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MASS SPECTROMETRIC DETERMINATION OF PESTICIDE RESIDUES

Prepared for publication by

P. T. HOLLAND

Ruakura Agricultural Centre, MAF, Private Bag, Hamilton, New Zealand

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Correspondence on the report should be addressed to the Secretary (1989–) of the Commission; Dr. P. T. Holland, Ruakura Agricultural Centre, MAF, Private Bag, Hamilton, New Zealand.

Mass spectrometric determination of pesticide residues

Abstract - A review is made of current approaches to mass spectrometry (MS) of pesticides, pesticide metabolites and related compounds such as PCB's and polychlorinated dibenzo-dioxins. Basic relationships between instrument sensitivity and detection limits in various operating modes are outlined. Recent developments in instrumentation are introduced such as 'bench top' GC-MS, LC-MS, MS-MS and surface ionisation techniques. Objective criteria are developed for interpretation of MS data for identification and quantitation of residues. The advantages of isotopically labelled internal standards to ultra trace analysis are highlighted. The recent literature on applications of MS to various pesticide classes are summarised. The conclusions are that requirements for detailed residue data on crop protection and environmentally significant chemicals will increasingly rely on MS techniques as detection limits are lowered and the number of chemicals grows. MS applications are increasingly becoming polarised between routine confirmation of identity and sophisticated structural elucidation or ultra trace analysis.

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1 INTRODUCTION

The confirmation and identification of trace residues is heavily dependent upon mass-spectrometry (MS) due to limitations in sensitivity or selectivity of alternative micro-analytical techniques. In many cases MS is used not only for identification or confirmation but also as the primary and preferred detection method, particularly in multi-residue trace analytical methods for environmental matrices e.g., US-EPA priority pollutant protocols, PCB analyses and dioxin analyses at the ng/kg level.

Gas chromatography coupled to MS (GC-MS) has dominated MS applications in the pesticide field. This technique has greatly benefited from development of bonded phase fused silica open tubular (FSOT) columns with high inertness and low bleed. Small, relatively inexpensive mass-spectrometers configured as dedicated GC detectors have made GC-MS more readily available to residue chemists. Furthermore ease of operation and maintenance are much improved over earlier generation or more complex instruments. Specialist mass-spectroscopy training is no longer a prerequisite for their operation.

Where analyte levels are too low for quantitation from full scan spectral data, selected ion monitoring (SIM) techniques can provide lower detection limits for specified compounds.

The ability to use stable isotope labelled analytes as internal standards has enabled methods based on mass-spectrometric determination that can provide unrivalled quantitative results at ultra-trace levels (µg/kg-ng/kg).

Alternatives to the standard electron impact ionisation (EI) such as chemical ionisation (CI, +ve or -ve) have been found more suitable for some residue problems. Coupled liquid chromatography-mass-spectrometry (LC-MS) and liquid surface ionisation mass-spectrometry (liquid-SIMS or FAB) have also become more routine. These 'soft ionisation' techniques are proving particularly useful for study of polar compounds including pesticide metabolites and conjugates (ref. 1, 2, 3, 4, 5). Newer techniques such as super critical fluid chromatography (SFC) and selected ion decomposition monitoring (SDM) using multiple analyser instruments (MS-MS) are also beginning to be applied to pesticide chemistry.

A number of reviews have outlined the broad problem solving ability of mass-spectrometry in the residue area and have given many interesting examples of applications (ref. 6-12, 2). These reviews generally have not examined the basic relationships between MS sensitivity and detection limits under different operating conditions or discussed objective criteria for interpretation of MS data to identify and quantitate residues. This review presents some background to these fundamentals. Some entry points are also given to the recent literature on applications of mass-spectrometry to pesticide chemistry.

Applications of mass-spectrometry to trace analysis of pesticide residues generally fall into five categories:

1. Decline studies: The test pesticide is applied to soil, crops, or administered to animals and residues are determined in samples taken at subsequent intervals. MS may be used in this type of study when the usual GC or LC techniques have proved unsuitable or where the high precision offered by labelled internal standards is required.

2. Confirmation of identity: Multi-residue screening procedures on food or environmental samples are often based on GC or LC chromatographic determinations. Legal enforcement of residue limits may require MS confirmation of putative residues.

3. Unidentified analytical responses (UAR): The above screening procedures can also reveal the presence of residue components which are additional to, or metabolites of, those for which the methods have been validated. Identification of these UAR's at the trace level is dependent on MS.

4. Environmental sample analysis: MS is the required determinative step in a range of analytical protocols for trace organic analysis of environmental samples, where formidably complex mixtures are often encountered at the µg/kg-mg/kg level. The protocols often call for GC-MS quantitation of a set of target analytes with isotopically labelled internal standards.

5. Metabolism studies: Pesticides, generally isotopically labelled, are administered to animals or applied to plants and the pathways of metabolism, degradation and excretion studied. MS assists identification of metabolites.

Fundamental requirements for these problems are to obtain MS data of quality such that:

1. Identification of the required residues is unequivocal or they are at least well characterised e.g., molecular weight and major fragments defined.

2. Quantitative estimates of the level of the residues in the samples can be made. For confirmation purposes or identification of unknowns semi-quantitative data may be adequate.

3. A detection limit can be assigned to the procedure where identification and quantitation are not established.

4. False positive or false negative results are avoided.

For a high degree of assurance on all these points, elaborate protocols and validation are required which cover all aspects of the method including sampling, extraction, clean-up, and the MS determinative step. These have reached the greatest degree of sophistication in recent methodology for polychlorinated dibenzo-dioxins and -furans, particularly TCDD.

2 INSTRUMENT PERFORMANCE

2.1 Sensitivity

It is useful to look in detail at some of the instrumental parameters that influence sensitivity and detection limits in various operating modes. These are two of the most important criteria for performance in residue analysis.

The absolute sensitivity for a mass-spectrometer is best expressed as the total electric charge collected at the detector (prior to electron multiplier) for a given sample input to the ion-source. This can be determined using the molecular ion of a test substance for example as coulombs collected at $^{m}/z$ 298 per microgram of methyl stearate. This molecular ion sensitivity S_m is of more general utility if expressed on a basis of the total ionisation (TI) of the test substance:

$$S_{TI} = S_m \times \frac{100}{A_m} \quad \text{coulombs/microgram}$$

where A_m is the abundance of the measured mass as a % of total ionisation.

Typical ranges of S_{TI} at low resolution for methyl stearate on modern instruments are:

EI	5×10^{-8} - 5×10^{-7} C/μg
CI (isobutane)	1×10^{-9} - 1×10^{-8} C/μg

For high resolution instruments S_{TI} decreases by 10-20 fold between 1,000 and 10,000 RP.

