Occupational Hygiene: Gas Chromatography☆

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Introduction

Industrial or occupational hygiene has been defined as the anticipation, recognition, evaluation and control of environmental factors or stresses arising in or from the workplace that may cause sickness, impaired health or significant discomfort. The factors causing stress encountered in the workplace are typically divided into 'physical' and 'chemical', although, increasingly, a biological component has been recognized as, for example, with infectious diseases.

Chemicals can occur as gases, vapors and mists and as solids in the form of dusts and fumes. Their hazard potential is related to their ability to react with or be absorbed by the skin or lungs. The physiological response to exposure is related to its frequency, duration and severity, the route of exposure, and the chemical make-up of the substance, as well as factors relating to individual susceptibility. Gases and vapors can cause problems in the lungs by irritation, or can be absorbed into the bloodstream to cause problems elsewhere in the body. Liquids may be absorbed through the skin with local irritation or systemic effects, while aerosols, both liquid and solid dispersions in air, can be deposited in various regions of the pulmonary system. In the lungs, certain dusts cause problems associated with their physical characteristics, while others are soluble and may be absorbed. Absorption of any

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chemical into the body may cause acute or chronic health effects in organs or tissues distant from the site of absorption. Exposure limits for chemicals are published by government and other agencies.

Monitoring of the environment is required to determine the nature and quantity of chemicals present, and also to evaluate the effectiveness of control measures. Monitoring is typically carried out through sampling, either of the air being breathed, or of surfaces which the skin or clothing may contact, or of the workers themselves through analysis of breath, blood or urine. Protocols have been established to standardize the methods of sampling and analysis. These methods are generally available, although they are often updated to meet the changing needs of hygiene investigations so that it is important to maintain a current awareness of the literature. Gas chromatography (GC) is one of a number of techniques used in the analysis of samples. It is used to separate the hazardous chemicals present in a sample, one from another, or from the matrix in which they are presented for analysis. Only a few years after gas/liquid GC was first described by James and Martin[1] Rushing reviewed both gas/liquid and adsorption chromatography (either referred to hereafter as GC) for occupational hygiene-related purposes.[2] The GC analyses he described included solvent analysis, determination of trace level contaminants (e.g., benzene contamination of paint thinners), and the determination of major and minor constituents of air. Although not specifically discussed by Rushing, he undoubtedly described isothermal GC analyses since temperature program operation was not yet common, and he mentioned that "a constant temperature heating chamber is extremely desirable" for GC analysis.[2] Rushing also noted a general lack of GC analysis sensitivity and the corresponding need to concentrate analytes prior to analysis, including through "adsorption on silica gel or charcoal." Referring to analyte retention time, Rushing also noted that "the technique measures a property which is not unique and thus it may be that other substances are responsible for part or all of the observed effect."[2] This problem can be resolved by orthogonal instrumentation, for example, whereby GC is combined with a mass spectrometric detector (GC-MS). Two (or more) co-eluting analytes can be determined by quantifying unique m/z values from the mass spectra of co-eluting chemicals. Analysis by GC most often occurs in a laboratory setting, but field-portable and person-portable GC instruments that employ simple detectors or even complex GC-MS instruments are also available.

Factors in the Selection of Sampling and Analysis Methods

The ideal method would be specific, sensitive, and free from interference. In addition, it would provide real-time continuous output as well as time-integrated results. Finally, it would be simple and cheap to operate. It is rarely possible to satisfy all these criteria in currently available technology and compromise is often necessary.

Air Sampling

There is substantial variation of hazardous chemical concentration in both space and time. To obtain accurate information concerning the airborne dose to the worker, it is necessary to sample air from the 'breathing zone'. Personal monitors therefore require an inlet port or sensor close to the face. The "breathing zone" is typically defined as a hemisphere of 30 cm radius facing forward from the face and centered between the nose and mouth. Thus it includes the upper area of the torso allowing attachment of samplers to shirt lapels or pockets. Special harnesses are sometimes also used, where samplers can be attached to the shoulder straps. These harnesses have the advantage of also providing points of attachment for battery-operated pumps. Temporal variability can be covered by taking a time-integrated sample. Regulated concentration limits normally are expressed in terms of 8 h (work-shift) averages, although short-term limits are also employed for compounds with more acute toxicity. The time period for short-term averaging is typically 15 min in the U.S., although other periods (e.g. 30 min) may be in use elsewhere. In addition, some regulations call for ceiling limits that cannot be exceeded under any circumstances. Although time periods for ceiling limit determinations are not stated, implying an instantaneous warning, in practice all monitoring equipment involves some time lapse. Equipment used for short-term sampling is often used to monitor ceiling values.

Whole air sampling

The simplest method for taking an air sample is to trap the air in an inert container. The air can be analyzed either in the laboratory or in a field-portable gas chromatograph, by direct injection using a gas-tight syringe or gas sampling loop. Alternatively the chemical content can be concentrated by secondary trapping using a sorbent-filled or cryogenically cooled trap, and then released by rapid heating. The containers used include glass syringes or bottles, bags made of various polymers (e.g. Tedlar®, Teflon®, Mylar®, Saran®)[3–5] or metal containers (stainless steel that has been electropolished, treated by the SUMMA® process or lined with fused silica).[6–10] However, all such containers are bulky, even though smaller canisters have been manufactured recently to hold 200–500 ml of air and which can be worn on a belt or harness. Flexible bags can be filled by passing air through a pump and into the bag. This has the advantage of being simple, but the disadvantage of allowing losses of sample by adsorption within the pump (as has been demonstrated for dichloromethane) or contamination from pump components (e.g. silicones). The alternative is to apply a vacuum to the outside of the bag, and there are specially designed cases for this purpose. While bags were once used for personal sampling, it is rare to see this today, because more convenient alternative sampling systems are available. There are issues of sample stability with whole-air samples in bags.[11–13] Tedlar is the most widely-used bag material, as collected vapors are generally stable within a Tedlar bag, but many aromatic and other compounds are not stable in these bags over periods greater than 24 h. Stability can depend on the type of fitting used, with polypropylene fittings providing greater stability than stainless steel. Photochemical reactions in transparent bags can be minimized by using opaque polymer or foil coverings. Tedlar bags can be

cleaned and re-used, but with an eventual risk of compromising their integrity. Rigid metal canisters offer greater stability over multiple uses. However, metal canisters have been only little used in industrial hygiene sampling.[9,10] The choice of internal finish to maximize the shelf-life of samples has changed over the years, with fused silica linings most popular today. For example, organic sulfur compounds are more stable in fused-silica lined canisters than in polished stainless steel. The expense of canisters ensures multiple re-use although carry-over to future samples is an issue when working from high concentrations to low, and contamination with oil mist renders a canister useless. However, high-pressure steam-cleaning units are available. Canisters are evacuated, and then either immediately filled by fully opening them, or filled slowly at a rate fixed through critical orifice flow-controllers. The size of canister and flow-controller can be matched to collect samples over different durations. Canisters may require a small amount of moisture to ensure compounds do not absorb to the walls. The Environmental Protection Agency uses 6-liter capacity cans for environmental monitoring of volatile organic hazardous air pollutants,[14] but smaller canisters are now available that can be worn as personal air samplers.

Active sorbent sampling

The implementation of regulated limit values for organic chemicals in air led to the development of sampling equipment to meet the combined needs of being lightweight, unobtrusive and carried by the worker, and of being able to provide time-weighted average (TWA) results. In the 1970s this resulted in a simple method for a wide range of gases and vapors using a battery-operated pump to pull air through a collection medium, such as a tube filled with a sorbent (**Figures 1** and **2**), and this is the most common procedure in use today, forming the basis of most published methods for air sampling for gases and vapors. Changing the type or

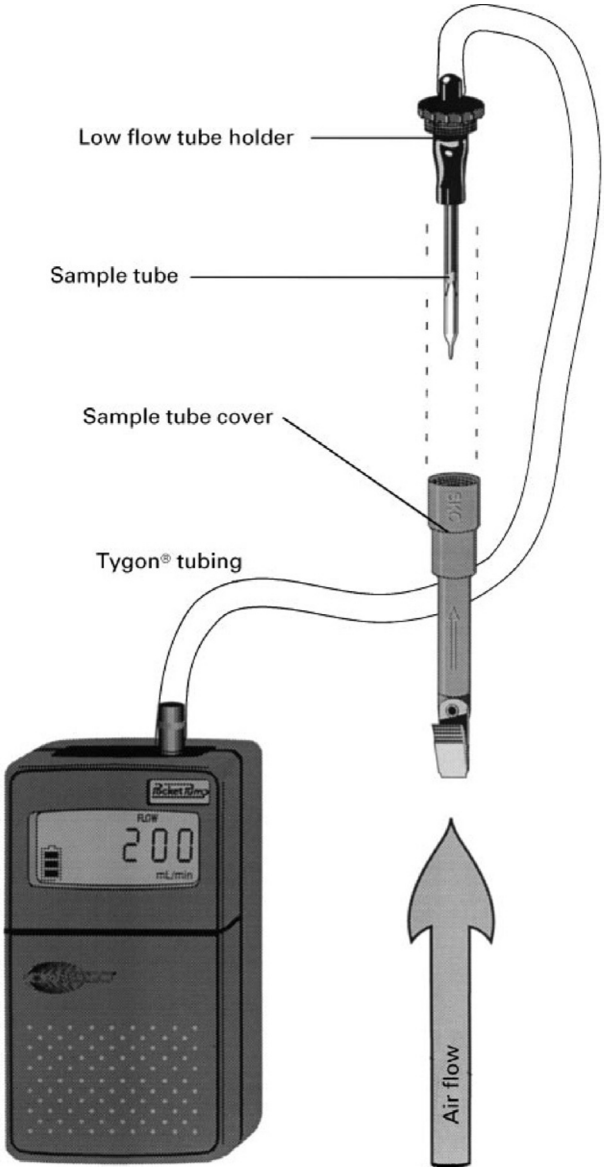

Figure 1 Typical personal air sampling train comprising sorbent tube and air-mover (pump). This is the commonest method of sampling worker exposure to hazardous gases and vapours. Provided courtesy of SKC Incorporated, used with permission.

Figure 2 Personal air sampling train attached to a worker. Provided courtesy of SKC Incorporated, used with permission.

quantity of sorbent extends the range of gases and vapors that can be collected. Another advantage with this approach is that an adjustable flow rate can be raised to obtain sufficient sample to exceed detection limits at low concentrations or lowered to reduce the sample so that saturation (breakthrough) does not occur at high concentrations. Sorbents generally can be classified as being of two types: those that react with the chemical of interest and those that use adsorption to collect airborne vapor molecules. The former type is preferred for gases that are not readily condensed at room temperatures, for chemicals that are unstable or reactive, or where the reaction product can be detected with a better sensitivity. Some examples are reaction of aldehydes to stable hydrazone derivatives with analysis by GC or high performance liquid chromatography (HPLC), and the reaction of ethylene oxide with hydrobromic acid to form bromoethanol, which gives a good response with an electron-capture detector.

The second type of sorbent, using microporous materials which have a high surface area for collection is more common. Silica gel was the first adsorbent to be used for this purpose,[15] although it was quickly replaced by activated carbons,[16] which can have surface areas as high as 1000 $m^2\ g^{-1}$ or more, with a network of large pores leading to successively smaller pores with diameters in the nanometer range. Molecules that enter this region are affected by the Van der Waals forces extending from the pore walls and from other molecules held in close proximity to them. Adsorption is strong and essentially complete at the low concentrations encountered in the air. Transport from the air stream to the sorbent is by molecular diffusion, and both diffusion and adsorption are relatively rapid. Thus only a small quantity of sorbent is required (as little as 100 mg) for effective removal of molecules from the air.[17] The adsorbed chemicals are liberated from the charcoal after sampling by application of a solvent, commonly carbon disulfide. Carbon disulfide is an attractive choice of solvent for several reasons. The molecule is relatively small and able to enter even micropores. It has a high heat of adsorption on charcoal and thus readily displaces the adsorbed molecules from sampling. It is a good solvent for hydrophobic compounds and alcohols can be added to improve the solubility of more hydrophilic compounds. However, its greatest advantage is its rapid passage through most chromatographic columns coupled with its very low response on a flame-ionization detector (FID). This is important because the solvent molecules typically outnumber the molecules of the analyte of interest by about a thousand to one and would otherwise likely interfere with their separation and quantification. The combination of charcoal adsorbent sampling, carbon disulfide desorption and analysis by GC-FID became the basis of most methods for volatile organic compounds developed by the U.S. National Institute for Occupational Safety and Health (NIOSH).[18] In the early days of industrial hygiene packed columns were used and typical injections could be as much as 5 μl. Today's updated methods using capillary columns require smaller injections and often involve split injections. Carbon disulfide is not without disadvantages. Benzene contamination may occur even in grades supposedly low in benzene. Some very volatile compounds, such

as 1,3-butadiene are difficult to detect and quantify when this desorption solvent is used due to co-elution with the solvent. Some compounds, such as amines, can react with carbon disulfide and the presence of carbon disulfide as a solvent can mask the occurrence of carbon disulfide in the sample. Dimethylformamide has been suggested as an alternative, because it also a good solvent and, because of its high boiling point, it elutes in a region that often has no other interest. Both solvents are, however, toxic. Solvent desorption with carbon disulfide is also not preferred when the detection is by mass spectrometry, as repeated contact with metal surfaces (e.g. a quadrupole assembly) can cause damage to this detector.

