The Metrologist

Edition 3 August 2016

Reagecon

www.reagecon.com

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Reagecon's Managing Director speaking at a recent event for the Irish Centre for Business Excellence Network.

Dean Meagher from Reagecon at a recent Biotech for Business event held by Shannon Applied Biotech Centre. Dean spoke about Reagecon's collaboration with Shannon Applied Biotech Centre and Limerick Institute of Technology on a number of GC-MS Methods.

Dear Customers, Readers and Business Partners

Welcome to the August Edition of The Metrologist.

Thanks for your support, feedback and encouragement, as a result of which Reagecon continues to grow rapidly. This year (2016) represents a milestone year, with the publication of our Physical and Chemical Standards Compendium.

The Compendium contains the largest and most diverse range of Physical and Chemical Standards ever published in one document, and brings our total offering of products to over 8,000 part numbers. The specific products contained within the Compendium are published within the following pages, but in addition to the product listings, the Compendium contains detailed specifications, matrix options, diverse pack sizes and a host of other important product details, which could be found in our previous catalogue. However, this Compendium differs from all other product presentations, in that it contains very detailed supporting technical and scientific information – hence the designation of Compendium. In the case of Organic Standards, we have presented some of this information in summary form in this publication (pages 15-23 inclusive). Further information will be presented in the next Metrologist. As a company we are proud of this new Compendium, the contents of which were decided upon, by you our customers, by telling us what you need, now and in the future.

This year also sees the launch of our new Global Metrology Centre, and the details and benefits of this are covered in detail here (pages 7 and 14). A centre such as this would normally be the preserve of government funded initiatives, and we are delighted as a private company to be able to bring the benefits of this centre to you.

Our technical staff and account managers are asked questions on a daily basis, about accreditations including the scope, features and benefits of such accreditations, particularly from our perspective of a Standards producer. We have endeavoured to answer these questions in as much detail as possible in a paper which is published on pages 8 – 12, with particular emphasis on ISO 17025 and the benefits it bestows on us as a Standards producer.

The development and production of high quality Conductivity Standards continues to be a cornerstone of Reagecon's output and growth. We continue to publish widely on this subject in the technical literature and this Metrologist contains a short technical article which has previously been published in poster format. The contents of this article emanated from a piece of market research which we conducted about 10 years ago, in which we discovered that a lot of analysts measuring conductivity did not use Quality Control materials, therefore, the use of such materials is emphasised in this paper.

Finally, Reagecon continues to exhibit, support local charities and attend conferences (sometimes providing speakers), and a representative selection of our endeavours in these areas is presented here in pictorial form. We will continue all of these activities into the future and as our business grows, all of these activities will escalate.

Ultimately though, for our business to grow, we need your support and to earn that support we must continue to strive everyday to improve our supply chain, value proposition, product range and every other aspect of our business that delivers value to you. On behalf of all in Reagecon, I can guarantee you that all of our daily efforts are, and will, centre around bringing you the best value available in the market.

Regards,
John J Barron
Managing Director

Reagecon Physical and Chemical Standards Compendium.

We have recently launched our new Reagecon Physical and Chemical Standards Compendium. Since the publication of our Physical and Chemical Standards and Reagents catalogue in 2013, substantial changes have occurred in the field of Analytical Chemistry. Stringent regulatory demands, combined with major economic implications and increased competitiveness, places necessity for validation on every analytical test performed, either in the laboratory or in the field. Not only must the correct result be obtained, but proof must also be provided of its fitness for purpose, validity and accuracy. Such proof must then be accessible, retrievable and presented in an easily understood format. Reagecon continue to respond to these challenges by presenting to its customers, an ever increasing range of highly specified, stable, traceable and certified standards.

The use of standards such as calibrators or control materials can greatly increase the possibility for the analyst to obtain the correct result and can provide definitive proof of the correctness of such a result from a technical perspective. Such materials can also be used for method validation, instrument qualification, verification and analyst qualification.

Since the beginning of 2011, we have developed a major pipeline of new products and we now have a broader and more comprehensive range of physical and chemical standards than any other producer worldwide. We are privileged to be able to present these new ranges to you, (in excess of 8,000 product numbers). This is the largest range of physical and chemical standards ever presented in one publication.

We hope you find this new compendium beneficial; that the products on offer match your technical specifications; represent value for money and that they will greatly enhance your ability to achieve valid and correct analytical results now and in the future. Many of the chapters and families of products contained within the compendium are introduced with detailed technical notes. Some of these notes are summarised and presented in this publication. On the remainder of this page and on pages 5 and 6 that follow, we introduce the various product families within the compendium and list some of the instruments used in the development, testing and production of these products.

Organic Standards

- Volatile Organic Compound Standards (VOCs)
- Phenol Standards
- Polycyclic Aromatic Hydrocarbon Standards (PAHs)
- Pesticide Standards
- Azo Dye Metabolite Standards
- Fatty Acid Methyl Ester & Fatty Acid Ethyl Ester Standards (FAME & FAEEs)
- Nitrosamine Standards
- Polybrominated Biphenyl Standards (PBBs)
- Polybrominated Diphenyl Ethers (PBDE) & Other Flame Retardant Standards
- Polychlorinated Biphenyl Standards (PCBs)
- Phthalate Standards
- Semi Volatile Organic Compound Standards (SVOCs)
- PIANO, PONA & PNA Standards
- Petrochemical Standards

Total Organic Carbon/Total Inorganic Carbon Standards

- Premium Range
- Quality Range
- Instrument Specific Range

Electrochemistry Standards

- Conductivity Standards
- pH Buffer Solutions
- Electrode Care & Maintenance Solutions
- Redox Standards
- Turbidity Standards
- Chemical Oxygen Demand
- Ion Selective Electrode Standards & Ionic Strength Adjustors

Standards for Anion & Cation Analysis

- ICP-MS/ICP-OES Standards
- Ion Chromatography Standards
- Atomic Absorption Standards
- Flame Photometry Standards

Titration

- Analytical Volumetric Solutions & Indicator Solutions
- Total Acid Number/ Total Base Number Standards & Reagents

Physiochemical Standards

- Colour Standards
- Spectrophotometry Standards
- Melting Point Standards
- Density Standards - Premium Range
- Density Standards - Quality Range
- Viscosity Standards
- ISO Guide 34 Certified Reference Materials: Sucrose in Water Standards
- Brix Standards (Stabilised)
- Refractive Index Standards
- Osmolality Standards
- Cryoscope Standards

Standards & Solutions in Compliance to Pharmacopoeias

- United States Pharmacopoeia Solutions
- European Pharmacopoeia Solutions
- Buffered Eluents
- Dissolution Media - Concentrates
- Dissolution Media - Ready to use

Industry Specific Standards & Reagents

- Dairy Standards & Reagents
- Standards & Reagents for APHA, AWWA & WEF Test Methods
- Wine Standards & Reagents
- Soil Testing Standards & Reagents
- Pulp & Paper Standards & Reagents

General Laboratory Standards & Reagents

- Laboratory Water
- Cleaning Solutions
- Analyst Qualification Sets

Techniques & Instruments Employed

Reagecon has an extensive range of scientific instrumentation. We have at least one and in some cases several of the instruments listed.

- Gas Chromatography (GC)
  - Flame Ionisation Detection (GC-FID)
  - Mass Spectroscopy (GC-MS)
- Liquid Chromatography
  - Mass Spectroscopy (HPLC-MS)
  - Ultra Violet Detection
  - Preparative
  - Reverse Phase
- Ion Chromatography (IC)
- Flame Atomic Absorption Spectroscopy (FAAS)
- Induced Coupling Plasma-Mass Spectroscopy (ICP-MS)
- Bingham Pycnometry
- Vibrational Densitometer
- Refractometer
- Polarimeter
- Osmometer
- Total Organic Carbon Analysers
  - Membrane Exclusion
  - Carbon Oxidisation
- Rotational Viscometer
- Ubbelodhe Master Viscometer
- Cryoscope
- Coulometer
- Auto Titrator
- Spectrophotometer
- Fourier Transform Infrared Spectroscope (FTIR)
- Colourimeter
  - Hunter Solid/Liquid
  - Tintometer
- Volumetric Karl Fisher
- Turbidimeter
- Conductometer
- pH Meter
- Differential Scanning Calorimeter
- Chemical Oxygen Demand (COD)
- Biological Oxygen Demand Assay Unit
- Ex-rated Solvent Facility
- Radley Combinatorial Chemistry Synthesiser
- Buchi Rotary Evaporator
- Melting Point Apparatus
- TBN/TAN Titrator
- Class ISO7 (Class 10,000) Cleanroom
- Solvent Manufacturing Plant

Global Metrology Development Centre

It is our great pleasure to announce the establishment of a Global Metrology Development Centre at our Headquarters in Shannon, Ireland. This is a unique achievement for a commercial organisation, as typically Metrology Centres or Metrology Laboratories are mostly State or Governmental organisations. It places at the disposal of our customers, immediate and direct access to a Metrology Centre of Excellence, a service offered by no other independent Standards manufacturer. In establishing the Global Metrology Development Centre, Reagecon will have created further differentiation from our competitors and ultimately offer you increased technical advantage.

