WELCOME TO ELLUTIA CHROMATOGRAPHY SOLUTIONS

We are an independent manufacturer of innovative chromatography instruments. Established in 1994 and formerly known as Cambridge Scientific Instruments Ltd, the company renamed as Ellutia Chromatography Solutions in 2010 and now have divisions in the UK, USA and Germany. Since then we have gone from strength to strength and supply our light, compact, yet highly sensitive GCs to a broad range of markets including education, brewing, materials testing and forensics.

We pride ourselves on our personalised, responsive service and ability to provide customised solutions to our customers’ challenges. Offering an ideal combination of agility and speed of service with a global outlook, and industry-shaping technological innovations, we have become the partner of choice for hundreds of customers.

Our instruments are designed and manufactured in the UK at the company headquarters in Ely, Cambridgeshire. The instruments are designed to be compact with great energy efficiency, whilst also delivering industry standard analytical performance.

Ellutia GC History

March 2017 Ellutia release 500 Series GC at Pittcon, our first GC to offer conventional air blown and ultra-fast direct heated chromatography functionality in one instrument

February 2017 Ellutia moves to new premises on Ely Business Park, Cambridge

2010 Cambridge Scientific Instruments re-brands to Ellutia

2007 300 Series GC, standalone ultra-fast GC System based around the concept of directly heating metal columns, released

2000 200 Series GC with patented Heat Recovery heating system released

1997 Cambridge Scientific Instruments work on the development of the EZ-Flash and EZ-Flash II Ultra-Fast GC Accessories

1994 Phillip James starts Cambridge Scientific Instruments after leaving Pye Unicam head of the chromatography division
The need for quality analytical testing in the cannabis industry is, as with the industry as a whole constantly increasing as further territories are legalizing for medicinal or recreational use. Throughout the supply chain from growers to extractors to processors in house testing can bring a great number of benefits.

Having worked and spoken with many people in the cannabis industry we at Ellutia can see that there is not only a need for testing but a strong desire to introduce it to their companies. However, we can also see that there is a lot of confusion and mis-information on what is achievable. Many have expressed concerns that the equipment will be too costly or that they require years of training to be able to operate it.

At Ellutia we hope to educate and help cannabis professionals to bring about change in the industry that will benefit everybody. Growers will be able to monitor and check their product more accurately. Extractors and processors are able to verify the materials they buy in are as expected and monitor their processes throughout. Finally end users are given greater confidence knowing that high quality testing has taken place right through the supply chain.

The compact 200 Series Gas Chromatograph from ellutia offers the perfect tool for a business looking to start cannabis testing. The compact size and lower cost make it a perfect tool for high quality analytical testing. Its capabilities can be further expanded with the addition of autosampler as sample numbers grow.

Ellutia understands that many customers in the cannabis industry may have never worked with scientific equipment such as a Gas Chromatograph before. Because of this we offer training and support specifically tailored to quickly and effectively bring people up to speed and capable of performing routine quality control applications regardless of their background.

**WHAT OUR CUSTOMERS SAY**

"We realised we needed more quality control. We first heard about Ellutia at a conference and began conversations about a partnership. We had looked at other companies, however, our feeling was that Ellutia was more sophisticated and better suited to our needs. The decision was made not just on the instruments that Ellutia could provide, but also on their expertise in chromatography."

— Terapéutico MÁ

"Four years in waiting for this (200 Series FID GC), searching worldwide for a compatible partner that can give us all we required. To think you have been under my nose all this time, I’m so happy to have found you and even better that you are top of your field in analysis technology and we speak the same language (technology requirements and language). It’s been a great journey to this point and now with science on board it’s going to get better for our patient members, thanks again."

— Shamanics.nl
Cannabis consists of the dried flowers of the female Cannabis L-Sativa plant, also known as hemp or marihuana, and contains a number of active substances, including Delta-THC and Cannabidiol (CBD). The physical effects of Cannabis are largely the result of THC, but other Cannabinoids including CBD, may also influence the effectiveness of the drug. The chemical composition of the Cannabis determines the positive and negative effects of each dose. There are many different strains of Cannabis plant, all having varying ratios of the active compounds. Strains are cultivated through cloning and cross breeding of different plants to achieve a new strain with a desired flavour or percentage of Cannabinoid.

