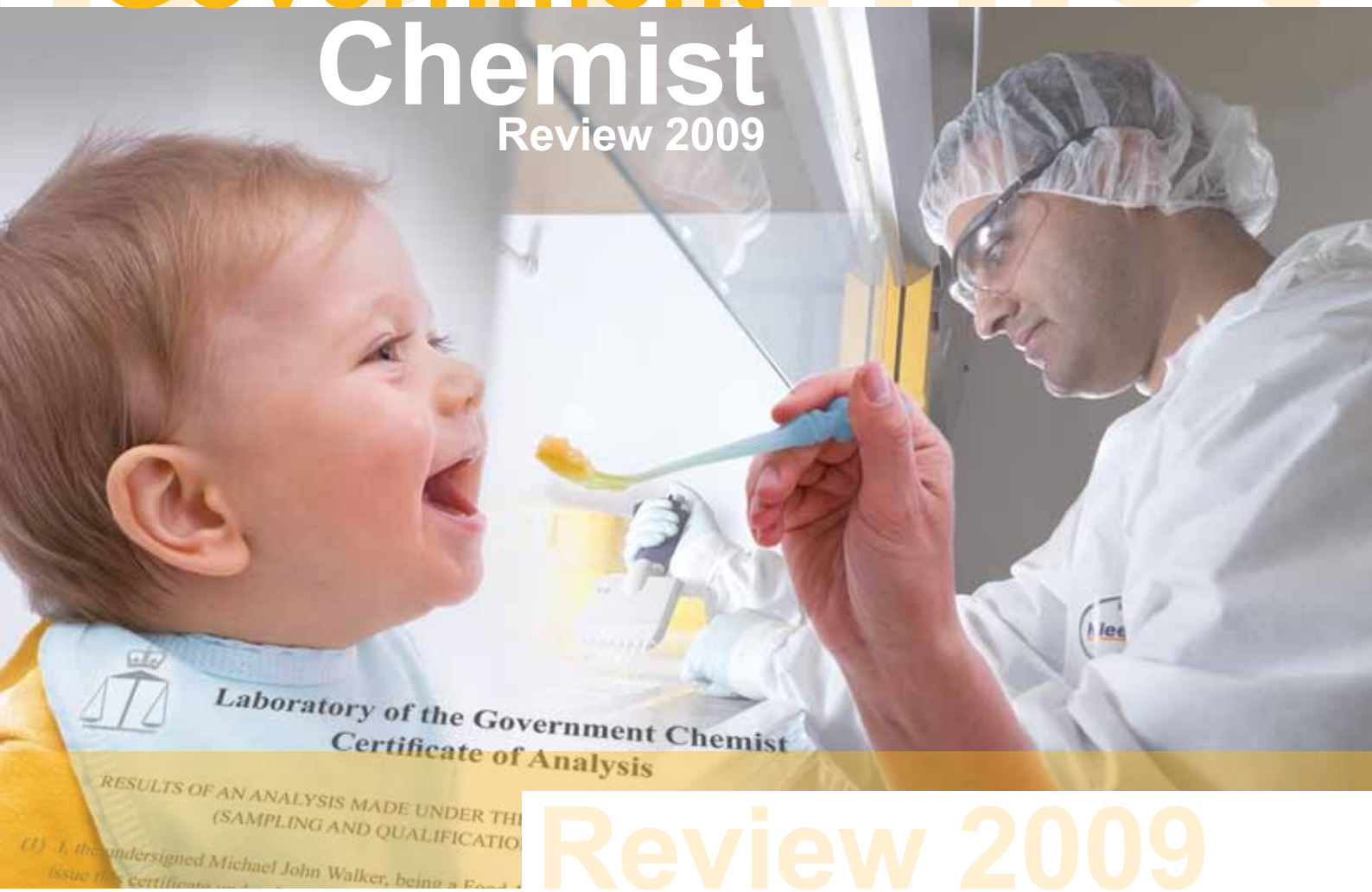
Government Chemist

Review 2009



Review 2009

Review 2009

Contents

Front cover: Rigorous laboratory procedures are required to support the control of food allergens and protect at-risk consumers
Above: Dionisis Theodosis measures water-soluble vitamins by UPLC

Government Chemist

Foreword

I am delighted to introduce the latest review of the work of the Government Chemist which covers a year of endeavour from a dedicated team of scientists delivering technical development, high quality analysis and knowledge transfer activities to support my roles and responsibilities to Government, industry and the wider community.

The resolution and also prevention of measurement disputes remains at the foundation of the role of the Government Chemist, and this review provides an overview of a diverse yet synergistic range of work that includes cases concerning chemical contaminants and allergen detection. The right of scientific appeal provides confidence in the regulatory process and protects industry through the facility to resolve conflict in an efficient and cost-effective way. For this reason other countries also retain a Government Chemist type function, and in Europe member states are required to provide mechanisms for supplementary expert opinion in respect of specific areas of food law.

I am very aware of the high priority that Government is rightly giving to the critical issue of global and UK food security, and of the desire of the public for greater choice. Sound measurement science underpins much of the evidence gathered for robust policy development and I welcome the Chief Scientific Adviser's cross-Government strategy for food research and innovation and share his vision of a framework to facilitate a more coordinated and collaborative approach between the public and private sector and consumer and other organisations in supporting this. I recognise also that questions have been raised over how technical, service and advisory excellence can be sustained within front line food and feed enforcement laboratories. These factors will inevitably result in new challenges for the regulatory framework, while impacting on food safety issues and on the potential for misdescription and fraud. Thus I believe maintaining high levels of scientific capability and responsiveness remains the key to fulfilling my role of arbiter in dispute resolution, particularly in anticipation of the changing and challenging times ahead.

The Government Chemist team remains vigilant of these developments and therefore, with strategic underpinning from LGC, continues to build scientific capability that will address current and future concerns and analytical challenges. For example, in this review we describe the application of new developments in mass spectrometry and immunoassay that should enhance our capacity to detect, reliably and sensitively, toxins and other banned compounds, and multiplex methods for genetic fingerprinting and allergen detection.

I have begun a strategic review of the varied demands on the Government Chemist, including support for consumer protection and effective regulation across a wide front, and the implied delivery needs. Your suggestions and feedback on requirements would be particularly welcome now, as formulation of the 2011-14 Government Chemist work programme is getting under way. Please contact Steve.Wood@lgc.co.uk, me, or any of my staff about this.

A feature of the Government Chemist function is the transparency of the work, some of which is described within this annual review, on the Government Chemist website, in technical publications and through presentation and dissemination events. With regard to transparency, I was pleased this year to have received the findings of a detailed independent audit, and I would like to thank Richard Burt and David Ray for their conscientiousness in delivering a comprehensive report. The audit forms part of the governance activities that are described in more detail within this review, and that enable LGC staff to maintain and enhance the high levels of integrity and independence that underpin the Government Chemist function.

I end this foreword by taking the opportunity to acknowledge the contribution of David Ferguson, the adviser to Government on the Government Chemist Programme, who has contributed to the monitoring of our work over a number of years. David steps down from this role in 2010 and we are indebted to him for his incisive questioning and helpful support. I hope you enjoy reading this review and that you will take the opportunity to attend some of the Government Chemist's dissemination events over the course of the year, the details of which can be found on the website *(www.governmentchemist.org.uk).*

Derek Craston
BSc PhD FRSC
Government Chemist

1 Remit and governance

The Government Chemist has science-based statutory functions under seven acts of Parliament. Most of these focus on public protection, particularly by providing confidence that sound measurement science informs regulatory activities in the food and agriculture sector. The statutory functions are framed by a wider ongoing Government Chemist function as adviser on analytical measurement science in relation to policy, standards and regulation. Independence and impartiality, backed up by sound governance arrangements, ensure that we discharge our remit in a credible and reliable manner.

Referee and adviser

The strategic role of the Government Chemist in underpinning effective regulation through sound measurement science has roots in the 19th century. At that time, chemical and biochemical reactions were becoming well enough understood for translation into innovative methods of determining what really went to make up widely traded natural products and consumer goods - or had surreptitiously been added to them. Historically, we became established as:

- The laboratory responsible for providing decisive expert opinion, based on analytical measurement, at a national level, particularly where the need arose under legislation to protect public health, safety and consumer rights. This status, while already laid down in the Sale of Food and Drugs Act, 1875, grew through the Fertilisers and Feeding Stuffs Act, 1893 to include a function as independent 'referee' should the initial results of analytical measurement be disputed
- More widely, a versatile, innovative Government laboratory, with the flexibility to analyse samples of all kinds and so meet the many and varied requirements of other departments and authorities.

Today, our functions embrace and build upon these two historical roles. Our statutory duties (Box 1) focus on protecting public safety, health, value for money and consumer choice. We spare public authorities, traders and the courts the costs of avoidable litigation, and our work as authorised analyst under the Hydrocarbon Oil Duties Act protects the public revenue - clear instances of the economic impact of analytical science in and through effective regulation[1]. Meanwhile, the range of demands and challenges faced over the years equips the Government Chemist to provide more widely scoped advice, for Government and other stakeholders including industry, on the way analytical science links into policy, standards and regulation.

[1] For an overview of mechanisms by which measurement delivers economic returns focusing on growth and productivity, see Swann GMP, The economics of metrology and measurement, National Measurement Office *(www.nmo.bis.gov.uk)*, October 2009, Table 3

Remit and governance

Box 1: The Government Chemist in legislation

The duties of the Government Chemist as referee analyst are defined in or under:

Food Safety Act 1990

Food Safety (Sampling and Qualifications) Regulations 1990

Food (Northern Ireland) Order 1989

Food Safety (Northern Ireland) Order 1991

Food Safety (Sampling and Qualifications) Regulations (Northern Ireland) 1991

Poultry Meat (Water Content) Regulations 1984

Natural Mineral Water, Spring Water and Bottled Drinking Water Regulations 2007

Materials and Articles in Contact with Food Regulations 2007

Plastic Materials and Articles in Contact with Food Regulations 2009

Agriculture Act 1970

Feed (Hygiene and Enforcement) Regulations 2005

Genetically Modified Animal Feed Regulations 2004

Medicines Act 1968

Farm and Garden Chemicals Act 1967

The Government Chemist is named and has other scientific responsibilities under:

Merchant Shipping Act 1995

Hydrocarbon Oil Duties Act 1979

Poisons Act 1972

The status and territorial extent of the Government Chemist are understood with reference to:

Freedom of Information Act 2000

Scotland Act 1998 (Cross-Border Public Authorities) (Specification) Order 1999

Scottish Parliament (Disqualification) Order 2007

Administrative Provisions Act (Northern Ireland) 1928

Government Chemist Regulations (Northern Ireland) 1928

The referee analyst function

Parliamentary acts and regulations lay down procedures for official sampling and analysis carried out as part of an investigation which may precede enforcement action against a business operator. The legal provisions may require a formal sample to be divided into equivalent portions or parts, so that each party has the chance to perform tests. As referee analyst, we provide an expert opinion, based on independent measurement, to resolve disputes over the results of tests carried out on behalf of the enforcement authority and the trader. For recent case studies, which relate to formal samples of food and feed, see section 2.

