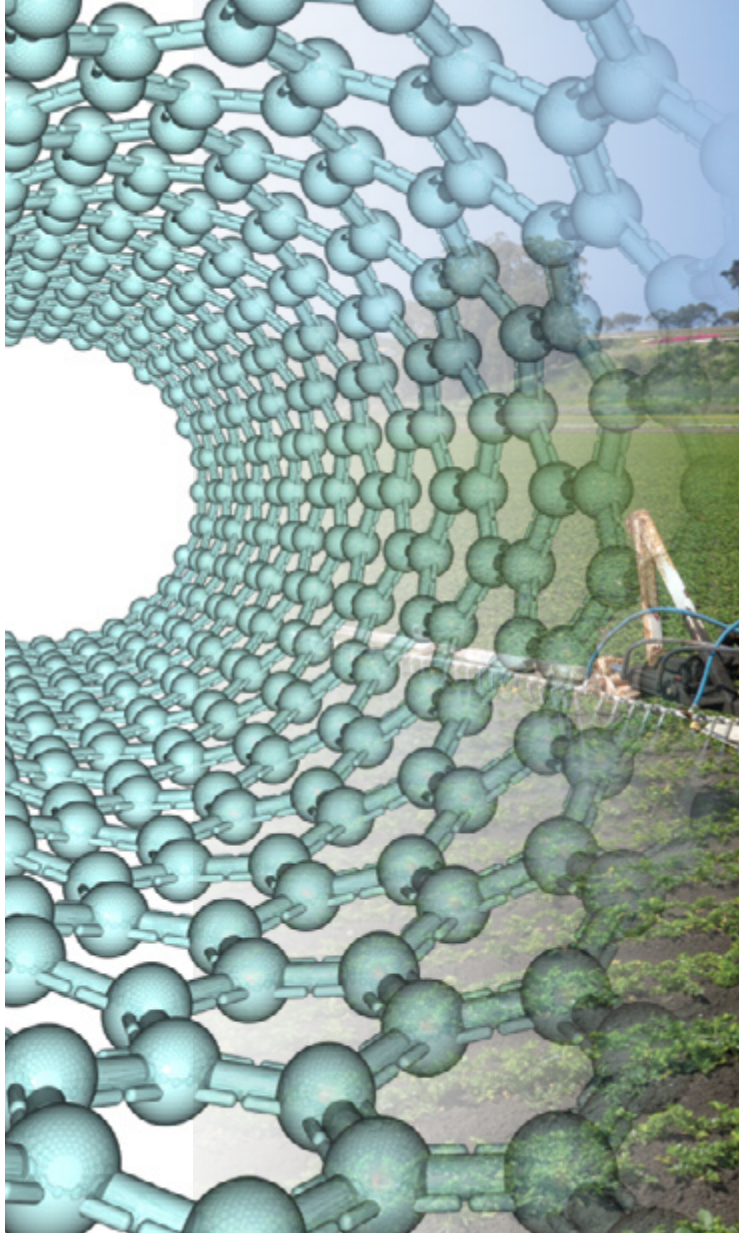


National Measurement Office

Government Chemist

Review 2012

the referee function adds value in the complex areas where global trade, measurement science and the law interact

Contents

Foreword

Government Chemist reviews seek to provide an annual update of our activity in the context of important issues of the time. Last year, for example, we described the Government Chemist Function in terms of its impact in assisting efficient and fair regulation against the backdrop of the “red tape challenge” and other efforts in the UK to reduce regulatory burden on industry. In this review we turn our focus to innovation – now well recognised as critical in supporting a sustainable and growing economy and buoyant food and agricultural industries.

Sound and innovative science has always been at the forefront of the delivery of our statutory role as a source of technical appeal in dispute resolution. Working with the best available validated technology provides confidence to industry, regulators and the legal system in the data and interpretation that we provide. This has been particularly so with the complexity of some of our recent case work described within section 2. Issues such as GM events in imported rice and leaching of formaldehyde into food from various forms of kitchenware required careful thought in both the technology applied and the design and control of associated methods. As ever I am indebted to the quality of the scientific team that diligently delivered this work.

I also acknowledge the endeavours of my research and advisory teams that developed techniques to meet the demands of current and predicted new issues in food and agricultural regulation as well as supporting industry and Government in scientific assessment and interpretation. Some of the research work is highlighted within section 3 of this review and covers areas as diverse as nanotechnology in food and cell based therapy. Continuing with the theme of innovation, we were also pleased this year to work with the Food Standards Agency, the Department of Environment Food and Rural Affairs, the National Measurement Office (NMO), LGC Standards, Campden BRI, Leatherhead Food Research and the Association of Public Analysts Educational Trust to organise and deliver a successful biannual scientific conference covering important topics such as food authenticity and the measurement of allergenic proteins.

Innovation rarely succeeds in isolation and of course requires adequate resources. I am grateful, therefore, for the continued support received from the NMO, and to the members of the Government Chemist Working Group who gave their valuable time to provide well informed advice to our work programmes.

I hope that you find the contents of this review useful and interesting. I will certainly appreciate any feedback you have on any aspect of our work, and on the future direction of our research and capability building activities.

Derek Craston
BSc PhD FRSC
Government Chemist

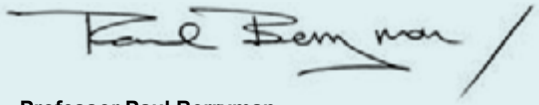
Note from the Government Chemist Working Group (GCWG)

I am very pleased to contribute to the 2012 Government Chemist Review as Chair of the NMO Government Chemist Working Group, GCWG.

GCWG plays a key role in the governance of the Government Chemist Programme. The working group is made up of stakeholders from industry, regulatory and policy officials, enforcement officers and Public Analysts and academics. We review quarterly progress reports and meet twice a year to provide independent scrutiny of referee casework, research and advice given by the Government Chemist. We also contribute to reformulation of the Programme on a rolling three year basis.

The diversity of measurement techniques, referee cases, advisory work and research described in this review is indeed impressive and its dissemination is regarded as helpful by all stakeholders. As Chief Executive of a leading food research organisation I appreciate only too well the ever increasing complexity of measurement science and the interpretation of findings in this area. Thus the safeguards offered by the Government Chemist to underpin the probity of official controls continue to add value.

In the context of the diversity and complexity of the scientific and legal issues arising in our deliberations I am especially grateful for the continuing hard work and dedication of my colleagues in the working group. It is also gratifying to note that our input and advice is appreciated and regarded as helpful both by the National Measurement Office and the Government Chemist.



Professor Paul Berryman
BSc, MChemA, PhD, MBA, FRSC, CSci
Chair, Government Chemist Working Group

1 Remit

The function of the Government Chemist was established 170 years ago to help protect the public from fraud, malpractice and harm and today this role continues. The Government Chemist uses – as has always been the case – up-to-date and authoritative measurement procedures and interpretative skills to act as a fair and independent arbiter to resolve disputes, continue to provide public protection and to contribute to effective and efficient regulatory enforcement in industrial sectors where chemical measurements are important. There is a continued need to develop these measurement techniques within our own laboratories and in collaboration with other organisations in order to respond to the potential future issues which may involve the Government Chemist.

The Government Chemist fulfils two functions, funded by the Department of Business, Innovation and Skills (BIS).

Statutory function

The Government Chemist has a science-based statutory function comprising duties prescribed under seven acts of Parliament. These duties (Box 1 on page 7) centre on public protection, safety, health, value for money, and consumer choice. Much of our work relates to scientific dispute resolution – 'referee analysis'. Based on independent measurement and expert opinion we resolve disputes between regulators and businesses, often without redress to legal process, thereby reducing the burden on the public purse. In these cases, the stakes can be high, so the credibility of the referee rests on first-class science, which is underpinned by the assignment of our home laboratory, LGC, as the UK's designated National Measurement Institute for chemical and bioanalytical measurement.

Legislation covering the food, agriculture and medicinal products sectors, where the safety of the consumer is of prime importance, contains equivalent provisions for the taking of official samples and subsequent analysis.

There are several routes for referral to the Government Chemist. The main route is The Food Safety (Sampling and Qualifications) Regulations 1990, which are invoked for many of the dispute resolution activities we undertake. These regulations state that test samples are divided into three parts by an authorised officer. The enforcement authority and trade party each receive one of these samples to perform independent analyses, while the third part of the sample is retained in case there is a dispute requiring the Government Chemist to act as referee.

In some circumstances a trader may ask for a referral to the Government Chemist without having their own portion of the sample analysed (a procedure known as 'supplementary expert opinion' - described on our website). For businesses, a successful appeal to the Government Chemist may avoid the effects of penalties prescribed under criminal law, potentially expensive compliance actions and, most seriously, loss of reputation and goodwill. Lastly, the referral sometimes comes from the court itself, with proceedings suspended pending the outcome.

Of course, when the Government Chemist's findings confirm those of the enforcement authority, the appropriate action to protect the public can proceed with all the more authority. But, regardless of the outcome, the scientific outputs of the case can be disseminated to all parties and the lessons of these can hopefully be learned to help reduce the possibility of recurrence. Dissemination of referee cases also takes place through scientific publications, seminars, workshops, training events and via our website, www.governmentchemist.org.uk.

► **Section 2 of this review looks at the year's completed referee cases.**

Unsurprisingly, the need for referee analysis often arises in novel or complex areas. Consequently, we need to look for emerging analytical issues and by targeting our R&D in these areas; we hope to be able better to respond to demands, as well as making the appropriate analytical measurements in shorter timescales. Dissemination of the measurement capability developed to stakeholders has led to the prevention as well as the resolution of disputes.

► **See Section 3 for an overview of R&D activities**

Advisory function

The Laboratory of the Government Chemist was originally founded in 1842 with the remit to detect adulteration of tobacco on behalf of HM Customs & Excise. It continued to develop after this time to become established for nearly half the 20th Century as a free-standing central department with a broad responsibility for the investigation and analysis of a wide range of samples and problems on behalf of other government authorities.

The Laboratory was privatised in 1996, whereupon an agreement between the Secretary of State for Trade and Industry and LGC was signed which underpinned the continuity of the broader public functions by appointing the Government Chemist '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'. This agreement is still relevant and highlights the importance of chemical and biochemical measurements in underpinning the UK economy. This function continues to be important as new technologies come on-stream and advice is needed to ensure these are adopted appropriately.

The principal mode of delivery for the advisory function is by responding to government calls for advice or published consultations, where there is a significant analytical science dimension. These responses provide relevant information specifically to the department or body issuing the consultation, and also to a broad range of stakeholders who have an interest in regulatory compliance and the associated measurement implications of this. Consultation Responses are published through the Government Chemist website. The advisory function also looks at emerging issues involving new regulation and analytical measurements and addresses these by means of small targeted projects or by publication through the Government Chemist blog[1].

► **See Section 3 for more about the wider advisory function.**

Governance

The Department for Business, Innovation and Skills (BIS) funds a programme to enable delivery of statutory casework, scientific advice and any work and research necessary for the ongoing effectiveness of the Government Chemist's functions. Within BIS, responsibility for both the Government Chemist and the wider UK National Measurement System rests with the National Measurement Office (NMO).

Arrangements are in place to ensure that the Government Chemist programme is delivered competently, and that scientific standards, impartiality, transparency and integrity are maintained. LGC has in place rigorous structures and procedures to ensure no conflicts of interest arise between work carried out under the statutory function and its commercial food analysis activities. The Government Chemist Working Group, GCWG, also plays a key role in the governance of the Government Chemist Programme.

