



Analytical Services

Chromatography
Mass Spectrometry
Method Development & Validation
Technology Transfer



Chromatography... every step of the way



crawfordscientific

Chromatography...every step of the way



Crawford Scientific with Hall Analytical Laboratories

With 120 years of combined experience in chromatography and mass spectrometry, Hall Analytical Laboratories in Partnership with Crawford Scientific offer a range of high quality development and analysis services to clients in all industry sectors.

Our successful service is built on three main principles:

- Excellent Communication & Customer Focus
- Analytical Science at the cutting edge performed by acknowledged experts
- Cost effectiveness based on highly efficient processes and high performance instrumentation

Customer Focus

In partnering with Crawford Scientific you gain the advantage of a highly experienced team with one main focus – delivering results!

We achieve this through:

- Extensive consultation and feedback
- High investment in technology
- Expert staff with time and knowledge to optimise results
- A fully accredited quality system
- Efficient and timely service with good project management
- Cost effectiveness
- Confidentiality





We recommend that you audit our laboratory – available at any time by prior arrangement

Regulatory Compliance/ Quality Framework

Together Crawford Scientific and Hall Analytical Laboratories provide a high quality service.

Our extensive experience guarantees total confidence in sampling handling and preparation, data acquisition and interpretation.

Our quality and project management systems ensure that all work is undertaken efficiently and enables us to update you regularly with progress reports.

Our facilities and analysis have been subjected to regulatory audits at the highest level and we have gained extensive regulatory compliance.

Milestones for Flexibility

Our expertise, client focus and management systems enable us to offer a Milestones approach to projects. Our study plans and work schedules contain Milestones which allow regular reviews and project termination or study plan amendment as required – **offering you a highly flexible and low risk solution to analytical outsourcing.**

Regulatory Compliance

**UKAS Accredited for the analysis of
Dioxins and Furans (BS/EN 1948)**

ISO/IEC 17025 approved quality system

GLP / cGMP Accredited

ISO 17025 Certified for Foams Analysis



Applications & Services

Industry / Application Areas -

- Pharmaceutical
- Environmental
- Petrochemical
- Geochemical
- Odours & Taints
- Essential Oils & Fats
- Forensic / Drugs of Abuse
- Polymer
- Foams & Textiles



Analytical Techniques

GC Techniques

- Capillary GC
- ECD / TCD / FID
- Split / Splitless
- Large Volume Injection (LVI)
- Headspace (HS) / Thermal Desorption (TD)
- Solid Phase MicroExtraction (SPME)

LC Techniques

- LC
- Capillary LC
- Ultrafast (Sub 2 μ m) LC
- Preparative HPLC
- DAD
- Fluorescence

MS Techniques

- LC-MS
- LC-MS/MS
- LC-MSn
- Electrospray / APCI
- Probe EI MS
- Accurate Mass GC-MS
- GC-EIMS
- GC-CIMS
- TD / HS GC-MS

Specialists in
compositional analysis
and structural elucidation



Instrumentation

Overview

We have state of the art instrumentation that allows us to carry out efficient and effective analysis according to your needs.

You can rely on Crawford Scientific to have the capability that you require to solve your problem. Whether this is a straightforward HPLC–UV method development, or a highly complex isolation and accurate mass determination of a trace component for structural elucidation, we will be able to provide the instrumentation and expertise to find the answers you need.

“ We found Crawford Analytical Services provided the answers that we needed with the minimum fuss, within our timescales and at a cost that was acceptable to our business. The best thing about this partnership is their excellent communication which gave us peace of mind ”

Blue Chip Pharmaceutical Client

Current Instrument Range

LC-MS

- LCQ-MS Deca XP
- QTof 2
- Micromass LCT
- Micromass Quattro Ultima

LC (+ Prep LC)