For electron impact (EI) of most organic compounds, S_{TI} values are not very dependent on molecular structure. More precise relative values for various compounds can be calculated from atomic additivity (ref. 13). Chemical ionisation (CI) sensitivities are more dependent on reagent gas and molecular structure. However sensitivity values when using methane reagent gas are similar (ref. 14) for compounds with oxygen or nitrogen functionality.

The absolute sensitivity specification S_{TI} can be used to estimate instrumental detection limits under a variety of conditions. The following formula calculates the flow rate of sample to the ion-source required for detection of N ions in a mass peak of relative abundance A_m present at the detector for time t_m.

$$F = \frac{N \cdot 1.6 \times 10^{-11}}{S_{TI} \cdot t_m \cdot A_m} \quad \text{pg/sec}$$

Taking the detection limit as N = 310 ions gives the limiting flow rate:

$$F_{dl} = \frac{5 \times 10^{-9}}{S_{TI} \cdot t_m \cdot A_m} \quad \text{pg/sec}$$

Note that this criteria for detection limit does not depend on the instrumental blank or noise level which can be extremely low for clean mass-spectrometer systems. Rather it is based on the counting statistics ($1/\sqrt{N}$) of the analyte signal itself. Peaks containing ca 300 ions will exhibit intensity fluctuations of ±10% (2δ). For chromatographic sample introduction the minimum detectable quantity (MDQ) for a peak T sec wide at half height is given by:

$$MDQ = F_{dl} \cdot T \quad \text{pg}$$

Consider detection limits for capillary GC-MS under three typical sets of instrumental condition:

1. Confirmation of pesticide residue identity using fast scanning.
   EI, 1000 RP, $S_{TI} = 5 \times 10^{-8}$ C/μg, GC peaks 3 sec half width
   A full spectrum every second: t_m = 0.5 msec
   Spectra to be reproducible for peaks down to 2% of TI: A_m = 2%
   F_{dl} = 100 pg/sec
   MDQ = 300 pg

2. Confirmation of pesticide residue molecular weight using fast scanning.
   CI, 1000 RP, $S_{TI} = 1 \times 10^{-9}$ C/μg.
   A full spectrum every second: t_m = 0.5 msec
   Reproducible detection of MH: A_m = 50%
   F_{dl} = 200 pg/sec
   MDQ = 600 pg

3. SIM quantitation of low level residues.
   EI, 1000 RP, $S_{TI} = 5 \times 10^{-8}$ C/μg
   Monitor 5 ions in a 0.6 sec cycle: t_m = 100 msec
   Choose major ions in spectrum: A_m = 10%
   F_{dl} = 0.1 pg/sec
   MDQ = 0.3 pg

For SIM at 10,000 RP, *MDQ* for a similar analysis would be 10-20 times higher i.e. 3-6 pg.

These instrumental limits can be met in practise when using EI or CI to run pure samples. As discussed in the section 2.2, the detection limit may be higher for the complete analytical system, influenced by factors in addition to the absolute MS sensitivity.

These formulae are useful to formalise the relationship between relative abundance of 'significant' ions, the time spent in measuring them, and detection limits. For example, the lower absolute sensitivity of CI may be compensated by the high proportion of ionisation carried by MH. It should be noted that the proportion of ionisation carried by M and other higher mass ions in EI can often be dramatically improved by operating at reduced electron energy (24-30 eV) and ion-source temperatures (150-180°). The later point is frequently commented on in relation to negative ion CI but is also valid in EI. The 'standard' source temperature of 250° is higher than required for integrity of chromatographic resolution of most pesticides and can lead to excessive fragmentation or thermal degradation.

2.2 Analytical detection limits

The instrumental limits to detection defined by the ion statistics of absolute sensitivity often do not apply to complete analytical systems due to two overriding factors.

1. Background: This can consist of responses due to coextractives or contaminants in the sample, GC column bleed, solvent, eluant (LC-MS), matrix (liquid-SIMS), or instrument contamination. Polymeric reagent gas ions in CI give a background continuum extending above $^m/_z$ 200. Background peaks can interfere with the measurements at the particular masses of interest. There can also be a general rise in the detector baseline due to scattered or metastable ions.

2. Sample losses or suppression: Sample adsorption in the inlet system can compromise low level detection and is reflected in non-linearity of response. It is often evident in GC-MS where the hot column and residual activity in the stationary phase support may be deleterious to polar compounds such as carbamate and phenyl urea pesticides.

Background due to contaminants or coextractives may be reduced by more rigorous attention to method blanks and sample clean-up. Sample preparation and clean-up procedures for mass-spectrometry have been reviewed (ref. 15). Increased resolution or changed selectivity in the chromatographic system can also solve individual problems. Mass-analyser selectivity against extraneous ions can also be increased by high-resolution (HR) or MS-MS techniques where available. Use of higher resolutions with SIM generally results in lower analytical detection limits despite the large reductions in absolute sensitivity. Similar improvements result from selected decomposition monitoring using MS-MS on multi-sector or triple quadrupole instruments (ref. 16).

The advent of bonded phase FSOT capillary columns has greatly assisted lowering of GC-MS detection limits by reducing both column bleed and residual column activity. However, pesticides that GC adequately at the ng level may still be severely degraded or lost at the pg level. These effects are exacerbated as columns age due to oxidation by traces of oxygen in the carrier gas and to contamination by sample coextractives. High levels of isotopically labelled internal standards may act as carriers to partially protect analytes from column activity. Such effects are unpredictable and not a universal panacea due to the unavailability or expense of many labelled pesticides.

Suppression of analyte response can also increase effective detection limits. Ion source outputs are often not very linear particularly when tuned for highest sensitivity. The presence of high levels of solvent or sample coextractives, can lead to suppression of ionisation of the analyte. This effect can be particularly acute in -ve CI where the electron plasma available for electron capture ionisation is limited. Source suppression phenomena limit the usefulness of higher analyser selectivity (HR-MS, MS-MS) in the analysis of crude extracts. A greater degree of sample purification is the only solution to such difficulties.

The remarkable efforts of laboratories specialising in the analysis of dioxins have resulted in procedures which can reliably detect TCDD at 1-10 ng/kg in a variety of matrices. These involve HRGC/HRMS detection of 500fg - 5pg TCDD with SIM of 3-5 masses.

These limits approach those predicted from the instrumental sensitivity (example eqn. 3 above). However, the exceptional stability of TCDD has allowed employment of extremely rigorous clean-up procedures resulting in extracts containing very little extraneous material. The stability of TCDD also reduces losses in the GC. Detection of low ng/kg levels of more polar compounds is difficult with present GC-MS technology due to the interference and column loss problems.

3 INSTRUMENTAL DEVELOPMENTS

3.1 'Bench top' GC-MS

The basic technology of quadrupole or magnetic sector mass analysers has remained stable over the past decade with incremental improvements in sensitivity, resolution, mass range, scan rate and data systems. The range of sample introduction and ionisation modes has also increased. Complementary to the increasing versatility and sophistication of specialist instruments has been the development of simple dedicated GC-MS units.