Other sorbents are used routinely for particular applications. Many of these are the same polymeric resin materials used in chromatographic column packings. The range of sorbents is large, and complicated by the number of trade names used (e.g. Porapak® N or Q, Chromosorb® 102, 104 or 106, Amberlite® XAD-2, XAD-4 or XAD-7, or Tenax® TA or GR).[19] One specific use for these sorbents is in thermal desorption, where the application of heat rather than a solvent is used to remove the collected chemicals.[20] Graphitized carbon blacks are also used in this application. Thermal desorption for industrial hygiene applications was developed in the United Kingdom, and the U.K. Health & Safety Executive features several methods in its series of Methods for the Determination of Hazardous Substances (MDHS). Thermal desorption avoids many of the disadvantages of using a solvent (interferences, reactions and masking) and is often promoted as offering a safer laboratory environment, and it is fully compatible with mass spectrometric detection. However, the main advantage is enhanced sensitivity, since with focusing (typically through a small sorbent tube held at sub-ambient temperature and then rapidly heated) much more of the sample can be delivered to the GC instrument resulting in greatly enhanced detection limits. This greater sensitivity can be very useful in the detection of low concentrations in the environment. The U.S. Environmental Protection Agency (EPA) has published a method using thermal desorption (TO-17)[21] for multiple organic vapors with an approximate range of 5–250 ppb. However, in industrial hygiene applications such sensitivity can be a cause of concern, since many peaks may be observed that have little consequence on health but may require identification and interpretation.

Needle trap and SPME sampling

Recent research in sorbent sampling has focused on the avoidance of solvent desorption which dictates the use of relatively large sorbent beds to avoid analyte breakthrough and yet still provide sufficient analyte mass to allow detection even with about a one thousand-fold solvent dilution. If solvent desorption can be avoided, the scale required for a sorbent-based sampler may be considerably smaller. One approach to accomplish this that has been increasingly studied is needle trap sampling where for instance a 21 gauge needle contains a short section of sorbent. Similarly as for thermal desorption methods that employ larger tubes loaded with sorbent (i.e., 89 mm length by 6.4 mm o.d.) a needle trap sampler may employ several beds of sorbents with differing sorption strength to allow sampling for analytes with a range of volatilities and sorption characteristics. As the analyte capacity of a very small sorbent bed is a concern, the use of a second needle trap sampler in series can allow for detection of breakthrough. In needle trap sampling either active or diffusive sampling is followed by insertion of the needle into the heated injector of a GC instrument for thermal desorption and analysis. Several desorption approaches are possible: the use of a syringe to manually flush a needle trap sampler, diversion of carrier gas flow through a needle trap sampler, and the use of a restrictive injector liner insert.[22] The latter approach is shown in **Figure 3**, where heated carrier gas flow within the injector passes into a side hole in the needle trap sampler when the tip of the needle bottoms out in a restrictive inlet liner. Out of the three approaches mentioned above, this most allows for normal GC operation for analysis of needle trap samples, as no valve operation or external gas flows are required. A recent review of needle trap sampling was completed by Lord et al.[23] The benefits that are possible with needle trap sampling for occupational hygiene applications include the ability to detect short term exposure limit concentrations over very brief durations (as solvent dilution is not necessary to complete analysis), and the solventless analysis process which improves safety in the analytical laboratory. The exhaustive nature of needle trap sampling offers easier calibration options compared to solid phase microextraction (SPME, discussed below) which by definition is a non-exhaustive sampling approach, and the elimination of solvent from the desorption process makes needle trap sampling a good candidate for use with field-portable GC instruments (discussed further below). Due to the small scale of the needle trap sampler compared to traditional sorbent tubes much smaller pumps and diffusive sampling devices based on this approach will allow for less obtrusive sampling for personal exposures.

While SPME sampling is most often used to passively sample (discussed below), in 2000 Koziel et al.[24] described dynamic SPME sampling where analyte uptake is controlled through a minimized boundary layer of analyte-depleted air near the SPME fiber coating surface. The method used an adsorptive coating (Carboxen™ particles in polydimethylsiloxane or CAR/PDMS), and by moving air past the extended SPME fiber at a velocity greater than 10 cm s^{-1}, a constant minimum boundary layer thickness was obtained. By applying known diffusion coefficient values the theoretical uptake of light aromatic analytes at constant concentrations over short (<1 min) periods was experimentally confirmed. Augusto et al.[25] used this approach to quantitatively sample similar analytes over very brief periods in an auto repair shop, and Hook et al.[26] used the same approach in a laboratory with a field-portable GC-MS instrument to quantitatively measure airborne concentrations of the chemical warfare agent sarin. The very brief sampling periods described were necessary to avoid saturation of the adsorptive fiber surface, demonstrating a limitation with this approach.

Diffusive sampling

An alternative to the use of pumps is to allow the molecules of the chemical being sampled simply to diffuse to the sorbent surface (**Figure 4**). Several styles of diffusive (also known as passive) sampler are available, some of which develop color reactions for

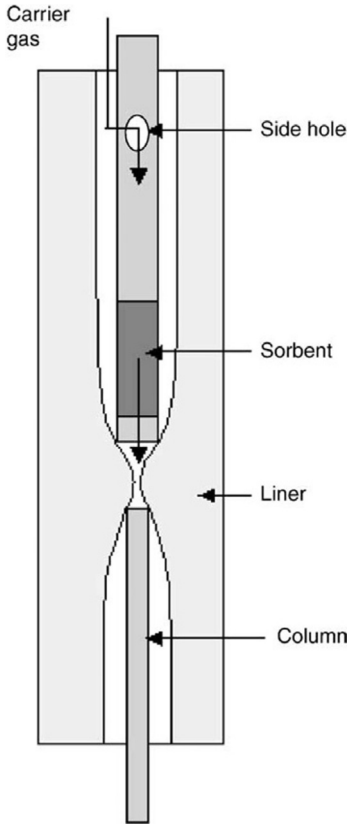

Figure 3 Diagram of the coupling of side hole needle trap sampler with a narrow-neck glass injector liner. The carrier gas enters the needle through the side hole, flows through the sorbent and facilitates the introduction of the desorbed analytes into the GC column. Reprinted from Wang et al.,[22] Copyright (2005), with permission from Elsevier.

Figure 4 Diffusive sampler attached to a worker. This method is more acceptable to workers but the uptake rate varies from chemical to chemical and cannot be altered by field hygienists. Provided courtesy of SKC Incorporated, used with permission.

on-site analysis, and others which contain the same types of sorbent used in the pumped tubes, and which are analyzed in a similar manner. Palmes and Gunnison[27] described quantitative diffusive sampling in 1973, using Fick's law of diffusion to predict sampling rates as determined by the cross sectional area A of a tubular sampling apparatus with length L. With a suitable sampling medium placed at the end of such a diffusion tube, as long as the analyte being sampled is trapped quickly and completely the concentration of airborne analyte will be near zero at the surface of the sampling medium and a concentration gradient will exist

from the atmospheric concentration at the diffusion tube entrance. With the sampling medium acting as a near-perfect sink, the mass of analyte taken up will correspond to the TWA analyte concentration throughout the period of sampling.[28] Sampling devices based on this approach often employ solvent desorption with subsequent GC analysis identical to that for a solvent-extracted sorbent tube, and the dimensions of A and L are defined to provide an uptake rate that will collect enough analyte to allow detection even after dilution in extraction solvent, but not so much as to cause saturation of the sorbent when the zero-sink condition will no longer apply. The most common form of a diffusive sampler available today is a sorbent retained behind a screen with diffusion occurring through the holes in the screen. One popular commercially available diffusive sampler has a diffusion space behind a microporous screen, while another has a plate with holes backed by a microporous screen, and yet another just uses a plate with holes as the diffusion path. These are known as "badge-type" samplers, and they have small diffusion length and large diffusion area, and thus collect relatively large numbers of molecules for analysis. The principle disadvantage of this type of sampler is a slow-down of uptake through starvation under low air-exchange (wind) conditions. While it is generally accepted that a worker's movements may allow sufficient air-exchange, this is not always the case. Nevertheless, many side-by-side field studies of these diffusive samplers with their actively pumped equivalent sorbent tubes have demonstrated equivalence in field studies, for example in sampling components of gasoline vapor.[29] However, in such field comparisons it is important to be aware of localized concentration gradients that can result in differences even between left and right lapels of workers.[30] Diffusive samplers are preferred by the workers, since they do not have to wear pumps, and by the hygienists, who do not have to calibrate and continually monitor the operation of these pumps, and they do not appear to bias exposure measurements.[31] One disadvantage is the inability to adjust the uptake rate, but the main disadvantage is the higher cost of diffusive samplers over sorbent tubes, which becomes evident when the cost of the pump is amortized over a large number of samples.[32] "Tube-type" samplers with a single opening and a relatively long path-length are less prone to wind velocity effects, but they have lower uptake rates and are consequently more likely to be analyzed using more sensitive methods, such as thermal desorption. They have been deployed for periods of several days or weeks in environmental sampling campaigns. A small "penlike" diffusive needle trap sampler was recently used in the field by Gong et al. over an 8 h period to collect aromatic hydrocarbon samples side-by-side with typical active charcoal tube sampling.[33] No significant differences were observed in the quantitative sampling results obtained using both approaches, and these researchers also showed that automated handling and injection of a side hole needle trap sampler was possible.

Since its inception in the early 1990s[34] SPME has played an increasingly important role in sample preparation, primarily for GC analysis. Sampling by SPME involves exposing a small (1 cm) fused silica fiber to analyte molecules, with a portion of these partitioning onto or into a polymeric fiber coating. A passive approach is most often used, with the entire length of the coated fiber extended from a needle for sampling. There are several benefits associated with the method as it is typically employed, primarily simplicity and the avoidance of solvent desorption. The method has been used for industrial hygiene-related GC analyses to complete both quantitative sampling and analysis of airborne organic vapors, and for rapid qualitative screening to establish organic constituents found in unknown samples. In the latter role SPME is used with GC-MS instrumentation, but in either case thermal desorption of analytes from a SPME fiber occurs in a standard split/splitless GC injector, producing a clean fiber coating ready for re-use. In addition to SPME for screening bulk materials and for air sampling, SPME has also been applied for biological monitoring applications discussed below. In 1999 Martos and Pawliszyn described the use of a SPME fiber for quantitative diffusive sampling with the SPME fiber retracted into a small needle having a very small value for A (0.00086 cm^2, determined by the needle diameter), and with user-selectable values for L to provide either rapid or slow sampling.[35] There is a much smaller analyte uptake compared to the larger dimensions of A typically used for diffusive samplers that are subject to solvent desorption, but the entire analyte mass may be injected into the GC. A number of absorptive and adsorptive SPME fiber coatings are commercially available. Adsorptive coatings are obtained by introducing porous particles into a PDMS coating. The attainment of equilibrium is not necessary to use SPME for quantitative air sampling, if as with equilibrium sampling the sample concentration does not change appreciably (i.e. for sampling over brief periods). In the early portion of an SPME uptake curve the quantity of analyte loaded into the fiber coating increases quite rapidly, and small variations in sampling time can produce relatively large variations in the mass of analyte collected from a constant analyte concentration. However, the example shown in **Figure 5** from Hook et al.[36] for the aromatic analytes shows that the uptake curve begins to flatten at around 1 min, making reproducible uptake practically achievable with a set pre-equilibrium sampling time. Schüpfer et al.[37] demonstrated that pre-equilibrium 10 min sampling of benzene, toluene, ethylbenzene and xylenes provided good sensitivity and reproducibility. Despite these advantages, direct SPME sampling of atmospheres with a fully-extended SPME fiber has not been sufficiently validated as to be published as standard, government-sponsored methods for industrial hygiene measurements in support of compliance with regulated or recommended exposure limit values. There are several reasons for this. For example, long-term (i.e. a full working shift) TWA sampling is not possible, gas-phase standards are required for calibration, and it is not possible to duplicate the analysis for quality assurance purposes, except by taking multiple samples. The use of SPME to rapidly screen for unknown organic analytes with GC-MS analysis has been repeatedly demonstrated, both in the field or with field-portable instrumentation,[36,38–40] and using laboratory instrumentation.[39,41] SPME sampling, especially in concert with on-site analysis, has been used to rapidly identify unknown air contaminants at various locations associated with emergency response activities. In 2011 Smith et al. described the use of a person-portable GC-MS instrument to rapidly screen several mixtures for correct ingredient listing in material safety data sheets that accompanied the products. While the vapor hazard ratio for the components disclosed to be present in a particular glue prioritized n-hexane as an exposure evaluation target, SPME/GC-MS analysis demonstrated that this compound was not actually present.[40]

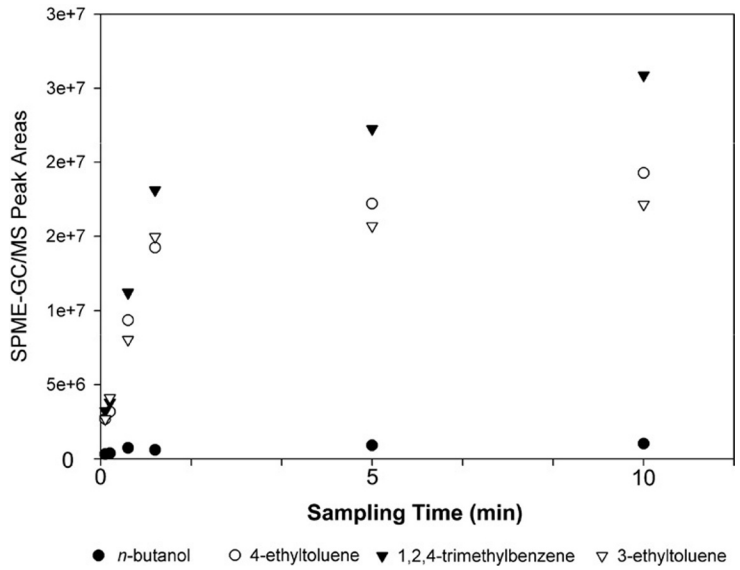

Figure 5 Uptake curves for SPME sampling of 1,2,4-trimethylbenzene, 3-ethyltoluene, 4-ethyltoluene, and *n*-butanol. The headspace above a mixture with equal volumes of each analyte was sampled using a commercially-available SPME fiber with 100 μm PDMS coating. From Hook et al.[36] Copyright (2002), with permission from Elsevier.