As Cannabis is a plant and not a chemically derived substance, it is very difficult to limit the presence of such a wide array of naturally occurring compounds and control content levels within any given dose.

The FDA has been involved with the medical and consumer communities in a lesser capacity, and has been highlighting the mislabelling of Medicinal Cannabis and its related products. In February 2015 the FDA issued six warning letters to suppliers of retail products claiming to contain various concentrations of CBD. They noted that the analysed concentration of CBD for these products were often vastly lower than the amount declared on the label, some showing zero detectable amounts of CBD. The following year, a further 8 companies were added to this list of false advertisers. A study carried out by Vandrey et al. looked at edible products available for purchase across a cross-section of U.S. metropolitan areas, and the results showed a large disparity between the declared CBD and Delta-THC content and the actual value - less than 50% of products sampled were labelled accurately. As these products are being consumed by ill and vulnerable patients, this inconsistency could result in a person receiving a minimal effect of treatment or conversely being overdosed and suffering potentially debilitating side effects. From a retail perspective, taxation of Cannabis products is calculated based on package size and not on the amount of active ingredient in the content. However, correct labelling is the only way for a patient to ensure they are receiving the correct dosage. Growers and dispensers need to protect themselves against future potential lawsuits – similar to the pharmaceutical industry, as well as protecting the consumer.

Potency testing evaluates the levels of each compound attributed to any health impact e.g. Cannabinoids – Delta-THC, Cannabinol (CBN) and Cannabindiol (CBD). The FDA has been involved with the medical and consumer communities in a lesser capacity, and has been highlighting the mislabelling of Medicinal Cannabis and its related products. In February 2015 the FDA issued six warning letters to suppliers of retail products claiming to contain various concentrations of CBD. They noted that the analysed concentration of CBD for these products were often vastly lower than the amount declared on the label, some showing zero detectable amounts of CBD. The following year, a further 8 companies were added to this list of false advertisers. A study carried out by Vandrey et al. looked at edible products available for purchase across a cross-section of U.S. metropolitan areas, and the results showed a large disparity between the declared CBD and Delta-THC content and the actual value - less than 50% of products sampled were labelled accurately. As these products are being consumed by ill and vulnerable patients, this inconsistency could result in a person receiving a minimal effect of treatment or conversely being overdosed and suffering potentially debilitating side effects. From a retail perspective, taxation of Cannabis products is calculated based on package size and not on the amount of active ingredient in the content. However, correct labelling is the only way for a patient to ensure they are receiving the correct dosage. Growers and dispensers need to protect themselves against future potential lawsuits – similar to the pharmaceutical industry, as well as protecting the consumer.

Potency testing evaluates the levels of each compound attributed to any health impact e.g. Cannabinoids – Delta-THC, Cannabinol (CBN) and Cannabindiol (CBD). The FDA has been involved with the medical and consumer communities in a lesser capacity, and has been highlighting the mislabelling of Medicinal Cannabis and its related products. In February 2015 the FDA issued six warning letters to suppliers of retail products claiming to contain various concentrations of CBD. They noted that the analysed concentration of CBD for these products were often vastly lower than the amount declared on the label, some showing zero detectable amounts of CBD. The following year, a further 8 companies were added to this list of false advertisers. A study carried out by Vandrey et al. looked at edible products available for purchase across a cross-section of U.S. metropolitan areas, and the results showed a large disparity between the declared CBD and Delta-THC content and the actual value - less than 50% of products sampled were labelled accurately. As these products are being consumed by ill and vulnerable patients, this inconsistency could result in a person receiving a minimal effect of treatment or conversely being overdosed and suffering potentially debilitating side effects. From a retail perspective, taxation of Cannabis products is calculated based on package size and not on the amount of active ingredient in the content. However, correct labelling is the only way for a patient to ensure they are receiving the correct dosage. Growers and dispensers need to protect themselves against future potential lawsuits – similar to the pharmaceutical industry, as well as protecting the consumer.

