Atomic spectrometry update. Clinical and biological materials, foods and beverages

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The literature reviewed this year has included a larger than usual number of interesting reports. The use of ultrasonication to extract analytes from samples is increasing and a review article on this technique has been published. Similarly, solid-phase micro-extraction now has an accepted place within atomic mass spectrometry. Using what appear to be mini-Chinese lanterns, powdered liver in small paper capsules was inserted into a flame-heated quartz cell for measurement of Cd by AAS. Novel designs of electrothermal atomisers made an appearance with a two-step atomiser (to preconcentrate and determine Hg in urine and drinking water) and a filter atomiser (which reduced background absorbance when measuring Cd and Pb in blood). More clinical applications involving collision cell technology for ICP-MS are being reported. However, the most interesting work this year has been made possible with multiple collector ICP-MS. This technique has uncovered the phenomenon of isotopic fractionation, whereby the body absorbs or incorporates into tissues one isotope of an element more than another. A sober reflection on the plethora of Se species reported in recent years suggests that much of the published work may not be very useful. Of the 16 Se species described in urine it is suggested that several had been mis-identified, and that selenosugars are probably more important than the trimethylselenonium ion. Exposure to As in drinking water in Bangladesh rumbles on with the discovery of high concentrations in wells that were purported to have been fitted with filtering devices. Also in drinking water was the unlikely discovery of As compounds that can be derived from chemical warfare agents. A number of residents of the affected area in Japan displayed uncommon central nervous system symptoms which could be attributed to these As compounds. Among the interesting forensic work reported, laser ablation-ICP-MS was seen to provide the opportunity to examine hair samples with greater chronological resolution than other techniques, a case of thallium poisoning was detected decades after the victim died, and an insight into the social history of Turkey in the 4–6th centuries AD was afforded by the analysis of goat bones!

1 Reviews and reference values

This review should be read in conjunction with the previous year's review[1] and with other related reviews in the series.[2–7] Clinical applications associated with instrumental developments were particularly highlighted in the ASUs featuring XRF.[2,3] Kubala-Kukas *et al.*[8] took results obtained by XRF to discuss data handling in order to determine LODs and to describe the distributions of results. In recent years there have been numerous studies of Se metabolites in biological specimens. Goenaga Infante *et al.*[9] reviewed speciation techniques applied to Se-rich foods and supplements. Attention was drawn to the importance of both Se-specific detection and molecular-specific determination and how the results could be interpreted with respect to their nutritional and cancer-prevention properties. The advantages of MS were emphasised. In an attempt to draw this disparate work together, Francesconi and Pannier[10] have prepared an *excellent review* drawing on 60 publications which reported a total of 16 Se species in urine. They concluded that several metabolites had been mis-identified, that the trimethylselenonium ion was not a major metabolite and that selenosugars were probably more important. Two further reviews addressed issues of sample preparation. In our previous ASUs, we have mentioned the importance of maintaining the structural integrity of species during the extraction and separation steps. This point was emphasised by Bernejo *et al.*[11] who proposed that enzymatic digestion and ultrasonication were suitably mild yet effective for speciation studies. Wrobel and Caruso[12] reviewed in considerable detail the pre-treatment and measurement of As and Se species in various sample types including urine. Koscielna[13] reviewed methods used to determine BrO_3^- in drinking water, including FI-ICP-MS and IC-ICP-MS. Despite the many techniques that may be used it was concluded that there is still a need for simple, low-cost reliable methods that can be used away from central laboratories.

The *reference range* for serum Se in adults was determined in samples collected from 26 adults living in Antwerp.[14] Specimens were collected each month for a year and their mean concentrations ranged from 71 to 99.3 ng ml^{-1}. These were similar to others reported from Belgian populations. The results were also compared against almost 100 studies in other European countries and the report has a valuable summary of all these previously published data. In addition, the month to month variation within each of the subjects was reported. In a mammoth piece of work, Bisse *et al.*[15] used AAS to measure the serum Si concentrations of 1325 healthy adults. Median values showed a small decrease with age in men but an increase in women up to the age of 45 y followed by a decline. The median values among the different age/sex groups were from 7.7 to 11.1 μmol l^{-1}. Zeiner *et al.*[16] used ICP-MS to determine Al, Co, Mo, Nb, Ni and Ti in urine samples from 100 residents of Budapest to establish normal creatinine adjusted concentrations. Median values (μg g^{-1} of creatinine) for this curious choice of elements were 9.9, 0.6, 53.5, 0.4, 1.5 and 8.5, respectively. Normal concentrations of Hg in 11 tissues and body fluids were measured in *post mortem* specimens from 50 male and 25 female Polish subjects. As would have been expected, the highest concentrations were found in liver (2.6–55) and kidney (3.2–170 ng g^{-1} wet weight).[17]

2 Reference materials and metrology

Christopher *et al.*[18] described in considerable detail the strategies and experimental work applied in a project for the *certification of elements in a NIST candidate fish SRM*, and also for the accurate measurement of Cd and Pb in blood CRMs. Unlike other value assignment procedures, ID was not performed, as it was required to measure all isotopes simultaneously. Therefore, a standard additions approach was adopted based on gravimetric rather than volumetric manipulations to increase the accuracy of sample handling. The procedure included the use of multiple internal standards and

a method to calculate analytical uncertainty was developed utilising regression and prediction uncertainties and quotient propagation of error formulae. The European Commission Institute of Reference Materials and Measurements organised an SI-traceable certification of methylmercury in tuna material.[19] Three new rice flour CRMs were produced in China for Cd by Zhao *et al.*[20] The bottled CRMs were subjected to 2.5 Mrad ^{60}Co for preservation and the homogeneity checked by AAS. The Cd contents of the three CRMs were determined using ID-MS. Isotope dilution was used for an SI-traceability study for the methylmercury content of tuna.[19] Further comprehensive details of an inter-laboratory comparison project using this material were also reported.[19,21]

Two studies were seen which referred to the Eurachem/Citac guide for determination of *analytical uncertainty*. A method for measuring Pt in plasma, ultrafiltrate and urine by ICP-MS was validated by Bettinelli,[22] who included assessment of the measurement uncertainty. In last year's Update, we referred to the work of Patriarca *et al.*,[23] who applied the protocol to the determination of Pb in blood by ETAAS and reported an expanded uncertainty of 16–20%, depending on concentration. This paper stimulated some correspondence in a subsequent issue of the journal[24–26] concerning the use of data on bias in the estimate of uncertainty. Patriarca *et al.* acknowledged a misprint in their original paper but supported their calculation model with reference to the Eurachem/Citac guide and also other authoritative documents. The issues raised by this correspondence indicate that the practical aspects and applications of measurement uncertainty are far from well established for clinical analyses but affirmed that their calculations were correct according to the Eurachem guide and also other authoritative documents. A full uncertainty budget was used to compare the performance of species specific single and 'approximate matching' double ID-MS in the determination of methylmercury by MC-ICP-MS in fish CRMs.[27]

3 Clinical and biological materials

3.1 Sample collection and preparation

3.1.1 Direct analysis. Few techniques are appropriate for *direct analysis without any sample preparation* but TXRF offers this, at least in principle. Marco and Herandez-Carabello[28] considered the difficulties associated with preparation and calibration for the analysis of biological samples. They discussed slurry sampling, Compton peak standardisation, *in situ* microwave digestion, *in situ* chemical modification, and internal standardisation. Examples of the methods that they developed were presented.

3.1.2 Collection and storage. As part of an evaluation of an AA spectrometer dedicated to measurement of Hg, Spevackova *et al.*[29] included a study of *sample stability in different containers*. No variations in the Hg content of blood were seen with polypropylene vessels but a time dependent increase was noted when polyethylene vessels were used. The contamination was attributed to either leaching from the polyethylene or diffusion from the external environment.

Analysts have struggled over the years with the *instability of certain trace elements in urine* and if anyone can come up with a solution to this problem it will be widely welcomed. Bornhurst *et al.*[30] conducted a rigorous study of the effects of preservative agents and temperature on the stability of 16 elements in urine for up to 65 days. While consistent concentrations were obtained for most conditions increases were seen for Al while Hg decreased over time. Boric acid and potassium pyrosulfate preservatives were liable to introduce contamination. The authors recommend storage at 4 °C without any additions. It is doubtful, however, if many analysts with any experience with measurements of Hg in urine will be convinced that such a simple approach would be really successful.

3.1.3 Extraction and digestion. As was mentioned above, sample preparation procedures for speciation work have been systematically reviewed.[11] Reports of practical methods indicate that the general conclusions expressed in the review are understood by analysts. In addition to *enzymic digestion and/or leaching, solvent extraction* can be employed. Torra *et al.*[31] followed this route to separate non-toxic from toxic As metabolites in urine while a similar process was employed to speciate As in hair.

A novel extraction procedure was adopted in a method to determine I in several different matrices.[32] Samples were placed with 10% v/v NH_3 solution in PTFE-lined digestion bombs and heated at 185 °C for 18 h. Results for CRMs, given by ICP-MS, were within the certified ranges. A conventional *acid leaching* method was shown to be simple and efficient for extracting CH_3Hg^+ from a variety of animal and plant tissues.[33] Samples were treated with 4 M HNO_3 at 55 °C and recoveries of added (CH_3Hg^+) enriched with ^{201}Hg were 93–96%. An attractively simple process was used by Mortari *et al.*[34] to prepare hair samples for the measurement of Se by HGAAS. Sample, and either HNO_3–H_2O_2 or H_2SO_4–HNO_3, in small, disposable polypropylene vials, were heated at 100 °C for 20 h. Sulfamic acid was added to minimise the influence of residual NO_x and results for a CRM were within 3% of the certified value. Kunze *et al.*[35] investigated further the problem associated with measuring Cr in blood and tissues by ICP-MS. An interference on isotopes 52 and 53 observed following digestion was attributed to residual carbon. They recommended using a Q-ICP-MS with DRC, SF-ICP-MS or ETAAS.

The measurement of *Pb in blood spots dried onto filter paper* was the subject of some controversy a few years ago and the protracted correspondence in *Clinical Chemistry* was reviewed in a previous Update.[36] DiMartino *et al.*[37] have now shown that if these samples are going to be used it is necessary to include 5 mM EDTA in the extraction solution to fully recover the Pb.

3.1.4 Preconcentration. Well established *techniques for preconcentration* of analyte were reported. On-line systems associated with complex formation on solid supports were seen for Cd,[38] Co and Ni in hair[39] and Pu in urine.[40] David *et al.*[41] developed a more elaborate off-line method for preconcentration and measurement of CH_3Hg^+ in biological RMs. The protocol involved extraction with CH_3COOH using microwave heating, derivatization and headspace solid-phase microextraction with a polydimethylsiloxane-coated silica fibre. Analysis

was completed by GC-ICP-MS *via* a specially constructed heated interface. Despite the complexity, reproducibility was <2% RSD and the LOD was 4.2 pg g^{-1}. Cloud point extraction, the alternative favoured preconcentration technique, featured rather less than in recent years but was used to determine As in hair and nail[42] and Cd and Pb in biological RMs.[43] Enrichment factors of 18–129 were obtained.

3.1.5 Solid sampling. Few examples of *solid or slurry sampling methods* were seen in this review period. Nomura *et al.*[44] described the steps of drying, grinding, checking particle size and homogeneity for the measurement of Cu and Zn by solid-sampling ETAAS. It is difficult to comprehend quite why such a convoluted process was thought to be necessary when there are much simpler methods available that are quick, less liable to contamination and straightforward. Simplicity was very much in mind when Liang *et al.* measured Hg in biological samples.[45] Samples, in 50% v/v *aqua regia*, were well mixed to give a stable slurry and introduced into an on-line FI-microwave digestion system with cold vapour generation AFS detection. The LOD was 0.06 μg l^{-1}. Seven recipes for preparing slurries prior to measurement of Hg and As by vapour generation ICP-AES were evaluated by dos Santos *et al.*[46] The methods included suspension in acid or alkaline media or in Triton X-100, with sonication and/or ozonation. All seven gave acceptable results for Hg with the CRMs tested but only two were satisfactory for Se. These were: (i) H_2O_2, sonication, addition of HCl, heating at 90 °C, and (ii) $K_2S_2O_8$, sonication, addition of HCl, heating at 90 °C. Both provided for release of Se from the organoselenium compounds in the samples but the latter method was recommended.

3.1.6 Speciation. Chromatographic separations are so well established that most reports now concentrate on the results rather than on the detail of the methodology. Encinar *et al.*[47] claimed to report the lowest ever LODs for Se by ICP-MS at less than 0.5 ng g^{-1} from a 450 mg serum sample. Their technique involved enzymic digestion, derivatization of selenomethionine (SeMet) and selenocysteine (SeCys) with iodoacetamide, HPLC and measurement of ^{77}Se and ^{80}Se with collision cell ICP-MS. The review by Francesconi and Pannier[10] of work with Se was mentioned above. Consistent with their observations relating to the importance of selenosugars were the findings of Gammelgaard *et al.*[48] who analysed urine samples from volunteers who had ingested Se-rich yeast. They pointed out that in some chromatographic systems Se-methylselenogalactosamine co-elutes with trimethylselenonium ion ($TMSe^+$) but that these species can be separated using cation exchange chromatography. When this latter procedure was used, no $TMSe^+$ was detected in any of the samples. One application of interest involved SEC with ICP-MS to separate metalloproteins in thyroid tissue.[49] Species that bound Cd, Cu, Pb and Zn were seen in healthy tissue but not in cancerous thyroid. The metalloproteins were not identified and their relevance to thyroid pathology is not known. Two *ingenious approaches to speciation* were described. By careful adjustment of pH, the cold-trapping conditions and the temperature gradient for subsequent release, Devesa *et al.*[50] were able to determine separately the AsH_3 generated from individual methylated metabolites of inorganic As. They showed the presence of As^{III}, As^{V}, MMA^{V}, MMA^{III}, DMA^{V}, DMA^{III} and $TMA^{V}O$ in cultured hepatocytes and/or urine. Zachariadis *et al.*[51] developed a dual channel FI manifold for the separate determination of Hg^{2+} and CH_3Hg^+. Dithiocarbamate complexes were formed in one channel, which included a PTFE column. The complex with Hg^{2+} was retained on the column while the methylated species was not adsorbed and was determined by CVAAS. Sample passing through the second channel was mixed with $SnCl_2$ which reduced only the Hg^{2+} for CVAAS. With this clever but simple arrangement, the Hg^{2+} and CH_3Hg^+ in urine samples were individually measured. Torres *et al.*[52] also developed a CVAAS procedure for Hg speciation. The vapour generated from samples treated with TMAH was directed to a quartz cell in the light path. At room temperature, only the vapour derived from Hg^{2+} absorbed light but, when the cell was heated by an air–C_2H_2 flame, the absorption signal was due to total Hg. The difference between the results was attributed to CH_3Hg. The validity of this procedure was confirmed by analysis of several CRMs.

3.2 Atomic absorption spectrometry

3.2.1 Flame AAS. *Ingenious ways to increase the sensitivity of FAAS* give testimony to the inventiveness of analytical chemists. da Costa *et al.*[53] developed a new solid sampling device. Dried, powdered liver samples were placed into small paper capsules for insertion into a flame-heated quartz cell for measurement of Cd. With low background signals and precision of <8% RSD, the LOD was 0.23 μg g^{-1} from a sample of 7 mg. Further design work with quartz slotted tube atom traps was reported by Yaman and Akdeniz[54] for measuring Cu and Zn in thyroid tissue. However, the 3.5-fold enhanced sensitivity is no greater than was obtained when work with the first slotted tubes was published more than 20 years ago. Bahircaoglu *et al.*[55] separated Cd, Cu, Ni and Zn in a liver CRM using a syringe based column filled with Chromosorb-103 resin. Depending on the pH and complexing agent added to the sample, either APDC or 8-hydroxyquinoline, specific elements were retained on the resin. Elution was achieved with HNO_3 in acetone and the analytes measured by FAAS.

3.2.2 Electrothermal AAS. A fundamental study this review year was that of Eleni *et al.*[56] on the *mechanism of atomisation of Pt*. They calculated activation energies for Pt at 1–8 ng in aqueous solution and in serum. An increase in activation energy with increasing mass of Pt suggested that, in H_2O, atomisation gradually changes from an adsorption to an evaporation process as more atoms are present. In serum, however, just one mechanism was observed that was thought to involve thermal desorption of Pt atoms from the carbon residues of the pyrolysed organic sample matrix.

An elegant *dynamic sampling system* allowed Mg and Zn to be measured by ETAAS in extracellular fluid from brain tissue of gerbils throughout an episode of cerebral ischaemia and reperfusion.[57,58] Fluid was sampled *via* a microdialysis probe inserted into the cortex. This was diluted on-line and injected into the AA furnace. Large decreases in concentrations were found in the fluid from the affected area of the brain during the ischaemia. Fernandez *et al.*[59] were able to measure V in urine

without any sample treatment or analyte enrichment. The atomiser was heated to 110 °C and three 60 µl volumes were sequentially injected with drying and pyrolysis steps between each injection. A chemical modifier containing BaF_2 and Triton X-100 was added to the urine. With this methodology, an LOD of 0.11 µg l^{-1} was achieved. An unusual diluent, 7.5 M NH_4OH, was used for the measurement of Co, Mn and Ni in serum.[60] Samples were diluted 2–4 fold and injected together with H_2O_2. Results reported for Seronorm RM were in good agreement with the certified values.

Apart from the use of BaF_2, recent work investigating *chemical modifiers* was mainly directed at the measurement of Se. After comparing Ir, Pd and Rh for their influence on analytical parameters, Piascik *et al.*[61] concluded that thermally reduced Rh was the most useful for the analysis of urine and allowed an LOD of 7.5 µg l^{-1}. In a similar study with human milk samples, Ir and Zr were used.[62] It was found that the best results were obtained with a mixed modifier. The absolute LOD was 0.41 µg l^{-1} but for the entire method, involving HNO_3 and H_2O_2 digestion, the LOD was 1.37 µg l^{-1}. Perhaps the most interesting work is that of Sahin *et al.*[63] who compared the responses obtained with Se^{IV}, Se^{VI}, SeCys and SeMet in the presence of Ni or Pd–Mg chemical modifiers. Thermostabilization was equivalent for all combinations using either an aqueous or serum sample matrix whereas sensitivities were variable among the four Se species. However, when either modifier was prepared in 2.5% HNO_3, the analytical responses were identical. These results may help to explain some of the differences that have been reported when samples have been analysed by ETAAS and by ICP-MS.

Simultaneous AAS featured in two publications. To measure As and Se in urine, Co was selected as an internal standard.[64] Matrix-matched calibration was preferred and the inclusion of Co provided for recoveries of 96% and 101% for As and Se, respectively, at a concentration of 10 µg l^{-1}. For the simultaneous determination of Cd and Pb in blood, samples were diluted in 0.2% HNO_3 and ethanol. The solutions were injected into a transverse heated filter atomiser at a temperature of 110–120 °C. The filter atomiser reduced non-specific absorption and obviated the need for chemical modifiers.[65]

3.3 Vapour generation procedures

A commercial instrument was evaluated for the *measurement of Hg in 1 cm segments from a single hair*.[66] The analyser included modules for sample combustion, amalgamation of the released Hg vapour with gold and AAS. The LOQ was defined as 0.01 ng of total Hg and the between-strand variability was 6.5 ± 2.8%. With such performance it is possible to monitor monthly Hg exposure by analysis of just a single hair. A similar combustion, amalgamation, Hg-analyser was evaluated for use with human hair and animal fur.[67] The analytical cycle was complete in less than 10 min and satisfactory results were obtained with a hair CRM and in interlaboratory studies.

Anthemidis *et al.*[68] developed what they called *an integrated gas–liquid separator which also functioned as the reaction cell* for Hg vaporisation. Sample volumes of up to 30 ml could be accommodated within the on-line system. The large volume gives the potential for high sensitivity. This is fine for water samples but is not relevant to most biological specimens. Using a 20 ml sample, the LOD is 0.02 µg l^{-1}.

Methods for measuring hydride-forming elements by *trapping the vapour within the graphite furnace* prior to atomisation are well described. In this last review period, similar systems have been reported for measuring Hg. Vil'pau *et al.*[69] employed a two-step atomiser consisting of a vaporiser and a furnace. Mercury vapour released from the sample, by heating the vaporiser, was transferred by an Ar gas flow to the inner walls of the furnace, where virtually 100% was trapped and then atomised by electrothermal heating. With 20 µl of urine, the LOD was 2 µg l^{-1} but the limit can be reduced further by repeated vaporisation and trapping in advance of the atomisation. The speciation work of Torres *et al.*[52] was described above (Section 3.1.6). In some preliminary work to optimise the vapour generation conditions, Hg vapour was trapped in an Au-treated graphite furnace and then re-atomised by heating. The LOD for this procedure was 0.001 µg g^{-1}. Both of these methods involving graphite furnace trapping were described as simple and afforded exceptional sensitivity compared with conventional CVAAS. Measurement of Hg by ICP-MS is problematic because of retention on the sampler tubing and it is not usually included in multi-element analyses. Therefore, this approach to Hg determination may become more widely used in the future.

Wang *et al.*[70] developed an automated *method for measuring Pb in blood by HG-AFS* which, with an LOD of 0.014 mg l^{-1}, was claimed to be more sensitive than HG-AES, ETAAS or HG-AAS (with or without in-atomiser trapping). The Pb in an acidified, digested sample was oxidised using $K_3Fe(CN)_6$, and then reacted with alkaline BH_4^- solution. The gaseous hydride was separated and swept to the atomiser. All facets of the procedure were optimised and a fast sampling rate, 120 h^{-1}, was possible. A second Chinese group used a dual-channel HG-AFS system to determine As and Se simultaneously.[71] Good results were reported for biological CRMs after preparation in a tartaric acid medium and recoveries of 92.5–95.5% and 101.2–108.4% were obtained for As and Se, respectively. See also the work in Sections 3.1.5[46] and 3.1.6.[50]

3.4 Atomic emission spectrometry

A *novel interface between the high pressure eluent from an on-line digestion system to an ICP-AE spectrometer* was developed by Bran *et al.*[72] This consisted of a porous polypropylene tube with an inner rod made of PEEK, which caused the liquid to flow through as a thin film. In this way there was a large effective surface for gas exchange to occur through the porous tube. Gaseous products, CO_2 and NO_x, were removed with an efficiency of >99% and the stability of the ICP is thereby maintained. Relative standard deviations and LODs were low and results with biological CRMs were good. Improvements in the analysis of serum by ETV-ICP-AES were observed by Chen[73] when samples were prepared as PTFE emulsions.

3.5 Mass spectrometry

3.5.1 ICP-MS

3.5.1.1 Quadrupole ICP-MS. The normal concentration of Cr in blood is around 1 µg l^{-1}, which is close to the LOD for

ETAAS. Thus, ICP-MS offers an attractive alternative technique for measuring this important essential element. However, Kunze *et al.*[35] have investigated the effect of the *interference from carbon* ($^{40}Ar^{12}C$, $^{40}Ar^{13}C$) on ^{52}Cr and ^{53}Cr measurements within the blood Cr reference range. They concluded that Q-ICP-MS cannot be used for determination in biological samples where concentrations are likely to be in the μg l^{-1} range.

A new *interface, to go between a capillary electrophoresis column and an ICP-mass spectrometer*, was developed and evaluated.[74] The interface was designed to generate volatile species, in this case from liver Cd-metallothionein isoforms separated by CE. Conditions for generation of the volatile species were optimised and performance was reported to be superior to any achieved using a Babington- or Micromist-based interface.

3.5.1.2 Sector field ICP-MS. Using SF-ICP-MS, Roduskin *et al.*[75] determined *20 elements normally present at very low concentrations in serum and urine* diluted tenfold with 2% HCl. High purity water and acid were necessary and there was evidence of release of some elements from the fabric of the sample introduction system. The LOQs for 13 elements were in the sub ng l^{-1} range. Two remarkably similar methods were described for measuring Pt using SF-ICP-MS. One was applied to environmental, food and urine specimens[76] while the other was used to examine post-mortem tissue samples.[77] Both involved sample digestion and membrane desolvation for sample introduction. In addition, both used the BCR-723 Road Dust CRM to validate the methods. One included an investigation of possible interference from HfO^+, the other employed ID for quantification. The LODs were not dissimilar at around 5 to 35 pg g^{-1}. The presence of Pt in lung tissue was attributed to environmental contamination from car catalysts.

3.5.1.3 Collision cell (dynamic reaction cell) ICP-MS. Many of the elements that are of general clinical interest are subject to polyatomic interferences with Q-ICP-MS. Thus, the recent availability of *affordable instruments with collision cell technology* has had an immediate impact with an increasing number of publications showing the usefulness of the technique for the applications previously undertaken using AAS. The determination of 23 elements in urine[78] illustrates the potential that is now being realised. Samples were diluted 1 + 4 with 1% HNO_3 and aspirated using a Babington nebuliser at a flow rate of 0.4 ml min^{-1}. The collision cell gas used was He for most elements and H_2 for Se. Operation was maintained for up to 500 samples without deterioration of performance. In a very specific study, Cd and Pb were determined in a blood CRM.[18] The collision gas was 8% H_2 and 92% He at a flow rate of 7 ml min^{-1}. To measure total Se in serum, a choice of isotopes is available and the collision cell is not necessarily required, but when several isotopes are determined, as when ID calibration is employed, use of the cell becomes necessary. This was the situation faced by Encinar *et al.*,[47] who included ^{77}Se-labelled SeMet in an assay to measure SeMet and SeCys in human serum. Turning from the routine to the exotic, an interference from U on ^{242}Pu was removed using the reaction cell with CO_2. This allowed for a simple measurement of Pu in urine with Tl as internal standard.[40] Preconcentration and matrix removal was effected from a 20 ml sample with TRU resin to give an LOD of 1.9 pg l^{-1}. Using O_2 as the reaction gas, Ejnik *et al.*[79] determined $^{235}U:^{238}U$ ratios in urine. The gas converted the $^{235}U^+$ and the $^{238}U^+$ to the UO_2 species with m/z values of 267 and 270, respectively, thus avoiding a polyatomic interference at 234.8. The LOQ for U was 0.1 pg ml^{-1}, while the LOD for the $^{235}U:^{238}U$ ratio was 3 pg ml^{-1}.

3.5.1.4 Multiple collector ICP-MS. To achieve the very best precision data, as required for isotope ratio measurements, multiple collector ICP-MS (MC-ICP-MS) should be used. The technique has revealed some curious human physiology in that, under certain circumstances, *the body appears to treat some isotopes differently* from others. Krayenbuehl *et al.*,[80] for example, showed that there are higher $^{56}Fe:^{54}Fe$ ratios in blood from haemochromatosis patients than in blood from healthy individuals. The ratios also correlated with total body Fe and with the severity of the disorder. Thus, the patients must absorb more of the heavier Fe isotope than do normal subjects. The $^{66}Zn:^{64}Zn$ and $^{68}Zn:^{64}Zn$ ratios were determined in human red cells and hair by Ohno *et al.*[81] The precisions of the ratio measurements (2SD) were 0.05 and 0.10 parts per thousand, respectively. No seasonal variations in the Zn ratios were seen in red cells from volunteers. However, the ratios in hair were significantly lower than in the red cells, revealing an isotopic fractionation within the body. Isobaric interferences, *e.g.* $^{64}Ni^+$ and $^{136}Ba^{2+}$, were eliminated by ion chromatography before measurement. The ratio $^{234}U:^{238}U$ is used to demonstrate whether there has been exposure to depleted uranium. Karpas *et al.*[82] determined the ratio in hair, nails and urine from volunteers who were given U in drinking water. Excellent correlations were obtained between the ratios in water and hair or nail but not with urine. The authors recommend hair as a sample to assess exposure to depleted uranium.

3.5.1.5 Laser ablation ICP-MS. The particular features of LA-ICP-MS were exploited by Becker et al. in two pieces of work. They were able to demonstrate the distribution of elements in 20 μm sections of the hippocampus area of the brain.[83] A focused laser beam produced craters of 50 μm diameter and ^{63}Cu, ^{56}Fe, ^{31}P, ^{32}S, ^{232}Th, ^{238}U and ^{64}Zn were measured by double focusing SF-ICP-MS. In a second project to establish a procedure for analysis of small amounts of dried urine for forensic investigations, they measured Th, U and the $^{235}U:^{238}U$ ratio by LA-ICP-MS.[84] Samples of either urine or synthetic urine standards were simply dried and then analysed. Recoveries of spiked analytes were from 91 to 104%. In an unusual application, a case of murder by poisoning with Tl was revealed 38 years after the event.[85] Acid digests of bones were analysed by ICP-MS and, at 1.07–2.63 μg g^{-1}, the Tl concentrations were much higher than in control samples. To determine the time between poisoning and death, fingernails were examined by LA-ICP-MS. A peak of Tl was seen 2.5 mm from the distal edge of the nail. A similar longitudinal analysis was applied to the measurement of Hg in single strands of hair.[86] The Hg was measured and, with a sampling spot size of

50 μm, each result corresponded to about 4 h growth, thus providing a far superior resolution than is possible with almost all other techniques. In describing how chromatography and ICP-MS may be linked together and applied to investigations relevant to the pharmaceutical industry, Marshall *et al.*[87] included the use of gel electrophoresis for protein separations. The analyses were performed by LA-ICP-MS.

