound. This technique is especially useful for measuring low levels of a toxic agent in a complex sample matrix. Because the spectra of all the compounds present contain fewer ions, there are fewer interferences at the mass being monitored. Reduced interferences result in lower method detection limits with complex samples. This technique is useful with many of the compounds on the EPA list. Agilent chemical ionization GC/MS systems are capable of switching between EI, PCI, and Electron Capture Negative Ionization (ECNI) modes, giving the greatest possible flexibility for both identification and monitoring.

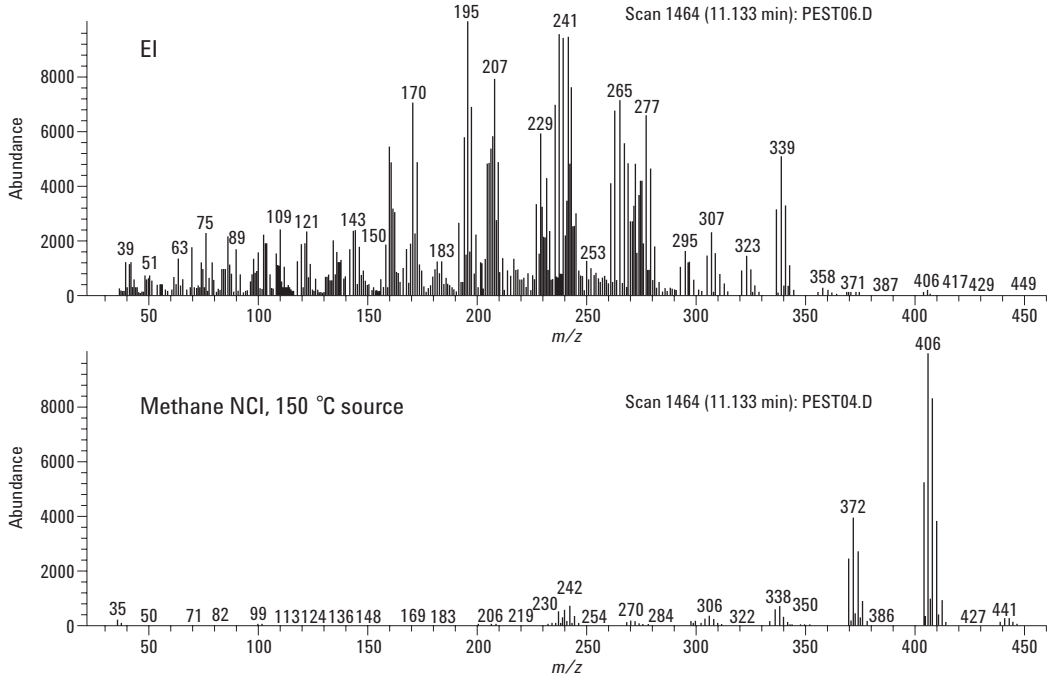

Figure 4. Mass spectrum of Endosulfan I in EI mode (top) and ECNI mode (bottom).

Table 2 lists the approximate quantitation limits expected for GC/MS in the various ionization and ion collection modes. Note that there exists significant variability in the response of the various target compounds, therefore these values are conservative estimates of performance for guidance purposes only.

Table 2. Approximate Quantitation Limits

Mode	Approximate quantitation limit (ng)
EI Scan	0.1 (0.5 ng for usable spectrum)
EI SIM*	0.01
PCI Scan	0.1
PCI SIM, Methane	0.01
ECNI Scan	0.002
ECNI SIM	0.0002

*Single ion monitoring

Another means of enhancing compound identification and lowering detection limits is to split the effluent of the GC column between the MS and other detector(s). For example, many pesticides and chemical nerve agents contain phosphorus. Therefore, a flame photometric detector (FPD) in the phosphorus mode can be employed in tandem with an MS. Since the FPD is very sensitive and selective for phosphorus (detection limit of approximately 1 pg P) compound detection is greatly facilitated especially at low levels in complex matrices. The Agilent GC/MS systems can be configured to collect chromatograms simultaneously from the MS and one (or two) additional GC detectors.

Sample Introduction into GC/MS

In the case of liquids, the sample can be injected directly into the GC/MS. For solid samples, a solvent like methylene chloride can be used to extract the toxic agent from the sample with subsequent injection of the extract into the GC/MS using the splitless mode. The ability of the inlet to switch between split and splitless is useful for samples covering a large range of agent concentration. In split mode, neat samples can be analyzed while keeping the largest peaks in the dynamic range of the detector. In the splitless mode, samples of the lowest agent concentration in extracts can be measured.