Direct coupling of capillary gas chromatographs to small quadrupole (mass selective detector or MSD) or ion-trap mass analysers (ITD) with personal computer based data systems has yielded relatively inexpensive, compact instruments. Their performance is more than adequate for much general pesticide work. A recent study of the MSD with 76 pesticides in food showed reliable identification could be obtained from full scan spectra at 400 ppb (10-20 ng) levels reducing to 10 ppb in SIM mode (ref. 17). The ITD in particular has remarkably high sensitivity with full scan spectra reported for subnanogram qualities (ref. 18).

Basic benchtop instruments do make compromises some areas that may be important for particular applications:

1. The source and analyser regions are not differentially pumped or bakeable which makes the analyser and electron multiplier detector susceptible to contamination. Analysis of crude extracts or samples with high levels of derivatising reagents is not recommended. The low pumping capacity may only allow the use of narrow bore GC columns or require splitting of the column effluent.

2. Selectivity in SIM experiments may be lower than for larger instruments which operate at nominal resolutions of 1000 or higher. This is because the resolution in bench top instruments at working masses may only be ca 300.

3. The ITD does not give large increases in sensitivity when operated in the SIM mode because of the pulsed ionisation/ion ejection sequence (ref. 19, 20). This is offset to a large extent by the inherently high sensitivity of the ion trap.

4. Direct probe or other sample introduction facilities are not fitted.

5. Ionisation mode is limited to positive EI. CI and MS-MS modes are available on special ion-trap models (ref. 21, 22).

6. Source temperature/ionising energy tend to be fixed at 220°/70 eV which may contribute to poor molecular ion intensity for some pesticides.

7. The mass range does not exceed 600 which may be lower than the molecular weight of some analytes e.g. perfluoroacyl derivatised compounds.

However bench top GC-MS instruments also have significant advantages:

1. Low cost. The base prices are of the order of 15-30% of those for more sophisticated instruments.

2. Simplicity of operation. The limited options and use of data system control, including automatic tuning, allow use by analysts with only modest training.

3. Reduced maintenance. The low parts count is likely to lead to fewer faults than on more complex instruments.

Overall bench top instruments are likely to have a significant impact on quality control in residue chemistry by verifying or supplanting many standard assays. They can also release more sophisticated MS instruments for specialised applications. Despite their many advantages it must be accepted that no current MS systems can match the linearity, long term reproducibility and reliability of standard GC detectors such as the electron capture or flame photometric detector.

3.2 Combined liquid chromatography – mass-spectrometry

Although a variety of LC-MS interfaces have been researched, the thermospray (TSP) system has gained the greatest acceptance to date (ref. 3, 23). It is a robust system that can accommodate reversed flow eluants containing volatile buffers at standard HPLC flow rates. Cationisation of analytes by protons, ammonium or adducts of these ions with solvent takes place in an expansion chamber following carefully graduated heating and vacuum vapourisation of the solvent. A sampling cone introduces ions to the mass analyser. Optimal ionisation of polar compounds, including pesticides, requires eluants with high water content and containing 0.1 M ammonium acetate (ref. 23). The spectra generally consist of molecular-adduct ions with little fragmentation. However thermal degradation can occur for some compounds such as carbamates (ref. 24, 25) unless the vapouriser temperature is reduced below the absolute sensitivity optimum. TSP sensitivity appears to be 10-100 times lower than for standard EI ionisation but polar pesticides such as urea herbicides and oxime carbamates that GC poorly yield molecular weight information by LC-TSP-MS. Negative ions can also be generated in the TSP interface by electron capture or anionisation by acetate or chloride. However sensitivities for carbamate or organophosphate pesticides, including chlorinated compounds have been found to be 10-100 times lower than for the positive ion mode (ref. 26, 27).

The utility of LC-TSP-MS has been demonstrated in screening for relatively non-volatile pollutants in water including a number of polar herbicides and insecticides that are difficult to gas chromatograph (ref. 28). Method detection limits were in the range 1-10 µg/litre for 29 analytes. Due to the low fragmentation, confirmation of identity mainly relied on molecular cation isotope ratios and MH/MNH_4 ratios.

The polar nature of many xenobiotic metabolites makes them candidates for TSP-MS. Other soft ionisation methods such as desorption chemical ionisation or liquid SIMS can often provide more informative spectra than TSP-MS. However these techniques generally require highly purified fractions whereas LC-TSP-MS can provide the sample fractionation directly. Reported applications to date have mainly involved drug metabolites. For example hydroxylated, glucuronide, glutathione and sulphate metabolites of various drugs have been determined in relatively crude extracts of bile, hepatocyte cultures, microsomal preparations and plasma (ref. 29-31).

The alanine conjugate of a methidation metabolite and the glutathione conjugate of prometryn have been identified by LC-TSP-MS (ref. 32).

Supercritical fluid chromatography (SFC) is a more natural coupling to MS. Recent developments (ref. 33, 34) indicate that many pesticides that do not GC well can be run in SFC. For example 11 carbamate and 4 acidic herbicides introduced to a CI source via FSOT-SFC gave full scan spectra to subnanogram levels (ref. 35).

3.3 Surface ionisation

Fast atom bombardment (FAB) or, preferably, liquid surface ionisation mass-spectrometry (LSIMS) has revolutionised the analysis of polar organic compounds. A beam of fast atoms or ions directly ionises the analyte from a liquid matrix. Recent developments of the technique are covered in comprehensive reviews (ref. 36, 37). Where previously hydrolytic, degradative and derivatisation chemistry was required prior to MS (EI) e.g. fenpropathrin metabolism in plants (ref. 38), much more direct analyses of intact conjugates or other polar metabolic products are now possible (ref. 1, 39-42). Provided samples are prepared to a good degree of purity, liquid SIMS spectra usually can be obtained for microgram quantities of sugar, glutathione and other conjugates (ref. 4, 5, 43). Positive ion mode has proved the most useful but negative ions can provide complimentary information and sensitivity is often higher for acidic compounds, e.g. sulphates (ref. 44) and nitrophenyl glucuronides (ref. 45). Liquid matrix selection is important for optimal results with SIMS and alkali cations must be removed to avoid weak spectra confused by adduct ions. Quantitative results have been obtained by using suitable internal standards (ref. 5, 44, 46). As well as molecular weight information, liquid SIMS spectra of conjugates generally contain fragment ions that can assist in assignment and location of the conjugation species. Daughter ion spectra of collisionally active MH anions from complex carbohydrates gave excellent structural information and eliminated the high matrix background (ref. 47).