3.5.1.6 Electrothermal vaporisation-ICP-MS. An alternative technique to remove interferences from the serum matrix is that of ETV. Li *et al.*[88] adopted this approach for *measuring seven refractory elements after five-fold dilution of the serum*. Vaporisation was facilitated by inclusion of a fluorinating agent, PTFE. The LODs were from 0.019 ng g^{-1} for W to 0.328 ng g^{-1} for Ba.

3.5.2 Other MS techniques: AMS, MIP-MS, SIMS. To study the tissue distribution following administration of 0.001–5 μg of ^{9}Be and ^{10}Be, samples were digested in HNO_3, H_2O_2 and $(NH_4)_2S_2O_8$, the Be precipitated with NH_4OH and converted to BeO by heating to 800 °C. The Be isotope ratios were then *measured by AMS with an exquisitely low LOD* of 0.8 attomol.[89] In a fascinating piece of archaeological detective work, the same technique was chosen to perform ^{14}C dating on mummified tissues and other contents of a coffin found in Pakistan. The inscription on the coffin implied that the mummy was that of a daughter of the Persian king, Xerxes, with a date of 518–465 BC. However, the ^{14}C data confirmed the remains to be a modern fake from 1994–6.[90]

Kawano *et al.*[91] developed a complicated procedure that eliminated any Ar interference on Se measured in biological CRMs. The method involved ID, slurry sampling, *in situ* fusion and ETV into an *MIP-mass spectrometer using N_2 as the plasma gas*. The fusion step was introduced to ensure isotopic equilibrium between the endogenous ^{80}Se and the ^{78}Se spike.

Distribution of elements in human hair was studied by Kempson and Skinner using TOF-SIMS.[92] They were able to differentiate between external contamination on the cuticle scales and internal incorporation within the medulla of the hair. Elements on the cuticle increase in concentration longitudinally from the scalp whereas signal intensities in the medulla progressively decrease, except for Si. The complex patterns of concentration in hair make the interpretation of results complicated.

3.6 XRF

Further work to measure *Pb in bone by* in vivo *XRF* continues although with less momentum than in recent years. Much of the development has been at just one or two centres but other facilities are now becoming active. Factors contributing to measurement uncertainty were studied in detail by Ahmed *et al.*[93] Superior data were obtained with a reduced source–skin distance, longer measurement time with a weaker source (3600 s, 0.42 GBq), and where the subject has a lower body mass index and less subcutaneous fat (*i.e.* male/female). A Chinese group found that, by normalising Pb X-rays to the coherent scatter and calculation of intensity : coherent intensity ratios, features such as the thickness of overlying tissue, bone shape, size mass and subject motion did not influence the results. Concentrations were calibrated against results from Pb-spiked plaster of Paris phantoms.[94] Elsewhere, established systems were applied to specific physiological questions in relation to Pb exposure.[95]

Analysis of isolated bone material was also undertaken. Using *μSR-XRF, Ca, Pb, Sr and Zn were determined in cortex and medulla of bone slices* along the length of the tibia. It was found that the concentrations of Pb and Zn were strongly correlated.[96] In an attempt to derive information concerning dietary and other living conditions in the 13th Century, femur bones and surrounding grave materials were analysed by TXRF.[97] Concentrations of Sr and Zn were constant in trabecular and cortical bone, and higher than in surrounding soil, suggesting that they represented the *in vivo* levels. For Cu and Pb, the concentrations in the outer bone were high but were lower in the inner cortical tissue. The concentrations of Fe and Mn were very high and similar to those in the soil. Marques *et al.*[98] used μSR-XRF to analyse teeth from patients with renal failure, some of whom were on long- term dialysis treatment. Twelve elements were determined but the only difference compared with teeth from healthy subjects was a higher Pb concentration. No explanation for this observation was offered.

More work with μSR-XRF was directed to the *distribution of Pb and other elements within brain compartments*. Using a 16 keV beam focused to a spot size of 5 × 3 μm, wax embedded brain slices of 20 μm thickness were surveyed. While certain elements were associated with particular structures in the brain, Pb was distributed throughout, but in varying concentrations in different areas.[99]

3.7 Multielement applications

3.7.1 Biological fluids. Materials handled by dental workers contain elements such as Hg, Pd, Pt, Rh and Ti. For this reason Iavicoli *et al.*[100] decided to measure these elements in serum and urine, using ICP-MS. Samples were collected from 20 workers and from 20 healthy controls. Concentrations of Ti were not different between the two groups. The concentrations of the other metals were so low that statistical analysis was not possible. These results are rather unexpected as all other studies demonstrate that most dental workers will have a small increase, at least of Hg, in these samples. Serum trace elements were measured in patients with Parkinson's disease.[101] It has often been suggested that Parkinson's disease may be associated with trace element perturbation, usually involving production of reactive oxygen species. In the study mentioned here, 12 elements were determined by ICP-AES and it was found that Al, Fe, S and Zn were decreased while Cu, K, Mg and P were increased, compared with controls. The results do not really shed any light on the mechanisms involved in this disorder. Nakamura *et al.*[102] set out to *measure the loss of trace elements during haemofiltration*. A model system was set up and evaluated using bovine blood. Loss of Cu, Cr, Mn, Se and Zn into the ultrafiltrate was demonstrated. It was recommended that active replacement of Cu, and especially Se, should be considered. Measurements of refractory elements in serum[88] and elements found at extremely low

concentrations in serum and urine[75] were described above (Sections 3.5.1.2 and 3.5.1.6).

Heitland and Koster[78] have shown that the *multi-element potential and sensitivity of ICP-MS can be realised for the routine analysis of urine samples*. Conditions employed included a five-fold dilution with 1% v/v HNO_3, a Tb internal standard, low flow rate Babington nebuliser, a torch with a 2.5 mm id injector and an octopole collision cell using either H or He gas. Long-term stability was demonstrated. With this work in mind, it should be possible for laboratories to achieve impressive workloads in the future. Rather more specific problems were also addressed. Exposure to Al, As, Ga, In and Sb in optoelectronic industries was monitored by analysis of blood and urine samples using ICP-MS.[103] Concentrations of As, Ga and In were increased compared with control subjects. Interest in possible roles for trace elements in cardiovascular disease is increasing and an association between blood Cd and Pb with peripheral arterial disease is recognised. In a further study, ICP-MS was used to measure nine elements in urine from 790 such patients as part of the US National Health and Nutrition Environment Survey (NHANES). Patients with peripheral arterial disease had higher levels of Cd and W compared with controls.[104] The results suggest new topics for investigation. As was mentioned above, Th and U in urine were measured by LA-ICP-MS.[84]

Samples of *saliva from 20 patients with taste disorders* were analysed by ICP-MS.[105] The concentrations of Mn and Zn, at 2.78 ± 1.23 and 47.22 ± 17.1 ppb. respectively, were lower that in healthy subjects, 4.48 ± 2.46 and 79.8 ± 42.6 ppb, respectively. While the group data show significant differences the obvious overlap between patient and control concentration ranges indicate that this approach is unlikely to be clinically useful.

In a series of papers, Massanyi and colleagues report on a challenging piece of work. They present the concentrations of *Cd, Cu, Fe, Ni, Pb and Zn in semen* collected from bulls and rams,[106] stallions[107] and foxes.[108] The results were compared with the incidence of pathological spermatozoa in the samples. Concentrations of the elements were quite different among the species examined. Multiple correlations between element concentrations and different types of sperm malformations were also reported but again there was no consistency from one species to another. This diversity of results indicates that the associations are unlikely to be causal and their relevance to reproduction is unclear.

3.7.2 Hair and nails. To determine whether head hair can be used as a marker of exposure, samples *were collected from children living in an REE mining area of China* and analysed for 16 REE.[109] Concentrations of Gd, La, Lu, Nd, Sc and Y were much greater than in control samples. Whether there is any significant absorption of these elements and any associated health problems has yet to be determined. Measurements of hair elements can be useful when there may be increased exposure but the relationship to concentrations in blood and other tissues is less convincing. Thus, the rationale for and the results from the studies of Charles *et al.*[110] and Wang *et al.*[111] require careful evaluation. Using PIXE to determine 11 elements, Charles *et al.*[110] monitored changes in the hair of cervical cancer patients undergoing radiotherapy. Wang *et al.*[111] reported that Ca, Cu, Fe, Mg and Zn in the hair of young women were positively correlated with the body mass index. Given that the concentrations of these elements in the blood are under tight homeostatic control, the results are difficult to interpret.

Concentrations of *eight elements were determined in fingernails* from individuals with occupational exposure and from controls.[112] The results showed significant correlations with a large number of unrelated clinical disorders. The relevance of these observations to possible causal involvement of any of the elements was not made clear. Use of finger- and toenails to investigate exposure to As[113] and a possible link to cutaneous melanoma[114] was also reported.

3.7.3 Neurological tissues. Projects to determine *the normal distribution of trace elements in different sections of the brain* proved to be popular in the past review year. Using LA-ICP-MS, Cu, Fe, P, S, Th, U and Zn were measured in sections of the human hippocampus.[83] Meanwhile, portions of rat brains were analysed by ICP-MS to show the distribution of four[115] and 16[116] elements. For the mouse, however, PIXE was chosen and the distribution of five elements determined.[117] Notwithstanding the accuracy, or otherwise, of the results, none of these projects were developed to relate the data to what is known about elements and their function in normal or pathological brain. Why, for example, set out to measure Th, U and V, which have no known involvement with neurological function? Rather it would seem simply to be an excuse to use the equipment. In another speculative study, 30 eyes from 16 subjects were dissected for measurement of Cd, Hg, Pb and Tl by ICP-MS in the different parts of the eye.[118] Cd and Pb were found in the retinal structures and at much lower concentrations in other samples. No Hg or Tl was detected at all. Whether these results have any significance to eye disease was not considered but Cd and Pb have never been described as causing ocular pathology. Contrast this with the work of Ide-Ektessabi and Rabionet,[119] whose interest is with conditions such as Alzheimer's and Parkinson's diseases. It has been proposed that oxidative stress is involved in the development and progress of such neurodegenerative conditions and, therefore, it is relevant to look for evidence for promoters of reactive oxygen species such as Fe^{2+}, Fe^{3+} and Cu. In this work, XRF and XANES were used to show the distribution and oxidative state of elements in human, mouse and monkey brain and the results were consistent with the hypothesis that oxidative stress is a factor in the aetiology of these diseases.

3.7.4 Miscellaneous tissues. In two separate studies, PIXE was used for the *analysis of joint tissues and uterine material*. Metal prostheses, such as artificial hip joints, are subject to wear and corrosion with release of debris into surrounding tissue. The mechanisms involved in these processes are poorly understood. Chassot *et al.*[120] obtained tissues *post-mortem* or during surgery and developed a methodology to investigate release of metals from the implant. Hormone replacement therapy has a beneficial effect in preventing post-menopausal osteoporosis but also has other effects including alterations to

serum trace element concentrations. To understand the changes associated with replacement therapy, Ynsa *et al.*[121] studied ovariectomised rats subjected to varying hormonal regimes. Concentrations of Ca, Cu, Fe, K, Mn, Se and Zn were determined in the uterine tissue using PIXE. Removal of the ovaries led to increases in Ca and Fe and decreases in Mn and Se concentrations. Hormones, except for progesterone, produced a recovery of the Fe, Mn and Se concentrations. Using SEC-ICP-MS, metal binding species were seen in healthy, but not in cancerous, thyroid tissue.[49] Ten types of tissues, removed at *post mortem*, were analysed for Cs, Th and U by a validated ICP-MS method.[122] The main target organs were the lung and kidney.

3.7.5 Pharmaceutical applications. General applications are discussed in Section 4 below. Use of specific elements having pharmacological or diagnostic importance, such as Fe, Gd and Pt, is described in the relevant paragraphs of Section 3.8.

3.7.6 Non-clinical biological analyses. Degryse *et al.*[123] used *data obtained from analysis of goat bones to speculate on the historical context during the fourth to sixth centuries AD*. The trace element concentrations in modern bones provided a model for comparisons with fossil bones found at the archaeological site of Sagalassos, in south west Turkey. The authors argued that the presence of elements associated with Palaeolithic pollution indicates that the goats were kept close to the town, *i.e.*, there was social insecurity during the 5–6th centuries. During the 4th century, lower uptake of pollutants implied that the goats grazed over a wider area, allowed by a more secure historical period.

3.8 Progress for individual elements

3.8.1 Aluminium. *The relationship between levels of Al in deciduous teeth and the incidence of dental caries* was investigated by Tanaka and colleagues.[124] The researchers measured Al in both enamel and dentin in three categories of teeth; sound teeth, carious teeth and amalgam filled teeth. Concentrations of Al were quantitatively determined using ETAAS. Concentrations of Al in enamel were significantly higher in healthy teeth (42.8 μg g^{-1}) compared with carious teeth (20.7 μg g^{-1}) and filled teeth (27.3 μg g^{-1}). Similarly, dentin Al was elevated in healthy teeth (36.2 μg g^{-1}) compared with carious teeth (15.1 μg g^{-1}) and filled teeth (17.2 μg g^{-1}). The authors hypothesised that Al may act as a cariostatic agent.

Yumoto *et al.*[125] investigated the uptake of Al from maternal milk into tissues of suckling rats. Lactating rats were injected, subcutaneously, with ^{26}Al labelled $AlCl_3$ from days 1–20 *post partum*. The tissue concentrations of ^{26}Al in suckling rats were quantitatively determined using AMS. During suckling, Al levels in the brain, liver, and kidney rose rapidly. On weaning, liver and kidney Al concentrations declined rapidly but brain Al remained elevated and had declined only slightly even 140 days after weaning.

3.8.2 Arsenic. Correira *et al.*[64] investigated *the use of an internal standard for the quantitative simultaneous determination of As and Se in urine using ETAAS*. Two potential candidates were selected, Co and Sn, based on their physicochemical characterisation, and the best precision and analytical accuracy was obtained with Co. Urine samples were simply diluted 1 + 2 v/v with 1% HNO_3 containing 80 μg l^{-1} Co and injected with a mixed Mg–Pd chemical modifier. Optimised pyrolysis and atomisation temperatures were 1400 °C and 2300 °C and matrix matched calibration standards were required, in addition to the Co internal standard, for reliable quantitative determination. The method was validated by analysing urine CRMs and reported LODs were 1.8 μg l^{-1} and 2.6 μg l^{-1} for As and Se, respectively.

As in previous reviews, however, much of the focus for analytical methods has been on As speciation rather than determination of total As. A comprehensive review of pre-treatment methods for the characterisation and quantitative determination of As and Se species in biological matrices was presented by Wrobel and Caruso.[12] The authors emphasised that appropriate pre-treatment procedures were critical when dealing with species that are often chemically labile. Devesa *et al.*[126] reported a method for the quantitative determination of seven inorganic and methylated As species from biological matrices using pH specific generation of arsines coupled with AAS. Improved boiling point separation of arsines was achieved by increasing the density of the chromatographic adsorbent used for cold-trapping the arsines and by subsequent modification of the temperature gradient for release of arsines from the cold trap. Reported absolute LODs ranged from 0.14 ng for TMAO to 0.4 ng for As^V. The authors used the method to study As species in cultures of primary human hepatocytes exposed to As. Kirby and colleagues[127] used two separate chromatographic systems coupled directly or *via* a HG system to an ICP-mass spectrometer for separation and quantitative determination of 13 As species in marine biological tissues. A cation exchange column with a 20 mM pyridine mobile phase at pH 2.2 was used to separate cationic species, whilst anionic species were separated on an anion exchange column with a $NH_4H_2PO_4$ mobile phase at pH 5.6. However, even with these conditions arsenous acid required an additional HG step for complete resolution from other As species. Schmeisser *et al.*[128] quantitatively determined arsenolipids in ten fish oil samples using normal-phase HPLC coupled with ICP-MS. The potential adverse effect of organic solvents in the HPLC eluent on the plasma was overcome by using a reduced column flow rate, chilled spray chamber and addition of O_2 to the plasma. All ten fish oil samples contained the same four to six arsenolipid species but in differing amounts, depending on the fish species. Quantitative determination was achieved by external calibration using triphenylarsine oxide or triphenylarsine sulfide and the sum of the As species equalled the total As content determined separately by ICP-MS following acid digestion.

Several groups reported the findings from biomonitoring studies of environmental As exposure. *Hair and nail As is frequently used as a biomarker for environmental As exposure*. Raab and Feldmann[129] investigated the stability of As species during their extraction from these matrices. Under the extraction conditions employed, they noted that inorganic and methylated As^V species were stable, but methylated As^{III} species and the thio analogue of DMA were not stable. Cloud-point extraction was used by Shemirani *et al.*[42] to

pre-concentrate As from digested hair and nail samples for quantitative determination using ETAAS. Arsenic in acid digests of hair and nails was oxidised to As^V with $KMnO_4$, complexed with molybdate in H_2SO_4 and extracted into Triton X-114 by centrifugation. Methanol was added to the surfactant phase to reduce the viscosity of the solution, and 20 µl volumes introduced into the graphite furnace for quantitative determination. With optimised extraction conditions, an enrichment factor of 52.5 was reported, giving an LOD of 0.01 µg l^{-1}. Meza *et al.*[130] monitored total As and As species (As^{III}, As^V, MMA and DMA) in urine samples from Mexican subjects exposed to high environmental concentrations of As in drinking water. Total As and As species were determined using HPLC-ICP-MS. Urinary As concentrations in the exposed population ranged from 18.9 to 93.8 µg l^{-1} and a positive correlation between As intake from water and total As in urine was observed. Speciation of As revealed DMA (47.7–67.1%) to be the major urinary As species, followed by inorganic As (16.4–25.4%) and MMA (7.5–10%). The authors observed that these relative proportions of DMA and MMA in urine were low compared with other reported values and they hypothesised that the difference in proportion of the As species in this population may be due to genetic polymorphism in the As methylating enzymes. Hong *et al.*[131] monitored urinary As and Cd levels in a Chinese population co-exposed to these elements. Urine As and Cd concentrations were determined using AAS and urinary albumin, β_2-microglobulin and n-acetylglucosaminidase were determined as effective biomarkers of renal dysfunction. The authors estimated the critical concentrations of As and Cd for a 10% excess level of risk above background for renal damage to be 102 µg g^{-1} creatinine for As and 0.88 µg g^{-1} creatinine for Cd.

Finally, Bohrer *et al.*[132] investigated As contamination of commercial parenteral nutritional solutions using HGAAS. The range of total As concentrations determined was 62 to 249 µg l^{-1} and in most solutions the concentration did not exceed the recommended limit of 0.1 mg l^{-1}. The authors also reported that during autoclave heating of solutions that contained reducing substances, such as glucose and amino acids, around 50% of the major contaminating species As^V was reduced to As^{III}.

3.8.3 Beryllium. *An extremely sensitive method for the determination of Be in biological samples using AMS* was described by Chiarappa-Zucca *et al.*[89] Tissue samples from mice administered intra-peritoneal injections of ^9Be and ^{10}Be were digested with HNO_3, followed by oxidation with H_2O_2–$(NH_4)_2S_2O_8$, precipitation of Be with NH_4OH and oxidation of precipitated Be to BeO by heating to 800 °C. The $^9Be:{}^{10}Be$ isotope ratio in the extracted BeO was quantitatively determined using AMS. The measured Be ratios in different tissues spanned four orders of magnitude, with highest levels determined in spleen and liver. An LOD of 0.8 amol l^{-1} was reported. The authors considered the method to be particularly suited to biological studies to investigate the molecular dosimetry of Be and the molecular targets associated with chronic beryllium disease.

3.8.4 Bromine. Lyon and colleagues[133] investigated *the influences of inorganic and organic serum components on the determination of Br using ICP-MS*. They established that Na and albumin were the major inorganic and organic species in 100-fold diluted serum which enhanced the ^{79}Br signal by around 13%. Plasma substitute was found to be an effective calibration material to matrix match for human serum and had the advantage of containing no endogenous Br. An LOD of 0.09 mg l^{-1} was reported and the results of analysis of Br in serum were in good agreement with results obtained by a reference method using ICP-AES

3.8.5 Cadmium. The group of Canario *et al.*[65] investigated the analytical performance of a transversely heated filter atomiser (THFA) for the quantitative determination of Cd and Pb in whole blood using simultaneous ETAAS. Blood samples were simply diluted five- or ten-fold with H_2O and injected into the filter atomiser, which was pre-heated to a temperature of 110–120 °C. Injection of a small volume of C_2H_5OH with the diluted blood sample improved the repeatability of analytical signal and periodic cleaning of the filter atomiser at a high temperature prevented the build up of carbonaceous residue in the furnace cavity. The use of a filter atomiser, rather than a graphite tube platform atomiser, gave a significant reduction in non-specific background absorption and satisfactory analytical recoveries without the usual need for a chemical modifier. The method was validated by analysing RMs and spiked blood samples. Reported LODs for Cd and Pb were 0.05 µg l^{-1} and 1 µg l^{-1}, respectively.

A number of relatively simple pre-treatment and enrichment procedures have been described for the determination of Cd in biological matrices. Maranhao *et al.*[43] applied the phenomenon of cloud point extraction to separate Cd and Pb from HNO_3–H_2O_2 digested biological samples for determination using ETAAS. The two analytes were complexed with *O*,*O*-diethyldithiophosphate (DDTP) in HCl and extracted into Triton X-114 by centrifugation. Acidified CH_3OH was added to the surfactant-rich phase prior to analysis by ETAAS, but no additional chemical modifier was needed to ensure thermal stability of the analytes for quantitative determination using atomisation temperatures of 1400 °C and 1600 °C for Cd and Pb , respectively. Enrichment factors of 129 for Cd and 18 for Pb were reported, giving LODs of 6 ng g^{-1} for Cd and 60 ng g^{-1} for Pb. The method was validated by analysis of five biological CRMs. A novel and very simple direct solid sampling method for the determination of Cd in biological samples using FAAS was described by da Costa *et al.*[53] Dried and milled samples of bovine and chicken liver, between 0.5 and 7 mg, were weighed into small paper capsules, which were introduced into a quartz cell heated by an air–C_2H_2 flame. The results obtained by using this method were comparable with those obtained by acid digestion and determination using ETAAS, and analysis of two CRMs gave results in good agreement with certified values. For a sample mass of 7 mg, an LOD of 0.23 µg g^{-1} was reported. The heated surface of a quartz T-tube was used as the trapping medium for on-line preconcentration of Cd in the method developed by Korkmaz *et al.*[134] Volatile Cd species were generated from acid digests of tomato leaves and oyster tissue CRMs using $NaBH_4$ and

trapped on the surface of the T-tube, which was heated to 350 °C. The Cd was re-volatilised by heating the tube to 1000 °C with introduction of H_2 for quantitative determination using AAS. An enrichment factor of 90 was reported, compared with conventional FI-HGAAS, giving an LOD of 1.8 pg ml^{-1} for an initial 6 ml sample volume.

Four groups have reported investigations into the health effects of environmental Cd exposure. Zhu and colleagues[135] investigated whether environmental Cd was associated with low bone mass in a Japanese population living near a smelter. Forearm bone mineral density measurements were made using single photon absorptiometry and urine Cd concentrations determined using ETAAS in a group of 790 residents living near the smelter and a non-exposed control population. The researchers reported that bone densities were negatively correlated with urinary Cd, suggesting a dose–effect relationship between Cd dose and bone mineral density. They remarked on the striking observation that there was a marked increase in the prevalence of fractures for both sexes in the Cd polluted areas compared with non-contaminated areas. Zeng *et al.*[136] investigated the possible effects of Cd exposure on human prostate. Volunteers from two Cd polluted areas and a control area in Southern China underwent a thorough clinical examination, including digital-rectal examination. Blood samples were taken for determination of circulating sex hormones and prostate specific antigen (PSA) using radio- and enzyme-immunoassay. Blood and urine samples were taken for determination of Cd using AAS, as indicators of Cd body burden. The reported results showed a clear dose–response relationship between Cd exposure and the prevalence of cases with abnormal levels of PSA. The authors concluded that chronic environmental Cd exposure is associated with injury to human prostate. Jurasovic *et al.*[137] reported the findings of a study to investigate the relationship between reproductive endocrine function and Cd body burden from cigarette smoking in Croatian men. After adjusting for confounding factors, the authors noted that blood Cd was significantly associated with a decrease in testis size and an increase in serum oestradiol, follicle stimulating hormone and testosterone. Finally, Zhang *et al.*[138] investigated the potential effects of environmental Cd exposure on pregnancy outcome. The authors determined Cd in whole blood, cord blood and placenta from healthy pregnant women living in a Cd polluted area of China. Blood and tissue Cd concentrations were determined using ICP-AES. Blood Cd concentrations ranged from 0.8 to 25.2 μg l^{-1} and placental Cd concentrations ranged from 0.084 to 3.97 μg g^{-1}. Statistical analysis showed no significant relationship between Cd exposure and immediate pregnancy outcome (premature labour or neonatal asphyxia). However, regression analysis did show that cord blood Cd, but not maternal blood Cd or placenta Cd, was negatively associated with neonatal birth height.

3.8.6 Calcium. Bacciotini *et al.*[139] demonstrated the potential of *ICP-MS as a technique for determining Ca bioavailability from alimentary sources*. The researchers calculated the bioavailability of Ca from high-calcium mineral waters given to 27 healthy volunteers. Mineral water samples were extrinsically loaded with ^{44}Ca and functional absorption of Ca from the oral dose was calculated from the determination of plasma Ca isotope ratios using ICP-MS. For an ingested Ca load of 3.18 mmol, the percentage absorption of Ca averaged 22.55% for men, 22.57% for pre-menopausal women and 21.62% for post-menopausal women. They concluded that bio-availability of Ca from water was comparable to that from milk.

3.8.7 Chromium. Studies have shown that measurable increases in the levels of ions such as Cr and Ni can be determined in the serum of patients with metal surgical implants. Kim and colleagues[140] described a cross sectional study to investigate serum Cr and Ni concentrations in 37 patients following spinal arthrodesis with stainless steel implants, a procedure to treat spinal deformity in adolescents. Concentrations of Cr and Ni were quantitatively determined using ICP-MS. The researchers reported abnormally high serum levels of Cr and Ni in all patients examined compared with normal reference values, and these elevated levels were significantly inversely related to time from surgery. Mean Cr and Ni levels in subjects who had undergone surgery less than two years previously were 2.7 μg l^{-1} and 3.8 μg l^{-1}, respectively. Mean Cr and Ni levels in subjects who had undergone surgery over four years previously were 0.3 μg l^{-1} and 0.9 μg l^{-1}, respectively. The authors concluded that serum levels of Cr and Ni were elevated after implant surgery and although they declined rapidly, they still remained above normal levels more than four years after surgery. The authors recommended that the long-term health implications of this metal exposure warranted further investigation. The research group of Back *et al.*[141] examined changes in serum Cr and Co levels in patients following a novel metal-on-metal hip resurfacing procedure. Serum Cr and Co levels were quantitatively determined using ETAAS and ICP-MS pre-operatively and sequentially at 3, 6, 9, 12 and 24 months post-operatively. An increase in serum Cr peaked at 9 months post-operatively whilst an increase in serum Co peaked earlier at 6 months. Concentrations of both metals then gradually declined over the next 15 months. No adverse effects on renal function were observed by the researchers during the two year study period.

Kunze *et al.*[35] re-emphasised the problem of C interferences on the determination of Cr in biological matrices using Q-ICP-MS and clearly demonstrated that C, added to a blank solution, produced signals at atomic masses 52 and 53 which were equivalent to normal blood Cr concentrations. They proposed that quantitative determination of Cr in biological matrices should be made using ETAAS, SF-ICP-MS or possibly Q-ICP-MS with a reaction or collision cell.

3.8.8 Cobalt. The research group of Ribeiro *et al.*[142] *compared two sample pre-treatment and introduction methods for the quantitative determination of Co in biological matrices using ETAAS*. For direct solid sampling, CRMs were ground to a mean particle size of 50 μm, whilst for alkaline treatment a 250 mg sample of CRM was mixed with 2 ml of 25% TMAH. The authors used a prototype high-resolution continuum source AA spectrometer to investigate spectral interferences, including background absorption, and to optimise temperature programmes for both sample types. Molecular absorption bands were observed for atomisation temperatures above

1800 °C, which the authors associated with formation of PO_x. Using the optimised thermal conditions, quantitative measurements were made using conventional line source ETAAS. The two methods were used to determine Co in six CRMs using aqueous calibration standards. Results obtained by both sample preparation methods were in good agreement with certified values and an LOD of 5 ng g^{-1} was reported.