From a technical perspective this centre will elevate Reagecon's status and knowledge base in the science of Metrology, to that of a Reference Centre.Technically the Centre will offer the following advantages

- Reduce Measurement uncertainty for pH, Conductivity, Refractive Index and Density by a full order of magnitude.
- Propel Reagecon into the Certified Reference Material space for these products.
- Increase our ability to publish more widely in the area of Metrology and participate in collaborative studies with research Metrology Institutions.
- Increase accuracy, precision, reproducibility and other metrological parameters for pH, Conductivity Refractive Index and Density initially, then followed by Viscosity, Colour and Osmolality.

From a marketing, image and perception value the Global Metrology Centre will yield significant customer impact. The tangible benefits in terms of outputs provided by the centre include, but are not limited to the following:

- A training facility for 300 international distributors on Metrology
- A training facility for 1,000 Irish customers on new products
- A training facility for our 25 Business Development staff on new products.
- Area for upskilling existing staff
- Provide an area for collaboration and research with National Metrology and National Reference Centres worldwide
- Establish Reagecon as a global Metrology Centre of excellence in the Science of Metrology
- Facilitate the rapid development of Certified Reference Materials in all four sciences of pH, Conductivity, Refractive Index and Density
- Form a platform for adding other Primary Reference Methods in areas such as Viscosity, Colour and Osmolality

The Role of Accreditations in the Production and Use of Standards and Reference Materials.

1.0 Introduction

Reagecon is the largest producer in the world of Standards, Reference Materials and Reagents. We are committed to providing you with products of the highest quality and the achievement and acquisition of Accreditations and Certifications has and continues to play a major part in that objective. Furthermore, Accreditations and Certifications are an integral part of our customer service value proposition, lead to competitive advantage and are an integral part of our business strategy.

Sometimes, there is confusion and lack of delineation in relation to the differences of Accreditations and Certifications and our interpretation of these differences in Reagecon are presented in Section 1.1 below. There is also a value in reiterating the benefits of these Reference Materials and Standards to you the user and how as a producer of such products, Accreditations give you confidence in the quality and integrity of the Standards, you use. Finally, although in the case of a producer of ISO 17025 accredited standards, it is the test procedure used in the assay and certification of the standards that is accredited rather than the standards themselves. All of the standards from the accredited company cover competence in the testing laboratory that involves sampling right through to production, dissemination and storage of the test results, records and certification. So, in the case of ISO17025 the major emphasis relate to the testing component of the process, but also the relationship between the testing component and other parts of the process that input on the testing component as presented in Section 1.3.

1.1 Reagecon's Commitment to Quality

We are committed to providing you with the highest quality Standards and Reference Materials, both accreditations and certification play a major role in that offering. Accreditation is a recognition of competence and Reagecon has held ISO17025 accreditations for the testing of several standards since 1989 and the list of Accredited Test Methods continues to grow. Reagecon has also been certified to ISO 9001:2009 (or its equivalent Certification) also since 1989 and recently the company has achieved ISO Guide 34 accreditations as a certified Reference Material for our first family of products. All of the certifications and accreditations achieved by the company are critical to our corporate evolution and the role played by each is presented in Figure 1 on the next page.

The relationship between ISO9001:2009, ISO17025 and ISO Guide 34 within Reagecon.

ISO 9001:2009

- General Quality Management System
- Does not provide specific accreditation for analytical result
- Does not specifically address stability or homogeneity
- Raw material quality accepted on basis of COA from approved suppliers
- Does not assess technical competence

ISO 17025

- Quality Management System specific to the analytical result
- Provides independent accreditation of the certified value and reported uncertainty of measurement
- Covers analytical and physical testing systems only
- Does not address stability, homogeneity, raw material quality or production validation

ISO Guide 34

- Cradle to Grave guarantee of certified result and reported uncertainty
- Raw materials must be Guide34 quality or extensively characterised
- Homogeneity and stability to be proven on every batch
- Test methods independently ISO 17025 approved
- Stability of every batch monitored 5 times during its lifetime
- Extensive production validation systems required
- Certified Reference Material

Figure 1

1.2.1 Why Use Reference Materials and Standards

Reference Materials and Standards are used in laboratories for a number of reasons as follows:

1) Instrument Calibration – almost all analytical chemistry is comparative – thus the concentration of an unknown analyte is compared with the concentration of a known or series of known analytes which calibrate the instrument. The use of a reputable Reference Material or Standard as a calibrant also establishes metrological traceability which in turn establishes comparability,thus, ensuring that analyses are comparable in time and place.
2) Control Material – the use of a Reference Material or Standard is a very effective and an almost universally mandatory means of Quality Controlling an unknown test result, provided matrix, homogeneity and stability are taken into account. The reference material may be used as a once off control, or can be used to verify that a measurement process is in statistical control, where repetitive testing is performed. This can also facilitate comparability. A study on the use of controls in conductivity measurement is presented elsewhere in this publication.
3) Method Validation – the validation of a test method provides objective evidence that the particular requirements of a test method are complied with and that the method is fit for purpose. The Reference Material or Standard enables metrological data pertaining to accuracy, precision, reproducibility, bias and uncertainty of measurement to be ascertained.
4) Instrument Qualification (IQ, OQ, PQ, MQ) – although such processes are the preserve of the Pharmaceutical Industry and are mandatory in that industry, they are seen in several industries as good laboratory practice and are now widespread as formal documentation processes or as fit for purpose processes (carried out less formally than in the Pharma Industry) in a whole host of other industries.
5) Proficiency Testing – here the test results of the Reference Materials or Standards are compared with the results of a statistically significant number of other laboratories and are a mandatory component of method validation and a mandatory component of the requirements of accreditation bodies for a laboratory that wishes to obtain an accreditation.
6) Analyst Qualification – in this instance the laboratory results are not compared with those of other laboratories, but compared with the analytical value obtained by the producer of the Reference Materials or Standard. The values obtained are generally withheld from the Analyst until after the test is performed and form an objective view of the level of training and competence of the analyst to perform a particular test.

Irrespective of application, it is an imperative that the producer of the Reference Materials or Standards be competent and accreditation is the most important means of determining and proving such competence.

This recognition of competence may relate to properties of the material produced such as stability or homogeneity, but certainly relates to the assigned values and their accuracy.

1.2.2 Why Use ISO 17025 Accredited Standards

ISO17025 accreditation demonstrates that analytical tests are performed in a technically valid manner, controlled by a rigorous quality system. ISO17025 examines all aspects of quotations and contracts, method development, method validation, equipment and personnel and routine performance of the analytical test method. The qualification, education, and training of all individuals involved in the process are scrutinized against their job responsibilities. Even the quality attributes of vendors and collaborators are checked, as well as every Quality Critical specification requirement.

To be ISO 17025 certified, a company must not only be consistent, but must also be proficient in testing the quality of their products. Using standards from a producer with this accreditation helps to ensure your laboratory is technically competent. ISO 17025 Accreditation is now an essential requirement for several types of laboratories and highly desirable for all other types of laboratories.

1.3 The Scope of ISO 17025

Documentation control, corrective & preventive actions, complaint handling, supplier & subcontractor management, non-conflicting organizational structure and internal audits are all part of the scope of ISO 17025. Figure 2 illustrates how the workflow steps involved interact, with particular emphasis on the testing component, which in figure 2 has been expanded out (green boxes)to emphasise the criticality of the testing component.
Some requirements impact on more than one workflow step:

- All analytical methods and procedures should be validated. This includes methods and procedures for sampling, testing and data evaluation.
- Equipment used for sampling and testing should be calibrated, tested, and well maintained. Material such as calibration standards should be qualified and traceable to System International (SI) units or to certified reference material.
- Nonconforming test results should be documented and controlled.
- Personnel should be qualified for their assigned tasks through education, experience, or training.
- Environmental conditions such as temperature, humidity, and electromagnetic interference should be monitored and controlled.

