



## EPP KEY EQUIPMENT

Edinburgh Pharmaceutical Processes [“EPP”] has superb facilities and technical equipment capabilities based across two sites which includes a dedicated Environmental Centre. Our sites are closely located outside Edinburgh, Scotland, and we offer facilities to handle large scale or complex projects.

Our experienced staff work across three core areas:

- Analytical and Screening including REACH and 5-Batch
- Environmental Sciences (eFate)
- Process Research and Development (R&D)

We specialise in:

- GLP 5-Batch analysis and Physico-chemical registration studies for Agrochemicals
- Custom synthesis of impurity, metabolite, and degradant reference standards.
- Re-certification of reference materials including GLP certification (with GLP NMR – qualitative analysis. We have our own NMR on-site).
- Reference Standard Management Service.
- Synthesise stable labelled reference materials.

We hold the following equipment and instruments across our two sites, which ensures we provide you a service of excellence.

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### Analytical & Screening Division

The Analytical & Screening Division uses several techniques including liquid chromatography, gas chromatography, spectrometry, and Karl Fischer analysis to provide quantitative and qualitative information on test substances. We hold on-site the following equipment:

#### Chromatography

Chromatography is one of the most powerful tools in the analytical laboratory and is used for the separation and analysis of mixtures of compounds of all types. Liquid chromatography systems feature detectors chosen according to the chemistry of the analytes of interest. Most detectors for HPLC are light absorbing detectors which focus on ultraviolet (UV) and visible (Vis) regions of the spectrum in the 190 - 900 nanometre (nm) wavelength range. Most analyses of organic analytes are in the ultraviolet range 190 - 350 nm.

#### High Performance Liquid Chromatography (HPLC)



At EPP HPLC separation is performed using the following instruments in conjunction with a range of detectors:

- **Agilent 1100 HPLC**
- **Thermo Ultimate 3000 HPLC**

EPP has the following detection systems:

- **UV Detectors - Diode Array Detector (DAD) and Variable Wavelength Detectors (VWD)**  
These are by far most popular detectors for LC. UV detectors can be fixed or variable wavelength and include diode array detectors (DAD or PDA). The UV absorption of the effluent is continuously measured at single or multiple wavelengths. Diode array detectors (DAD) can measure the entire wavelength range in real time whilst also allowing single-wavelength data acquisition. Two lamps in these detectors ensure the highest light output from 190 to 950 nm for low detection limits over the UV and Visible wavelength range.
- **Fluorescence Detector (FLD)**  
This type of detector is a useful tool to detect compounds which fluoresce. Fluorescence detection is typically more sensitive than UV detection. The detector can be used, when typical detection systems such as UV and MS are not suitable for the required applications.
- **Evaporative Light Scattering Detector (ELSD)**  
The detector identifies analytes with uniform sensitivity regardless of their spectroscopic properties. The detector removes the mobile phase through evaporation and then makes a light scattering measurement of the dried analyte particles. The output is directly related to the mass of the analyte particles. This type of detector is a useful tool to detect compounds with little or no UV response. The detector can be used, when typical detection systems such as UV and MS are not suitable for the required applications.

### **Ion Chromatography (IC)**

Ion chromatography is performed using a **Dionex Ion Chromatograph**. This system can be operated in anion and cation mode and employs electrochemical detection which allows characterization of ions in the sample.

### **Gas Chromatography (GC)**

Gas chromatography is used to separate mixtures of species in solution by vapourising a solution of the test substance. Detection of the analyte is performed by Flame Ionisation detection (FID) or Mass Spectrometry using the following systems:

- **Agilent 6890N GC system with FID**
- **Thermo Trace 1300 GC with FID and ISQ EI LT MS**



## Chromatography Data Capture Systems

**Chromeleon 7.2 CDS** is primarily used as the main data capture system for chromatography systems in the Analytical division. Chromeleon 7.2 enables full instrument control and data processing for High Performance Liquid Chromatography (HPLC), Gas Chromatography (GC) and Ion Chromatography (IC) in a GLP environment i.e., the system provides full audit trails, restricted user access, automated processing, and electronic archiving of data. This computerized system has been fully validated according to GLP.