3.8.9 Copper and zinc. Yaman and Akdeniz[54] examined various designs of slotted quartz tube atom trap for the quantitative determination of Cu in human thyroid tissue using FAAS. The optimised design gave a 3.5-fold enhancement in sensitivity. The authors used the method to compare Cu levels in healthy and cancerous thyroid tissue and reported increased concentrations of Cu in cancerous tissue.

Nomura and colleagues[143] *systematically examined the principal factors affecting the analytical precision and accuracy of Cu and Zn determinations in bovine liver using ETAAS with solid sampling*. Bovine liver samples were prepared using different drying procedures, including freeze drying and microwave drying, and either ball or cryogenic milling. A tungsten–rhodium chemical modifier was required for accurate Zn determination and satisfactory calibration for both elements was obtained with aqueous standards. The studies indicated that accurate determination of Zn is more dependent on the sample pre-treatment than Cu, and that the best microhomogeneity was achieved with microwave drying and cryogenic milling. Concentrations of Cu and Zn determined in a bovine liver CRM were in good agreement with the certified values and values determined using a microwave digestion-FAAS reference method.

The serum concentrations of Cu and Zn in 80 severely malnourished children were investigated by Thakur *et al.*[144] using AAS. A mean serum Cu level of 0.74 μg ml^{-1} was determined in the malnourished group compared with 1.19 μg ml^{-1} for a healthy control group. Similarly, a 'significantly lower' serum Zn level of 2.59 μg ml^{-1} was determined in the malnourished group compared with 3.92 μg ml^{-1} in the control group. (However, the review team note that these Zn values are 39.6 and 60.0 μmol l^{-1}, respectively, which are considerably above what one could normally expect in children and suggest contaminated samples, for example, from normal Vacutainers used to collect the blood samples.) The trace element deficiency was associated with reduced superoxide dismutase activity, hypoproteinaemia and anaemia. The authors concluded that the trace element deficiency and depleted anti-oxidant activity could be contributory factors to the pathophysiology of protein malnutrition. The sensitive technique of LA-ICP-MS was used by Becker *et al.*[83] to examine the spatial distribution of Cu, uranides and Zn in thin sections of human brain hippocampus. The surface of the brain sections was raster scanned with a focused laser beam in a cooled laser ablation chamber specifically developed for the measurements. Quantitative determinations were obtained using laboratory prepared matrix matched standards. The authors also examined the use of calibration solutions introduced through a micro-nebuliser inserted directly into the ablation chamber. The researchers observed that uranides were homogeneously distributed at concentrations in the very low ng g^{-1} range. By contrast, a non-homogeneous layered distribution was observed for both Cu and Zn.

—Cereal based complementary foods can contain high levels of phytic acid, which binds strongly to trace elements and can affect their absorption. Egli and colleagues[145] investigated the effect of de-phytinisation of complementary foods on the absorption of Cu and Zn in adults. Untreated and de-phytinised food samples were labelled with ^{70}Zn and ^{65}Cu stable isotopes and given to volunteers. Faecal concentrations of the Cu and Zn isotopes were determined using TIMS and the apparent absorption of both elements estimated from the faecal excretion of non-absorbed isotope labels. Apparent Zn absorption was significantly higher from the de-phytinised food sample but apparent fractional Cu absorption was not affected by de-phytinisation. The authors proposed further work to examine the long-term benefits of de-phytinisation of complementary foods, particularly for young children. The efficiency of uptake of Zn from aqueous doses of $ZnSO_4$ was investigated by Tran *et al.*[146] Aqueous $ZnSO_4$ was labelled with ^{70}Zn or ^{68}Zn and orally administered to healthy adult volunteers in three pairs of Zn doses in three phases (one dose per phase). An *i.v.* dose of ^{67}Zn was also administered one hour after the first oral dose of each pair. Daily urine samples were collected for up to 15 days following administration of the Zn labels. Zinc isotope ratios were determined using ICP-MS and fractional absorption of Zn calculated from the dual isotope ratios. Absorption of Zn was best described by a saturable dose response model with a maximum Zn absorption of 13 mg for the largest doses. The authors concluded that increasing aqueous doses of Zn above 20 mg resulted in small and progressively diminishing increases in Zn absorption.

Abnet *et al.*[147] described the findings of a study to investigate the relationship between oesophageal tissue Zn concentrations and oesophageal cancer risk. Tissue concentrations of Zn in fixed oesophageal biopsy samples, collected in 1985 as baseline samples for a prospective observational study, were determined using XRF. Tissue Zn concentrations were determined in tissues from 60 eventual cases of oesophageal cancer and 72 control subjects. Cox proportional hazards models were used to estimate hazard ratios for the association of Zn and other elements with the risk of cancer. The risk of developing cancer was significantly lower for subjects in the highest quartile of tissue Zn concentrations. No association was observed between tissue Cu, Fe or Ni concentration and the risk of oesophageal cancer. The authors concluded that XRF may be used to assess relationships between essential and toxic elements and disease risk in banked tissue samples. Finally, Flinn *et al.*[148] presented data to show a relationship between enhanced Zn consumption and impaired cognitive function in rats. Rats were administered high levels of Zn (10 ppm $ZnCO_3$) in drinking water for periods of up to nine months. Increased brain Zn levels were confirmed by microprobe SR-XRF. When tested with a series of cognitive experiments, rats administered the Zn enriched water were found to have impaired reference and working memory compared to control rats.

3.8.10 Gold. *Ionisation and percutaneous absorption of Au are recognised prerequisites for contact sensitisation and*

elicitation of an allergic reaction to the metal. Moller and colleagues[149] investigated the percutaneous absorption of Au following occlusive patch testing with gold sodium thiosulfate (GSTS). Patients were patch tested with 0.5%, 2% and 5% GSTS in petrolatum and blood samples taken prior to testing and on day 3 or day 7 of application. Concentrations of Au in the blood samples were quantitatively determined using ICP-MS. Median blood Au levels increased from 0.03 μg l^{-1} on day 3 to 0.34 μg l^{-1} on day 7 and this increase was similar in both gold allergic and non-allergic patients.

3.8.11 Iodine. Bing *et al.*[32] described *a simple pre-treatment procedure for the determination of I in biological matrices*. Iodine was extracted from hair, kelp and tea samples into a 10% NH_3 solution heated to 185 °C for 18 h in PTFE lined steel pressure bombs. The concentration of I in the resulting extract solution was quantitatively determined using ICP-MS with ^{126}Te as an internal standard to correct for matrix interferences and instrumental drift. An impressively low LOD of 0.003 ng ml^{-1} was reported, which corresponded to an LOQ of 0.1 ng g^{-1} for the original solid sample. The method was validated by analysing a series of Chinese CRMs. The authors considered that the NH_3 extraction method had significant advantages over an alternative sintering method, being a simpler procedure with lower procedural blanks and better sensitivity and reproducibility.

3.8.12 Iron. *The full potential of ICP-MS for elemental isotope measurements in clinical applications is now being realised and many exciting studies are being reported*. In the work described by Krayenbuehl *et al.*,[80] the Fe isotope ratios in blood samples from patients suffering from hereditary haemochromatosis were compared with isotope ratios in blood from healthy individuals. The $^{56}Fe:^{54}Fe$ isotope ratio was quantitatively determined using MC-ICP-MS. Blood from haemochromatosis patients had a higher $^{56}Fe:^{54}Fe$ ratio than blood from healthy individuals. Furthermore, the isotope ratio showed a significant correlation with total body Fe accumulation, severity of disease and need for regular phlebotomy to reduce Fe re-accumulation. The authors concluded that the blood of patients with hereditary haemochromatosis contains a higher proportion of heavier Fe isotopes and that this difference was due to isotope sensitive Fe absorption in the intestine.

The bioavailability of Fe from five different iron salts used to fortify infant formulas was investigated by Dominguez *et al.*[150] Infant formula was fortified with iron lactate, diphosphate, sulfate, encapsulated sulfate or EDTA–Fe^{III}. A two-stage *in vitro* enzyme treatment was developed to simulate newborn digestion, the first using pepsin at pH 5 and the second using pancreatin at pH 7. The dialyzable fraction, considered to be equivalent to the fraction available for absorption, was determined using ICP-AES with an axial plasma. The researchers considered EDTA–Fe^{III} to be the most suitable Fe salt for fortification of infant formula. A new approach to Fe fortification of infant formula using micro-encapsulated ferrous fumarate (sprinkles) was investigated by Tondeur *et al.*[151] The researchers examined the absorption of different doses of Fe from sprinkles added to a maize based complementary food given to infants with different Fe and haematological status. They used a dual stable isotope technique with determination of Fe isotopes using ICP-MS. The sprinkles were labelled with ^{57}Fe and infants were also administered a ^{58}Fe tracer intravenously. Blood samples were taken prior to administration of the tracers and 14 days later and the absorption of Fe estimated from corrected erythrocyte incorporation of ^{57}Fe. The authors reported that mean Fe absorption was 8.2% in infants with iron deficiency anaemia, 4.48% in infants with iron deficiency and 4.65% in iron sufficient infants. They concluded that Fe was satisfactorily absorbed from the sprinkles and met published requirements for absorbed Fe.

3.8.13 Lead. *Results presented by Martin et al.*[152] *on the distribution of Pb in a hair sample collected from a lead smelter worker clearly demonstrated the impact of surface contamination on Pb concentrations determined in this matrix*. Hair Pb was determined using SR-XRF and a mathematical model produced to imitate the scan signal obtained from the hair sample. The results indicated that direct deposition from the environment was the most important source of Pb in the hair sample analysed. This observation has an important bearing on the study described by Strumylaite *et al.*[153] and indeed other groups who have advocated hair samples for bio-monitoring of occupational and environmental exposure to toxic elements. The group measured Pb in hair samples from workers in a ceramic plant and a non-exposed control population. Hair Pb was quantitatively determined using AAS. Mean hair Pb in the exposed group was 7.6 μg g^{-1} compared with a concentration of 3.2 μg g^{-1} in the control group. The authors proposed that hair measurements could be used to identify Pb exposure in epidemiological studies. However, the results of Martin clearly indicate that hair measurements cannot be considered a substitute for blood Pb measurements in assessing Pb absorption from the workplace or environment. The merits of portable instruments for large-scale field studies of occupational and environmental Pb exposure continue to be assessed. Taylor *et al.*[154] determined blood Pb concentrations in 243 occupationally exposed subjects, working at altitude in the Peruvian Andes, using a portable ASV instrument. Duplicate samples were also analysed by a reference method using ETAAS. The mean blood Pb concentration determined using ETAAS (46 μg dl^{-1}) was significantly higher than the mean value determined by ASV (32 μg dl^{-1}). The authors could not clearly establish the cause of the discrepancy but advised that blood measurements on populations living at altitude made using portable ASV instruments should be treated with caution. Wang *et al.*[70] described a very sensitive screening method for blood Pb levels in the Chinese population using HGAFS. Lead hydride was generated from acid digested blood samples using $K_3Fe(CN)_6$ and tetrahydroborate and swept directly into the atomiser of the fluorescence spectrometer. A thorough study of factors affecting the method was presented and, with optimised conditions, an LOD of 0.014 mg l^{-1} was reported. The authors claimed the performance to be superior to direct injection ETAAS and atom trapping HG-AAS and comparable to ICP-MS. Zoeger *et al.*[96] used μ-SR-XRF to investigate the distribution of Pb and Zn in slices of human bone. The

authors observed that Pb was localised mainly at the outer border of cortical bone and was very strongly associated with Zn distribution.

Several groups have reported the results of studies investigating the relationship between Pb exposure and health status or incidence of disease risk in adult and infant populations. The relationship between moderate accumulative exposure to Pb and development of cataracts was investigated by Schaumberg *et al.*[155] The study population was a subset of the US normative ageing study group, a longitudinal epidemiological study of ageing men that has been reported in previous ASU reviews. The selected group was restricted to men over 60 who had received eye examinations as part of the study. Data on bone Pb concentrations were obtained from measurements taken between 1991 and 1999 using K shell XRF and eye examination data for the period following bone Pb measurements was reviewed. An increased risk of cataracts was noted for men in the highest quartile of tibia and patella Pb levels compared with men in the lowest quartile. The authors concluded that the epidemiological data suggested accumulative Pb exposure may be an important but previously unrecognised risk factor for cataracts.

3.8.14 Magnesium. The group of Yang *et al.*[57,58] developed a particularly sensitive method for *monitoring dynamic changes in brain Mg levels using dual-probe microdialysis coupled with ETAAS*. Gerbils were subjected to transient focal cerebral ischemia by occlusion of the middle cerebral artery and common carotid artery. Extracellular fluid dialysate samples were collected, during and after occlusion, from microdialysis probes inserted in both sides of the brain cortex. The dialysates were diluted with H_2O and injected directly into the graphite tube for quantitative determination of Mg. An LOD of 0.03 $\mu g\ l^{-1}$ was reported. During cerebral ischemia, extracellular Mg levels fell significantly to 41% of the baseline value before occlusion, but returned to 67% of baseline within 60 min of reperfusion. The authors hypothesised that the derangement of Mg could be an important factor in the progression of brain cell injury.

3.8.15 Mercury. This review period has seen attention return to investigations of total Hg levels in biological samples rather than Hg speciation studies. *Despite problems associated with hair trace element analysis, some of which are highlighted in the section on lead in this review, the use of hair for biomonitoring of Hg exposure continues to be advocated by research groups*. Legrand and colleagues[66] took this approach further by describing a method for monitoring Hg exposure using a single strand of hair. Mercury was determined directly from the hair sample using a commercial mercury analyser that combined sample combustion with gold amalgamation and AAS. The authors determined Hg concentrations in hair from 12 women exposed to Hg and compared the results with those obtained from an established method involving digestion of a hair bundle sample and determination of Hg using CVAAS. The researchers reported a "1 : 1 relationship" between the results obtained by the two methods. Variability between individual hair strands from the same subject was reported to be 6.5%. The authors concluded that the single hair method was suitable for monitoring Hg exposure on a regular (monthly) basis. Two research groups presented the findings of studies on occupational exposure to Hg in dental practitioners. Ritchie *et al.*[156] examined Hg exposure in 180 dentists from the West of Scotland. Urine, hair and nail samples were taken for determination of Hg , using CVAAS for urine and ICP-MS for hair and nail measurements. Environmental measurements of Hg were also made in eight different work areas of their surgeries. In over 67% of surgeries visited, environmental Hg concentrations in one or more areas exceeded the occupational exposure standard. Dentists were found to have urinary Hg levels around four times higher than an unexposed control population, but, in all but one subject, the urinary Hg level was below the UK HSE health guidance value of 20 $\mu mol\ mol^{-1}$ of creatinine. The researchers considered that urine Hg was a better indicator of Hg exposure than either hair or nail Hg concentrations. Karahalil *et al.*[157] determined urine Hg excretion in 20 Turkish dentists using CVAAS. Concentrations of Hg in urine samples from the dentists were around three times higher than a control group (6.29 $\mu g\ l^{-1}$ *versus* 1.97 $\mu g\ l^{-1}$, respectively). They considered that dentists were at risk of significant Hg exposure and that careful attention to simple hygiene measures such as avoidance of spills, floor cleaning and ventilation should be taken to minimise the risk of exposure. The review team note that these findings are consistent with observations made some 25 years ago on Hg exposures in dental practitioners. A comprehensive report on 'reference' Hg concentrations in human tissues was presented by Lech and Sadlik.[17] Tissue samples taken from 75 autopsies of inhabitants of Southern Poland were homogenised and digested with H_2SO_4–HNO_3 for quantitative determination using CVAAS. The highest mean Hg levels were determined in kidney (35.9 $ng\ g^{-1}$) and liver (15.5 $ng\ g^{-1}$) compared with levels between 2 and 4 $ng\ g^{-1}$ in all other tissues analysed. The reported concentrations were lower than levels previously reported for Korean and Japanese populations.

A very sensitive method for the determination of methylmercury in a variety of biological specimens was described by Davies *et al.*[41] using SPME-ICP-MS. Tissue samples were microwave digested with CH_3COOH and methylmercury derivatised and extracted using headspace SPME on a polydimethylsiloxane coated silica fibre. Methylmercury was quantitatively determined using capillary GC-ICP-MS. The authors reported an LOD of 4.2 $pg\ g^{-1}$. They validated the method by analysing a range of CRMs and determined methylmercury concentrations in eggs collected from colonies of seabirds on islands in the Bering Sea and Gulf of Alaska.

A novel method for sequential speciation of Hg was described by Zachariadis *et al.*[51] using IC coupled on-line with CVAAS. The method was based on the selective adsorption of pyrrolidine dithiocarbamate (PDC) complexes of Hg onto a chromatography column packed with PTFE. Inorganic Hg-PDC was retained on the column, whereas methylmercury–PDC was not adsorbed and was directly reduced on-line by reaction with $NaBH_4$ and thermal dissociation for quantitative determination of Hg using AAS.

3.8.16 Platinum group elements. *A number of sensitive methods for the determination of platinum group elements (PGEs) have been described in this review period.* Rudolph *et al.*[158] determined 'background' concentrations of Pt in human tissues using ID SF-ICP-MS with membrane desolvation and USN sample introduction. Lung, liver and kidney samples, from five autopsies, were prepared for analysis by a combination of microwave and open vessel digestion. Very low LODs were reported in all three tissue types: 20 pg g^{-1} in both lung and liver and 35 pg g^{-1} in kidney. Tissue Pt levels determined in the tissues ranged from 0.03 ng g^{-1} to 1.42 ng g^{-1}. The authors hypothesised that the levels of Pt in lung tissue may reflect environmental levels of Pt arising from car catalysts. Fragniere *et al.*[76] also described a sensitive method for the quantitative determination of Pt in biological and environmental matrices using ICP-SF-MS with a membrane desolvation unit for sample introduction. The use of a membrane desolvator greatly reduced oxide formation and the interference of HfO^+ on the Pt signal. An LOD of 0.5 ng l^{-1} was reported for Pt in human urine.

Eleni *et al.*[56] reported a comprehensive investigation of the mechanism of Pt atomisation when aqueous and serum samples are analysed using ETAAS. Activation energies for Pt in both solution matrices were calculated using both chemical and physical approaches previously described by Rojas-Olivares and L'vov , respectively. With increasing masses of Pt in aqueous solution, a change in atomisation mechanism from adsorption to evaporation was hypothesised. In contrast, the activation energy for increasing masses of Pt in serum indicated a single mechanism which involved thermal desorption of Pt from the carbon residue generated by pyrolysis of the organic serum matrix. Platinum group elements are widely used in dentistry for fillings and prosthetic work. Iavicoli *et al.*[100] monitored occupational exposure to PGEs in dental workers through the determination of PGEs in serum and urine using ICP-MS. Blood and urine samples were taken from a group of 20 dentists and 20 healthy unexposed controls. The very low mean serum and urine concentrations of Pd, Pt and Rh did not allow any significant statistical comparison between the two groups. The authors considered that determination of Pd, Pt and Rh in urine and serum was not useful in assessing occupational exposure in dental workers. Maharaj[159] presented findings on the determination of Pt in silicone breast implant materials using ICP-MS. The concentration of Pt found in the different materials were: 0.26–48.9 μg g^{-1} for implant gel, 3–28.9 μg g^{-1} for elastomer, 5.8–125.3 μg g^{-1} for double lumen and 5.8–8 μg g^{-1} for foam. Concentrations of Pt in surrounding capsular tissue ranged from 0.003–0.3 μg g^{-1}. The author concluded that all silicone breast implant materials may be a source of significant Pt exposure for individuals with such implants.

Introduction of automobile catalytic converters containing PGEs has raised concerns over the environmental impact of bioaccumulation of these elements. A comprehensive review of the routes of transfer of PGEs from the environment to biological systems was presented by Ek *et al.*[160] The same group examined the bioaccumulation of PGEs in raptors (birds of prey).[161] They considered the use of raptors to be particularly useful for investigating the environmental impact of PGEs as they inhabit both urban and rural environments and represent the top end of the food chain. Concentrations of Pd, Pt and Rh in raptor blood, faeces and tissues were determined using ICP-MS. No evidence of significant bioaccumulation of PGEs in liver or kidney was observed. The results, however, did indicate a greater mobility gradient into biological systems for Pd than for Pt and Rh.

The pharmacokinetics of a novel Pd based photodynamic therapy drug, palladium bacteriopheophorbide (WST09), were investigated by Brun *et al.*[162] Tumour bearing mice were administered a single bolus injection of WST09. At various time points following injection, blood and tissue concentrations of Pd were quantitatively determined using ETAAS. Biphasic kinetics were observed in plasma, liver and kidney tissues, and clearance from these organs was rapid. No selective accumulation was observed in any tissue compared with plasma. The authors hypothesised that the therapeutic effects of the drug may be due to vascular targeting from the drug in circulation rather than selective accumulation in tumour tissue.

3.8.17 Rare earth elements. *The value of scalp hair as a biomarker of exposure to rare earth elements (REEs)* was investigated by Tong *et al.*[109] Scalp hair samples were collected from children aged 11–15 years, living in an area of Southern China mined for rare earths. Sixteen rare earth elements were determined in the digested samples using ICP-MS. The authors found that for all sixteen elements, measured levels in the hair samples from children in the mining area (*e.g.*, La 0.14–6.93 μg g^{-1}, Lu 0.2–13.3 ng g^{-1}, Y 0.03–1.27 ng g^{-1} and Gd 12.2–646 ng g^{-1}) were significantly higher than in children from a non-mining reference area (*e.g.*, La 0.04–0.4 μg g^{-1}, Lu 0.4–3.3 ng g^{-1}, Y 0.03–0.29 ng g^{-1} and Gd 8.3–64.3 ng g^{-1}) and much higher than values previously reported in the literature. The distribution pattern of elements in the hair samples reflected the environmental distribution of rare earths in the mine and surrounding area. The authors considered that children living in the mining area should be regarded as a high-risk group for REE exposure.

Gadolinium–DTPA is often used as a contrast agent for magnetic resonance imaging (MRI). Loreti and Bettmer[163] combined SEC with ICP-MS to determine Gd and Gd–DTPA (diethylenetriaminopentaacetic acid) in urine following *i.v.* administration of the contrast agent to a patient undergoing MRI. The researchers observed no conversion of Gd–DTPA to free Gd^{3+} or other species and calculated that the administered Gd–DTPA was almost completely excreted in the urine within one day.

3.8.18 Selenium. *The quantitative determination of total Se in human serum and other biological solutions by ETAAS can be complicated by the different thermal behaviours of the Se species present in these matrices.* Sahin *et al.*[63] examined the effect of the chemical modifiers, Ni or Pd–Mg, on the thermal stabilities of Se species in both aqueous and serum solutions. They reported that equal analytical sensitivities for Se species could only be achieved with these chemical modifiers in the presence of HNO_3. When these conditions were achieved, quantitative determination using ETAAS could be achieved with a single

Se species as the calibration standard. Reported absolute LODs for Se were 37 pg with a Ni chemical modifier and 35 pg with a Pd–Mg modifier. Two papers described slurry-sampling procedures for the determination of Se in biological CRMs. Dos Santos[46] investigated seven slurry preparation procedures for the simultaneous quantitative determination of Hg and Se using on-line CV-ICP-AES. The author observed that analytical results in agreement with certified values for Se were only obtained with slurry sampling procedures that involved heating with the oxidising agents H_2O_2 or $K_2S_2O_8$. The adopted sampling procedure involved suspension in $K_2S_2O_8$, sonication, addition of HCl and heating to 90 °C, prior to on-line HG with HCl and $NaBH_4$. An LOD of 0.1 μg g^{-1} was reported for a sample mass of 20 mg in a 15 ml sample volume. Kawano *et al.*[91] described a method for Se determination in CRMs using slurry sampling ETV-ID-MIP-MS. A fusion step, using NaOH as an alkaline flux, was introduced into the thermal programme to fuse the biological sample and obtain isotope equilibration between Se in the sample and the ^{78}Se spike solution. The use of a nitrogen MIP avoided the interference of $^{40}Ar^{40}Ar$ dimer on Se determination. The method was validated by analysing biological CRMs and an LOD of 90 ng g^{-1} was reported.

A thorough critical review of previous studies on Se metabolites in urine was undertaken by Francesconi and Pannier.[10] A detailed comment on this work is given in the introduction to this ASU review. In light of the observations made in the critical review, the study presented by Gammelgaard *et al.*[48] merits highlighting. The authors determined two selenosugar metabolites, Se-methylseleno-*N*-acetylgalactosamine (Se-Gal-*N*-Ac) and Se-methyl-selenogalactosamine (Se-Gal-NH_2), using LC-DRC-ICP-MS. Samples were simply diluted 1 + 1 v/v and Se metabolites separated on a reversed-phase column using an eluent of 200 mM ammonium oxalate–5% CH_3OH. Three nebulisation systems were examined for introduction of the eluent into the plasma, an MCN, a DIN and a USN, and the best performance was obtained with an MCN. The authors used the method to examine urinary excretion of Se following administration of Se enriched yeast to 8 volunteers. Following Se intake, urinary excretion of Se-Gal-N-Ac increased from 2.6 to 11.6 μg l^{-1} and Se-Gal-NH_2 from 1.4 to 1.9 μg l^{-1}. Encinar *et al.*[47] described a method for the determination of selenoaminoacids in serum using HPLC coupled with ID-DRC-ICP-MS. Selenocysteine in the sample was derivatised with iodoacetamide and samples were enzymatically digested with lipase and protease. The total selenoaminoacid fraction was separated by SEC and the specific SeMet and carboxymethylselenocysteine species isolated by capillary HPLC. Selenomethionine was quantitatively determined by measurement of the $^{77}Se:^{80}Se$ ratio in the SeMet peak using a ^{77}Se-labelled SeMet spike. The accurately determined SeMet was used as an internal standard for determination of SeCys in the same chromatogram. The authors claimed the lowest ever reported LOD of 0.5 ng g^{-1} for a 450 mg serum sample.

Borawska *et al.*[164] investigated the food types that best affected Se status in Se adequate and Se deficient subjects. Serum Se concentrations were determined in 129 subjects using ETAAS. The authors suggested that frequent consumption of ham, tea and honey might be effective in improving Se status in Se deficient individuals. Akinloye *et al.*[165] examined Se status in fertile and infertile Nigerian men. Serum and seminal plasma Se was quantitatively determined using ETAAS. The authors reported that there appeared to be a physiological balance between serum and seminal plasma Se in fertile men but that a disturbance in this Se balance has a significant influence on spermatogenesis.

3.8.19 Silicon. Recent past ASU reviews have reported a number of studies on reference values for individual trace elements in human populations. In this review period, Bisse and colleagues[15] reported *reference values for serum Si in a healthy adult population*. Concentrations of Si in serum samples from 1325 healthy adults, aged between 18 and 91 years, were determined using AAS. A median serum Si concentration of 9.5 μmol l^{-1} was reported for men aged between 18 and 59 years, which decreased to 8.5 μmol l^{-1} for men aged between 60 and 74 years. For women, the median serum Si concentration rose from 10 μmol l^{-1} at 18–29 years, to 11.1 μmol l^{-1} at 30–44 years and then declined to 9.2 μmol l^{-1} at 45–59 years. In all subjects aged over 74 years, the median Si concentrations were 7.7 μmol l^{-1} for men and 8 μmol l^{-1} for women. The authors considered these changes in Si concentration with age to be important in relation to future studies on the health effects and medical implications of Si.

3.8.20 Strontium. Peltz-Csaszma *et al.*[166] described a method for *the determination of Sr in human brain tissue using ETAAS*. Brain samples were digested by microwave heating under high pressure in Parr bombs. Optimised thermal conditions for quantitative determination of Sr were pyrolysis at 1500 °C and atomisation at 2500 °C, using $La(NO_3)_3$ as a chemical modifier. An LOD of 0.057 μg l^{-1} was reported, which the review team considers to be surprisingly low for ETAAS. The authors noted that brain Sr concentrations showed considerable inter-individual variability with reported values between 20 and 450 ng g^{-1} dry weight.

3.8.21 Thallium. An interesting medico-legal application of ICP-MS was described by Hann *et al.*[85] The researchers re-examined *a homicide by Tl poisoning, which took place 38 years previously*. *They determined concentrations of Tl in several bone samples using SF-ICP-MS*, after microwave assisted acid digestion of the bone samples. Bone Tl concentrations ranged from 1.07 to 2.63 μg g^{-1}, which were up to 170 times higher than levels of Tl determined in bones of people who had died of natural causes. The researchers also determined the distribution of Tl in a thumbnail of the victim using LA-ICP-MS in an effort to assess the time interval between poisoning and death of the victim.

