

# Cannabis Testing Laboratory Solutions



# We are the cannabis testing instrument experts.

When purchasing analytical equipment, it is important to know that you are not just buying an instrument but investing in your lab's future.

Shimadzu not only provides the instrumentation and software, plus optional FDA 21 CFR Part 11 compliance software for required labs, but also the technical knowledge and support to help your lab be successful. We can assist with method development, instrument training, and many other areas of support like maintenance to ensure your systems are constantly operating at an exceptional level.

From seed to sale, from accurate cannabis potency profiles to reliable, highly sensitive pesticide analysis, let us deliver scalable, turnkey solutions to meet your testing needs for today and tomorrow.



**C**annabis growers benefit tremendously from cannabis testing. Whether meeting state requirements or certifying a product, laboratory testing reduces your risk and ensures delivery of a quality product. Routine cannabis testing services include potency, screening/determination of terpenes, and analysis of heavy metals, pesticides and residual solvents.



**S**himadzu provides you with the leading cannabis testing analytical instrumentation. Our rigorously tested methods, expansive platforms and expert team of scientists are readily available to help your cannabis testing laboratory succeed. Talk to us today about your analytical testing needs.



**A**s medicinal and recreational cannabis markets continue to grow, analytical testing will ensure that consumers are receiving accurately labeled products that are free from contamination. Shimadzu is ready to assist you as you grow your laboratory. We also offer instrument research platforms and a variety of leasing programs to meet evolving requirements.

# Delivering total cannabis lab testing solutions for:



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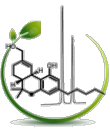
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## Software Compliance/ Research Platforms

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Information on the following pages reflects recommended platforms for each analysis/test. Some techniques, such as LC-MS/MS or GC-MS/MS, may be applicable for multiple analyses. Please contact your salesperson for more details.



# Potency Testing by HPLC

The Cannabis Analyzer for Potency captures the spirit of an Analyzer - a comprehensive package integrating instrument hardware, software, consumables, and analytical workflow. Includes a certified reference material (CRM) mixture of target compounds. Also includes a service package to cover preventive maintenance and warranty for three years, plus free technical support for the life of the product. The solution is ready to use after one day of installation and testing, and requires no time-consuming method development on the part of the analyst.

Target Compound List	
THCV	Tetrahydrocannabivarin
$\Delta^8$ -THC	$\Delta^8$ -Tetrahydrocannabinol
$\Delta^9$ -THC	$\Delta^9$ -Tetrahydrocannabinol
THCA	$\Delta^9$ -Tetrahydrocannabinolic acid
CBD	Cannabidiol
CBDa	Cannabidiolic acid
CBDV	Cannabidivarin
CBN	Cannabinol
CBG	Cannabigerol
CBGA	Cannabigerolic acid
CBC	Cannabichromene

✦ Turnkey HPLC Analyzer

✦ Choice of 3 Proven HPLC Methods

✦ 3 Years Warranty & Preventive Maintenance



**High Throughput HPLC Method Package** – Designed for analysis of the 10 most commonly requested cannabinoids in under 8 minutes. This is the original method developed by Shimadzu in collaboration with industry laboratories. (Does not include THCV.)

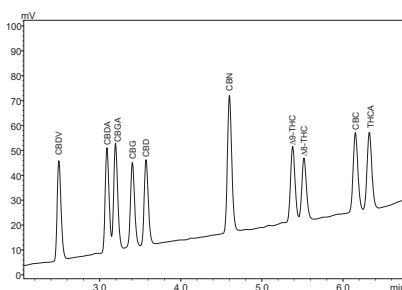


**High Sensitivity HPLC Method Package** – Adds THCV to the target analyte list, with an instrument cycle time of under 10 minutes. The short analysis time produces the sharpest chromatographic peaks for the best overall sensitivity.

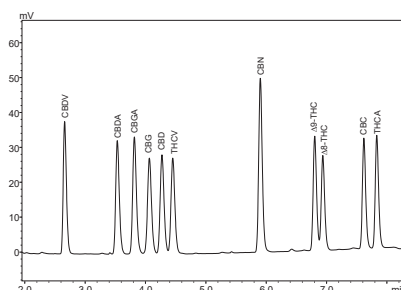


**High Resolution HPLC Method Package** – Presents full baseline resolution for all 11 compounds and an analysis time under 30 minutes. This method is preferred for research purposes, or when additional compounds must be added to the analysis in response to new state regulatory requirements.