Sampling for semi-volatile compounds

Semi-volatile chemicals, such as pesticides, polychlorobiphenyls, and polyaromatic hydrocarbons, are normally sampled using a filter prior to the sorbent tube.[42–49] A range of filters is available, including glass or quartz fiber, cellulose ester and polymeric membranes (e.g. polyvinyl chloride, polypropylene, polycarbonate, polytetrafluoroethylene), as well as a range of sorbents, including polyurethane foam. This same arrangement can also be used where mists of volatile components are encountered, such as with oil mists and metalworking fluids. The filter is extracted with a solvent, which may be the same as that used for the sorbent portion of the sample. In fact, since these arrangements are not able to accurately distinguish aerosol and vapor phases (because of vapor absorption on the filter and particle evaporation from the filter), the filter and sorbent collection media are normally combined for desorption and analysis. Adsorbent-coated vapor denuders followed by filters are able to make a better distinction between vapor and particle phases, but are not often used for this purpose, even though knowledge of phase composition can be useful in understanding exposure routes and designing controls. Recently, such devices have been optimized for the collection of oxidant reaction products in air, such as carbonyl compounds, including carboxylic acids.[50]

Biological Sampling

Many occupational hygiene methods involve the analysis of breath, urine or blood samples. GC analysis may involve the chemical of interest or a metabolite such as the s-phenylmercapturic acid content of urine used as a monitor of benzene exposure. While breath sampling is the least invasive, it may not be the best estimate of exposure over a period of time, and is often the most variable. Urinary analysis is also quite variable, and correction for concentration is often made using the analysis of the creatinine component. Blood is the most difficult fluid to take on a regular basis, but blood is used in some regulations (e.g. for lead (Pb) exposure), and several organic vapors can be measured, most normally through headspace sample collection. The American Conference of Governmental Industrial Hygienists (ACGIH) TLV® booklet includes a listing of Biological Exposure Index (BEI®) values.[51] The most common procedure is to measure organic vapors in urine after headspace collection. The following chemicals with BEI's can be analyzed in urine through headspace analysis: acetone, dichloromethane, methanol, methyl ethyl ketone, methyl isobutyl ketone, 2-propanol (as acetone), tetrahydrofuran, toluene and trichloroethylene. Headspace analysis is particularly simple, and provides good results provided sample container losses are accounted for and transfer to the analytical system is rapid. Solvent in urine generally shows closer correlation with the exposure intensity than the corresponding metabolite(s), but it does not correlate as well as solvent in blood when the vapor concentration is low (e.g. < 10 ppm toluene).[52] Other organic compounds and their metabolites can be measured directly. Hydrolysis is required in the measurement of butoxyacetic acid as a marker for 2-butoxyethanol, furoic acid for furfural, cyclohexanol or 1,2-cyclohexanediol for cyclohexanol and cyclohexanone, and phenol as itself after liberation from its conjugates. For other analytes, e.g. 2,5-hexanedione for hexane and methyl ethyl ketone exposure, hydrolysis is not recommended. Other markers can be measured after derivitization. Examples are 1,2 dihydroxy-4-(N-acetylcysteinyl)-butane as a marker for 1,3-butadiene and p-nitrophenol for parathion. Other useful marker metabolites are s-phenylmercapturic acid for benzene and mandelic acid or phenylglyoxylic acid for styrene. There are some other chemicals for which gas-chromatographic procedures have been developed, but for which other procedures, especially liquid chromatography,

are generally preferred. For example, the analyte 2-thiothiazolidine-4-carboxylic acid as a marker of carbon disulfide exposure can be determined by gas chromatography, but it is not the preferred procedure; the same is also true of methylhippuric acids as a marker of exposure to xylenes.

Breath samples may be collected in special containers, or passed through sorbent tubes to concentrate the chemicals of interest.[53] The sample can then be introduced into a gas chromatograph using a gas-sampling loop, or through solvent or thermal desorption of the sorbent. The humidity of the exhaled breath is an interfering factor, as is also the presence of chemicals produced by normal biological processes within the body. The SPME technique is well suited for the pre-concentration of specific analytes before analysis.[54–56] Chemicals that are analyzed in breath for comparison of levels to BEI's include 1,1,1-trichloroethane, tetrachloroethylene and trichloroethylene. Styrene, tetrachloroethylene, toluene, trichloroethylene and 1,1,1,-trichloroethane (as trichloroethanol) can be measured in blood. Blood and urine samples are more difficult to analyze directly because of the matrix. Urine samples can be injected into a GC if the injection liner is replaced frequently, but blood contains surfactants and is a much more difficult medium. Liquid–liquid or liquid–solid extraction, static and dynamic head space analysis, or SPME have all been used as sample preparation techniques. Special care must be taken in the timing of the sample in relation to the work-periods, and also in the taking of the sample. For example breath samples should be of end-exhaled air, and blood samples should be of venous rather than capillary blood. In addition, some standards are based on total urinary excretion and others on urinary concentration. The sample container and the presence of sample preservatives are also important.

Analysis of biological samples

While gas chromatography is often the preferred technique for the analysis of organic compounds in the laboratory, many chemical of concern and their metabolites are highly polar, water-soluble compounds and liquid chromatography therefore can be the preferred analytical technique. As an example, much biological monitoring is performed with respect to pesticide exposures, especially to farm-workers and their families. A recent review of analytical methods for biological monitoring of exposure to pesticides[57] examined various classes of pesticides and herbicides (organophosphates, organochlorine, pyrethroids and phenoxyacetic acid herbicides) and concluded that most methods employed chromatography of some sort with mass spectrometric detection. While gas chromatography still appears to be the most widely employed technique, the authors also noted a recent trend towards more widespread use of liquid chromatography coupled with tandem mass spectrometry. Biological analysis also has to take into account the source of exposure, since even exposures to workplace chemicals such as benzene can have contributions from other sources (in this case including gasoline and cigarette smoking). Thus recent biomarker studies suggest environmental exposures to benzene are typically in the sub to low ppb range.[58] In addition to measuring biomarkers of exposure it is also possible to measure biomarkers of effect, for example chemically induced oxidative stress in cells from exposure to anaesthetic agents which results in aldehydic products of lipid peroxidation that can be analyzed in urine by gas chromatography with electron capture detection after derivitization with O-(2,3,4,5,6-pentafluorobenzyl)-hydroxylamine hydrochloride.[59]

Sources of Methods for Air Sampling with GC Analyses

NIOSH has been responsible for the NIOSH Manual of Analytical Methods (NMAM), now in its fourth edition. The NMAM is the largest repository of methods in the world, and many of its methods have been adopted by government agencies in other countries, such as the Health and Safety Laboratory of the U.K. **Table 1** gives a list of commonly used NIOSH methods for organic vapors together with the chromatographic columns used. Most of the methods use carbon disulfide (sometimes with a polar modifier) as the desorbing solution, and flame ionization detection. Another source of occupational hygiene sampling and analysis methods is the GESTIS database available at http://www.dguv.de/ifa/en/gestis/analytical_methods/index.jsp (Accessed May 16, 2013).

Validation of Methods

The validation of methods should encompass all stages of the method, including both the sampling and analysis steps. The NMAM contains details of the NIOSH method validation objectives, and a detailed validation manual for pumped sampling methods has been published.[60] In addition, NIOSH developed a protocol for the validation of diffusive samplers, which has been used commercially.[61] NIOSH has also supported the American Society for Testing and Materials (ASTM) Standard D6246 for evaluating the performance of diffusive samplers.[62] The US Occupational Safety and Health Administration (OSHA) Methods Manual contains similar documentation.[63] The U.K. Health and Safety Executive also has standard method validation protocols that similarly include the verification of numerous details needed to complete defensible sampling and analysis such as method precision, safe sampling volume, sample storage stability, effect of humidity on analyte sampling and analysis, etc. (e..g., as described in MDHS 27 for diffusive samplers).[64]

Sorbent Selection for Air Sampling Methods

The choice of chromatographic analysis procedure is intimately associated with the selection of the sorbent and the desorption procedure. Both the column type and the detector possibilities depend on the type of sample finally presented for analysis. While published methods give guidance, experienced analysts can develop or modify procedures to meet most eventualities. For example,

Table 1 Commonly used Methods for analyzing multiple related organic compounds in workplace air from the National Institute for Occupational Safety and Health Manual of Analytical Methods 4th Edition, DHHS/NIOSH Publication Number 2003-154, Cincinnati, OH. GC column evaluated for the Method is shown as well as a list of chemicals for which the Method has been validated. Detection and quantitation in each case is by FID

Method 5515 Polynuclear aromatic hydrocarbons	*Method 1500 Hydrocarbons BP 36–126 °C*	*Method 1501 Hydrocarbons aromatic (A)*	*Method 1501 Hydrocarbons aromatic (B)*	*Method 1003 Hydrocarbons halogenated (A)*	*Method 1003 Hydrocarbons halogenated (B)*	*Method 1550 Naphthas*	*Method 1450 Esters I*	*Method 1405 Alcohols Combined*	*Method 2555 Ketones I*
Column: 30 m × 0.32 mm ID, 1-μm DB-5	Column: 30 m × 0.32 mm ID, 3-μm 100% dimethyl polysiloxane	Column: 30 m × 0.32 mm ID, 1-μm polyethylene glycol	Column: 30 m × 0.53 mm ID, 3-μm Crossbonded® 35%diphenyl, 65% dimethyl polysiloxane	Column: 30 m × 0.32 mm ID, 1.8-μm diphenyl/dimethyl polysiloxane (Rtx®-502.2)	Column: 30 m × 0.53 mm ID, 3-μm Crossbonded® 35%diphenyl, 65% dimethyl polysiloxane	Column: 30 m × 0.32 mm ID, 1-μm DB-1	Column: 30 m × 0.32 mm ID, 0.5-μm DB-Wax	Column: 30 m × 0.32 mm ID, 0.5-μm polyethylene glycol	Column: 30 m × 0.53 mm ID, 3-μm Crossbonded® 35%diphenyl, 65% dimethyl polysiloxane
Acenaphthene	Benzene	Benzene	*p*-*t*-Butyltoluene	Bromoform	Benzyl chloride	Petroleum ether	*n*-Amyl acetate	*n*-Butyl alcohol	Acetone
Acenaphthylene	Cyclohexane	Ethylbenzene	Cumene	Carbon tetrachloride	Chlorobromomethane	Rubber solvent	*sec*-Amyl acetate	*sec*-Butyl alcohol	Methyl ethyl ketone
Anthracene	Cyclohexene	Toluene	α-Methylstyrene	Chlorobenzene	*o*-Dichlorobenzene	Petroleum naphtha	*n*-Butyl acetate	Isobutyl alcohol	2-Pentanone
Benz[a] anthracene	*n*-Heptane	Xylene (o, m and p)	Styrene	Chloroform	*p*-Dichlorobenzene	VM&P naphtha	*sec*-Butyl acetate	*n*-Propyl alcohol	Methyl isobutyl ketone
Benzo[b] fluoranthene	*n*-Hexane			1,1-Dichloroethane	1,2-Dichloroethylene	Mineral spirits	*t*-Butyl acetate	Allyl alcohol	2-Hexanone
Benzo[k] fluoranthene	Methylcyclohexane			Ethylene dichloride	Hexachloroethane	Stoddard solvent	2-Ethoxyethyl acetate	Diacetone alcohol	Di-isobutyl ketone
Benzo[ghi] perylene	*n*-Octane			1,1,1-Trichloroethane	1,1,2-Trichloroethane	Kerosene	Ethyl acrylate	Cyclohexanol	Cyclohexanone
Benzo[a]pyrene	*n*-Pentane			Tetrachloroethylene	1,2,3-Trichloropropane	Coal tar naphtha	Isoamyl acetate	Isoamyl alcohol	
Benzo[e]pyrene	Toluene			Trichloroethylene			Isobutyl acetate	Methyl isobutyl carbinol	
Chrysene							Methyl isoamyl acetate		
Dibenz[a,h] anthracene							*n*-Propyl acetate		
Fluoranthene									
Fluorene									
Indeno[1,2,3-cd] pyrene									
Naphthalene									
Phenanthrene									
Pyrene									

the analysis of benzene may vary depending on whether benzene has been collected as part of a simple or complex mixture, and whether it is necessary to quantify only the benzene or all components, whether the sample was collected on charcoal or a polymer sorbent, whether the desorption is with a simple solvent or a mixture or by heat, and whether detection is by flame ionization (FID), photoionization (PID) or mass spectrometry (MS). Silica gel is a highly polar and quite strong adsorbent, useful for very polar compounds such as methanol or amines. Strong adsorption of water is a problem when this sorbent material is used for other chemicals. Because of this, silica gel is used in specific applications, such as the collection of methanol with subsequent desorption by water and analysis on a packed Tenax column with FID. Charcoal is the most widely used sorbent for organic vapors. Various sources of charcoal are used, but in all cases the porosity has been enhanced by activation. Charcoals normally require solvent desorption. Anasorb® 747 is a popular charcoal from petroleum precursors that has wide application in OSHA methods.[65] Ambersorb®s are charcoals derived from controlled carbonization of organic polymers. Porous polymer sorbents include cross-linked styrene and divinyl benzenes, which can have relatively large pores (Chromosorb 102, Amberlite XAD-2) or smaller micropores (Chromosorb 106, Porapak or Hayesep Q, Amberlite XAD-4). Polar sorbents derived from acrylonitrile (Chromosorb 104, Amberlite XAD-7) or pyrrolidones (Porapak N, R) are also used. Tenax has a very small surface area and is normally only used for sampling low concentrations. It has the advantage of having a very low adsorption capacity for water. Because of its higher surface area and adsorption capacity, hydrophobicity, and compatibility with both solvent desorption and thermal desorption, Chromosorb 106 has been generally regarded as the most suitable polymer for occupational hygiene sampling.[66] However, if thermal desorption is used the upper temperature limit of Chromosorb 106 is only 250 °C, compared with 350 °C for Tenax or Carbotrap® (a graphitized carbon), rendering it unsuitable for the collection of semi-volatile components. Styrene polymers such as chromosorb 106 also tend to have significant background when used for thermal desorption of the low concentrations found in ambient or residential indoor air, so that Tenax or Carbotrap are better. Graphitized carbons are available in different surface areas (e.g. Carbotrap C is approximately 10 $m^2\ g^{-1}$ and Carbotrap B is approximately 100 $m^2\ g^{-1}$) and are used with thermal desorption in environmental applications. They have been used less often in occupational hygiene investigations, although NIOSH has documented a semi-quantitative screening method involving tubes containing multiple layers of sorbents including graphitized carbons in combination with carbon molecular sieves.[67] Carbon molecular sieves, such as the Carboxen™ series, can be used to sample the most volatile compounds, but have the disadvantage of also trapping large amounts of water vapor from atmospheres of high humidity. Sorbents are specified in the methods, but the literature[19,20] can also be consulted to assist in selecting the most appropriate sorbent. Field sampling personnel should always consult with their analytical laboratory.