Capability building

The duty to perform referee analysis spans a huge range of substances or properties to be determined (analytes). Moreover, analytes may be present in a wide variety of sample types (matrix materials, or matrices). We try to foresee areas of likely demand, and upgrade the capability to determine analytes in matrices that may present complex measurement issues. To read about projects supporting this aim, go to section 3.

Strategic skills and knowledge

Our ability both to imbibe and disseminate best practice depends on LGC's designation as the National Measurement Institute for chemical and bioanalysis. As the home laboratory of the Government Chemist, LGC strategically underpins our access to state-of-the-art technology and expertise. For more on strategic R&D, consult section 4.

The wider advisory function

The wider advisory function of the Government Chemist is formally established by our appointment to the Secretary of State 'as a source of advice for HM Government and the wider analytical community on the analytical chemistry implications on matters of policy and of standards and of regulations'. We contribute to Government-led dialogue and debate within this field of expertise. We also help protect the environment and human health by tackling measurement issues linked to potentially hazardous substances, often in conjunction with industry. For an overview of our wider advisory work, turn to section 5.

The future

The referee analyst function has served the UK well for many years as guarantor of public safety, health and choice. Regulators, businesses, and, ultimately, the courts are spared much of the cost and delay which could arise from technical errors or uncertainties in front line analytical measurement.

We live in a world of increasing innovation and industrial competition, linked to growing demand for lean, effective regulation. The referee analyst function provides efficiency savings to both industry and the regulatory authorities. Meanwhile, in our advisory capacity, we harness innovation to improve and ease regulatory compliance and enforcement. Hence the Government Chemist function as a whole remains, and is continuing to evolve as, a central pillar for proportionate enforcement and effective technology transfer.

Organogram

The roles and responsibilities of those LGC staff directly responsible to the Government Chemist are clearly and independently defined (Figure 1). In addition, scientists and other professionals throughout the Laboratory are on hand to contribute advice and expertise. Analytical scientists undergo relevant training and develop expertise through related R&D as well as by participating in appropriate proficiency tests. Nominated Officers, who have overall responsibility for case supervision, prepare and sign certificates of referee analysis. Only the Government Chemist or Deputy, once satisfied that a case has been properly completed, may countersign.

Governance

The National Measurement Office (NMO), an executive agency of the Department for Business, Innovation and Skills (BIS), underpins the Government Chemist on behalf of the UK Government. As our sponsor department, BIS funds the Government Chemist Programme to enable delivery of statutory casework, scientific advice, and related activities such as R&D in support of those functions.

An independent adviser, appointed by NMO, provides expert scrutiny of the Government Chemist Programme on a quarterly basis, and liaises over additional good governance measures. For example, he assisted the definition of quality systems that safeguard against the potential for conflicts of interest, by embedding rigorous methods for evaluating external enquiries received across relevant LGC operations.

In the latter part of 2008, the independent adviser coordinated a broadly-based external audit which had been commissioned by the Government to examine our remit and functions. The report, published early in 2009, contained several strategic findings. Briefly:

- The Government Chemist function is held in high regard, delivers excellent quality measurement science for stakeholders, and fulfils the need for an independent and impartial service
- Maintaining the historic ties with LGC has worked well, and should continue to do so
- Stakeholders should have an increasing role in shaping the Government Chemist Programme; horizon scanning to foresee emerging regulation, technologies and threats; knowledge transfer; and partnership to maximise the value of the wider advisory function.

What more, then, can be done to foster the role of stakeholders? So far, the Government Chemist Advisory Group (GCAG) has continued meeting on a six-monthly basis to review and inform our progress. This group brings together Public Analysts, local and port health authorities, trade and research associations, Government departments and agencies. GCAG is currently chaired by the Government Chemist Science Manager, but plans are well advanced for the group to be reconstituted, and potentially widened, with a new remit to advise NMO directly on our activities. This arrangement is likely to be established as we begin to formulate the next Government Chemist Programme, which is due to commence in April 2011.

Meanwhile, many of our ongoing activities would benefit from wider collaboration or partnership. Most of these are likely to build on what is reported below. If you would like to discuss any aspect of our work, please refer to Figure 1 for a suitable contact point.

Remit and governance

Figure 1:
Government Chemist contact points

Derek Craston
Government Chemist
Derek.Craston@lgc.co.uk

Ian Lumley
Government Chemist Deputy
Ian.Lumley@lgc.co.uk

Steve Wood
Programme Manager
Steve.Wood@lgc.co.uk

Rita Harte
Assistant Programme Manager
Rita.Harte@lgc.co.uk

Peter Colwell
Project Manager,
Statutory Function
Pete.Colwell@lgc.co.uk

Selvarani Elahi
Nominated Officer
Selvarani.Elahi@lgc.co.uk

Malcolm Burns
Project Manager
Malcolm.Burns@lgc.co.uk

Kirstin Gray
Analysis Manager
Kirstin.Gray@lgc.co.uk

Michael Walker
Science Manager and
Nominated Officer
Michael.Walker@lgc.co.uk

John Francis
Project Manager,
Advisory Function
John.Francis@lgc.co.uk

Peter Roper
Nominated Officer
Peter.Roper@lgc.co.uk

Contact

Email: government.chemist@lgc.co.uk Phone the LGC switchboard: +44 (0)20 8943 7000

2 Casework

We received seven formal cases for arbitration in 2009:

- Five in the capacity of statutory referee, under the provisions of the Food Safety Act 1990
- One further food sample in respect of which the right to a supplementary expert opinion, deriving from the EU Official Control Regulation, was exercised
- And one sample of animal feed, submitted in accordance with the provisions of the Agriculture Act 1970.

The following pages highlight some of the year's completed cases, showing how the interplay of regulatory diligence and scientific rigour makes each formal sample[2] a unique challenge.

A flexible service

Food and feed business operators whose products have been sampled for analysis have a right in accordance with Article 11(5) of Regulation (EC) No 882/2004 *on official controls* to a supplementary expert opinion (SEO). This is exercisable by reference to any official control laboratory (OCL) and in certain circumstances by appeal to the Government Chemist. Alternatively, UK legislation continues to offer an evidence-rich route - the OCL and the trader each obtain test results and have scope to review all aspects of the science before taking up any outstanding measurement issues with the referee. The company can choose which procedure to follow, and the decision may prove significant.

We continue to charge a nominal administrative fee of £250 for referee analysis. However, the rigour with which a referee case is conducted, along with the expert opinion brought to bear, brings with it a significant cost; it is fitting to conduct SEO casework to the same standard and so habitual recourse to the SEO route is a significant challenge to the resourcing of the Government Chemist. Therefore, in consultation with the Government Chemist Advisory Group, which consists of independent stakeholder representatives, we decided to raise the price of SEO to £1,500 per sample this year. This still falls well short of the real cost to the Exchequer, and the sum is unlikely to deter any trader with secure grounds for submitting a sample.

[2] A sample taken for analysis under statutory enforcement provisions, such as regulation 6 of the Food Safety (Sampling and Qualifications) Regulations 1990

Casework

Nitrofurans

Nitrofurans, once widely used as veterinary antibiotics, are now known to be carcinogenic and are prohibited in the food chain. The related official controls are underpinned by Decision 2002/657/EC *concerning the performance of analytical methods and the interpretation of results* as amended. Because nitrofurans are rapidly broken down *in vivo*, certain metabolites are recognised as markers to indicate their previous use in the food. Nitrofurans are of such concern that no maximum residue limit can be set[3]. Instead, the requirement is to be confident that they are not present.

A rather complicated history attaches to a formal sample of frozen prawns which we received for the determination of nitrofurans. The sample had been taken under the Food Safety Act 1990, and with regard to an EU Decision on emergency measures applicable to crustaceans imported from India and intended for human consumption. As required by food legislation, the sample was divided into three portions. From the first portion, assigned for testing on behalf of the Port Health Authority, a result was reported at a level of 2.6 μg kg^{-1} for the semicarbazide metabolite, indicating that nitrofurans may have been present. Unusually, the food business operator broke the seal of the second portion and further divided the sample under official supervision for analysis on his behalf by two independent laboratories. The provision of facilities for such analysis in the UK is not extensive, and one of these subdivided portions found its way, without disclosure that it was involved in an official sampling exercise, to LGC, where it was routinely analysed.

Upon receipt of the official third portion for referee analysis (referee sample), we were informed of the sample history and acted promptly to prevent any possible conflict of interest in relation to the sub-portion tested by LGC. This included ensuring that Government Chemist staff, separate from the area of LGC which analysed the previous sub-portion, managed the case and prepared the referee sample (Figure 2), and all the while remained unaware of the sub-portion result. A full case-specific method validation package was prepared by residue analysts having no prior involvement with the sample and under the direct supervision of Government Chemist staff.

Figure 2: Prawns were coned and quartered, shelled, washed, and finally blended as a prelude to referee analysis for nitrofuran metabolites

We deployed a variation of our UKAS-accredited procedure based on acid hydrolysis of the homogenised prawns to release the residue markers. These were extracted, derivatised and determined by LC-MS/MS, establishing detection limits below the EU minimum required performance limit for marker metabolites of four nitrofuran compounds. We used this method to determine triplicate sample aliquots on each of three days, and concluded that the sample did not contain nitrofuran metabolites at concentrations greater than the detection capability.

[3] Within the framework of Regulation (EC) No 470/2009 *laying down Community procedures for the establishment of residue limits of pharmacologically active substances in foodstuffs of animal origin*, which recently superseded Regulation (EEC) No 2377/90

Aflatoxins

We continued to receive formal samples for the determination of aflatoxins - metabolites that are genotoxic carcinogens derived from certain moulds which can develop on natural products, such as fruit and nuts, under adverse climatic and storage conditions.