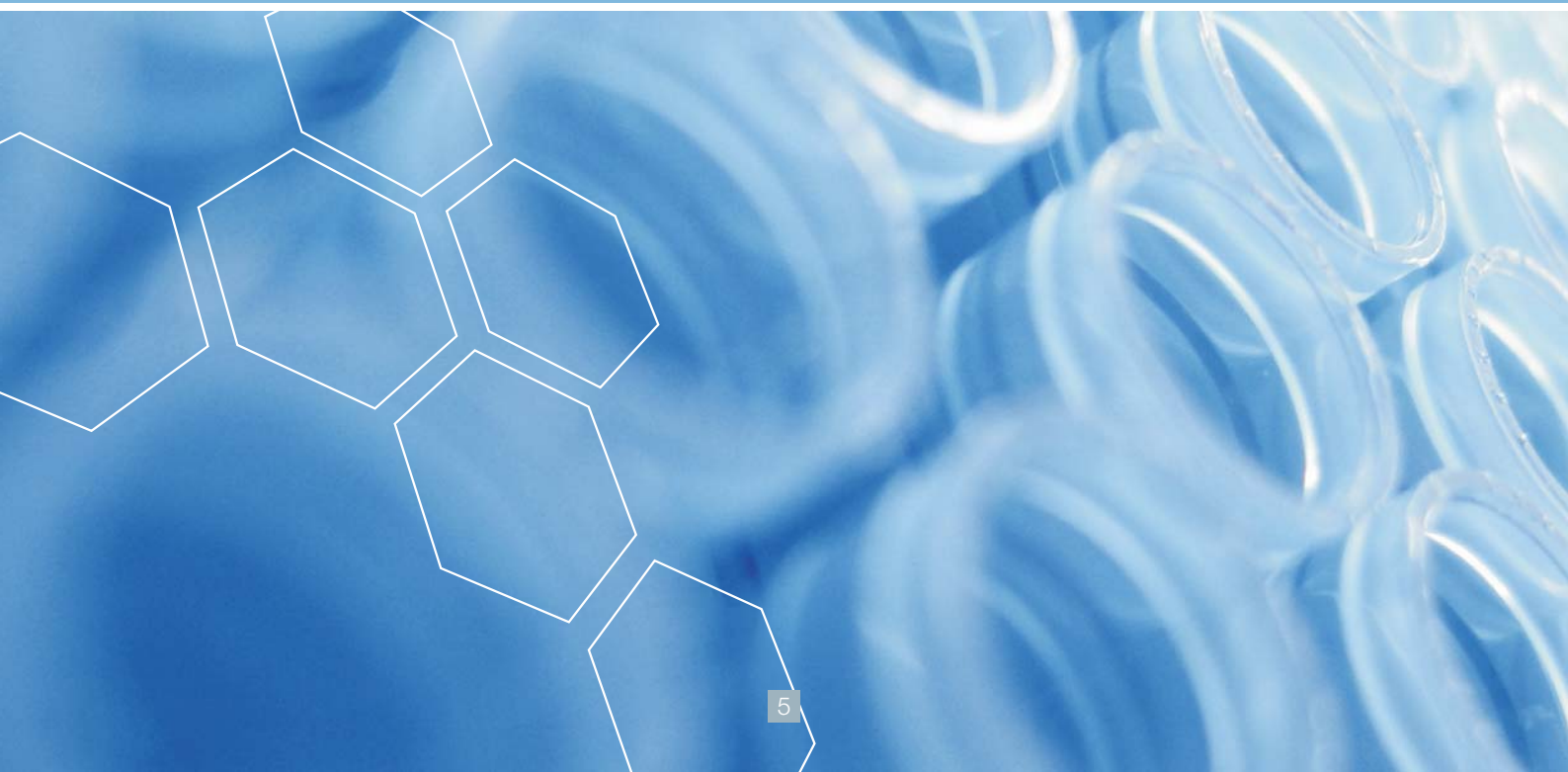
- Agilent 1100 series LC with DAD / Fluorescence
- Waters 2790 system with 996 DAD
- Waters 2690 system with 996 DAD
- Gilson Prep LC system

GC-MS

- Autospec M
- Autospec Q
- Agilent 6890/5973 GCMS (EI & CI)
- MD800 Fisons MS

GC

- Agilent 6890
- Agilent 5890
- MD 8000



“ Crawford Scientific Analytical Services have provided vital answers to our team through their expertise in characterizing unknown components and their ability to isolate and identify a critical degradation product from our API ”

Blue Chip Pharmaceutical Client

Pharmaceutical Analysis

Overview

We provide expert analytical solutions for all stages of pharmaceutical development and manufacturing support processes.

Our mass spectrometry services provide answers in structural analysis and the identification of unknowns using a range of accurate mass instrumentation coupled with preparative HPLC.

We develop methods for a range of analyses from high throughput chemistry using Fast HPLC to more complex stability indicating methods with Mass Spectral detection.

Our growing international reputation in the analysis of extractable components from container/closure systems is built on excellence in mass spectrometric analysis coupled with extensive knowledge of the chemistry involved.

Whilst we excel at technically challenging analyses we also provide analytical solutions for more routine analyses such as Residual Solvents Analysis.

Our laboratory practices and administration systems are MHRA accredited and we have hundreds of satisfied customers within blue chip pharmaceutical companies.