The group provides the necessary independent scrutiny of the programme and offers advice to the NMO regarding future priorities. The GCWG meets twice a year to oversee and discuss the delivery, planning and quality of the programme, and also has oversight of the scientific standards of the programme. The GCWG is tasked by the NMO to advise on:

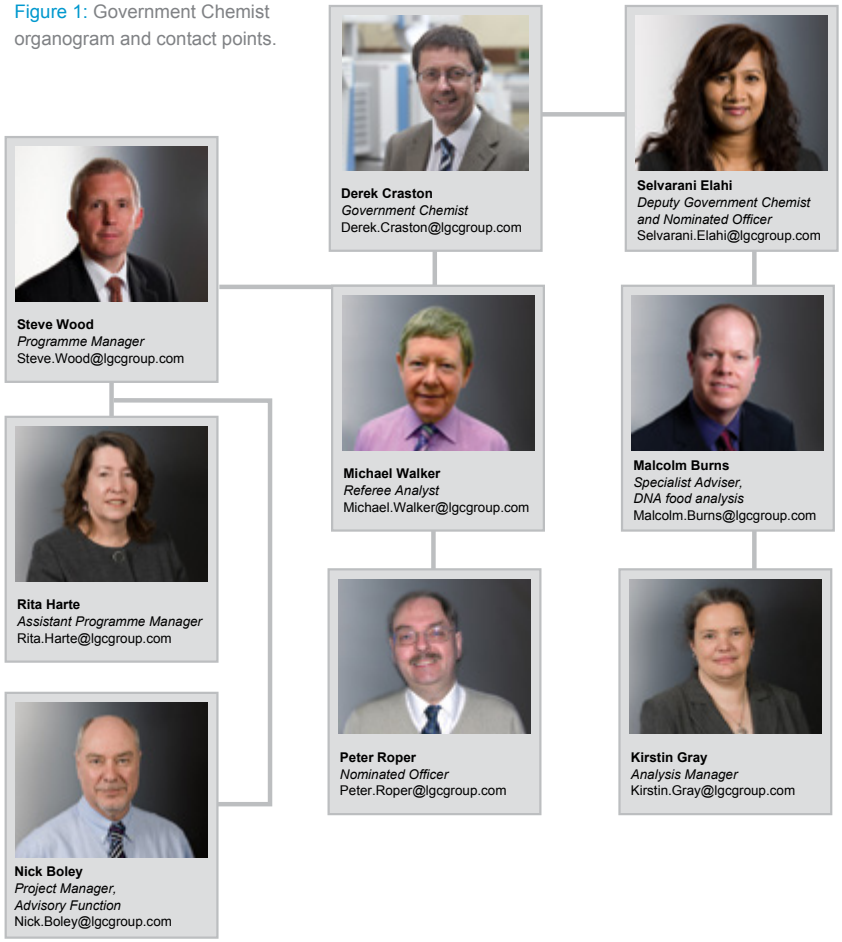
- The effectiveness and impact of the Programme in providing an independent, expert service to resolve disputes between food control authorities and food traders on analytical results and their interpretation;
- The medium to long term Government Chemist research and development work aimed at preventing disputes arising;
- The progress of the current projects in meeting technical milestones and targets; and
- The formulation and prioritisation of new projects to maintain and develop the capabilities needed to discharge the GC functions (i.e. Capability Building, Knowledge Transfer, Regulatory Foresight and Statutory Analysis).

The GCWG comprises representatives of regulatory and enforcement bodies, industry, trade associations and academia, with a broad range of backgrounds, skills and interests.

Readers will note that the front cover of the 2012 review now includes the Board of Trade crest. This is as a result of discussions with the Cabinet Office regarding branding of the Government Chemist as part of the Government's consistent branding initiative.

[1] http://governmentchemist.wordpress.com/

Figure 1: Government Chemist organogram and contact points.



National Measurement Office

The current Government Chemist programme

The current Government Chemist programme, covering 2011-2014, commenced in April 2011. The programme reflects the prioritisation exercise carried out by the GCWG, and is similar in structure and themes to the 2008-2011 programme:

- Intelligence gathering: horizon-scanning projects on the scientific implications of policy development, emerging legislation, changes to existing legislation and enforcement trends
- Capability building: innovative and relevant R&D which aims to reflect potential needs for future casework under the Government Chemist's statutory role
- Statutory activities: work carried out in relation to individual cases that are referred to the Government Chemist under his statutory function as defined in Acts of Parliament
- Knowledge transfer: improved dissemination of regulatory and analytical developments to a wide range of stakeholders, to stimulate improvement of standards of measurements, the understanding of the regulatory environment and to help industry to innovate concerning new products and processes.

Work has already commenced to develop the next Government Chemist programme, due to operate from 2014 to 2017, and to identify areas where activity should be targeted. The planning for the new programme is also looking at effective ways to improve communications through the modern mechanism of social media.

People

LGC staff who directly support the Government Chemist function have clearly and independently defined roles (Figure 1). Within this framework, there are particular requirements for the management of statutory casework:

- Nominated officers, one of whom holds the requisite statutory qualification[2], have overall responsibility for case supervision. They prepare and sign Government Chemist certificates of analysis
- Only the Government Chemist or Deputy, once satisfied that the case has been properly completed, may countersign.

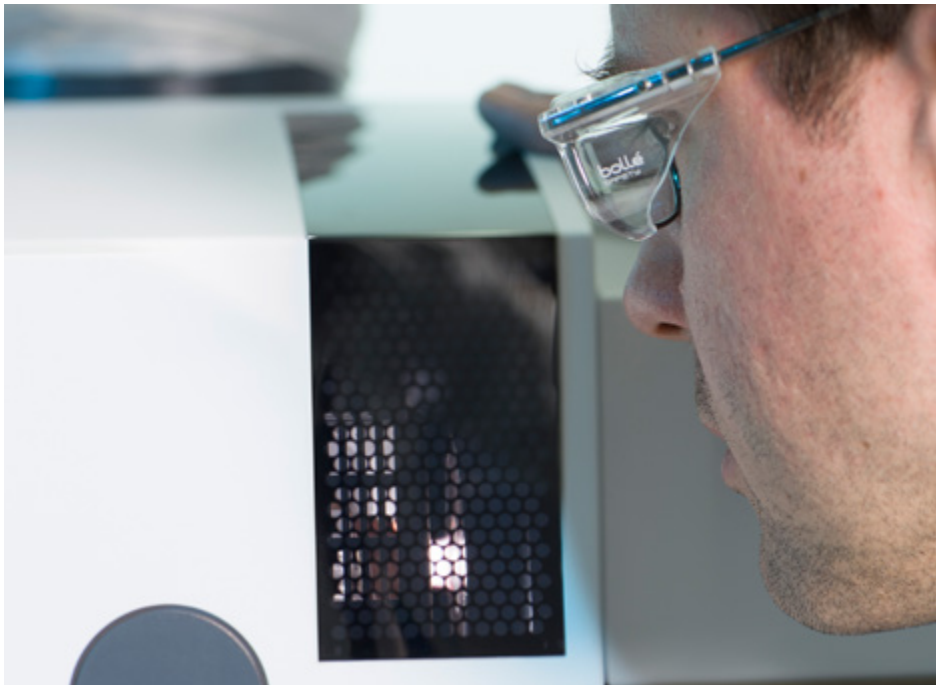
The staff who carry out work under the Government Chemist's statutory function continually demonstrate their competence through participation in an extensive variety of appropriate proficiency testing schemes and collaborative studies. The diverse nature of LGC's scientific activities therefore leads to a wide range of skills and specialisms being available in-house. Many of the staff who are involved in delivering the programme have carried out research and development work, often of an internationally-collaborative nature, which gives them the capability to contribute positively and efficiently to their work.

[2] All work is overseen by Michael Walker, a nominated officer holding the statutory MChemA qualification

Collaboration

The work we carry out within the Government Chemist programme is very broad; but we are not always fully equipped to undertake everything we consider to be appropriate within the programme. Consequently we are always happy to collaborate with stakeholders and are looking constantly to seek new stakeholders to become involved in our work with the intention of being better able to respond to the future challenges of potential casework. Our work on allergens continues to be a good example of this as we collaborate with patient groups and, through the University of Manchester, with academic partners, the food industry, regulators and allergen detection kit manufacturers. Thus our research projects aim to develop scientific capabilities which will benefit public health, safety and well-being, and the wider scientific community, including those UK manufacturing industries which depend on sound analytical measurement and understanding of regulations.

If you would like to get involved with any aspect of our work, or for more information on our work, please contact us at Government.Chemist@lgcgroup.com or go to the website (www.governmentchemist.org.uk).



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[1]

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 (England) Regulations 2012

Materials and Articles in Contact with Food (Scotland) Regulations 2012

Materials and Articles in Contact with Food (Wales) Regulations 2012

Materials and Articles in Contact with Food (Northern Ireland) Regulations 2012

Agriculture Act 1970

Feed (Hygiene and Enforcement) Regulations 2005

Genetically Modified Animal Feed Regulations 2004

Human Medicines Regulations 2012

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

Administrative Provisions Act (Northern Ireland) 1928

Government Chemist Regulations (Northern Ireland) 1928

[1] Due to be superseded in 2013

2 Science underpinning sound dispute resolution

Referee casework arises most frequently under the Food Safety Act 1990 or the Agriculture Act 1970.

Formal samples taken under statutory enforcement provisions are divided into parts for analysis on behalf of the authorities, the food and feed business operator (FBO) and, when required, the referee. During 2012, 14 cases were referred to the Government Chemist – 13 in connection with the Food Safety Act and 1 in accordance with the provisions of the Agriculture Act. Further information about some of these cases is presented later in this section.

The Referee function

Referee casework is a demand led service which has been at the core of the Government Chemist's function since 1875. It guarantees fair treatment for industry and enforcement alike by authoritative adjudication on disputes on analytical results or their interpretation in the food and feed official control system.

We maintain the even-handed credibility of this referee role by stringent governance of the function and painstaking analytical rigour. Our aim is to safeguard consumers, regulators, the agrifood sector and the courts from unwitting errors in measurement science.

Some of the problems that arose were in areas familiar to us, such as aflatoxins in imported food and vitamins and minerals in animal feed. But, interestingly, three issues, all in relation to imports, were presented that had not previously been appealed:

- questions on the migration of formaldehyde from melamine kitchen wear,
- allegations of GMOs in rice and
- a dispute on carbon monoxide in fish.

Analytical results must be interpreted in increasingly complex scientific legal and policy contexts, and as these new areas demonstrate, in an increasingly global supply chain.

When a referral is received we begin with a case meeting; the default analytical strategy is multi-replicate analyses on more than one day to provide a case specific measurement uncertainty. Analysis of certified reference materials, if available, blanks and spiked blanks is performed to provide a high level of analytical confidence. All significant analytical steps are witnessed by a second scientist, the resulting dataset is independently evaluated by statisticians, a certificate is drafted and reviewed by a qualified person, as defined in Food Safety (Sampling and Qualifications) Regulations, and finally the case file is brought to the Government Chemist, or Deputy, for review. If all steps are satisfactory the Government Chemist will allow the certificate to be released. Along with the high-end analytical equipment deployed these measures are aimed to give the food business owners, the courts and regulators the necessary assurance that the appellate function is discharged to the highest possible professional standards.

Formaldehyde migration from melamine kitchenware

The thermosetting plastic ”melamine” is used to manufacture a diversity of inexpensive food contact articles intended for repeated use. Melamine is a chemical (a monomer) which, when mixed with formaldehyde, forms melamine resin, a polymer. This resin is also referred to as simply melamine, and we will do so here. Articles made from melamine are used extensively in picnic sets and by children in the form of cups and plates, often printed with popular motifs, and in kitchenware such as bowls and ladles. In its native form the polymer is a polycondensation product of the monomers formaldehyde and melamine and residues of both may remain in the finished product although formaldehyde release appears to be hydrolysis rather than diffusion controlled. Thus both compounds are on the EU monomer positive list with specific migration limits[3].

Formaldehyde is an interesting example of a compound that occurs in food both from natural and man-made sources. Its toxicology is complex; it is known to be capable of sensitising some people to allergic contact dermatitis and there is evidence that it is a carcinogen.[4,5]

As a result of continuing reports of non-compliance with migration limits, including those for formaldehyde, Regulation (EU) No 284/2011 laid down conditions and procedures for the import of polyamide and melamine plastic kitchenware originating in or consigned from the People’s Republic of China and Hong Kong Special Administrative Region, China. The Food Standards Agency also highlighted the migration of formaldehyde in melamine ware in a National Coordinated Risk Based Food and Feed sampling programme 2011-12. In due course sampling and analysis at import led to three referee cases on disputed results for migration of formaldehyde in the early part of 2012. Two of the cases were for supplementary expert opinions (SEO) and one was a UK dispute.

The powers of the Government Chemist to act in relation to food contact materials derives from successive national measures[6] on Materials and Articles in Contact with Food implementing and enforcing a group of European Directives and Regulations designed to protect consumers’ health and remove technical barriers to trade[7]. The measures cover food packaging materials, cutlery and dishes, food processing machinery, food containers and materials and articles in contact with water for human consumption.