Solvent Versus Thermal Desorption

There are significant drawbacks to the use of solvents for the recovery of chemicals from sorbent samples, not the least of which is the added hygiene and safety burden of handling a solvent such as carbon disulfide. Solvents do not always give 100% recovery, and recoveries significantly less than 75% may be associated with increased variability in the precision of recovery. It may be difficult to optimize a solvent for best recovery of a mixture of polar and nonpolar chemicals, and the solvent may interfere with the analysis of chemicals in the mixture. There are special problems relating to the adsorption of water from atmospheres of high humidity, and its subsequent release from the sorbent on addition of the desorbing solvent. For example, charcoal can adsorb large quantities of water (hundreds of milligrams per gram) from atmospheres of humidity greater than 50%. This water is displaced by carbon disulfide but does not mix with it. Polar compounds such as acetone can partition into the separate water phase causing an apparent drop in recovery. Several options have been developed to deal with polar compounds, including adding a polar modifier (e.g. 2-propanol or dimethylformamide) to carbon disulfide, or switching to an altogether different solvent (e.g. 95% dichloromethane/5% methanol). However, it is difficult to substitute entirely for carbon disulfide because of its low FID response and its good recovery of nonpolar compounds. New carbon sorbents such as Anasorb 747 exhibit much better adsorption and desorption properties under these conditions. When using polymer sorbents, care must be taken in the choice of recovery solvent. While styrene polymers are compatible with most solvent systems, Tenax will swell in some solvents, and pyrrolidone polymers may dissolve.

Thermal desorption is an alternative where a sorbent tube is heated while a stream of carrier gas removes the collected vapors. Because this transfer can take several minutes the recovered vapors are usually focused in a secondary trap. There are several varieties of secondary trap in common use, including large sorbent traps kept at ambient temperature, open capillary tubes cooled cryogenically, and narrow-bore sorbent traps kept at sub-ambient temperatures by Peltier cooling. The latter method provides for rapid transfer of the analytes to the column when the small secondary trap is heated, with effective transfer of compounds in the range C_2–C_{30}, and without risk of ice blockage or condensation of permanent gases such as oxygen. Some specialized analyses of thermally labile compounds such as nerve agents or vesicants may require derivatization prior to desorption. Thermal desorption methods have existed since the mid-1970s, but this approach has not significantly replaced solvent desorption in most countries for several reasons. Efficient thermal desorption requires a sorbent with less attraction for the vapors of interest than charcoal. The use of sorbents with lower surface areas and smaller capacity can lead to premature breakthrough of the sample during the sampling period. Sorbent tubes for solvent desorption are designed with a 'back-up' sorbent section that can be analyzed to detect such breakthrough but sorbent tubes for thermal desorption are not. There are also quality assurance issues that must be addressed, for example, in calibrating the analysis (standards must be added as solutions to blank tubes and then the solvent removed), using internal standards (more easily added to a solvent) or making multiple analyses (which for thermal desorption analyses used to require taking multiple samples). Water management can also be a problem with thermal desorption of real-world samples. The

transfer of desorbed water onto a capillary chromatographic column can alter the pressure gradient across the column and the polarity of the system, changing both retention times and peak areas. Where sorbent tubes contain hydrophilic sorbents their performance can be improved by drying the sample with 300 ml of helium prior to desorption. Thermal desorption is often used for the analysis of canister samples, with the contents of the canister being drawn through the secondary trap or focusing tube, which is then desorbed and analyzed. Water management may also be necessary in the analysis of canister samples. The U.K. Health and Safety Laboratory is the main source of published thermal desorption methods for occupational hygiene analyses, but NIOSH has one thermal desorption method for semi-quantitative investigations.[67]

One important major advantage of thermal desorption is the possibility of increasing the quantity of sample that can be placed on the chromatographic column by means of the secondary focusing trap. Recent developments in optimizing the technology now allow complete on-column injection of an entire sample, improving detection limits as much as two orders of magnitude over solvent injections. This is very useful for ambient and indoor air investigations at ppb levels, and also makes the system attractive for workplace analyses where there are chemicals with exposure limits at 1 ppm or below (e.g. benzene). When using thermal desorption for such trace analyses particular attention must be paid to the background levels of the sorbent (typically no more than 1 ng per component and 10 ng total) and handling, transport and storage procedures for the tubes. Thermal desorption also has potential applications in the analysis of biological samples, either through sorbent trapping from breath, or from direct heating of blood or urine samples. Both solvent and thermal desorption systems can be automated. Woolfenden recently reviewed sorbent-based thermal desorption, and described improvements and new applications for this sampling and analysis approach.[20] Accessories are now available for collection of analyte vapors from exhaled breath and emissions from products and materials onto standard 89 mm length thermal desorption tubes. Also, recent equipment models that allow re-collection of split flow during thermal desorption onto a clean tube overcome the problem with thermal desorption being considered as a "one shot" method. Most of the desorbed analyte collected during sampling is not analyzed when a high split ratio thermal desorption method is used, and re-collection can allow for several analytical events from a single sample. Sample re-collection is also used to verify analyte recovery in several international thermal desorption standards.[68,69]

Types of Columns

When methods were being selected and validated in the early 1970s capillary chromatography was not far advanced commercially. Nor was it particularly necessary, since neither sensitivity nor selectivity was an issue. Typical occupational exposure limits at that time ranged from 10 to 1000 parts per million by volume of air for an 8 h TWA concentration. Assuming a full-shift sample using a sample tube operated at 20 ml min^{-1} (approximately 10 l of air), the tube could contain up to 10 mg of sampled chemical. Even if this were diluted in several milliliters of solvent, a single injection into the gas chromatograph typically contained micrograms of the chemical. In addition, chemicals were less often used in complex blends, so that interfering peaks were less common. Typically, the only separation required was between the solvent, a single chemical in the sample and an internal standard. This was achieved easily with 1/8th inch (3.2 mm) packed columns, even in isothermal mode, and this procedure could be extended to cover many simple solvent mixtures used in industrial applications.

Packed columns continue to be used today for analysis of permanent gases, such as the sulfur gases (sulfur dioxide, sulfur trioxide, hydrogen sulfide, carbonyl sulfide, carbon disulfide and mercaptans), or for very volatile compounds such as 1,3-butadiene. The packings are typically zeolite or carbon molecular sieves, or, in the case of the two examples just given, alumina-PLOT columns have been used. However, as occupational exposure limits continue to fall (on average by an order of magnitude between 1980 and 1990), and the number of regulated chemicals increases and complex mixtures become more common, there is a distinct move towards the use of capillary columns, which is supported by laboratories wishing to speed up analytical procedures. This has been recognized by NIOSH, which has recently updated the methods in the NMAM to include capillary columns. The typical modern occupational hygiene laboratory will have a collection of capillary columns from 15 to 100 m length, both microbore ($\leq$0.32 mm) and megabore (0.53 mm), with different stationary phase films and thicknesses. A standard all-purpose column might be a DB-1 or DB-5 or equivalent. A typical example of a complex analysis is the determination of trace benzene (ACGIH TWA threshold limit value (TLV®) for 2013 is 0.5 ppm[51]) in the presence of gasoline (see **Figure 6**).

Resistive Column Heating

Writing of portable GC instruments only a little more than ten years ago Burroughs and Tabor noted that "portable instruments must compromise between the need for power required to achieve high temperatures (greater than approximately 100 $\pm$ °C) or temperature programming, and the need to minimize weight by limiting battery size."[70] Thus, very early field-portable GC instruments operated at ambient temperature, and as instrumentation designs progressed relatively low isothermal heating was used.[71] In about the last ten years however substantial improvements have been made to the capabilities of field-portable GC instruments, with the most important being the commercial availability of low thermal mass (LTM) GC column assemblies which are resistively heated. In combination with the advent of high power density Li-ion batteries, when the heated zones of a portable GC instrument are kept as small as possible and are well-insulated, high temperature operation and even rapid column temperature programming are now possible. For instance, the shift away from convection oven column heating to the use of LTM column

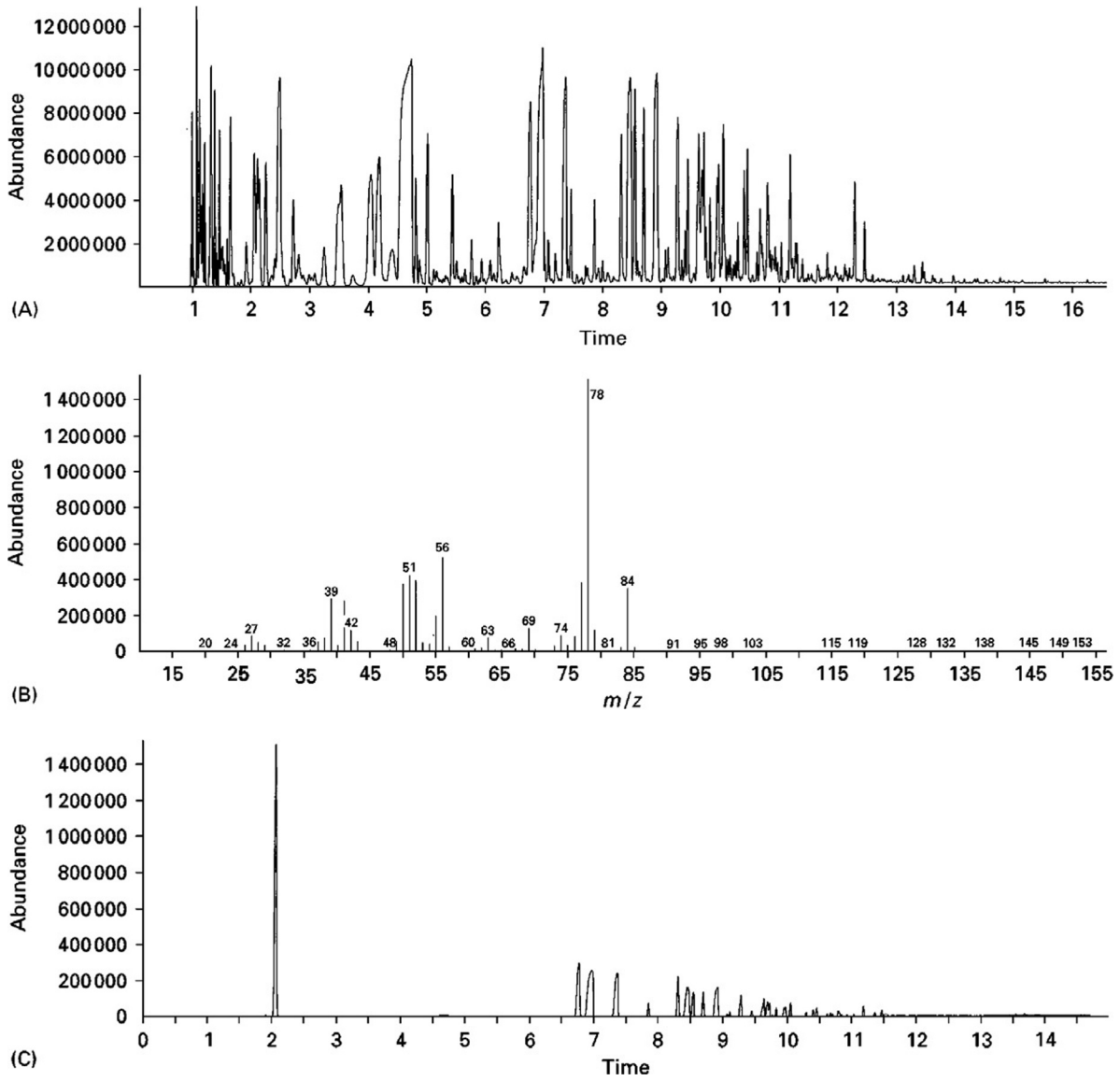

Figure 6 Determination of benzene in gasoline using GC-MS. The GC column was a 5% phenylmethylsiloxane HP-5MS. (A) Total ion chromatogram (note an FID trace would be similar). Retention time of benzene is 2.06 min. (B) Mass spectrum of peak at 2.06 min resolves interference from a C6H12 compound. (C) Single ion scan at *m/z* 78 can be used to quantify benzene.

assemblies with resistive heating has allowed the construction of portable GC systems (to be discussed below) capable of fast temperature ramping, even in one case for up to twenty analysis events over a two-hour period while operating on battery power.[40]

The migration away from packed GC columns towards small diameter open tubular columns that occurred in the 1980s was made possible by the use of high-purity fused silica for column construction, and this provided a strong and inert inner surface onto which a variety of stationary phases could be bonded. The small diameter open tubular GC column is capable of high resolution separations, and also coincidentally has a very low thermal mass. In 1984 as the fused silica open tubular GC column design was replacing the older packed column design Lee et al. recognized the potential to greatly reduce the heating power requirement and increase the speed of column heating with direct resistive heating of the more modern open tubular column which has a much smaller thermal mass compared to an entire convection oven.[72] While a number of resistive heating approaches have been tried, a relatively simple design was described by Ehrmann et al. in 1996 where two separate wires were placed along the length of an open tubular fused silica column, with one wire used to read back column temperature through temperature-dependent changes to resistance, while the other was used to heat the column with the application of voltage producing heat.[73]

In 2001, Sloan et al. described a resistive column heating approach developed earlier by Mustacich and co-workers where a Ni/Cr resistive heating wire was placed within a ceramic fiber sheath, and this was wound in a bundle with a fused silica column.[74] The ceramic fiber sheath prevented hot spots along the column, and helped to distribute heat within the LTM column assembly that

was completed by wrapping the resulting toroid with Al foil. A thin Pt wire was also included within the LTM column assembly, and as the temperature within the column assembly changed, the resistance of this temperature sensing wire would also change predictably. Microprocessor control cycled voltage to the Ni/Cr wire in response to readings from the Pt sensing wire, providing for very fast temperature program operation while using much less power compared to a convection oven; less than 100 W was needed even when ramping at rates as high as 120 °C min^{-1} up to a final LTM assembly temperature of 270 °C. This resistively heated LTM column began to be marketed commercially by RVM Scientific around 2001, and the product line was purchased by Agilent Technologies in 2008 for use in an Agilent field-portable GC-MS instrument. Additionally, the RVM (now Agilent) LTM column design is supplied to three other field-portable/person-portable GC-MS manufacturers. More recently, Stearns et al. described two additional approaches to resistive heating of an LTM column assembly in 2010;[75] either a single Ni wire or Ni cladding over a fused silica capillary is used to both heat an LTM column assembly and to sense temperature through changes to electrical resistance, and these resistive column heating methods have been commercialized by Valco Inc. (VICI).