252-californium plasma desorption (Cf-PD) mass spectrometry was shown to offer advantages over LSIMS identification of simple monoglucosyl conjugates of sulphonyl ureas and other compounds (ref. 48). Because of the relative absence of matrix peaks in Cf-PD, molecular ions and structurally significant fragment ions to below $^{m}/z$ 100 could be easily observed whereas glycerol matrix peaks frequently obscured LSIMS spectra below $^{m}/z$ 200.

Matrix background has been reported to be reduced in continuous flow FAB where the sample is delivered to the ionisation stage in a dilute glycerol/solvent mixture (ref. 49). A further advantage of this technique is the possibility for combined LC-LSIMS which has now been realised for microbore HPLC of tryptic digests (ref. 50).

LSIMS has helped clarify metabolic pathways of a number of herbicides in plants. EPTC was shown to be conjugated to glutathione (GSH) with further metabolism to malonyl-cysteine or malono-3-thiolactic acid conjugates (ref. 51). Metribuzin, acifluorfen, propachlor and tridiphane also formed conjugates with GSH or homo-GSH in soy bean (ref. 52, 53, 43, 54). Chlorsulfuron was found to be hydroxylated and conjugated with glucose in corn (ref. 55).

Field desorption (FD) techniques have largely been superseded by LSIMS. For example, LSIMS (positive and negative ions) was more effective in the study of sulphuric acid conjugates of the rice fungicide pyroquilon (ref. 56). However, FD can be superior for determination of less polar compounds e.g., peracetates of mono- to tri-glucoside conjugates of the acid moiety from fenvalerate (ref. 57).

3.4 MS-MS techniques

Double focussing or multiple analyser (tandem) instruments have the capability to examine fragmentation of ions outside the primary ion source (ref. 16). Fragmentations can be enhanced by passing ions through a gas cell. High energy collisions (several keV) are obtained in magnetic sector instruments and such decompositions are classed as collisionally induced (CID). Triple quadrupole instruments use the middle quadrupole as a trapping cell to promote multiple low energy (5-30 eV) collisions (collisionally activated decompositions, CAD). Analyser conditions can be chosen to scan the daughter ions of a chosen parent, the parents of a chosen daughter or the parent ions giving rise to the same neutral loss (constant neutral loss). With modern instrument control by data system, these experiments can be carried out with ease and flexibility. Such experiments are of great utility in delineating fragmentation routes and mechanisms, information that is often not obvious in standard spectra. The use of isotope data in interpreting CAD spectra has been discussed (ref. 58).

In analogy to SIM, selected decomposition monitoring (SDM) increases the sensitivity of CID/CAD experiments by concentrating on particular parent-daughter transitions. This mode of operation gives high selectivity and MS-MS instrumentation is being increasingly applied to trace analysis problems. Detection limits have been lowered or sample clean-up and chromatographic procedures simplified (ref. 16, 59, 60). For example sulphonamide drug residues in pig livers could be determined by CAD-SDM experiments on relatively crude extracts (ref. 61). The pioneering work by Hunt et al. (ref. 62) demonstrated that MS-MS can be used as a broad range screening technique. Seven constant neutral loss scans and a parent ion scan during direct probe sample introduction of sediment extracts enabled a wide range of pollutants to be determined. Cautionary notes however are appearing about excessive optimism in the use of MS-MS for routine screening of crude extracts to low detection limits (ref. 63, 64). Problems of ion source contamination and high background noise indicate that some sample clean-up, possibly combined with a low resolution chromatographic introduction system, is advisable.

MS-MS techniques are likely to prove useful in metabolism studies using liquid SIMS or LC thermospray ionisation where fragmentions are weak or obscured by matrix derived peaks. The ability of MS-MS instruments to perform constant neutral loss experiments also provides a rapid means of identifying conjugate type (ref. 65).

4 IDENTIFICATION AND QUANTITATION

4.1 Data acquisition

Positive identification of low level residues in a complex matrix presents the analyst with a number of problems that are exacerbated when there is also a requirement for accurate quantitation. As discussed in section 2.1, there is a trade-off of information content for sensitivity as experimental conditions are changed from full spectra scanning to selected ion monitoring using reduced numbers of mass channels. Full scan spectra should be obtained wherever possible for semi-quantitative confirmation of residues. The high sensitivity and selectivity of modern GC-MS instruments enables this in many situations to below 0.1 mg/kg although more concentrated and cleaned-up extracts may be required. Spectral averaging and subtraction facilities in the data system can be used to remove contributions from background or partially resolved contaminants. However, attempts to 'clean-up' very weak spectra where background mass peaks predominate may lead to spectra of dubious validity. Information for identification may be limited if the spectra contain only one or two prominent peaks e.g. MH^+ from soft ionisation techniques or spectra are dominated by low mass ions of little structural significance. Quantitations from full scan spectra are usually based on mass chromatograms generated from stored data using ion masses

characteristic for the analyte. The analyser cycle time should be fast enough to permit at least 3-5 scans to be acquired over the chromatographic peaks.

SIM procedures are preferred for very low level residue determinations or where accurate quantitation is required. The higher sensitivity and faster cycle times possible with SIM result in more reproducible responses. This may be particularly important in experiments employing isotopically labelled compounds. However, depending on the number of ions monitored, the information content is reduced over complete spectra which increases the risk of incorrect assignments. A high degree of reliance should not be placed on results of SIM analyses unless extensive checking has determined the extent of possible interferences. The minimum number of ions to use in selected ion monitoring is dependent on other selectivity in the system (sample clean-up, chromatographic resolution, mass resolution) and how characteristic the masses chosen are for the analyte. For most pesticide work, 2-3 ions, preferably including the molecular ion, have been found adequate (ref. 17).

4.2 Identification criteria

The literature contains a number of different criteria for confirmation of identity dependent on application. Mass-spectral identification is based on four comparisons of sample response to a standard.

4.2.1 Correspondence of appearance time

This will usually be retention time in a chromatographic system but could also be time to maximum evaporation rate from a direct probe. Using capillary GC with external standard provides reproducibility of Rt to about 5 parts in 1000. Furthermore this correspondence should cover all the masses measured for the compound.

4.2.2. Appearance profiles should be discrete

Again this mainly applies to chromatographic sample introduction. It is a requirement for resolution of analyte from other sample components where they have ions in common. Suitable criteria are for analyte mass chromatogram peaks to exhibit valleys of at least 25% from other components and that the analyte mass-chromatogram peaks be of uniform half-width.

4.2.3 Spectra should match in mass and relative intensity

The relative intensity criteria necessary to establish correspondence of spectra at the trace level have been variously proposed as ±10% or ±20% maximum difference in ratios of prominent ion intensities relative to ratios in the standard (measured either as peak heights in individual spectra or as areas of mass chromatogram peaks). Using isotope peaks of chlorine for this comparison enhances the confirmation of an analyte containing chlorine (but does not increase the differentiation between similar chlorinated compounds).