Potency testing evaluates the levels of each compound attributed to any health impact e.g. Cannabinoids – Delta-THC, Cannabinol (CBN) and Cannabindiol (CBD). The FDA has been involved with the medical and consumer communities in a lesser capacity, and has been highlighting the mislabelling of Medicinal Cannabis and its related products. In February 2015 the FDA issued six warning letters to suppliers of retail products claiming to contain various concentrations of CBD. They noted that the analysed concentration of CBD for these products were often vastly lower than the amount declared on the label, some showing zero detectable amounts of CBD. The following year, a further 8 companies were added to this list of false advertisers. A study carried out by Vandrey et al. looked at edible products available for purchase across a cross-section of U.S. metropolitan areas, and the results showed a large disparity between the declared CBD and Delta-THC content and the actual value - less than 50% of products sampled were labelled accurately. As these products are being consumed by ill and vulnerable patients, this inconsistency could result in a person receiving a minimal effect of treatment or conversely being overdosed and suffering potentially debilitating side effects. From a retail perspective, taxation of Cannabis products is calculated based on package size and not on the amount of active ingredient in the content. However, correct labelling is the only way for a patient to ensure they are receiving the correct dosage. Growers and dispensers need to protect themselves against future potential lawsuits – similar to the pharmaceutical industry, as well as protecting the consumer.

Potency testing evaluates the levels of each compound associated to any health impact e.g. Cannabinoids – Delta-THC, Cannabinol (CBN) and Cannabindiol (CBD).
Potency in Cannabis was tested by using a readily available standard to show that the compounds can be clearly and easily detected when using an Ellutia 200 Series Gas Chromatograph.

A liquid sampling technique was used when testing for potency. The molecule sizes and volatility are very varied, and as a consequence of this, liquid sampling is the most efficient and easiest technique to use. We have found that using a headspace prevents the sample from being fully represented.

The samples were placed in an EL3000A liquid autosampler, and then it was left to run. The 200 Series Gas Chromatograph with an FID (Flame Ionisation Detector) analysis condition are shown on the left. The GC and Autosampler forms an efficient, time saving and cost effective combination. As shown in figure 1, all components normally found when testing potency were detected.

For more information on this application, equipment used or ordering, please visit: www.ellutia.com or email: info@ellutia.com.

**Equipment used**

**Main Instruments**
- 200 Series GC with FID
  - Part no. 20500130
- Ellution Software
  - Part no. 23001001
- Colibrick
  - Part no. 23001022
- EL 5 30 m x 0.25 mm x 0.25 µm column
  - Part no. 51100157

**Liquid Autosampler**
- Ellutia EL3100A - Automatic Liquid Sampler - 15 position
  - Part no. 30500011
- Ellutia EL3000A - Automatic Liquid Sampler - 121 position
  - Part no. 30500010
- GC Mounting Kit for EL3100A/EL3000A Autosampler
  - Part no. 30500018

**Accessories**
- 7000 Series Flowmeter
  - Part no. 21007000
- 5µl Syringe
  - Part no. 20511202
- 2ml Short-cap Screw Thread Vials
  - Part no. 20511101
- Pre-assembled Short Blue Screw Vial Closures
  - Part no. 20511102
**ACIDIC & NEUTRAL CANNABINOID ANALYSIS**

Cannabinoids are found in both a neutral and acidic form. When testing for cannabinoid content users are commonly looking for the total available for a given cannabinoid. This total cannabinoid content is calculated by combining the amount of neutral cannabinoid present with the amount of neutral cannabinoid that could be created by the decarboxylation of the acidic version present. When testing by GC the heat of the injection port and column oven cause total decarboxylation of the acidic versions so only the neutral versions will be present. This means that the values for the neutral cannabinoids detected is the total available.

Previously if the analyst had wanted to detect both the neutral and acidic versions HPLC would have been the preferred method. This is now possible to perform on GC with some additional sample preparation to derviatise the sample before analysis. The derivatisation changes the chemical composition of the acidic cannabinoid such that it no longer converts to the neutral version in the heat of the GC so can then be detected separately.

**Example Cannabis Derivatisation Procedure**

An aliquot of the individual standards and the 12 Cannabinoid stock solution were independently evaporated to dryness under a nitrogen stream at approximately 100 ml min⁻¹.

Derivatisation agent, BSTFA + 1% TCMS (CAS No. 25561-30-2, CF₃C≡NSi(CH₃)₃OSi(CH₃)₃(l)) to that of a dried sample was added and the vials heated at 90 °C.

After 30 minutes, samples were removed from the heating mantle and allowed to cool to room temperature, the excess derivatisation agent was evaporated until dry as above and single standards were reconstituted in MeOH.
Calculating The Total Available Cannabinoid Value From Acidic and Neutral Results.