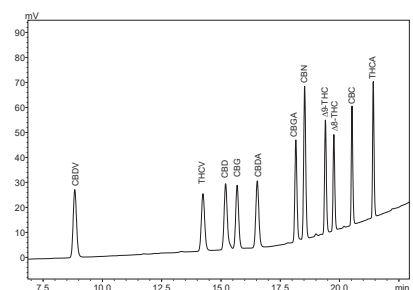
High Throughput Method

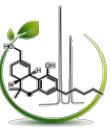


High Sensitivity Method



High Resolution Method

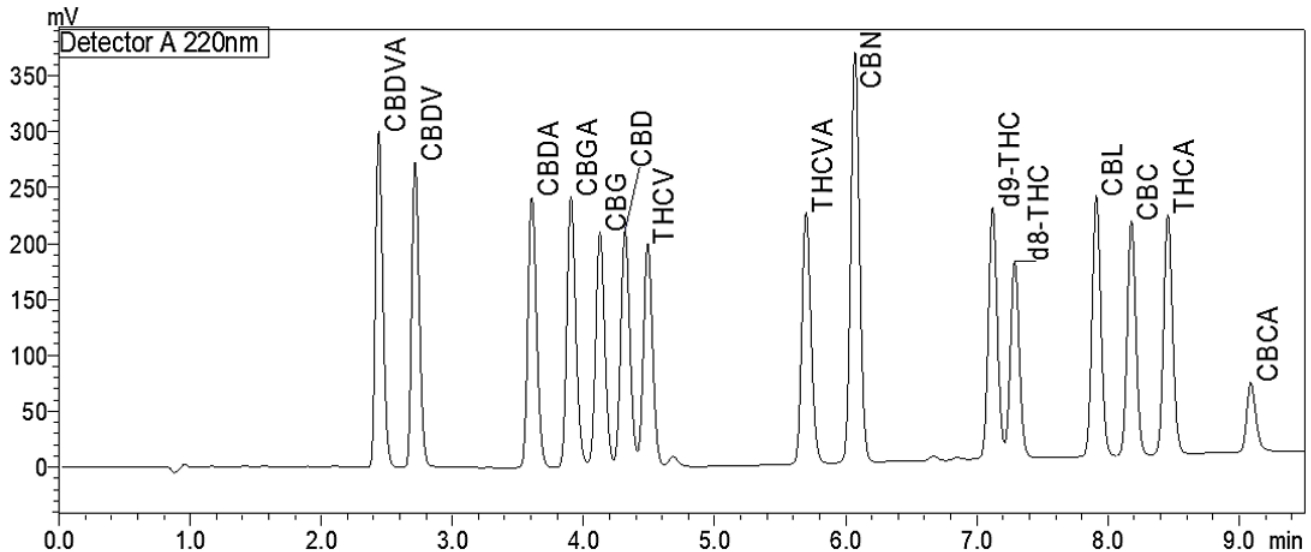




# Potency Testing by (U)HPLC

## HPLC Analysis

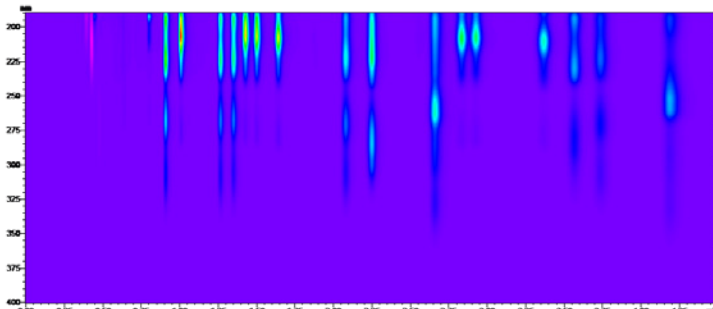
The Shimadzu Cannabis Analyzer has been extended to include the analysis of 15 cannabinoids in 15 minutes. The cannabinoid list is the same as on page 4 with the addition of CBDVA, THCVA, CBCA, and CBL. The method uses Shimadzu's 11-part cannabinoid mix (220-91239-21) plus the four individual standards. For the full application, request Shimadzu's Application News No. HPLC-032.



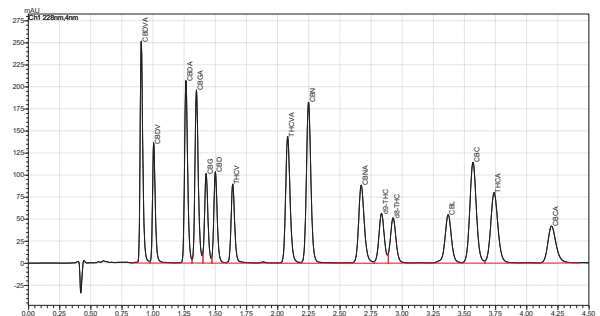
Analysis of 15 Cannabinoids with the Shimadzu Hemp Analyzer

## UHPLC Analysis

Shimadzu's Nexera-i (LC-2040C 3D) UHPLC with a photodiode array (PDA) detector offers a solution to 16 cannabinoid analysis. The cannabinoid list is the same as on page 4 with the addition of CBNA, CBDVA, THCVA, CBCA, and CBL. The method uses Shimadzu's 11-part cannabinoid mix (220-91239-21) plus the five individual standards. UV-Vis detectors provide the absorption at fixed wavelengths (i.e. 220 nm). The key advantage of the PDA detector over a standard UV-Vis detector is that the full absorption profile from 190-400 nm is recorded. PDA detectors are often used in the pharmaceutical industry to determine peak purity. For the full application, request Shimadzu's Application News No. HPLC-020.