Strict control measures are in place to prevent contaminated consignments entering the UK. Regulation (EC) No 1881/2006 imposes concentration limits for total aflatoxins and for the B_1 form, a specific metabolite of concern, while Regulation (EC) No 401/2006 lays down methods of sampling and analysis.

An agreed sampling protocol reflects the fact that mould contamination tends to be patchy rather than evenly distributed; so from a single formal sample taken by Port Health Authorities, up to three subsamples are produced for analysis. For our part, to obtain a high level of confidence in the results of referee analysis, we typically test every subsample three times on each of three days alongside appropriate control materials. Accompanying samples are spiked with known quantities of aflatoxins so that the proportion recovered from analysis can be factored into the final measurement.

After performing an optimised solvent extraction, we isolate the aflatoxins by immunoaffinity chromatography, separate them by liquid chromatography (LC), and react them to form derivatives which can be measured by a fluorescence detector with high precision. We also confirm the identity of the measured toxins by LC-tandem mass spectrometry (LC-MS/MS).

One referee case involved roasted pistachio nuts (Figure 3). The legal limit for aflatoxin B1 in nuts is 2 μg kg^{-1}. The Public Analyst reported that one of the subsamples contained 8.0 ± 2.2 μg kg^{-1} of aflatoxin B_1, but the importer's laboratory found a concentration of 2.5 ± 0.6 μg kg^{-1}. Because the confidence interval for the importer's result straddles the legal limit, the two results were effectively at variance.

The Government Chemist's result was 7.8 ± 0.2 μg kg^{-1}, in close agreement with the Public Analyst. Our confirmation of non-compliance resulted in re-export of the pistachio consignment.

A sample of fig paste was received for analysis via the SEO route. In this case, evidence of compliance with EU legal limits was available from the country in which the figs had been processed, sampled and analysed. Perhaps because of mould growth during transit, tests conducted for the Port Health Authority indicated that aflatoxin concentrations were in excess of the legal limits when the consignment arrived in the UK.

Again, our results confirmed those of the Public Analyst, and in consequence, the consignment was re-exported.

Figure 3: A slurry must be created to help ensure that toxins derived from mould growth are sampled representatively

Sabotage?

Although some may imagine that referee analysis is a somewhat genteel pursuit - delivered by experts, for experts - in practice it has much in common with police-led criminal law enforcement. After all, public health and wellbeing are at stake. Our scientists routinely work to forensic standards, such as by conserving the chain of evidence, going the extra mile to increase confidence in the results, and attending court when required to give expert testimony.

Last year's Government Chemist Review touched on the part played by staff in progressing a novel and costly case of suspected sabotage involving peanuts, a recognised food allergen. We are now in a position to provide a fuller case history. It may be recalled that a disgruntled employee was alleged to have contaminated a nut-free food factory, which incurred shutdown, clean-up and product recall costs reportedly totalling £1.2 m.

Our forensic evidence for this case utilised a dedicated laboratory suite, originally built to exclude potential cross-contamination when measuring allergens in formal food samples, and incorporating best practice such as:

- A step-over barrier to demarcate the clean zone
- Air handling considerations
- Gown-style laboratory wear, colour-coded to ensure that each operational area remains isolated
- Optimal use of disposable equipment
- Swabbing protocols to test for contamination of the laboratory environment with allergens
- No access if an analyst has consumed the allergen under test within the last 24 hours.

We were asked to explore two lines of evidence:

- We examined two exhibits of clothing allegedly belonging to the defendant - overalls and tracksuit bottoms - and detected peanut protein after swabbing the inside surfaces of the pockets (Figure 4)
- Counsel for the defence then requested experiments to establish the conditions under which peanut protein could be transferred to fabric after handling, and if it would remain on the hands after washing. We reported that handling a peanut for 10 seconds transferred enough peanut protein to the fingers for it to be recovered from fabric even after 10 successive finger/fabric contacts (Figure 5).

The trial, which took place before the Recorder of Nottingham, lasted over two weeks. The defendant pleaded not guilty to offences involving the possession of materials for contaminating goods, making it appear that goods had been contaminated with intent to cause public alarm, injury, economic loss and threats to kill. The defence established that the peanuts were found in the factory, and the clothing exhibits seized, by the same management team, raising a possibility that peanut protein may have been transferred inadvertently to the pockets. In the light of this evidence, the jury was unable to agree a verdict, and was discharged by the judge. The Crown Prosecution Service considered a retrial, but it was decided that there was no realistic prospect of a conviction, and the defendant was acquitted.

This forensic work provided further insight into the scope and performance of ELISA-based allergen testing methods, the potential for cross-contamination and the design of control procedures, all of which can be carried forward to any future cases requiring referee analysis.

Figure 4: We examined forensic exhibits for traces of peanut protein

Figure 5: We conducted systematic experiments to establish whether peanut protein was detectable after typical day-to-day handling

Casework

Animal feed

The ruminant feed ban, which includes a prohibition on ruminant protein being fed to cattle, is a fundamental protection measure against the spread of transmissible spongiform encephalopathies, considered by most scientists to be the origin of the invariably fatal human brain disease vCJD. Thus several regulations combined to protect consumers when a lorry ostensibly carrying cattle feed subject to the Organic Products Regulations 2009 was stopped by the Vehicle and Operator Services Agency (VOSA). The inspector suspected that the lorry had previously transported meat and bone meal, contamination of cattle feed with which would breach not only legislation protecting consumer choice, but also the safety measures contained in the national Transmissible Spongiform Encephalopathies Regulations of 2008. Acting in accordance with Part IV of the Agriculture Act 1970, the inspector took a formal sample, divided it, and submitted the first part to the Veterinary Laboratories Agency (VLA). The analyst reported that muscle fibres and terrestrial animal bone were present. However, a laboratory acting on the owner's behalf tested the second part of the sample, and did not detect meat and bone meal. Both laboratories employed microscopy methods.

The part of the sample retained as required by the 1970 Act was then sent to the Government Chemist. We analysed it in accordance with Commission Directive 2003/126/EC *on the analytical method for the determination of constituents of animal origin for the official control of feedingstuffs*. We sieved and milled the sample, which consisted mainly of pellets, to isolate fractions in which any adventitious contamination might tend to accumulate. We then prepared a series of slides for reflected and transmitted light microscopy, staining with Alizarin Red dye to highlight possible bone tissue (Figure 6). We detected 85 fragments with the characteristics of terrestrial animal bone, as well as hairs having features consistent with bovine or porcine origin - effectively confirming the VLA's findings. Alternative techniques - immunoassay and DNA-based - were validated, but found insufficiently sensitive to detect the low levels of contamination present in this sample reliably.

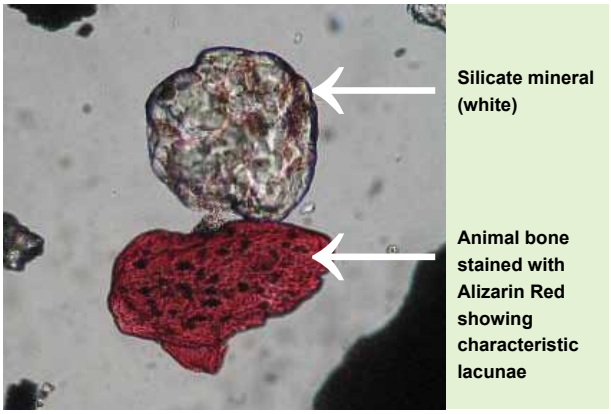


Figure 6: The morphology of fragments stained by Alizarin Red contributed to our opinion that constituents derived from terrestrial animals were present in a sample of cattle feed

The inspector launched proceedings against the haulage company, which, after pleading guilty, was fined £25,000 and ordered to pay £4,500 in costs.

Dispute avoidance

The parties to a dispute over scientific measurement can save themselves the costs and heartache of a court case by appeal to the referee analyst. However, sometimes we can help those affected to resolve uncertainties even earlier in a case investigation.

For example, a Public Analyst recently tested a formal sample described as basmati rice by a DNA microsatellite method, and found that it did not comply with the sectoral code of practice, which requires 93 % of the grains to meet the description. A separate retained sample was sent to an independent laboratory, which reported borderline compliance after taking into account an overall uncertainty of 6.4 %. We advised on the case at several stages. After reviewing the available science, such as whether measurements had been based on individual grains, and the control materials matched to the age and milling of the sample, we advised that further sampling and analysis would be feasible. In fact, no further action was taken because it appeared that the manufacturer might reasonably plead due diligence, a defence recognised by section 21 of the Food Safety Act 1990 and other sectoral legislation. In conjunction with stakeholders, we are exploring the possible production of sampling guidance.

3 Underpinning the referee function

We continue to perform a wide range of R&D relating to food and feed measurement science. The primary aim of our underpinning studies is to maintain an effective and credible referee function. Knowledge transfer activities support this aim whilst enabling our findings to be more widely applied, particularly by business operators and the official controls community.

The topics reported in this chapter are arranged under the key themes of consumer safety, nutrition and choice, although in practice they may contribute to more than one of these strategic goals.

Consumer safety

Aflatoxins

If climatic and storage conditions are favourable, aflatoxin-producing strains of the moulds *Aspergillus flavus* and *A. parasiticus* can grow on foodstuffs. Aflatoxins are potent genotoxic carcinogens as well as acute toxins. Of the 18 known chemical forms, aflatoxin B_1 usually predominates, and is subject to statutory concentration limits in food types considered to be at risk of contamination. There are similar statutory limits for the sum of the concentrations of four major aflatoxin forms - B_1, B_2, G_1 and G_2.

Analytical control methods generally include sophisticated procedures to isolate aflatoxins from the many other constituents of food and feed samples. It is clearly important to recover a representative proportion of the aflatoxins present for measurement, and to do so consistently. Recoveries are assessed by measuring control materials to which known quantities of aflatoxins have been added. This spiking procedure had been built into a sampling protocol agreed with the UK Port Health Authorities, but uncertainty remained about the optimal timing. Were it a mere matter of convenience, some laboratories might choose to spike the samples in the afternoon and extract the aflatoxins on the next working day, while others would opt for a within-day protocol. We designed experiments to compare these alternatives for three common sample types: peanuts, figs and chillies.

Our statistical evaluation showed that higher recoveries resulted when contact between the aflatoxin spike and the control material was relatively brief, although the significance of the effect was different for each food type. From a risk management perspective, the ideal spiking protocol might be designed to reflect the proportion of the aflatoxin content which is bioavailable in real food samples; however, in the first instance, the priority may be to foster a consensus on timing of this procedural step.