All routine tasks should be performed according to written procedures

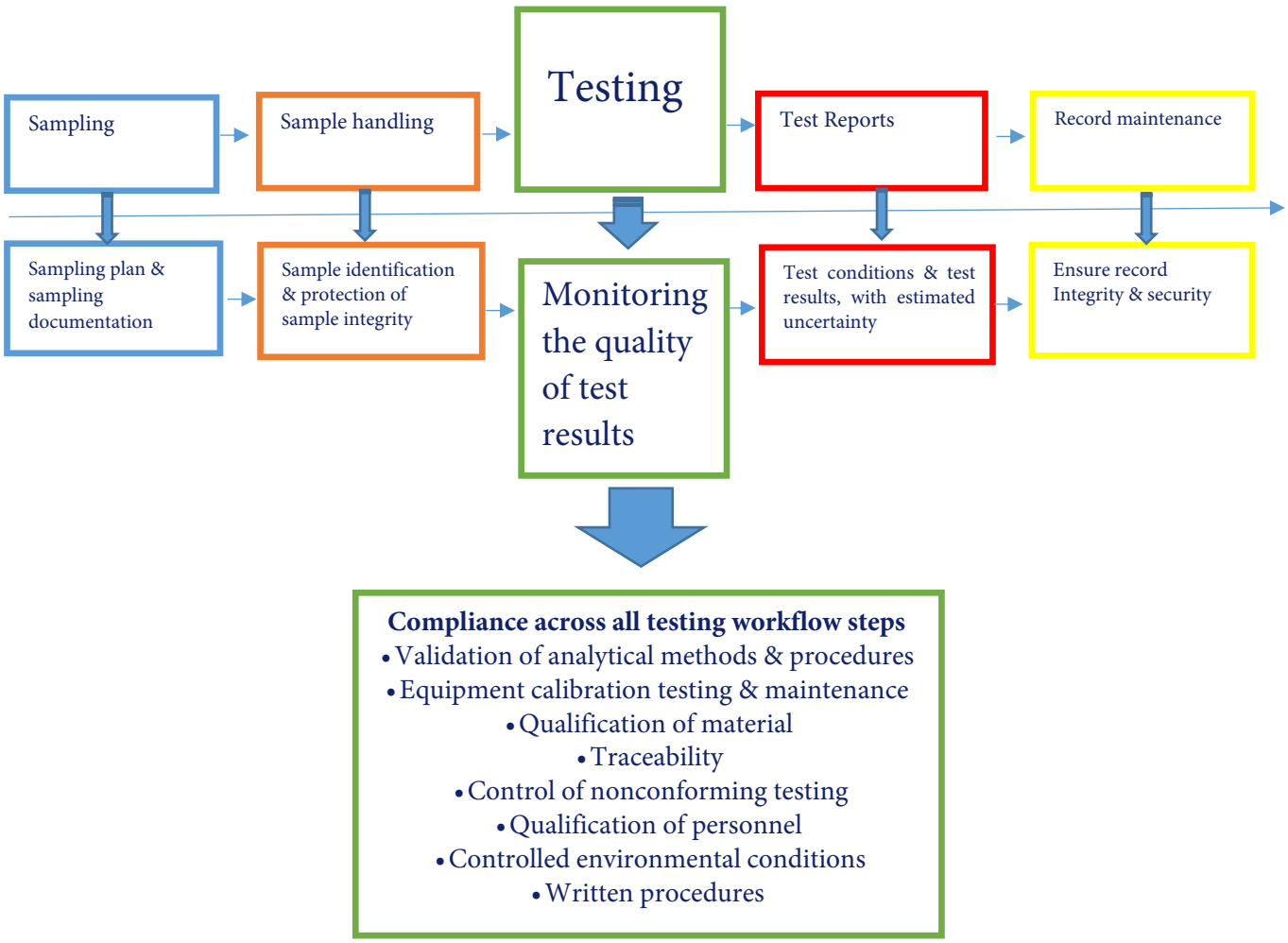

ISO17025 Requirements for Testing Laboratories
Sampling
Sample handling
Testing
Test Reports
Record maintenance
Sampling plan & sampling documentation
Sample identification & protection of sample integrity
Monitoring the quality of test results
Test conditions & test results, with estimated uncertainty
Ensure record Integrity & security
Compliance across all testing workflow steps
• Validation of analytical methods & procedures
• Equipment calibration testing & maintenance
• Qualification of material
• Traceability
• Control of nonconforming testing
• Qualification of personnel
• Controlled environmental conditions
• Written procedures

Figure 2

Current Accreditations

Accreditations/ Certifications ISO 9001:2008

- Registration number 19.2769
- Accreditation held since May 1988
- Certificate of Registration of Quality Management System covering the manufacture and distribution of chemicals, reagents, consumables, apparatus, safety and scientific equipment. The provision of IQ/OQ, equipment maintenance and calibration services.
  The provision of Vendor Managed Inventory (VMI) services to allow customers to outsource the management and replenishment of their consumables and equipment.

Accreditations ISO 17025:2005

- ISO 17025:2005 (264T Testing accreditation)
- Accredited since May 1988 for some products
- pH Buffers
- Conductivity
- Titration
- Brix 0% - 60%
- Refractive Index 1.3331 – 1.6581
- Density 0.65 – 1.03 g/l
- ICP-OES, ICP-MS
- Colour and Spectrophotometry
- Melting point
- Viscosity
- Density 1.03 g/l – 3.1 g/l
- IC standards


Irish National Accreditation Board

Accreditation Certificate

Reagecon Diagnostics Ltd.

Testing Laboratory

Registration number: 264T


NSAI

Certificate of Registration
of Quality Management System
to I.S. EN ISO 9001:2008

Reagecon Diagnostics Ltd
Shannon Free Zone
Shannon
Co. Clare

Accreditations ISO 17025:2005

- ISO 17025:2005 (265C Calibration accreditation)
- Accredited since July 2010
- Balance, Volumetric and Temperature Calibration Laboratory


Irish National Accreditation Board

Accreditation Certificate

Reagecon Diagnostics Ltd.

Reference Material Producer

Registration number: 001Rm

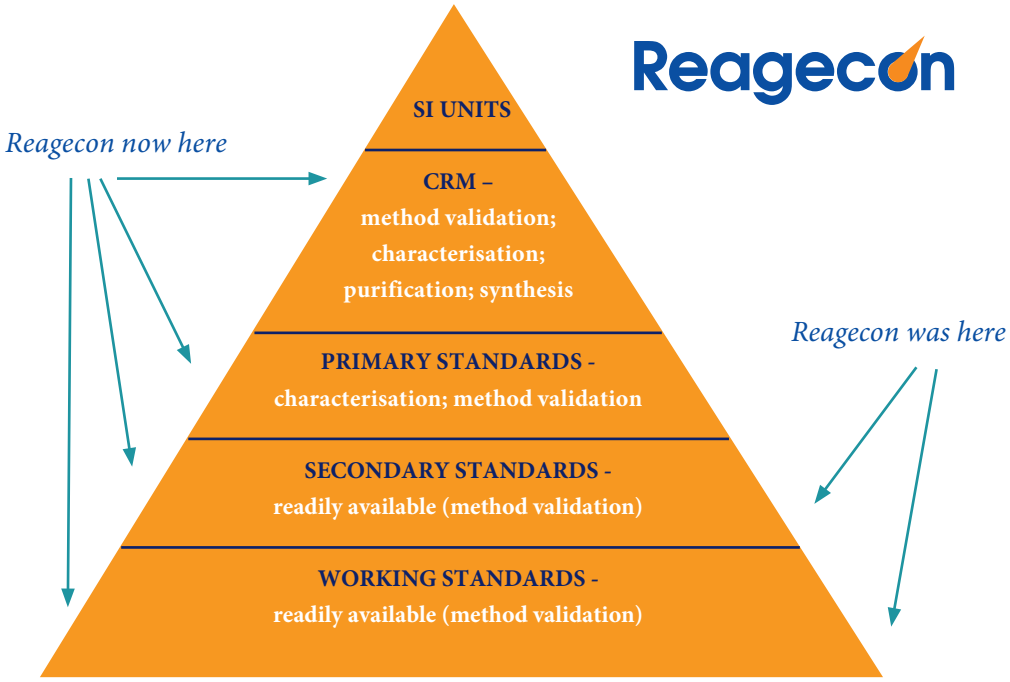
Accreditations ISO Guide 34

- ISO Guide 34 (001RM)
- Accredited since April 2014
- Accredited Producer of Reference Materials
- Only company in Ireland with this accreditation
- Production of materials used for the calibration of scientific instruments and the validation of test methods
- ISO Guide 34 accreditations demands a set of stringent requirements that ensures all aspects of the production of reference materials are carried out with measureable and traceable quality
- The Guide's comprehensive requirements includes production planning, raw material selection and characterization, assignment of certified values, uncertainty, traceability, homogeneity and stability, as well as packaging, documentation, supply chain and logistics.

The Reagecon Hierarchy of Standards

Traditionally, Reagecon's manufactured products fitted into the classification of working/secondary standards. The development and production of such standards was consistent with our main technical competencies (method validation/accreditation) at that time.

Standards Value Chain:



Since 2011, we have escalated dramatically the range of working and secondary standards that we offer. Because of our recently developed ability to perform raw material characterization we are now also producing primary standards and certified reference materials. In the past the production of standards at the higher end of the value chain such as Primary Standards and Certified Reference Materials was the preserve of government funded agencies such as the National Institute of Science and Technology (NIST) in Washington, DC. Now, due to affordable technology, a number of privately funded companies have developed and are marketing primary standards and Certified Reference Materials. These companies generally have well-developed characterisation, purification and synthesis capability. Reagecon has grasped these opportunities with enthusiasm and are a leading producer of such materials.

As a producer of Metrological Standards we are concerned with enabling the end user (analyst) to achieve an analytical result that is fit for purpose and to provide proof of the correctness of that result. These two objectives are achieved by optimizing :

- Accreditations
- Accuracy
- Sensitivity
- Reproducibility
- Comparability
- Traceability
- Precision
- Limit of Detection (LOD)
- Measurement uncertainty

As a Metrology Company, it is a basic requirement that we have detailed knowledge and skills in the Chemical and Biological Sciences, Physics, Statistics, and Engineering. As a manufacturer of metrological products it is mandatory that we have skills and expertise in automation, programmable logic controllers, (PLC's), cleanroom technology and lean (5S, Kaizen, Value Stream Mapping).

Because Metrology forms such a core component of Reagecon's technology platform and is a key Competitive Advantage of the Company, in 2016, we established in Shannon a new Global Metrology Development Centre. The features and benefits of this centre are detailed on page 7 of this publication.