Calibration of relative ion abundance levels using the reference compound decafluoro-triphenyl phosphine has been recommended for contract applications of US-EPA Method 625 to analysis of base/neutrals and acids in waste waters. Unfortunately this has led to anomalies as the criteria developed on early quadrupole instruments (ref. 66) are inapplicable to magnetic sectors due to the superior transmission of high mass ions in the latter. Revised standards have been proposed (ref. 67).

In the absence of standards, mass spectral identifications become more tenuous but library or literature data may be adequate for known compounds.

For complete unknowns such as new pesticide metabolites, detailed spectral interpretation based on experience with related compounds can generally lead to hypotheses for structures. Elemental compositions from medium - high resolution mass measurements are valuable and can be obtained using fast scanning GC-MS on modern instruments. Stable isotope labelling in conjunction with GC-MS also provides a powerful means of identifying pesticide derived components in complex mixtures (ref. 68). Mixing pesticide labelled with ^{13}C, ^{15}N or D atoms with unlabelled pesticide in approximately 1:1 ratio produces mass-spectra with characteristic isotope cluster peaks. This technique has been extensively used in drug metabolism studies (ref. 69). The metabolism of methidathion provides an example in the pesticide field (ref. 32). However, MS alone is rarely acceptable for structural elucidation. Confirmation by other techniques will generally be required, preferably including synthesis.

4.3 Mass spectral libraries

Where full scan mass spectral data has been obtained on samples of food or environmental origin for determination of a range of residues, identifications will rely on comparisons of spectra to those of standards. These standards may be run at the same time in which case the identification is trivial governed by the criteria given in section 3.2. However, in wide ranging studies, initial identification may depend on comparisons to library spectra.

Large mass spectral data bases are available for computer searching either through dedicated mass-spectrometer data systems or by 'on-line' access via terminal/modem/ telephone to central facilities. Predominant amongst these compilations are those from NIH-NBS, Wiley and MSDC (ref. 70-72). The MSDC data can also be accessed through the 8 peak index compilation available in printed form. These data bases contain 50,000-100,000 spectra and represent a tremendous resource when dealing with complete unknowns. Even if the unknown is not matched, information may be obtained on related compounds which can assist in structural elucidation. However, these compilations are not always the ideal adjunct to mass-spectral studies on pesticide or environmental pollutants because of the following factors:

1. The spectra are almost exclusively EI. They are therefore of virtually no use when dealing with CI or other ionisation techniques.

2. Instrumental conditions often do not match. Analyser type, source temperature, ionising energy and method of sample introduction all can affect the relative abundance of ions. Differences in spectra reduce the possibility of obtaining high match scores.

3. By their very nature the large data bases have a low efficiency of searching with the vast majority of spectra being totally unrelated to the problem at hand. This can lead to slow and possibly expensive searches.

4. Spurious matches may be generated. This may be advantageous when dealing with complete unknowns, but hampers automated search approaches to processing large volumes of GC-MS data such as may result from screening of environmental samples.

5. Despite their large scope the data bases are by no means all inclusive and have significant omissions in the pesticide area for some of the newer compounds and for metabolites. However the NBS library has been reported to contain spectra of 72 out of 76 common pesticides (ref. 17).

These disadvantages can be at least partly overcome by use of libraries more specific to pesticide residue studies, with spectra preferably generated by GC-MS on a similar instrument. A number of published spectral collections deal with compounds in the pesticide, toxicological, or environmental areas (ref. 73-76). Automation of the search procedure is well within the capabilities of modern data systems. This provides a means of relieving the analyst of the burden of preliminary interpretation of the large volumes of data that can be generated by GC-MS. Introduction of GC retention indexes improved the accuracies of matching in a system for confirmation of residues in food (ref. 77). Automated procedures for calculation of PCB concentrations have also been developed (ref. 78, 79) and extended to chlorinated pesticides (ref. 80). A programme which uses isotopic cluster analysis has been developed to automatically extract spectra of chlorinated compounds from GC-MS data (ref. 81).

4.4 Quantitation criteria

Where accurate quantitative data is required, instrument calibration should follow general principles for environmental analysis (ref. 82) which recommends at least 3 concentration levels analysed in triplicate. The concentration range of interest should be bracketed and no data should be reported beyond the range of calibration of the methodology.

One of the major advantages of MS in trace organic analysis is the possibility to use isotopically labelled internal standards. These greatly improve quantitation and analytical quality control by providing accurate correction for, and measure of, losses. Calibration is straightforward where isotopic incorporation in the standard is so complete that no contribution is observed to the major ion masses in the unlabelled analyte. Non-linear calibrations occur if significant overlap occurs although approaches to linearise the data are available (ref. 83). With deuterated compounds there is the possibility of isotopic-exchange. Physical separation of unlabelled and labelled analytes in HPLC or GC have also been reported (ref. 84). SIM procedures with short cycle times are therefore preferable in experiments employing isotopes to ensure relative amounts are accurately determined.

Surrogate internal standards (compounds similar to the analyte, often isomeric) also provide improvements in analytical precision where labelled pesticides are not available (ref. 80, 85). Multiple standards are recommended where the analytes span a wide retention time range (ref. 85).

Injection technique also can have a considerable effect on reproducibility in GC-MS with on-column injection being generally preferred over split-splitless for sensitive compounds (ref. 85, 86).

With unknown compounds or pesticides where no standards, are available semi-quantitative estimates of concentration should still be made. Total ion current (TIC) responses using

the relatively non-specific EI or CI (CH_4) ionisation can be roughly calibrated using hydrocarbon or other suitable standards. Such estimates are invaluable in establishing a correspondence between MS response to the analyte and that observed in other analytical systems.

4.5 Estimation of detection limit

The IUPAC definition of detection limit should be applied to the analytical system wherever possible (ref. 87). The minimum detectable concentration is given by $3S_B/S$ where S_B is the standard deviation of the analytical system blank response and S is the sensitivity factor relating instrument response to concentration of analyte in the sample. A minimum of 10 blanks are recommended to estimate S_B. The application of this definition is straightforward in principle where a field blank sample is available.

Two practical difficulties however often arise in trace organic analysis. Firstly, true field blank samples (identical in all respects except for absence of analyte) are frequently unavailable. Control samples which are essentially free of analyte are often used, even if they may not necessarily contain the same range of other residues as the actual samples. Secondly, many trace analytical procedures are exceedingly time consuming and the running of large numbers of blanks may be impractical, particularly if only a small number of actual samples are involved.