3.8.22 Uranides. This review period has seen continued interest in the investigation of human exposure to uranides. *Whereas studies described in recent past reviews have focused on exposures in military personnel, this review period has seen attention also turn to environmental exposures*. A comprehensive study of Cs, Th and U concentrations in human autopsy tissues was reported by Wang *et al.*[122] The uranides were quantitatively determined using ICP-MS with Rh as an internal standard to compensate for matrix effects. Tissue samples

were digested with HNO_3–$HClO_4$ and measurements made without any further sample enrichment or separation procedures. The main target organs for Th and U were identified as the lung and kidney. Urinary U determination is considered by some research groups to be the best biological monitoring medium for exposure to depleted uranium. Ejnik *et al.*[79] described a method for the determination of total U and the $^{235}U:^{238}U$ ratio in human urine using ICP-MS with a dynamic reaction cell (DRC). Quantitative measurements were made using ^{233}U as an internal standard and O_2 as the reaction gas in the DRC. An LOD for total U of 0.1 pg ml^{-1} was reported. Westphal *et al.*[167] determined total U and U isotope ratios in spiked synthetic urine samples using Q-ICP-MS with a large bore, high efficiency, direct injection nebuliser (DIHEN) for sample introduction. Severe matrix effects from the high dissolved solids were corrected with ^{233}U as an internal standard. Results obtained with this method were compared with results obtained from other laboratories using α-spectrometry and Q-ICP-MS with a conventional nebuliser. The DIHEN system gave the most accurate results over the concentrations studied. Becker and colleagues[84] described a novel approach for the determination of Th and U concentrations in urine. Urine samples were dried and Th and U directly determined in the dried films using LA-ICP-MS. Recoveries of Th and U from spiked synthetic urine samples were 91–104%. The authors considered the method to be of potential interest to forensic science investigations where only very small urine samples may be available.

Epov *et al.*[40] developed a rapid method for the direct determination of Pu in urine using ICP-MS with a DRC and ^{205}Tl as an internal standard. Preconcentration of the analyte from the urine matrix was achieved on-line using FI with an ion exchange resin column and desolvation nebulisation introduction into the plasma. Use of the DRC avoided the need for sample pre-treatment to separate Pu from U. An LOD of 1.9 pg l^{-1} was reported for ^{242}Pu. Karpas *et al.*[82] determined $^{234}U:^{238}U$ ratios in hair, nail and urine samples from 45 individuals who had consumed U in their drinking water. Quantitative determination was made using MC-ICP-MS. Good correlations were observed between measured U ratios in the contaminated water and hair (0.97), hair and nail (0.98), hair and urine (0.91) and nails and urine (0.89). The authors argued that U in the biomonitoring matrices could be directly linked to the exposure source (water) and that hair was particularly attractive as a biomonitoring sample as it was a bioaccumulator and, therefore, could be used to assess exposure to U long after subjects had left areas of suspected contamination.

3.8.23 Vanadium. Two European research groups examined levels of V in tissues of aquatic invertebrates and seabirds following contamination of the French Atlantic coast with oil from the wrecked tanker 'Erika'. Over a one-year period, Chiffoleau *et al.*[168] monitored both Ni and V in soft tissues of mussels and oysters using ETAAS, and in scallop shell growth bands using LA-ICP-MS. Soft tissues were analysed every two weeks and shell growth bands every three bands. The measured concentrations of Ni and V in the survey samples were compared with reference data gathered from a French national monitoring database. Mean concentrations of Ni in both mussels (1.8 μg g^{-1}) and oysters (1.2 μg g^{-1}) were comparable with reference data over the entire monitoring period. In contrast, a sharp increase in V concentrations was observed five months after the accident in both mussels (4.6 μg g^{-1}) and oysters (3.2 μg gl^{-1}) compared with reference values (1.4 μg gl^{-1} and 1.3 μg g^{-1}, respectively). Similarly a V peak in the time profiles of scallop shell growth bands was found at the same period. The authors considered both monitoring approaches to be suitable for environmental monitoring following chemical spills. Kammerer *et al.*[169] determined V in liver and kidney tissue from oiled seabirds that had subsequently died in wildlife care centres. Vanadium concentrations were quantitatively determined using AAS and ranged from 30 to 77 ng g^{-1} for liver and 52 to 72 ng g^{-1} for kidney. These values were not significantly different from values determined in dead seabirds found later on beaches with no traces of pollution from the wreck. The authors concluded that neither kidney nor liver V concentrations are suitable biomarkers for recent exposure of seabirds to oil pollution.

Colina and colleagues[170] described a method for the separation and quantitiative determination of V^{IV} and V^{V} species in mussel and fish tissue samples using reversed phase ion-pair LC coupled with ICP-MS. The V species were separated on a C_8 reversed phase column, as EDTA complexes, using a mobile phase containing 0.06 M CH_3COONH_4–10 mM tetrabutylammonium hydroxide–10 mM $NH_4H_2PO_4$–2.5 mM EDTA, thereby minimising the adverse effect of organic solvents on the sensitivity of V determination. Fernandez *et al.*[59] described a method for the determination of V in urine using ETAAS with repeated sample injection into a pre-heated tube atomiser. Urine samples were diluted with 0.3% Triton X-100 and BaF_2 was added as a chemical modifier. Three 60 μl volumes of the diluted urine were sequentially injected into the graphite tube atomiser, pre-heated to 110 °C. An LOD of 0.11 μg l^{-1} was reported and analytical recoveries from spiked samples were 96–103% for V additions of 0.8 to 3.5 μg l^{-1}.

A comprehensive summary of analyses in the fields of clinical and biological materials can be found in Table 1.

4 Analysis of drugs and pharmaceuticals, medicinal plants and supplements

Applications of ICP-MS within the *pharmaceutical industry* were discussed by Marshall *et al.*[87] They referred to (i) the use of Cu and Fe in derivatization reactions so that compounds with amine or carboxylic acid groups can be detected after LC separation, (ii) analysis of plasma samples, *e.g.* for Br-labelled peptides, (iii) analysis of materials from solid-phase beads used in combinatorial chemistry and (iv) LA-ICP-MS to determine phosphate in proteins after electrophoretic separation. Work to investigate the effectiveness and the pharmacokinetics of new metal-containing pharmacological agents continues to be undertaken, particularly with anti-cancer drugs based on Pt.

Sources of *medicinal plants and ethnic pharmaceuticals* now being reported are increasing (Table 2). In recent years traditional Chinese medicines have been the focus of attention, following earlier interest in Indian and Pakistani remedies. During the last year, results of analyses of medicines from

Table 1 Analyses of clinical and biological materials

Element	Matrix	Technique; atomisation; presentation	Sample treatment/comments	Ref.
As	Macroalgae supplements, seaweeds	MS;ICP;HPLC MS;ICP;HPLC-HG	The determination of 13 As species in marine biological extracts was reported. Two chromatographic systems (a Supelcosil LC-SCX cation-exchange column, eluted with a 20 mM pyridine mobile phase, pH 2.2–2.6, flow rate 1.5 ml min^{-1}, at 40 °C and a Hamilton PRP-X100 anion-exchange column, eluted with 20 mM $NH_4H_2PO_4$ buffer, pH 5.6, flow rate 1.5 ml min^{-1}, at 40 °C), were used. An additional HG step was required to separate arsenous acid from other As species	230
As	Human hepatocytes, mouse urine	AA;HG;L	An improved method for the determination of As species by means of pH dependent HGAAS was reported. LODs ranged from 0.14 ng As (TMAO) to 0.40 ng As (As^V). Linear range was 0.5–100 ng As. Recovery was between 85 and 124% and precision varied from 1.0 to 14.5% in various biological matrices	50
As	Ayurvedic herbal medicines	XRF;-;-	The content of As, Hg and Pb in Ayurvedic herbal medicines from South Asia sold in the Boston area was determined. Daily intake of As, Hg and Pb from these medicines, calculated using manufacturers' dosage recommendations, were above US Pharmacopeia and US Environmental Protection Agency regulatory standards	336
As	Urine	AA;ETA;L	A method based on solvent extraction was applied to separate nontoxic (AB) from toxic As species (As^{III}, As^V, DMA and MMA) in urine samples from residents in Barcelona, Spain. Samples were analysed by means of Zeeman corrected ETAAS, with a Ni–Mg modifier	337
As	Essential oils	AA;ETA;L	Samples from lavender (*Lavendula angustifolia*) and rose (*Rosa damascena*) oils were diluted with ethanol or isopropanol, respectively, prior to analysis by longitudinal Zeeman-effect ETAAS. Equivalent response from 4 As species (As^{III}, As^V, MMA, DMA) was achieved with 0.05 g l^{-1} L-cysteine–2.5 μg Pd–100 μg citric acid as modifier. Transverse-heated endcapped graphite atomisers with integrated pyrolytic graphite platforms, pre-treated with Zr–Ir, were used. Calibration was by solvent-matched standard solutions of As^{III}, for 4- and 5-fold diluted samples of lavender and rose oil, respectively, and by standard additions for lower dilutions. LODs were 4.4 and 4.7 ng g^{-1} As in lavender and rose oil, respectively. RSD was between 8 and 17% for both oils. An alternative procedure based on low temperature plasma ashing in O_2 followed by ETAAS, provided LODs of 2.5 and 2.7 ng g^{-1}, in lavender and rose oil, respectively, and RSD within 8–12% for both oils. The results from both procedures were in good agreement	338
As	Marine organisms	AA;HG;L AE;ICP;HPLC	The complete decomposition of 6 organic As compounds (MMA, DMA, TMAO, tetramethylarsonium iodide, AC and AB) from marine organisms were investigated using three acid mixtures (HNO_3–$HClO_4$; HNO_3–$HClO_4$–HF; or HNO_3–$HClO_4$–H_2SO_4). Both MAA and DMA were decomposed completely by any of the mixed acids at temperatures $\geq$ 200 °C. An HNO_3–$HClO_4$–H_2SO_4 mixture and temperatures $\geq$ 320 °C were required to decompose the most difficult species (AC and AB), followed by evaporation to dryness for the complete decomposition of AB. Analysis by HPLC-ICP-AES showed all As in the residue to be As^V	233
As	Tap water, hair and nails	AA;ETA;L	A new method for the preconcentration and determination of As^{III} and As^V in tap water and total As in biological samples by cloud point extraction and ETAAS was described. After treating As^V with	42

Table 1 (*continued*)

Element	Matrix	Technique; atomisation; presentation	Sample treatment/comments	Ref.
			MoO_4^- in H_2SO_4 at 55 °C, As species were quantitatively extracted into Triton X-114 and concentrated by centrifugation. After addition of CH_3OH, to allow pipetting by the autosampler, 20 µl of solution + 10 µl of the modifier (0.1% m/v $Pd(NO_3)_2$) were injected. Total inorganic As was determined by the same method, after oxidation of As^{III} to As^V with $KMnO_4$. As^{III} was calculated by difference. An LOD of 0.01 µg l^{-1}, with enrichment factor of 52.5, was achieved for a 10 ml sample. The linear range was 0.02–0.35 µg l^{-1}. RSDs were <5%	
As	Hair	AF;HG;L	As and Se were determined simultaneously in human hair samples digested in a microwave oven with HNO_3. NO_x were eliminated by removing gases from above the digested solution with an Ar stream. Linear range for both analytes was 0.5–100 µg l^{-1}, LOD 0.2 µg l^{-1} and RSD (repeatability) 1% for Se and 2% for As. No mutual interference was observed. An RM was used for validation	339
As	Hair, nail, skin	-;-;-	An extraction method for As species from hair, skin and nail was developed and the stability of different As species during the extraction process was investigated	129
As	Human hair, nails and urine, groundwater and water extracts from soils	MS;ICP;HPLC	The determination of diphenylarsinic acid in human and environmental samples by means of combined SEC-HPLC and ICP-MS was reported. Most samples were analysed directly after filtration, but for hair and nails digestion with alkali, extraction into diethyl ether and re-dissolution of the extract in water, was necessary. LOD was <1 ng l^{-1}	340
As	Chinese herb (*Ligusticum chuanxiong Hort*)	AF;HG;L	8-Hydroxyquinoline was used as a masking agent to eliminate severe interferences from Pb^{2+} and Cu^{2+} on the determination of As species (As^{III}, As^V and organic As) and to remove the atomic fluorescence of As^V which interfered with the signal of As^{III}	172
As	Urine	AA;ETA;L	As and Se were determined by simultaneous ETAAS using Co as internal standard, chosen on the basis of physico-chemical characteristics and a preliminary comparison with Sn. Urine samples were diluted 1 + 2 to final concentrations of 1.0% (v/v) HNO_3 and 80 µg l^{-1} Co^{2+}. The modifier was 20 µg Pd–3 µg Mg and pyrolysis and atomisation were carried out at 1400 and 2300 °C, respectively. Characteristic masses were 47 ± 1 pg (As) and 72 ± 2 pg (Se), LODs were 1.8 ± 0.1 (As) and 2.6 ± 0.1 (Se) µg l^{-1}. Matrix-matched standards were necessary for calibration. Recoveries from 8 urine samples spiked with 10 and 25 µg l^{-1} As and Se were 96 ± 6% and 95 ± 6% (As) and 101 ± 7% and 97 ± 4% (Se)	64
As	Nails	AF;-;L NAA;-;-	Within the framework of a study of nail As as a biomarker of As exposure from well water in Inner Mongolia, pooled samples of finger- and toenails from 32 subjects were analysed for total As by both instrumental NAA and AFS. Mean nail As values (±SEM) were 14.8 ± 2.4 (NAA) and 19.4 ± 2.8 µg g^{-1} (AFS), $r = 0.93$, $p < 0.0001$. As in toenails from 314 subjects, determined by NAA, was significantly correlated ($r = 0.84$, $p < 0.0001$) with As in well water samples collected from their households and analysed by AFS	341
As	Biological samples	AF;HG;L	A new method was proposed for the simultaneous determination of As and Se by HG coupled with double-channel non-dispersive AFS. Linearity range was up to 20 µg l^{-1} (As) and 32 µg l^{-1} (Se). LODs were 0.13 (As) and 0.12 (Se) µg l^{-1}. RSD% was 2.7% (As, 4 µg l^{-1}) and 1.9% (Se, 8 µg l^{-1}). Recoveries from 4 biological samples and 2 biological CRMs were 92.5–95.5% (As) and 101.2–108.4% (Se)	71
Au	Blood	MS;ICP;L	Au levels were determined in blood of 66 patients before and after patch testing with gold sodium	149

Table 1 (*continued*)

Element	Matrix	Technique; atomisation; presentation	Sample treatment/comments	Ref.
			thiosulfate and found significantly higher after (median 0.34 *versus* 0.03 μg l^{-1}) in all patients, both allergic and non-allergic to gold	
Be	Mouse blood and tissue (spleen, liver, femur, lung, and kidney)	AMS;-;-	AMS was applied to investigate molecular targets involved in chronic beryllium disease. Be was determined at attomole levels in blood and tissues from mice given known doses of ^{9}Be and ^{10}Be by intraperitoneal injection. Sample preparation involved digestion with HNO_3, oxidation with H_2O_2 and $(NH_4)_2S_2O_8$, precipitation of Be with NH_4OH and conversion to BeO at 800 °C. Be concentration in the original sample was calculated from the measured $^{10}Be:^{9}Be$ ratios; these ranged from 10^{-10} to 10^{-14} and LOD was 3.0×10^{-14}, *i.e.*, 0.8 amol of ^{10}Be	89
Bi	Chinese medicines	AF;HG;L	The effect of different digestion procedures and proportions of reagents for HG were investigated. Under optimised conditions, linear range was 0.1–200 μg l^{-1}, LOD 0.094 μg l^{-1}, instrumental RSD 0.55% and recovery ranged from 94% to 107%	342
Br	Serum	MS;ICP;L AE;ICP;L	Plasma substitute, which contains no endogenous Br, was proposed for matrix matching when analysing Br in 100-fold diluted serum by ICP-MS. Other sources of C, *e.g.*, sucrose, did not work as well in compensating for the enhancement (about 13%) of the ^{79}Br signal in a serum matrix. The proposed method compared well with an established ICP-AES procedure. LODs for the ICP-MS and ICP-AES methods were 0.09 and 0.8 mg l^{-1}, respectively	133
C	Bone, skin, muscle tissue	AMS;-;-	^{14}C dating by AMS on samples from a mummy recently found in Pakistan revealed it to be a modern fake	90
Ca	Human milk	XRF;-;-	EDXRF with an annular ^{241}Am and ^{55}Fe sources was applied to the determination of Ca. The sample preparation and determination methods were reported	219
Ca	Nails	AA;F;-	Finger- and toenail clippings were dissolved in HNO_3 prior to analysis. The Ca and Mg content of nail samples from 169 women and 115 men between 20 and 80 years of age decreased with age and were related to bone mineral density	343
Cd	Blood	AA;ETA;L	A transverse heated filter atomizer (THFA) was applied to the determination of Cd and Pb in blood by ETAAS. Blood samples, diluted 5 to 10 times with water, were injected in the THFA at 110–120 °C. In comparison with conventional transverse heated graphite atomisers with a platform, THFA allowed a significant reduction of non-specific background absorption. Recovery of Cd and Pb was >90% without modifiers. Addition of ethanol improved repeatability. High temperature cleaning steps every 15–20 cycles were necessary to prevent build-up of solid residues. LODs were 0.05 (Cd) and 1 (Pb) μg l^{-1}, respectively	65
Cd	Biological samples, sea-water	AA;F;FI	The on-line preconcentration of Cd, based on complexation with ammonium *O,O*-diethyldithiophosphate and solid phase extraction on Amberlite XAD-4, was reported. Different preconcentration times (from 30 s to 5 min) gave LODs ranging from 1 to 5 μg l^{-1}. RSD was around 3%. The analysis of 5 CRMs did not show significant differences from the certified values (*t*-test, 95% CL). Recovery from enriched sea-waters ranged between 93 and 108%. The method could be coupled to other measuring analytical techniques	38
Cd	Metallothioneins (rabbit liver)	MS;ICP;CE	An alternative CE-ICP-MS interface, based on volatile species generation, was developed, evaluated and compared with the conventional sample introduction systems *via* nebulisation, using the speciation of Cd–metallothioneins (MTs) in rabbit	74

Table 1 (*continued*)

Element	Matrix	Technique; atomisation; presentation	Sample treatment/comments	Ref.
			liver as a model. LODs for Cd–MTs were almost one order of magnitude better than those from a conventional Babington nebuliser	
Cd	Medicinal plants	AA;FF;TS	Batches of 24 samples (5 mg), placed in polypropylene minivials with a mixture of oxidising agents (200 μl conc. HNO_3–150 μl 30% v/v H_2O_2) were heated in both closed-vessel (4 min) and focused (10 min) microwave ovens. Cd (up to 0.80 μg g^{-1}) and residual C (0.30–0.45%) were determined by thermospray flame furnace AAS and CHN elemental analysis, respectively. The method was assessed by analysis of CRMs (BCR 281 Rye Grass and NIST 1577b Bovine Liver) as well as by comparison with conventional microwave assisted decomposition	203
Cd	Biological CRMs	AA;ETA;L	Samples, digested with H_2O_2–HNO_3 in a microwave oven, were treated with *O,O*-diethyldithiophosphate in an HCl medium and the resulting complexes of Cd and Pb were quantitatively extracted in a Triton X-114 rich phase (cloud point extraction) by centrifugation. CH_3OH acidified with 0.1 mol l^{-1} HNO_3 was added to the surfactant-rich phase prior to analysis by ETAAS. Pyrolysis temperature was 700 °C for both elements and atomisation temperatures were 1400 and 1600 °C for Cd and Pb, respectively, without modifiers. Thermal stability was attributed to the high P content from the complexing agent and the matrix itself. LODs were 6 and 40 ng g^{-1}, with enrichment factors of 129 and 18, for Cd and Pb, respectively. The analysis of 5 biological CRMs gave results in agreement with the certified concentrations (*t*-test, 95% CL)	43
Co	Pharmaceutical products (vitamins)	AA;F;L AA;ETA; L AE;ICP;L	Samples (about 0.5 g) were digested in a microwave oven with 6 ml HNO_3–1 ml H_2O_2 and Co concentrations were determined by spectrometric and electrometric (ASV) techniques using the standard additions method	344
Co	Blood, tissues (mouse)	AA;ETA;L	Blood and tissue samples (about 0.3 g) from mice exposed to Co in drinking water were dried at 110 °C and digested in a water-bath at 80 °C with 700 μl of a 1 + 1 mixture of HNO_3–30% H_2O_2. The digest was further diluted with water prior to analysis. Quantification was achieved by the standard additions method. RSD was <5%. LODs were 0.03 μg L^{-1} for blood and 0.03 ng g^{-1} for tissues	345
Co	Soil and human hair samples	AA;F;FI	Co and Ni were determined after complexation with 2,3-dihydroxynaphthalene, at pH values of 2.0–8.0, adsorption of the complexes onto a C_{18} microcolumn and elution with acidified CH_3OH (pH 2). Enrichment factors were 725 (Co) and 600 (Ni), with a 1 min preconcentration time and a sample throughput of 30 h^{-1}. LODs were 0.1 μg l^{-1} and RSDs 2.5–2.6% at 10 μg l^{-1} (Co or Ni). No significant interference was observed from other common electrolytes (Fe, Zn, Cu)	39
Co	Serum	AA;ETA;L	Co, Mn and Ni were determined in human serum, treated with 7.5 M NH_4OH, followed by a 2–4-fold dilution with water, and injected onto the graphite furnace with H_2O_2. Treatment with NH_4OH reduced sample viscosity. Drying steps between 80 and 110 °C were maintained for 180 s. Characteristic masses for all elements were better than those from recommended methods. Measured concentrations of Co, Mn and Ni in Seronorm™ CRMs were 1.09 μg l^{-1} ± 1.6%, 10.1 μg l^{-1} ± 5.3% and 5.49 μg l^{-1} ± 1.1%, respectively, in good agreement with the certified values	60
Co	Pharmaceutical and biological (hair, nails, blood	AA;ETA;L	Samples were microwave digested. Calibration, by the standard additions method, was linear in the range 0.1–10 μg l^{-1}. The method was compared with ASV	346

Table 1 (*continued*)

Element	Matrix	Technique; atomisation; presentation	Sample treatment/comments	Ref.
	and urine) samples			
Co	Biological CRMs	AA;ETA;L	Two procedures for sample preparation (solid sampling and alkaline digestion with TMAH) were compared. For solid sampling, CRMs were ground to a particle size ≤ 50 μm. For alkaline treatment *ca.* 250 mg of the sample were placed in a polypropylene flask with 2 ml of 25% m/v TMAH and deionized water. A prototype high-resolution continuum source AA spectrometer, providing 3-D spectral plots, was used to investigate spectral interferences. A continuous background signal with pyrolysis temperatures <700 °C and molecular absorption bands with atomization temperatures >1800 °C were identified. Optimised furnace conditions were developed and applied on a conventional line-source AA spectrometer. Results for 6 CRMs, using calibration with aqueous standards, were in agreement with certified values (*t*-test, 95% CL) and LOD was 5 ng g^{-1}	142
Cr	Blood, tissues	MS;ICP;L AA;ETA;L	Interferences, at masses 52 and 53, from residual C content in the determination of Cr, at the μg L^{-1} level, in digested biological samples were investigated by GC-MS and ETAAS analysis of acid digested samples	35
Cr	Parenteral solutions	AE;ICP;FI	The on-line preconcentration (70-fold enrichment factor) and speciation of Cr was achieved by retention of Cr^{III} on activated C at pH 5.0. The total Cr content was determined after a reduction step. Cr^{VI} concentration was obtained by difference. LOD for the preconcentration of 25 ml of sample was 29 ng l^{-1}. The method was linear up to at least 60 μg l^{-1}. RSD at 5 μg l^{-1} was 2.3% (peak height)	347
Cs	Autopsy tissues	MS;ICP;L	The determination of Cs, Th and U in acid digested (HNO_3–$HClO_4$) human autopsy tissues (bone, heart, intestinum tenue, kidney, liver, lung, muscle, stomach, spleen and thyroid gland), with Rh as the internal standard, gave LODs between 5.7 and 17.8 pg ml^{-1} and recoveries (from liver samples) from 96% to 107%. RSDs ranged from 4.8 to 8.9%	122
Cu	Thyroid tissue	AA;F;L	The sensitivity of Cu measurements with different designs of the quartz tube in a slotted tube atom trap in FAAS was assessed. A sensitivity improvement of 3.5-fold was achieved. Cu content was higher in cancerous *versus* non-cancerous human thyroid tissues	54
Cu	Blood serum	AE;ICP;ETV	A remarkable improvement in the analytical performances of a method for the direct determination of trace elements (Cu, Fe) in human serum by ETV-ICP-AES and slurry sampling was achieved using a PTFE emulsion as a fluorinating agent to promote the vaporization of the analytes from the graphite furnace. LODs were 1.4 ng ml^{-1} (Cu) and 2.9 ng ml^{-1} (Fe). RSD were $<6.0\%$ after optimization of the operating conditions	73
Cu	Plasma	AA;ETA;L	Fast furnace programs were evaluated for the determination of Cu and Zn in blood plasma samples from children with the Down syndrome. LODs were 0.1 μg l^{-1} for both analytes and characteristic masses of 5.3 pg (Cu) and 0.9 pg (Zn) were observed with a 20 μl sample injection volume. The lack of bias was demonstrated by the analysis of 2 CRMs and recovery studies (100.6% and 100.2%, for Cu and Zn, respectively). RSD was 0.97% (Cu) and 1.21% (Zn). Samples from 35 children with Down syndrome and 35 controls were analysed	348
Fe	Blood serum	AE;ICP;ETV	See Cu, ref. 73	73
Fe	Cocaine	AA;-;-	A method for the indirect AA determination of cocaine *via* formation and liquid–liquid extraction of the Fe^{III}–cocaine complex was developed. In 5 M	349

Table 1 (*continued*)

Element	Matrix	Technique; atomisation; presentation	Sample treatment/comments	Ref.
			HCl, cocaine was protonated and associated with tetrachloroferrate prior to its extraction into 1,2-dichloroethane. LOD was 0.1 ng cm^{-3} cocaine in water, RSD 0.07% and linear range up 50 ng cm^{-3} cocaine	
Fe	Blood	MS;ICP;L	The $^{56}Fe:^{54}Fe$ ratio was determined in blood samples from 30 patients with homozygous C282Y haemochromatosis and healthy controls by a newly developed technique based on MC-ICP-MS. Patients with haemochromatosis had higher $^{56}Fe:^{54}Fe$ ratios which significantly correlated with total-body Fe accumulation, severity of clinical disease, and the need for regular phlebotomies to prevent Fe accumulation	80
Gd	Urine	MS;ICP;SEC	Gd^{3+} and its complex with DTPA, a MRI contrast agent, were determined simultaneously in urine from a patient given Gd–DTPA *i.v.* Most Gd-DTPA (>99%) was excreted within 1 day and no Gd^{3+} was detected	163
Hg	Biological samples, water	AA;CV;G	A sequential injection system for CVAAS, based on a new integrated gas–liquid separator (GLS), operating also as a reactor, was developed. Sample and reductant were sequentially loaded into the GLS and the released Hg vapour was transferred to the AA cell by an argon flow. With a 20 ml sample volume, linearity was in the range 0.05–5.0 μg l^{-1}, LOD 0.02 μg l^{-1} and RSD 2.6% at 1.0 μg l^{-1}	68
Hg	Human hair, horse fur	AA;-;-	The performance of a commercially available Hg analyser, based on sample combustion, gold amalgamation and AAS. Analysis of a CRM (NIES 13) and samples from an international interlaboratory ($n > 16$) comparison study were in good agreement with target values. RSD was <5%. Total analysis time per sample was <10 min	67
Hg	Blood	AA;-;L	Polyethylene vessels were found to be a source of Hg contamination, but no significant variations of the Hg content was observed in blood samples and control materials collected and stored in commercial polypropylene vials over a 30-day period	29
Hg	Blood, brain, kidney, muscle (mouse)	AF;CV;-	The distribution of Hg in neonatal mice, following injections of methylmercury, ethylmercury or Thimerosal, was studied in timed collections of samples of blood and tissues	350
Hg	Ayurvedic herbal medicines	XRF;-;-	See As, ref. 336	336
Hg	Biological materials (seabird eggs), CRMs	MS;ICP;GC	Methylmercury was determined in biological samples (seabird eggs) and CRMs (NIST SRM 1566b Oyster Tissue, 13.2 ng g^{-1} and SRM 1946 Lake Superior Fish Tissue, 397 ng g^{-1}) by a novel method, based on ICP-MS coupled with GC *via* a novel heated interface. Sample preparation involved microwave extraction with acetic acid, followed by derivatization and headspace SPME with a polydimethylsiloxane-coated silica fiber. RSD was 2% and LOD 4.2 pg g^{-1}, as Hg, based on a 0.5 g sample	41
Hg	Blood	AA;CV;G	The validation of a method based on CVAAS for the determination of Hg in human red blood cells was reported. LOD and LOQ were 1.84 and 4.03 μg l^{-1}, respectively. Linearity was verified between 5 and 40 μg l^{-1} Hg, with correlation coefficients for calibration straight lines always ≥ 0.99. RSD was 5.51% (repeatability) and between 4.89 and 5.44% (intermediate precision), respectively. A CRM (NIST SRM 966, Toxic Metals in Bovine Blood) was analysed. The robustness of the method was evaluated by changing some of the experimental conditions, using a fractional factorial experimental design	351