Reagecon Organic Standards- John J Barron

Since 2011, we have escalated dramatically the range of working and secondary standards developed and we have moved up the value chain to include primary standards and Certified Reference Materials , because of our recently developed ability to perform raw material characterisation. We are now the largest producer in the world of Physical and Chemical Standards and Certified Reference Materials.

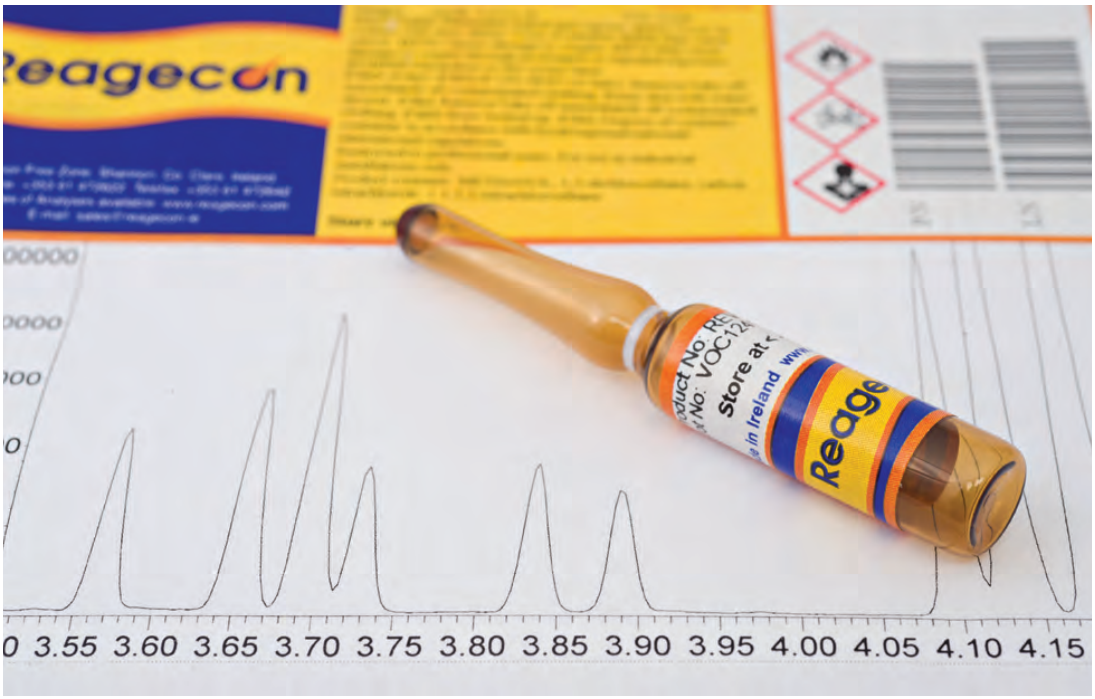
Included in these have been the development of Organic Standards . We now offer an extensive range of organic standards which are listed below.

- Volatile Organic Compound Standards (VOCs)
- Phenol Standards
- Polycyclic Aromatic Hydrocarbon Standards (PAHs)
- Pesticide Standards
- Azo Dye Metabolite Standards
- Fatty Acid Methyl Ester & Fatty Acid Ethyl Ester Standards (FAME & FAEEs)
- Nitrosamine Standards
- Polybrominated Biphenyl Standards (PBBs)
- Polybrominated Diphenyl Ethers (PBDE) & Other Flame Retardant Standards
- Polychlorinated Biphenyl Standards (PCBs)
- Phthalate Standards
- Semi Volatile Organic Compound Standards (SVOCs)
- PIANO, PONA & PNA Standards
- Petrochemical Standards

In the following pages, we will present detailed technical notes, pertaining to the necessity to measure these materials, brief details of their chemical composition, health and safety effects and other relevant details including analytical method of choice for the following:

Azo Dye Metabolite Standards
Fatty Acid Methyl Ester & Fatty Acid Ethyl Ester Standards (FAME & FAEEs)
Nitrosamine Standards
Polybrominated Biphenyl Standards (PBBs)
Polybrominated Diphenyl Ethers (PBDEs) & Other Flame Retardant Standards
Polychlorinated Biphenyl Standards (PCBs)
Phthalate Standards

Similar information will be presented on the remaining families of products in the next edition of The Metrologist.



Azo Dye Metabolite Standards

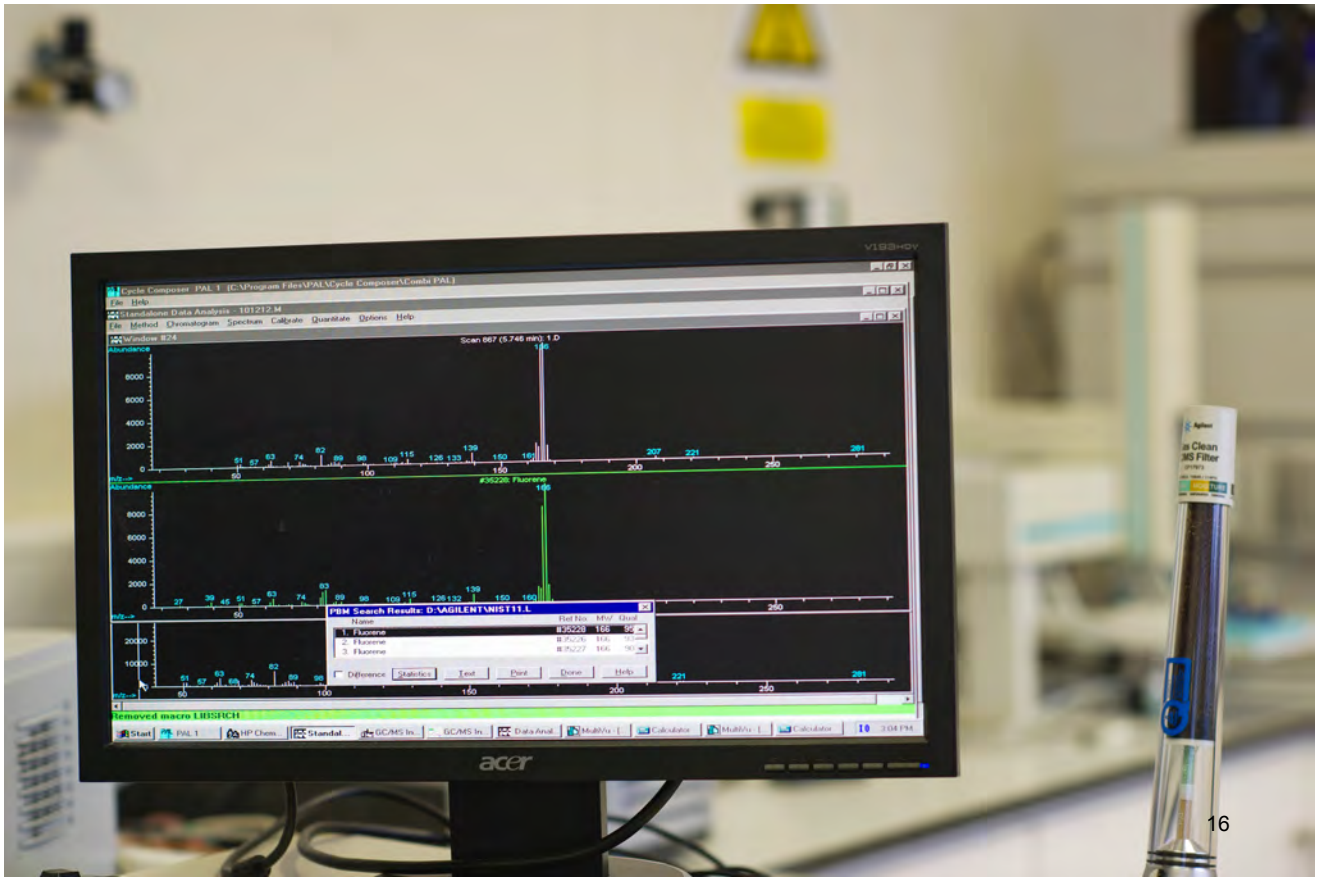
Introduction

Azo-dyes are a large class of synthetic organic dyes that contain nitrogen in the form of an azo group (-N=N-), as part of their molecular structures. They are used in many areas such as the food, cosmetic, textile, leather, nutrition, plastic and pharmaceutical industries. During the past 50 years, the amount of azo-dyes used in foods has increased by 500%. When compared to natural dyes, synthetic food dyes provide many advantages. Synthetic dyes are cheaper, more easily available, last longer and can achieve colour and hue variations otherwise not possible using natural colourants. They also provide superior colour fastness and colour intensity.