An alternative means of sample introduction is static headspace sampling in which the sample is heated in a sealed vial and the headspace sampled after some specified period of time. Headspace sampling has two distinct advantages. The first is that it works well with very volatile analytes such as gases and low boiling solvents. Consequently, this technique is useful for incidents involving chlorine, ammonia, sulfur dioxide, chloroform, etc. In addition, since samples are often injected directly into the GC as a liquid, it is important to make sure the samples are free of particulates and that nonvolatile materials are kept to a minimum. Therefore, a second important advantage of headspace is its ability to analyze “dirty” sample without the need for additional sample preparation such as filtration or solid phase extraction. The limitation of this technique is that analytes must have sufficient vapor pressure at the temperature to which the vials are heated. The Agilent 7694 headspace sampler has a 44-sample tray and can run sample analyses under complete automation with the GC/MS system.

A third sample introduction technique is that of thermal desorption. The technique is especially useful for detecting trace levels of volatile and semi-volatile compounds in the atmosphere. In a typical thermal desorption analysis, 10–20 L of air sample are drawn through the sample trap with a small vacuum pump. Volatile and semivolatile compounds in the air are retained and concentrated in the sample trap then thermally desorbed. Because the concentration factor is so high, compounds can be measured at extremely low levels. Concentrations on the order of 50 ng/M^3 of air should produce a usable spectrum with 1 ng/M^3 detectable in single ion monitoring mode.

Thermal desorption analysis is limited to those compounds in the volatility range of about C_2 to C_{36}. Also, most inorganic gases like chlorine, ammonia, and sulfur dioxide cannot be analyzed with the technique. For those compounds which are amenable to the technique, the combination of thermal desorption and the GC/MS provide an extremely sensitive analytical method for measuring toxic compounds in air.

Liquid Chromatography/Mass Spectrometry (LC/MS)

A substantial number of the organic compounds and pesticides in the EPA list are not amenable to analysis by gas chromatography. Some have vapor pressures that are so low as to prevent vaporization. Others are thermally labile and would decompose in the GC. For these types of compounds, liquid chromatography is the preferred separation technique to interface to the MS.

The Agilent Liquid Chromatography Mass Selective Detector (LC-MSD) is a rugged benchtop LC/MS that is cost-effective, and easy to use in routine applications. In the LC-MSD, the effluent from the LC enters the ionization source where it is nebulized into an aerosol. The sample constituents are ionized and the ions separated by mass to charge ratio. There are three principal types of ionization source used for LC/MS: atmospheric pressure electrospray ionization (ESI); atmospheric pressure chemical ionization (APCI); and atmospheric pressure photoionization (APPI). The choice of ionization source is based on the specific types of compounds to be analyzed. In practice, many compounds can be ionized with all three sources, but will perform optimally with only one of the three. Part of the development of an LC/MS method is the selection of the appropriate ionization technique and optimization of the operating parameters. The source modules in Agilent LC/MS systems are easily interchangeable to facilitate method development.

While the relatively simple spectra obtained make it fairly easy to determine the molecular weight of the analyte, more fragmentation is often desired for structural determination or for confirmation of identity. If required, additional fragmentation can be obtained using a technique called collision induced dissociation (CID). Unlike GC/MS, however, there is no large library of spectra that can be searched to identify unknowns. In LC/MS, a method is developed for a group of analytes and the spectra of standards are recorded under the specific conditions used in that method. The spectra obtained are then used to confirm the identity of compounds found when the method is run on actual unknown samples.

For laboratories that need to determine the structures of unknowns and/or need to run analyses in particularly complex matrices, the LC-MSD Trap offers useful additional capabilities. Principal among these is that of MS^n. This powerful technique allows analysts to deconstruct molecules to determine their structure or to generate unique ions with which an analyte can be selectively detected in the presence of a complex matrix with the highest signal to noise ratio.

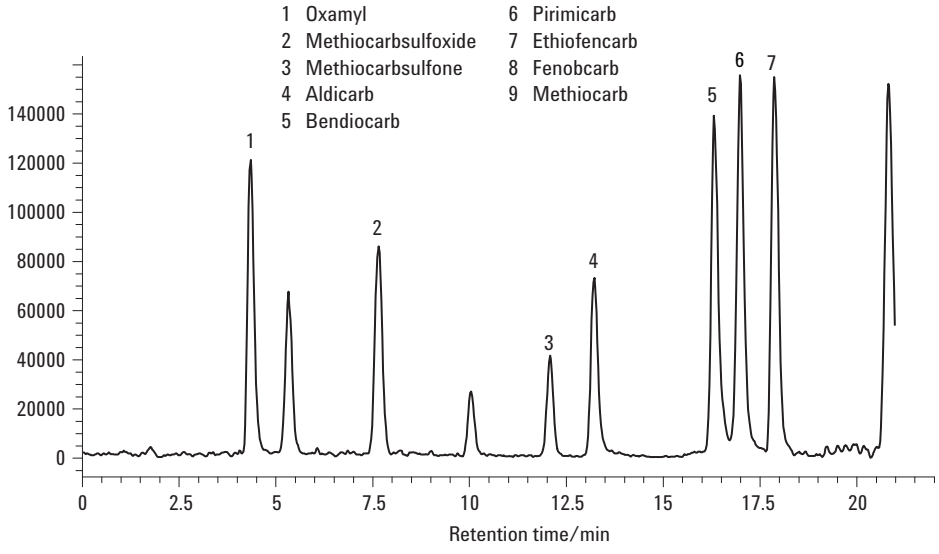

Figure 5. The positive ESI TIC for a mixture of nine carbamate pesticides [5] at a concentration of 1 ppm. Three of these compounds, Aldicarb, Oxamyl, and Methiocarb, are on the EPA Hazardous Substances list.