Table 1 (*continued*)

Element	Matrix	Technique; atomisation; presentation	Sample treatment/comments	Ref.
Hg	Drinking water, sea-water, urine	AA;CV;L	A novel method for the sequential Hg speciation at ng l^{-1} levels was developed. A column packed with PTFE turnings was used to separate inorganic Hg, as $Hg(PDC)_2$, from the sample solution. The PDC complex of methylmercury was not adsorbed and could be determined directly after reduction by $NaBH_4$ and subsequent on-line thermal dissociation of the resulting hydride. Inorganic Hg in the presence of methylmercury was determined in a parallel manifold	51
Hg	Drinking water and urine	AA;ETA;L	A new method was developed for the direct determination of Hg by ETAAS, using double vaporization in a two-step atomizer with a purged vaporizer. The sample, placed in the vaporizer of a two-step atomizer, was dried, vaporized, and the vapour transferred by an argon flow to an unheated atomizer cell where it was trapped by the cell inner surface. Preconcentration could be achieved by repeating these steps. Atomic Hg vapour was then generated by heating the atomizer cell. With a single sample transfer, LODs were 0.24 μg l^{-1} for 100 μl drinking water and 2.0 μg l^{-1} for 20 μl urine. The method was tested by analysis of CRMs and recovery tests	69
Hg	Tissues of benthic organisms and plant material	MS;ICP;GC	An extraction method based on acidic leaching was developed for measurement of methylmercury (MeHg) in benthic organisms and plant material by GC-ICP-MS. The method was evaluated by recovery of species specific ID with $Me^{201}Hg$ and analysis of CRMs. Samples were digested with 5 ml of 4 M HNO_3 at 55 °C followed by aqueous phase ethylation. The solution was stable for 1 week. The method was applied to real samples of benthic invertebrates and inter-laboratory comparisons were conducted using lyophilized zooplankton, chironomidae, and notonectidae samples	33
Hg	Biological samples (CRMs)	AA;CV;L AA;ETA;CV	Inorganic Hg was determined in biological samples, treated at room temperature with TMAH, by CVAAS. Total Hg was measured by the same technique, heating the quartz cell in an air–C_2H_2 flame. Organic Hg was calculated by difference. In addition, total Hg was determined by CV-ETAAS, obtained by retention of Hg vapour in a heated Au-treated graphite tube, in order to optimise vapour generation conditions. Total Hg concentrations by both techniques were in agreement and corresponded to certified values (*t*-test, 95% CL). RSD was <10%. LODs by CVAAS were: 0.13 μg g^{-1} (total Hg) and 0.025 μg g^{-1} (Hg^{2+}). LOD for total Hg by CV-ETAAS was 0.001 μg g^{-1}	52
Hg	Chinese medicine (*Wanshi Niuhuang Qingxin*)	AF;CV;L	Improved sensitivity for the determination of inorganic and total Hg in a traditional Chinese medicine (*Wanshi Niuhuang Qingxin*) by CVAFS was obtained by addition of thiourea and citric acid, which greatly enhanced the AF signal of Hg. LOD for total Hg was 7.6 ng l^{-1}, RSD ranged from 1.56% to 3.28% and analytical recovery from 90.3% to 110.3%	173
Hg	Brain, kidney and liver tissue (rat)	AA;-;-	Methylmercury was determined in rat tissues by AAS, with O_2 combustion and gold amalgamation, after toluene extraction and back extraction to an aqueous medium. From the experimental recoveries of methylmercury added to rat brain, kidney and liver homogenates (83.6–86.7%), a correction factor of 0.85 was applied to calculate the actual methylmercury content. The concentrations of methylmercury determined by this method were in agreement with those calculated, as difference, by total and inorganic Hg estimated with other established procedures	352

Table 1 (*continued*)

Element	Matrix	Technique; atomisation; presentation	Sample treatment/comments	Ref.
Hg	Hair (single strand)	AA;-;S AA;CV;L	A method for the determination of Hg in a single human hair strand using a commercial Hg analyser was developed and compared with conventional CVAAS, using hair samples from 12 women with a wide range of Hg exposure. The average RSD between hair strands was 6.5 ± 2.8%. Absolute LOQ was 0.10 ng of total Hg	66
Hg	Oyster tissue and CRMs	AE;ICP;Sl	Seven procedures for slurry preparation of biological samples, involving different combination of reagents (*aqua regia*, HCl, H_2O_2, TMAH, $K_2S_2O_8$, Triton X-100), sonication, ozonation and/or heating at 90 °C, were evaluated for the simultaneous determination of Hg and Se by on-line chemical vapour generation coupled to axial view ICP-AES. The analysis of CRM TORT-2 (Lobster Hepatopancreas) by all procedures gave results in agreement with the certified Hg value, whereas only procedures involving the addition of either H_2O_2 or $K_2S_2O_8$, followed by sonication, addition of HCl and heating at 90 °C, gave acceptable values for the Se content. Treatment with $K_2S_2O_8$ gave LODs of 0.08 μg g^{-1} (Hg) and 0.10 μg g^{-1} (Se), for a sample mass of 20 mg in a final volume of 15 ml	46
I	Biological samples, soil and sediments	MS;ICP;L	Samples of soil, sediment and biological materials were digested overnight in pressurised, PTFE-lined, stainless steel bombs, using 10% v/v NH_3 at 185 °C, prior to determination of I by ICP-MS. LOD, in the sample solution, was 0.003 ng ml^{-1} and LOQ, referred to the solid sample, was 0.01 μg g^{-1} dry mass. The method was validated by the analysis of CRMs	32
Mg	Extracellular fluid	AA;ETA;L	Mg concentrations in extracellular fluid samples from the brain of gerbils subjected to transient focal cerebral ischemia were monitored *via* on-line microdialysis coupled with ETAAS. Extracellular fluid samples were collected *via* a microdialysis probe inserted into the right cortex before, during and after inducing ischemia. The LOD of 0.03 μg l^{-1} was better than previously reported (from 0.50 to 3.00 μg l^{-1}). Mg concentrations significantly decreased to 41% of baseline during cerebral ischemia and gradually returned to 67% of baseline after 60 min of reperfusion	58
Mg	Brain	AA;ETA;L	A coupled microdialysis–ETAAS system was developed to monitor dynamic changes of extracellular Mg and Zn in the cortex of gerbils subjected to focal cerebral ischemia	57
Mg	Nails	AA;F;-	See Ca, ref. 343	343
Mn	Serum	AA;ETA;L	See Co, ref. 60	60
Ni	Mussel/oyster soft tissue; scallop shell	AA;ETA;L MS;ICP;LA	Following the "Erika" wreck off the French coast, Ni and V concentrations were monitored in mussel (*Mytilus edulis*) and oyster (*Crassostrea gigas*) soft tissues by ETAAS and in scallop (*Pecten maximus*) shells by LA-ICP-MS	168
Ni	Serum	AA;ETA;L	See Co, ref. 60	60
Pb	Bone	AA;ETA;L	A method for the determination of Pb in bone by ETAAS was reported, based on calibration with aqueous Pb solutions containing $NH_4H_2PO_4$ as modifier. LOD was 0.07 ng ml^{-1} (*i.e.*, 0.022 μg g^{-1}) in the original sample. RSD% was 3.5% and bias was tested by the analysis of NIST SRM 1846 "Bone Meal"	353
Pb	Blood	AA;ETA;L	See Cd, ref. 65	65
Pb	Ayurvedic herbal medicines	XRF;-;-	See As, ref. 336	336
Pb	Blood	AA;ETA;L	EDTA 5 mM was found to be essential for the complete release of Pb from dried blood spots on filter paper, a method of sample collection applied for neonatal screening	37
Pb		AF;HG;G		171

Table 1 (*continued*)

Element	Matrix	Technique; atomisation; presentation	Sample treatment/comments	Ref.
	Chinese medicines		In a novel method for the determination of Pb traces, samples of traditional Chinese medicines were digested at high pressure with HNO_3–H_2O_2 and Pb concentration determined by HG-AFS. LOD was 0.08 μg l^{-1} and RSD 0.34%	
Pb	Blood	AA;ETA;L	The performance of a portable ASV instrument for the determination of Pb in blood was assessed by comparison with ETAAS, using paired blood samples from 243 employees working at about 3800 m (Peru). Mean blood Pb by ETAAS (46 ± 16 μg dl^{-1}) was significantly higher than the mean value by ASV (32 ± 11 μg dl^{-1} (paired *t*-test; $P < 0.0001$), and the difference increased as the measured blood Pb concentration decreased	154
Pb	Blood	AF;HG;L	A low cost procedure for the screening of blood Pb with automated sequential injection HGAFS was developed, for the screening of blood Pb levels in Chinese children. PbH_2 was generated from an acid solution, using $K_3Fe(CN)_6$ as an oxidising agent, by reaction with alkaline BH_4, separated from the reaction medium in a gas–liquid separator and swept directly into the atomiser. Under optimised conditions, LOD was 0.014 mg l^{-1}, RSD 0.7% (at 2.0 μg L^{-1}) and sampling frequency 120 h^{-1}. The sensitivity of the procedure was comparable to ICP-MS. The method was assessed by analysis of CRMs (frozen cattle blood GBW 09139 and GBW 09140) and spiked human whole blood samples	70
Pb	Biological and environmental CRMs	MS;ICP;GC	Species specific ID and GC-ICP-MS were applied for the determination of trimethyllead (Me_3Pb^+) in biological and environmental samples. GC-ICP-MS, after derivitization with tetraethylborate, and reverse ID analysis were used to determine the isotopic composition and concentration of the spike solution. The method was validated by analysis of CRM 605 Urban Dust, which is certified for Me^3Pb^+ and used to determine the Me^3Pb^+ content in CRM 580 (sediment) and six biological CRMs (DORM 2, CRM 278, CRM 422, CRM 463, CRM 477, MURST-ISS-A2). The observed values ranged from 0.3 to 17 ng g^{-1} (as Pb), *i.e.*, up to 20% of total Pb, except for MURST-ISS-A2 and CRM 580 (sediment), in which concentrations were <LOD (0.09 ng g^{-1})	235
Pb	Hair	XRF;-;-	SR-XRF was applied to study the distribution of Pb in a hair sample collected from a lead smelter worker. The model could apply equally to other thin cylindrical samples	152
Pb	Bone (fish)	AE;ICP;L	A procedure for determining low levels of Pb in bone by axially viewed, multichannel-based, ICP-AES was developed. Sample pretreatment involved wet acid digestion in a pressurised microwave-heated system. The Co 228.615 nm reference line was chosen for internal standardisation, to compensate for matrix effects from Ca and HNO_3. LOD was 0.11 μg Pb g^{-1} dry mass. Instrumental precision at 10 μg L^{-1} ranged from 6.1 to 9.4% and the precision of the sample preparation step was 5.4%. The measurement of SRM 1486 gave a value of 1.32 ± 0.04 μg g^{-1} *versus* the certified one of 1.335 ± 0.014 μg g^{-1}. Comparison on various fish bone samples showed good agreement with differential pulse ASV. The multi-element capability of this technique could be exploited for the simultaneous determination of other elements	354
Pb	Bone (tibia)	XRF;-;-	Bone (tibia) Pb was measured *in vivo* by ^{109}Cd K-shell XRF in two groups of young adults from Vermont (USA) and New Brunswick (Canada). Mean Pb values were 0.7 μg g^{-1} (Vermont) and 0.5 μg g^{-1} (New Brunswick). Mean uncertainty was lower (2.6 μg g^{-1} *versus* 4.1 μg g^{-1}) in the New Brunswick	93

Table 1 (*continued*)

Element	Matrix	Technique; atomisation; presentation	Sample treatment/comments	Ref.
			group, owing to the use of reduced source-to-skin distance (5 mm) and longer measurement time (3600 s) with a weaker radioisotope source (0.42 GBq). Measurement uncertainty tended to increase with body mass index and was higher in women compared with men, for a given body mass index	
Pb	Biological CRMs	AA;ETA;L	See Cd, ref. 43	43
Pb	Teeth	MS;ICP;L AE;ICP;L	The concentrations of Pb, Sr and Zn were determined by ICP-MS and ICP-AES in deciduous teeth from living individuals and permanent teeth from historical burial sites. Pb isotope ratios were used to identify areas of residence. Sr and Zn concentrations in teeth reflected the individual nutritional and environmental history	355
Pd	Egg, faeces, blood, liver and kidney (raptor)	MS;ICP;L	Pd, Pt and Rh concentrations were determined by ICP-MS in biological samples (eggs, blood, liver, kidney and faeces) from raptors (sparrowhawk (*Accipiter nisus*), peregrine falcon (*Falco peregrinus*) and gyrfalcon (*Falco rusticolus*))	161
Pt	Breast implant material	MS;ICP;L	Individuals with silicone breast implants may be at risk of Pt exposure, since Pt was determined in breast implant materials at concentrations within the ranges: 0.26–48.90 μg g^{-1} (silicone breast implant gel), 3.05–28.78 μg g^{-1} (elastomer), 5.79, 25.27 μg g^{-1} (double lumen), 5.79–8.36 μg g^{-1} (foam) and 0.003–0.272 μg g^{-1} (capsular tissue)	159
Pt	Egg, faeces, blood, liver and kidney (raptor)	MS;ICP;L	See Pd, ref. 161	161
Pt	Water, serum	AA;ETA;L	The atomisation of Pt from aqueous solutions and serum samples was investigated	56
Pt	Biological fluids (plasma, ultrafiltrate and urine)	MS;ICP;L	A method for the determination of Pt in plasma, ultrafiltrate and urine samples from patients treated with antitumour agents was developed. LOQs in the three matrices were 1.0, 0.1, and 2.0 μg l^{-1}. The method was validated according to the FDA criteria and the uncertainty of measurement in the different matrices was estimated according to the EURACHEM/CITAC Guide	22
Pt	Environmental, food and urine samples and CRMs	MS;ICP;L	A method was developed for the quantification of Pt in digested environmental, food and urine samples, by means of SF-ICP-MS, in low resolution mode. The use of a desolvation device combined with a membrane unit for sample introduction gave a $HfO^+ : Hf^+$ ratio of 0.01% (50 times lower than with a standard introduction system). The method was validated by analysis of CRM BCR 723 Road Dust and recovery tests on spiked peat and hay samples. LODs were: 4.5 ng kg^{-1} dry weight for environmental and food samples (*i.e.* 0.2–1.8 ng kg^{-1} wet weight) and 0.5 ng l^{-1} for urine samples	76
Pt	Human autopsy tissues (lung, liver and kidney)	MS;ICP;L	After microwave digestion followed by an open vessel treatment, samples were analysed by SF-ICP-MS with an ultrasonic nebulisation/membrane desolvation system for sample introduction and ID. LODs were 20, 20 and 34 pg g^{-1} dry weight for lung, liver and kidney tissue, respectively. Pt levels in tissues from 5 individuals ranged between 0.03 and 1.42 ng g^{-1}	77
Pu	Urine	MS;ICP;FI	The procedure involved on-line matrix separation, Pu preconcentration on an ion-exchanger TRU resin and sample introduction by FI, desolvation and nebulisation *via* a commercial APEX device. The use of DRC eliminated interferences from U. ^{205}Tl was the internal standard and ^{175}Lu was used as yield tracer. LOD for ^{242}Pu in 10 ml urine was 1.9 pg l^{-1}. The rapid (<11 min) method was assessed by recovery tests on urine from non-exposed volunteers	40
Rh		MS;ICP;L	See Pd, ref. 161	161

Table 1 (*continued*)

Element	Matrix	Technique; atomisation; presentation	Sample treatment/comments	Ref.
	Egg, faeces, blood, liver and kidney (raptor)			
Se	Blood serum	MS;ICP;HPLC MS;ICP;SEC	A method was developed to determine selenoamino acids in human serum samples, with a collision cell and species specific ID. Sample preparation involved treatment with lipase and protease, after derivatisation of the SeCys residues with iodoacetamide, followed by isolation of the selenoaminoacid fraction (by SEC) and further separation of SeMet and carboxymethylated SeCys (by capillary HPLC). Quantification of SeMet was carried out by ID with ^{77}Se-labeled SeMet as a spike and the determination of the ^{77}Se : ^{80}Se ratio in the SeMet fraction. The SeCys concentration in the same sample was then determined using SeMet as an internal standard. A modification of the HPLC-ICP-MS interface allowed an LOD of <0.5 ng g^{-1} to be achieved. RSD was $<5\%$	47
Se	Urine	-;-;-	Sixty publications, from 1969 to date, reporting a total of 16 Se metabolites in urine of humans or rats, were critically assessed. It was suggested that, in many studies, incorrect structures might have been assigned to Se metabolites. In particular, the relative abundance of $TMSe^+$ and selenosugars was revisited	10
Se	Se-enriched supplements	MS;ICP;HPLC MS;MS;ES	A method for the speciation of Se compounds present in extracts of Se-yeast and Se-methylselenocysteine based supplements was reported. ES-MS/MS coupled with RP, ion pair HPLC was used to identify such species and SEC, anion-exchange and RP, ion pair HPLC coupled with Q-ICP-MS with USN for their quantitation. Sample preparation involved either accelerated solvent extraction or sample digestion with proteolytic enzymes. With USN, LODs were up to 6-fold lower (in the range of ng l^{-1}) than those obtained with pneumatic nebulisation and the newly developed method allowed improved separation of minor Se species	241
Se	Organ tissue (rat)	AA;ETA;L	Se was determined in 10 rat's organs after microwave aided digestion with (10 : 3) HNO_3–H_2O_2. $PdCl_2$ (50 μg ml^{-1}) was used as modifier. Charring and atomisation temperatures were 1200 °C and 1800 °C, respectively. Linear range was 0–80 ng ml^{-1}, LOD 1.83 ng mL^{-1}, RSD $<8\%$ and the average recovery rate 97.6%	356
Se	Garlic, urine (rat)	MS;ICP;HPLC	Capillary HPLC, using multi-mode gel filtration columns, was evaluated for the separation of naturally occurring selenocompounds with ICP-MS detection	247
Se	Hair	AA;HG;L	Two procedures for wet decomposition of human hair samples were compared. These involved treatment with HNO_3–H_2O_2 and H_2SO_4–HNO_3, respectively, using small disposable polypropylene vials. Analytical steps from weighing to dilution were performed in the same polypropylene vial. After weighing (10 ± 3 mg) and reagent addition, decomposition was performed in a conventional oven (20 h, 100 °C). Addition of sulfamic acid prior to HGAAS measurements minimised interferences from residual NO_x. The analysis of a hair CRM gave results $>97\%$ of the target concentration. Absolute LOD was 1.2 ng, corresponding to 0.12 μg g^{-1} in the dry sample	34
Se	Hair	AF;HG;L	See As, ref. 339	339
Se	Urine	AA;ETA;L	With a mixed Pd–Rh–Ir modifier, LOD, on a 1.0% v/v HNO_3 solution, was 7.5 ± 1.2 μg l^{-1} for a 20 μl injection volume. Characteristic mass was 4.3 pg (water) and 6.8 pg (urine)	61
Se	Biological CRMs	MS;MIP;Sl		91

Table 1 (*continued*)

Element	Matrix	Technique; atomisation; presentation	Sample treatment/comments	Ref.
			Se was determined in slurry samples of biological CRMs using ETV with *in situ* fusion, N_2 MIP and MS with ID. The slurry sample with a ^{78}Se spike and NaOH as an alkaline flux, was injected into the ETV unit. An *in situ* fusion step was performed just before the pyrolysis step, to achieve equilibration between natural Se and the ^{78}Se spike solution. The use of N_2 as plasma gas eliminated isobaric interferences at m/z = 78 and 80. LOD was 90 ng g^{-1} and RSD between 8 and 15%. Analysis required <30 min per sample including slurry preparation	
Se	Urine	AA;ETA;L	See As, ref. 64	64
Se	Liver (animal)	AA;HG;L MS;ICP;L	HGAAS and ICP-MS were compared for the determination of Se in liver samples from domestic animal species. Samples were digested with $Mg(NO_3)_2$ and HNO_3, for HGAAS and ICP-MS, respectively. Using ^{82}Se for quantitation and Y as internal standard, the ICP-MS method gave a LOD of 0.12 μg g^{-1}. The paired analysis of 310 liver samples, evaluated by the mean difference plot method, confirmed the reliability of ICP-MS for quantitation of tissue Se at $\leq$ 2 μg g^{-1}	357
Se	Biological samples	AF;HG;L	See As, ref. 71	71
Se	Oyster tissue and CRMs		See Hg, ref. 46	46
Se	Urine	MS;ICP;LC	Two Se metabolites, Se-methylseleno-*N*-acetylgalactosamine and Se-methylselenogalactosamine, were quantified in human urine by LC-DRC-ICP-MS, using the standard additions method within a linear range of 0.5–100 μg L^{-1} Se. Sample pretreatment consisted of 1 + 1 dilution and RP chromatography using 200 mM CH_3COONH_4–5% CH_3OH as eluent at pH 9.25. LODs were 0.1 μg Se l^{-1} and 0.2 μg Se l^{-1}, respectively, and RSDs were 3.1% and 1.7%, at 2 μg l^{-1} Se, and 1.0% and 0.7% at 10 μg l^{-1} Se. For sample introduction, a microconcentric nebuliser in combination with a cyclonic spray chamber performed better than a DIN and an USN. The method was applied to the analysis of urine from volunteers given selenised yeast	48
Se	Water, serum	AA;ETA;L	Different chemical species of Se (*e.g.* different oxidation states) may exhibit different analytical behaviour in ETAAS. The addition of 2.5% HNO_3 in the presence of nickel (5–10 μg) or palladium–magnesium (0.5 μg and 5 μg, respectively) as modifiers was essential to achieve equal sensitivity for different Se species (Se^{IV}, Se^{VI}, SeMet and SeCys) in both aqueous and human serum samples, so that calibratiμon based on a single species (Se^{IV}) was effective	63
Se	Human milk	AA;ETA;L	The performance of different modifiers (Zr, Ir and an Ir–Zr mixture) was investigated. Maximum pyrolysis temperatures were 800 °C (Zr), 1000 °C (Ir) and 1200 °C (Ir–Zr). Values observed for Se characteristic mass were 73.3, 18.0 and 14.7 pg, with Zr, Ir and Ir–Zr, respectively, and the corresponding LODs were 2.0, 0.50 and 0.41 μg l^{-1}. A 2 μg Zr–2 μg Ir mixture was applied to the determination of Se in human milk, digested with HNO_3–H_2O_2 in a microwave oven, using matrix-matched standards for calibration. LOD was 1.37 μg l^{-1}, characteristic mass 48.8 pg, RSD (repeatability) <5% and recovery between 93 and 105%. The Se content in samples of milk from 9 Greek women ranged from 16.7 to 42.6 μg l^{-1}	62
Sr	Brain	AA;ETA;L AE;ICP;L	The Sr content of various brain regions was determined in autopsy samples from Alzheimer's patients and controls. After sample dissolution by	166

Table 1 (*continued*)

Element	Matrix	Technique; atomisation; presentation	Sample treatment/comments	Ref.
			microwave-assisted or high-pressure Parr-bomb digestion, Sr was determined by ETAAS, using pyrolysis at 1500 °C and atomization at 2500 °C, with 0.4% $La(NO_3)_3$ as modifier. LOD was 0.057 ng ml^{-1} and characteristic mass 1.0 pg. Ca and Mg content of the same digested samples were measured by ICP-AES. The methods were assessed by analysis of NIST SRM 1577 Bovine Liver and recovery tests. In contrast to Ca and Mg, Sr concentrations showed large individual differences	
Sr	Teeth	MS;ICP;L AE;ICP;L	See Pb, ref. 355	355
Th	Autopsy tissue	MS;ICP;L	See Cs, ref. 122	122
Th	Urine	MS;ICP;LA	A new analytical procedure was developed for the determination of Th and U concentrations and the $^{235}U:^{238}U$ isotope ratio in dried, homogenised, urine samples. Recovery of Th and U from spiked synthetic urine ranged from 91 to 104%. At U concentrations of 0.1 ng ml^{-1}, RSD% was 7%	84
Tl	Bone	MS;ICP;LA	By means of SF-ICP-MS in conjunction with LA for the determination of Tl in bone samples in a case of homicide, the results of previous analyses of total Tl concentration by ETAAS were confirmed and further information was obtained on the spatial distribution of Tl in a thumbnail of the poisoned person	85
U	Autopsy tissue	MS;ICP;L	See Cs, ref. 122	122
U	Urine	MS;ICP;L	ICP-MS, coupled with a large-bore DIHEN, was used to determine U concentration and isotopic ratio in synthetic urine. Loss of signal intensity, due to the high total dissolved solid content, was compensated for by using ^{233}U as an internal standard. The method showed better performances than alpha-spectrometry and Q-ICP-MS with a conventional nebuliser, for both isotope ratio (<5%) and absolute quantitation (<2%) precision	167
U	Urine	MS;ICP;LA	See Th, ref. 84	84
U	Urine	MS;ICP;L	A method based on ICP-MS with a DRC and ^{233}U as an internal standard was applied to identifying depleted U in urine by measuring both total U and the $^{235}U:^{238}U$ ratio. Analyses were performed with and without O_2 as reaction gas, which converted ionised U isotopes into their oxides with a 90% efficiency. Urine samples (n = 15) with known U concentration were used for validation. LOD for total U was 0.1 pg ml^{-1} in urine and RSD 1–2%. LOD for the $^{235}U:^{238}U$ ratio was 3.0 pg ml^{-1} in urine. Analysis of 21 patient samples allowed the correct identification of previous exposure to depleted U	79
V	Bird liver and kidneys	AA;-;-	Hepatic (30–77 ng g^{-1}) and renal (52–72 ng g^{-1}) wet weight concentrations of V did not correlate with recent exposure to fuel in seabirds	169
V	Mussel/oyster soft tissue; scallop shell	AA;ETA;L MS;ICP;LA	See Ni, ref. 168	168
V	Urine	AA;ETA;L	Three 60 µl volumes of diluted urine were sequentially injected into the atomiser, preheated to 110 °C, at a flow-rate of 0.5 µl s^{-1}. Drying and pyrolysis steps were carried out after each injection. 100 mg L^{-1} BaF_2–0.3% v/v Triton X-100 was used as modifier. With this preconcentration, LOD and LOQ improved from 0.54 to 0.11 µg l^{-1} and from 1.82 to 0.37 µg l^{-1}, respectively. Recoveries varied from 96.0 to 103% for V additions ranging from 0.8 to 3.5 µg l^{-1}	59
Zn	Brain	AA;ETA;L	See Mg, ref. 57	57
Zn	Human erythrocytes and hair	MS;ICP;L	$^{66}Zn:^{64}Zn$ and $^{68}Zn:^{64}Zn$ isotope ratios were measured by MC-ICP-MS, after elimination of potential interfering species (*e.g.*, $^{64}Ni^+$ and $^{136}Ba^{2+}$) by ion chromatography. Precision (2SD) was 0.05‰	81

Table 1 (*continued*)