However, since the use of synthetic food colouring has become widespread, many allergic and other immune reaction disorders, have increasingly been reported. The reductive cleavage of the azo bond leads to the formation of aromatic amines which may be mutagenic, carcinogenic or allergenic. For instance, acid red 85 and direct blue 6, are both capable of reductively splitting to produce carcinogenic benzidine. Likewise, Sudan II and disperse yellow 7 are capable of splitting to form p-phenylenediamine and aniline, while disperse orange 3 can split only to p-phenylenediamine. [1]

Legislation

Colour Directive 94/36/EC outlines the permitted natural and synthetic colours with their approved applications and limits in different foodstuffs (Commission, 1994) and the use of azo-dyes which can be reduced into toxic amines is prohibited in Europe, US and many other countries. The safety of food colours and other food additives in the EU is evaluated by the European Food Safety Authority (EFSA). Since 2009, the expert Scientific Panel of EFSA assess all of the permitted food colours (45 in total) which had been approved for use in the EU giving priority to those synthetically produced and then to those obtained from natural sources mainly carotenoids. Since new scientific data became available, there have been changes in the legislation, many additives which were initially authorised for used in the past, are currently not permitted in food products in the EU. Unfortunately, there are reports of food adulteration by using dyes unauthorised for food which are often hazardous.



Illegal Adulteration

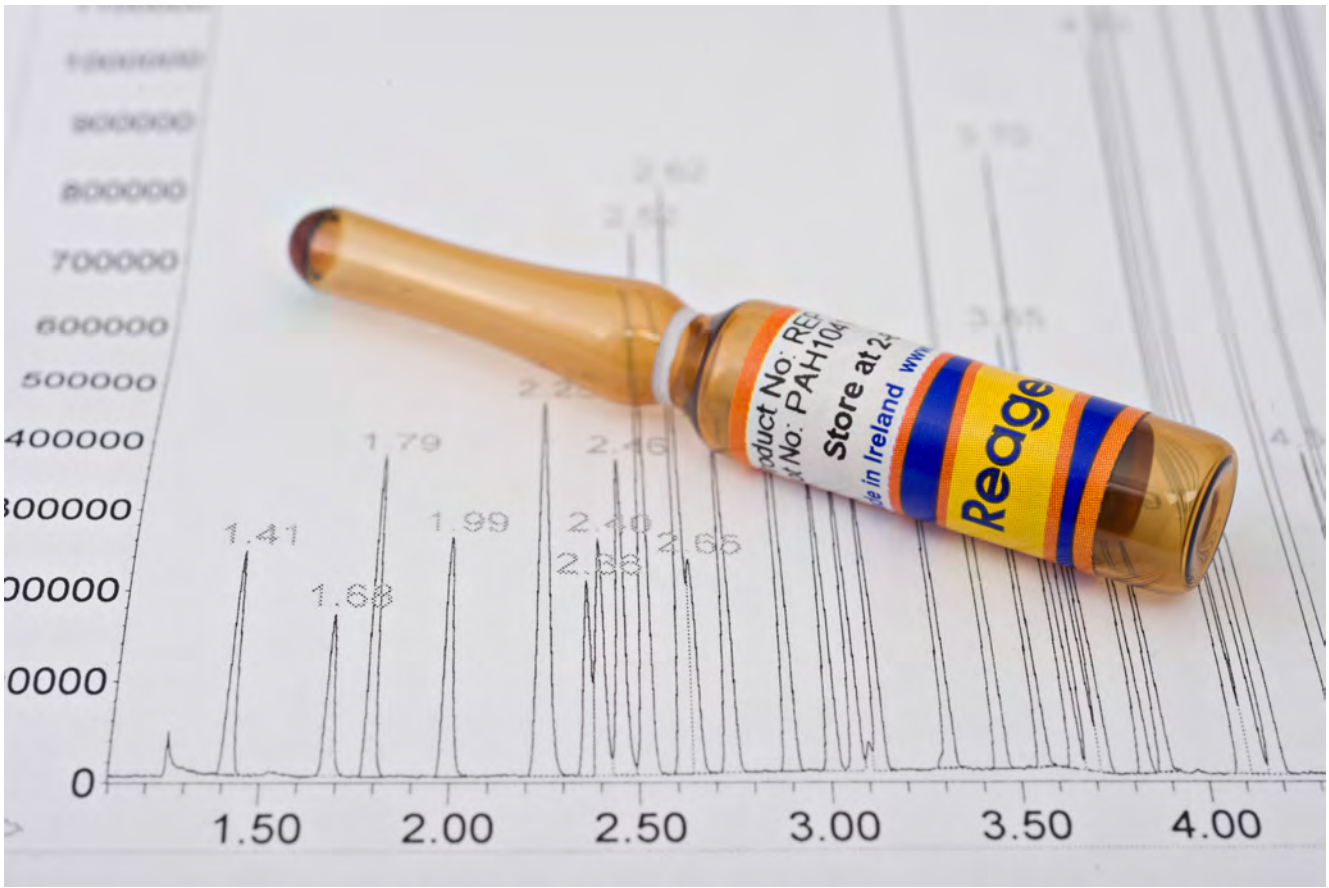
There have been many notifications from several EU Member States via the Rapid Alert System for Food and Feed (RASFF) of the occurrence of Sudan I, II, III and IV, para red, rhodamine b, and orange 2 in chilli and curry powder and processed products containing chilli or curry powder, sumac, curcuma and palm oil among others. There have also been occurrences of azo dyes released from clothing and textiles, which may be accidently ingested intradermically or orally by people wearing such clothes. Textile workers are also at risk.

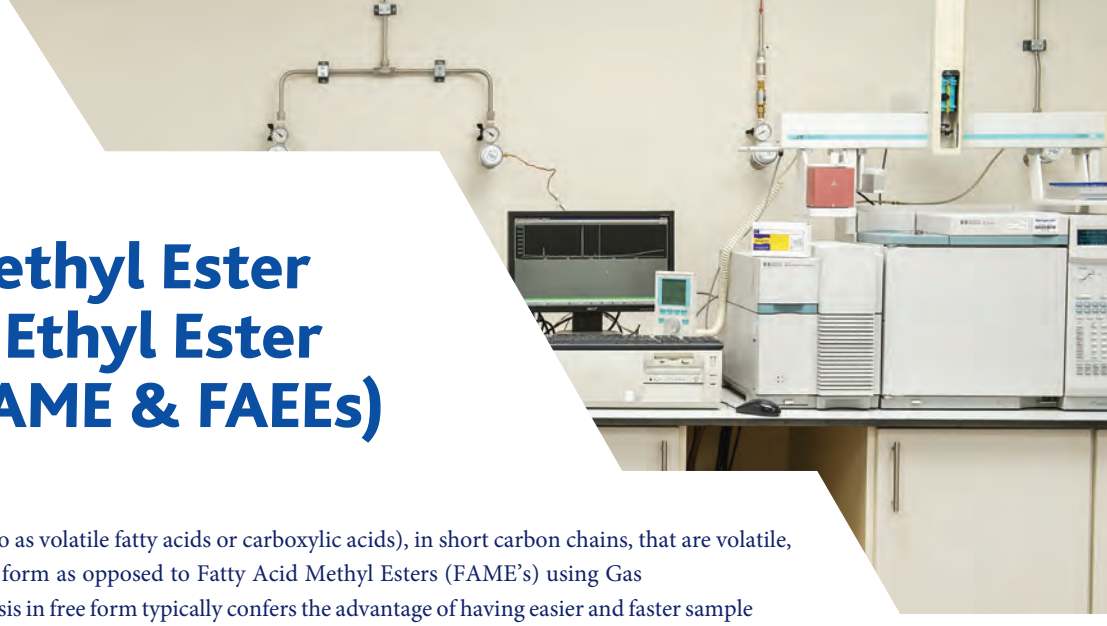
Metabolite Standards

Efficient analytical methods for the determination of food colorants are of utmost importance since their illegal presence in food threatens consumer's safety. Up to now, most methods are focused to detect dyes so far found illegally present in food. There are no methods focused in the detection of aromatic amines derived from azo dyes which may potentially appear illegally in food and show carcinogenic effects in humans.

In a study funded by and participated in by scientists in Reagecon, we have taken account of this consideration and have tried to fill this void. For example, we have provided and published a rapid, accurate and precise method for the identification and quantification of various synthetic food colourant products in paprika. As always, our principle role has been to characterise, purify, validate and offer high quality standards for these products and disseminate these into the marketplace. Further details can be found at www.reagecon.com

(1) Report 6/14 Chemicals in textiles - risks to human health and the environment. KEM Swedish Chemicals Agency, Stockholm, 2014





Fatty Acid Methyl Ester & Fatty Acid Ethyl Ester Standards (FAME & FAEEs)

Free fatty acids (also referred to as volatile fatty acids or carboxylic acids), in short carbon chains, that are volatile, are typically measured in free form as opposed to Fatty Acid Methyl Esters (FAME's) using Gas Chromatography (GC). Analysis in free form typically confers the advantage of having easier and faster sample preparation and avoids the formation of derivatisation artefacts. However, free fatty acids may be difficult to analyse because these highly polar compounds tend to form hydrogen bonds causing column adsorption problems or in the case of unsaturated fatty acids the slight difference between different compounds may be difficult to distinguish without the neutralisation step involved in esterification.

The esterification of fatty acids is an important tool for both characterising fats and oils and for determining the total fat content in foods and foodstuffs. It is also an important technique for assessing the quality and purity of biofuels. Fats are extracted using a non-polar solvent, saponised to acids and analysed by gas chromatography (GC). GC is an important technique for fats and oils analysis because accurate results can be obtained for complex as well as simple sample matrices. Several compendium from organisations such as the Association of Official Agriculture Chemists (AOAC), American Oil Chemists Society (AOCS) and the European Pharmacopoeia (EP) contain derivatisation procedures. FAME's may be produced from vegetable oils, animal fats or waste cooking oils by transesterification. In this process a glyceride reacts with an alcohol in the presence of a catalyst forming a mixture of fatty acid esters and an alcohol thus producing biodiesel. Using triglycerides as the fat source, results in the production of glycerol.