It is not possible to escape the statistical imperatives if an accurate estimate of the detection limit is required. However, limited blank testing may be acceptable if more conservative detection criteria are adopted. Thorough sample clean-up can lead to very low blanks in GC-MS with only non-specific background noise signals in the analyte retention region. The detection limit is often reported as the concentration equivalent of 2-3 times the peak-peak noise (averaged over all significant mass channels). As the p-p criteria corresponds roughly to $4S_B$, this equates to a 10 S_B/S definition. A valid estimate of noise includes both high and low frequency perturbances over a time interval of several peak widths. All detection limit estimates should be backed by full recovery tests with low level spikes close to the detection limit.

4.6 Anomalous detection

False negatives: There is always the possibility of non-detection when the analyte is actually present in the sample extract. Ion-source suppression phenomena or adsorption in the inlet system are likely causes, aside from instrument malfunction or tuning shifts. Internal standards, preferably isotope labelled, allow affected runs to be detected. If these are not available, then response of the system to analyte must be verified in the presence of matrix components. This can only be ensured by re-running of sample extracts with a spike of analyte at levels close to the detection limit. Responses of analyte in the usual recovery experiments (control samples spiked before extraction) are a guide but not infallible when operating near the detection limit on complex environmental samples.

False positives: Positive responses can also occur when the analyte is not present in the sample extract. Depending on how stringently the above detection criteria are applied, there is possibility for false identification due to interfering substances. These are most likely to arise where SIM is being used in trace analysis of samples where no true field blank exists. Even the highly selective techniques used for dioxin analysis do not completely eliminate interferences at the ng/kg level. For example, $M\text{-}Cl_2$ ions from polychlorinated diphenyl ethers overlap M from polychlorinated dibenzofurans. Including extra SIM masses such as diagnostic fragment ions or full spectral scanning can detect this type of problem.

5 COMPARATIVE STUDIES ON PESTICIDES AND POLLUTANTS

The wide range of conditions now available for MS of pesticides make published spectral data and comparative studies very useful. The text edited by Karasek, Hutzinger and Self (ref. 89) has chapters covering mass-spectra (principally EI) of the major pesticide and pollutant classes. Tables 1-5 summarise other recent studies.

5.1 Organochlorine insecticides

The principal development in MS of organochlorine insecticides (Table 1) has been NCI techniques which offer sensitivity similar to the normal GC-electron capture detector. Optimal operating conditions and mechanisms have been clarified (ref. 90-93). LC-MS techniques have failed thus far to attain the sensitivity required for most residue work on organochlorines (ref. 94).

TABLE 1. Mass-spectrometry of organochlorine insecticides

Reference		Comments
Sauter et al. 1986	14	Priority pollutants
Alford-Stevens et al. 1986	80	US-EPA Method 680
Benoit et al. 1986	95	PCB's and 21 OC insecticides in water
Wells and Cowan 1983	85	Water pollutants; choice of internal standards
Hargesheimer 1984	96	PCB's and OC pesticides in water, CI (CH_4)
Miyazaki et al. 1986	97	OC pollutants in human milk
Jansson and Wideqvist 1983	98	Chlordane and toxaphene, NCI
Stemmler and Hites 1985	90	Bridged cyclic chlorinated insecticides, NCI
Gooch and Matsumura 1985	99	Toxaphene
Swackhammer et al. 1987	100	Toxaphene, NCI
Miyazaki et al. 1985	101	Composition of chlordane
Miyazaki et al. 1986	102 103	Residues of chlordane in various species
Suzuki et al. 1983	104	HCH isomers in water - SIM with deuterated I.S.'s
Yost et al. 1984	59	HCB and TCP in urine and serum, HRGC-MS vs GC-MS-MS
Artigas et al. 1988	105	Lindane and metabolites, NCI

5.2 Polychlorinated biphenyls (PCB's)

Although these industrial pollutants are not pesticides, they are often present in environmental matrices along with organochlorine pesticide residues and they pose similar analytical difficulties. Early quantitation using mass-spectrometry relied on chlorination level assays using LRGC-MS-SIM calibrated against PCB formulation standards (ref. 11). High resolving power FSOT columns can virtually completely separate the complex mixtures (209 possible congeners) and this had led to assays based on individual congener quantitation (ref. 111). This has enabled more detailed studies on the toxic coplanar or non-ortho congeners and on preferential metabolism and bioaccumulation. Recent research is summarised in Table 2.

TABLE 2. Mass-spectrometry of PCB's

Reference		Comments
Pellizzari et al. 1985	106	Review
Capel et al. 1985	78	Congener analysis of Aroclors
Alford-Stevens et al. 1985	107	ECD vs MS detection
Gebhart et al. 1985	108	Response factors
Voyksner et al. 1986	109	Optimisation of CI (CH_4)
Heidmann 1986	110	Isomer specific analysis
Alford-Stevens et al. 1986	79	Congener analysis of Aroclors
Ballschmiter et al. 1987	111	Individual congeners

TABLE 2. (cont.)

Reference		Comments
Shore et al. 1986	112	$^{13}C_{12}$-PCB i.s.'s
Guevremont et al. 1987	113	Oxygen enhanced NCI
Kannan et al. 1987	114	Coplanar content of PCB formulations
DeKok et al. 1987	115	Hydroxy-PCB derivatives
Haraguchi et al. 1987	116	Methylsulfonyl-PCB metabolites
Fuerst et al. 1987	117	Ion trap analysis of Ugilecs (tetrachlorobenzyl toluenes)
Porte et al. 1988	118	NCI-SIM confirmation in fish

5.3 Organophosphorus, carbamate and pyrethroid insecticides

Table 3 summarises recent research which has explored diverse MS techniques for these compounds. SCFC-MS appears a very promising technique for providing high resolving power and minimal decomposition of labile pesticides (ref. 34).

TABLE 3. Organophosphorus, carbamate and pyrethroid insecticides

Reference		Comments
Stan & Kellner 1982	119	Survey of 52 OP's, NCI
Wilkins et al. 1985	120	90 OP sulfide, sulfoxides, sulfones
Cairns et al. 1984	121	Isofenphos and metabolites, CI
Singh et al. 1986	122	13 OP's in plasma, EI/CI
Roach and Andrzejewski 1986	58	23 OP's Comparative data on EI-MIKES, CI-MS-MS
Hummel and Yost 1986	123	26 OP's +ve and -ve, CI-MS-MS
Roach and Carson 1987	62	Omethoate, parathion and azinphosmethyl, CI-MS-MS
Cairns and Sigmund 1987	124	Etrimfos and dimethoate on crops, CI-MS-MS
Parker et al. 1982, 1985	125, 126	-ve ion and chloride ion spectra of OP's, LC-MS (DLI)
Voyksner et al. 1984	127	+ve and -ve ion spectra OP's and carbamates, LC-MS (DLI)
Voyksner and Haney 1985	23	OP's and triazines, LC-MS (TSP)
Barcelo Voyksner 1987	128	Carbamates, LC-MS
Barcelo et al. 1987	129	Optimisation for 10 OP's, LC-MS (DLI)
Stamp et al. 1986	130	20 carbamates, CI (CH_4 or NH_3), GC-MS (CI)
Kalinowski et al. 1986	35	11 carbamates, 4 acid herbicides, SFC-MS (CI)
Cairns et al. 1987	24	Aldicarb and metabolites, LC-MS (TSP)
Lidgard et al. 1986	131	+ve and -ve ion spectra of 7 SP's

5.4 Herbicides and fungicides

These diverse classes contains many pesticides that are not very suitable for GC. LC-MS techniques are therefore of great interest. Table 4 summarises recent research.