When calculating the total available cannabinoid content from the neutral and acidic results, it is not as simple as simply adding the two values together. When an acidic cannabinoid decarboxylates, it loses CO$_2$ to become the neutral version. This means the difference in molecular weight must be taken into account.

THCA has a weight of 358g per mol as it decarboxylates it becomes THC which has a weight of 314g per mol. This allows us to calculate that for every 1 unit of THCA that decarboxylates, we will have 0.877 (314/358) the amount of THC.

So the calculation for total available THC is

\[
\text{THC (total available)} = \text{THC} + (0.877 \times \text{THCA})
\]

This same process can be applied to calculate the total available for other cannabinoids present.
As a pharmaceutical drug, Cannabis should be rigorously tested to comply with stringent rules and regulations regarding quality and safety of the product. As there is currently no centralised regulatory body for Cannabis quality control, responsibility for testing falls to the dispenser, manufacturer and even the individual consumer - if they are growing their own for personal medical use.

As Cannabis is now effectively legalised at state level in the United States, but has remained illegal at Federal level, the usual routes for substance regulation cannot be applied. The Food and Drug Association (FDA) is normally at the forefront of ensuring consumer safety, but they are effectively restricted from completing effective drug trials, as the DEA official position means they cannot provide illegal substances for testing. The absence of this data means the FDA are unable to provide relevant regulations, resulting in the FDA declaring Cannabis as not safe for human consumption. However, Delta-THC, the main psychoactive ingredient in the L-Sativa plant has been an FDA approved drug for over 25 years. This has helped influence the general opinion that Cannabis itself should also be an FDA regulated substance.

Cannabis has an abundance of different strains with many different side effects. In order for medicinal Cannabis to be regulated and prescribed correctly to treat specific ailments, strain determination is essential.

Flavour profiling would be applicable for determining strain identity through levels of compounds responsible for distinctive tastes and smells e.g. Terpenes.

<table>
<thead>
<tr>
<th>GC Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Injector Temperature</td>
</tr>
<tr>
<td>Detector Type</td>
</tr>
<tr>
<td>Detector Temperature</td>
</tr>
<tr>
<td>Carrier Gas Type</td>
</tr>
<tr>
<td>Stimulated Constant Flow</td>
</tr>
<tr>
<td>Split Flow</td>
</tr>
<tr>
<td>Column Type</td>
</tr>
<tr>
<td>Temperature Program</td>
</tr>
<tr>
<td>Initial Temperature</td>
</tr>
<tr>
<td>Ramp 1</td>
</tr>
</tbody>
</table>

Flavour profiles in Cannabis were tested by using a readily available standard to show that the compounds can be clearly and easily detected when using an Ellutia 200 Series Gas Chromatograph.

A liquid sampling technique was used when testing for Terpenes. This is so that all molecules can be equally represented in the injected sample. Headspace would not be recommended for this task, due to larger molecules struggling to reach the gas phase. It is hard to find a headspace temperature where all molecules can be equally sampled when analysing Terpenes. The samples were placed in an EL3000A liquid autosampler. The 200 Gas Chromatograph with an FID (Flame Ionisation Detector) analysis conditions are shown above. The GC and Liquid Autosampler is a cost effective addition to any lab.
Figure 1 - A 1.0 uL injection of a 625 ppm Terpene mix standard

1. a-Pinene
2. Camphene
3. b-Pinene
4. b-Mycene
5. d3-Carene
6. a-Terpinene
7. p-Cymene
8. d-Limonene
9. Ocimene
10. g-Terpinene
11. Terpinolene
12. Linalool
13. iso-Pulegol
14. Geraniol
15. b-Caryophylene
16. a-Humulene
17. Nerolidol
18. Guaiol
19. a-Bisabool

**Equipment used**

**Main Instruments**
- 200 Series GC with FID
  Part no. 20500130
- Ellution Software
  Part no. 23001001
- Colibrick
  Part no. 23001022
- EL 5 30 m x 0.25 mm x 0.25 µm column
  Part no. 51100157

**Liquid Autosampler**
- Ellutia EL3100A - Automatic Liquid Sampler
  - 15 position
    Part no. 30500011
- Ellutia EL3000A - Automatic Liquid Sampler
  - 121 position
    Part no. 30500010
- GC Mounting Kit for EL3100A/EL3000A Autosampler
  Part no. 30500018