Rapeseed, sunflower, soybean and palm oils are the most common raw materials used for the production of biodiesel. Using methanol in the transesterification process has the advantage that the resulting glycerol can be separated simultaneously during the transesterification process. When using ethanol, the ethanol needs to be free of water and the oil needs to have a low water content as well, to achieve an easy glycerol separation. Where ethanol is used it is fatty acid ethyl esters (FAEE's) that are produced. The end products of the transesterification process are raw biodiesel and raw glycerol. After a cleaning step biodiesel is produced. The purified glycerol can be used in the food and cosmetic industries as well as in the electrochemical industry and as a substrate for anaerobic digestion. Reagecon offers several FAME and FAEE individual compounds and mixtures which can be used to calibrate the GC instrument prior to analysis or as Quality Control Materials during analysis. Deuterated versions are also available for use as internal standards. Such products may be offered as neat materials or in pre-prepared liquid matrices.

Nitrosamine Standards

Nitrosamines are products that are formed by the chemical reaction of amines and nitrogen containing agents such as nitrates, nitrogen oxides or nitrous acids. The products can be detected in air, water, soil, beverages, milk, cosmetics and in the alimentary tract of both humans and animals. Nitrosamines are now classified as known carcinogens and much attention in particular is being paid to the presence of a substance called N-Nitrosodi-Methylamine (NDMA) and several other nitrosamines in drinking water. This substance is accidently produced during a process called chloramination which is used in water treatment plants to reduce or eliminate trihalomethane levels in drinking water.

The occurrence of several nitrosamines including NDMA has been documented in recycled water, effluent, industrial waste water discharges and sewage sludge. All of these are sources of groundwater contamination and all have the potential to move from groundwater into the potable water system. NDMA is now considered a priority pollutant and a number of local, national and international authorities have set regulatory guidelines for this and other nitrosamines in drinking water. Apart from NDMA, N-Nitrosomethyethylamine (NMEA), N-Nitrosodiethylamine (NDEA), N-Nitrosopyrollidine (NPYR), N-Nitrososodi-N-Propylamine (NDPA), N-Nitrosopiperidine (NPIP) and N-Nitrosodi-N-Buthylamine (NDBA) are all considered significant.

Since nitrosamines may only be present in various matrices in ppb of ppt levels a high degree of sensitivity in sample management is necessary to monitor their presence. High quality, pure and well characterised standards are an imperative for successful qualitative and quantitative detection and measurement. Reagecon offers neat, single and multi component Standards for Nitrosamine analysis. These Standards are characterised and screened for identity, purity, stability and homogeneity. The products are prepared and certified gravimetrically and verified using GC-MS.

Polybrominated Biphenyl Standards (PBBs)

Polybrominated biphenyls (PBB's) which may also be called brominated biphenyls, or polybromobiphenyls, are the bromine analogs of Polychlorinated biphenyls (PCB's). Like PCB's, they are man made, hazardous to mammalian health, controlled, or prescribed environmentally but not nearly as commonly used as PCB's in industrial applications.

Like PCB's there are 209 possible congeners which differ from each other in the number and position of the bromine atoms in the two phenyl rings. Also like the PCB's the benzene rings can rotate around the central bond that connects the rings allowing planar and non-planar configurations. These differences in molecular structure are highly relevant in terms of the interaction with different receptors in determining possible toxicological or pathological properties of PBB's.

The products are used as flame retardants and form a subset of the brominated flame retardant group. The products are added to polymers and fibres and have made their way into several types of consumer goods, including computer peripherals, electrical goods, textiles and some furniture products, always to render them, less flammable. PBB's are also highly lipophilic and will accumulate in lipid rich tissues. There is significant evidence of hazards to human health from these products which are certainly proven to be absorbed through the gastrointestinal tract. Such pathological effects include evidence of poor neurodevelopment, specific cancers, and hormonal effects on fertility. Some evidence of immunotoxicity has also been reported.

Reagecon is developing a growing offering of PBB congeners mostly in ready to use format in an isooctane matrix. However, customised matrices, mixtures and other concentrations are also available upon request. Some of the congeners are also offered in neat form. For additional information on this rapidly growing range please visit www.reagecon.com

Polybrominated Diphenyl Ethers (PBDEs) & Other Flame Retardant Standards

Polybrominated Diphenyl Ethers (PBDE's) are a subgroup of the wider brominated flame retardant family. Structurally, they are similar to Polychlorinated Biphenyls (PCB's) and like PCB's there are, in total, 209 different congeners or isomers. The compounds are classified according to the average number of Bromine atoms in the molecule.

The congeners occur as mono-, di-, tri-, tetra-, penta-, hexa-, hepta-, octa-, nono-, and decabromodiphenyl ethers and the numbers of each respectively are 3, 12, 24, 42, 46, 42, 24, 12, 3, and 1, all adding up to 209 in total. The three main commercial mixtures that were available on the market include pentaBDE, octaBDE and decaBDE. The pentaBDE mixture contains tetrabromates, hexabromates and traces of tribromates in addition to the pentabromates. OctaBDE includes hexa, hepta, nona and decabromates as well as the octa congeners. There are no known natural sources of PBDE's, although some evidence exists in the literature that PBDE variants may be produced by marine organisms, but all commercial mixtures were man made.

PBDE's have been used in a wide variety of products as flame retardants, including building materials, electronics, furnishings, motor vehicles, household appliances, plastics, foams and textiles. Like PCB's, these products exhibit high lipophilicity and therefore accumulate in fatty tissues. Unlike PCB's, they are easier to degrade because of the weaker bromine bonds and unlike PCB's there is less concern about their toxicity upon degradation.

There is evidence from animal studies that PBDE's are injurious to health, but the evidence is spurious, and specific effects are not clearly elucidated. There is evidence of the products acting as endocrine disruptors, possibilities that they may act as a teratogen and some studies have identified neurodevelopmental toxicity in mice.

Humans may either ingest orally or through the respiratory tract. Waters used in the manufacture of PBDE containing products are at high risk of contamination and pose risks if ingested. Staff in repair or recycling plants are also at risk but inhalation or food ingestion in a domestic context also poses potential health hazards. The products have also been detected in dust, sludge and wastewater effluent and there is no doubt about their ability to bioaccumulate. Detection methods include GC, GC-MS and various LC combinations.

Polychlorinated Biphenyl Standards (PCBs)

Introduction

Polychlorinated biphenyls (PCB's) are man made organic chemicals derived from combining between 1 and 10 chlorine atoms with biphenyls, a molecule that is composed of two benzene rings. When all of the possible positions of the chlorine atoms on the benzene rings are taken into account, a total of 209 configurations are possible and these are called congeners.

Of these 209 congeners about 130 have been used in commercial preparations, since the introduction of the products into the marketplace by a company called Swann Chemical Company, which commenced production in 1929. Synthesis at laboratory scale began in 1881 and from then significant amounts of PCB's were already being released into the environment.

Applications

The commercial uses of PCB's were based on the products being good insulators, chemically stable and of low flammability. Therefore, they were used for a range of applications that include: coolants and insulating fluids for capacitors and transformers, hydraulic fluids, cutting oils, copying paper, plasticisers in paints and cements, additives in PVC coatings and as pesticide extenders. They also had a myriad of other commercial uses, description of which is beyond the scope of this document.

Often PCB's were sold as commercial mixtures under trade names, including Aroclor's, which is a brand name of Monsanto. Such Aroclor's had a four digit numbering system, with the first two digits referring to the number of carbons in the two benzene rings (12 in the case of PCB's) and the second two digits referred to the percentage of chlorine by mass in the mixture, although there are exceptions to this nomenclature. Aroclor's varied in terms of what they were used for, depending on availability and suitability for particular applications.

Presence in the Environment

PCB's are highly resistant to oxidation or reduction processes, which makes them stable and persistent pollutants (POPs). They are unstable in water, which makes them more stable in the environment chemically and either intentional or natural destruction may lead to the generation and release of extremely toxic materials such as Dibenzodioxins and Dibenzofurans through partial oxidation.

Many rivers, lakes, buildings and other sites are contaminated by PCB's and they have been found also in soil and air. Because of their lipophilic properties, they are to be found in foodstuffs and at various points of the food chain.

Health Effects

PCB's are readily absorbed through skin, but can also be absorbed through polyvinyl chloride (PVC) or latex rubber. However, most human absorption is through the alimentary or respiratory routes and once ingested they may change in chemical structure. One of the physical properties of PCB's includes lipophilicity which causes bioaccumulation in both adipose tissue and in liver tissue.

Persons exposed to very high levels may experience skin lesions, liver damage, ocular lesions, lowered immunity and irregular menstrual cycles by interference with estradiol. Generalised symptoms can include headaches, fatigue and cough. More severe symptomatic outcomes may include cancers, sexual, skeletal, and mental under-development in both sexes. In fact, evidence of reduced levels of certain thyroid hormones could have an adverse effect on every physiological process within the body.