The analysis of the samples was informed by guidance issued by the European Reference Laboratory for Food Contact Materials and began with exposure of the plastic material at 70 °C for two hours to 3 % v/v aqueous acetic acid food simulant to mimic the worst case scenario in actual use. The work was very classical in nature, an iodometric titration against the primary standard potassium iodate being used to characterise a stock calibrant solution of formaldehyde. The analytical finish applied two well known reactions, one with chromotropic acid and the other with pentane-2,4-dione (acetylacetone) stoichiometrically to produce coloured reaction products for the spectrometric determination of migrated formaldehyde[8]. Since the test items were intended for repeated use, each item was exposed to fresh food simulant in three consecutive tests with formaldehyde concentrations reported from the third (final) exposure of each test specimen. In each instance three replicates were analysed alongside exposed food simulant spiked with formaldehyde and blank (unexposed) simulant. As is usual a case specific measurement uncertainty was derived and applied in appraisal of the results.

Several interesting issues of interpretation arose across the three cases.

Commission Regulation (EU) 10/2011 on plastic materials and articles intended to come into contact with food limits the transfer of formaldehyde from plastic materials to a maximum of 15 milligrams of formaldehyde per kilogram of food, mg kg^{-1}, applying the real surface to volume ratio in actual or foreseen use. A derogation, related to container volume, can reduce the numerical magnitude of the results by applying a surface to volume ratio of 6 dm^2 per kg of food. However, in a precautionary manner, the derogation does not apply to items for infants and young children. The packaging of the first of the cases bore text strongly suggestive of use for infants and young children. We therefore disapplied the derogation and the referee results, supporting those of the public analyst, were above the limit of 15 milligrams of formaldehyde per kilogram of food, mg kg^{-1} which comply with the criminal burden of proof. The consignment was refused entry into the UK.

[3] K. H. Lund, J. H. Petersen, 2006, Migration of formaldehyde and melamine monomers from kitchen- and tableware made of melamine plastic, Food Additives and Contaminants, 23, 948-955

[4] Lois Lehman-McKeeman, 2010, Paracelsus and Formaldehyde 2010: The Dose to the Target Organ Makes the Poison, Toxicol. Sci. 116, 361-363

[5] Hermann M. Bolt, Peter Morfeld, 2012, New results on formaldehyde: the 2nd International Formaldehyde Science Conference

[6] The Materials and Articles in Contact with Food (England) Regulations 2012, No. 2619, the Materials and Articles in Contact with Food (Scotland) Regulations 2012, No. 318, the Materials and Articles in Contact with Food (Wales) Regulations 2012, No. 2705 (W. 291) and the Materials and Articles in Contact with Food Regulations (Northern Ireland) 2012, No. 384

[7] European Commission, Food Contact Materials, http://ec.europa.eu/food/food/chemicalsafety/foodcontact/index_en.htm accessed 29.01.13

[8] According to CEN/TS 13130-23, Materials and articles in contact with foodstuffs – Plastics substances subject to limitation – Part 23: Determination of formaldehyde and hexamethylenetetramine in food simulants.

The second case proceeded in a similar manner but the results showed that of the four plates analysed, three exhibited migration of formaldehyde above the permitted maximum but one did not. Moreover, owing to item to item dispersion rather than analytical variance, the results straddled the limit as shown in Figure 2. Thus we could not interpret these results as a non-compliance to the criminal burden of proof. However Commission Regulation (EU) 10/2011 permits plastic materials and articles to be placed on the market only if they comply with certain conditions, which include good manufacturing practice as set out in Commission Regulation (EC) No 2023/2006. Hence we concluded that overall the sample failed to demonstrate compliance with good manufacturing practice by way of lack of consistency and control to ensure conformity with the rules applicable to them[9]. Again the consignment was refused entry into the UK.

In the last case on formaldehyde migration in 2012 we confirmed the public analyst's analytical results but differed on the interpretation of the way in which the analytical findings are calculated in relation to the surface to volume ratio and upheld the defence findings in the case. The consignment was therefore allowed onto the UK market.

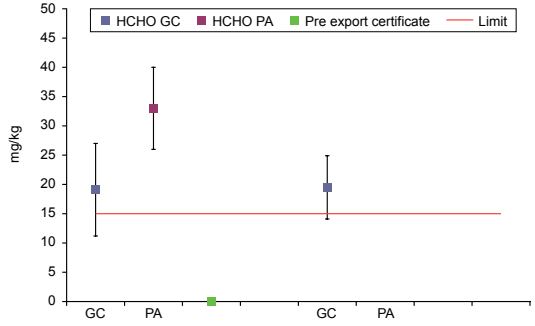


Figure 2: Graphical illustration of formaldehyde (HCHO) results in a referee case on food contact migration, GC = Government Chemist, PA = Public Analyst, CT = Chromotropic acid results, AcAc = Acetyl acetone results. Note the pre-export certificate result well below the limit.

Genetically Modified Organisms and rice

EU law[10] prohibits the placing on the market of genetically modified (GM) food unless it is officially authorised. Such an authorisation must demonstrate that the GM food does not have adverse effects on health or the environment and that it does not mislead the consumer. In addition the GM food must not differ from the food it is intended to replace to such an extent that its normal consumption would be nutritionally disadvantageous. Similar provisions apply to GM animal feed.

There are no genetically modified rice products authorised in the European Union[11] but from 2006 onwards some rice products originating in or consigned from China, were discovered to be contaminated with the unauthorised genetically modified rice Bt 63. The Chinese authorities took steps to control the presence of unauthorised GM rice, however unauthorised GM rice including other varieties continued to be found in rice imported into the EU. As a consequence, the EU requires rice imports from China to be accompanied by an analytical report demonstrating the absence of GM rice. From December 2011 all rice imports from China have been subject to inspection, sampling and analysis and in 2012 we began to see referrals of disputed results from such official sampling and analysis.

There are reportedly[12] some 25 genetically modified rice varieties that may be a source of contamination of rice products imported from China. It appears that no relevant details are currently officially available regarding full DNA sequence information for many of the GM rice varieties said to be produced in China. Accordingly, the normal recommended specific methods of analysis are limited and in the light of this Commission Decision 2011/884/EU requires screening tests[13]. The screening tests must be performed by real-time polymerase chain reaction, (PCR) according to the method published by the European Union reference laboratory for genetically modified organisms in food and feed (EU-RL GMFF) for certain generic genetic elements. GM plants are generally produced by

[9] We are grateful to Emma Bradley of FERA for suggesting that we explore this interpretation Using Real Time PCR, version of 21 December 2011.
[10] Regulation (EC) No 1829/2003 of the European Parliament and of the Council of 22 September 2003 on genetically modified food and feed
[11] Commission Decision 2011/884/EU Recital 8.
[12] European Reference Laboratory for Genetically Modified Food and Feed, EU-RL GMFF Guidance on the Application of P-35S, T-NOS and CrylAb/Ac Methods for the Detection of Genetically Modified Rice Originating from China Using Real Time PCR, version of 21 December 2011.
[13] Commission Decision 2011/884/EU Annex II Para 3

inserting a transgenic sequence that encodes for a desired trait into the host genome. The trait sequence is typically bounded by regulatory promoter and terminator sequences, some of the most common being the 35S promoter derived from Cauliflower Mosaic Virus (P35S) and the nopaline synthase terminator (TNOS) derived from *Agrobacterium tumefaciens.* Thus P35S and TNOS are useful screening targets together with a prevalent insect resistance trait sequence representing genes encoding for the genetically engineered *Bacillus thuringiensis* endotoxins CrylAb/Ac, globular protein molecules, which accumulate in crystalline form. The most common chemistries used to produce a signal downstream of PCR are the use of a specific fluorescent probe (TaqMan) or DNA binding (intercalating) fluorescent dyes (e.g., SYBR Green I). In SYBR Green chemistry the fluorescent dye binds to the minor groove of DNA, but may also bind to nonspecific PCR products and primer dimers. To address this, the first derivative of fluorescence against temperature is plotted to pinpoint the DNA fragment melting point (dissociation of the double stranded DNA, the melting curve). Based on this melting temperature, a direct property of the DNA fragment nucleotide content, it is possible to distinguish nonspecific fragments from specific PCR products.[14]

In general multi-day, multiple replicates of the samples are analysed by a specialist team of molecular biologists. Positive and negative controls are assayed (certified reference materials for Bt11, Mon810, LLRICE62; no-template aqueous controls; wild-type rice), and real-time PCR assays for a rice taxon-specific phospholipase D (PLD)[15]). Two real-time PCR instruments from separate manufacturers are deployed and interpretation of results is based both on instrument default automatic threshold settings and expert judgement of amplification curves and melting temperature plots. Where required, and applicable, confirmatory procedures are applied for example based on those of the GMO National Reference Laboratories of Germany.[16]

In total five GM cases were initiated in 2012 although one was abandoned by the applicant before substantial laboratory work had been carried out. Of the remaining four, three upheld the findings of the importers' laboratory in that no GM rice was detected. In one case the public analyst's finding of GM rice was upheld. Each case threw up different issues of interpretation of the analytical findings and dialogue is continuing on GM rice detection methodology, acknowledged to be analytically and interpretively problematic, with an importer and the laboratories involved.

Mycotoxins - aflatoxins

Aflatoxins are a chemically related group of genotoxic carcinogens derived from Aspergillus moulds, which pose a high risk to the safety of food produce. They remain prominent in casework with four cases in 2012 in each of which we upheld the public analysts' findings. Several cases generated extensive correspondence with the importers in which we explained in detail sampling and analytical aspects.

Nitrofurans

Once widely used as veterinary antibiotics, these compounds are now prohibited in food in the EU because they can cause cancer. Based on our experience in a series of referee cases in 2010 and 2011 when we overturned the majority of public analysts' findings we published advice on nitrofuran analysis on the Government Chemist website. As a result only one case was referred in 2012 and our findings upheld those of the Official Control Laboratory (Public Analyst).

Animal Feed

There have been many examples of food safety incidents originating from animal feed, hence regulation of feed should continue to be an important facet of enforcement activity. One referee case involving two official samples was referred in 2012. As in previous years the determination of vitamins A and E was at issue, together with copper. Our analyses upheld Official Control Laboratory (Public Analyst) findings.

[14] Sylvia R. M. Broeders, Sigrid C. J. De Keersmaecker, and Nancy H. C. Roosens, 2012, How to Deal with the Upcoming Challenges in GMO Detection in Food and Feed, Journal of Biomedicine and Biotechnology, Article ID 402418
[15] Mbongolo Mbella et al., (2011) "SYBR®Green qPCR methods for detection of endogenous reference genes in commodity crops: a step ahead in combinatory screening for Genetically Modified Crops in food and feed products" Eur. Food Res. Technol. 232:485-496
[16] Bundesamt für Verbraucherschutz und Lebensmittelsicherheit, Guideline detection of genetically modified rice 26 March 2012

Carbon monoxide in fish

Regulation No 1333/2008 of the European Parliament and Council of 16 December 2008 on food additives[17] implemented by the Food Additives (England) Regulations 2009 restricts the use of additives in foods to those included in the Community list. Carbon monoxide is not permitted to be added to food but is known to be used to enhance the colour of some fish, including fresh tuna. This effect arises because of the enhanced binding capacity of carbon monoxide to the ferrous iron Fe(II) in myoglobin and haemoglobin delaying its subsequent oxidation to the ferric ion Fe(III), and a transition from a pleasant pink colour to a less desirable dark brown colour. However formation of toxic histamine proceeds, potentially masked by the apparently fresh colour. A referee case was received in late December 2012 and was reported in 2013.

Conclusions

The referee function remains a demand led service clearly required in the UK and especially in the complex areas where global trade, science and the law interact. While some problems appear to have been dealt with, e.g. nitrofurans, disputes still arise in familiar areas such as aflatoxin and animal feed analyses. Referee areas new to the Government Chemist appeared in 2012 on the migration of formaldehyde from melamine kitchenware, on GM rice and on carbon monoxide in fish. These brought exciting scientific and interpretational challenges and prompted stimulating dialogue with scientific colleagues in other laboratories and with traders, enforcement officers and policy officials. Particular thanks go to the Government Chemist Working Group for their advice and continued keen interest in referee casework and to Professor Duncan Thorburn Burns, Emeritus in the Queen's University of Belfast, for input on the publication of our research findings and helpful discussions on the more refractory analytical puzzles that inevitably come to the Government Chemist for resolution.

[17] Consolidated version 2008R1333 — EN — 03.12.2012 — 007.001 — 1

3 Impact

The impact of the work of the Government Chemist programme is broad and the effects can be seen in a number of ways.