Element	Matrix	Technique; atomisation; presentation	Sample treatment/comments	Ref.
			for the $^{66}Zn:^{64}Zn$ ratio and 0.10‰ for the $^{68}Zn:^{64}Zn$ ratio, respectively. The inter-individual and seasonal variations of the Zn isotope ratios in blood were evaluated and, in one subject, blood and hair Zn isotope ratios were compared	
Zn	Plasma	AA;ETA;L	See Cu, ref. 348	348
Zn	Teeth	MS;ICP;L AE;ICP;L	See Pb, ref. 355	355
Various	—	XRF;-;-	This annual review of XRF covered instrumental and analytical developments as well as applications. Among others, biological and clinical (including biomonitoring) applications were reported, thus indicating an increased utilisation of the technique in these areas	2
Various	Biological and clinical samples	XRF;-;-	Procedures for sample preparation and calibration for the direct analysis of biological samples by TXRF were reviewed. Examples included slurry sampling, *in situ* microwave digestion, *in situ* chemical modification and Compton peak and internal standardisation	28
Various	—	-;-;-	The state-of-the art of enzymatic digestion as a method for sample preparation prior to total determination and speciation of chemical elements by atomic spectrometry was critically reviewed. The combination of enzymatic digestion and ultrasonication, by either bath or probe, was indicated as an emerging, promising technique. Guidelines for its implementation were provided	11
Various	Biological and pharmaceutical samples	MS;ICP;HPLC MS;ICP;LA	This paper reviewed applications of LC and capillary LC coupled with ICP-MS in areas of interest for the pharmaceutical industry, including the profiling of element content (in particular Br, for the study of Br-labelled peptides) in biological samples such as human plasma and investigations of the use of LA-ICP-MS for the determination of protein phosphorylation on electrophoresis gel blots	87
Various	Biological and environmental CRMs	AE;ICP;L	An improved method for the on-line digestion of biological and environmental samples prior to analysis by ICP-AES was developed, including a novel type of interface for gas removal. The method was tested by the analysis of biological and environmental CRMs	72
Various	Skin	PIXE;-;-	Micro-PIXE, in association with other ion beam microanalysis techniques, was used to characterize different epidermis models, based on their content and distribution of elemental ionic species	358
Various	—	XRF;-;-	This annual review of XRF covers instrumental developments and a survey of applications in various fields, including forensic, biological, clinical and speciation studies	3
Various (4)	Botanic and biological samples	AA;ETA;L	A comprehensive investigation of Sc, Ru, Sc–$(NH_4)_2HPO_4$, Ru–$(NH_4)_2HPO_4$, Sc–Ru and Sc–Ru–$(NH_4)_2HPO_4$, as modifiers for the determination of Cu, Mn, Pb and Zn in botanic and other biological samples was reported. With a Sc–Ru–$(NH_4)_2HPO_4$ mixture in Triton X-100 0.5% (v/v) as modifier, LODs and characteristic masses were: 0.32 μg l^{-1} and 5.6 pg (Cu), 0.09 μg l^{-1} and 0.1 pg (Mn), 0.72 μg l^{-1} and 16.3 pg (Pb), 0.03 μg l^{-1} and 1.1 pg (Zn), respectively. The analysis of CRMs after dilution with 0.2% (v/v) HNO_3 showed good agreement with the certified values	359
Various (4)	Bone	XRF;-;-	The distribution of Pb and other elements (Ca, Sr and Zn) in slices of human bone was studied using μSR-XRF at beamline L of the HASYLAB facility in Hamburg, Germany, with a focused synchrotron X-ray beam of about 15 μm in diameter	96
Various (4)	Human eyes (autopsy tissue)	MS;ICP;L	30 autopsy eyes of 16 subjects were and the concentrations of Cd, Hg, Pb and Tl were determined in ocular tissues, ocular fluids and blood samples. Cd	118

Table 1 (*continued*)

Element	Matrix	Technique; atomisation; presentation	Sample treatment/comments	Ref.
			and Pb were found in all pigmented ocular tissues studied. In the retina, Cd was present in all samples (mean, 1072 ± 489 ng g^{-1}) but Pb only in 9 (30%) of the 30 eyes (mean, 53 ± 54 ng g^{-1}). Hg and Tl were not detected in any of the samples	
Various (4)	Blood plasma and synovial fluid	AA;-;L	The concentrations of Cu, Fe, Se and Zn in synovial fluid and blood plasma samples from patients with rheumatoid and osteoarthritis were investigated by AA (Cu, Se, Zn) and colorimetric (Fe) methods	360
Various (5)	Human milk	AE;-;L AA;-;L	B, Cu, Fe, Se and Zn concentrations were determined in timed collections of milk from mothers of full-term and premature infants. Milk samples were digested with HNO_3–H_2O_2 in PTFE tubes prior to analysis by AES or AAS. In contrast to other elements, B concentrations were stable over time in milk samples from mothers of full term babies	361
Various (5)	Bile and pancreatic ducts	AE;ICP;L	Age-related changes of element (Ca, Fe, Mg, P, S) contents in the common bile and pancreatic ducts and their correlations were investigated. Only Mg changed significantly with ageing	362
Various (5)	Brain (mouse)	PIXE;-;-	Brain samples from 4 genetic mouse strains (C57BIack6/SJL, C57Black6/D2, SJL and C3H) were freeze-dried and analysed by means of PIXE and Rutherford backscattering spectrometry to establish reference values for Ca, Cu, Fe, K and Zn content of the white and gray matter of the *cerebellum* and *corpus callosum*	117
Various (7)	Human serum	MS;ICP;ETV	Ba, Ce, Cr, La, Mo, V and W were determined simultaneously in 5-fold diluted human serum. PTFE, as a fluorinating reagent, was used as modifier. LODs were 0.328 (Ba), 0.038 (Ce), 0.229 (Cr), 0.031 (La), 0.050 (Mo), 0.18 (V) and 0.019 (W) ng mL^{-1}. RSDs, at serum concentrations of 2 ng mL^{-1}, were in the range 4–15%	88
Various (7)	Brain	MS;ICP;LA	To obtain images of element distribution in 20 μm thin sections of human brain tissue (*Hippocampus*), the sample surface (80 mm^2) was scanned with a focused laser beam (wavelength 213 nm, diameter of laser crater 50 μm and laser power density 3×10^9 W cm^{-2}) in a cooled LA chamber developed for this application. Ion intensities of $^{63}Cu^+$, $^{56}Fe^+$, $^{31}P^+$, $^{32}S^+$, $^{232}Th^+$, $^{238}U^+$ and $^{64}Zn^+$ were measured by coupling LA with double-focusing SF-ICP-MS. Cu, Th, U and Zn concentrations were quantified using matrix-matched standards. An inhomogeneous distribution (layered structure) was observed for Cu, P, S and Zn, whereas Th and U were more evenly distributed	83
Various (8)	Bone	XRF;-;-	The suitability of TXRF to evaluate the distribution and *post-mortem* uptake of Ba, Ca, Cu, Fe, Mn, Pb, Sr and Zn in human bones from the 13th century was investigated. TXRF was applied to quantification and profiling of the elements throughout long bones	97
Various (8)	Teeth (Steller sea lion)	PIXE;-;-	The concentration and distribution of 8 elements (Br, Ca, Cu, Fe, Mn, Pb, Sr and Zn) in the teeth of Steller sea lions (*Eumetopias jubatus*) collected from the North Pacific from 1968 to 1999 were determined by PIXE and evaluated as possible indicators of temporal and spatial variations of trace element pollution	363
Various (8)	Liver (chicken)	MS;ICP;SEC	A method was developed for multi-element (Cu, Fe, Hg, Mn, P, S, Se and Zn) speciation in chicken liver cytosol. Separation parameters (25 mM Tris-HCl buffer, 50 mM KCl, pH 6.8, 1 ml min^{-1}) were optimised. RSD was $<10\%$ and recovery between 82 and 102%. Interactions between the liver extracts and the column material were investigated: Cu, Fe, Hg, S, Se and Zn were mainly associated to high and medium M_r (4300–45 kDa), Mn to high (116 kDa)	364

Table 1 (*continued*)

Element	Matrix	Technique; atomisation; presentation	Sample treatment/comments	Ref.
			and low (0.03 kDa) M_r species and P to low M_r species (5.5 kDa)	
Various (9)	Fish tissue, blood (CRMs)	MS;ICP;L	A multi-element quantification strategy was implemented for the measurement of As, Cu, Fe, Mn, Rb, Se, and Zn levels in a candidate fish tissue NIST SRM and measurement of Cd and Pb in two clinical, whole blood CRMs by ICP-MS with collision cell. The approach used to estimate uncertainties of the results from standard additions calibrations, using regression analysis and quotient propagation of error formulae, was reported	18
Various (10)	Herbal drugs	AA;F;L AE;F;L AE;ICP;L	Al, B, Ba, Ca, Cu, Fe, K, Mg, Mn and Zn were determined in 26 herbal drugs after sample dissolution. The analysis of NIST 1573a Tomato Leaves gave values between 91 and 102% of the target concentrations. Metal concentrations in drug samples originated from medicinal plants (Serbia) were reported and evaluated using a chemometric approach	365
Various (14)	Urine	AE;ICP;L	Al, Ba, Ca, Co, Cr, Cu, K, Mg, Na, Ni, P, Sr, Ti and Zn concentrations were determined in urine from patients with fluorine or arsenic fluoride poisoning. RSD ranged from 0.24% to 2.47% ($n = 10$) and average recoveries from 90.4% to 100.5%	366
Various (16)	Hair	MS;ICP;L	16 REEs were determined in scalp hair samples from 60 children, aged 11–15 years, living in mining and surrounding areas in southern China. Higher concentrations were observed in samples from subjects from the mining area, compared with controls and the literature. The distribution pattern reflected that in the mine	109
Various (16)	Brain tissue (rat)	MS;ICP;L	SF-ICP-MS was applied to the simultaneous determination of Ag, As, Bi, Cd, Co, Cr, Cu, Fe, Hg, Mn, Ni, Pb, Se, U, V and Zn in specific regions of the brain of healthy Wistar rats. Concentrations ranged from 2 ± 1 (Cr in diencephalon) to 7558 ± 450 ng ml^{-1} (Fe in olfactory bulb) and LODs from 5 (U) to 300 pg ml^{-1} (Fe). The method was validated by analysis of NIST SRM Bovine Liver 1577B and recovery tests	367
Various (17)	Medicinal plants	XRF;-;-MS;ICP;L AE;ICP;L	The concentrations of 17 elements (Al, As, Ca, Cu, Fe, K, Mg, Mn, Na, P, Pb, Rb, S, Si, Sr, Ti and Zn) in five medicinal plants (*Taraxacum officinale Weber, Eucalyptus globulus Labill, Plantago lanceolata L., Matricaria chamomilla L.* and *Mentha piperita L.*) were determined in the bulk raw plants (WDXRF and EDXRF) and in their infusions (ICP-MS and ICP-AES)	225
Various (20)	Blood serum, urine	MS;ICP;L	A method based on SF-ICP-MS, with a sample-introduction system designed to provide enhanced sensitivity, was developed to determine low abundance elements (Ag, Au, Bi, Hf, Ir, Nb, Os, Pd, Pt, Re, Rh, Ru, Sb, Ta, Te, Tl, U, W, Y and Zr) in urine and serum samples from the general population. Samples were 10-fold diluted with 2% HCl. Using high purity water and acids, LOQs for 13 analytes were <1 ng l^{-1}. Further improvements of LOQs were hampered by release of analytes (Ag, Au, Bi, Sb, Tl, U, Y and Zr) from the sample-introduction system itself. Only for Pd, Rh and Ru, residual unresolved spectral interferences may still be present	75
Various (23)	Urine	MS;ICP;L	The routine determination of 23 elements (As, Ba, Be, Cd, Co, Cr, Cu, In, Li, Mn, Mo, Ni, Pb, Pt, Rh, Sb, Se, Sn, Tl, U, V, W and Zn) in urine by ICP-MS with an octopole collision cell was reported. Urine samples were 5-fold diluted (v/v) with 1% (v/v) HNO_3. Sample introduction was *via* a robust Babington nebuliser and a torch with an injector tube with an inner diameter of 2.5 mm. Sample aspiration	78

Table 1 (*continued*)

Element	Matrix	Technique; atomisation; presentation	Sample treatment/comments	Ref.
			rate was 0.4 ml min^{-1}. Helium, 3.2 ml min^{-1} (for As, Ba, Cd, Cr, Cu, Mo, Mn, Ni, Rh, V, Zn) or H_2, 3.4 ml min^{-1} (for Se) were used as collision gas. LODs for undiluted urine ranged from 0.4 ng L^{-1} (U) to 143 ng l^{-1} (Se). Results for method validation, including external quality assurance, and the analysis of 63 real urine samples from non-exposed human subjects, were reported	

Mali, Malaysia, Manipur and Brazil have been presented, together with additional data on Indian and Chinese medicines sold in Europe and the USA. Publications divide into those with an emphasis on method development and speciation (particularly using AFS[171–173]) and those which report element concentrations (using a range of techniques). As in previous years, some preparations were found with concentrations of elements, such as Pb, in excess of allowable limits, while others were deemed perfectly safe. Elements that influence plasma glucose concentrations were at no more than trace concentrations in plants used to treat diabetes.[174,175]

Given the incidence of Fe deficiency in children from many countries throughout the world, and the difficulties in tolerating Fe-supplements, the formulation of microencapsulated *ferrous fumarate 'sprinkles'* may prove to be a significant development.[151] Absorption of Fe from this product, which can be added to simple foods, appeared to be very effective in this relatively small study. The developing interest in Se and its species in yeast-based supplements is described below in Section 5.6.4.

5 Analysis of foods and beverages

5.1 Sampling and sample preparation

The need for *suitable sub-sampling* techniques prior to analysis is very important although this receives little attention in the literature. In the case of solid sampling ETAAS, Nomura *et al.*[44] found that microwave drying followed by heating in a stove at 60 °C to constant weight and cryogenic milling gave the lowest RSD for the determination of Cu and Zn in bovine liver. Krystek and Ritsema[176] compared different sub-sampling techniques in the determination of Hg species. Use of partially thawed frozen shark fillet led to significant differences in the Hg concentration which was on average a factor or two lower than in the fully thawed out fillet.

5.1.1 Extraction. *Pressurised solvent extraction* was evaluated for a range of tri-substituted organotins. The technique offered good analyte preservation, speed of extraction and precision but inferior LODs when compared with solid–liquid extraction.[177] Enzymic digestion of rice for As speciation (using IC-ICP-MS as detection) compared favourably with extraction with trifluoroacetic acid.[178] The enzymic route allowed the tentative identification of dimethylthioarsinic acid in the two rice samples cooked in As-contaminated water.

Solid-phase microextraction is being used extensively across the analytical spectrum. SPME is an established technique in molecular MS, but is cited less frequently in atomic MS. Davis *et al.*[41] constructed a heated interface for the SPME-GC-ICP-MS determination of methylmercury, yielding an LOD of 4.2 pg g^{-1}. SPME was also used to concentrate and separate sample from matrix in the determination of volatile species during the production and subsequent *in vitro* gastric digestion of commercial products. Inorganic Se was metabolised to at least five different volatile species, predominantly dimethyl selenide and dimethyl diselenide.[179] In a further application of SPME, samples were digested using KOH–NaOH, derivatized using phenylation and the resulting hydrides SPME trapped and introduced to a pyrolysis GC-AF system.[180] Chromium(VI) species were separated from Cr^{III} by solid-phase extraction with APDC.[181] The As species diphenylarsinic acid (DPAA) was extracted from well and sea-water onto Oasis® HLB cartridges and eluted with C_2H_5OH prior to determination by ETAAS. Fe^{III} reduced recovery of DPAA but EDTA improved retention.[182]

In an evaluation of *ultrasound-assisted extraction*, optimum compromise conditions were 7 ml extraction volume, 3.7 M HNO_3, sonication for 35 min, ultrasound frequency 17 kHz, and water-bath temperature 65 °C.[183] Copper and Fe were extracted on-line from seafood samples by a robust, fast and simple continuous ultrasound-assisted extraction system. This was connected *via* FI to an on-line FAA spectrometer.[184] In a second paper,[185] the group used the method to determine Zn in meat. Focused ultrasound in conjunction with HNO_3–H_2O_2, 1 + 2, was used for extraction. The required sample treatment time was only 60 s.[186]

5.1.2 Digestion. Work continues on the use and comparison of more *traditional digestion techniques*,[187,188] microwave-assisted digestion[189,190] and focused-microwave digestion.[191] Bing *et al.*[32] demonstrated that 10% v/v NH_3 in a PTFE-lined stainless steel bomb at 185 °C for 18 h was required for determining I by ICP-MS. The method was shown to have a precision of 1.82–4.32% RSD using Chinese CRMs. Mineralisation procedures for Cu, Fe, Se and Zn were compared with respect to precision, recovery and sensitivity.[187] Although a closed vessel microwave system gave good recoveries for chicken meat, with the animal feed it was necessary to include HF to prevent losses of Zn due to residual siliceous material.

Ultrasound sonication techniques are becoming more prevalent in sample preparation. The use of ultrasound to assist digestion compared favourably with microwave digestion of

Table 2 Analysis of foods and beverages

Element	Matrix	Technique; atomisation; presentation	Sample treatment/comments	Ref.
Al	Orange juice	SF-MS;ICP;L	Al migration from aseptic paperboard packaging into orange juice was studied over periods up to 1 y. There was no evidence of migration. The LOD was 5 μg l^{-1}	328
Al	Foodstuffs	AA;ETA;L	The effect of Al containing food additives on total Al content of a range of US foodstuffs was investigated. Some products contained up to 180 mg per serving	368
As	Drinking water	AA;HG;FI	In a study of 533 Bangladeshi women, the findings suggested that chronic As exposure may increase the risk of fetal and infant death	369
As	Drinking water	AA;HG;FI	In a further study of the Bangladesh/Indian As contamination crisis, one village was investigated in detail. Although filtration systems had been supplied, 149 of 825 residents interviewed showed As lesions and the authors reported villagers were ill-informed about the risks	300
As	Drinking water	AA;HG;L	In a contrast to the Bangladeshi papers, this study reported As concentrations in well water from Central Appalachia, USA. The incidence of As-related cancers and other diseases in the region was high and 6% of samples had As concentrations above a new US Environmental Protection Agency maximum contamination level of 10 ppb	299
As	Drinking water	AA;ETA;L	The cloud point extraction approach, using Triton X-114 as non-ionic surfactant, was used to determine As^{III} and As^{V} at LODs of 0.01 μg l^{-1} for a 10 ml sample	42
As	Well water	AA;ETA;L MS;ICP;HPLC	Highly elevated levels of As in well water, 4.5 ppm, were found to be associated with bis(diphenylarsine)oxide, diphenylarsinic acid and phenylarsonic acid. Apparently these compounds are linked with chemical weapons and the authors suggested they were derived from such. How the compounds came to be present in Japanese well water is an unanswered and important question	301
As	Beer, juice, soft drinks	MS;ICP;HPLC	Anion exchange with a mobile phase of K_2HPO_4–KH_2PO_4, 0.05 × 10^{-3} M, was used to separate As^{III}, As^{V}, DMA and MMA	231
As	Seaweed	-;-;-	A study of *Hizikia fusiforme* edible seaweed suggested that the bioaccessibility of As_i increased with cooking. The authors published an additional work covering similar ground327	326,327
As	Bangladeshi foodstuffs	AA;ETA;L	As contamination of groundwater in Bangladesh and West Bengal has been frequently reported in ASU reviews. In this study, foods imported into the UK from Bangladesh were analysed and found to contain 2–3 times higher levels of As than similar foods produced in the UK, although still inside permissible limits	281
As	Marine organisms	AA;HG;L AE;ICP;L	The conditions to achieve complete decomposition of 6 As species (MMA, DMA, AC, AB, TMAO, TMI) were investigated. To decompose AB, the most stable species, extreme conditions of HNO_3–$HClO_4$–H_2SO_4 heated to 320 °C were required	233
As	Fish, shellfish	AF;HG;HPLC	12 species were investigated using LC-photo-oxidation-HG-AFS	293
As	Rice, rice cereal, oyster, dogfish, mushroom extracts	MS;ICP;HPLC	11 As species were separated using anion exchange and a mobile phase of 10 mM ammonium phosphate–30 mM boric acid at pH 8.5. As species separated included As^{III}, AS^{V}, DMA, MMA, AB, TMA and arsenosugars	232
As	Fish tissues, molluscs, plants	-;-;-	A useful review of arsenolipids presented structures of natural arsenolipids (and derivatives), their distribution, biogenesis in algae and invertebrates, synthesis, and also biological activity	370
As	Fish, fish oils	MS;ICP;L MS;ICP;HPLC	10 fish oils were used as samples for a detailed study of arsenolipids. All of the oils contained the same 4–6 lipids	128
As	Fish	MS;ICP;HPLC	Samples were microwave digested using ethanolic NaOH. The LOD was 3 ng g^{-1} and the method was not suited to oily fish such as mackerel	371
As	Molluscs	MS;ICP;LC MS;ES;LC	A new arsine sulfide containing an analogue of a known arsenosugar was identified in 4 species of mollusc	229
As	Seafood	MS;ICP;L	6 As species were characterised in 33 extracts from Korean seaweed, shrimp, fish and shellfish. Unusually AC was the species found in highest concentrations, up to 69 mg kg^{-1}	372
As	Fish, oyster	MS;ICP;CE	As^{III}, As^{VI}, MMA, DMA, AB and AC were determined at LODs of 0.3–0.5 ng As ml^{-1}	215
As	Rice	MS;ICP;LC ES-MS;-;HPLC	As was speciated in rice before and after cooking in contaminated drinking water. Absorption rates were high (> 89%). Dimethylthioarsinic acid was tentatively identified in 2 of the samples	178
Bi	Milk shakes	AF;HG;FI	An interesting approach to a slightly unusual application was described. Samples were treated for 10 min on-line using sonication in 8% v/v *aqua regia*. The LOD was 1.67 ng g^{-1} and good	109

Table 2 (*continued*)

Element	Matrix	Technique; atomisation; presentation	Sample treatment/comments	Ref.
			agreement with a microwave-assisted digestion method was reported	
Br	Drinking water	-;-;-	Methods for determining bromate were reviewed. The authors concluded there remains a need for low cost methods	13
Br	Vegetables	XRF;-;-	Samples from a Japanese market contained exceptionally high (1000–16200 ppm dry weight) levels of Br, possibly due to improper application of the fumigant, methyl bromide	220
Ca	Mineral water	MS;ICP;L	Some individuals have diets deficient in Ca. Unfortunately, most dietary sources are high in fat. In the reported study, which used samples extrinsically labelled with ^{44}Ca, the bioavailability from Ca-rich mineral waters was found to be as good as milk	139
Ca	Maize	MS;ICP;L	Absorption of Ca from tortillas prepared from low-phytate maize was significantly greater than from tortillas prepared from control maize	277
Cd	Tap water	AA;ETA;CV	Cd was determined with an LOD of 0.2 ng ml^{-1} using the technique of catholyte variation electrochemical hydride generation AAS. A laboratory-made electrolytic cell with lead–tin alloy as cathode material was used for HG	210
Cd	Tea	AE;ICP;L	Cd was precipitated in a mini-column containing polyurethane foam and 2-(5-bromo-2-pyridylazo)-5- diethylaminophenol as precipitating agent. The precipitate was eluted using 20% v/v HNO_3 and taken for measurement using ICP-AES equipped with a USN	373
Cd	Vegetables	AA;-;L	Cd, Hg and Pb were determined in Nigerian produce. Some exceptionally high concentrations of Pb, *ca.* 16 μg g^{-1}, were found and linked to high soil concentrations in farms close to highways	278
Cd	Salt	AA;F;L	Cd and Pb were extracted from solution using dithizone and IBMK. The LODs were 0.3 and 4.2 ng g^{-1}, respectively. A computer programme allowed the 2 elements to be determined sequentially in the extract	200
Cd	Tomato leaf SRM, Oyster SRM	AA;ETA;CV	Hydrides of Cd species were formed by reaction with $NaBH_4$ and then trapped in a purpose-built quartz tube held at 350 °C. The LOD for 3 min collection was 1.8 pg ml^{-1}	134
Cd	Dried fruit, legumes		A continuous ultrasound-column preconcentration-FAAS procedure yielded LODs of 0.011–0.014 μg g^{-1}	207
Co	Foods, beverages	MS;ICP;L	150 Australian foods and drinks were analysed in a comprehensive study	256
Cr	Mineral water	AA;ETA;L	Cr^{VI} species were separated from Cr^{III} by solid-phase extraction with APDC	181
Cu	Bovine milk, fruit juice	AA;FF;TS	Untreated sample, 300 μl, was injected into the carrier, 0.014 M HNO_3, and introduced into a hot nickel tube. The LODs for Cu and Zn were 2.2 and 0.91 μg l^{-1}, respectively. Good results were achieved for RMs	201
Cu	Foods	AA;F;L	Cu was determined in a wide range of Brazilian retail foods. Highest concentrations were found in beef liver	255
Cu	Complementary foods	TIMS;-;L	The effect of dephytinization of a cereal-based complementary food on Cu and Zn apparent absorption was studied using extrinsically labelled stable isotopes. Dephytinization was found to be beneficial for Zn absorption but not Cu	145
Cu	Seafood, meat	AA;F;FI	Cu and Fe were extracted on-line from seafood samples by a robust, fast and simple continuous ultrasound-assisted extraction system. This was connected *via* FI to an on-line FAA spectrometer. In a second paper,[185] the group used the method to determine Zn in meat	184, 185
Cu	Chocolate	AA;ETA;Sl	Sample, 0.2 g, was sonicated for 15 min in 2 M HCl. The LOD was 0.4 μg g^{-1}	374
Fe	Seafood, meat	AA;F;FI	See Cu, refs. 184 and 185	184, 185
Fe	Pulses, rice	AA;F;L	HNO_3–30% H_2O_2, 4 + 3, was used for closed vessel microwave digestion as part of a procedure to determine Fe, Mn and Zn	190
Fe	Infant formula	AE;ICP;L	The bioavailability of 5 different Fe salts was determined. EDTA–Fe^{III} was the preferred option. An *in vitro* method to simulate infant digestion was developed and used also to determine the effect of Fe concentration on Cu and Zn bioavailability	150
Fe	Fortified food, blood	MS;ICP;L	A new approach to treating Fe deficiency was described. Microencapsulated ferrous fumarate sprinkles were added to a maize porridge and provided to infants with different Fe and haematological status. ICP-MS was used to determine erythrocyte incorporation of ^{57}Fe and ^{58}Fe. The authors concluded that the sprinkles met and surpassed requirements for Fe absorption	151
Hg	Drinking water	AA;CV;L		51

Table 2 (*continued*)

Element	Matrix	Technique; atomisation; presentation	Sample treatment/comments	Ref.
			Methyl and Hg_i were sequentially speciated by selective retention of Hg_i on a PTFE packed column. A dual manifold was used to determine the 2 species	
Hg	Drinking water	AA;ETA;L	Sample was placed in the furnace of a 2 step atomizer and dried and vaporized. The vapour was carried in an Ar stream to an unheated vaporizer and trapped on the walls. The Hg was then atomized, yielding LODs of 0.24 μg l^{-1} for a 100 μl sample and a single transfer	69
Hg	Tap water	AA;ETA;CV	A comparison of the suitability of Ir, W or Zr for coating and trapping hydrides in a graphite cuvette found Ir most suitable. The LOD was 1 ng ml^{-1}	211
Hg	Vegetables	AA;-;L	See Cd, ref. 278	278
Hg	Rice	AF,ETA;GC	Methyl- and ethylmercury were determined in 25 rice samples from 15 Chinese provinces, with the former being found in the range 1.9–10.5 ng g^{-1}, the latter absent	273
Hg	Cultivated mushrooms	AA;HG;L	Hg content of *Agaricus bisporus* (variety K-23), reportedly the world's most cultivated mushroom, was found to be 10-fold lower than wild mushrooms	286
Hg	Oyster	AE;ICP;HG	7 slurry procedures for the simultaneous determination of Hg and Se were evaluated. Low recoveries of Se with 5 of the approaches indicated the need for strong oxidizing agents such as H_2O_2 or $K_2S_2O_8$ in the reaction medium	46
Hg	Fish and shellfish SRMs, biological samples	MS;ICP;GC	SPME is an established technique in molecular MS, but is cited less frequently in atomic MS. In this paper the authors constructed a heated interface for the SPME-GC-ICP-MS determination of methylmercury, yielding an LOD of 4.2 pg g^{-1}	41
Hg	Fish	AF;-;GC	In a further application of SPME, samples were digested using KOH–NaOH, derivatized using phenylation and the resulting hydrides SPME trapped and introduced to a pyrolysis GC-AF system	180
Hg	Shark steaks	MS;ICP;GC	Samples were dissolved in TMAH, derivatized in sodium tetraethylborate, extracted into isooctane and introduced into the gas chromatograph. The signal was stabilized by adding Xe to the GC carrier gas. The same procedure was applied by the authors[176] to investigate the influence of freeze-thaw on analytical results	176, 238
Hg	Tuna	MS;ICP;GC	ID was used in a detailed account of the SI-traceable certification of methylmercury content. Further comprehensive details of certification of tuna were given in another report[21]	19, 21
Hg	Tuna	MS;ICP;ID	^{202}Hg was spiked into the sample which was then microwave digested using HNO_3–H_2O_2	218
Hg	Fish CRMs	MS;ICP;L	A full uncertainty budget was used to compare the performance of species specific single and 'approximate matching' double IDMS in the determination of methylmercury by MC-ICP-MS	27
I	Tea	MS;ICP;L	I was extracted in screw-top PTFE-lined stainless steel bombs using a 10% v/v NH_3 solution at 185 °C for 18 h followed by direct ICP-MS measurement using ^{126}Te as internal standard. The LOD was 0.003 ng ml^{-1}	32
I	Cow's milk, human milk	MS;ICP;L	A German study investigated I content of milk from 32 lactating mothers, and from cows' milk. A sub-group of the women also consumed I supplements. The results showed a significant increase in human milk I content from a 1994 study and that the I supplements led to no increase in I in human milk	263
I	Foods, milk	MS;ICP;ID	A range of Swiss foods was analysed, using the enriched isotope ^{129}I. Bread and milk were found to be significant sources of I	259
I	Seaweed	MS;ICP;HPLC	I was speciated using a multidimensional HPLC (SEC-RP); the results revealed the presence of monoiodotyrosine and diiodotyrosine in *Wakame*	375
Mg	Fruit, vegetables	AA;-;L	A detailed study of 22 sample types evaluated the link between chlorophyll-bound Mg and human nutrition. However, the study showed the link to be of little relevance	260
Mn	Pulses, rice	AA;F;L	See Fe, ref. 190	190
Mo	Foods, formula milk, human milk	MS;ICP;L	Mo status of the Japanese population was evaluated. Mo in several plant foods was more than 0.5 μg g^{-1}; in particular Mo content in several seeds and pulses was more than 1 μg g^{-1} while that in most animal foods was less than 0.1 μg g^{-1}	254
Ni	Soft drinks	AA;ETA;L	The application of Co as internal standard led to improved accuracy and precision	376
Ni	Shellfish	AA;ETA;L MS;ICP;LA	Ni and V were measured by ETAAS (mussels, oysters) or LA-ICP-MS (scallops), following an accidental oil spill in Brittany. The results showed the monitoring of V in mollusc tissues is able to	168