Phthalate Standards

Phthalates are esters produced by esterification of phthalic acid with different alcohols. They are the most commonly used plasticisers, which are added to plastics to increase their flexibility, transparency and durability. Phthalates may be classified into two groups, based on molecular weight, comprising low molecular weight phthalates (ester side-chain lengths, one to four carbons) which include dibutyl phthalate (DBP), diethyl phthalate (DEP) and dimethyl phthalate (DMP) and high-molecular-weight phthalates (ester side-chain lengths, five or more carbons), which include bis (2-n-ethylhexyl) phthalate (DEHP) and dinonyl phthalate (DINP). These compounds can be found in a wide range of products, including adhesives and glues, electronics, medical devices, tubing, packaging, cosmetics, children's toys and food. Their presence in different products of everyday use means they can be found in all parts of the environment.

Since phthalates are incorporated in the polymer matrix in almost all plastic materials, these can easily migrate into foods and drinking water from the packaging or bottling material. Thus phthalates can bioaccumulate in tissues and in the food chain. Phthalates are poorly biodegradable and are potentially toxic. They have been associated with a number of health problems that include endocrine, respiratory, neurological and reproductive disorders. Several phthalates have been prioritised as significantly hazardous substances by many protection organisations.[1] For example, certain phthalates have been identified as priority hazardous substances by the European Union (EU), the US Environmental Protection Agency (EPA) and other international organisations.

In order to protect the consumers, sensitive and reliable methods for rapid detection of phthalates present in food and food contact materials are clearly needed. Although, liquid chromatography-mass spectrometry (LC-MS) methods for phthalates have been described, gas chromatography-mass spectrometry (GC-MS) is the preferred method for phthalate measurement due to the high reproducibility and specificity obtained.

Irrespective of analytical methodology, there is a requirement for high quality, pure, well characterised phthalate standards. Such standards have recently been developed in this laboratory and we have as part of this work, participated in a significant study on the quantification of phthalates in commercially available drinking water from different producers. Furthermore, this study provides specific data about the concentration of DBP and DEHP attributable to the migration of phthalates from food contact materials.[1]

[1] Improved method for rapid detection of phthalates in bottled water by gas chromatography–mass spectrometry
Paz Otero[a], Sushanta Kumar Saha[a], Siobhan Moaneaa, John Barron[b], Gerard Clancy[b], Patrick Murray[a]

[a] Shannon Applied Biotechnology Centre, Limerick Institute of Technology, Moylish Park, Limerick, Ireland

[b] Reagecon Diagnostics Limited Shannon Free Zone, Shannon, Co. Clare, Ireland.

Exhibitions 2016

As part of our programme of Exhibitions, Reagecon again participated in the Analytica Trade Fair in Munich. The show was very successful and we are delighted to present a few images of the exhibition. In total Reagecon have exhibited at several Trade Shows this year and the upcoming venues are highlighted in red. We look forward to seeing you there..

Month	Date	Show-Location
Jan	27-29	HTC-14 Ghent
March	15-17	Eurolab -Warsaw
	17-18	Loborama-Brussels
	20-23	Arablab -Dubai
	30-31	ForumLabo-Paris
April	31/3-2/4	China LabExpo-Guangzhou
	13-15	Lab Indonesia-Jakarta
	26-29	KOREAlab-Kintex
May	9--12	AchemAsia-Beijing
	10-13	Analytica-Munich
	22-24	CISILE-Beijing
Oct	10-13	Analytica China-Shanghai
	20-21	Reagecon's Metrology Centre launch
Nov	2--3	WWEM-Telford
	7-10	ADIPEC Abu Dhabi UAE
	10-12	Turkchem Eurasia-Istanbul

OBTAINING ACCURATE CONDUCTIVITY MEASUREMENTS

Authors: John J. Barron, Colin Ashton, Leo Geary & Bernard Gleeson – Reagecon Diagnostics Ltd

Conductivity is an extremely common analytical technique. Due to the simplicity of the equipment required, it can be measured quickly and cheaply. However, there are a number of factors that need to be taken into account to ensure that these measurements are accurate and fit for purpose so that decisions made based upon conductivity test results are correct:

1. Instrument Selection

- Required accuracy of results is the overriding selection factor.
- Take account of the instrument's temperature measuring accuracy – this may be the biggest error source.
- Be aware of specifications stating the accuracy as "% f.s." – this means % of the full scale of the instrument's measuring range and not % of the measured value

2. Sensor Selection

Conductivity sensor selection is made based upon the conductivity range of the samples being measured. Modern conductivity sensors are capable of giving linear response over several decades; but it is not possible to cover the entire practical conductivity range with a single sensor.
Figure 1 shows the linear ranges of sensors with different cell constants

FIGURE 1 : TYPICAL MEASURING RANGES OF SENSORS WITH DIFFERENT CELL CONSTANTS (k)

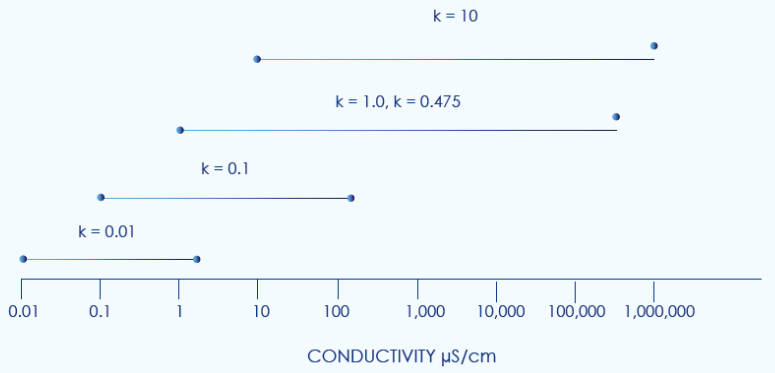


Figure 1

3. Temperature Effects

Conductivity is a temperature dependent parameter. Table 1 gives the temperature dependency for a range of solutions

Temperature Depency of Solutions

Solution	Temperature Coefficient of Variation %/ °C at 25 °C
Ultrapure Water	5.50
NaOH 5%	2.01
NaOH 30%	4.50
HCl 5%	1.58
HCl 30%	1.52
KCl 5%	2.01
KCl 30%	1.68
Fresh Water	~ 2.0

Table 1

Conductivity instruments are equipped with a temperature compensation function. This has practical benefits, but also limitations:

- Comparisons of measurements made at different temperatures are possible, as the instrument reports an expected conductivity value at a reference temperature (usually 25°C).
- Field measurements are practical, particular with instruments equipped with non-linear temperature compensation specified in ISO 7888(3) (suitable for natural waters, such as groundwater and river water).
- Temperature compensation must be appropriate to the sample type.
- For high accuracy do not use temperature compensation; but ensure all the samples are at the same temperature
- The Pharmacopoeias stipulate that temperature compensation cannot be used for the laboratory measurement of purified water samples(4,5).

4. Selection and use of Calibration Standards

Conductivity instruments multiply the input signal from the sensor by the Cell Constant to give their reported value. The Cell Constant is assigned during calibration by measuring the response to a Calibration Standard. As all of the subsequent sample measurements will be affected by the calibration process, it is essential that the Calibration Standard is suitable and used correctly:

- It should be of high accuracy – your measurements cannot be more accurate than your Calibration Standard.
- It should be traceable to SI units (usually via traceability to primary standards, such as those produced by NIST). If this is not the case then your conductivity measurements are not traceable to SI units and so you are not entitled to quote your readings in SI units.
- Ideally, the manufacturer should hold ISO 17025(6) accreditation – this gives an independent guarantee of the traceability and validity of how its value was assigned.
- To ensure contamination does not occur, rinse the measuring container to drain before filling and rinse the sensor to drain with the Calibration Standard before placing it in the measurement aliquot. The same approach should be used when measuring samples

5. Proof of the correct result

Many analysts cover all of these previous points; but this does not give any proof that their sample measurements are correct. If the only standard used is the Calibration Standard then this assumes that the sensor and instrument give perfectly linear response. Apart from at the calibration value, this gives no knowledge of how your system performs

FIGURE 2: CALIBRATION ALONE DOES NOT ASSURE CORRECT TEST RESULTS

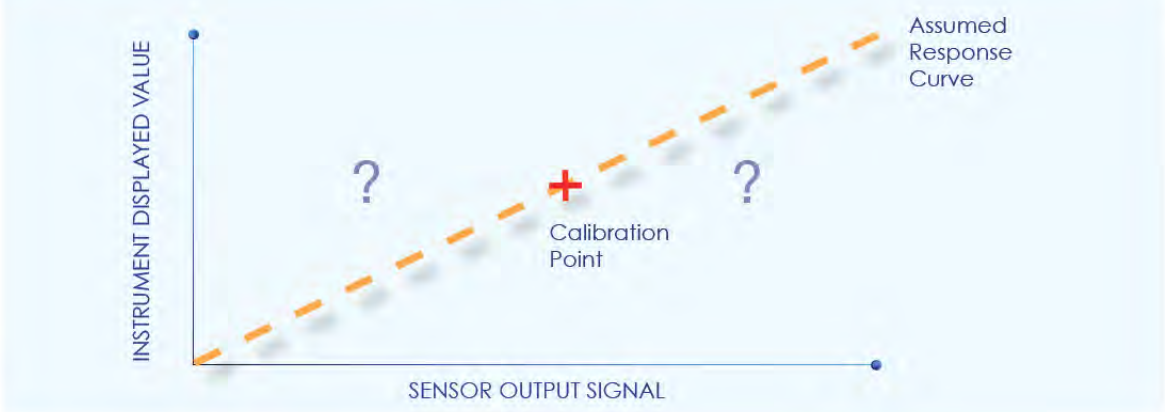


Figure 2

To give assurance of results requires the use of Control Standards and also an understanding that the role of the Calibration Standard is merely to accurately assign the Cell Constant. For the Calibration Standard selection:

- If the instrument has pre-defined Calibration Standard values then use these values, as this will automate the calibration process.
- When measuring low conductivity then use a Calibration Standard near the upper end of the cell's linear response range (typically 200µS/cm for sensors with a nominal Cell Constant of 0.1cm-1) to limit errors from the instrument's resolution.
- Some instruments have a number of discreet overlapping measurement ranges that each use a separate Cell Constant and so each need a Calibration Standard.