Research projects are carried out to support the future work of the Statutory Function for example by horizon scanning to identify measurement topics which are likely to become more important. These are not just aimed at the referee analyses carried out by the Government Chemist, but also for the wider measurement community to prevent disputes by promoting best measurement practice in these emerging areas. This is disseminated through knowledge transfer activities, and a list of publications is given later in this section. The advisory function of the Government Chemist provides advice on analytical measurement subjects to Government, the European Commission, and the wider stakeholder community.

All these activities are aimed firmly at predicting future regulatory issues within the chemical and biochemical measurements sphere, whilst providing a secure base for more efficient and cost-effective regulations.

Horizon Scanning

Preparedness for future problems is enhanced by our horizon scanning of the scientific implications of policy development, emerging and changing legislation, and enforcement trends. We publish our foresight activities, such as our reviews on legislation with a commentary on the associated scientific context, on our website. We collaborate with IFST, Defra and the APA Training Committee, gaining and sharing insights on developments in the food industry and the official food and feed control system. An exciting novel aspect of our horizon scanning is our collaboration with Kingston University, co-funded by the Food Standards Agency, to enhance intelligence gained from our multinational food recalls datasets. This study explores the usefulness of interactive data mining of emerging or re-occurring temporal trends in global food safety and authenticity issues. It stems from the expertise and experience in Kingston University in the application of novel algorithms in Network Analysis coupled with web-based visualisation of the outputs.

Nanomaterials in foods – The next big measurement challenge?

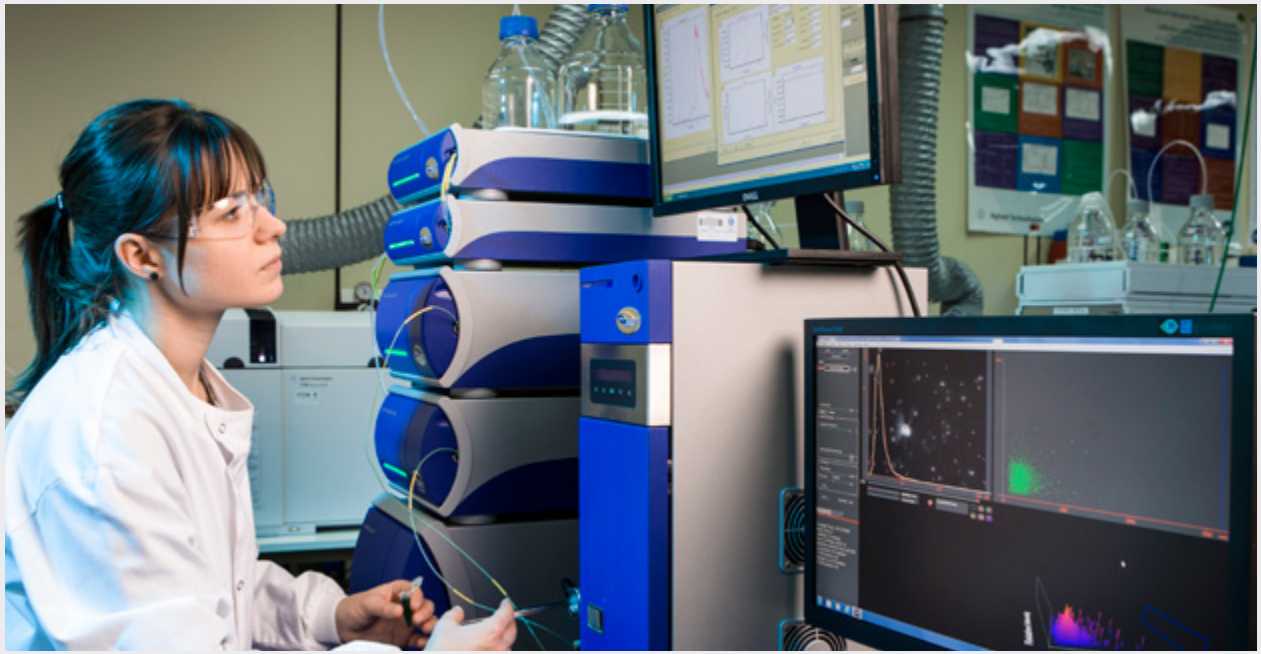
The issue

The novel properties of nanomaterials have led to their increased use in foods and other consumer products over the last decade. The addition of nanomaterials to foods has the potential to offer a number of benefits to industry and consumers. These include creating foods with unaltered taste but lower fat, salt or sugar levels, or with improved colour or anti-caking properties. Nanotechnology may also have significant benefits for food packaging, enabling food to be kept fresh for longer. However, despite the potential benefits, nanomaterials may present new risks as a result of their unique properties and there are concerns about the toxicological hazards that some might present. Regulatory and scientific assessment of products containing nanomaterials requires an understanding of exposure to both humans and the environment. This, in turn, requires validated and traceable measurement methods for product characterisation, and reference materials for method validation and calibration.

To date, the analysis of nanomaterials has focused on the development of methods to characterise materials for their physical properties in their powder form or in very simple matrices. There is a pressing need for traceable methods and reference materials for nanomaterial characterisation in complex matrices such as food, to support upcoming regulation and to enable more effective quality control of existing products. The extraction of nanomaterials from complex solid samples, without altering their properties, is a particular analytical challenge. It is also important to be able to distinguish between naturally occurring nanoparticles and those intentionally added to foodstuffs (known as 'engineered nanomaterials' (ENM)).

The solution

Given the complexity of the majority of consumer products, the use of single measurement techniques for nanomaterial characterisation has often resulted in ambiguous results. The use of multi-method approaches has therefore been proven to be essential for providing reliable results. Such approaches have the advantage of combining techniques that can provide information on a range of properties of nanomaterials, including size, size distribution, elemental composition and isotopic ratios, surface charge, shape, agglomeration and aggregation. Such information is essential for the unambiguous characterisation of nanomaterials in complex environments. To address these measurement challenges, LGC scientists have developed a systematic approach for the evaluation and development of methods for the extraction and characterisation of nanomaterials in complex samples. This approach uses asymmetric field flow fractionation (AF4) coupled on-line to inductively coupled plasma mass spectrometry (FFF-ICP-MS) with UV visible and multi-angle light scattering (MALS) detection. AF4 is a method which allows the separation of particles with diameters in the range 1 nm to 100 µm, while ICP-MS is an established technique for elemental analysis. The coupled technique used in combination with MALS can therefore provide information on the size distribution of particles and their size-based elemental chemical composition. Recent research at LGC has focused on the analysis of silicon dioxide (SiO_2) nanoparticles – which are used to thicken pastes and as anti-caking agents – in commercial coffee creamers. Samples have been spiked with known amounts of food grade SiO_2 nanoparticles to study extraction conditions in the presence of a complex matrix. In addition, sample preparation procedures that mimic the preparation of coffee creamer in everyday use have been applied to obtain meaningful results regarding the size and size distribution of the particles. Studies are ongoing with the ultimate aim being the development of reference methods which can be used to support regulation and in the characterisation of ENM-containing reference materials.



Genetically Modified Organisms (GMOs) in the Food chain

The Issue

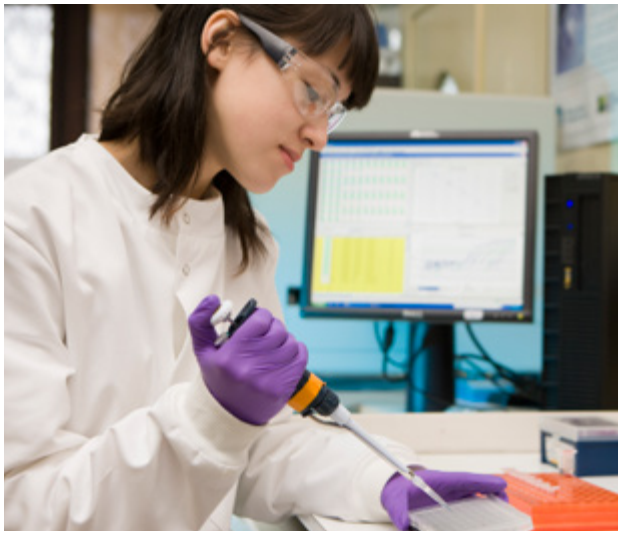
Last year, on 12 January 2012, Commission Implementing Decision 2011/884/EU came into force. This regulation describes emergency measures regarding the importation of unauthorised genetically modified rice in rice products which originate in China, and it repealed an earlier decision regarding rice containing the unauthorised genetically modified organism (GMO) 'Bt63' (2008/289/EC). This product was found in imports to the EU from 2007.

Commission Implementing Decision 2011/884/EU stipulates that all consignments of rice or rice products originating from, or consigned from, China, must be sampled at the point of entry into the EU. Sampling for official control must be carried out at a frequency of 100 % on all consignments, i.e. all consignments arriving at EU points of entry must be sampled. It also contains prescriptive descriptions for lot, increment sample, bulk sample, laboratory sample and analytical sample. The Decision prescribes that each consignment must be accompanied by an analytical report for each lot and a health certificate. Sampling and analysis must be carried out according to Annex II based on Commission Recommendation 2004/787/EC, rendering previous guidance on sampling and analysis obsolete. If a consignment which contains rice is not accompanied by the analytical report and health certificate the consignment must be re-dispatched to the country of origin or destroyed. When the results of sampling and analysis show compliance with EU law the consignment must be released for free circulation.

Measurement solutions to detect illegal GMO rice

There are no genetically-modified (GM) rice varieties currently approved for use in the European Union. In support of the repeal of Commission Decision 2008/289/EC (3 April 2008), the European Union Reference Laboratory for Genetically Modified Food and Feed (EURL-GMFF), established by Regulation (EC) No. 1829/3004, was requested to carry out an in-house verification study to assess the performance of P35S, TNOS and CryIAb/Ac methods as a screening approach for the detection of genetically modified rice in food products. For this, P35S, TNOS and CryIAb/Ac SYBR Green Real-time PCR methods and a P35S/TNOS duplex TaqMan Real-time PCR method were assessed by the EURL-GMFF for their performance in detecting these markers in rice material.

There are reportedly over 25 genetically modified rice varieties that may be a source of contamination of rice products imported from China. However, relevant details of their molecular structure and DNA sequence information are not currently officially available. Consequently normal recommended specific methods of analysis are not applicable and in light of this Commission Decision 2011/884/EU requires screening tests. The screening tests must be performed by real-time PCR according to the method published by the EU-RL GMFF for at least the following genetic elements: DNA sequences characteristic for the 35S promoter derived from Cauliflower Mosaic Virus (P35S) the nopaline synthase terminator (TNOS) derived from Agrobacterium tumefaciens and the genetically engineered CryIAb/CryIAc.



The EURL-GMFF advocated the use of the SYBRGreen screening method for the detection of Chinese GM rice varieties, over the use of the TaqMan method as the former was supposed to be able to identify more of the Chinese GM rive varieties than the later as it was more generic. Additionally, at the time of going to press, there was no validated TaqMan approach for the third Chinese GM rice genetic element of CryIAb/Ac.

During the year, we received four very complex referee cases for the detection of Chinese GM rice. These were particularly challenging although our preparedness from our membership of the European Network of GMO Laboratories, ENGL, was of considerable help.

EU Regulation 619/2011 stipulates zero-tolerance of EU unapproved varieties in feed samples. This is technically regarded as 0.1 % m/m of a particular ingredient, chosen as this is the lowest level detectable on a repeatable basis. Prior to the 2012 referee case, the GC had previously not experienced GM testing at this level. As the Commission proposes to extend this limit to food, there is a greater likelihood of a referee case occurring. There is also potential for a referee case as a consequence of the ruling of the European Court concerning GM pollen in honey. In addition, there is a proposed revision to the Chinese GM rice legislation (2011/884/EU) to extend the scope to any products that originate from China that have rice present as an ingredient, further increasing the likelihood of referee cases. The GC continues to follow developments in this field through involvement as the UK National Reference Laboratory (NRL), in the European Network of GMO Laboratories (ENGL) and through its R & D activities.

Controlling allergens in food

The Issue

Food allergy is an increasingly prevalent global health problem. Susceptible individuals develop an immunological response to specific food proteins, which leads to symptoms ranging from lip tingling to life threatening anaphylaxis. Cures for allergies remain experimental. Usually the only option for allergy suffers is to identify the food type causing the reaction and cut it out of their diet entirely. Often this also means excluding the ingredient from the diets of others that share the same meals as the sufferer, and in extreme cases from the environment in which the sufferer lives and works. The discipline required to follow exclusion diets is notoriously difficult, and the detrimental effects on nutritional balance, food enjoyment and costs affect the quality of life of huge numbers of individuals in the developed world. Furthermore, this number is growing.