Portable Gas Chromatographs

To date, portable gas chromatographs have not been used for compliance monitoring by OSHA, nor have they replaced traditional personal sampling methods. Portable gas chromatographs have the advantage of near real-time response, which can be combined with observation of the work activity, for example by video monitoring, to gauge the effect of different work practices and control measures. Other applications include exhaled breath analysis, measuring the penetration of organic chemicals through protective clothing, providing assurance of safe entry into confined spaces, monitoring at hazardous waste sites and spills, and the protection of deployed military forces. The earliest portable GC method evaluated by NIOSH involved a PID for analysis of trichloroethylene published in 1987 (updated in 1994).[76] At that time, the columns were large bore and unheated, so that interference from other chemicals was likely. No interferences were evaluated as part of the method validation and the user was cautioned not to rely on results from complex atmospheres. In 1994, NIOSH also published a method for benzene determination by portable GC-PID,[77] and again the limitations of the equipment available at the time meant a caution was necessary that in the presence of significant interference the limit of detection could approach or exceed typical limit values. These methods were intended more for the direct determination of benzene in air, although it allowed longer-term samples through collection of air over time into a sample bag. In 1998, a NIOSH method for perchloroethylene in end-exhaled breath and air was published.[78] The high humidity of exhaled breath was considered likely to influence the PID, and so sampling was through a dessicant into the sampling bag. The dessicant caused a potentially correctable negative bias, as did sample storage in the bag over time. The microbore column evaluated was able to separate perchloroethylene from common metabolites and chemicals likely to be present in dry-cleaning situations. A method for ethylene oxide in sterilization facilities[79] is of little use now that ethylene oxide has been largely superseded in hospitals. A method for ventilation testing using sulfur hexafluoride involves GC-ECD,[80] while a method for carbon dioxide uses GC-TCD.[81] Though the program of evaluating portable GC instrumentation was not extended beyond the late 1990s by NIOSH, more recently, a Division of NIOSH evaluated the performance of some portable handheld PIDs (without GC inlet), but without resulting in the publication of specific NIOSH methods.[82]

Several of the detectors used in GC, especially the FID and the PID, are often used as stand-alone instruments for 'total' hydrocarbon or VOC analysis, and these are often calibrated to a standard concentration of an alkane (or alkene) in air. These detectors may also be used with a portable gas chromatograph to transfer laboratory analytical techniques to the field. In the past, some GC instruments operated at ambient temperatures, but these were limited to analysis of gases and very volatile compounds; currently most have some capability for either isothermal column heating or temperature programming. Both packed and capillary column instruments are available, but since the introduction of capillary columns in the early 1980s these have become standard. A detection limit of 0.1 ppb is claimed by one manufacturer (probably for an ECD), but most are higher, up to 0.1 ppm using PID or FID-equipped instruments. Some are available with an option for different detector or injector types. Most can be linked to a personal computer for data analysis. Several transportable GC instruments exist that require mains power but a number of person-portable GC instruments are available with the capability to operate in some cases for up to 8 h. The commercially-available person-portable instruments are relatively large and heavy, and none are truly considered 'personal' samplers. Burroughs and Tabor reviewed portable gas chromatographs in 1999,[70] defining a portable gas chromatograph as "one which weighs less than approximately 50 lbs. (20 kg), and is capable of operating independently of external power" (hereafter referred to as "person-portable GC instrumentation). Burroughs and Tabor noted that manufacturers "reduced both the size and weight of the analytical equipment, yet at the same time included options such as internal batteries and cylinders for carrier gas not necessary for laboratory instruments." As was the case in 1999, four non-orthogonal detectors are still widely used: the PID, the FID, the ECD, and the TCD. A first generation person-portable GC instrument with a mass spectrometric detector (GC-MS) that met the 20 kg definition of "person-portable" was marketed beginning in the 1990s, and has been updated with improvements several times in the intervening years. A second generation person-portable GC-MS instrument capable of extended operation time and fast column temperature ramping to >300 °C has been developed recently by incorporating resistive column heating as previously discussed, and both of these GC-MS instruments will be discussed further below. The available person-portable GC instruments described by Burroughs and Tabor in 1999 allowed "samples to be introduced directly from the environment, or to be collected in inert plastic bags or evacuated containers for injection."[70] This approach allows such GC instruments to process time-integrated samples with introduction from a gas-tight syringe, or from a built-in sample loop filled by an internal pump to give semi-'real time'

measurements. Much work has been completed to develop and use new solventless analyte concentration methods with person-portable GC systems, exemplified by SPME[83] and needle trap sorbent devices.[71] Also, traditional thermal desorption methods have been adapted to commercially-available person-portable and transportable GC-MS instruments.

Portable GC instruments are substantially more expensive compared to a simple handheld detector such as a handheld PID which has no separation capability. In addition to the cost to acquire portable GC instrumentation, transportation and attainment and maintenance of user proficiency should also be considered. A common problem encountered by users of portable GC instrumentation is that "compressed gases (for carrier gas or instrument calibration) cannot be taken aboard passenger aircraft either as checked or carry-on luggage"[70] although electrolytic generation of H_2 carrier gas from pure water has been used, especially in van-mounted instrumentation, to avoid this problem. When used, radioactive sources (e.g. found in an ECD) also complicate air transportation. In some cases ambient air may be used as a GC carrier gas, and while this limits the column operating temperature and detection limits and separations are not as good as with helium, no compressed gases are required for instrument operation if the detector is a PID, or an FID with hydrogen generated by electrolysis of water. Prior to about the year 2000, column temperature ramping was not common for person-portable instruments (defined as not only weighing <20 kg, but also being capable of operating with battery power and self-contained carrier gas) due to the prevalence of convection oven heating at that time. Not only is repeated heating of a relatively large convection oven a problem for a battery-powered instrument, but lengthy cool-down times are also problematic. However, as described earlier, the commercial availability of resistively heated LTM column modules has revolutionized the ability to aggressively heat the GC column for both transportable and person-portable GC instruments with a very small column module that uses little power and cools fairly rapidly at the end of a run. Person-portable GC instruments with a variety of non-orthogonal detectors are currently produced by Photovac (recently acquired by Inficon) and PID Analyzers LLC. Until recently the Photovac Voyager was available as an intrinsically safe person-portable GC with a PID and an optional ECD. The Photovac Explorer™ is stated to be virtually the same instrument, although without intrinsic safety certification. A range of detectors are available for the Model 312 person-portable GC manufactured by PID Analyzers LLC, including PID, TCD, FID, flame photometric detector (FPD), far uv (FUV) detector, and a catalytic combustion detector. Both of these person-portable GC instruments employ relatively low-temperature isothermal heating in a small convection oven to conserve battery life. Details regarding the more commonly encountered detectors found in these person-portable GC detection systems (as well as in laboratory GC instruments) are discussed below.

Transportable and Person-Portable GC-MS

The need for high-certainty data to protect deployed military forces has driven substantial development in transportable and person-portable GC-MS instruments in the recent past, and these advances are briefly described below. The GC-MS systems operated by military organizations for field chemical detection and identification typically employ solvent-free sample introduction methods such as SPME, needle trap sampling, and thermal desorption approaches.

Field-portable GC-MS instruments

Field-portable GC-MS instruments that employed convection oven column heating were built in relatively small numbers during the 1980s and 1990s. An example is the Viking 572 instrument described by Eckenrode in 2001.[84] This instrument was used to rapidly address air quality concerns related to extensive forest fires to guide selection of appropriate sampling methods and locations for later traditional analyses that were completed in a laboratory. As summarized by Smith and Driscoll,[85] two primary benefits typically result from the use of field-portable GC-MS, and these were demonstrated in Eckenrode's work: "(1) The ability to identify unknown analytes within minutes or hours, and (2) The ability to rapidly change sampling and analysis strategies based on immediate feedback. These factors are critical in situations where the public health is threatened, as traditional sampling and analysis approaches (even when expedited) can take from hours to days to provide actionable data," and, even longer, if the wrong analyses are requested.

The Viking instrument included an on-board two-stage thermal desorption capability and a direct membrane inlet to the mass spectrometric detector for very rapid determination of high-purity volatile analytes without the benefit of chromatographic separation. A heated injector was included with the capability for traditional liquid and SPME injections. The convection oven design exposed limitations related to excessive power consumption and limited temperature programming and cooling rates. Also, this instrument required an external supply of carrier gas and battery operation was not possible. The revolutionary improvements in heating rates and power consumption made possible by the advent of commercially-available LTM GC column assemblies around 2001 led Smith et al. to demonstrate the improved performance possible for a transportable GC-MS instrument in 2005. They added a LTM column assembly to a Viking instrument and demonstrated rapid separations of chemical warfare agent analytes (including a high molecular weight T-2 toxin) in under 3 minutes.[86] In this paper the construction of a small transportable GC-MS instrument was also demonstrated by combining a LTM column assembly and heated injector to an Agilent 5973 mass spectrometric detector. This configuration can be considered as the forerunner to the commercially-produced Agilent 5975T instrument, which combines the operating characteristics of the well-known commercial transmission quadrupole detector with the reductions in size, weight, and power consumption associated with the use of resistive column heating.

At about the same time Griffin Analytical (since purchased by FLIR) developed the Griffin 450 transportable GC-MS instrument that combined a resistively heated LTM column assembly with a cylindrical ion trap mass spectrometer. Due to the use of internal ionization, this ion trap design displays mass spectra with evidence for ion/molecule interactions, e.g. production of protonated

molecular ions and dimers, and this varies depending on the mass of a specific analyte which is injected.[87] This instrument includes a docking port and an internal focusing trap that receives analytes sampled remotely by a handheld pump module that contains several stainless steel thermal desorption tubes. Upon docking to the transportable GC-MS instrument, power and helium carrier gas are transferred to the module for thermal desorption.

Person-portable GC-MS instruments

Variants of the Hapsite™ person-portable GC-MS instrument (Figure 7) have been available since the 1990s. All of these use a linear quadrupole detector separated from an open tubular GC column by a polymeric membrane. The need for the membrane interface results from the use of a nonevaporative getter (NEG) vacuum pump to avoid a mechanical MS vacuum system. The earliest version of the Hapsite™ had no provision for analyte concentration, as air was pumped into a fixed-volume sample loop for direct injection with no analyte preconcentration. A small internal sorbent trap and associated valving were added around 2001, and several years ago the Hapsite ER™ was introduced with the capability for thermal desorption of a SPME fiber or an 89 mm thermal desorption tube. However the "extended range" version cannot complete these types of analyses unless operating on stable external power due to the higher temperatures used for the heated zones compared to analysis of a direct air sample through an approximately 1 m heated inlet (typically kept at 40 °C). The analysis speed and chromatography for the version of this instrument that was available in the early 2000s (first variant with analyte concentration capability) were described in 2004.[88] The various configurations of this instrument made available over the years and similar details for a second-generation person-portable GC-MS instrument (discussed immediately below) have been described by Smith in a recent review that covers advances in person-portable GC.[71]

In 2008, Contreras et al. described a toroidal ion trap mass spectrometer that was interfaced with a resistively heated LTM GC column module, with a total weight of <13 kg.[89] Refinements to this instrument were largely driven by the U.S. Department of Defense, and at this writing a commercial product weighing 14.5 kg has been available for several years, co-marketed by Torion Technologies and Smiths Detection. The heated zones of this instrument are considerably smaller than those of the larger 19 kg Hapsite™ instrument, and a direct MS interface is made possible with mechanical vacuum pumping. Initially sample introduction was limited to SPME, but injection from a side-hole needle trap sampler is now possible. Also, a small modular battery-powered sample desorption module is available for desorption of standard 89 × 6.4 mm o.d. tubes onto a needle trap sampler to allow collection of high-volume samples on the bigger tube. The needle trap sampler (with analytes desorbed from the large sorbent tube) focuses the analytes in a small sorbent volume for efficient injection, in analogous fashion to secondary trapping by a laboratory-based thermal desorption system. The modular approach is different than that taken by the developers of the larger first-generation instrument which includes an onboard air sampling pump and a pre-concentration trap for integrated air sampling, and one performance difference is the ability to start and operate the newer instrument on battery power for up to two hours. Also, the range of volatility for potential analytes is greater for the Torion instrument due to the use of small, high temperature heated zones along a well-insulated analyte flow path. Smith et al. demonstrated the ability to detect high molecular weight polychlorinated biphenyl compounds with the newer GC-MS instrument.[40] The LTM GC column module used in the second-generation instrument is a 5 m section of 0.10 mm i.d. column with 1.5 μm 5% phenyl polydimethylsiloxane stationary phase, and this narrow bore column lessens the vacuum demand placed on the mechanical pumping system used. Also, the mechanical pumping demands are somewhat aided by the use of an ion trap detector (which has less stringent vacuum demands compared to a transmission quadrupole instrument). As with the transportable Griffin instrument discussed above, internal ionization and ion storage lead to the production of non-standard mass spectra. The second-generation person-portable GC-MS instrument is depicted in Figure 8, and a chromatogram produced with analyte introduction from a side-hole needle trap is shown in Figure 9.