TABLE 4. Herbicides and fungicides

Reference		Comments
Geerdink et al. 1987	94	Cl attachment -ve ionisation of acidic herbicides, LC-MS (DLI)
Lopez-Avila et al. 1986	132	2,4-D and dicamba. Deuterated internal standard SIM assay
Meemken et al. 1987	133	Phenoxy herbicides
De Felip et al. 1989	134	2,4-D and MCPA
Begleg and Foulger 1988	135	Triclopyr in plants, NCI
Bardalaye et al. 1985	136	Terbutryn and metabolites
Viden et al. 1987	137	Triazines
Parker et al. 1982	138	Triazines, LC-MS (DLI)
Voyksner et al. 1987	139	Triazines, LC-MS-MS (TSP)
deWit et al. 1988	140	Trifluralin and metabolites, NCI, LC-MS (DLI)
Barcelo 1988	141	Linuron and cyanazine, LC-MS (TSP)
Shalaby 1987	142	Sulfonyl ureas, methyl ureas, uracils, LC-MS (TSP)
Voyksner 1987	128	Methyl ureas, carbamates, LC-MS (TSP)
Bardalaye et al. 1984	143	Oryzalin, N-methyl derivative
Patumi et al. 1987	144	Fluazifop in soil, methyl ester derivative
Stemmler and Hites 1987	145	Dinitrophenols, dinitroanilines, NCI
Cairns and Siegmund 1984	146	Iprodione and metaboilites, CI
Cairns and Siegmund 1986	147	Dichlofluanid, CI
Prigge and Naumann 1985	148	Quintozene and metabolite, NCI
Cairns et al. 1987	149	Quintozene and metabolite, CI
Ripley 1985	150	Acylanalines
Cairns et al. 1989	151	Triadimefon, CI, MS-MS

5.5 PCDD's and PCDF's

These compounds have been identified as industrial by-products of manufacture of chlorinated phenols, phenoxy herbicides, PCB's and certain other chlorinated aromatics. They have also been shown to be formed during combustion of materials containing a source of chlorine e.g. municipal waste and during chlorine bleaching of wood pulp. Their high toxicity, particularly the 2,3,7,8 substituted congeners, has led to extensive research to delineate their distribution and environmental fate. This research may have reducing direct relevance to pesticide chemistry due to the cessation of 2,4,5-T manufacture. However, all chlorinated carbon compounds, still important feedstocks to many agrochemicals, contribute to the environmental burden via municipal waste incineration and other disposal routes (ref. 152). The methods for determining PCDD's and PCDF's to ng/kg levels in various matrices also provide outstanding examples of the power of modern mass-spectrometry. Quantitative aspects of the techniques have reached a high degree of sophistication and, driven by the imperatives of regulatory requirements, strict analytical quality assurance (QA) criteria have been developed. Thus, the analysis of PCDD's and PCDF's provides important pointers to developments in all areas of trace analysis by mass-spectrometry.

Until recently methodology has concentrated on 2,3,7,8-TCDD, the most toxic isomer. However, other congeners are also of toxicological concern and are often present at higher levels e.g. in fly ash (ref. 152) or pentachlorophenol and 2,4-D (ref. 153). There are 75 possible PCDD isomers, 22 in the tetrachloro congener class, while there are 136 possible PCDF's with 78 tetrachloro isomers. Ensuring specificity for 2,3,7,8-TCDD or 2,3,7,8-TCDF requires chromatographic resolution from all other isomers. Polar cyanosilicone stationary phases fulfil this requirement. Liquid crystal smetic phases have also recently been demonstrated to have excellent selectivity for 2,3,7,8 substituted congeners (ref. 154, 155).

In addition to isomer specificity, methods must demonstrate adequate selectivity against a variety of other potentially interfering compounds. In particular PCB's and organochlorine insecticides may be present in samples at 10^3-10^6 higher levels. These and a variety of other polychlorinated pollutants produce ions that can overlap those being monitored for PCDD's and PCDF's (ref. 88, 156, 157). Clean-up procedures designed to remove the majority of these compounds can provide extracts of some matrices suitable for screening by HRGC-LRMS (ref. 88, 158). However for confirmation and identification of positive samples at the ng/kg level detection systems with higher selectivity than LRMS (EI) are generally required.

HRMS (EI) has been the basis for highly selective detection of 2,3,7,8-TCDD (ref. 159-161). Resolutions of 10,000 are adequate to separate TCDD's from all other possible chlorine containing compounds or fragments that can give the 4 chlorine isotope pattern at m/z 320/322/324. The high sensitivity specifications of modern magnetic sector instruments has enabled analyses at 10,000 RP with superior detection limits to those obtainable at low resolution on quadrupole instruments (ref. 162).

MS-MS instrumentation has also been shown to be very selective (ref. 156, 163, 164). Collision-induced dissociation (CID) on mass-selected parent ions allowed the measurement in the second analyser of the M-OCl daughter ions. Results in regard to sensitivity, repeatability and linearity for 2,3,7,8-TCDD at the pg level were comparable to HRMS and selectivity was rather better against interference from PCB's at 10^3-10^5 higher levels (ref. 156). However, ion-source and inlet system non-linearities in the presence of matrix components meant that a relatively high degree of sample clean-up was still required to achieve reliable results (ref. 164).

Electron impact has been the dominant ionisation method for PCDD's and PCDF's. Sensitivity has been reported as ten times lower with CI (CH_4) (ref. 165). These authors gave EI response factors for 37 of the 38 possible TCDF isomers for use in SIM analyses where all standards may not be available. Relative response data has also been obtained for the 22 TCDD isomers (ref. 166). Due to the differences in spectra between various instruments, this type of data must be used with caution in calibrating assays for a wide range of isomers.

Negative ion detection can be highly sensitive for PCDD's and PCDF's as for other polyhalogenated compounds. HRGC-LRMS (NCI) has proved particularly useful as a screening technique for the higher congeners (ref. 88, 158, 162). Sensitivity for TCDD's was much lower than for higher congeners although optimisation of conditions has been studied (ref. 91). NCI (N_2O/CH_4) utilises OH^- anions to affect a variety of ionisation reactions. Oehme and Kirschmer (ref. 167) have shown OH^- to be a very sensitive and selective reagent for TCDD. Furthermore substantial differences in negative ion spectra were observed amongst the TCDD isomers. Thus utilisation of ionisation chemistry can provide selectivity for LRMS as an alternative to more expensive HRMS or MS-MS instrumentation.