Mycotoxins

Although recent official controls have focused particularly on aflatoxins, many other mycotoxins - toxic metabolites produced by fungi - are subject to Regulation (EC) No 1881/2006 *setting maximum levels for certain contaminants in foodstuffs*, as amended. These vary widely in chemical structure, ranging from the relatively simple patulin, found in rotting apples, to intricate molecules such as the fumonisins which typically affect corn.

We set out to develop LC-MS/MS methods able to detect and quantify a range of mycotoxins with high confidence at concentrations appropriate to the regulatory limits. We first reviewed literature methods, and concluded that:

- Extraction with two solvents, having complementary properties, is needed to recover the whole range of mycotoxins acceptably
- Advances in LC miniaturisation should enable generic column packings to replace bespoke, costly immunoaffinity chromatography (IAC) media
- Each modern variant of mass spectrometry (ion trap, time of flight, triple quadrupole) has potential advantages for this application, as do the different ionisation techniques that can accompany them
- Achieving the best detection limits will depend on being able to switch deftly between mass analysis of positive and negative ions
- Internal standards, created by adding molecules resembling natural mycotoxins to samples early in the analytical procedure, will be needed to help ensure reliable measurement.

R&D confirmed many of these conclusions. We could measure preparations of all the mycotoxins in a single, dual-injection procedure utilising LC-MS/MS in both positive and negative ESI modes, with the exception of patulin, which, owing to its chemical structure, requires a different approach. Data are interpreted with reference to isotopically labelled mycotoxin preparations, which have analytical properties as close as possible to those of the naturally occurring molecules. After introducing a dual-solvent extraction procedure, we were able to omit IAC. The LC-MS/MS method is being optimised for increasingly complex sample types; we established suitable parameters for wheat flour, and extension to cereal-based baby foods is in progress.

Nutrition

Vitamins

Traditional microbiological assay (MBA) methods for vitamins are time-consuming, and can be temperamental. We plan to evaluate modern alternatives over a wide front, so as to support industry compliance, official controls, and possible referee analysis in connection with legislation such as the Food Labelling Regulations 1996, the Food Supplements Regulations 2003 and the Feeding Stuffs Regulations 2000. Current objectives are to:

- Progress the determination of vitamins in food supplements. Lessons learnt from a previous collaborative trial are being used to plan a follow-up study that focuses on the key measurement parameters
- Develop LC methods for folic acid and folates in foods. A comparison of MBA and LC methods for folates in beer and breakfast cereal is in progress
- Evaluate new immunoaffinity clean-up (IAC) columns for isolating vitamin B12 from foods and supplements. We developed an IAC-LC method capable of recovering sub-parts per million concentrations of this vitamin from a variety of products, including multivitamin tablets, yeast extract, infant milk formula and breakfast cereal
- Investigate the feasibility of LC-MS for the simultaneous determination of B-group vitamins in foods and feeds. A literature survey concluded that this is a challenging goal, but R&D plans are well advanced
- Explore techniques for the determination of chiral forms of vitamins and related compounds. Again, a literature survey is under way, focusing on biotin, vitamin C and vitamin E (tocopherol). As usual we aim to develop methods that could easily be reproduced by laboratories supporting regulatory compliance and enforcement.

Underpinning the referee function

Consumer choice

Genetically modified organisms (GMOs)

Within the EU, Regulation (EC) No 1829/2003 maintains legal requirements for the authorisation and labelling of GMOs, as well as food and feed products containing or produced from them. Overseas, commercial GM food and feed technology is getting more sophisticated, and the detection of unauthorised GMOs within the EU is becoming more common. We monitor EU legislation, particularly border control measures that may impact on laboratory testing. For example, unauthorised GM CDC Triffid Flax (Event FP967) has recently been found in the majority of EU member states. Earlier in the year, regulatory databases provided evidence of a surge in product recalls linked to the unauthorised GM maize variety MON 88017.

The appointment of LGC as the National Reference Laboratory (NRL) for GM food and feed in March 2009, which will further underpin UK measurement capability, was accompanied by positive steps to ensure that Government Chemist staff remain independent. We carry out complementary research, targeted on technologies that could benefit the referee function.

For example, our trials of digital PCR for the determination of GM rice and maize indicated that:

- The new technology is suitable for absolute single molecule detection of DNA derived from GMOs
- The digital technique is much more sensitive than real-time PCR. This will allow sensitivity limits in EU validated protocols for the detection of GMOs to be re-evaluated and more accurately defined
- We need to foster technology transfer by seeking consensus on rigorous protocols for comparing real-time and digital PCR technologies.

We also initiated an independent, comparative trial of commercial DNA analysers that employ capillary electrophoresis (CE), based on a GM detection method approved by the Food Standards Agency, which will establish key figures of merit such as repeatability data.

We maintain preparedness in this and other key areas through proficiency testing (PT) schemes. For example, we were among the 58 laboratories that tested two PT samples circulated by the Genetically Modified Materials Analysis Scheme (GeMMA) in January 2009. We correctly determined that a variety of herbicide-resistant GM soya was absent in one sample, and present in the other. Moreover, our positive result (1.02 % by mass) was in close agreement with the independently assigned value (1.05 %), even though we had to apply unfamiliar reference materials and a new EU validated measurement protocol.

DNA methods to tackle food fraud

Food adulteration has a long and murky history. There is usually an economic motive; this may override any safety considerations, let alone the consumer's right to decide what to eat. We launched a project to update the application of DNA techniques for the detection and quantitation of potential food adulterants.

High-value ingredients such as meat are at relatively high risk of fraudulent replacement with cheaper species or cuts. Building on advances in bioinformatics, we began a systematic review of real-time PCR techniques for beef, lamb and pork by using the world-class National Center for Biotechnology Information (NCBI) Basic Local Alignment Search Tool (BLAST) to evaluate potential cross-reactivity between the DNA of food-producing animals and that of the primer sequences on which test methods depend. The results will inform practical tests to define the species specificity of available primers more precisely.

Irradiation

The treatment of food with ionising radiation (X-rays, gamma rays or beams of electrons) is a preservation technique subject to the Food Labelling Regulations 1996 as amended, and to authorisation for specific uses under the Food Irradiation Regulations 2009. Supply chains for globally traded ingredients can conceal the use of unauthorised irradiation, or fail to pass on data required for labelling purposes. It is good practice to screen ingredients for irradiation by the photostimulated luminescence (PSL) technique.

Statutory casework in this field is relatively infrequent, but challenging. We are collaborating to extend the range of sample types amenable to a reference measurement method based on thermoluminescence (TL) detection of energy from the irradiating process trapped in silicate minerals in the food. For herbs, spices and other foods silicate mineral inclusions can serve as indicators of prior irradiation.

However, highly processed or blended products may contain limited quantities of silicate minerals, and it can be difficult to extract enough material for TL analysis. The harmonised European standard method (BS EN 1788:2001) indicates the quantity of silicate materials needed, but this is unlikely to be apparent upon initial inspection of a food sample. Hence we established a generic pre-screening method to show whether the recovery of silicate materials is likely to be satisfactory, based on dry ashing with a fusion aid then silicon determination by inductively coupled plasma optical emission spectrometry (ICP-OES). We went on to demonstrate an effective hydrolytic method for extracting the intact silicate inclusions from starchy food products.

We also developed awareness of supply chains for bulk ingredients which we can be confident have not been irradiated. These are needed to prepare matrix-matched control samples containing known proportions of irradiated materials.

Knowledge transfer

We aim to share knowledge with all stakeholders, by organising and participating in a variety of relevant events as well as through the traditional channels of scientific correspondence and discourse. For example, we participated regularly in:

- The Food Standards Agency Sampling and Co-ordination Working Group, giving expert advice for instance through the Feed Sampling Guidance sub-group and ensuring synergy with training activities undertaken by us and the APA
- The LACORS Sampling and Analysis Working Group, presenting a detailed mid-year update on Government Chemist activities and advising on analytical and interpretive issues in food and feed regulation
- The Food Law Group, learning about upcoming food law and discussing topics such as the relationship between local authorities and the Local Better Regulation Office under the Regulatory Enforcement and Sanctions Act 2008.

Following advice in the audit of the previous (2005-08) programme we have sought to ramp up our dissemination of the Government Chemist function with speaking engagements covering casework and related issues. These were delivered to a wide range of stakeholders including academics in Belfast and Dublin, 27 regulatory affairs managers from 21 food companies at a Leatherhead Research International seminar, the FSA, Public Analysts, the European Food Law Association and at several international conferences.

We place increasing priority on outreach to overseas institutes with a potential role in official controls or in safeguarding global supply chains[4]. In October, five LGC staff - including the Government Chemist, Deputy, and Science Manager - visited the Republic of Korea's National Measurement Institute (KRISS). The Foreign & Commonwealth Office sponsored this initiative to foster mutual understanding of official food safety regulation, and closer collaboration on connected measurement issues.

During the visit, Government Chemist staff presented at a conference on food safety. Our presentations highlighted the benefits of reference materials, method validation and proficiency testing, in sound measurement science in general and deployed to adjudicate disputes. Korean scientists provided insights into emerging food contaminant issues, and discussed cooperation on food allergens, GMOs and laboratory accreditation to ISO/IEC 17025. We plan to continue joint working through a reciprocal visit in mid 2010 for wide-ranging discussions on food safety and food security.

[4] 'The UK has a strong track record in the application of science and scientific advice to government. As more decisions are taken internationally, and more scientific advice is provided internationally, the UK needs to engage ever better with international organisations and processes so we can contribute to global good practice.' Government Office for Science, *Science & engineering in government: an overview of the Government's approach*, October 2009, URN 09/1291

Underpinning the referee function

Government Chemist conference

Our annual dissemination event, *Resolving Disputes in the Food Network*, was held on 30 April at the Westminster Conference Centre. The events are chaired alternately by eminent figures from the industrial and regulatory communities, and on this occasion we were delighted that Paul Berryman, CEO of Leatherhead Food Research, agreed to take the helm. The 57 participants were drawn from Public Analyst laboratories, the Food Standards Agency, Port Health Authorities and a wide range of interested organisations, while the increased representation from the food industry this year was particularly welcome.