Figure 7 Hapsite™ person-portable GC-MS instrument deployed in the field. (1) Sample collection probe; (2) control keypad on instrument faceplate; and (3) interface for attachment of the instrument to a servicemodule containing mechanical vacuum pumps (service module usable only when AC power is available). From Smith et al.[88] Copyright (2004), with permission from Elsevier.

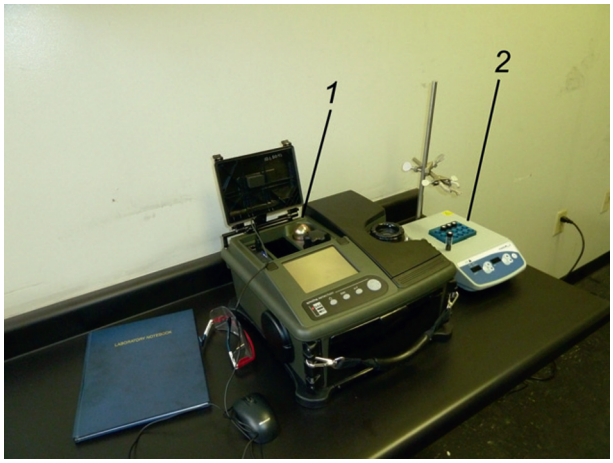

Figure 8 Guardion 8™ person-portable GC-MS instrument operating in the field. (1) Disposable high pressure helium bottle, and (2) heater block to control the temperature of material during SPME sampling from within a sealed vial. From Smith.[71] Copyright (2012), with permission from Elsevier.

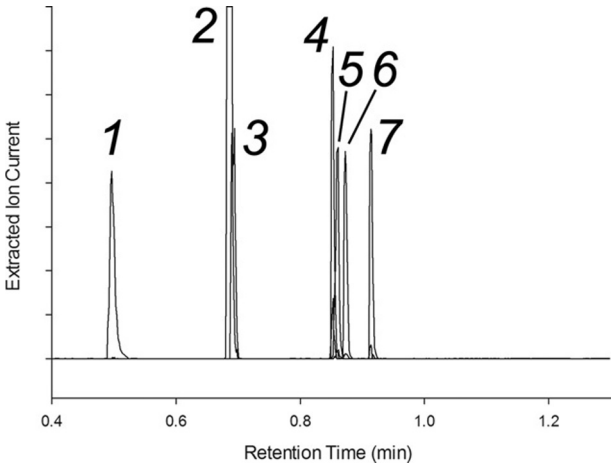

Figure 9 GC-MS analysis using person-portable toroidal ion trap instrument described in the text. Extracted ion traces produced from a needle trap sample (1.5 mg carboxen™ 1000 behind 2.0 mg Tenax TA™ in a 19 gauge needle), 25 ppm nominal analyte concentrations. The respective relevant *m/z* values for extracted ion traces are indicated for target BTEX analytes and internal standards: (1) benzene (*m/z* 78), (2) toluene-d_8 internal standard (*m/z* 98), (3) toluene (*m/z* 91), (4) bromopentafluorobenzene -internal standard (*m/z* 117), (5) ethylbenzene (*m/z* 91), (6) p-xylene (*m/z* 91), (7) o-xylene (*m/z* 91). Air sample collected for target analytes by pulling a twenty ml volume of air through the needle trap device with a gas-tight syringe, followed by sampling a known volume of the internal standard vapors. The resistively heated column was held at 30 °C for 10 s, followed by ramping to 270 °C at 120 °C min^{-1}. From Smith.[71] Copyright (2012), with permission from Elsevier.

Types of Detectors

Flame Ionization Detector (FID)

First described in the literature in 1958,[90] the FID has been the traditional detector of choice in industrial hygiene analyses. It has widespread utility since the majority of organic compounds burn in a hydrogen-oxygen flame, producing ions. The movement of these ions in an electric field results in a measurable ion current. It has a very wide linear range. With packed columns, limits of quantitation range typically from 2 ng to 20 ng of analyte per injection. The sharper peaks obtained with capillary columns can allow quantitation at lower concentrations, but this must be balanced against the smaller sample loading possible onto a capillary with less capacity. Sample loading can be increased by using megabore capillary columns, or by preconcentration at the injection stage. Overall limits of quantitation of 0.1–1 ng per injection are possible. Halogenated hydrocarbons do not provide as many ions in the flame and therefore have lower relative detector response. In addition, reactions with remnant ions from the carbon disulfide solvent can alter the response of halogenated hydrocarbons at low concentrations. Handheld FID detectors without separation have been used for many years. However, a worldwide low ppm concentration of methane in ambient air limits the use of stand-alone FID to the detection of hydrocarbons at higher ppm concentrations. The use of a GC separation method thus improves detector sensitivity. The need for pure H_2 to support the FID combustion flame adds complexity to logistical concerns when this

detector is to be used in a field-portable instrument, although the PID Analyzers Model 312 person-portable GC addresses this issue by using H_2 as the carrier gas when this detector is included, and the same gas supply is used for the FID combustion flame.

Photoionization Detector (PID)

As currently used, the PID was first described as a GC detector in 1976.[91] Whether used as a stand-alone (handheld) detector or as a GC detector, one of the positive attributes of a PID is that a special detector gas is not required. This makes the PID a good choice for a portable GC detector (where it appears more often than in the laboratory) when target analytes exhibit ionization potential values that will allow detection. The PID is very useful, for example, for the detection of aromatic hydrocarbons in the presence of aliphatic hydrocarbons (e.g. benzene in gasoline). Importantly, the use of a PID as a GC detector avoids the well-known problems that occur when a PID is used as a stand-alone detector: humidity,[92–94] high concentrations of methane (which absorbs uv energy but is not ionizable nor detectable using typical PID lamps),[95] and either high or low oxygen concentrations[96] have been shown to effect the ability to quantitatively detect a target analyte with a handheld PID. Oxygen has a ionization potential (IP) of 13.61 eV and thus is not detected by a handheld PID equipped with any of the commonly used PID lamps, however Driscoll found that a negative GC-PID peak was produced when O_2 eluted into this detector.[97] This was attributed to the quenching of cations by O_2^- produced in the ion chamber by electron capture. Issues such as this must be considered when a handheld PID is used in the field, but when an analyte elutes from a GC column into a PID after separation from other injected components present in a sample, the influence of other atmospheric gases and vapors is eliminated.

Thermal Conductivity Detector (TCD)

The TCD is acknowledged to lack the sensitivity of many other detectors, and thus it is not commonly used in the laboratory except for an application such as whole-air composition analysis with an adsorptive stationary phase capillary or packed column. However its simple operating principles and suitability for use in field applications where the measurement of percent composition of gases and light vapors account for its continued availability in a person-portable instrument such as the PID Analyzers Model 312 GC system. The TCD may be used behind a short packed column suitable for the separation of light gases. For instance the National Institute for Occupational Safety and Health (NIOSH) method 6603 for CO_2 by gas chromatography (portable)[81] was published with a description of a GC/TCD method that used a 1.5×6 mm i.d. stainless steel column packed with Porapak QS stationary phase to separate CO_2 from other gases typically present in ambient air.

Electron Capture Detector (ECD)

The ECD operates through the attenuation of current from a steady stream of electrons emitted from a source. When the applied accelerating voltage is constant analytes with a high electron affinity that elute from a GC column enter the detector and capture a portion of the electrons, reducing the current at the detector anode, and producing a signal that corresponds to the presence of analytes with affinity for electrons. The ECD is often used in the industrial hygiene laboratory for specialized applications, for example, to measure halogenated compounds such as organochlorine herbicides and polychlorinated biphenyls. Its high sensitivity also allows detection of halogenated derivatives, such as bromoethanol from the hydrobromination of ethylene oxide, a suspect carcinogen with a low exposure limit value. Since Lovelock described the ECD in 1960[98] a radioactive electron source has typically been used, often ^{63}Ni (typical for laboratory GC instruments) as with the Photovac Explorer™. Tritium (specifically titanium titride adsorbed to a stainless steel foil) is used in the ECD of the field-portable Lagus Autotrac instrument manufactured by Lagus Applied Technology, Inc. for measurement of SF_6 tracer gas.

Nitrogen-Phosphorous (thermionic) Detector (NPD)

The NPD is a delicate detector making use of ionization of certain compounds in the presence of hydrogen on the surface of a heated catalytic bead. It is not used in the field but it has an extraordinary sensitivity for certain organonitrogen and organophosporous compounds, and is used in the industrial hygiene laboratory for the direct analysis of organophosporous pesticides and the indirect analysis of formaldehyde after derivitization with hydroxymethylpiperidine (HMP). In the latter analysis, HPLC with UV analysis of 2,4-dinitrophenylhydrazone derivatives is often preferred because of its wider general application to other aldehydes, but in the analysis of acrolein in air the HMP derivatization and GC-NPD analysis procedure has the advantage of high sensitivity, and excellent separation of a single peak.

Flame Photometric Detector (FPD)

Brodey and Chaney described the FPD in 1966, and noted that when compounds that contain either sulfur or phosphorous are burned in a hydrogen flame, emission occurs respectively at 324 and 520 nm.[99] The use of dual channel photometry allows for both sulfur and phosphorous emissions to be monitored simultaneously. An improved version of this detector was described by Atar et al. in 1991, where the resolution of emission over time is possible when a short duration flame pulse is repeated.[100] In addition to detection of analytes that contain either sulfur or phosphorous as with a standard FPD, the pulsed FPD (PFPD) allows

the detection of other elements due to differences in emission timing that are element-specific. The PFPD is offered as a detector on the MINICAMS transportable GC that is marketed by OI analytical. The MINICAMS instrument is well-known in the chemical warfare agent (CWA) demilitarization community, as it has been widely used for environmental monitoring during CWA destruction mandated by multilateral international treaty. Several stand-alone FPD detectors without GC have also been marketed (Proengin, France) for use by military organizations and first responders in potential cases of chemical warfare agent use.

Mass Spectrometric Detectors

Mass spectrometry (MS) has become popular for the analysis of trace organic components in the atmosphere through methods promulgated by the U.S. Environmental Protection Agency (EPA).[101] A quote from EPA researchers published in 1975 explains the rise of GC-MS at that time in response to the study of environmental contamination and summarizes the importance of GC-MS: "any technique that left ambiguity in the analytical results was likely to lead to continual controversy and litigation."[102] The development of linear quadrupole detectors has allowed the rapid scan of spectra in the timescale of a capillary peak, and when the spectra are matched to a reference library compound identification is possible, especially when this information is cross-referenced to specific compound retention times (typically following Van den Dool and Kratz linear temperature program retention indices).[103] However, because MS detectors have been costly to purchase and maintain, while FIDs have had adequate sensitivity and the compounds of interest are usually known in advance, MS methods have not often been developed for occupational hygiene analyses. This is changing and a recent example from the NMAM (method 2539)[104] is a screening method for aldehydes (**Figure 10** and **Figure 11**). In investigations of the quality of ambient or indoor air, the dilution of the sample by solvent desorption effectively puts most contaminants below the limits of quantitation of both the FID and MS, and the use of desorption solvent also precludes detection of analytes that elute during a typical solvent delay time for MS startup. The mass spectrometer therefore is most suitable in combination with thermal desorption for sampling multiple unknown contaminants, often at low concentrations. For this application a semi-quantitative NIOSH screening method (method 2549)[67] has been developed. MS in single-ion mode can increase detection limits by a factor of 10 or more. Two examples are given showing the usefulness of the MS detector in compound identification and quantitation. Both involve the analysis of benzene in complex samples. In **Figure 6** the single peak at the retention time of benzene is resolved in the MS scan as a mixture of benzene and another compound (possibly cyclohexane). In **Figure 12(B)** the single peak is resolved into benzene and butanol. In both cases benzene could be quantified at low concentrations without interference by measuring the *m/z* 78 ion in single ion mode. Mass spectrometric detection has become popular for the GC analysis of field samples collected onto thermal desorption tubes in occupational hygiene investigations, especially with respect to nuisance odors.

Quality Assurance

The number of samples taken per investigation will depend on the number of exposed workers and the perceived extent of any problem and may vary from one to several hundred. The best choice of laboratory for analyzing occupational hygiene samples is one that specializes in such samples and accepts them on a routine basis. Laboratories may voluntarily participate in Proficiency Analytical Testing (PAT) schemes or, once they have established proficiency in these schemes, request accreditation by various recognized bodies. In the U.S. the proficiency samples for organic solvents include aliphatic, aromatic and chlorinated hydrocarbons, alcohols, ketones and esters. Many other countries have similar proficiency testing and accreditation programs. For example, the U.K. Health and Safety Laboratory operates the Workplace Analysis Scheme for Proficiency (WASP).

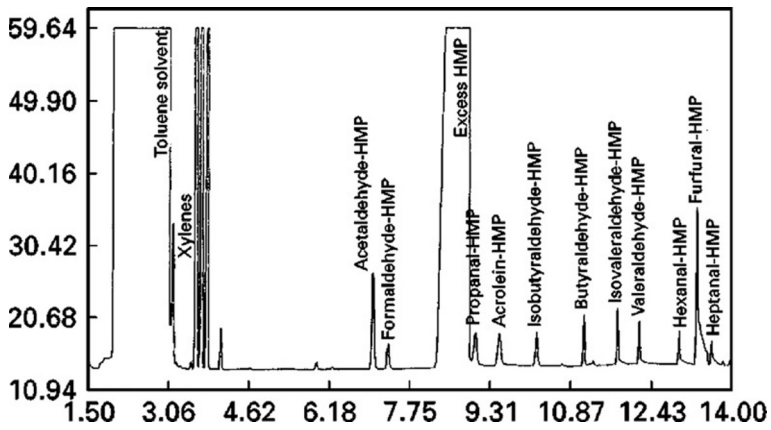

Figure 10 Determination of multiple aldehydes as their derivatives with 2-hydroxymethylpiperidine. Total ion chromatogram of aldehyde mix from spiked sorbent tube separated on a 15 m DB-1301 column.