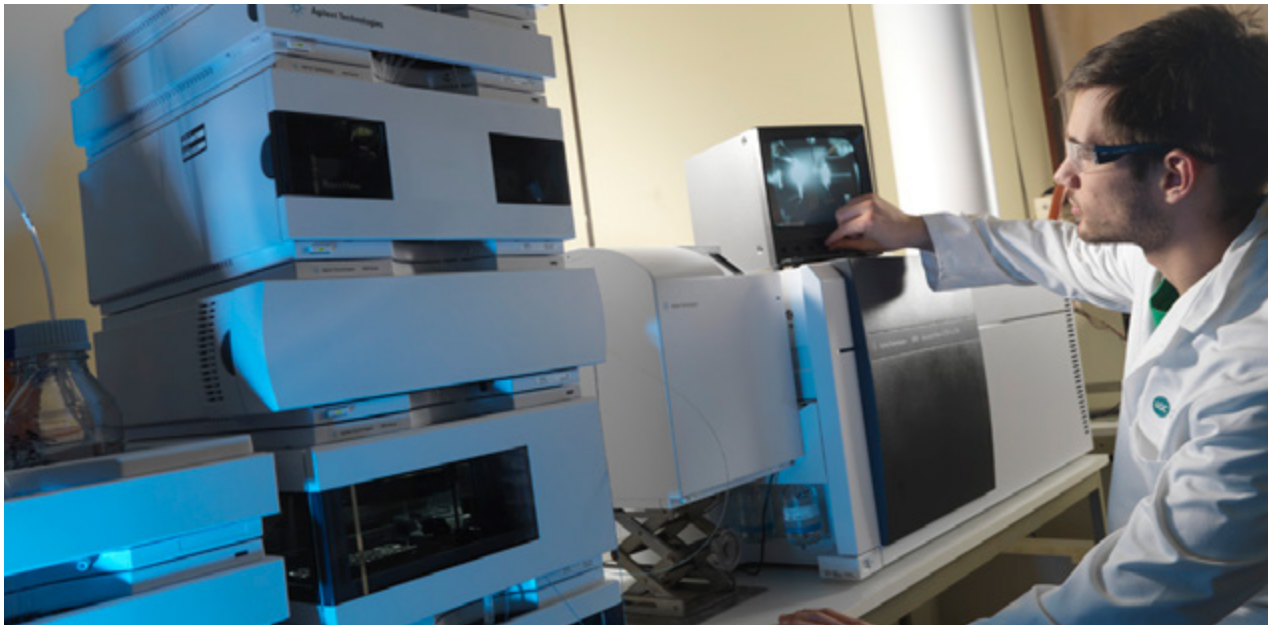
In response to this serious societal issue, food regulators have been busy introducing measures to protect consumers, mainly in the form of legislation and compulsory labelling requirements of pre-packaged food. In Europe the inclusion of any of 14 major allergens in prepacked food, defined by Annex IIIa to Directive 2000/13/EC (as amended), triggers specific labelling requirements. Such labelling requirements will be extended in 2014 to non-pre-packaged food such as that produced by catering establishments.

Under European and UK food law it is an offence to sell food that is unsafe for allergic consumers, particularly if specifically intended for their consumption. One significant challenge therefore is in the definition of “unsafe”. Many food experts consider that the introduction of thresholds or the definition of a ‘minimum eliciting dose’ for specific food allergens will deliver major improvements for all stakeholders. However, there remains a need for fit for purpose analytical methods that can be adopted across the food industry to underpin risk management, and secure compliance with quantifiable thresholds.

Measurement solutions to underpin food safety

Scientists at LGC have been putting their expertise to work on the development of robust measurement methods for the accurate quantification of allergenic proteins in food. The initial allergen protein of interest was lysozyme, an egg allergen protein, at low ppm levels in solution in wine as model liquid matrix. Several steps were optimised and validated to ensure lysozyme was fully recovered from wine and could be accurately quantified through the use of isotope dilution mass spectrometry and isotopically labelled standards. A quadruple time of flight mass spectrometer has been used in method development to check for recovery of the protein/peptides from the wine matrix and a triple quadrupole has been employed for the quantification experiments. The project was finalised in April 2012 and lysozyme was successfully quantified in white wine at the 1 ppm level with an expanded uncertainty lower than 5 %. A paper describing these results has recently been accepted by JAOAC (in press).

The target allergens of the GC 2011-2014 programme of research are milk allergen proteins, which are amongst the most common causes of allergies in children. The aim of this work is the development of an SI-traceable method for quantification of alpha s1 casein in aqueous solution. Preliminary experiments are being performed to evaluate the applicability of the method for quantification of low levels of casein in solid food matrices such as biscuits. The goal of this work is to enable standardisation and intercomparability of measurements across the food industry, and to support enforcement of legislation. This will play an important part in facilitating allergen risk management in the future, for the wider benefit of our society.



Accelerating Cell therapies

LGC is a leading contributor to standards development supporting the characterisation of novel cell-based therapies and the quality of cell-based technologies. Our cell biology group delivers research to develop robust measurement solutions to support this emerging industry. Cell therapies are derived either from a patient's own cells (autologous therapies), or from cells or tissues derived from unrelated donors, or tissue banks (allogeneic therapies) and formulated into a product that can be applied to larger groups of patients. These medical treatments promise to deliver a step change in therapy for various debilitating diseases and injuries that are currently not effectively addressed by conventional drug therapies.

However, there are fundamental challenges associated with bringing a new cell therapy product to market. There is an intricate regulatory environment that companies have to navigate and comply with, which requires a thorough understanding of the cell product characteristics which must be maintained during a costly regime of clinical trials and evaluation. This includes measurement of desired attributes such as concentration of active components, identity, homogeneity, quality, stability and functionality of the cells. LGC's NMI function has a leading role in helping guide cell therapy organisations through this environment through the delivery of Publicly Available Specifications (pre-standards) in collaboration with the British Standards Institute and other thought leaders in the cell therapy sector. The following PAS guidance documents have been published with leading input from LGC:

- PAS 83:2012. Developing human cells for clinical applications in the European Union and the United States of America.
- PAS 93:2011. Characterization of human cells for clinical applications.

Measurement solutions for cell therapies

Obtaining reliable and reproducible characterisation data is crucial for bringing new cell therapies to market. This is a particular challenge in cell biology, where the product is alive and has very dynamic characteristics. Cell assessment currently relies on visual microscopic inspections, which inevitably incur an element of subjectivity of the operator, as well as measurement of fluorescently tagged cells and molecular by-products which provide a general assessment of large cell populations. Our NMI research is geared to developing robust measurement solutions to enable manufacturers of cell therapies to assure the quality of their products, and deliver effective and safe therapies to patients by bridging the different scales of observations, from single cell measurements to large cell populations found in the drug products. Our cell biology laboratories are equipped with leading edge technologies for cell imaging such as time lapse laser scanning confocal microscopy, laser dissection microscopy, and high-throughput epifluorescence/bright field automated scanner.

Through the application of a multi-parametric high throughput single cell analysis method developed at LGC, it has recently been possible to understand and quantify the intrinsic heterogeneity of a cell therapy population that is currently being evaluated in the first European human clinical trial for stroke patients by the company ReNeuron. The technique has enabled the direct comparison of this product with a related cell therapy population with no clinical efficacy.

Our unique approach to integrated multiparametric measurements uses a range of state of the art measurement platforms, combined with the development of well characterised cell models and test environments. In this way LGC is able to provide a robust framework for the assessment of cell characteristics with relevance to a range of applications from drug screening and in vitro cytotoxicity measurements, to the quality assurance of cell therapies, tissue engineering and rapid cell authentication. Many of our approaches can be automated and standardized, removing the limitations of operator subjectivity, and opening new avenues for the development of standardized and inter-comparable measurement practice.

Knowledge Transfer

The Government Chemist strongly supports the wide dissemination of knowledge to regulators, academics, policy makers, the food industry and professional bodies, and believes that this is a fundamental part of his function and that this a key aspect of promoting innovation. In this section, we highlight how we disseminate information using both traditional channels such as scientific papers, posters, conferences and lectures, and specialised working groups, collaborative events, training and web-based media.

A conference, organised under the Government Chemist programme, was held on 8th and 9th May in London entitled "Safe Authentic Food: Policy & Enforcement: Challenges and Opportunities". This conference was supported by a number of partners: Food Standards Agency, the Department for Environment, Food and Rural Affairs (Defra), LGC Standards, Leatherhead Food Research, Campden BRI, National Measurement Office, and the Association of Public Analysts Educational Trust.

Over 100 people attended on each of the two days, and they were treated to a range of topical talks from experts from industry, regulation, policy and enforcement.

The scientifically iconic and historic venue of the Royal Society on Carlton House Terrace provided a fitting backdrop to the event. Some feedback from delegates and speakers regarding the conference included:

> *"I had a great time and found the conference very useful, hopefully LGC will be able to host this event again as it gave me an insight into some of the ongoing developments and allowed me to explore some areas we would like to develop further."*

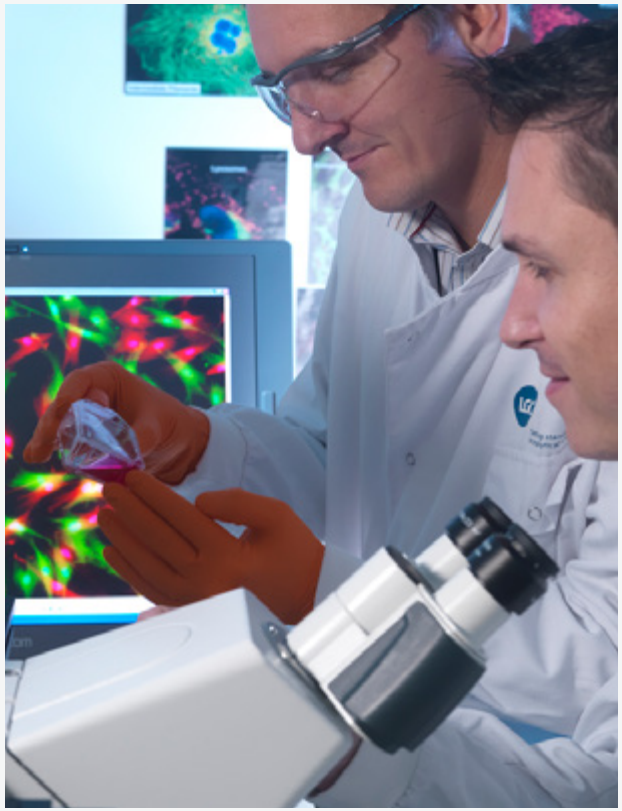
> *"Thank you again for the opportunity to participate at the conference. It was excellently organised and the venue was stunning."*

> *"I really enjoyed it – thank you for inviting me."*

The presentation slides from the conference are available on the Government Chemist website http://www.governmentchemist.org.uk/Events.aspx?m=93&amid=1447. Short papers from the conference have been prepared by a number of contributors and published in the Journal of the Association of Public Analysts, an open access peer reviewed journal available at http://www.apajournal.org.uk/html/japa_vol_40_pg_60-80.html.

Some highlights of the conference papers include:

- Margaret Gilmore, Board member of FSA gives an overview of the Agency's remit and how it interacts with enforcement and the food industry in managing incidents.
- Helen Grundy of the Food and Environment Research Agency (FERA) provides an overview of Food Authenticity and Food Fraud Research.
- Mark Roe and Paul Finglas of the Institute of Food Research write on IFR's Food Databanks. This 4-year project (2009-2013), funded by the Department of Health, to review, update and maintain UK data on the composition of foods, will culminate in the publication of the 7th edition of McCance and Widdowson's 'The Composition of Foods'. The project is supported by the British Nutrition Foundation, LGC Ltd, Eurofins Laboratories Ltd and The Royal Society of Chemistry.
- Kerstin Gross-Helmert describes the role of the European Food Safety Authority: Fostering Scientific Cooperation in Europe. Kerstin's theme that scientific cooperation within Europe and beyond is crucial to help ensure that the food we eat is safe is one we all wholeheartedly subscribe to.
- Yuk Cheung provides a paper from our 2010 conference on her own views on laboratory services operating in an increasingly competitive market.
- From within LGC Milena Quaglia describes the application of protein mass spectrometry to the analysis of allergens. Milena discusses exact matching isotope dilution mass spectrometry, IDMS, successfully applied to a model system of lysozyme in wine.