We presented the casework and supporting studies that we had completed as referee analyst over the preceding year, highlighting best practice and lessons learnt which may help traders and enforcement authorities to avoid disputes in the future. A central topic was food fraud, with speakers ranging from Franz Ulberth, Head of Food Safety and Quality at the JRC-IRMM, to LGC's Rebeca Santamaria-Fernandez. Franz reported initial findings from a European project aiming to distinguish organic and conventionally produced wheat based on the total nitrogen content, the protein pattern and stable isotopes of nitrogen. Rebeca outlined advances in isotope ratio measurement, currently being applied to identify counterfeit drugs, which could be extended to improve the detection of adulterated food.

Building on highly positive feedback, plans are well under way for the next annual event, *Setting Standards in Food Analysis*, which will be held at the Churchill Museum and Cabinet War Rooms, London, on 28 and 29 April 2010. In an historic setting this will be a unique opportunity to hear from and network with scientists and policy officials from influential stakeholders in the food standards sector, representing the regulator, industry, research bodies and the referee analyst.

Under the auspices of the National Measurement Office and the APA Educational Trust, the conference will address developments in food safety, authenticity and analysis, and is supported by:

- The Food Standards Agency
- Leatherhead Food Research
- Campden BRI
- LGC Standards
- The Government Chemist.

For details, please contact: Kirstin.Gray@lgc.co.uk

Churchill Museum and Cabinet War Rooms, HCA Auditorium, London

4 Strategic underpinning

We receive an increasingly diverse and complex range of samples for referee analysis. This suggests that, as we would wish, UK laboratories progressively adopt the science and technology to deal with more familiar and foreseeable measurement scenarios, while continuing to seek our opinion on those at the leading edge.

That we are able to provide such opinion is largely a consequence of LGC's globally networked role as the UK designated National Measurement Institute (NMI) for chemical and bioanalysis. The NMI also underpins the analytical rigour which characterises the Government Chemist function, enabling us to access and adopt international best practice, for example in the design and statistical interpretation of experiments. Here we highlight some of the NMI-led measurement R&D which we hope to see widely exploited for the benefit of stakeholders over the coming decade.

Strategic underpinning

Underpinning protein measurement

For many years, scientists have attempted to represent molecules in the common currency of the natural sciences - the SI base units of mass (kilogram) and amount of substance (mole) - to assure traceability and improve the accuracy and comparability of measurement. This aim continues to drive the development of reliable, quantitative measurement techniques that can then be validated for specific applications. Success will enable the results of working analytical methods to be expressed in terms of global standards, creating a level playing field for international trade and its regulation. Thanks to improved mass spectrometry technology and new methodologies, traceability to the fundamental units of measurement is now realisable.

Traceable quantification of biologicals is, however, still a demanding task due to the complexity of the samples and the lack of standards.

An approach established by LGC in conjunction with other National Measurement Institutes relies on enzymes to prepare fragments (peptides) in a mass range that is amenable to LC-MS/MS techniques derived from mainstream analytical chemistry (Figure 7). An aspect of this work is definitive metrology, which requires painstaking method development and a full investigation of uncertainties such the inherent variability of the source material, the efficacy of purification steps and the reproducibility of sample preparation procedures.

Studies are facilitated by access to a range of high performance mass spectrometers. Typically, optimisation of enzymatic digestion and selection of peptides to be used in quantification are performed on a quadrupole time-of-flight (QToF) machine, because of its high mass resolution and data acquisition rate. Quantification is carried out on triple quadrupole (QqQ) instruments, for high accuracy and selectivity.

As confidence in the methodology builds, practical working methods become feasible. Take for example the determination of allergenic proteins in food. Existing analytical methods based on ELISA and real-time PCR can be both sensitive and easy to use. However, reliability and quantitation are areas of concern, and could be addressed by comparison with an independent, internationally traceable method. As a first step in this direction, we chose a relatively straightforward model system - lysozyme protein in wine, which is potentially present as a preservative and owing to the use of egg white as a fining agent. Development of a dedicated LC-MS/MS method for egg lysozyme in wine commenced in November, early results were encouraging and validation is in prospect. While the full protocol entails considerable sample preparation, a variant intended for rapid screening, which employs a short pre-column to fractionate the sample, also shows promise.

LC-MS/MS is capable of quantifying many substances with high confidence in a single experiment (multiplexing). This is significant for the official control of allergens, as the measurement requirements relate to a well-defined list of substances.

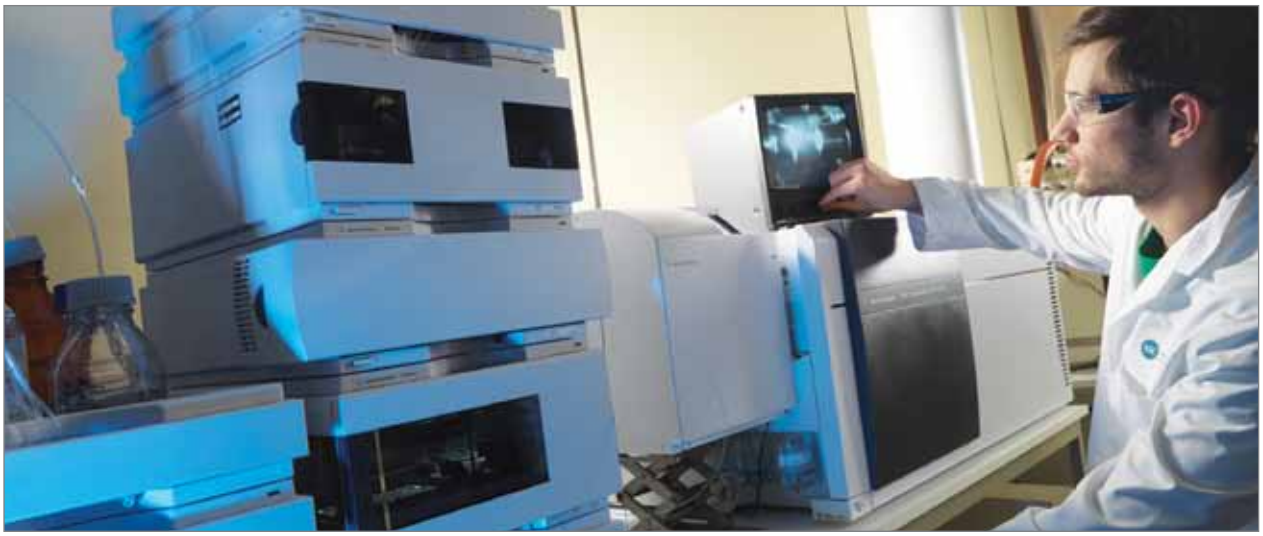


Figure 7: Mass spectrometry offers a sound scientific basis for the global intercomparison of protein measurements

Evaluating ion mobility spectrometry techniques

Ion mobility spectrometry (IMS) is the family name for a developing cluster of techniques which has already found niche application, notably in the security and forensic sectors. The IMS family shares a key feature with mass spectrometry, namely the ingenious use of electric fields to direct and select charged particles (ion optics). Whereas mass spectrometric analysis relies on the ratio of ionic mass to charge, IMS separation is based on molecular shape, and therefore has the potential to identify and quantify each of a group of isomers present in a sample. LGC is exploring the potential of IMS to underpin critical decision making in fields such as clinical chemistry and sports science, either as a complementary stand-alone approach or in combination with the mass spectrometer.

Simple IMS instruments separate charged particles (ions) in a tube along which a uniform electric field is applied. In the presence of a suitable carrier gas, each ion attains a characteristic velocity, and the time taken to traverse the tube is measured.

With NMO funding, LGC is evaluating a variant technique, high field asymmetric waveform IMS (FAIMS). Ions are elicited from the sample by the versatile electrospray (ESI) technique widely used in mass spectrometry. FAIMS employs a second, tunable electric field to harvest ions of interest. These pass on into an adjacent triple quadrupole mass spectrometer (MS/MS) for definitive identification. By acting as an ion filter, the FAIMS-MS combination can eliminate many substances which might otherwise interfere with measurement, improving confidence in the overall result.

Testosterone is well known as a performance-enhancing substance controlled in conjunction with the World Anti-Doping Agency (WADA). Endogenous levels of this hormone in the low parts per billion range are of clinical interest, while abuse is more likely to be detected by monitoring changes in its concentration relative to an inactive isomer, epitestosterone. Both isomers are excreted as glucuronide compounds, and are often measured in this guise because urine sampling and testing schemes are well established. But before the ratio of the two isomers can be determined, they must be separated unequivocally. LGC demonstrated that LC-FAIMS-MS/MS could resolve and quantify these isomers. FAIMS could increase confidence in the results of the analysis by removing other unidentified, potentially interfering, substances which are often observed in urine extracts (Figure 8). This method resulted in excellent agreement with the consensus mean of the laboratories that participated in an international trial organised by the Consultative Committee for Amount of Substance (CCQM).

Case-by-case validation remains necessary, as the effects of operational variables on FAIMS data are just beginning to be assessed, and poor ion transmission may hinder or prevent the determination of trace concentrations of some substances. However, the technique appears promising for the isolation of individual isomers, or the removal of isobaric interferences. It is likely to prove its worth in tackling complex sample types, for example when investigating suspected food adulteration, and particularly where the development of a bespoke method is justified by the existence of a significant risk to health or the environment.

LGC is collaborating with the University of Loughborough to improve understanding of the parameters affecting IMS measurement quality. The joint project also extends to:

- Evaluation of travelling wave IMS (TWIMS), again utilising the testosterone model
- Development of standards to improve the diagnostic accuracy of conventional IMS analysers.