Our measure of success – repeat business!

Typical Services Available

HPLC / GC Method Development

- Fast HPLC for Combinatorial analysis
- Target Compound Analysis (MS where required)
- Method Development (GLP, cGMP)
- Full Method Validation (ICH Q2A, Q2B)

Target Compound Identification / Profiling

- Identification & characterization of New Drug Substances (ICH Q6A)
- Metabolite ID
- Extractable Profiles from Container / Closure systems (ICH Q6A)

Stability Indicating Analysis

- Method Development
- Product / Process Related Impurity / Degradant isolation and characterisation (ICH Q3A, Q3B)

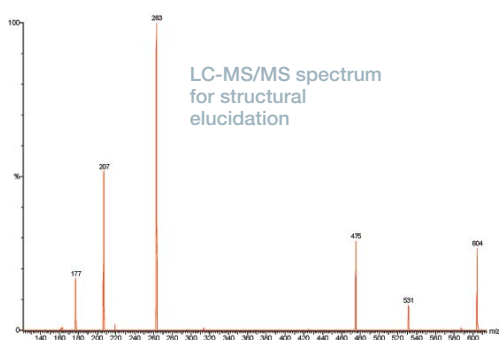
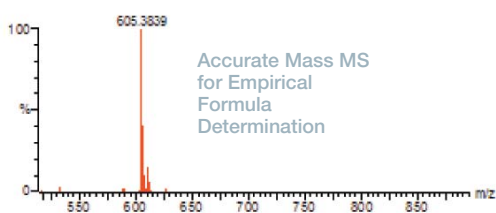
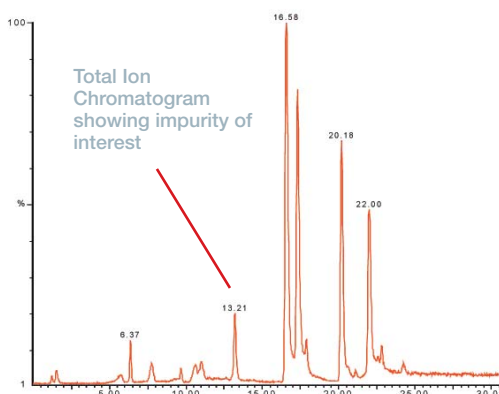
Production / Process Support

- Residual Solvent Testing (ICH Q3C)
- Process Troubleshooting
- Production Investigation
- Cleaning Validation (Method Development) (CFR 21 Part 211.67)



We specialise in Method Transfer and all methods developed can be efficiently transferred to your laboratory

Pharmaceutical Analysis



Structural Analysis

Our range of mass spectrometers coupled to both HPLC and GC are used to assist clients identify, characterise and, when required, quantify unknowns. Some examples are cited below:

Characterisation of Product or Process related Impurities or Degradants

- Preparative HPLC is used to isolate and concentrate the impurity of interest
- Molecular or Pseudomolecular weight information may not provide adequate information on either the structure or empirical formula of the analyte
- High resolution LCMS is employed to elucidate elemental composition and Tandem LCMS techniques may be used for structural information via collisionally induced dissociation
- GC-MS may be used where the impurity is volatile and library matching is combined with spectral interpretation for a tentative match
- Other techniques such as Solids Probe Electrospray MS and/or Pyrolysis/GC-MS may be used for involatile analytes unsuited to traditional HPLC or GC Analysis
- NMR analysis can also be undertaken to confirm molecular structure of the isolated impurities where required.

Pharmaceutical Analysis

Efficient and Accurate Approach to Testing

Compounds likely to migrate from container / closure systems might include:

- Monomers
- Initiators
- Antioxidants
- Antistatic Agents
- Heat Stabilisers
- Elastomers / Lubricants
- UV Absorbers
- Fillers
- Flame Retardants
- Modifiers & Coupling Agents

Controlled Extraction Studies Approach :

1. Extraction appropriate to component
2. General Screen for Extractables Profile (GC-MS / LC-MS)
3. Specific Screen for compounds of particular toxicological interest
 - Nitrosamines, PAHs, 2-Mercaptobenzothiazols
4. Appropriate Controlled Extraction Study using GC-MS (EI & CI), LC-MS (+ve & -ve)
5. Other supporting analysis and unknown characterisation as required.



Extractable & Leachable Analysis

This area of growing regulatory significance provides many challenges in the development and analysis of inhalation and injectable drug products.