Advice

We continued to respond to requests for advice from a wide range of stakeholders. Many concern disputed analytical results but were resolved by advice rather than referee cases. Allergen determination, food authenticity, nitrogen factors and choking hazards featured, all regular topics of enquiry. Stemming from work carried out by the Government Chemist some years ago several enquires on methods of analysis for chondroitin were received and an update to our website report was prepared as a response. Scientists in the Government Chemist's team are regularly asked to act as expert reviewers of papers submitted to learned journals and this along with the diversity of requests for advice continue to confirm the Government Chemist as a trusted and authoritative source of information and scientific opinion.

Training

The Government Chemist acquires a great deal of expertise and knowledge through discharging the statutory function. This forms the basis of material which can be used in the provision of training for practising analysts.

Malcolm Burns, Principal Scientist and Special Adviser to the Government Chemist, organised a knowledge transfer event for Public Analysts and food industry analysts on the subject of designing DNA primers to help with food authenticity testing. This event was jointly funded through Defra, the FSA and the GC programme. This was a follow up to the training course on the use of DNA sequencing for food testing. The event consisted of a series of presentations and discussions regarding the design of primers and the use of DNA databases, as well as an interactive workshop for using DNA databases to help design suitable primers for species identity. Pragmatic guidance was given on how to select, design, order and test PCR primers for species identification.

> *"As always, LGC has put together a comprehensive course run by extremely knowledgeable staff" – Course attendee*

Delegates commented on how well the event was organised, the quality of the training material and facilities, and the opportunity to discuss and network with fellow scientists. They remarked that it gave them the confidence to apply the principles of PCR primer design and DNA sequencing in their own laboratories, and how they had been given the knowledge to overcome some of the issues that laboratories had been encountering with "problem" food samples. Delegates also requested that Defra and LGC consider running additional dissemination activities, including training on DNA extraction techniques from different food matrices.

The Government Chemist cooperates with the APA Educational Trust by way of a service level agreement to provide training focused on the needs of official food and feed control scientists (public analysts) but available to all. Training is organised by Michael Walker in his capacity as part-time APA Training Officer under the GC Programme. The principal activity is an annual week long residential course at Reading University supplemented by seminars on topical issues. This year the residential course took place from 23rd – 27th April and attracted 19 delegates, 10 for the whole week and 9 for specific individual sessions. The majority of delegates were from Public Analyst Laboratories with Reading University, FSA and LGC making up the remainder. The teaching consisted of a mix of lectures; laboratory practical sessions and interactive exercises. Two novel sessions were incorporated this year:

- Dietary fibre, delivered by Klaus Englyst and Paul Lawrance, covering the output of FSA funded work on dietary fibre analysis performed at LGC and
- An evening interactive session on court techniques and the role of the expert witness.

The course was, as always, intensive for the delegates but reflects the pressures in a modern official food and feed control (Public Analyst) laboratory. Some of the delegates are studying for the Mastership in Chemical Analysis, the statutory qualification required to practice as a Public Analyst and several sessions were devoted to demystifying the exam process and encouraging other delegates to consider taking the qualification. Some of the lectures were given by Public Analysts currently in practice while others were from experts outside the profession. This enabled mutually beneficial contact to be made and once again networking was a much valued informal aspect of the event. All delegates recorded that they enjoyed the course and considered that it met their expectations to a high degree. A full report on the event is available on the Government Chemist website http://www.governmentchemist.org.uk/dm_documents/Analysis__Examination_of_Food_2012_wXtLy.pdf. The Government Chemist is grateful to the APA Educational Trust, the FSA and the Analytical Chemistry Trust Fund for financial support for this training.

Reflecting the increasing application of advanced mass spectrometry based equipment in their laboratories. In September, 8 Official Food Control analysts visited LGC for an intensive one day course on LC-MS/MS. The course, delivered by LGC speakers, was designed for staff in Public Analysts laboratories that have recently bought (or are about to acquire) these instruments, and provided an up to date refresher on both theoretical and practical guidance on instrument selection and method development.

Gavin O'Connor gave a succinct introduction and a description of the fundamentals of atmospheric pressure ionisation (API), followed by Chris Mussell who talked about coupling LC to MS and Chris Hopley who covered identification of unknown compounds. Gavin also provided an overview of mass analysers.

"Hints and tips from experienced analysts rather than just pure theory", were noted highlights of the day, emphasising the significance and success of this type of seminar. A donation was made to the British Mass Spectrometry Society for use of their teaching material.

Recognising the increasing time and funding constraints that organisations face, we are also embracing electronic means of communication and organised a training innovation in October (a webinar) on 'Allergen management in the Food Industry'. The attendees were a mix of APA and IFST laboratory and food industry personnel. IFST Certificates of Attendance were issued to participants who requested them and the feedback was that the content of the webinar was excellent and should be repeated. The presentation is available on the ***Safe*Food** Food Allergy & Food Intolerance Networks http://safefoodallergy.ning.com/

The Wider Advisory Function

The Government Chemist also has a role to provide advice on subjects with analytical measurement aspects to both Government (including the European Union) and the wider community of stakeholders, which includes industry, academe and local Government. This is done by means of the provision of specific advice pertaining to aspects of measurement topics on a broad range of policy and regulatory developments, and also providing a proactive scientific and measurement-based support service to those industries where chemical measurements are key to their business.

Addressing scientific issues with stakeholders

We have continued to follow developments of both the UK Chemical Stakeholder Forum (UKCSF) and the Hazardous Substances Advisory Committee (HSAC), successor body to the Advisory Committee on Hazardous Substances (ACHS), by attending meetings of these bodies and, where appropriate, making contributions to relevant discussions. One specific area to highlight in this context is the European Commission's recommendation[18] for a definition of a nanomaterial. Many eminent toxicologists were not happy with the proposal, but our view was that the definition, although far from perfect, could be implemented easily as it contained clear, objective and quantitative rules. More subjective definitions, favoured by some experts, are very difficult to measure and could therefore create issues in enforcement.

We have continued to provide advice through our responses to a wide range of official consultations (see Box 2). These consultations are carried out by the Government (including devolved administrations), Standards bodies or the European Union, to obtain the input of both interested and expert stakeholders on proposed new legislation or regulations, prior to enactment and are considered by legislators to be an important part of the development process for new legislation and regulation. The Government Chemist is well-placed, through his expertise in a breadth of matters in analytical science, to respond authoritatively and independently to a wide range of consultations which have chemical or bioanalytical measurement implications.

Box 2. Our Public Consultation Responses

British Standards Institute	Draft PAS 377:2012 - Consumables used in the collection, preservation and processing of material for forensic science
Food Standards Agency	Food Additives (England) (Amendment) and the Extraction Solvents in Food (Amendment) (England) Regulations 2012
British Standards Institute	Draft PAS 820:2012: Laboratory-identifiable forensic codes – Classification for performance when exposed to artificial weathering
Food Standards Agency	Review of the Food Safety (Sampling & Qualifications) Regulations 1990*
National Measurement Office	Consultation on the Implementation of the Restriction of Hazardous Substances in Electrical and Electronic Equipment (RoHS) Directive
National Measurement Office	OIML review of Recommendation 100 Atomic Absorption Spectrometer systems for measuring metal pollutants in water
Food Standards Agency	Informal consultation on proposed new limits for the release of metals from ceramic materials and articles into food*
Department of Health	Consultation on Front of Pack Nutrition Labelling*
DG Environment (European Commission)	Consultation on EU Implementation Plan (UIP) for Persistent Organic Pollutants (POPs)
Food Standards Agency	The Food (Miscellaneous Amendment and Revocation) (England) Regulations 2013
Maritime & Coastguard Agency	Consultation on Draft National Contingency Plan for Marine Pollution from Shipping and Offshore Installations (NCP)
Defra	Fish Labelling (England) Regulations 2010, Amendment to the list of Commercial Designations for Fish September 2012*
Department for Transport	Enforcement Procedures against Drink Drivers and Other Offenders – A Consultation Document

* These consultation responses were also sent to the appropriate department within the devolved administrations in Wales, Scotland and Northern Ireland

[18] http://ec.europa.eu/environment/chemicals/nanotech/index.htm#definition: "Nanomaterial" means a natural, incidental or manufactured material containing particles, in an unbound state or as an aggregate or as an agglomerate and where, for 50% or more of the particles in the number size distribution, one or more external dimensions is in the size range 1 nm - 100 nm.
In specific cases and where warranted by concerns for the environment, health, safety or competitiveness the number size distribution threshold of 50% may be replaced by a threshold between 1 and 50%.
By derogation from the above, fullerenes, graphene flakes and single wall carbon nanotubes with one or more external dimensions below 1 nm should be considered as nanomaterials."

Specific questions which we addressed included:

- The need to ensure that good quality measurement science is incorporated into regulation where enforcement depends on effective measurement
- The need to ensure that proposed regulation and legislation are compatible with existing analytical capability, including state-of-the-art capability and the availability of appropriate certified reference materials, to enable effective implementation where measurements play a potentially key role
- The importance of sampling as a key component in the analytical measurement chain, particularly where the provision of a representative sample is key to accurate measurements for legal purposes
- The importance of appropriate and accurate statistical processes in properly interpreting analytical measurement data
- The importance of clear and unambiguous technical documentation which does not allow for different interpretations
- The use of existing quality standards, particularly ISO/IEC 17025, as a valid means of identifying a laboratory's competence

Dissemination

During 2012 we launched the Government Chemist blog[19] which we use to communicate stories and issues where legislation and regulation meet analytical measurements. The blog is aimed to be informal and a means to make stakeholders aware of a range of issues of interest.

Taking our advice into new areas

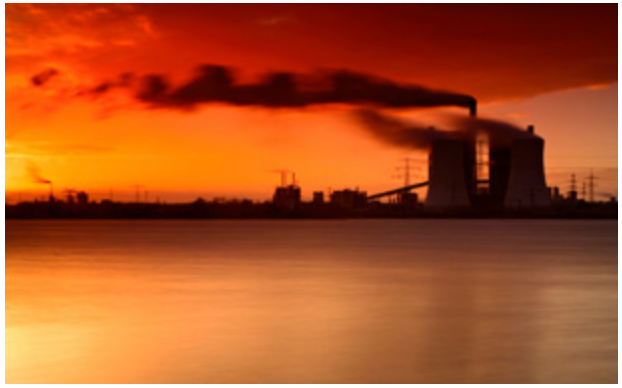
We sought the opinion of stakeholders to determine which sectors we needed to get more involved to help with the understanding and implementation of issues within important legislation such as the Registration, Evaluation, Authorisation and restriction of Chemicals (REACH) and the Classification, Labelling and Packaging of Substances and Mixtures Regulation (CLP). As a consequence we identified the enforcement sector – mainly within local authorities – as an area where we were able to help.

As a result we organised a seminar on enforcement issues in REACH and CLP, designed particularly for those with an analytical measurement dimension sto their role. This was held at the Red Rose Suite at Old Trafford Cricket Ground, Manchester (home of Lancashire County Cricket Club) and was very well attended by 60 delegates, many of whom were from local authorities in the north-west of England.

The talks were of a high quality and covered the various issues from different perspectives:

- Andrew Smith, the Public Analyst for Lancashire gave a presentation on the enforcement issues in REACH and CLP on regulation from a Public Analyst and Local Authority perspective.
- Hannah Doherty of the Chemical Regulation Directorate (CRD) within HSE gave a presentation on the CLP regulation, including the transition between CHIP and CLP. She explained what CRD would look for when conducting an inspection for CLP in a laboratory situation as well as the enforcement strategy within HSE.
- Derek Craston, the Government Chemist, gave a presentation which explained the role of the Government Chemist and the designated National Measurement Institute at LGC, which form part of the measurement infrastructure of the UK that seeks to support industry and Government in setting and enforcing regulation and in product development and compliance.
- Kevin Thurlow, of LGC Standards, tackled the thorny issue of Safety Data Sheets. He said that compliant SDS are necessary, but far too many of them in the public domain are not very good. He gave an overview of the production of SDS for LGC Standards, concentrating on the need for good communication, and showing some of the errors that are commonly found in published SDS. He explained that clear identification of the product, good sources of data and a consistent approach are vital.
- Christopher Summers of the Environment Agency gave a presentation which covered the enforcement activities and responsibilities of the Agency, which regulates a variety of restricted substances which potentially impact the environment and could subsequently have an affect on human health. The Agency's remit now includes REACH, POPs (Persistent Organic Pollutants), PCB (Poly-Chlorinated Biphenyls), F-gas (Fluorinated Greenhouse Gases) and ODS (Ozone Depleting Substances) regulations.
- Mark Selby of Denehurst Chemical Safety gave a talk on Substances of Very High Concern (SVHCs) in Articles. He believed that the main problem for industry is the need to trust suppliers of articles to both know what substances are present in the article, and to then declare these correctly. The onus is on those in the supply line to ensure suitable information is provided along the supply chain to ensure that the presence of SVHCs is communicated.