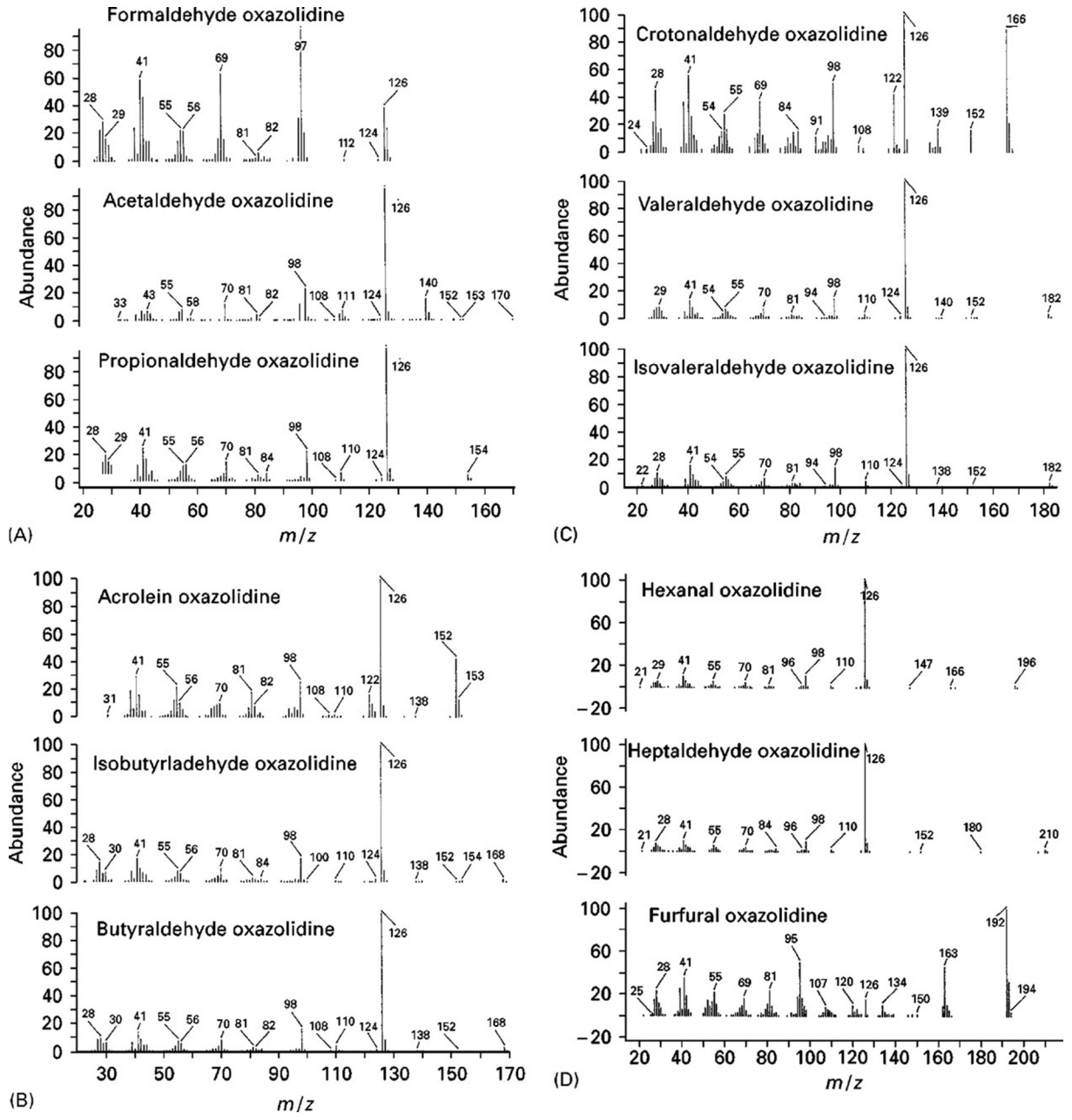

Figure 11 Determination of multiple aldehydes as their derivatives with 2-hydroxymethylpiperidine. Individual 70 eV electron ionization reference spectra obtained using a Hewlett Packard 5970 mass selective detector, *m/z* 20–400 scan (30 m DB-1 column).

In addition to documentation of methods and practices, the following specific elements are considered appropriate for good analytical practice:

Initial calibration verification. This is based on a range of standards diluted from a stock solution. Multiple points encompassing the expected sample range are used to create a calibration curve. If the samples fall outside this range, further standards are prepared. The response of the detector to the standards, and their correlation coefficient, should be within control limits. Field-portable detectors may use packaged calibration gases.

Continuing calibration verification. At least one of the standards used for the initial calibration is repeated each 10–20 injections (or more frequently if considered desirable).

Internal standards. An internal standard is useful to compensate for minor variations in the sample size injected into the GC, but because it may mask a chemical of interest internal standards are not always employed where the sample is not well characterized.

Reagent blanks. The solvent used to make up standards and desorb samples is checked for contamination. This procedure is essential if low concentrations of analyte are to be determined.

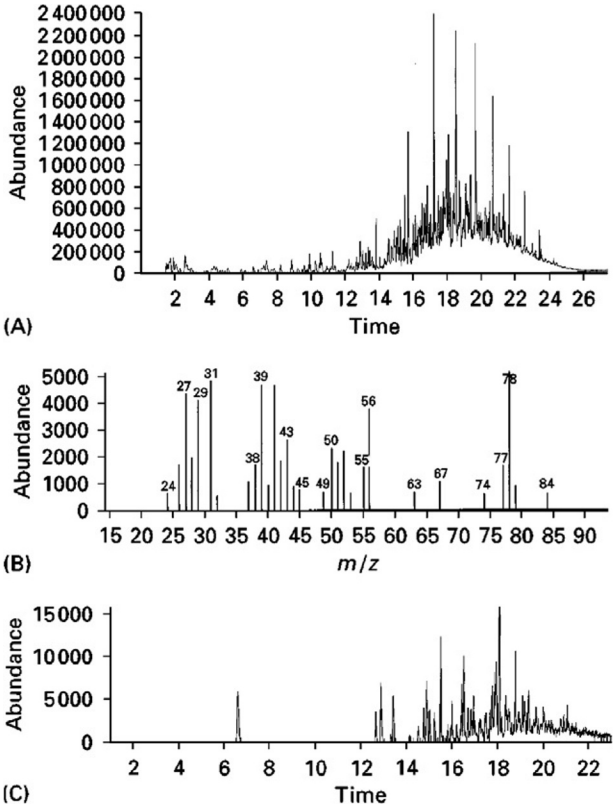

Figure 12 Air sample taken during asphalt paving operations analyzed by thermal desorption/GC-MS (30 m DB-1 column). (A) Total ion chromatogram. Retention time of benzene is 6.6 min. (B) Mass spectrum of peak at 6.6 min showing the presence of butanal in addition to benzene. (C) Single ion chromatogram of *m/z* 78 benzene ion, eliminating other hydrocarbon interferences.

Matrix blanks. The sampling medium is checked for contamination.

Matrix spikes. A known quantity of the analyte is added to a blank sample medium, which is carried through the full analytical procedure to ensure proper recovery.

Replicates. Used to ensure the precision of analysis. Particularly useful at low sample concentrations.

External standards. Known concentrations of the chemical of interest obtained from a source other than the laboratory. Standard mixtures of commonly analyzed chemicals are obtainable from speciality sources.

Other quality assurance methods used less often include: using a surrogate (a compound that behaves similarly to that of interest, but which can be separated, such as a deuterated analogue, which is used in the same way as a matrix spike with actual samples), matrix additions (direct addition of known quantities of the chemical of interest, which are subtracted from the final result) and splitting the sample (division of the sample for separate analyses).

The Future

Very recently, concerns have been raised over "emerging contaminants", such as organophosphate triesters, new phthalates and phthalate substitutes, perchlorate, organic UV filters, and polycyclic siloxanes, and a need to measure these in human matrices.[105] In all cases chromatography and mass spectrometry were the techniques of choice, because of their selectivity and sensitivity for measurements at ng g^{-1} levels. Traditional occupational hygiene sampling and analysis is already facing problems with sensitivity. As an example one can cite the NIOSH method for acrylonitrile.[106] The NIOSH recommended exposure limit is 1 ppm, but the lower limit of the current method is only slightly less at 0.7 ppm. Several other chemicals (e.g. benzene, 1,3-butadiene, vinyl chloride, ethylene oxide, etc.) have exposure limits close to the lower limit of their respective method ranges. In almost no case has an exposure limit been raised – the limit for benzene fell from 100 ppm (1946) to 25 ppm (1961) to 10 ppm (1978), and the current TWA TLV® is 0.5 ppm. Clearly the challenge is to find more sensitive methods of detection. One route is to use capillary chromatography, another is to use thermal desorption, and another is to use MS detection. The combination of all three can yield a sensitivity of around 0.1 ng per sample (equivalent to 0.03 μg m^{-3}, or 0.1 ppb, for a 3-L sample). One problem with such a combination is the cost, which can be as much as ten times that of the analysis of a conventional charcoal tube by solvent desorption and GC-FID. The advent of fast GC systems may lower the cost by allowing a greater daily sample throughput.

Another issue for the field is the long turn-around time for the result (sometimes weeks). Detectors that can give on-site results are clearly preferable. Based on trends for low-power heating of modern fused silica columns and micro-miniaturization such as micro-fluidics and surface-acoustic wave (SAW) detectors (the 'GC-on-a-chip') this may become achievable in the near future.

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References

1. James, A. T.; Martin, A. J. P. *Biochem. J.* **1951**, *50*, 679–690.
2. Rushing, D. E. *Am. Ind. Hyg. Assoc. J.* **1958**, *19*, 238–245.
3. Apol, A. G.; Cook, W. A.; Lawrence, E. F. *Atmos. Environ.* **1967**, *1*, 515–519.
4. Seila, R. L.; Lonneman, W. A.; Meeks, S. A. *J. Environ. Sci. Health A* **1976**, *11*, 121–130.
5. Rothwell, R.; Mitchell, A. D. *Clean Air* **1977**, *7*, 35–36.
6. McClenny, W. A.; Pleil, J. D.; Evans, G. F.; Oliver, K. D.; Holdren, M. W.; Winberry, W. T. *J. Air Waste Manage. Assoc.* **1991**, *41*, 1038–1318.
7. Kelly, T. J.; Holdren, M. W. *Atmos. Environ.* **1995**, *29*, 2595–2608.
8. Ochiai, N.; Daishima, S.; Cardin, D. B. *J. Environ. Monit.* **2003**, *5*, 997–1003.
9. LeBoeuf, R. F.; Stefaniak, A. B.; Virji, M. A. *J. Environ. Monit.* **2012**, *14*, 977–983.
10. Occupational Safety and Health Administration, Partially Validated method 2120: Volatile Organic Compounds in Air. OSHA Salt Lake Technical Center, Sandy, UT, http://www.osha.gov/dts/sltc/methods/partial/pv2120/pv2120.html. Accessed May 16, 2013.
11. Posner, J. C.; Woodfin, W. J. *Appl. Ind. Hyg.* **1986**, *1*, 163–168.
12. Wang, Y.; Raihala, T. S.; Jackman, A. P.; St. John, R. *Environ. Sci. Technol.* **1996**, *30*, 3115–3117.
13. McGarvey, L. J.; Shorten, C. V. *Am. Ind. Hyg. Assoc. J.* **2000**, *61*, 375–380.
14. U.S. Environmental Protection Agency, Compendium Method TO-14A, Determination of Volatile Organic Compounds (VOCs) In Ambient Air Using Specially Prepared Canisters With Subsequent Analysis By Gas Chromatography; Cincinnati, OH, 1999.
15. Van Mourik, J. H. C. *Am. Ind. Hyg. Assoc. J.* **1965**, *26*, 498–509.
16. Reid, F. H.; Halpin, W. R. *Am. Ind. Hyg. Assoc. J.* **1968**, *29*, 390–396.
17. Harper, M. *Ann. Occup. Hyg.* **1993**, *37*, 65–88.
18. White, L. D.; Taylor, D. G.; Mauer, P. A.; Kupel, R. E. *Am. Ind. Hyg. Assoc. J.* **1970**, *31*, 225–232.
19. Harper, M. *J. Chromatogr. A* **2000**, *885*, 129–151.
20. Woolfenden, E. *J. Chromatogr. A* **2010**, *1217*, 2685–2694.
21. U.S. Environmental Protection Agency, Compendium Method TO-17, Determination of Volatile Organic Compounds in Ambient Air Using Active Sampling Onto Sorbent Tubes; Cincinnati, OH, 1999.
22. Wang, A.; Fang, F.; Pawliszyn, J. *J. Chromatogr. A* **2005**, *1072*, 127–135.
23. Lord, H.; Zhan, W.; Pawliszyn, J. *Anal. Chim. Acta* **2010**, *677*, 3–18.
24. Koziel, J.; Jia, M.; Pawliszyn, J. *Anal. Chem.* **2000**, *72*, 5178–5186.
25. Augusto, F.; Koziel, J.; Pawliszyn, J. *Anal. Chem.* **2001**, *73*, 481–486.
26. Hook, G. L.; Jackson Lepage, C.; Miller, S. I.; Smith, P. A. *J. Sep. Sci.* **2004**, *27*, 1017–1022.
27. Palmes, E. D.; Gunnison, A. F. *Am. Ind. Hyg. Assoc. J.* **1973**, *34*, 78–81.
28. Harper, M.; Purnell, C. J. *Am. Ind. Hyg. Assoc. J.* **1987**, *48*, 214–218.
29. Purdham, J. T.; Sass-Kortsak, A. M.; Bozek, P. R. *Ann. Occup. Hyg.* **1994**, *38*, 721–740.
30. van der Wal, J. F.; Moerkerken, A. *Ann. Occup. Hyg.* **1984**, *28*, 39–47.
31. Cherrie, J. W.; Lynch, G.; Bord, B. S.; Heathfield, P.; Cowie, H.; Robertson, A. *Ann. Occup. Hyg.* **1994**, *38*, 827–838.
32. Nothstein, G. L.; Hahne, R. M. A.; Spence, M. W. *Am. Ind. Hyg. Assoc. J.* **2000**, *61*, 64–68.
33. Gong, Y.; Eom, I.-Y.; Lou, D.-W.; Hein, D.; Pawliszyn, J. *Anal. Chem.* **2008**, *80*, 7275–7282.
34. Arthur, C. L.; Pawliszyn, J. *Anal. Chem.* **1990**, *62*, 2145–2148.
35. Martos, P. A.; Pawliszyn, J. *Anal. Chem.* **1999**, *71*, 1513–1520.
36. Hook, G. L.; Kimm, G. L.; Hall, T.; Smith, P. A. *Trends Anal. Chem.* **2002**, *21*, 534–543.
37. Schüpfer, P. Y.; Huynh, C. K. *J. Occup. Environ. Hyg.* **2008**, *5*, 490–500.
38. Smith, P. A.; Kluchinsky, T., Jr.; Savage, P. B.; Erickson, R. P.; Lee, A. P.; Williams, K.; Stevens, M.; Thomas, R. J. *Am. Ind. Hyg. Assoc. J.* **2002**, *63*, 284–292.
39. Smith, P. A.; Sheely, M. V.; Hakspiel, S. J.; Miller, S. *Am. Ind. Hyg. Assoc. J.* **2003**, *64*, 189–195.
40. Smith, P. A.; Roe, M. T. A.; Sadowski, C.; Lee, E. D. *J. Occup. Environ. Hyg.* **2011**, *8*, 129–138.
41. Hout, J. J.; Hook, G. L.; LaPuma, P. T.; White, D. W. *J. Occup. Environ. Hyg.* **2010**, *7*, 352–357.
42. Kennedy, E. R.; Abell, M. T.; Reynolds, J.; Wickman, D. *Am. Ind. Hyg. Assoc. J.* **1994**, *55*, 1172–1177.
43. Kennedy, E. R.; Lin, J. J.; Reynolds, J. M.; Perkins, J. B. *Am. Ind. Hyg. Assoc. J.* **1997**, *58*, 720–725.
44. Lewis, R. G.; Brown, A. R.; Jackson, M. D. *Anal. Chem.* **1977**, *49*, 1668–1672.
45. American Society for Testing and Materials. ASTM D4861–11 Standard Practice for Sampling and Selection of Analytical Techniques for Pesticides and Polychlorinated Biphenyls in Air. ASTM International, West Conshohocken, PA.
46. Raina, R.; Hall, P. *Air Soil Water Res.* **2010**, *3*, 57–66.
47. Arnold, J.E., Method 5503 Polychlorobiphenys (issue 2). National Institute for Occupational Safety and Health (NIOSH) Manual of Analytical Methods, 4th ed., DHHS/NIOSH Publication Number 2003–154, Cincinnati, OH. http://www.cdc.gov/niosh/docs/2003-154/pdfs/5503.pdf. Accessed May 16, 2013.
48. Neumeister, C.; Key-Schwartz, R., Method 5800 Polycyclic Aromatic Compounds, Total (PACs). National Institute for Occupational Safety and Health (NIOSH) Manual of Analytical Methods, 4th ed., DHHS/NIOSH Publication Number 2003–154, Cincinnati, OH. http://www.cdc.gov/niosh/docs/2003-154/pdfs/5800.pdf. Accessed May 16, 2013.
49. Kuusimäki, L.; Peltonen, K.; Mutanen, P.; Savela, K. *Ann. Occup. Hyg.* **2003**, *47*, 389–398.
50. Wells, J. R. *J. Environ. Monit.* **2012**, *14*, 1044–1054.