## Water Analysis

Moisture meters are used to measure the amount of water in each substance using Karl Fischer titration. The titration can be performed in two different ways using either a volumetric or coulometric process. EPP has the capability to perform both types of titrations.

- **Coulometric Water Determination**

The water content of a sample is measured by coulometric determination (electrochemical titration). Coulometric determination allows accurate analysis of low levels of water, typically <1% w/w. The vaporiser attachment can be used when test substances are not directly soluble in the anode solution.

- **Volumetric Water Determination**

In a volumetric titration the reagent addition is performed automatically using a motor driven piston burette. At EPP the volumetric process is typically used for samples with a water content of 1-100% w/w.

## Mass Spectrometry

LCMS systems are Liquid Chromatographs with a mass spectrometer as a detector. At EPP, Ion Trap Mass Analyser systems are used on GLP regulatory studies for the qualitative analysis of a wide range of chemical compounds.

Mass spectrometry (MS) is an analytical technique that measures the mass-to-charge ratio ( $m/z$ ) of charged particles (ions). While the mass analyzer applies the electric and magnetic fields to sort the ions by their masses, the detector measures and amplifies the ion current to calculate the abundances of each mass-resolved ion.

The mass spectrum can be used to determine the mass of the analytes, their elemental and isotopic composition, or to elucidate the chemical structure of the sample. This is one of the techniques used for confirmation of identity of test substances for 5-Batch Analysis.

## Ion Trap Mass Analysers

Ion traps are used for a combination of electric or magnetic fields to capture charged particles, known as ions. These are often found in a system isolated from an external environment. As a storage device, the ion trap acts as an 'electric-field test-tube' for the confinement of gaseous ions either positively charged or negatively charged. The confining capacity of the ion trap arises from a trapping potential well formed when appropriate potentials are applied to the ion trap electrodes. This allows us to obtain high sensitivity full scan MS along with in-

depth MS<sup>n</sup> (CRM) capabilities. A single quadrupole offers Selected Ion Monitoring. A triple quadrupole adds Selected Reaction Monitoring. A linear ion trap goes further by enabling Consecutive Reaction Monitoring where a selected ion is fragmented into a product ion and the resulting product ion further fragmented in additional consecutive steps. Each additional fragmentation step makes compound identification more certain and facilitates structural characterization.

At EPP, LCMS is performed using the following instruments:

- **LTQ XL™ Ion Trap with Agilent 1100 HPLC-DAD**
- **LCQ™ Deca XP MS with Agilent 1100 HPLC-DAD**
- **LCMS Thermo Finnigan LCQ Advantage with Agilent 1100 HPLC-DAD**

This ion trap mass spectrometer is used for high productivity LC/MS/MS results and is easily upgraded to MS<sub>n</sub> performance.

#### **Additional Qualitative Techniques**

- **Shimadzu IRSpirit with ATR**

In the Analytical division FT-ATR spectroscopy is used qualitatively for the analysis of solid and liquid samples. This technique provides further information on the structure of the test substance and is one of the techniques used for confirmation of identity of test substances for 5-Batch Analysis

- **Bruker AV500 NMR Spectrometer**

In the Analytical division NMR is used qualitatively for the analysis of solid and liquid samples. This technique provides further information on the structure of the test substance and can be used as a technique for confirmation of identity of test substances for 5-Batch Analysis. Compounds can be identified using 1D spectra from <sup>1</sup>H, <sup>13</sup>C and other nuclei.

#### **UV Spectrophotometry**

Spectrophotometry is a standard and inexpensive technique to measure light absorption or the amount of chemicals in a solution. It uses a light beam which passes through the sample, and each compound in the solution absorbs or transmits light over a certain wavelength. EPP uses a **Shimadzu UV-1900** which is a double-beam UV-Vis Spectrophotometer using LO-RAY-LIGH™ diffraction grating technology to support the following study types:

- To generate UV-VIS spectra for various test items. The spectra are used to measure the absorbance maxima of the sample. The molar extinction coefficient can then be calculated using the absorbance maxima data. (OECD Test 101).
- For quantitative measurement of test items against standard curves employing single wavelength measurements.

## Research & Development Division

We have a custom synthesis house specialising in the production of analytical reference standards related to agrochemicals and pharmaceuticals.