Full details of all the presentations can be found on the Government Chemist website (www.governmentchemist.org.uk)



[19] http://governmentchemist.wordpress.com/

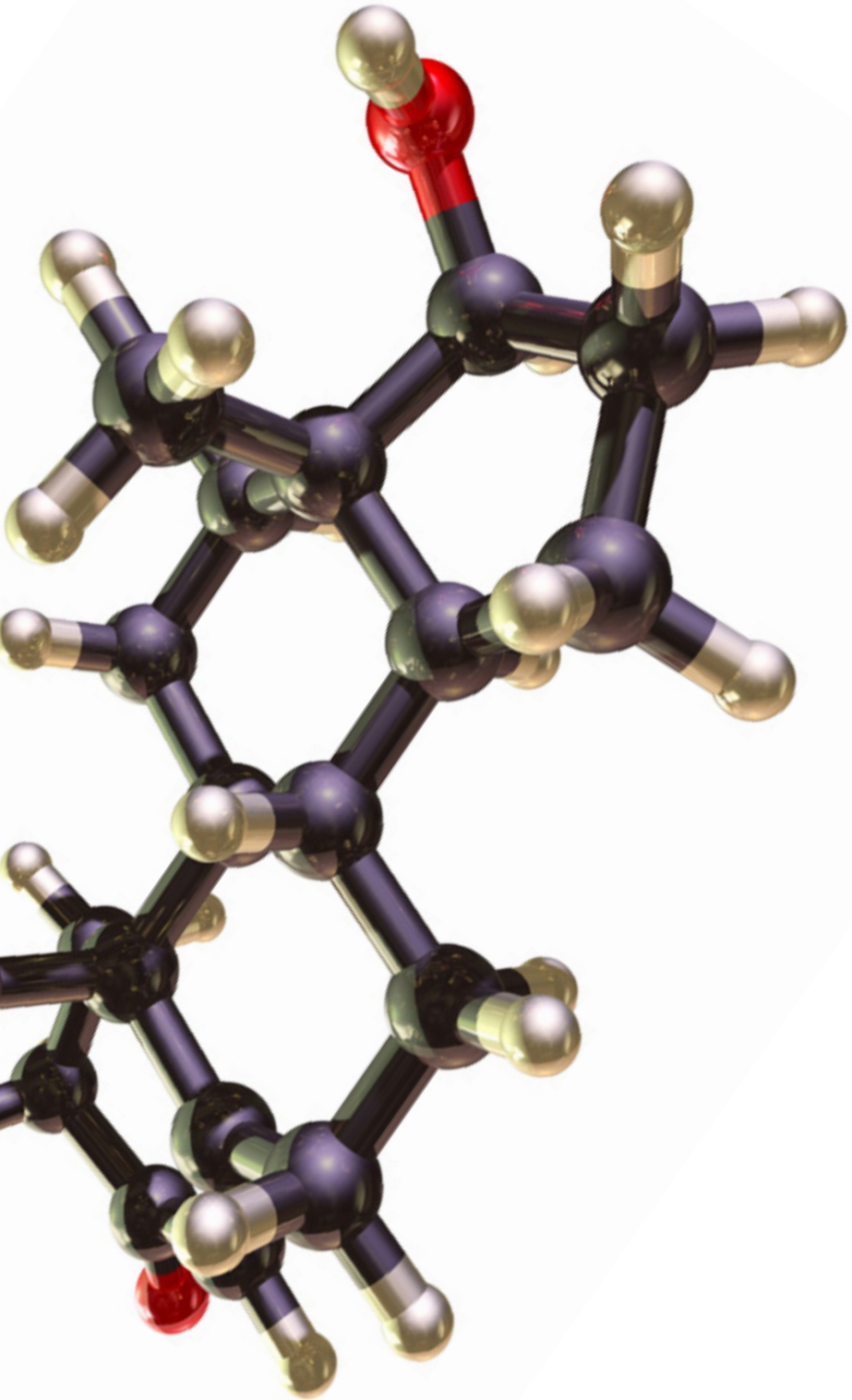
Micro-funded Studies

The prioritisation process undertaken by the GCWG prior to the commencement of the 2011-2014 programme identified a number of proposed project areas which they felt were appropriate for small-scale funding, and might also lead to increased activity in areas which are beneficial to industry. They considered that these smaller projects should be undertaken with a potential for further funding in the future, if appropriate.

Studies which have been concluded in the last year include:

- The qualitative determination of chromium species in landfill leachate by LC-ICP-MS. This is a novel method which has the potential to be transferred to other matrices where chromium speciation is important, particularly taking into account the legislative restrictions on chromium (VI) in various sectors.
- The determination of formaldehyde in food contact materials. Although focused on food the method developed has applications in many areas such as cosmetics where formaldehyde is banned but can be produced in situ.
- The quantitative measurement of arsenic species in landfill leachate by inductively-coupled plasma-mass spectrometry (ICP-MS). A method has been developed and a report outlining this is available on the Government Chemist website.

In addition, work has been planned in other areas considered to be of importance at the current time, including methods for the characterisation of nanoparticles according to the proposed EU definition of a nanoparticle.



Chemical Nomenclature

Substance identity is very important in attaining compliance with legislation, particularly relating to chemical safety. REACH requires accurate naming of chemicals so that correct procedures can be followed to use chemicals safely, or to deal with problems efficiently if they occur.

It is also important to use correct names in publications to aid communication. A paper reporting high-class research can be rendered worthless if it is not clear which chemicals are involved.

Kevin Thurlow has been a member of IUPAC's Advisory Committee to Chemical Nomenclature and Structure Representation Division (VIII) since its inception in 2002. He has also represented the Government Chemist on RSC's "Committee on Standards in Nomenclature, Terminology, Units and Symbols" (CSN) since 1991.

The former committee is "virtual". Members are invited to comment on draft proposals and documents and to participate in drafting of new or revised recommendations for chemical nomenclature.

The RSC committee meets once a year. Most members are concerned with education (both school and university), but there are representatives of BSI and scientific societies. LGC input is appreciated as it brings in an industrial and regulatory focus, more practical than theoretical, which is otherwise absent from the committee.

LGC assists Department of Justice in the preparation of amendments to legislation, specifically by supplying accurate chemical names and descriptions so that legislation can deal with "legal highs". It is important that the correct chemicals or families of chemicals are banned, whilst allowing harmless chemicals, or legitimate medicines to be items of trade. Many of the "legal highs" are chemically very similar to legitimate products. Care must be taken in drafting technical aspects of legislation to ensure structurally similar but harmless compounds are not inadvertently caught by the law.

Finally, the names of element 114 (flerovium, Fl) and element 116 (livermorium, Lv) have now been confirmed by the IUPAC Committee.

Publications

Publishing peer-reviewed papers is integral to our work enabling transparency to the analytical community. The following were published in 2012:

Burns M & Bushell C, Feasibility Study into the Use of DNA Sequencing for the Identification of Probiotic Bacteria, Journal of the Association of Public Analysts (Online), 2012, 40, 28-38

Button J, Reference materials – why quality matters, The Column, 2012, 8, 11, 11-14

Cryar A, Pritchard C, Burkitt W, Walker M, O'Connor, G & Quaglia M, A Mass Spectrometry-based Reference Method for the Analysis of Lysozyme in Wine and the Production of Certified Reference Materials, Journal of the Association of Public Analysts (Online), 2012, 40, 77-80

Dean L & Braybrook J, LGC - Clinical about clinical measurement, Bioanalysis, 2012, 4, 2, 125-131

Devonshire A, Sanders R, Wilkes T, Taylor M, Foy C & Huggett J, Application of next generation qPCR and sequencing platforms to mRNA biomarker analysis, Methods, 2013, 59, 1, 89-100

Domann P, Spencer D & Harvey D, Production and fragmentation of negative ions from neutral N-linked carbohydrates ionized by MALDI, Rapid Communications in Mass Spectrometry, 2012, 6, 4, 469-479

Fox B, Devonshire A, Baradez M, Marshall D & Foy C, Comparison of reverse transcription–quantitative polymerase chain reaction methods and platforms for single cell gene expression analysis, Analytical Biochemistry, 2012, 427, 2 178-186

Mazur M, D.Theodosis, B.Subaskaran, S.Taylor & P.Taylor, Ultra High Performance Liquid Chromatographic Determination of Aflatoxins with Fluorescence detection using Kobra Cell for post column derivatisation, poster at WMF meets IUPAC conference, October 2012

Mussell C, Overcoming rejection – Metrological Traceability for Immunosuppressant Therapeutic Drug Monitoring Assays, IADTMCT Compass, 2012, 11, 4, 13-15

Nischwitz V & Goenaga-Infante H, 2012, Improved sample preparation and quality control for the characterisation of titanium dioxide nanoparticles in sunscreens using flow field flow fractionation on-line with inductively coupled plasma mass spectrometry, J. Anal. At. Spectrom., 2012, 27, 1084-1092

O'Connor G & Dean L, Making measurement matter, IUPAC Chemistry International, 2012, 34, 1, 4-7

D.Theodosis, K.Gray, M.Mazur, B.Subaskaran & P.Colwell, Investigation in to the effect of spiking times on Aflatoxin Recovery, poster at Safefood Network Biotoxins conference, November 2012

Walker M, Beyond Reasonable Doubt, Chemistry and Industry, 2012, 76, 11, 24-27

Walker M J, Forensic investigation of a sabotage incident in a factory manufacturing nut-free ready meals in the UK, In: J Hoorfar ed. Case Studies in food safety and authenticity, Woodhead Publishing 2012, pp288-295.

Walker M, Colwell P, Biesenbruch S, Stuart B & Thorburn Burns D, Forensically Robust Determination of the Illegal Dye Dimethyl Yellow in a Refractory Curcuma Oleoresin–Surfactant Matrix–a Case Study, Food Analytical Methods, June 2012, online publication

Walker M, Gray K, Hopley C, Bell D, Colwell P, Maynard P & Thorburn Burns D, Forensically Robust Detection of the Presence of Morpholine in Apples–Proof of Principle, Food Analytical Methods, 2012, 5, 4, 874-880

Whale A, Huggett J, Cowen S, Speirs V, Shaw J, Ellison S, Foy C & Scott D, Comparison of microfludic digital PCR and conventional quantitative PCR for measuring copy number variation, Nucleic Acids Research, 2012, 40, 11, e82

Glossary

See the International Vocabulary of Metrology[20] for the current definitions of terms used in measurement science

AF4	Asymmetric field flow fraction, a variant of field flow fractionation (FFF)
APA	Association of Public Analysts
BIS	Department for Business, Innovation and Skills
BSI	British Standards Institution
CHIP Regulations	Chemicals (Hazard Information and Packaging for Supply) Regulations
CLP	Regulation (EC) No 1272/2008 on classification, labelling and packaging (CLP) of substances and mixtures, as amended
CRM	Certified Reference Material – Material with accurately known traceable concentration of one or more components for use in calibration or validation of methods of analysis
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
DfT	Department for Transport
DH	Department of Health
ECHA	European Chemicals Agency
EFSA	European Food Safety Authority
ENGL	European Network of GMO Laboratories
EURL-GMFF	European Union Reference Laboratory for Genetically Modified Food and Feed