Extractables are 'compounds that can be extracted from elastomeric, plastic compounds or coatings of the container and closure systems when in the presence of appropriate solvents under vigorous conditions.'

Whilst information may be available on the composition of the polymeric or rubber component from the manufacturer – this may be considered unreliable, incomplete and will not include information on extractable materials such as surface contaminants or materials absorbed into the component matrix over time as a result of processing and handling.

As a result of many years experience we have defined a strategy for performing **Controlled Extraction Studies** which satisfies the PQRI requirements, whilst presenting the client with a highly cost effective and efficient approach to the Controlled Extraction Study.

Controlled Extraction Studies give information useful for on-going component quality monitoring, biological risk assessment and can identify components for **Leachable Studies**. Leachable compounds pose a risk in that they may influence the delivered dose, react with the active pharmaceutical or other formulated ingredients and hence compromise the efficacy of the drug product.

Experience in developing validated analytical methodology for quantitative study of leachable compounds allows our team to accurately and efficiently assess the accumulated level of the leachable species throughout the shelf life of the product. This data can then be used to assess the biological risk posed by the accumulation of the potential migratory species.

Established track record of client Extractable & Leachable data being successfully submitted to FDA and other licensing authorities.

Determination of Residual Solvents

Residual Solvent analysis is required under ICH Topic Q3C when 'production or purification processes are known to result in the presence of such solvents'. The guidelines set limits on residual solvent levels and recommend methods for both qualitative and quantitative analysis.

USP Residual Solvents methods <467> are radically changing (July 2008) and the procedure now requires a different approach (similar to the current EP methods):

- Preliminary GC Screening
- Confirmatory analysis using dissimilar column chemistry
- Identification of any solvent identified under both analyses above
- Quantitative analysis

There are now 57 solvents listed as either Class 1 (unacceptable due to toxicity), Class 2 (solvents without adequate Toxicological Data) or Class 3 (least toxic, preferred solvents), all of which need to be screened and if identified subsequently quantified under proposed USP (and existing EP) guidelines.

We offer an expert service for the analysis of residual solvents which includes:

- GC-MS Screen using alternative selectivity columns (with Thermal Desorption as required)
- GC (or GC-MS) quantitation of Class 1 Solvents
- Identification and Quantitation of Class 2/3 solvents (or solvent residues)
- Expert spectral interpretation where required
- Method development, validation (ICH Q2A, Q2B) and Technical Transfer of the method.

Cleaning Validation

21 CFR 211.67 requires that cleaning of manufacturing and storage equipment is undertaken to ensure no toxic or physiologically active substances remain.

Many manufacturers now use Total Organic Carbon (TOC) Analysis for cleaning validation studies – assuming that all carbon detected is due to residual drug substance and/or drug product as appropriate.

Limits for this analysis are typically 1/1000 of the lowest therapeutic dose of the previous drug substance (or 10ppm whichever is lower) or the LD50 limit of the cleaning detergent used.


Whilst TOC analysis is useful for the broad estimation of residual detergents and other carboniferous material – it is unhelpful when issues develop regarding identification and quantification of specific contaminating materials.

We have developed a range of target analysis services which allow the identification and quantitation of contaminating materials which allows efficient troubleshooting and remediation of issues relating to cleaning of process equipment.

Our services include:

- Rapid identification of contaminants in Cleaning In Place (CIP) or Out of Place (COP)
- Small molecule and detergent identification and quantitation
- Analysis of swabs, wipes, rinse and immersion solutions to sub ppm levels of detection
- Identification and quantitation of contaminants identified via Total Organic Carbon (TOC) and Non Purgable Organic Carbon (NPOC) techniques.





“ Just a great solution to our environmental analysis requirements – a trusted partner!! ”

Global Chemical Manufacturing Client

Environmental Analysis

Overview

Our team has developed an extensive range of accredited Environmental analyses from a wide range of sample types – providing you with rapid, high quality analytical solutions.

Our laboratories are UKAS accredited for the sampling and analysis of waters and air emissions and the analysis of soils. Our extensive range of analytical, sampling and extraction equipment allows us to handle a wide range of matrix types for a suite of compounds of environmental interest, including:

- Air
- Soils
- Sediments
- Waste and Potable Waters
- Foodstuffs
- Tissue
- Vegetation

Our newly improved facilities and optimised methodology ensure a swift turnaround time and highly competitive pricing. We are able to offer a fast turnaround premium service for urgent samples when required.