Table 2 (*continued*)

Element	Matrix	Technique; atomisation; presentation	Sample treatment/comments	Ref.
			identify contamination due to oil spills, and similar information might be obtained *a posteriori* by analysing daily growth bands of scallop shells	
Pb	Vegetables	AA;-;L	See Cd, ref. 278	278
Pb	Salt	AA;F;L	See Cd, ref. 200	200
Pb	Moonshine	AA;ETA;L	Last years review referenced work being undertaken by the US authorities to assess the risk posed by moonshine consumption. In this report Pb levels ranged from 5–599 ppb, mean value of 80.7 ppb. Perhaps the ethanol content posed a greater risk, being up to 66%	320
Pb	Wine must	AA;ETA;L	Focused ultrasound in conjunction with HNO_3–H_2O_2, 1 + 2, was used for extraction. The required sample treatment time was only 60 s	186
Pb	Wine	MS;ICP;ID	Exact-matching ID was used as part of a high accuracy method utilised in an international intercomparison study	234
Pb	Seafood	MS;ICP;GC	A trimethyllead spike was synthesized from ^{206}Pb enriched metallic Pb and used for the determination of trimethyllead by GC-ID-ICP-MS. The LOD was 0.09 ng g^{-1}	235
Pt	Foods, SRMs	SFMS;ICP;L	A desolvation system and a membrane unit were used to reduce oxide interferences. LODs of 4.5 ng kg^{-1} in fresh foods were obtained	76
Pt	Indian mustard, maize	MS;ICP;L ASV;-;L	Using hydroponically grown plants, Pt uptake was evaluated following microwave sample digestion	377
Ra	Well water	SF-MS;ICP;LC	^{226}Ra was determined by SF-ICP-MS following removal of alkaline metal interferents. This approach yielded an LOD of 0.189 pg l^{-1}	378
Ra	Mineral water	SF-MS;ICP;L	The LOD for ^{226}Ra was 0.02 fg ml^{-1}	379
Se	Milk	AA;HG;L	Se distributions in milk, whey, fat and micellar casein phases were separated and measured by ultracentrifugation followed by microwave digestion and then HGAAS. The highest proportions (47–73%) were in the whey fraction	269
Se	Milk	AA;ETA;L	HNO_3–H_2O_2 with microwave digestion combined with a Zr–Ir modifier yielded LODs of 1.37 μg l^{-1}	62
Se	Milk	AA;ETA;L	As and Ge were added as internal standards *via* autosampler. They yielded a notable improvement in precision	209
Se	Foods	AA;ETA;L	129 subjects participated in a study to determine which foods best affect serum Se in subjects with Se concentrations below or above 70 μg l^{-1}, (the concentration considered to be sufficient for optimum glutathione peroxidase activity). It was concluded that frequent consumption of ham, tea and honey may be effective to improve the Se concentration in the sera of Se-inadequate subjects. Alcohol may have been associated with Se loss	164
Se	Cereals, bread	AA;ETA;HG	An FI-HG-ETAAS method using *in situ* trapping onto iridium-coated platforms. The method was applied to the determination of Se in doped and undoped cereals and bakery products	246
Se	Beverages, water	AA;ETA;L	A tungsten–rhodium carbide coating on the integrated platform of a transversely heated furnace or tungsten coating with co-injection of $Pd(NO_3)_2$ was used as a permanent modifier	208
Se	Oyster	AE;ICP;HG	See Hg, ref. 46	46
Se	Yeast	MS;-;GC	Papers on Se speciation in yeast continue to proliferate. In this useful publication, the authors compared 14 common extraction methods used in the determination of Met and SeMet. Interestingly, a number of oft quoted enzymic procedures gave very low recoveries. A 4 M methanesulfonic acid reflux digestion was found to be the most efficient for both analytes	243
Se	Yeast	MS;ICP;GC MS;-;GC	^{74}Se enriched SeMet was used to determine SeMet by ID. Samples were digested by refluxing, 16 h, in methanesulfonic acid then derivatized using CNBr and extracted into $CHCl_3$. The LOD was 0.9 μg g^{-1}. The impact of alternative acids and derivatizing agents was discussed. A linked work by the same authors is described above[243]	216
Se	Indian mustard, selenized yeast	MS;ICP;HPLC	Hydroponic cultures were used to evaluate Se metabolism in *Brassica*. S-(methylseleno)cysteine was found for the first time in shoots and roots when grown in the presence of Se^{IV} and Se^{VI}	380
Se	Yeast dietary supplements	ES-MS;-;HPLC	6 Se species were separated using a C_{18} column and a mobile phase containing the ion pairing agent tetraethylammonium chloride	240
Se	Yeast, dietary supplements	MS;ICP;HPLC ES-MS;-;HPLC	The paper was noteworthy for including an evaluation of accelerated solvent extraction amongst a number of other analytical protocols. Se-methylselenocysteine was characterised in the yeast, which was of interest as this is believed to be metabolised in animals and humans to methylselenol, an anti-carcinogenic compound	241

Table 2 (*continued*)

Element	Matrix	Technique; atomisation; presentation	Sample treatment/comments	Ref.
Se	Selenized yeast	MS;ICP;LC	Acid hydrolysis, which released 81% of the total Se, was followed by ID-LC-MS or LC-ICP-MS for characterisation of an RM. SeMet comprised 79% of the extracted Se	244
Se	Selenized yeast	MS;ICP;LC	Following proteolysis and two-dimensional LC, *i.e.*, size exclusion anion exchange, SeMet was found to constitute 80% of the Se in the sample. The authors suggested that other reported results may be negatively biased	242
Se	Selenized yeast	MS;ICP;HPLC	The same research group as in ref. 242 applied their two-dimensional LC approach with species specific ID for the accurate determination of an Asp-Tyr-SeMet-Gly-Ala-Ala-Lys peptide directly in a tryptic digest of an aqueous extract of selenized yeast	381
Se	Selenized yeast	AE;MIP;GC	SPME was used to concentrate and separate sample from matrix in the determination of volatile species during the production and subsequent *in vitro* gastric digestion of commercial products. Se_i was metabolised to at least 5 different volatile species, predominantly dimethylselenide and dimethyldiselenide	179
Se	Garlic	AF;ETV;HPLC	An online UV photolysis and UV/TiO_2 photocatalysis reduction device and an electrochemical vapor generation cell were used to couple HPLC to AFS. LODs for Se species were in the range 2–10 ng ml^{-1}	245
Se	Garlic	MS;ICP;HPLC	Multi-mode gel filtration HPLC columns of capillary size were evaluated for the separation of naturally occurring selenocompounds	247
Se	Chicken liver, kidney and muscle	MS;ICP;L MS;ICP;HPLC	A new procedure, described as enzymatic probe sonication, was claimed to offer advantages in terms of speed, simplicity and safety over traditional methods. Se species were extracted unchanged	194
Se	Brazil nuts	MS;ICP;SEC MS;ICP;CE	In a comparison of different extraction procedures, the best solubilisation of proteins was achieved using 0.05 M NaOH and 1% SDS in Tris/HCl buffer (0.05 M, pH 8)	239
Sn	Vegetables, SRMs	AA;ETA;L	An ultrasonic probe extraction procedure was described An end-capped Zr–Ir coated transverse heated tube was used and an LOD of 0.03 μg g^{-1} achieved	193
Sn	Vegetables	-;-;-	Accelerated solvent extraction was evaluated for a range of trisubstituted organotins. The technique offered good analyte preservation, speed of extraction and precision but inferior LODs when compared to solid–liquid extraction	177
Te	Drinking water	AF;HG;IC	The LODs were 0.6 and 0.7 μg l^{-1} for Te^{VI} and Te^{IV}, respectively	382
Te	Milk	AF;HG;Sl AF;HG;L	Te was leached from samples using *aqua regia* sonication and the resulting slurry merged with $NaBH_4$ and HCl to obtain results for Te^{IV}. Another portion of the slurry was mixed with KBr and passed through a reaction coil inside a microwave oven, reducing quantitatively Te^{VI} to Te^{IV}, which was measured using HGAFS	214
Te	Garlic	AA;F;HG	Samples were spiked with $La(NO_3)_3$, introduced into a resin and mixed with NH_3 buffer, which co-precipitated Te with $La(OH)_2$. The LOD was 0.03 μg l^{-1}	383
Th	Drinking water	MS;ICP;L	Analytical procedures, LODs, observed background distributions, and the results of U isotope ratio tests were presented	384
U	Drinking water	MS;ICP;L	See Th, ref. 384	384
U	Drinking water, hair, toenail, urine	MS;ICP;L	$^{234}U:^{238}U$ was determined using MC-ICP-MS. The results conclusively proved a link between drinking water consumption and exposure	82
V	Shellfish	AA;ETA;L MS;ICP;LA	See Ni, ref. 168	168
V	Fish, mussel	MS;ICP;HPLC	V^{IV} and V^{V} were separated as EDTA complexes	170
Zn	Seafood, meat	AA;F;FI	See Cu, refs. 184 and 185	184, 185
Zn	Bovine milk, fruit juice	AA;FF;TS	See Cu, ref. 201	201
Zn	Pulses, rice	AA;F;L	See Fe, ref. 190	190
Zn	Foods	AA;F;FI	Samples were treated with H_2SO_4–30% H_2O_2, then measured using FI with the gradient calibration procedure. This involves electronic selection of different segments along the gradient and electronic dilution and calibration where a multipoint curve can be constructed using a single sample injection	204
Zn	Potatoes	AA;-;L	Zn content in normal and blight contaminated potatoes was measured. Blighted potatoes were Zn depleted and the authors speculated that consumption of such potatoes could result in neural tube defects in infants, although presumably this would only be the case if there were no other sources of Zn in the diet	282
Zn	Complementary foods	TIMS;-;L	See Cu, ref. 145	145

Table 2 (*continued*)

Element	Matrix	Technique; atomisation; presentation	Sample treatment/comments	Ref.
Various (4)	Beer	AA;FF;TS	Following ultrasonification, beer was introduced into a hot nickel tube *via* a flow of air or 0.14 M HNO_3. The LODs for Cu, Mn, Pb, and Zn were 2.2, 18, 1.6, and 0.9 μg l^{-1}. Also see ref. 201	202
Various (25)	Turkish tea	AE;ICP;L	Optimum infusion for extraction of nutritional elements was determined	304
Various (45)	Milk	MS;ICP;L	Room temperature acid sonication for 10 min was used prior to quantitative or semi-quantitative analysis with Rh as internal standard	192
Various (7)	Wines	EDXRF;-;S	A simple and sensitive method was described. The liquid residue was pre-concentrated by chelating with APDC and then filtered under vacuum. A miniaturised low power X-ray tube was used (Cu, Fe, Mo, Ni, Pb, V, Zn)	221
Various (8)	Edible seaweed	AA;F;L	In an evaluation of ultrasound-assisted extraction optimum compromise conditions were 7 ml extraction volume, 3.7 M HNO_3, sonication for 35 min, ultrasound frequency 17 kHz, and water bath temperature 65 °C	183
Various (8)	Fresh water fish	AA;F;L	With Bangladesh already afflicted with As contaminated drinking water, this study showed that Bangladeshi lake water fish are, in some cases, contaminated with elevated levels of Pb	385
Various (30)	Jamaican foods	NAA;-;-, AA;F;L AA;ETA;L	A comprehensive study of 5 Jamaican food categories found higher levels than many other countries, with Cd being the principal source of concern	250
Various (18)	Foods	-;-;-	Results of the first French Total Diet Study, incorporating 1080 composite food samples, were reported	252
Various (5)	Brassicas	AE;ICP;L	Brassicas are important sources of minerals including Ca, Fe, K, Mg and Zn. In this useful study, the effect of cultivar and season were determined for the named elements. Typically a two-fold difference in accumulation among 22 cultivars was found	279
Various (6)	Tea	AE;ICP;Sl	Slurry atomisation using the Generalised Standard Additions Method, in which both the sample mass and the volume of standard solution are altered, compared favourably to more conventional approaches (Al, Ba, Ca, Mg, Mn, Zn)	386
Various (6)	Rice, Food RM	AE;ICP;Sl	Two very similar papers from the same author described slurry sampling followed by ETV for sample introduction. A PTFE emulsion was utilized as fluorinating agent to promote vaporization. In the interests of economy, the authors had apparently written identical abstracts for both journals (Cu, Cr, Fe, La, V, Zn)	387, 388
Various (16)	Honey	TXRF;-;L	A Slovenian study of 8 honey varieties (lime, acacia, *etc.*) found statistically significant differences between them	222
Various (15)	Honey	AE;ICP;L AE;F;L	73 samples from 7 botanical varieties were classified with >90% accuracy using chemometrics	331
Various	Cheeses	AE;ICP;L	A further example of combining analytical data with chemometric methods for the geographical characterization of food products, in this case buffalo milk mozzarella cheeses originating from two areas of Southern Italy	335
Various (5)	Durum wheat and derived products, wheat CRMs, drinking water	MS;ICP;L AE;ICP;L	An interesting pair of papers firstly described method development, and secondly, application of the method to investigate the transfer of contaminants through the food chain and the effects of processing. Milling, purity of ingredient water, deposition from plant air and metal release from equipment were critical issues in contamination (Cd, Cr, Fe, Ni, Pb)	270, 389
Various (10)	Wheat	MS;ICP;ID	Exact-matching double ID–ICP-MS was used for the high accuracy analysis of a candidate sample for a proficiency testing scheme (Cd, Cu, Cr, Hg, Mo, Ni, Pb, Se, Sn, Zn)	217
Various (4)	Chicken, animal feed	MS;ICP;L AE;ICP;L	Mineralisation procedures for Cu, Fe, Se and Zn were compared with respect to precision, recovery and sensitivity. Although a closed vessel microwave system gave good recoveries in the chicken, with the feed it was necessary to include HF to prevent losses of Zn due to residual siliceous material	187

milk[192] and wine.[186] An ultrasonic probe was also used to extract Sn in a study of various RMs[193] and to assist in an acid leaching process for the determination of major and trace elements leading to an RSD <5%.[183] Ultrasound has been used to enhance enzymic digestion of various chicken tissues to enable Se speciation.[194] Bermejo *et al.*[11] reviewed this powerful combination of sample digestion techniques.

5.1.3 Preconcentration. A method for determining methylmercury using *headspace preconcentration* of the hydride

vapour in a single drop containing Pd^{II} or Pt^{IV} was developed by Gil *et al.*,[195] giving a 40-fold preconcentration factor. The hydrogen evolved in the headspace generated Pd^0 or Pt^0, thus sequestering the methylmercury. Validation against two fish CRMs gave LODs of 5 ng ml^{-1} and 4 ng ml^{-1} using Pd^{II} and Pt^{IV}, respectively.

An *on-line preconcentration* procedure, prior to Cd analysis by ultrasonic nebulisation ICP-AES, employed a conical mini-column packed with polyurethane foam in which Cd^{II} was precipitated with 2-(5-bromo-2-pyridylazo)-5-diethylamino-phenol.[196] Using 20% HNO_3 as eluant, a 20-fold preconcentration factor was achieved in the determination of Cd in teas. Similarly, total As was determined using *in situ* reduction of As^V with L-cysteine on a mini-column loaded with alumina prior to HG-AAS, achieving a 7-fold preconcentration factor.[197] Off-line preconcentration and separation of Hg^{II} in tap water from co-existing metal ions using Duolite GT-73 resin in HCl media was demonstrated.[198] The oxalate-form of Dowex-1 resin was found to selectively adsorb Cr^{VI} in the presence of Cr^{III} in potable water, allowing a 25-fold preconcentration.[199] Using a liquid–liquid extraction with dithizone followed by IBMK, Amorim and Ferreira[200] were able to determine Cd and Pb in table salt, attaining a concentration factor of 80 and LODs of 0.3 ng g^{-1} and 4.2 ng g^{-1}, respectively. This work allowed the levels of these elements to be estimated in table salt consumed in Salvador City, Brazil.

5.1.4 Speciation. *The split between technique development and applications this year is more balanced than in previous years*. Half of the applications concern the measurement of As species and these, with the applications concerning other elements, are described in the appropriate sections below. Chromatography coupled to ICP-MS is the technique of choice for over half of all studies specifically for speciation, although AFS and AAS with CV or GC techniques continue to be used. Whilst HPLC is widely used as the separation technique, a number of other chromatographies have been used, including IC, CE and SEC-HPLC.

5.2 Atomic absorption spectrometry

5.2.1 Flame AAS. It appears that Brazil is the main centre for new developments in FAAS. The 'flame-furnace' work has been described in our last two or three Updates and the group working on this technique applied the system to the direct analysis of fruit juices, milk and beer[201,202] and medicinal plants after microwave digestion.[203] Using FI to mix samples with diluent and introduce them into the hot nickel tube, analysis rates of 40 h^{-1} were achieved and LODs were in the low μg l^{-1} range for Cd, Cu, Fe, Mn and Zn. An *unusual solid sampling device* was developed by da Costa *et al.*[53] Liver samples were dried, powdered and then placed into small paper capsules, which were inserted into a flame-heated quartz cell for measurement of Cd. There were low background signals and the precision was $<8\%$ RSD. Using a 7 mg sample, the LOD was 0.23 μg g^{-1} and the authors claim that as little as 0.5 mg can be analysed. As with many solid sampling procedures the drying, milling and weighing steps increase the overall analysis time, complexity and vulnerability to contamination.

Most other work involving FAAS (much of it carried out at the Analytical Chemistry Department, University of Santiago De Compostela, in Spain) is focused on developing *sophisticated FI systems* to carry out preparative work such as extraction, preconcentration, calibration, for sequential (multi-element) analyses.[184,185,200,204–207]

5.2.2 ETAAS. ETAAS is a mature technique and has been available to the analytical scientist for more than 30 years. Despite this, interesting developments continue to be reported in the literature. The advent of SIMAAC instruments has seen a number of methods, developed by one research group in particular, which allow *the use of internal standards in ETAAS*. Oliveira *et al.*[208] spiked samples and standards with 500 μg l^{-1} As for the determination of Se in a range of foods including fruit juices and milks. The use of the internal standard improved RSDs from 6 to 3% in comparison with conventional analysis. The same authors used a similar approach[209] to determine Se in milk, evaluating both As and Ge as the internal standard. The latter offered improved sensitivity and RSD and both gave recovery values in the 99–105% range compared with the 70–80% range without internal standardisation. Finally, they determined Ni in soft drinks using a transversely-heated atomiser and 50 μg l^{-1} Co as internal standard. Again, significant improvements in RSD were recorded and the authors claimed the results obtained with the internal standard were better than those without.

A *new method for the determination of Hg was described*,[69] *which utilised a two-step atomisation* process. Sample was placed in the vaporiser of the atomizer, dried, and vaporised. The vapour was then transferred to a second unheated atomizer cell *via* an Ar flow and trapped on the inner surface. This step could be repeated to preconcentrate the Hg. The cell was then heated and the Hg measured using AA. For a 100 μl sample of drinking water the LOD was 0.024 μg l^{-1}.

Numerous *papers on permanent modification continue to appear*. Kumar *et al.*[193] used a zirconium–iridium transversely heated furnace as part of an interesting method that involved ultrasonic extraction to quantify Sn in RMs. The LOD was 0.03 μg g^{-1} and precision 2–4% RSD. In the procedure for the determination of Se using an As internal standard,[208] described earlier in this section, the authors also utilised either tungsten–rhodium carbide or a tungsten coating with co-injection of $Pd(NO_3)_2$ as permanent modifiers. Pyrolysis and atomisation temperatures of the optimised system were 1300 and 2100 °C, respectively. In a systematic study[44] of the solid sample determination of Cu and Zn in bovine liver, tungsten–rhodium permanent modification was found to be essential for the Zn measurement. The absolute detection limits were 1.6 and 1.3 ng, respectively. An extension of tube coatings for chemical modification is to use the coatings as a trapping medium, as discussed in the following section.

5.3 Vapour generation procedures

Interesting work has been carried out where *analytes were vaporised, trapped onto the surface of a graphite furnace* and then atomised by heating for measurement by AAS. Arbab-Zavar *et al.*[210] constructed an electrolytic cell with a lead–tin alloy as the cathode and produced the hydride of Cd from tap

water. When the parameters were optimised the LOD was 0.2 ng ml^{-1}. Similarly, they also generated Hg vapour[211] and found that of the trapping agents investigated, Ir coated graphite was the most effective and provided an LOD of 1 ng ml^{-1} and an RSD of 3%. Methods for the removal of a wide range of potential interferents were also considered in the study. To separate, preconcentrate and measure methylmercury in fish RMs, Gil *et al.*[195] investigated the formation of the organometal hydride in the headspace of a closed vial. The hydride was then trapped onto a 3 µl drop of a solution of either Pd or Pt, effecting a 40-fold preconcentration, and determined by ETAAS with an LOD of 5 ng ml^{-1}.

To determine Hg in Chinese medicines, Yang *et al.*[173] used AFS. They looked at conditions which influence the oxidation of Hg^{2+} and the fluorescence, and opted to use thiourea with citric acid as a sensitizing agent. Interferences from other ions were also investigated and eliminated. The *cold vapour generation* of Cd was exploited by Korkmaz *et al.*[212] to determine this metal in food RMs by AFS. These workers found that the vapour could be trapped on the inlet arm of the quartz T-tube if this was maintained at 350 °C. Further heating to 1000 °C and a flow of gas released the Cd into the analytical part of the fluorimeter. The length of the reaction coil, and concentrations of HCl and $NaBH_4$, were important to obtain the best results and, when optimised, the LOD was 1.8 pg ml^{-1}.

Interferences in the generation of hydride vapour from As species in a Chinese herb were investigated by Deng *et al.*[172] Addition of 8-hydroxyquinoline eliminated the interference caused by Pb and Cu and also suppressed any signal from As^{V}, thereby allowing the measurement of As^{III}. Bismuth and Te were measured by HGAFS in milk shakes and milk, respectively.[213,214] Samples were sonicated for 10 min with *aqua regia* and then assayed using an FI system for addition of HCl diluent and $NaBH_4$. The FI manifold was arranged so that reagents were pumped and mixed only as and when required. With this 'multicommutated flow' arrangement, the consumption of reagents was four-fold less compared with a conventional continuous flow system and the volume of waste products was halved. In addition, the analysis rate was more than doubled.

5.4 Inductively coupled plasma-mass spectrometry

This technique has now matured to an extent that most papers focused on the application rather than instrumental development. While HPLC is the standard chromatography interface, CE[215] and IC[216] were also used.

Although *isotope dilution* ICP-MS is used for accurate determinations in CRM metrology[217] and measurement uncertainty,[27] it also found application in the determination of Hg in tuna fish tissue.[218]

5.5 Other techniques

The majority of other techniques published during this review period use *X-ray fluorescence*. For a review of these techniques see Potts *et al.*[2] Energy-dispersive XRF methodology was the most widely used technique and found application for Ca determination in human milk,[219] Br in vegetables[220] and multielement determination in a variety of matrices.[221–226] In an interesting paper in Japanese, Ishii *et al.*[227] showed that a dry-battery XRF had sufficient capability for the analysis of crops, notwithstanding the low power of the X-ray output. *Particle-induced X-ray emission* and Rutherford backscattering was also used to assess a multielement determination in tomato purées.[228]

5.6 Progress on individual elements

5.6.1 Arsenic. Yeh and Jiang[215] described the use of a 70 cm × 75 µm fused-silica capillary to separate six *arsenic species* in fish RMs using 15 mM tris buffer containing 15 mM SDS with a voltage of 22 kV. An LOD of 0.3–0.5 ng ml^{-1} was achieved. Ion chromatography ICP-MS and ES-MS-MS allowed Fricke *et al.*[229] to identify a new arsine sulfide-containing analogue of a known arsenosugar, referred to as As(498). Thirteen As species were determined in marine biological samples using cation- and anion-exchange HPLC, but in order to separate arsenous acid, an additional hydride-generation step was required.[230] A method to assay the arsenic species As^{III}, As^{V}, DMA and MMA in soft drinks, beers and juice was developed by Coelho *et al.*,[231] giving LODs of 0.2, 0.2, 0.3, 0.5 ng ml^{-1}, respectively. They used an anion exchange column with a 5 mM K_2HPO_4–KH_2PO_4 mobile phase at pH 8.5 to achieve separation before detection with ICP-MS. Paproski and Le[232] introduced 30 mM boric acid into the ammonium phosphate mobile phase in anion exchange HPLC to selectively modify the retention of arsenosugars, thus allowing 11 As species to be assayed in different matrices. In order to assay the total As in marine organisms, a method for the complete decomposition of MMA, DMA, AC, AB, TMAO, and tetramethylarsonium iodide was investigated by Narukawa *et al.*[233]. This was achieved using HNO_3–$HClO_4$–H_2SO_4, heated to a set-point of 320 °C, the most extreme condition being needed to fully decompose AC. The cloud point extraction approach, using Triton X-114 as non-ionic surfactant, was used to determine As^{III} and As^{V} at LODs of 0.01 µg l^{-1} for a 10 ml sample.[42]

5.6.2 Lead. Very little work appears to have been focused on developments for lead. *Exact-matching ID* was used as part of a high accuracy method for determining Pb in wine and achieved an expanded uncertainty of <2% at the 95% confidence level.[234] A trimethyllead spike was synthesized from ^{206}Pb enriched metallic Pb and used for the determination of trimethyllead by GC-ICP-ID-MS, achieving an LOD of 0.09 ng g^{-1}.[235]

5.6.3 Mercury. Several methods have been developed for *total Hg and Hg species*, mostly to improve throughput or accuracy.[218,236–238] Methyl- and inorganic mercury were sequentially speciated by selective retention of inorganic Hg as its complex with APDC on a PTFE packed column.[51]

In a *direct ETAA* method for the determination of Hg in water and urine, the sample was placed in the vaporizer of a two-step atomizer, dried and vaporized. The vapour was carried in an Ar stream to an unheated vaporizer and trapped on the walls. The Hg was then atomized, yielding LODs of 0.24 µg l^{-1} for a 100 µl sample and a single transfer.[69] A comparison of the suitability of Ir, W or Zr for coating and

trapping Hg vapour in a graphite cuvette found Ir most suitable. The LOD was 1 ng ml^{-1}.[211]

Seven *slurry procedures* for the simultaneous determination of Hg and Se were evaluated. Low recoveries of Se with five of the approaches indicated the need for strong oxidizing agents such as H_2O_2 or $K_2S_2O_8$ in the reaction medium.[46] In a further application of SPME for the determination of methylmercury in fish products, samples were digested using KOH–NaOH, derivatized using phenylation and the resulting derivatives SPME trapped and introduced to a pyrolysis GC-AF system.[180] Krystek and Ritsema[238] speciated mercury and methylmercury in shark fillets by GC-ICP-MS. Samples were dissolved in TMAH, derivatized with sodium tetraethylborate, extracted into isooctane and introduced into the GC. The signal was stabilized by adding Xe to the GC carrier gas. The same procedure was applied by the authors to investigate the influence of freeze-thaw on analytical results[176] (see Section 4.1).

Isotope dilution was used for an *SI-traceability study* for the methylmercury content of tuna.[19] Further comprehensive details of an inter-laboratory comparison project using this material were also reported.[19,21] A full uncertainty budget was used to compare the performance of species specific single and 'approximate matching' double ID-MS in the determination of methylmercury by MC-ICP-MS in fish CRMs.[27]

5.6.4 Selenium. In a comparison of different *extraction procedures* prior to Se determination in nut proteins, Kannamkumarath *et al.*[239] identified the best solubilisation of proteins to be achieved using 0.05 M NaOH and 1% SDS in Tris–HCl buffer (0.05 M, pH 8). A new procedure, described as enzymic probe sonication, was claimed to offer advantages in terms of speed, simplicity and safety over traditional methods. Se species were extracted unchanged.[194]

The ongoing challenge to *identify and measure selenium species* in yeast and yeast-based dietary supplements shows no sign of abating. Landaluze *et al.*[179] used SPME to concentrate and separate samples from the matrix in the determination of volatile species during the production and subsequent *in vitro* gastric digestion of commercial supplements. The species were separated by multicapillary GC and detected by MIP-AES. Dumont *et al.*[240] set out to identify and characterise the major Se species in yeast. Six Se species were separated using a C_{18} column and a mobile phase containing the ion pairing agent tetraethylammonium chloride. Detection was by ES-MS-MS. Goenaga Infante *et al.*[241] employed 'accelerated solvent extraction' where Se in yeast was extracted with a solution containing 0.1 mM phenylmethane sulfonyl fluoride and 0.01% dithiothreitol, with five repeat cycles at 100 °C and 1500 psi. Several Se-containing species were detected by HPLC-ICP-MS. The procedure was compared with hydrolysis using a mixture of protease and lipase at 37 °C for 16 h and similar results were obtained. These workers also showed that by using ultrasonic nebulisation, formation of H- and O-based polyatomic interferences was reduced and that detection limits were improved by up to 600%.[241] Proteolytic digestion was also used by Polatajko *et al.*[242] Various species were identified in the samples. Selenomethionine is the major compound but Se-methylselenocysteine,[241] dimethylselenide and diethylselenide[179] were also reported.