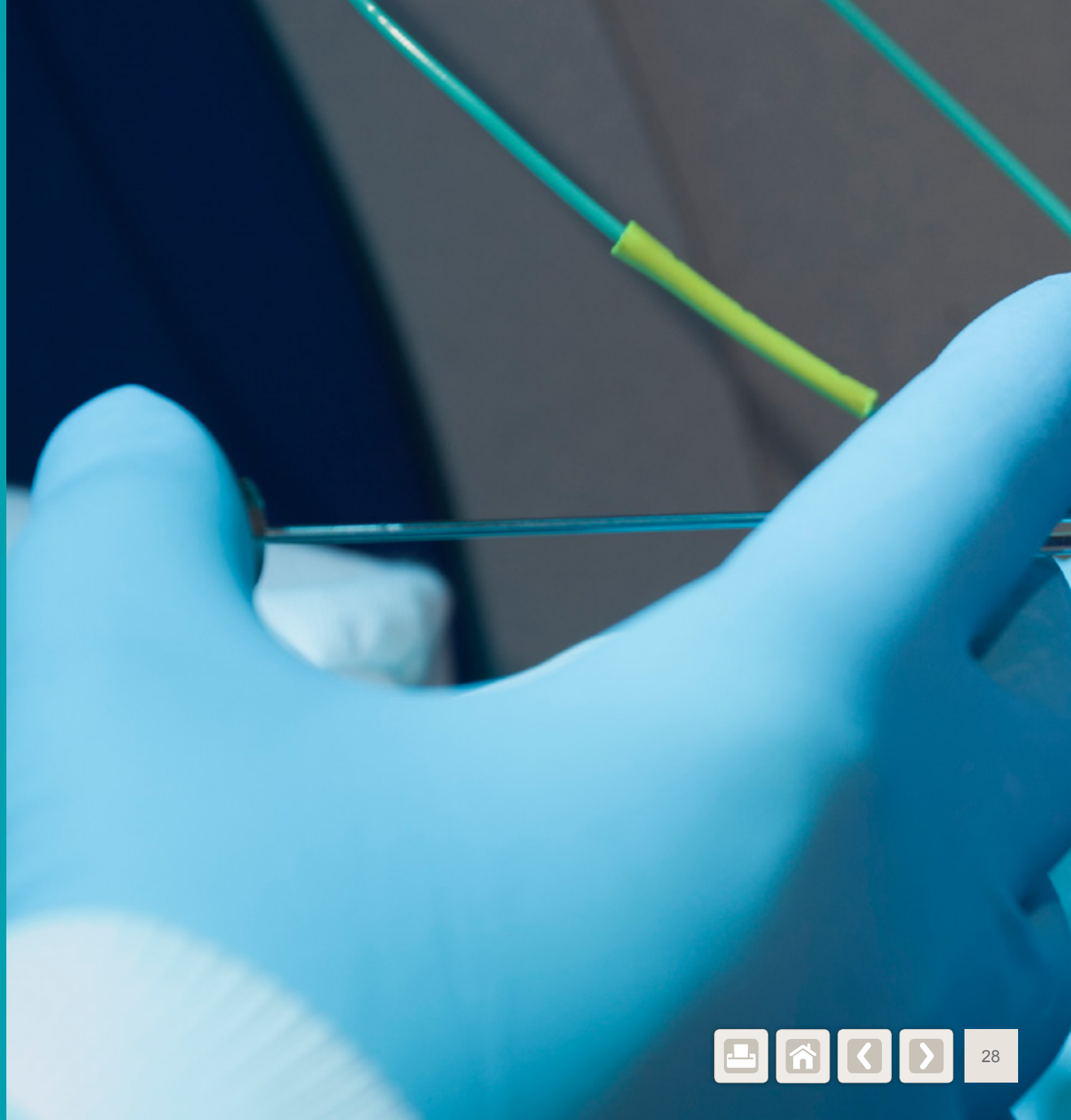
FBO	Food or feed business operator
FERA	Food and Environment Research Agency
FFF	Field flow fractionation – separation technique which separates particles according to their mobility
FSA	Food Standards Agency
GCWG	Government Chemist Working Group
Gene expression	Production of a characteristic biomolecule (RNA) from the genomic sequence, which may be followed by translation into specific proteins
GMO	Genetically-Modified Organism
HSAC	Hazardous Substances Advisory Committee. Expert committee providing advice to Government on hazardous substances, toxicology, risk assessments.
ICP- MS	Inductively coupled plasma mass spectrometry – a modern technique for determining the chemical elements in a sample
IFST	Institute of Food Science and Technology
in vitro	Performed with laboratory or industrial media and instruments, rather than in a living organism
IRMM	JRC Institute for Reference Materials and Measurements
IUPAC	International Union of Pure and Applied Chemistry
JAOAC	Journal of the Association of Official Analytical Chemists. A leading international journal for analytical measurement topics supporting legislation.

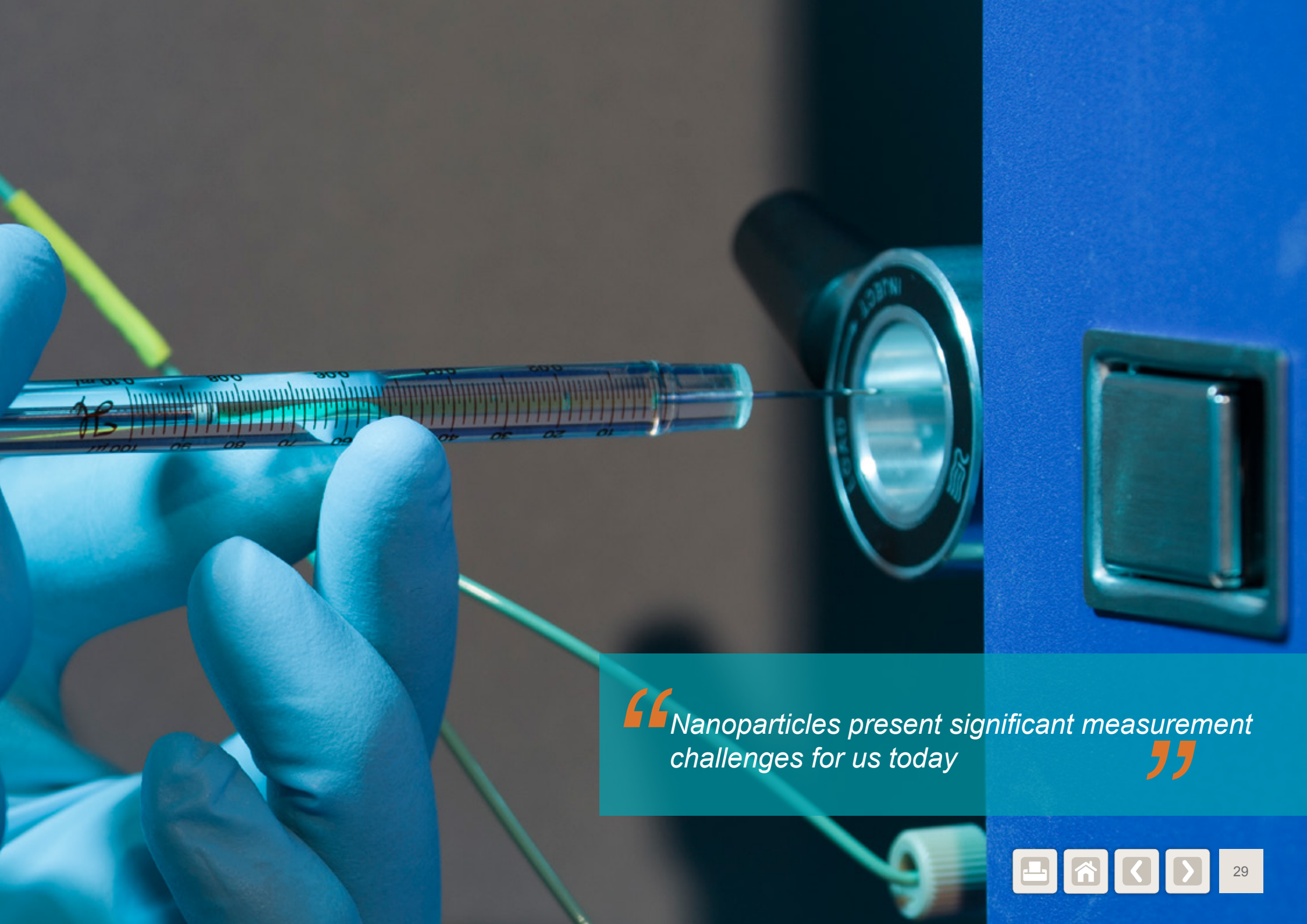
[20] International Bureau of Weights and Measures, International vocabulary of metrology – basic and general concepts and associated terms (VIM), Third Edition, JCGM 200:2008, 2008, www.bipm/org/utils/common/documents/jcgm/JCGM_200_2008.pdf

Glossary

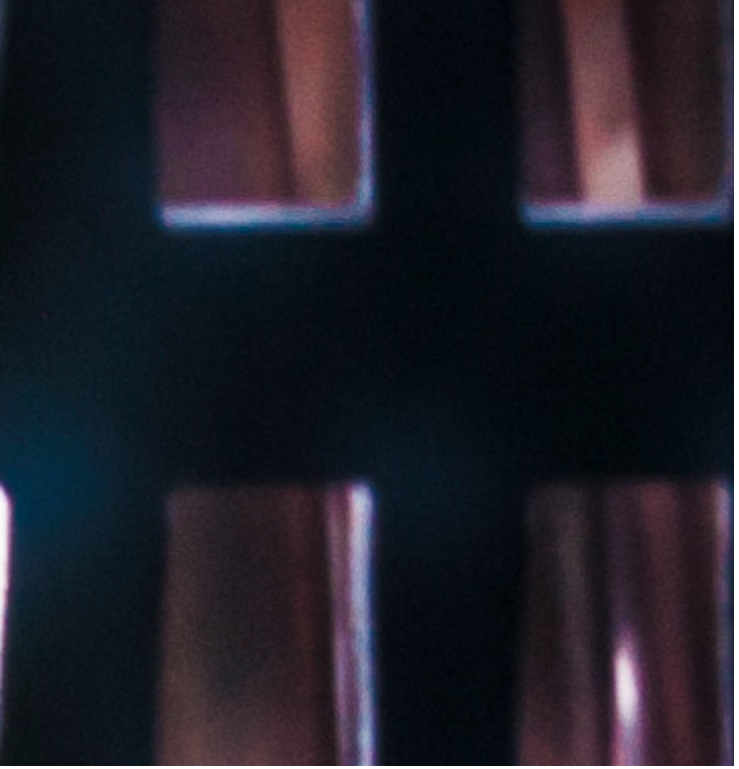
LC-MS/MS	Liquid chromatography-tandem mass spectrometry
MALS	Multi-angle light scattering, a detection method used with field flow fractionation (FFF)
MChemA	Mastership in Chemical Analysis – this Royal Society of Chemistry qualification is required for appointment as a Public Analyst or as an Official Food Analyst
Microarray	Compact array of biomolecular probes - typically either DNA or protein - which can be used to acquire data simultaneously on the composition of a sample
MRPL	Minimum required performance limit in animal products (see Decision 2002/657/EC concerning the performance of analytical methods and the interpretation of results)
Multidimensional GCGC	Gas chromatography carried out in more than one dimension. Components separated in one dimension are then separated in another dimension using different separation criteria.
NMI	National Measurement Institute
NMO	National Measurement Office
OIML	Organisation Internationale de Métrologie Légale (International Organization of Legal Metrology)
Official Food Analyst	A person qualified under the Food Safety (Sampling and Qualifications) Regulations (1990 and/or 2013) (see also MChemA and Public Analyst)
PCR	Polymerase chain reaction, a technique used to amplify DNA sequences so that they can be identified
POP	Persistent Organic Pollutant. Substance which has a long half-life in the environment.

Port Health Authority	Special type of local authority created to ease administration at seaports where the port area is covered by more than one local authority, responsible for carrying out checks on food and feed consignments
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
Quantitative analysis	Measurement, with results expressed as a number and a unit, of the quantity of a target substance in a sample, e.g. 10 $mg.kg^{-1}$
REACH	Regulation (EC) No 1907/2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals, as amended
Referee analysis	Impartial analysis by the GC to help resolve disputes relating to test results obtained on behalf of two independent parties
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
ROHS	Restriction of Hazardous Substances Directive, which restricts the use of certain hazardous substances in electrical and electronic equipment
SEO	Supplementary expert opinion in the context of Regulation (EC) No 882/2004 on official controls, Article 11(5)
SVHC	Substance of Very High Concern (under REACH)
Toxicogenomics	Investigation of the toxic mechanism and potency of substances based on the way they affect the activity of genomic DNA
UKAS	United Kingdom Accreditation Service





“Nanoparticles present significant measurement challenges for us today”



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