Our expertise, superb facilities and instruments enable us to undertake a diverse range of chemical reactions including the complex synthesis of chiral and isotopically labelled compounds. Indeed, we have worked on impurity and metabolite reference standards associated with over 200 active ingredients.

We can work on a scale ranging from milligrams to kilograms (used for non-clinical research purposes). Our range of synthetic services are supported with insightful guidance and advice. In addition, we are also able to support your in-house team with synthetically challenging problems, optimising the manufacturing process.

- **Agilent 1100 HPLC System with Diode Array Detector.**  
The Agilent 1100 HPLC System guarantees the most efficient mixing and pulse-free solvent delivery for consistently fast and accurate results. The system's optimized design using a quaternary pump allows variable stroke volumes for stable solvent flow
- **Biotage SP4**  
The Biotage approach to sample purification involves the use of automated flash chromatography. By using pre-packed flash columns and a fully automated instrument, target molecules from synthetic reactions are rapidly isolated with a focus on maximised recovery.
- **Biotage Isolera one**  
Isolera One is equipped with Spektra. Spektra features include simultaneous UV-detection on all wavelengths and baseline correction. The unique behaviour of the lambda-all functionality, together with the uniquely designed baseline correction enables detection of poor UV absorbing compounds.
- **Biotage Microwave reactors**  
These are designed to enhance the ability to perform chemical reactions under controlled conditions on a laboratory scale. Microwave chemistry is based on the efficient heating of materials by "microwave dielectric heating" effects.
- **H-cube flow hydrogenator**  
The H-Cube<sup>®</sup> Mini Plus is a safe, powerful, and affordable flow reactor which generates high-pressure hydrogen with the electrolysis of water, allowing chemists to perform catalytic hydrogenations from atmospheric pressure and room temperature to 100 bar and 100 °C in minutes.
- **Photoreactor**  
We have is a 400W UV photoreactor capable of using volumes up to 2L.

- **PARR 4842 pressure hydrogenator (600ml)**

Parr Shaker type hydrogenators provide compact and easily operated systems for treating chemicals with hydrogen in the presence of a catalyst at pressures.

- **Preparative HPLC – SHIMADZU prep-HPLC 20A**

Shimadzu modular Prep HPLC comprising of:

2x LC20AR pumps  
SIL20A Prominence auto sampler  
CBM-20A Communication bus module  
SPD-20A Prominence UV/vis detector  
FRC10A fraction collector.

For semi-prep applications, the LC-20AR delivers solvent flow rates up to 20 ml/min, to support separation on analytical columns up to 20 mm I.D. and semi-preparative columns.

The system can be configured to suit a variety of purposes, with manual injection and isocratic separation to fully automated with autosampler injection and gradient elution. The solvent delivery unit and number of fractions collected can be selected to suit the recovery volume.

### **Bruker AV500 NMR Spectrometer**

EPP has its own in-house GLP compliant, NMR facility supported by a dedicated and highly experienced NMR operator with many years' experience in the field. As a result, we can offer a standalone NMR service to clients in addition to supporting our other EPP services.

Our NMR spectrometer is a Bruker Avance 500MHz running Topspin and Icon NMR. Samples can be run automatically with our 60-position sample changer. We can offer NMR experiments for  $^1\text{H}$ ,  $^{13}\text{C}$ ,  $^{31}\text{P}$  and other relevant nuclei (excluding  $^{19}\text{F}$ ). We have experimental methods in place for 1D, 2D and Quantitative NMR. The instrument is fitted with variable temperature control, pulsed field gradients and shaped pulses.

We can identify compounds using 1D spectra from  $^1\text{H}$ ,  $^{13}\text{C}$  and other nuclei, and various 2D experiments, including COSY, HSQC, NOESY and HMBC. Experiments using other 2D methods and other nuclei can be set up if required.

We can undertake quantitative NMR experiments to characterise materials and to certify standards examples being Ethephon, Glyphosate and Glufosinate.