In an extension of their work, Yang *et al.*[243] compared *14 common extraction methods* used in the determination of methionine (Met) and SeMet. Interestingly, a number of often quoted enzyme procedures gave very low recoveries. A 4 M methanesulfonic acid reflux digestion was found to be the most efficient for both analyses. In a second paper,[216] this extraction was used for the determination of SeMet in yeast in which the extracted SeMet was derivatized with CNBr and extracted into $CHCl_3$. Subsequent determination was by GC-ICP-MS using species specific ID with ^{74}Se enriched SeMet. The LOD was 0.9 μg g^{-1}. In a third paper,[244] Met and SeMet were determined by ID-LC-MS or LC-ICP-MS for characterisation of an RM. SeMet comprised 79% of the extracted Se.

Looking for a procedure suitable for certifying a candidate yeast RM for the SeMet concentration, Sturgeon and his colleagues *evaluated 14 published extraction methods* and obtained very different outcomes. The protocol included ID using ^{74}Se-enriched SeMet to compensate for losses during the analyses. Refluxing with 4 M methanesulfonic acid or prolonged enzymic hydrolysis using protease XIV at 37 °C were the most efficient procedures.[243] Extraction with HCl and TMAH were not effective, nor were several other enzyme preparations. Measurement of the extracted SeMet was undertaken by GC-MS following derivatization using methyl chloroformate. In a second publication,[216] workers from this group determined SeMet using GC-ICP-MS following methanesulfonic acid reflux, CNBr derivatization and extraction into $CHCl_3$. Results were compared with the CG-MS measurements and were very similar when measuring $^{78}Se:^{74}Se$ or $^{82}Se:^{74}Se$ ratios (GC-ICP-MS) or $SeCN^+$ fragments with m/z ratio of 106 : 100 (GC-MS). As a consequence of including the ^{74}Se-enriched SeMet the precision was less than 0.6% RSD and the LOD was 0.9 μg g^{-1}. Finally, this team developed an LC-ICP-MS method to measure SeMet and achieved equivalent results with either ID or standard additions calibration.[244] Using the different methods described in these papers the proportion of the total Se present as SeMet varied from 63.9 to 67%.

An online UV photolysis and UV-TiO_2 photocatalysis reduction device, together with an *electrochemical vapour generation cell* has been proposed by Liang *et al.*[245] as an interface to couple HPLC to AFS. Detection limits for Se species were in the range 2–10 ng ml^{-1}. An FI-HG-ETAAS method using *in situ* trapping onto Ir-coated platforms was applied to the determination of Se in doped and undoped cereals and bakery products.[246] In a method for the determination of Se in milk by ETAAS after microwave digestion with HNO_3–H_2O_2, the preferred modifier was a Zr–Ir mixture which yielded an LOD of 1.37 μg l^{-1}.[62] A tungsten–rhodium carbide coating on the integrated platform of a transversely heated furnace or a tungsten coating with co-injection of $Pd(NO_3)_2$ were used as permanent modifiers for the determination of Se in a range of foods and beverages.[208] To minimise matrix interferences in the determination of Se in milk by ETAAS, As and Ge were added as internal standards *via* the autosampler and yielded a notable improvement in precision.[209]

Capillary-sized (0.5 and 0.8 mm id) gel filtration columns have been used by Ogra and Suzuki[247] for the separation of

naturally-occurring selenocompounds in *selenised garlic*. These were separated, following a direct 100 nl injection, with satisfactory sensitivity and better S/N ratio than conventional HPLC. In a study of Se species in Se-enriched shiitake mushrooms and vegetables,[248] extraction using 0.2 M HCl only released 20% Se. A protease digestion released large quantities of SeMet from mushrooms cultivated on selenite-enriched beds but not from those from selenate-enriched beds for which a cell wall digestive enzyme worked better. The results indicated that the main Se species in the shiitake enriched with selenite or selenate was SeMet bound to protein or selenate bound to polysaccharides in the cell wall, respectively.

5.6.5 Other elements. A flow injection micro-column technique using 8-hydroxyquinoline-loaded silanised silica gel, with HNO_3 as eluant, allowed Chen *et al.*[249] to achieve *separation of Al species* in tea infusions, coffee and tap water. An LOD of 0.2 ng ml^{-1}, an RSD of 4.2% and a recovery of 95–108% were attained. An interesting approach to a slightly unusual application described the analysis of Bi in milk shakes. Samples were treated for 10 min on-line using sonication in 8% v/v *aqua regia*. The LOD was 1.67 ng g^{-1} and good agreement with a microwave-assisted digestion method was reported.[213]

5.7 Single and multielement applications in food and beverages

5.7.1 Dietary intake studies. The majority of studies on the *dietary intake of metals* are country specific and show no predominance for any particular element.[250–253] The Mo content in food consumed in Japan was assessed by ICP-MS.[254] The overall Mo intake of the Japanese population is estimated as 225 μg d^{-1} with the principal dietary source being rice followed by soy bean products. The authors showed that while the Mo content of most animal foods was less than 0.1 μg g^{-1}, that of cereals was greater than 0.5 μg g^{-1}. With little data being available for the Cu content of Brazilian food, Ferreira *et al.*[255] undertook analysis of a range of samples purchased from retail stores in south east Brazil using FAAS. The highest content of 60.6 μg g^{-1} fresh weight was found in beef liver with the lowest of 0.1 μg g^{-1} fresh weight in milk and fish fillets. Hoskin *et al.*[256] surveyed the Co content of Australian food by ICP-MS and concluded the data were comparable to those of other countries. The Se content of numerous foods purchased on the Slovenian market was determined by Smrkolj *et al.*[257] Selenium in high protein foods ranged from 33 to 689 ng g^{-1}, while vegetables and fruit ranged from 0.3 to 77 ng g^{-1}. Additionally, the daily mean intake of Se by the Slovenian military was estimated as 87 μg. The exposure of the population of eastern Poland to three heavy metals was measured through a duplicate diet approach by Marzec and Schlegel-Zawadzka[258] using FAAS and CVAAS. Cadmium and Pb exposure did not exceed 58% of the provisional tolerable weekly intake (PTWI) while Hg was even lower at a maximum of 16%.

The I content of the Swiss diet was studied by Haldimann *et al.*[259] using ID-ICP-MS with enriched ^{129}I. Bread and milk were identified as significant sources of iodine, contributing 58 and 29 μg d^{-1}, respectively. The estimated consumption of 140 μg d^{-1} was recognised as being below the acceptable level for adequate nutrition of 150 μg d^{-1}. The contribution to the intake from the consumption of iodinized salt did not appear to have been adequately considered. The relevance of chlorophyll-bound magnesium was explored by Bohn *et al.*[260] by determining the amounts of chlorophyll by HPLC and Mg by AA. The median concentrations of Mg were 122 μg g^{-1} and ranged from 48 μg g^{-1} in grapes to 849 μg g^{-1} in spinach. The authors estimate that, given that less than 1% of the total Mg was chlorophyll-bound, it is of little significance to magnesium nutrition. The lead content of the diet of the population of the Canary Islands was assessed using ETAAS and was found to be <70 μg d^{-1}.[261]

5.7.2 Human milk and infant formula. In a study to assess the Mo content of the Japanese diet,[254] human milk was shown to have a median content of 4.5 ng ml^{-1} (range 2.0–8.8 ng ml^{-1}) while formula milk was typically 2–3 ng ml^{-1} leading to the Japanese infant Mo intake being estimated at 2–4 μg d^{-1}. The *day-to-day variation in Cu, Fe and Zn in the breast milk* of Guatemalan mothers was assessed, using ICP-AES, in order to define a sample-taking regime. The daily variation was low enough to allow one milk sample to be taken for a reliable estimate of the Zn concentration but two samples taken on consecutive days were necessary for Cu and Fe.[262] Ekcini *et al.*[219] showed EDXRF to be suitable for the determination of the Ca concentration in human milk while WDXRF has been validated against a number of other techniques for the determination of six macro- and three trace elements in infant cereal matrices.[224] Iodine in human milk and cows' milk was studied by Bader *et al.*[263] using ICP-MS. The I level in the human milk ranged from 33 to 348 μg l^{-1} (mean 169 μg l^{-1}) regardless of whether the mothers took supplements. The cows' milk had a mean concentration of 178 μg l^{-1}. Cadmium, Hg and Pb concentrations have been assessed in human milk in Slovakia by ETAAS and CVAAS, and whereas the PTWI were not exceeded, the study showed that of the factors studied, only the mother's active/passive smoking at home significantly increased Pb levels in breast milk and amalgam teeth fillings appeared to increase Hg levels.[264]

The bioavailability of Fe in *infant formula* was assessed by Dominguez *et al.*[150] by subjecting doped formula to a short incubation with pepsin and pancreatin and measuring Fe by ICP-AES. Of the five Fe salts used to fortify the formula (sulfate, lactate, diphosphate, encapsulated sulfate and Fe^{III}–EDTA), the latter appears to be the most adequate. An article in Japanese[265] described a simple method for the determination of Rb content in infant formula by FAAS. There was a significant difference in the Rb content between follow-up formula (10.7 ± 2.9 μg g^{-1}) and young infant formula (5.3 ± 1.7 μg g^{-1}).

5.7.3 Milk and dairy products. Four trace elements (Cu, Cd, Ni and Zn) were determined using FAAS in *milk collected from cows, goats and ewes*.[266] The same technique was used to survey the heavy metal content in Turkish white cheese.[267] The results of both studies agree with previous work but indicated that the Ni concentration in ewe's milk in the former study was the highest reported in the literature. The effect of sub-clinical

mastitis on mineral levels in cows' milk was investigated by Yildiz and Kaygusuzlu.[268] Calcium levels in the milk serum from affected cows were significantly lower than from healthy cows while levels of Fe and Zn were elevated.

Forty-five elements were determined in *liquid and powdered milks* by ICP-MS, following sonication with acid for 10 min.[192] A procedure for determining Se in cows' milk was developed by Muniz-Naveiro *et al.*[269] using HGAAS after microwave-assisted acid digestion, for which LODs were typically 0.075 μg l^{-1}. The total content of Se varied from 8.5 to 21 μg l^{-1} with the highest concentration being found in the whey. The total Te content in commercially available milk ranged from 1 to 10 ng ml^{-1} when determined using HGAFS.[214] This technique was also used by Ventura-Gayete *et al.*[213] to allow a highly sensitive method of determining Bi in milk shakes following an off-line sonication with *aqua-regia*. Samples from the Spanish market yielded a range of concentrations from 4.2 to 15.0 ng ml^{-1}.

5.7.4 Cereals, flour and rice. The heavy metal content, especially Cd and Pb, in *cereal products*[270,271] and rice[20,272] continues to hold the interest of some researchers. To investigate the content of methylmercury and ethylmercury in rice across 15 Chinese provinces, Shi *et al.*[273] developed a GC-AFS technique. In these samples only methylmercury was detected with a range of 1.9–10.5 ng g^{-1}, accounting for 7–44% of the total Hg measured. Methods continue to be developed for determining total Se and Se species in this class of food[246,274,275] (see 5.6.4). The Se content of cereals grown on soils treated with Se-doped fertilizer ranged from 128 to 1045 ng g^{-1} (wet weight).[246] The range of Se content from bakery products made from cereal grown on un-doped soils was 7.7–68.0 ng g^{-1}, whereas that of the corresponding cereal crops did not exceed 100 ng g^{-1} (wet weight).

Mateos *et al.*[276] used ETAAS following an acid digestion (using HNO_3, H_2SO_4 and $HClO_4$) to determine the Cr content in a wide variety of *breakfast cereals*. The results ranged from 0.12 ± 0.01 μg g^{-1} for bran cereals to 0.35 μg g^{-1} for wheat, oat, rice and corn cereals. The binding effect of phytic acid, commonly present in cereal foods (4 mg g^{-1}), to elements such as Cu and Zn was evaluated by Egli *et al.*[145] using a dephytinized foodstuff (<0.03 mg g^{-1}) and labelled ^{65}Cu and ^{70}Zn. The apparent fractional Zn absorption was significantly higher from dephytinized cereals—although the Cu absorption did not appear to change—and highlighted the need to remove phytic acid when preparing complementary cereal-based foods. The bioavailability of Ca was similarly determined in low-phytate maize by the use of labelled Ca with ^{44}Ca administered in water during meal and ^{42}Ca administered *i.v.* after the meal. The mean fractional absorption was significantly greater in low-phytate maize.[277]

5.7.5 Vegetables, fruits and nuts. The impact of growing *leafy green vegetables in the proximity of highways* in Nigeria on their Cd, Hg and Pb levels was assessed by Bakare *et al.*[278] using AAS. The Pb content of nearly 17 μg g^{-1} in samples grown close to the highway was double that of samples from distant farms, and Pb in the soil and irrigation water was equally higher. Kospell *et al.*[279] studied the variability of some mineral elements in different cultivars of *Brassica oleracea* using ICP-AES. On average, a two-fold difference was found and this was thought useful for selecting appropriate cultivars for delivering higher nutritional benefits. Using EDXRF, Tirasoglu *et al.*[280] also determined trace element levels in *Brassica*, a widely grown crop throughout the year in Turkey.

Al Rmalli *et al.*[281] highlighted the possibility of foodstuffs imported into the UK from Bangladesh having higher levels of As. Using ETAAS, the authors show that the average As content of studied foods was 54.5 μg kg^{-1} (range 5–540 μg kg^{-1}) and that *vegetables grown in Bangladesh* have As concentrations two- to three-fold higher than those grown in the UK which, although below recommended limits, could be an additional source of As to certain population groups in the UK. Ulman *et al.*[282] proposed that potatoes affected by blight were deficient in Zn and, when eaten by pregnant mothers, their consumption could pose a threat to the foetus. However, the figures quoted in this paper do not substantiate this.

Radish plants were used by Tlustos *et al.*[283] as *an indicator of As uptake from three different soil types doped with DMA*. Soil properties were shown to significantly affect the transformation of As species. Mendil[284,285] used microwave digestion and AAS to determine trace metals including Cd and Pb in mushrooms collected in Turkey, while Vetter[286] used CVAAS to assess the Hg content of the mushroom *Agaricus biporus*, which showed it to be an order of magnitude lower than the reported values for wild mushrooms.

Ali-Mohamed and Khamis[287] studied the mineral content of Bahraini date palm seeds and other imported grains. They found the Pb content to be higher than Cd. PIXE has also been used to analyse a range of Mexican tomato purées for comparison against brands from other countries; these were found to fall within accepted limits.[228] Lui *et al.*[288] have determined the trace element content of soy bean by AAS. High Br levels (1000–16200 ppm) in vegetables available in an Osaka market were determined by XRF and ascribed to *fumigation with methyl bromide*.[220] The mineral content of Brazilian coconut water was assayed using ICP-AES without prior mineralization.[289]

The *Se distribution and speciation in proteins of Brazil nut* (*Bertholletia excelsa*) was studied by Kannamkumarath *et al.*[239] A Superdex 200 SEC column linked to ICP-MS following solubilisation of samples by 0.05 M NaOH and 1% SDS allowed the authors to establish that Se was associated with two of three distinct M_r fractions at 107 and 50 kDa. By using CE-ICP-MS, which was demonstrated to allow the separation of Se^{IV}, Se^{VI}, selenocystine and SeMet, the Se was found to be present mainly in the latter form. Other trace metals were considered in another paper.[290]

5.7.6 Meat products. A fast on-line method using ultrasound-assisted FI-FAAS has been developed by Yebra-Biurrun *et al.*[185] for the determination of *Zn in meat products*, with a LOD of 0.6 μg g^{-1}. The same authors extended the technique to Cd by incorporating an on-line concentration column using Chelate P with aminomethylphosphoric acid groups to achieve an enrichment factor of 20.5.[206]

By studying the correlations between the Cd contents of various pig organs, hair and faeces from abattoirs across

Hungary, Gyori *et al.*[291] concluded that good on-farm indicators for contamination in porcine products were faeces for Cd and blood for Pb. All Cd and Pb levels, measured by AAS, were below legal limits. De Oliveira *et al.*[292] demonstrated that chromium oxide, measured by XRF, was a good *marker for digestibility* of high grain beef fed on varying nitrogen-source diets.

5.7.7 Fish and seafood. *Arsenic species* were studied in a range of marine species collected from the Aegean Sea. In all samples, AB was the predominant species (concentration from 2.7 to 23.1 μg g^{-1}) while arsenosugars were detected only in mussels (*Mytulis galloprovincialis*).[293] Tinned fish (five varieties) marketed in the southern USA were assayed for 13 elements by ICP-AES. Several instances of metal content exceeding guidelines were noted.[294] Heavy metals were determined in sediments and shellfish from Trinidad and Venezuela,and correlations were established,indicating that mussels were a better biological indicator of heavy metal contamination in sediments than oysters, while oysters provided indicators of Cu and Zn contamination.[295]

In an article in Japanese, Tamaru *et al.*[296] measured a range of elements in scallop tissue, using ICP-MS and ICP-AES methods developed on oyster tissue CRM. In particular, by using shale and sea-water, they estimated the *accumulation factor of Cd* to be the highest amongst the 30 elements. Using ICP-MS, Pourang *et al.*[297] studied the accumulation of 20 trace elements in five sturgeon species cultivated in the Caspian Sea. As well as noting that heavy metals were below international guidelines for human consumption, certain growth factors were correlated with the elemental composition: Cd with weight and Ga and Ba with length.

5.7.8 Drinking water and non-alcoholic beverages. The problem of arsenic-contaminated *drinking water* is much studied around the world.[298,299] However, a report by Rahman *et al.* in a WHO bulletin this year[300] highlighted that 91% of wells tested in one arsenic-affected village in West Bengal had an As concentration >10 μg l^{-1} (WHO and EPA Level) and 63% are >50 μg l^{-1} despite arsenic-filtering devices being fitted. The mean daily As intake of adults in the Yaqui Valley, Mexico, has been assessed at 65.5 μg d^{-1} by Meza *et al.*[130] using HPLC-ICP-MS. The major compound excreted in urine was DMA followed by inorganic As and MMA.

Ishazaki *et al.*[301] reported on uncommon clinical central nervous system symptoms they attributed to As compounds derived from *chemical weapons*. They demonstrated the presence in drinking water of bis(diphenylarsine) oxide, diphenylarsinic acid and diphenylarsonic acid, compounds that can be derived from diphenylchloroarsine and diphenylcyanoarsine, both chemical warfare agents. The concentrations reported are exceptional and leave the reader wanting to know more.

The presence of *uranium (U) has been investigated in drinking water in Moravia* by Halata *et al.*,[302] where a median value of 1.09 ± 10.36 μg l^{-1} was determined by ICP-MS. Karpas *et al.*[303] studied the absorption of U in hair, urine and toenails from drinking water and found a strong correlation. Bacciottini *et al.*[139] compared the bioavailability of Ca in high-calcium mineral waters with that of milk using enriched ^{44}Ca and measurements by ICP-MS. Both milk and Ca-rich mineral water were shown to have similar absorption factors. Finally, Koscielna[13] provides a review of determining bromate in drinking water (see Section 1).

The *health benefits of drinking tea* are increasingly reported. The elemental content is also receiving attention, from a general point of view of understanding the concentrations,[304–307] to a study in Chinese on the adsorption behaviours of Cd and Pb[308] on green and black tea, where the recovery of Pb^{II} was more than that of Cd^{II} when the pH was <6 and *vice versa* at pH $>$ 6. It was also reported that elution of the metal ions was difficult using water at 25 °C.

5.7.9 Wine and other alcoholic drinks. As a widely consumed beverage around the world, *it is essential that wine is assessed for the presence of metals toxic to the consumer or which affect the stability of the product*. Capelo *et al.*[186] have developed a fast sample preparation method (only 60 s) for determining Pb in must by ETAAS using focused ultrasound with HNO_3–H_2O_2, avoiding a microwave digestion. Myors *et al.*[234] employed ID-ICP-MS to ensure that high-accuracy methodology was available and Tasev *et al.*[309] described a method using HGAAS to determine inorganic and total As. Conventional and fast thermal programs in ETAAS were compared by Catarino *et al.*[310] for determining Cu in wines. This conventional technique, involving Pd and Mg matrix modifiers, gave the better sensitivity, while the fast technique required only dilution by a factor of 5 and avoided possible contamination. De Lima *et al.*[311] determined Pb and Cd in the vineyard soil as well as the grapes and wine.

Differentiation of wines by geographical origin, so effectively achieved by using trace elements over the years, relies heavily on the relationship of the soil mineral content to that of the grape, must and hence wine. Mackenzie and Christy[312] clearly demonstrated that soil cation chemistry does have an influence on wine grape composition. Several elements (Ba, Ca, Pb, Sr) could be correlated with sugar concentration and titratable acidity which have an influence on the quality of the wine grape. The work of Tokalioglu *et al.*[313] on grapes grown in contaminated soils corroborated this and the relationship between soil and grape concentrations was particularly significant for Cd, Fe, Mn, Pb and Zn. This also resulted in these elements being suitable for bioavailability studies in contaminated soil–plant systems. The wines of several wine-growing regions have been analysed to determine their mineral fingerprints, undoubtedly to allow geographical differentiation. Work has been carried out on wines from numerous growing regions.[221,311,314–319]

Because of its illicit production, the *health-threatening attributes of moonshine* are understandable. The Pb content of 60% of the samples analysed by Holstege *et al.*[320] using ETAAS was higher that the EPA limit in water of 15 ppb, indicating that chronic drinkers are likely to suffer from Pb poisoning. Following the development of a continuous-flow method for measuring Pb by FAAS, de Pena[205] determined the Pb content of 28 Venezuelan home-made spirits based on agave, raw and white cane sugar, with results ranging from 12.6 to 370 μg l^{-1}.

5.7.10 Other foods. Honey has generally been analysed to determine mineral content[321–323] or specifically toxic status.[324] *Edible seaweeds* have not been specifically addressed in previous Updates but a handful of publications now draw attention to this source of nourishment. Total I in two edible seaweeds, Kombu (*Laminaria digita* japonica) and Wakame (*Undaria pinnatifida*) was determined by ICP-MS after acid digestion.[325] The concentrations were 4170 and 226 μg g^{-1}, respectively, indicating species-dependent enrichment. Using SEC and ion exchange chromatography of extracts, it was seen that most was present as the iodide but that Wakame also contains mono- and diiodotyrosine, probably bound to proteins. *Hizikia fsuiforme* seaweed contains high concentrations of inorganic As (approximately 100 μg g^{-1}). Laparra *et al.* assessed the bioavailability of As (as inorganic, As^{III} and As^{V})[326] and arsenosugars[327] in raw and cooked *Hizikia* seaweed with an *in vitro* gastrointestinal digestion method. Boiling increased the bioaccessibility of inorganic As from a maximum of 66.5 to 84.4% and also altered the As^{III}/As^{V} relationship. When raw, As^{III} dominates after the gastric/gastrointestinal process.

5.8 Packaging. The *migration of Al from aseptic laminated paperboard was studied* by monitoring the Al content of orange juice stored in the packaging at 23 °C for up to one year.[328] Results revealed that there were no time-dependent changes in Al concentration.

5.9 Authentication of food

With the granting of increasing numbers of *Protected Designations of Origin* (PDO) in the European Union, more methods for characterising products have been seen, many of which require several high specification analytical techniques. Apart from wine authentication (see 5.7.9), this area is still the subject of investigation around the world for other foodstuffs. A methodology for determining the country of origin of garlic by comparing trace element profiles has been devised by Smith[329] using high-resolution ICP-MS. Likewise, pistachio nuts can be differentiated by a number of trace elements and other chemical markers. Using linear discriminant analysis, 95% of samples were correctly classified into the three regions of production: Turkey, Iran and California.[330] Honey has similarly been analysed to differentiate botanical origin[222,331] and geographical origin.[332] Classification of Brazilian coffees and cane-sugar spirit (Cachaca) was less successful with coffees only being separated into roasted and instant soluble types and home-made and industrial Cachaca being discriminated.[333]

Having a high added-value, olive *oil is often the subject of adulteration*. Zeiner *et al.*[334] demonstrated that the levels of Al, Ca, Co, Cu, K, Mn and Ni differ according to region and could be used as a tool for authentication. Data from other techniques are often required to improve statistical discrimination. One such study[335] involved the use of trace elements, along with Stable Isotope Ratio Mass Spectrometry and NMR, for the differentiation of buffalo milk and Mozzarella cheese. In this instance, only the NMR and IRMS data proved to be discriminatory.

6 Appendix

Abbreviations used in this update

AA Atomic absorption
AAS Atomic absorption spectrometry
AB Arsenobetaine
AC Arsenocholine
AES Atomic emission spectrometry
AF Atomic fluorescence
AFS Atomic fluorescence spectrometry
AMS Accelerator mass spectrometry
APDC Ammonium pyrrolidine dithiocarbamate
ASU Atomic spectrometry update
ASV Anodic stripping voltametry
BCR Bureau Communité de Référence
CE Capillary electrophoresis
CL Confidence limits
CRM Certified reference material
CV Cold vapour
CVAAS Cold vapour AAS
CVAFS Cold vapour AFS
DDTP *O,O*-diethyldithiophosphate
DIHEN High efficiency direct injection nebuliser
DIN Direct injection nebuliser
DMA Dimethylarsinic acid
DRC Dynamic reaction cell
DTPA Diethylenetriaminepentaacetic acid
EDTA Ethylenediaminetetraacetic acid
EDXRF Energy dispersive XRF
ES-MS Electrospray MS
EPA Environmental Protection Agency
ETA Electrothermal atomisation
ETAAS Electrothermal atomisation AAS
ETV Electrothermal vaporisation
FAAS Flame AAS
FF Flame furnace
FI Flow injection
GC-MS Gas chromatography-MS
HG Hydride generation
HG-AAS Hydride generation AAS
HG-AFS Hydride generation AFS
HPLC High-performance liquid chromatography
HSE Health and Safety Executive
IBMK Isobutyl methyl ketone
IC Ion chromatography
ICP Inductively coupled plasma
ICP-MS Inductively coupled plasma-mass spectrometry
ID Isotope dilution
LA-ICP-MS Laser ablation-ICP-MS
LC-ICP-MS Liquid chromatography-ICP-MS
LOD Limit of detection
LOQ Limit of quantitation
MC Multiple collector
MCN Microconcentric nebuliser
MIP Microwave induced plasma
MMA Monomethylarsonic acid
M_r Relative molecular mass
MRI Magnetic resonance imaging
MS Mass spectrometry

NAA Neutron activation analysis
NIST National Institute of Standards Technology
PDC Pyrrolidine dithiocarbamate
PGE Platinum group elements
PIXE Particle-induced X-ray emission
PTFE Poly(tetrafluorethylene)
PTWI Provisional tolerable weekly intake
Q-ICP-MS Quadrupole ICP-MS
REE Rare earth elements
RM Reference material
RSD Relative standard deviation
RP Reversed phase
SDS Sodium dodecylsulfate
SEC Size exclusion chromatography
SeCys Selenocysteine
Se-Gal-N-Ac Se-methylseleno-*N*-acetylgalactosamine
Se-Gal-NH_2 Se-methyl-selenogalactosamine
SeMet Selenomethionine
SF-ICP-MS Sector field ICP-MS
SI Système International
SIMAAC Simultaneous multi-element analysis with a continuum source
SIMS Secondary ion MS
Sl Slurry
SPME Solid phase microextraction
SRM Standard reference material
SR-XRF Synchrotron radiation XRF
THFA Transversely heated filter atomiser
TIMS Thermal ionisation MS
TMAH Tetramethylammonium hydroxide
TMAO Trimethylarsine oxide
$TMSe^+$ Trimethylselonium ion
TOF Time-of-flight
TS Thermospray
TXRF Total reflection XRF
USN Ultrasonic nebuliser
UV Ultraviolet
WDXRF Wavelength dispersive XRF
WHO World Health Organisation
XANES X-ray absorption near-edge structure
XRF X-ray fluorescence

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