The multipole geometry ion trap can be used as a mass analyzer to generate conventional mass spectra. It can also hold or trap an ion of a specific mass and eject other ions out of the trap. The trapped ion can then be collided with helium atoms and fragmented. This process is referred to as MS/MS. An ion from this second generation spectrum can be trapped and fragmented, leading to MS^3. This trapping of ions and subsequent fragmentation is the process called MS^n. The ion trap software contains tools that allow the automatic acquisition of MS/MS data and software to aid in the determination of structures obtained from MS^n analysis. This type of analysis can be completed on pg levels of the target compound making the ion trap approach a powerful tool for solving difficult analytical problems.

Inductively Coupled Plasma Mass Spectrometry (ICP-MS)

Approximately 10% of the compounds in the EPA list are compounds that contain a toxic metal. In some cases, as with mercury, the metal itself is highly toxic. In other cases, toxicity is directly related to the form in which the metal is bound as in the case of organotin compounds. In both of these cases, ICP-MS is the method of choice.

In ICP-MS, liquid samples are introduced into a high temperature plasma (~6700 °K), ionized, separated in a quadrupole mass analyzer, and detected. The inherently high sensitivity and low background associated with this technique results in detection capability for most metals in the single to sub-ppt range. In addition, current state-of-the-art detector technology enables nine orders of linear dynamic range. A particularly powerful capability of ICP-MS, which is based upon each element's unique isotopic fingerprint, is the ability to perform semi-quantitative analysis for nearly the entire periodic table including radionucleides in a matter of minutes.

Typically, ICP-MS provides total metals concentration for any given analyte. If species specific information is desired, an LC or GC can be interfaced to an ICP-MS to provide organometallic speciation as shown in Figure 6. The primary benefit of using LC or GC interfaced to ICP-MS is the excellent detection capability for the metal species relative to GC/MS or LC/MS.

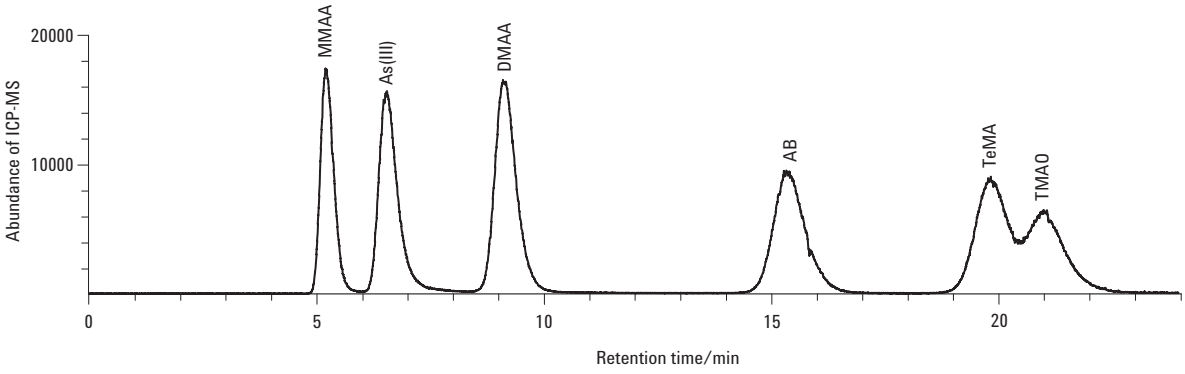

Figure 6. Speciation of organoarsenic compounds using LC-ICP-MS (20 µL injection).

Summary

Preparedness for the analytical response to a release of toxic industrial compounds presents significant challenges to the laboratory. The breadth of potential compounds accompanied by their varying chemical and physical properties often requires that multiple techniques be deployed to provide comprehensive analytical capability. This document has outlined several measurement tools well suited for this task using the EPA's published list of hazardous substances as a reference point. In addition, several options for sample introduction have been discussed. A summary of the techniques discussed and their applicability to the analysis of toxic industrial compounds is given in Table 3.

Table 3. Summary of Analytical Techniques for the Analysis of Toxic Industrial Compounds

Classification	GC/MS	LC/MS	ICP-MS
Organic compounds	X	X*	
Pesticides	X	X*	
Inorganic compounds			X
Gases	X		
Organometallic compounds	X	X*	X**

*Compounds that are thermally labile or have very low vapor pressures

**Provides total metals concentration. Species information requires interfacing with a LC or GC

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