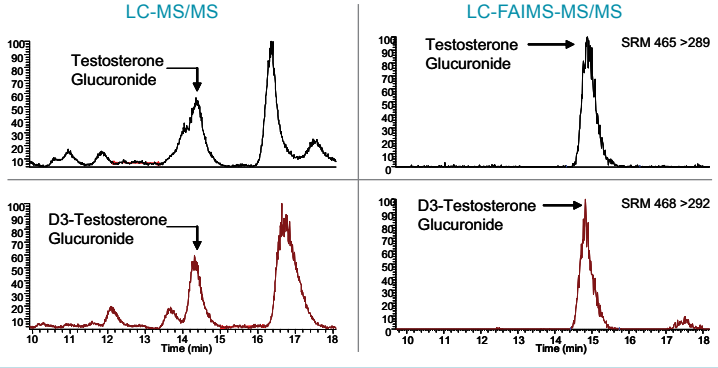


Figure 8:
Determination of testosterone glucuronide extracted from urine.
Top: by removing isobaric interferences, FAIMS improved confidence in the estimation of peak areas.
Bottom: the identity of the observed peak was confirmed by the behaviour of isotopically-labelled testosterone glucuronide, which had been added to the extract earlier in the analytical procedure.
Horizontal axes: LC run time.
Vertical axes: percentage of maximum peak height.
SRM: selected reaction monitoring was performed for the stated transitions in ionic mass/charge ratio

Strategic underpinning

Toward robust electrochemiluminescence detection

Recognising that the widespread acceptance of a novel measurement technology hinges on effective translational R&D, the NMO Chemical and Biological Metrology (ChemBio) programme[5] is funding the evaluation of promising immunoassay platforms. The latest of these is electrochemiluminescence (MSD™ ECL), in which an electrode is chemically coupled to the emission of a characteristic red light when the substance under test is present. This operating principle promises to enhance assay performance by constraining measurement to the region near the electrode and avoiding the need for incoming light.

Building on an earlier proof of principle for the detection of walnut protein in chocolate, LGC is working to widen the valid application of MSD™ ECL (Figure 9). The central issues are to establish comparability with other assay platforms, and to provide confidence in the measurement of real samples. Quite apart from how much of the substance under test they contain, there are significant compositional differences from sample to sample in most fields of analytical measurement, and science must find a way to ensure that these variations do not interfere unduly with the assay results. To tackle this issue, LGC is developing a normalisation protocol.

One way forward is to measure suitable control materials alongside each set of samples. It is desirable to choose control materials that respond to many forms of sample-to-sample variation, and so can be used flexibly. LGC selected six proteins to represent a broad spectrum of possible analytes, taking into account molecular weight, isoelectric points and structural variation. Protein concentrations were chosen to cover the wide (10^6-fold) dynamic range of the technique. This control set was successfully applied to the ECL monitoring of human ovarian cancer progression.

Traditional techniques for cell surface profiling, such as flow cytometry, can consume several million cells. The feasibility of reducing cell numbers was explored by detecting surface proteins on cultured mammalian cell lines using MSD™ ECL technology. This method has broad applicability to cell-based studies given that the expression profiles of selected surface markers may serve as a cell quality indicator prior to any downstream application. Proof of concept studies showed selected surface protein detection, using only 10s of cells for a typical high throughput platform assay.

We expect the range of ECL applications to expand, with the potential for further assays for food allergens, contaminants and biomarkers on the horizon.

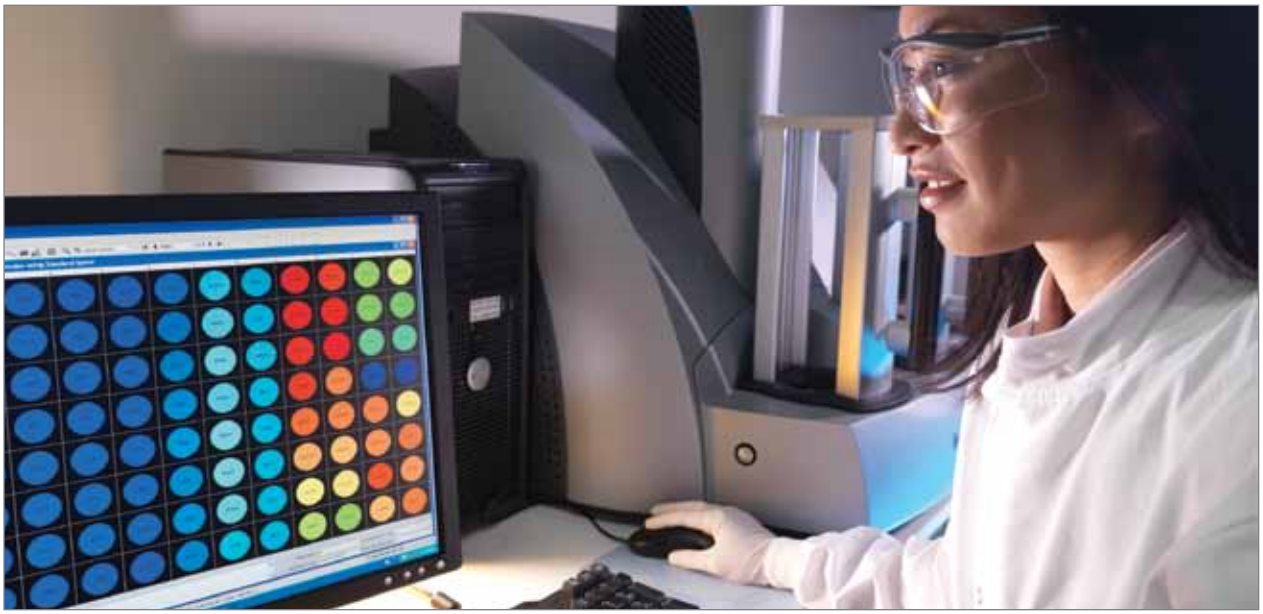


Figure 9: Susan Pang is developing normalisation models to enable wider use of enhanced assay platforms, such as Meso Scale Discovery's Sector Imager 6000

[5] *www.nmschembio.org.uk*

5 The wider advisory function

The Government Chemist works to foster the scientific underpinning needed for effective policy, standards and regulation through

- Dialogue and debate
- The development of scientific advice
- Partnership and networking activities.

The wider advisory function

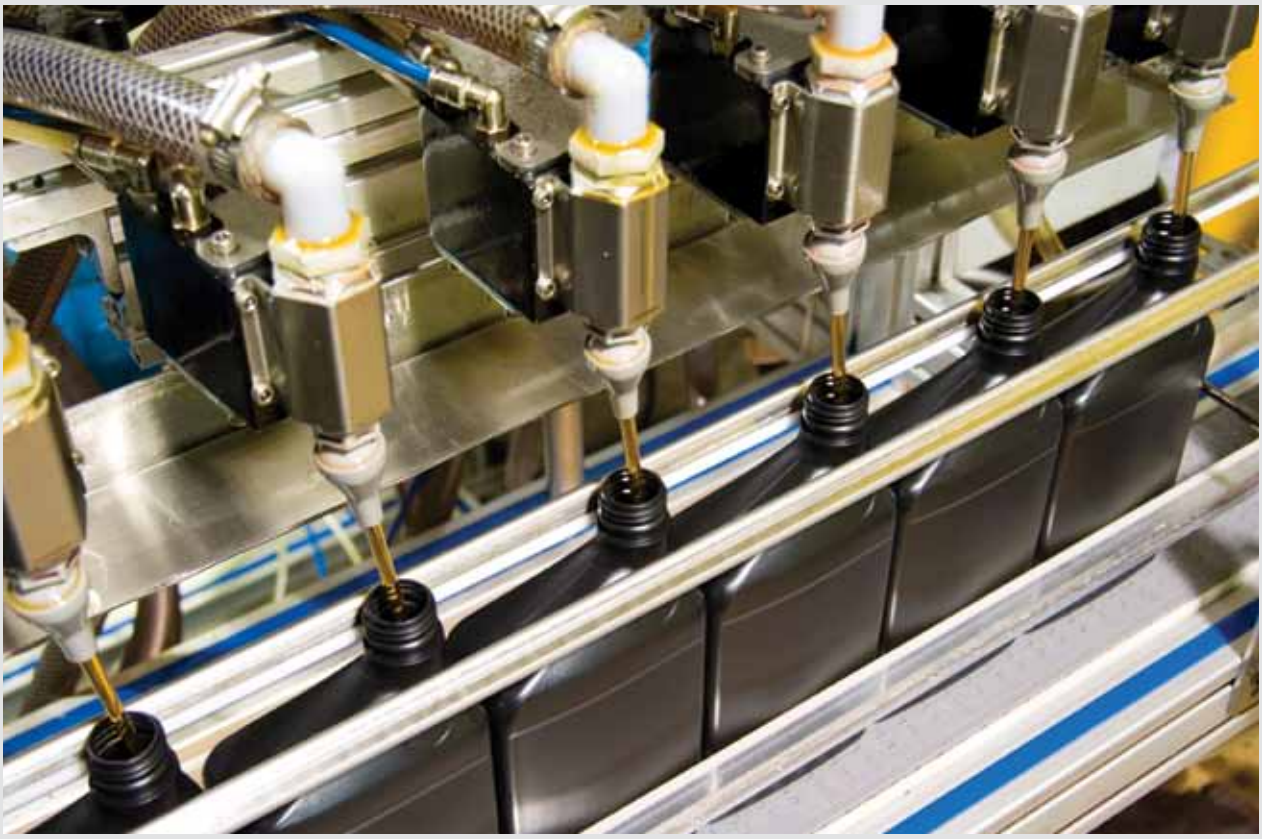
The benefits of measurement and effective regulation

Across Government and society, there is growing awareness that science and innovation are as necessary for sustained economic growth as in responding proactively to the great environmental and demographic challenges of our century. This year, alongside advice on specific analytical methods and related regulation, we contributed to public dialogue at a more strategic level, primarily to build understanding of the part played by analytical measurement in effective regulation and in securing wider benefits through policy, standards and legislation founded on sound science (Box 2). It may be of interest to collate some of the underlying themes:

- Measurement science is a truly objective, reliable and credible policy making tool. Modelling techniques can be valuable, but they should be used judiciously, under the watchful eyes of the relevant experts, and adequately underpinned and benchmarked by real-world measurement
- Regulatory and technical guidance for businesses, particularly SMEs, needs to set out clear criteria for deciding when measurement is required. The costs of testing need to be factored into regulatory impact assessments
- As regulation expands to cope with emerging technologies and markets, the demands on measurement science increase. Innovative methodologies will also be needed to develop, implement and enforce solutions to global challenges such as food security and the mounting environmental impact of increasingly complex pollution trends. The case may be growing for a more visible and coordinated way of keeping pace with these pressures. At least, resources for sampling and analysis performed on behalf of regulatory enforcement authorities need to reflect changing requirements.