If properly selected, the Control Standard gives full assurance of the correct result(7):

- The Control Standard should have similar properties to the samples – i.e. similar conductivity value and similar matrix (usually aqueous).
- If the samples have a wide range of conductivity values then a number of Control Standards will be required.
- The Control Standard should be handled as described above for Calibration Standards, to ensure contaminations does not occur.
- If an acceptable reading is obtained for the Control Standard then this not only proves that the instrument is functioning correctly; but also that the sensor gives linear response, the calibration process was performed correctly, temperature effects do not give significant errors, the operator has not contributed significant errors and that the entire measurement process yields valid results.

The Use Of Appropriate Control Standards Gives Full Confidence In The Complete Conductivity Measuring System And Method So That There Is Proof That The Conductivity Measurements Are Correct.

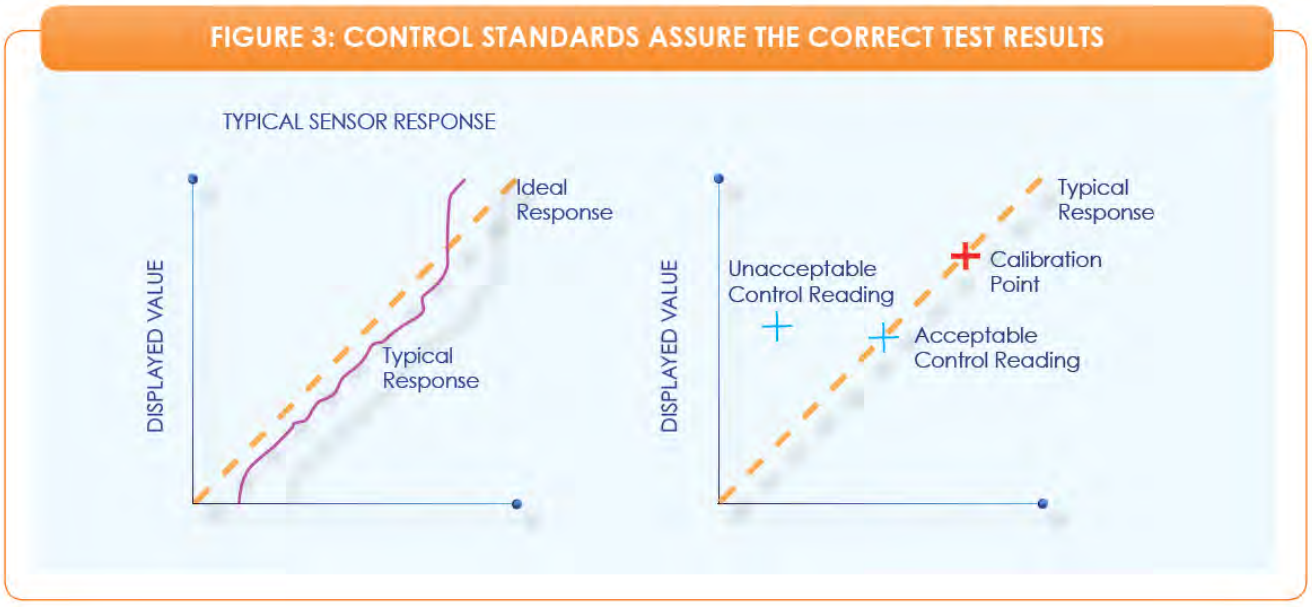


Figure 3

6.0 References

1. Barron JJ & Ashton C., 2007,"The Selection, Use, Care and Maintenance of Sensors for Accurate Conductivity Measurement"
2. Barron JJ. & Ashton C., 2006, "The Effect of Temperature on Conductivity Measurement"
3. ISO 7888 "Water Quality – Determination of Electrical Conductivity"
4. United States Pharmacopoeia, Monograph <645>: "Water Conductivity"
5. European Pharmacopoeia Monographs 0008, 0169 & 1927
6. ISO 17025 "General Requirements for the Competence of Testing and Calibration Laboratories"
7. Barron JJ. & Ashton C., 2004, "The Application of Good Laboratory Practice in the Selection and Use of Accurate, Traceable Conductivity Standards" *

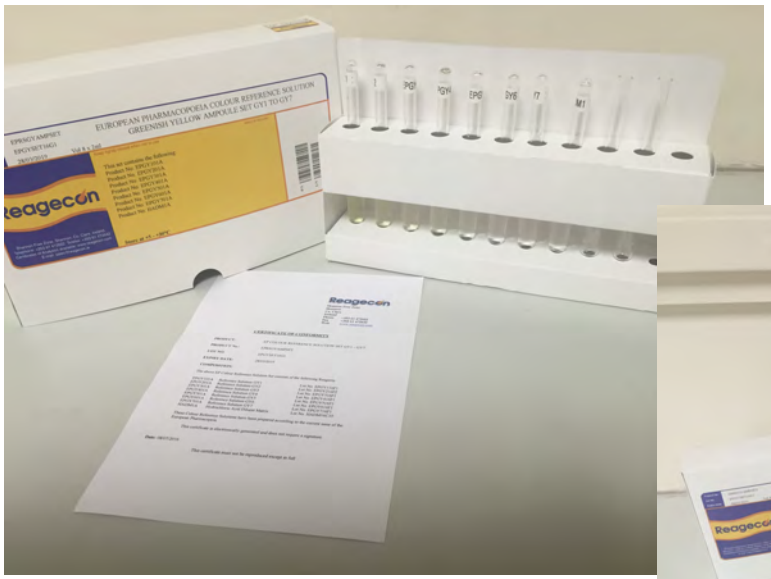
New Products Launched

Examining the degree of coloration of liquids in the range brown – yellow – red is described in the European Pharmacopoeia. Preparation of the required colour reference solutions, however, is complex and time-consuming. Hence, Reagecon's ready-to-use reference solutions can save you time and money.

Therefore we have recently launched a Range of Ready to Use Colour Kits in Compliance with European Pharmacopeia.

All 37 color reference solutions described in chapter 2.2.2 of the Ph Eur – are available as convenient, easy to use kits. Each kit (B, BY, Y, GY and R) contains a set of cuvettes with the respective solutions as well as empty sample cells (developed for Ph Eur method I). To perform the analysis, simply fill the sample in the empty cuvette, place it alongside the color comparison solutions in the rack provided, and compare colors in diffused daylight, viewing horizontally against a white background.

Item No.	Item Description
EPBSET	European Pharmacopoeia Reagent Colour Reference Solution Set B1 to B9
EPBYSET	European Pharmacopoeia BY Colour Reference Solution Set, containing BY1 to BY7
EPGYSET	European Pharmacopoeia GY Colour Reference Solution Set, containing GY1 to GY7
EPRSBAMPSET	European Pharmacopoeia Colour Reference Solution Brown Ampoule Set B1 to B9
EPRSBYAMPSET	European Pharmacopoeia Colour Reference Solution Brownish-Yellow Ampoule Set BY1 to BY7
EPRSGYAMPSET	European Pharmacopoeia Colour Reference Solution Greenish-Yellow Ampoule Set GY1 to GY7
EPRSRAMPSET	European Pharmacopoeia Colour Reference Solution Red Ampoule Set R1 to R7
EPRSYAMPSET	European Pharmacopoeia Colour Reference Solution Yellow Ampoule Set Y1 to Y7
EPYSET	European Pharmacopoeia Y Colour Reference Solution Set, containing Y1 to Y7



Reagecon Staff Supporting Local Charities

Reagecon Management and staff are delighted to support various fundraising initiatives and charitable organisations throughout the year. A small collection of photos from our support of these are presented below.

Some of Reagecon's staff supporting the Irish Cancer Society's Daffodil Day fundraising event .

We regularly support Ireland National Children's Hospital Temple Street and have taken part in The Trick Or Treat for Temple Street Campaign for the past 3 years, as well as supporting this very worthy cause with coffee mornings and other events.

Reagecon

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Reagecon Diagnostics Ltd.

Shannon Freezone, Shannon, Co. Clare, Ireland
Tel: +353 61 472622 • Email: sales@reagecon.ie • Fax: +353 61 472642

www.reagecon.com