The QA criteria for identification and quantitation of PCDD's and PCDF's, in particular 2,3,7,8-TCDD are of general interest. A basic tool in defining and achieving these criteria has been the use of isotopically labelled internal standards. Current methodology calls for an internal standard added at initial extraction with $^{13}C_{12}$ labelled 2,3,7,8-TCDD being preferred. Where higher congeners are being studied a $^{13}C_{12}$ labelled PCDD is also added for each chlorination level (Rappe et al. 1987). Following sample extraction and clean-up, a second 'recovery' internal standard is added prior to final concentration of the extract for injection into the GC-MS. This standard has been variously $^{13}C_6$- or $^{13}C_{12}$-1,2,3,4-TCDD or $^{37}Cl_4$-2,3,7,8-TCDD which are either mass or chromatographically resolved from both the analyte and the first internal standard. The ratios of responses in the respective SIM mass channels for analyte and internal standard molecular ions relative to ratios in calibration runs using mixtures of pure standards gives the quantitation of the analyte (generally 2,3,7,8-TCDD) directly. The relative responses of first and second internal standard measure the absolute recovery of TCDD through the complete method.

The internal standard responses also allow 'in-run' determination of other QC factors such as chromatographic and mass-spectrometer resolutions (ref. 169).

Recent published methodology for 2,3,7,8-TCDD and other TCDD isomers in fish tissue (ref. 168), human adipose tissue (ref. 159), human serum (ref. 160) and soil or water

(ref. 161) have reached a high degree of consensus on methodological steps required for QA at the ng/kg level using HRGC-HRMS techniques. These typically include:

1. Development of highly specific sample extraction and clean-up procedures which eliminate major and minor co-extractives and provide high recovery of PCDD's and PCDF's. The internal standard $^{13}C_{12}$-2,3,7,8-TCDD is added at 0.5-1.2 ppt (liquids) or 24-50 ppt (solids) prior to extraction. The recovery standard $^{13}C_{12}$-1,2,3,4-TCDD is added to the extract immediately prior to GC-MS.

2. Use of long cyanosilicone FSOT GC columns to ensure isomer specificity for 2,3,7,8-TCDD.

3. Use of computer controlled SIM at 10,000 resolution to cycle around sets of peak tops (M,M + 2 for analyte and internal standards: 319.897, 321.894, 331.937 and 333.934). A constant bleed of a reference compound such as perfluorotributylamine provides a peak for use as a lock mass which is included in the SIM cycle to correct for slight shifts in the magnet setting.

4. Demonstration of linear calibration using a set of 3-5 mixed standards each analysed in triplicate.

5. Demonstration of adequate recovery of internal standard (60-120%) and of TCDD in spiked field blank or control samples.

6. Demonstration of adequate selectivity by running of 'worst case' field samples or samples spiked with a range of potential interfering compounds.

7. Running of field samples in a daily routine which includes initial instrument tuning for resolution and sensitivity, checking of column resolution and response calibration (standard at 1 level), running of sample extracts in batches of 3 plus a QC sample extract (prepared from a spiked pool sample).

8. Quantitation of responses using sums of integrated peak areas for M and M + 2 for TCDD and internal standards.

9. Checking of individual run data to ensure that it meets the following criteria:

   (i) Ratio of 320/322 within 95% confidence interval of ratio obtained for standards.

   (ii) Signal:noise greater than 3:1 for both 320 and 322 TCDD peaks and greater than 10:1 for ^{13}C-TCDD i.s. peaks.

   (iii) Retention times for 320 and 322 peaks within 1 scan of each other and RRT to $^{13}C_{12}$-TCDD within 2 ppt of that in standard runs.

   (iv) Peaks all of uniform width at half-height indicating absence of partially resolved interferences.

   (v) Recovery of internal standard between 40% and 120%.

   TCDD is classed as not detected (ND) if these criteria are not all met. Inadequate recovery of internal standard or apparent interferences indicate a need to reanalyse the sample.

10. Other TCDD isomers can also be quantitated using published response factors if relevant S:N, ion ratio and retention time criteria are met.

11. For added specificity or confirmation the M + 2 - OCl fragment ion can also be monitored. Overall sensitivity is compromised but the added assurance may be necessary in the analysis of samples containing high levels of other pollutants such as contaminated soil.

12. Participation in inter-laboratory comparisons involving exchange of samples and standards to monitor systematic errors.

Adherence to strict QA protocols has resulted in remarkably precise data. Soil residues in the range 15-2000 ng/kg were measured with a precision of 11-25% (ref. 161). Much of the variation was attributed to sampling. Precision for TCDD in spiked pork fat or human adipose tissue at the low ng/kg level was in the range 6-19% (ref. 159). Pooled human serum was determined to contain 25.8 ng/litre TCDD with a CV of 13%. These sets of data were also supported for accuracy by inter-laboratory studies. Thus the empirical relationship observed by Horwitz (ref. 170) from earlier trace analysis studies showing an increase in CV by power of 2 for each power of 10 decrease in concentration is no longer valid. CV's for TCDD at the ng/kg level are no higher than commonly observed for pesticide residues at the mg/kg level.

6 CONCLUSIONS

There is an ever increasing range of crop protection chemicals many of which are active at very low rates. There are also greater demands from regulatory authorities and the public for detailed knowledge on the fate and distribution of residues. The power and flexibility of mass-spectrometry in trace organic analysis is therefore likely to be called upon to an even greater degree in the future. Instrumental developments have led to a polarising of mass-spectrometry applications to pesticide chemistry. Simple bench top instruments now dominate much routine pesticide residue confirmation work while increasingly sophisticated instruments are being used for difficult problems in structural elucidation, metabolism and ultra-trace analysis. Approaches to improved determination of polar pesticides and metabolites such as liquid surface ionisation-MS and liquid chromatography-MS are becoming more standard. They are therefore likely to be included in formal analytical protocols in the same way GC-MS was officially adopted a decade ago. Highly selective GC-MS techniques using isotopically labelled internal standards can greatly improve precision and accuracy of trace analysis once the overriding problems of adequate sub-sampling and accurate standards are overcome.

To obtain optimal results requires a good understanding of the fundamentals of the techniques being employed and a knowledge of the mass spectral characteristics of the compound types being studied. This review has attempted to bring these two aspects together for the benefit of pesticide chemists and others in the trace analysis field. In particular the criteria for mass-spectrometric detection and identification need careful examination. The diversity of mass-spectrometry instrumentation and applications requires that user training also must be given full attention.

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