Box 2: Our public consultation responses highlighting strategic issues or advice

All Party Parliamentary Group on Food and Agriculture for Development	Parliamentary inquiry into the UK's role in tackling the challenge of global food security until 2050
DECC	Amendments to The Offshore Chemicals Regulations 2002 and The Offshore Petroleum Activities (Oil Pollution Prevention and Control) Regulations 2005
Defra	Secondary legislation for England and Wales under the Marine and Coastal Access Bill: Part 4 Marine Licensing
Food Standards Agency	Draft guidance on legal compliance and best practice for business documentation - materials and articles in contact with food
	Review of the FSA regulatory framework
	The draft Contaminants in Food (England) Regulations 2009
	The Food Standards Agency Strategy for 2010 to 2015
House of Commons Science and Technology Committee	Bioengineering
House of Lords Science and Technology Committee	Setting science and technology research funding priorities
Royal Society	The Fruits of Curiosity: science, innovation and future sources of wealth



Sound science for REACH compliance

We have followed the progress of the REACH Regulation[6] from its formative stages, aiming to clarify and communicate the measurement implications. By 30 November 2010, companies producing or importing high tonnages of chemicals, together with those responsible for certain potentially high-risk substances, must submit a detailed registration dossier to the European Chemicals Agency (ECHA). The dossier will need to include a scientifically valid substance identity, as well as data on hazard, risk and use - the credibility of which also depends ultimately on analytical science.

In March, we updated our advice on REACH registration, this time aiming to help companies align each of their products with an appropriate substance information exchange forum (SIEF)[7]. In keeping with the wishes of our stakeholders, this update was informed by case studies drawn from four groups of substances - dyes, reactive organometallic products, surface-active agents, and silicon compounds - chosen to explore a wide range of measurement issues, and developed in consultation with industry.

Key issues include:

- Each SIEF submits a joint specification for one REACH substance to ECHA. SIEF members also submit individual specifications
- It is helpful if all affected companies can agree on commissioning analytical work and, in some circumstances, to be bound by the results
- Decisions need to be informed by fit-for-purpose measurements, that are trusted and meaningful within and between related SIEFs
- Measurement alone will not determine SIEF membership; chemical hazard is also a consideration. But for this reason, quantifying potentially hazardous impurities or isomers can be critical
- Because various aspects of REACH will demand measurement data, it may be cost-effective to carry out - or, as a minimum, plan and schedule - the analytical work at the outset, ensuring that the scope and rigour take account of later compliance points.

[6] Regulation (EC) No 1907/2006 *Concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals*, as amended

[7] Analytical issues relating to chemical substance definition under REACH: *www.governmentchemist.org.uk/Publications.aspx?m=77&amid=730*, with Supplement on dyes: *www.governmentchemist.org.uk/Publications.aspx?m=77&amid=731*

The wider advisory function

One giant leap

The Government Chemist had coordinated events on the analytical implications of REACH in Runcorn (2006), London (2007) and Huddersfield (2008). This year, based on our understanding of the way chemical manufacturers and users are clustered within the UK, we decided that the Humber region was a priority venue. We had learnt that coordinating events with regional partners could boost impact, hence we approached Humber Chemical Focus and the University of Hull, who agreed to collaborate.

As a result, in Hull on 12 November, and with barely a year in hand before the first REACH registration deadline, over 60 minds were concentrated wonderfully upon the theme *Better analysis: one giant leap toward REACH compliance*[8]. Industry specialists, scientists, regulators and other interested stakeholders met to share knowledge of the ground rules and find practical ways forward.

The Government Chemist's keynote address stressed that confidence in measurement data rests on understanding and controlling the inherent uncertainties. LGC presented a review of modern techniques for the characterisation of industrial chemicals ranging from clays and pigments to refinery products. Measurement has a variety of functions in connection with REACH registration:

- Given an industrial product with a well-defined composition, the aim is to identify the substance chemically and to quantify all the significant constituents

Glyn Hughes (Humber Chemical Focus), Derek Craston (Government Chemist) and Alan Handley (LGC) discuss the measurement implications of REACH

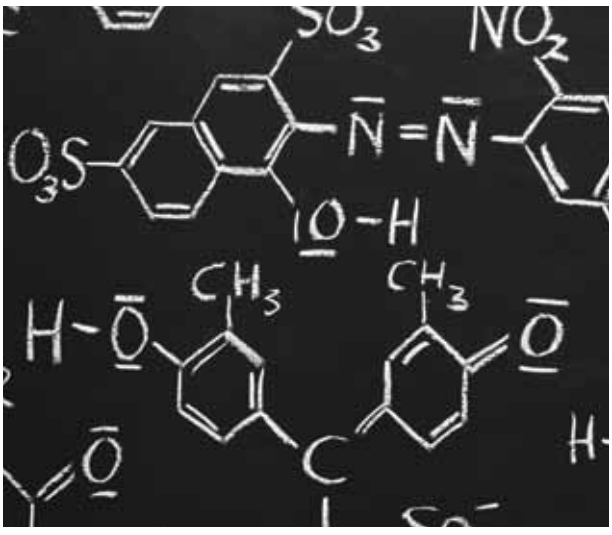
- But for substances of unknown or variable composition, complex reaction products or biological materials (UVCBs), fingerprinting and specialised probe techniques may be needed.

Alongside registration, the practical implications of the REACH authorisation and restriction processes are starting to bite. At Hull, Richard Hawkins, Head of the Environment Agency's Chemical Compliance Team, outlined the targeting and prioritisation of action to enforce ongoing restrictions on the marketing and use of chemicals, which now operate as part of REACH. LGC highlighted measurement strategies needed to support the efforts of supply chains to comply with the 0.1 % by mass limit on a growing number of substances of very high concern (SVHC) in manufactured articles.

Casting the net wider

LGC has a unique role as the Government Chemist's research and technology platform. As well as making available their own skills and knowledge, scientists across the laboratory help to create and develop the networks and partnerships needed to advise on increasingly challenging and complex analytical requirements. A proportion of this work is delivered through committee structures, for example the:

- RSC Atomic Spectroscopy Group
- Forensic Isotope Ratio Mass Spectrometry (FIRMS) Network
- IUPAC Advisory Subcommittee on Chemical Nomenclature and Structure Representation
- IUPAC task group on the determination of selenomethionine in selenized yeast supplements
- Human Genetics Commission (HGC).



[8] For details, go to *www.governmentchemist.org.uk/Events.aspx?m=93&amid=830*

Publications

Braybrook J, Realising point of care testing. Journal of Physics: Conference Series, 2009, 178, 12001

Brookman B, Finch H, Proficiency testing in the phytochemical industry - development of the PHYTAS scheme. Planta Medica, 2009, 75, 993

Burns M (editor), EU Co-Extra, Procedure for the experimental design and validation of novel methods and guidelines for data processing, method validation and good data handling practices. EU Sixth Framework Programme, project number 007158, 2009

Burns M, Sanders R, Burrell A, Strawberry and raspberry fruit differentiation using the Agilent CE 2100 Bioanalyzer, Agilent Technologies application note 5990-3327EN (2009)

Colwell P, Walker M, Axford I, Crane J, Jelly mini-cups: evaluation of a choking hazard, a case study from the Government Chemist's Programme. Fourth International Symposium on Recent Advances in Food Analysis, 2009, A-39, 171

Colwell P, Walker M, Gray K, Detection of animal remains in an organic cattle feed. Fourth International Symposium on Recent Advances in Food Analysis, 2009, J-35, 477

Ellison SLR, Performance of MM-estimators on multi-modal data shows potential for improvements in consensus value estimation. Accreditation and Quality Assurance, 2009, 14, 411-19

Ellison SLR, Barwick VJ, Duguid Farrant TJ, Practical statistics for the analytical scientist - a bench guide. Royal Society of Chemistry, second edition, 2009

Encheva V, Shah HN, Gharbia SE, Proteomic analysis of the adaptive response of *Salmonella enterica* serovar Typhimurium to growth under anaerobic conditions. Microbiology, 2009, 155, 2429-41

Gale N, Debenham P, French DJ, Howard R, McDowell DG, Brown T, Oligonucleotides and uses thereof. International patent publication number WO/2009/053679, 2009

Gaunt W, Whetton M, Regular participation in proficiency testing provides long term improvements in laboratory performance: an assessment of data over time. Accreditation and Quality Assurance, 2009, 14, 449-54

Goenaga-Infante H, Borrego AA, Peachey E, Hearn R, O'Connor G, Barrera TG, Ariza JLG, Study of the effect of sample preparation and cooking on the selenium speciation of selenized potatoes by HPLC with ICP-MS and electrospray ionization MS/MS. Journal of Agricultural and Food Chemistry, 2009, 57, 38-45

Gray K, Walker M, Colwell P, Authenticity of fruit sauce in ice cream. Fourth International Symposium on Recent Advances in Food Analysis, 2009, J-13, 455

Gray K, Walker M, Patel I, Singh M, Colwell P, Persistence of peanut protein on hands and clothing. Fourth International Symposium on Recent Advances in Food Analysis, 2009, K-10, 504

Green FM, Stokes P, Hopley C, Seah MP, Gilmore IS, O'Connor G, Developing repeatable measurements for reliable analysis of molecules at surfaces using desorption electrospray ionization. Analytical Chemistry, 2009, 81, 2286-93

Hill S, Santamaria-Fernandez R, Accurate quantification of cadmium, chromium, mercury and lead in plastics for RoHS compliance using the Agilent 7500ce ICP-MS, Agilent Technologies application note 5990-5059EN (2009)

Juresa D, Entwisle J, Goenaga-Infante H, Simultaneous measurement of sulfur and selenium in NIST 1568a Rice Flour. Agilent ICP-MS Journal, 2009, 37, 3

Kaur-Atwal G, O'Connor G, Aksenov AA, Bocos-Bintintan V, Thomas CLP, Creaser CS, Chemical standards for ion mobility spectrometry: a review. International Journal for Ion Mobility Spectrometry, 2009, 12, 1-14

Le Goff T, Joseph B, Wood S, Development and accreditation to ISO/IEC 17025 calibration status of a melting point measurement facility for the UK. Journal of Thermal Analysis and Calorimetry, 2009, 96, 653-62

Le Goff T, Mazlum S, Wood S, Production of a Solvent Yellow 124 "euromarker" reference material certified for purity. Fuel, 2009, 88, 2025-31

Le Goff T, Wood S, Improvement of the traceability of reference materials certified for purity: evaluation of a semi-preparative high-performance liquid chromatography approach. Analytical and Bioanalytical Chemistry, 2009, 394, 2183-92

Publications

Mansuet-Lupo A, Henke J, Henke L, Blank C, Ernsting A, Kozlowski P, Rouger P, Van Huffel V, A paternity case with three genetic incompatibilities between father and child due to maternal uniparental disomy 21 and a mutation at the Y chromosome. Forensic Science International: Genetics, 2009, 3, 141-43