We are constantly seeking ways to improve our service by reducing sample preparation time, analytical costs and detection limits. Full method blanks with each sample batch and appropriate QC sample preparation ensure confidence in our analytical results. QC results for recovery of internal standards and instrument calibration curves are far superior to the limits allowed in the standard protocol. Limits of detection are calculated separately for each targeted congener in each sample, giving a more accurate assessment of matrix interference.

Typical Services Available

Dioxin and Furan Analysis

UKAS accredited Dioxin analysis to BS/EN 1948, the European harmonized protocol for stack measurements from hazardous waste incinerators as well as to USEPA Method 23. This includes the preparation and supply of UKAS accredited XAD traps for sample collection.

Other Matrices:

Accredited Dioxin analysis methods to USEPA 1613 for soils, sediments, waters, waste waters, ash and dust have been developed. Tissue, lipid and vegetation methods are also available.

PCB analysis

Targeted PCB analysis in environmental samples such as soils, sediments and foods using high resolution GCMS.

PAH Analysis

Semi-volatile PAH analysis can be performed using either low resolution or high resolution GCMS to reduce chemical interferences and to achieve lower detection levels.

Species of Specific Environmental Interest

Methods have been developed which enable the following groups of materials to be identified and quantified:

- Volatile Organic Compounds (VOC'S)
- Semi-volatiles
- Sulphur compounds
- Pesticides / Herbicides



Petrochemical Analysis

Overview

Oil and oil related samples are some of the most complicated mixtures to analyse. The identification of trace components within these complex matrices requires a good understanding of the appropriate chromatographic and mass spectrometric techniques. The widely varying component concentration in these oil and petrochemical samples adds further complications when trying to perform quantification studies

We use a combination of approaches including high-resolution GC-MS with various spectral experiment types to identify and quantify analytes or categories of analytes within intractable matrices. We have the capability of sampling solids, liquids and gases to ensure that we can provide the full range of services that you require.

We have provided both qualitative and quantitative data to clients for many years for clients within the petrochemical and associated industries and have built an enviable reputation for problem solving and troubleshooting.

Whether you need a simple additive identification or a complex analysis involving detailed compositional or dopant analysis – we can provide over 100 years of combined experience in petrochemical and related analyses.

Typical Services Available

Oil Industry Services

- Source rock correlation
- Bio-diesel analysis (including Glycol quantitation ASTM D 2982)
- Oil based sample compositional analysis with full inhibitor profiling
- Wax and Oxygenate analysis in crude, fractioned oils and synthetic formulations
- Sediment and water analysis for hydrocarbon profile
- Oil gas breakdown products for transformer breakdown investigations / turbine flushing support analysis
- Incident / contamination analysis - including full profiling, identification and remediation
- Lubricated equipment failure analysis

Petroleum Industry Services

- Contamination speciation analysis
- Fuel and light-end fingerprinting
- Petroleum contamination analysis
- Cargo contamination analysis
- Compliance testing
- Odour / taint analysis
- Detergent inclusion analysis
- 'One-off' characterisation and quantitation
- Characterisation of processing additives
- Fuel Development support



Services Chart

Low & High Resolution LC-MS

- Primary Metabolites
- Pharmaceutical assay
- Quantitative DMPK analysis
- MDA, TDA analysis of foams
- Accurate mass LC-MS for characterisation
- Oil Analysis
- Food Adulteration

Low & High Resolution LC-MS/MS

- Metabolite Identification
- Impurity preparation and identification
- Bioanalytical and DMPK
- Extractable and Leachable profiling
- Dyes
- PAH, TPH, BTEX, VOC's and PCB analysis

High Resolution GC-MS

- Dioxins/Furans/PCB's
- Pesticides
- Organophosphates
- Biomarkers

Low Resolution GC-MS

- Volatiles & Semi-Volatile Organics in plastics, polymers, fabrics etc.
- Pyrolysis by flash or MSSV
- Dynamic Headspace Analysis
- Drugs of Abuse
- Oil and petrochemical contamination and characterisation studies

Analytical Partnerships

We recognize that University spin-off and smaller start-up companies in the Biotechnology and Pharmaceutical sectors often require analytical support in bringing products to market.

Working to GLP and ICH guidelines we offer a wide range of flexible, competitively priced support packages tailored around your needs.

Our extensive equipment range and staff experience enables us to assist emerging companies throughout their product development lifecycle.

Testing Services

- Structural analysis
- Purification and isolation
- Method development and validation
- Product assay
- Stability indicating analysis / impurity & degradant profiling
- Technical method transfer
- On-site training
- Pilot scale cleaning validation support
- Extractable and Leachable analysis

Contact Information

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Chromatography... every step of the way