51. American Conference of Governmental Industrial Hygienists. 2013 TLVs® and BEIs® Based on the Documentation of the Threshold Limit Values for Chemical Substances and Physical Agents & Biological Exposure Indices. ACGIH, Cincinnati, OH.
52. Ikeda, M. *Toxicol Lett.* **1999**, *108*, 99–106.
53. Lindstrom, A. B.; Pleil, J. D. *Biomarkers* **2002**, *7*, 189–208.
54. Amorim, L. C.; de L. Cardeal, Z. *J. Chromatogr. B* **2007**, *853*, 1–9.
55. Waidyanatha, S.; Zheng, Y.; Rappaport, S. M. *Chem. Biol. Interact.* **2003**, *145*, 165–174.
56. Mills, G. A.; Walker, V. *J. Chromatogr. A* **2000**, *902*, 267–287.
57. Margariti, M. G.; Tsakalof, A. K.; Tsatsakis, A. M. *Ther. Drug Monit.* **2007**, *29*, 150–163.
58. Weisel, C. P. *Chem Biol Interact.* **2010**, *184*, 58–66.
59. Orhan, H. *J. Sep. Sci.* **2007**, *30*, 149–174.
60. Kennedy, E. R.; Fishbach, T. J.; Song, R., Eller, P. M.; Shulman, S. A. Guidelines for Air Sampling and Analytical Method Development and Evaluation, Publication No. 95–117; U.S. Department of Health and Human Services (NIOSH): Cincinnati, OH, 1995.
61. Harper, M.; Guild, L. V. *Am. Ind. Hyg. Assoc. J.* **1996**, *57*, 1115–1123.
62. American Society for Testing and Materials. ASTM D6246-08(2013), *Standard Practice for Evaluating the Performance of Diffusive Samplers*; ASTM International: West Conshohocken, PA, 2013, DOI: 10.1520/D6246-08R13.
63. Eide, M.; Simmons, M.; Hendricks, W. *Validation Guidelines for Air Sampling Methods Utilizing Chromatographic Analysis*. U.S. Department of Labor (OSHA): Salt Lake City, UT, 2010.
64. Health and Safety Executive. Methods for the Determination of Hazardous Substances, MDHS 72 *Volatile Organic Compounds in Air*; HSE, London, U.K., 1992.
65. Harper, M. *Analyst* **1994**, *119*, 65–69.
66. Brown, R. H. *Analyst* **1996**, *121*, 1171–1175.
67. Grote, A. A.; Kennedy, E. R., Method 2549 Volatile Organic Compounds (Screening), National Institute for Occupational Safety and Health (NIOSH) Manual of Analytical Methods, 4th ed., DHHS/NIOSH Publication Number 2003–154, Cincinnati, OH.
68. ASTM Standard D6196-03(2009), *Standard Practice for Selection of Sorbents, Sampling and Thermal Desorption Analysis Procedures for VOCs in Air*; ASTM International: West Conshohocken, PA, 2013, DOI: 10.1520/D6196-03R09.
69. ISO Standard 16000–6:2011, *Indoor Air – Part 6: Determination of Volatile Organic Compounds in Indoor and Test Chamber Air by Active Sampling on Tenax TA Sorbent, Thermal Desorption and Gas Chromatography using MS or MS-FID*; International Organization for Standardization: Geneva, Switzerland, 2011.
70. Burroughs, G. E.; Tabor, M. W. *Appl. Occup. Environ. Hyg.* **1999**, *14*, 159–162.
71. Smith, P. A. *J. Chromatogr. A* **2012**, *1261*, 37–45.
72. Lee, M. L.; Yang, F. J.; Bartle, K. D. *Open Tubular Column Gas Chromatography, Theory and Practice*. Wiley: New York, NY, 1984; pp 107–110.
73. Ehrmann, E. U.; Dharmasena, H. P.; Carney, K.; Overton, E. B. *J. Chromatogr. Sci.* **1996**, *34*, 533–539.
74. Sloan, K. M.; Mustacich, R. V.; Eckenrode, B. A. *Field Anal. Chem. Tech.* **2001**, *5*, 288–301.
75. Stearns, S. D.; Cai, H.; Koehn, J. A.; Brisbin, M.; Cowles, C.; Bishop, C.; Puents, S.; Ashworth, D. *J. Chromatogr. A* **2010**, *1217*, 4629–4638.
76. Posner, J.C., Method 3701 Trichloroethylene by Portable GC. NIOSH Manual of Analytical Methods, 4th ed., DHHS/NIOSH Publication Number 2003–154, Cincinnati, OH.
77. Burroughs, G.E., Method 3700 Benzene by Portable Gas Chromatography. NIOSH Manual of Analytical Methods, 4th ed., DHHS/NIOSH Publication Number 2003–154, Cincinnati, OH.
78. Burroughs, G.E.; Sweet, N., Method 3704 Perchloroethylene (Portable GC) in Exhaled Breath and Air. National Institute for Occupational Safety and Health (NIOSH) Manual of Analytical Methods, 4th ed., DHHS/NIOSH Publication Number 2003–154, Cincinnati, OH.
79. Burroughs, G.E., Method 3702 Ethylene Oxide by Portable GC. National Institute for Occupational Safety and Health (NIOSH) Manual of Analytical Methods, 4th ed., DHHS/NIOSH Publication Number 2003–154, Cincinnati, OH.
80. Burroughs, G.E., Method 6602 Sulfur Hexafluoride by Portable GC. National Institute for Occupational Safety and Health (NIOSH) Manual of Analytical Methods, 4th ed., DHHS/NIOSH Publication Number 2003–154, Cincinnati, OH.
81. Woebkenberg, M.L., Method 6603 Carbon Dioxide. National Institute for Occupational Safety and Health (NIOSH) Manual of Analytical Methods, 4th ed., DHHS/NIOSH Publication Number 2003–154, Cincinnati, OH.
82. Coffey, C.; Lebouf, R.; Lee, L.; Slaven, J.; Martin, S. *J. Occup. Environ. Hyg.* **2012**, *9*, 670–680.
83. Ouyang, G.; Pawliszyn, J. *Trends Anal. Chem.* **2006**, *25*, 692–703.
84. Eckenrode, B. A. *J. Am. Soc. Mass Spectrom.* **2001**, *12*, 683–693.
85. Smith, P. A.; Driscoll, J. N. Field-Portable Gas Chromatography. In *Important Instrumentation and Methods for the Detection of Chemicals in the Field*; Smith, P. A.; Cook, G. W., Eds.; American Industrial Hygiene Association: Falls Church, VA, 2013; pp 115–130, Chapter 9.
86. Smith, P. A.; Sng, M. T.; Eckenrode, B. A.; Leow, S. Y.; Koch, D.; Erickson, R. P.; Jackson Lepage, C. R.; Hook, G. L. *J. Chromatogr. A.* **2005**, *1067*, 285–294.
87. Smith, P. A.; Jackson Lepage, C.; Lukacs, M.; Martin, N.; Shufutinsky, A.; Savage, P. B. *Int. J. Mass Spectrom.* **2010**, *295*, 113–118.
88. Smith, P. A.; Jackson Lepage, C. R.; Koch, D.; Wyatt, H. D. M.; Hook, G. L.; Betsinger, G.; Erickson, R. P.; Eckenrode, B. A. *Trends Anal. Chem.* **2004**, *23*, 296–306.
89. Contreras, J. A.; Murray, J. A.; Tolley, S. E.; Oliphant, J. L.; Tolley, H. D.; Lammert, S. A.; Lee, E. D.; Later, D. W.; Lee, M. L. *J. Am. Soc. Mass Spectrom.* **2008**, *19*, 1425–1434.
90. McWilliam, I. G.; Dewar, R. A. *Nature* **1958**, *181*, 760.
91. Driscoll, J.; Clarici, J. *Chromatographia* **1976**, *9*, 567–570.
92. Chelton, C. F.; Zakraysek, N.; Lautner, G. M.; Confer, R. G. *Am. Ind. Hyg. Assoc. J.* **1983**, *44*, 710–715.
93. Barsky, J. B.; Que Hee, S. S.; Clark, C. S. *Am. Ind. Hyg. Assoc. J.* **1985**, *46*, 9–14.
94. Smith, P. A.; Jackson Lepage, C.; Harrer, K. L.; Brochu, P. J. *J. Occup. Environ. Hyg.* **2007**, *4*, 729–738.
95. Nyquist, J. E.; Wilson, D. L.; Norman, L. A.; Gammage, R. G. *Am. Ind. Hyg. Assoc. J.* **1990**, *51*, 325–330.
96. Mouradin, R. F.; Flannery, J. P. *Am. Ind. Hyg. Assoc. J.* **1994**, *55*, 1084–1086.
97. Driscoll, J. N. *J. Chromatogr.* **1977**, *134*, 49–55.
98. Lovelock, J. E.; Lipsky, S. R. *J. Am. Chem. Soc.* **1960**, *82*, 431–433.
99. Brodey, S. S.; Chaney, J. E. *J. Gas Chromatogr.* **1966**, *4*, 42–46.
100. Atar, E.; Cheskis, S.; Amirav, A. *Anal. Chem.* **1991**, *63*, 2064–2068.
101. Finnigan, R. E. *Anal. Chem.* **2004**, *66*, 969A–975A.
102. Heller, S. R.; McGuire, J. M.; Budde, W. L. *Environ. Sci. Technol.* **1975**, *9*, 210–213.
103. Van den Dool, H.; Kratz, P. D. *J. Chromatogr.* **1963**, *11*, 463–471.
104. Grote, A.A.; Kennedy, E.R., Method 2539 Aldehydes, Screening, National Institute for Occupational Safety and Health (NIOSH) Manual of Analytical Methods, 4th ed., DHHS/NIOSH Publication Number 2003–154, Cincinnati, OH.
105. Dirtu, A. C.; Van den Eede, N.; Malarvannan, G.; Ionas, A. C.; Covaci, A. *Anal Bioanal Chem.* **2012**, *404*, 2555–2581.
106. Gagnon, Y. T., Method 1604 Acrylonitrile, National Institute for Occupational Safety and Health (NIOSH) Manual of Analytical Methods, 4th ed., DHHS/NIOSH Publication Number 2003–154, Cincinnati, OH.