Moroz OV, Burkitt W, Wittkowski H, He W, Ianoul A, Novitskaya V, Xie J, Polyakova O, Lednev IK, Shekhtman A, Derrick PJ, Bjoerk P, Foell D, Bronstein IB, Both Ca^{2+} and Zn^{2+} are essential for S100A12 protein oligomerization and function. BMC Biochemistry, 2009, 10, 11

Peachey E, Cook K, Castles A, Hopley C, Goenaga-Infante H, Capabilities of mixed-mode liquid chromatography coupled to inductively coupled plasma mass spectrometry for the simultaneous speciation analysis of inorganic and organically-bound selenium. Journal of Chromatography A, 2009, 1216, 7001-06

Petroczi A, Naughton DP, Mercury, cadmium and lead contamination in seafood: a comparative study to evaluate the usefulness of Target Hazard Quotients. Food and Chemical Toxicology, 2009, 47, 298-302

Pritchard C, Quaglia M, Mussell C, Burkitt WI, Parkes H, O'Connor G, Fully traceable absolute protein quantification of somatropin that allows independent comparison of somatropin standards. Clinical Chemistry, 2009, 55, 1984-90

Santamaria-Fernandez R, Giner Martínez-Sierra J, Marchante-Gayón JM, García-Alonso JI, Hearn R, Measurement of longitudinal sulfur isotopic variations by laser ablation MC-ICP-MS in single human hair strands. Analytical and Bioanalytical Chemistry, 2009, 394, 225-33

Santamaria-Fernandez R, Hearn R, Wolff JC, Detection of counterfeit antiviral drug Heptodin and classification of counterfeits using isotope amount ratio measurements by multicollector inductively coupled plasma mass spectrometry (MC-ICPMS) and isotope ratio mass spectrometry (IRMS). Science and Justice, 2009, 49, 102-06

Schutte ME, Devonshire A, Bokhari M, Foy C, Przyborski S, Marshall D, Increased expression of liver specific functional markers in primary cells grown in a 3D cell culture environment. Toxicology, 2009, 262, 26

Sheridan B, Harris N, New glossary of terms used in regenerative medicine: standardization continues to emerge as regenerative medicine matures. Regenerative Medicine, 2009, 4, 621-22

Walker MJ, Colwell P, Elahi S, Gray K, Lumley I, Food allergen detection: a literature review 2004-2007. Journal of the Association of Public Analysts, 2008, 36, 1-18

Walker MJ, McShane J, Burns DT, Canavan P, Flanagan A, A cross-border method validation for the determination of sweeteners in soft drinks. Journal of the Association of Public Analysts, 2009, 37, 1-14

Wheeler SF, Domann PJ, Harvey DJ, Derivatization of sialic acids for stabilization in matrix-assisted laser desorption/ionization mass spectrometry and concomitant differentiation of α2→3- and α2→6-isomers. Rapid Communications in Mass Spectrometry, 2009, 23, 303-12

Yang I, Kim S-K, Burke DG, Griffiths K, Kassir Z, Emslie KR, Gao Y, Wang J, Foy CA, Pardos-Pardos AC, Ellison S, Domann PJ, Fujii S-I, Park S-R, An international comparability study on quantification of total methyl cytosine content. Analytical Biochemistry, 2009, 384, 288-95

Glossary

aflatoxins	mycotoxins produced by certain *Aspergillus* moulds that can grow on food or feed unless it is properly stored
analyte	constituent or property which we desire to determine by analysis of samples
APA	Association of Public Analysts
bioengineering	the application of engineering principles to biology and medicine
BIS	Department for Business, Innovation and Skills
BSI	British Standards Institution
capillary electrophoresis	family of high performance techniques that use narrow-bore fused-silica capillaries to separate charged substances in an electric field
CCQM	Consultative Committee for Amount of Substance (international body for metrology in chemistry)
CEN	Comité Européen de Normalisation (European Committee for Standardization)
chiral	resulting in a distinct chemical structure when reflected, as if through a mirror; everyday analogies are left and right hands or screw threads
coning and quartering	dividing a particulate sample by repeatedly piling it into a conical shape, flattening out, splitting into four, and combining the opposite quarters
CRL	Community Reference Laboratory
DECC	Department of Energy and Climate Change
Defra	Department for Environment, Food and Rural Affairs
derivatisation	chemical modification of a substance, typically without changing its core structure, for example to facilitate measurement
determination	we use this term broadly, to mean qualitative analysis (detection or identification), quantitative measurement, or both
digital PCR	PCR variant based on determining presence or absence of a target DNA sequence in each of many small subsamples
dry ashing	strong heating of an organic material such as a food sample, with oxygen present but without added water, resulting in a mineral residue
ECHA	European Chemicals Agency
EFSA	European Food Safety Authority
electrochemiluminescence	luminescence produced by electrode reactions (IUPAC definition)
ELISA	enzyme-linked immunosorbent assay (a type of immunoassay)

Glossary

ESI	electrospray ionisation: droplets emerging from a fine needle evaporate and break up in an electric field. Dissolved substances are released as ions
EU Co-Extra	the largest ever EU Framework project aimed at evaluating the coexistence of GM and non-GM commodities in the food and feed supply chain
FCO	Foreign & Commonwealth Office
fingerprinting	comparison with data from samples of known identity, to seek a match
flow cytometry	counting and characterisation of individual cells or particles which are presented to the measuring instrument in a stream of fluid
FSA	Food Standards Agency
GC-MS	gas chromatography-mass spectrometry
genome	one full set of an organism's DNA, containing one copy of each gene
genotoxic carcinogen	substance which can damage genetic material and cause cancer. Regulation (EC) No 1881/2006 *setting maximum levels for certain contaminants in foodstuffs* implies that there is no concentration below which a genotoxic carcinogen may be considered safe
hydrolysis	chemical breakdown or transformation of a substance by reaction with water
IAC	immunoaffinity clean-up/chromatography: isolates a substance by means of its reaction with antibodies
ICP-MS	inductively coupled plasma mass spectrometry – a modern technique for determining the chemical elements in a sample
IDMS	isotope dilution mass spectrometry; a technique capable of outstanding accuracy
immunoassay	measures or detects a substance by means of its reaction with antibodies
ion mobility spectrometry (IMS)	size-related separation of ions accelerated through gas by an electric field, with ToF measurement
ion trap	device for spatially confining ions using electric and/or magnetic fields. These fields can be varied to eject ions below a chosen m/z. The remaining ions can be fragmented and/or scanned out of the trap for m/z measurement
IRMM	JRC Institute for Reference Materials and Measurements
IRMS	isotope ratio mass spectrometry; separates and measures isotopes of a constituent element to help trace sample history
ISO	International Organization for Standardization
ISO/IEC 17025	the international standard *General requirements for the competence of testing and calibration laboratories*
isobaric	having the same mass (therefore not differentiated by simple MS)

Glossary

isoelectric point	pH at which a molecule bears no overall electric charge
isomer	one of a pair or group of molecules with the same elementary composition, but differing in structure (topology or spatial distribution of the atoms)
IUPAC	International Union of Pure and Applied Chemistry
JRC	European Commission Joint Research Centre
LACORS	Local Authorities Coordinators of Regulatory Services
LC	liquid chromatography
LC-MS	liquid chromatography-mass spectrometry
LC-MS/MS	liquid chromatography-tandem mass spectrometry
microsatellite marker	DNA containing consecutive repeats of a short sequence. The variety or species of origin can often be deduced from the total lengths of certain markers
mitochondrion	component of biological cells that contains maternally-inherited DNA
MS	mass spectrometry
MS/MS	tandem (two-stage) mass spectrometry; ions selected from the first analysis can be fragmented for further study in the second
multiplex	measuring a number of analytes at the same time
mycotoxins	toxins produced by moulds, which can grow on poorly stored food or feed
m/z	mass to charge ratio
NMI	National Measurement Institute
NMO	National Measurement Office
NRL	National Reference Laboratory
OCL	official control laboratory
organometallic	any species of chemical containing a carbon atom bound directly to a metal atom
PCR	polymerase chain reaction, a technique used to amplify DNA sequences so that they can be identified
peptide	chain consisting of amino acids (the chemical building blocks for proteins); may be formed by fragmenting a protein
photostimulated luminescence	used to test whether a sample has been exposed to ionising radiation. Electrons trapped on irradiation and later released by light of a suitable wavelength are detected optically

Glossary

proficiency testing	analysis of portions of an independently prepared sample by a number of laboratories, and assessment of their performance from the results returned
Public Analyst	analytical scientist appointed under statute by UK local authorities to provide an official food or feed control function and scientific advice for the enforcement of many acts of Parliament
quadrupole	comprises four parallel rods, electrified in such a way as to retain or transmit ions of a given mass to charge ratio
REACH	Regulation (EC) No 1907/2006 *Concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals*, as amended
real-time PCR	determination of DNA sequences as they are generated by PCR amplification
referee function	duty of the Government Chemist under acts of Parliament to provide impartial analysis in the resolution of disputes relating to the enforcement of regulation
RSC	Royal Society of Chemistry
SEO	supplementary expert opinion in the context of Regulation (EC) No 882/2004 *on official controls*, Article 11(5)
SIEF	REACH substance information exchange forum
SME	small and medium-sized enterprise
surface-active agent	substance, such as a detergent, emulsifier or wetting agent, that functions by reducing surface tension
thermoluminescence (TL)	used to determine whether a sample has been exposed to ionising radiation. Electrons trapped on irradiation and later released by heating are detected optically
ToF	time of flight: the time taken for particles such as ions to travel a fixed distance is measured, and used to identify them
traceability	the property of the result of a measurement or the value of a standard whereby it can be related to stated references, usually national or international standards, through an unbroken chain of comparisons all having stated uncertainties (ISO International Vocabulary of Basic and General Terms in Metrology, 1993)
UKAS	United Kingdom Accreditation Service
uncertainty	parameter, associated with the result of a measurement, that characterises the dispersion of the values that could reasonably be attributed to the property being measured
vCJD	variant Creutzfeldt-Jakob disease, a rare and fatal human neurodegenerative condition

Governme

Setting standards in analytical science

Queens Road, Teddington, Middlesex TW11 0LY, UK
Tel: +44 (0)20 8943 7000 Fax: +44 (0)20 8943 2767
www.lgc.co.uk

2405/TK/0410