## Environmental Science (eFate) Division

We specialise in working with difficult substances including unstable and volatile molecules as well as chemical substances of unknown or variable composition, complex reaction products and biological materials (UVCB). We hold the following equipment onsite:

- **Centrifuge**  
A centrifuge is a laboratory device that is used for the separation of fluids, gas, or liquid, based on density. Separation is achieved by spinning a vessel containing material at high speed; the centrifugal force pushes heavier materials to the outside of the vessel.
- **Beckman Coulter Allegra 6R Centrifuge**  
The Allegra 6R is ideal for cell culture, plasma, and other general-purpose separations. This rotor reaches a maximum speed of 3,750 RPM.
- **Beckmann Coulter 18 Microcentrifuge**  
The Beckman Coulter Microfuge 18 Centrifuge is a microprocessor-controlled compact bench top centrifuge that generates centrifugal forces required for a wide variety of applications, including pelleting of DNA, RNA, and proteins and cell virus isolation.
- **Beckmann DU 640 UV/Vis spectrometer**  
UV-Vis spectrophotometer for liquids and solids ensuring this is the ideal equipment for routine measurements.
- **FLSmidth Essa LM201 Pulverising Mill**  
The user-friendly LM201 can be fitted with 800, 1000 or 2000 cc single disc-type grinding bowls, and the standard size ring-and-roller grinding bowls. It typically grinds to 95% minus 75 microns in approximately three minutes.
- **FT-IR AVATAR 360 IR**  
This FT-IR spectrometer offers a packaged solution for the entire FT-IR process, from receiving the sample to successfully communicating the results.
- **Hobart Laboratory Homogeniser**  
Sample mixer used to homogenise sediment or soils spiked with the active / test item.
- **Perkin Elmer Sample Oxidiser Model 307**  
The 307 Sample Oxidizer is an automatic preparation and oxidization system for both single and dual radiolabelled samples containing 3H and/or 14C for use in liquid scintillation counting. The 307 Sample Oxidizer ensures reliable combustion of biological, environmental, and industrial samples.
- **Total Organic Carbon Analyzer**  
A TOC analyser allows you to monitor water purity levels throughout your process as well as validate the cleaning methods you use to maintain your drug manufacturing equipment.

- **Shimadzu TOC-L CPH**

The TOC-L series of TOC analysers adopts the 680°C combustion catalytic oxidation method. While providing an ultra-wide range of 4 µg/L to 30,000 mg/L, these analysers boast a detection limit of 4 µg/L through coordination with NDIR. This is the highest level of detection sensitivity available with the combustion catalytic oxidation method. In addition, the combustion catalytic oxidation method makes it possible to efficiently oxidize not only easily decomposed, low-molecular-weight organic compounds, but also hard-to-decompose insoluble and macromolecular organic compounds.

- **Agilent 1100 HPLC with Flow Scintillation Analyser**

The flow scintillation analysis is used to quantify the radioisotope label on organic compounds such as biochemicals, drugs, and metabolites separated from complex mixtures by High Performance Liquid Chromatography (HPLC).

- **Liquid Scintillation Counter (LSC)**

Liquid scintillation counters are mainly used for counting beta-emitting elements (<sup>3</sup>H, <sup>14</sup>C, N, O, P, S) because their radiation (charged particles) has a short range in solids and liquids. Liquid scintillation detectors differ from well counters in that the PM tube is within a light-tight box. The substance to be "counted" (e.g., tissue sample) is incubated with a chemical scintillator (PPO, BBOT) whose purpose is to emit light, which is then detected by the PM tube.

- **Packard Tri-Carb 2100TR**

This Liquid Scintillation Counter is a computer-controlled, benchtop liquid scintillation analyser for detecting small amounts of alpha, beta, and gamma radioactivity.

- **Packard Tri-Carb 2500TR**

This LSC has a built-in electrostatic controller minimizes the effects of static electricity. The automatic data reduction feature includes averaging of repeat sample counts, percent Coefficient of Variation (CV), low count rejection, and result normalization.



### Get in Touch

If you are interested in finding out more or how you can work with EPP in any of our areas of expertise please email us at [enquiries@eppltd.com](mailto:enquiries@eppltd.com)

If required, we also have Chinese and Russian speaking scientist on-site.

Meet the Team at [www.eppltd.com/about-us/meet-the-team/](http://www.eppltd.com/about-us/meet-the-team/)

For further information on what we do visit [www.eppltd.com](http://www.eppltd.com)

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