**Accessories**
- 7000 Series Flowmeter
  Part no. 21007000
- 5µl Syringe
  Part no. 20511202
- 2ml Short-cap Screw Thread Vials
  Part no. 20511101
- Pre-assembled Short Blue Screw Vial Closures
  Part no. 20511102

For more information on this application, equipment used or ordering, please visit: www.ellutia.com or email: info@ellutia.com.
RESIDUAL SOLVENTS IN CANNABIS

When Cannabis components are extracted, several potentially harmful compounds are used in the process. They can be left in the extraction and cause harm to consumers. Residual solvents analysis will determine if any solvents have been found within the finished product, and this ensures that consumers are not at risk. Testing for residual solvents is essential.

Hydrocarbon gases as well as organic solvents are used to extract essential oils from cannabis for medicinal products. Residual solvents are any solvents used in extraction that remain in the extracted product. They can be consumed by users in significant quantities.

If Cannabis was to be brought into line with other pharmaceutical testing, each batch of Medicinal Cannabis would need to be tested for potency, flavour profiling and residual solvents. Some manufacturers may use cheap materials in order to produce the products cost-effectively and have a higher profit margin. These cheap materials may have high levels of dangerous solvents. Residual solvents that are left in the final product can adversely affect patients. For example, if a product that retains high levels of ethanol is used to treat children, it could cause liver damage.

As a result of this danger, testing needs to be taken very seriously due to the harmful nature and severe consequences that the solvents can cause.

Residual solvents in Cannabis were tested by using a readily available standard to show that the compounds can be clearly and easily detected when using an Ellutia 200 Series Gas Chromatograph.

In order for residual solvents to be extracted, the components will need to enter the gas phase, and so headspace sampling was used for this purpose. The samples were placed in a headspace autosampler and the sample was heated to encourage the volatile compounds to excite and enter the gas phase. Once this has happened, sampling can take place. The gas sample was injected into the 200 series GC-FID. The GC conditions can be found on the previous page. The GC paired with the EL2000H headspace autosampler creates a low cost, reliable and efficient combination.

As shown in figure 1, all components normally found when testing residual solvents were detected, and detected clearly with low noise output.

<table>
<thead>
<tr>
<th>GC Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Injector Temperature: 230°C</td>
</tr>
<tr>
<td>Detector Type: FID</td>
</tr>
<tr>
<td>Detector Temperature: 240°C</td>
</tr>
<tr>
<td>Carrier Gas Type: Hydrogen</td>
</tr>
<tr>
<td>Constant Pressure: 4.65 psi</td>
</tr>
<tr>
<td>Split Flow: 70 ml min⁻¹</td>
</tr>
<tr>
<td>Column Type: EL-VOC 60 m x 0.32 mm x 1.8µm</td>
</tr>
<tr>
<td>Initial Temperature: 40°C (hold 4 mins)</td>
</tr>
<tr>
<td>Ramp 1: 4°C min⁻¹ to 200°C (hold 3 mins)</td>
</tr>
</tbody>
</table>
A 10 μL volume of a 25 mix standards was placed in a 20 ml headspace vial and held at 100°C for 45 minutes within an Ellutia 2t Static Manual Headspace module. A 0.5 ml gas sample was taken and injected into Ellutia 200GC-FID. The chromatogram of the headspace injection is shown below.

Figure 1 - A 0.5 μL injection of a Residual Solvent mix standard

1. Methanol, 10. iso-Butanol, 18. 4-Methyl-2-Pentanone, 25. Cyclohexanone
2. Ethanol 11. Tetrahydrofuran, 19. 2-Ethoxyethanol,
3. 2-Propanol, 12. Methyl Cellusolve, 20. iso-Butyl Acetate,
5. Methyl Acetate, 14. iso-Propyl Acetate, 22. Butyl Acetate,
6. 1-Propanol, 15. n-Butanol, 23. Methyl Cellosolve Acetate,
7. sec-Butanone, 16. 1-Methoxy-2-Propanol, 24. 2-Ethoxyethyl Acetate
8. 2-Butanone, 17. n-Propyl Acetate, 25. Cyclohexanone
9. Ethyl Acetate,