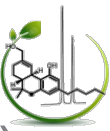


Analysis of 16 Cannabinoids with the Shimadzu Nexera-i (LC-2040C 3D) UHPLC with PDA



4.5 minute separation of 16 Cannabinoids by UHPLC-PDA





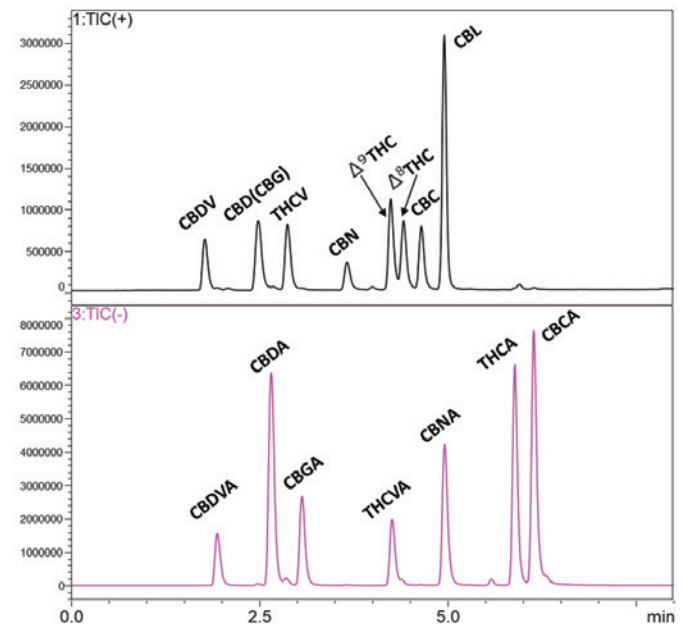
# Potency Testing by LC-MS(/MS)

Some labs require a higher level of confirmation of the cannabinoids than a UV-Vis or photodiode array (PDA) detector can provide as described on page 4-5. That is where LC-MS and LC-MS/MS come in to play. The advantages of LC-MS(/MS) are improved sensitivity (S/N), selectivity, and mass identification. As long as each cannabinoid has a unique mass (does not pertain to isotopes), complete baseline resolution is not required. These LC-MS(/MS) methods are also capable of measuring 16 or more cannabinoids.

## LC-MS Analysis

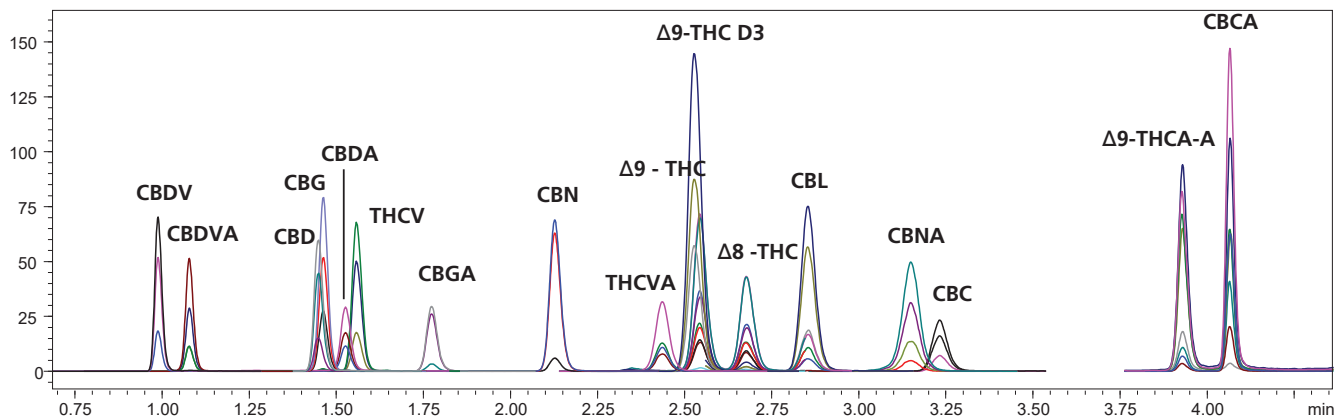
Added confidence in identification can be obtained using a single quadrupole MS and in-source fragmentation. The cannabinoid list is the same as on page 4 with the addition of CBNA, CBDVA, THCVA, CBCA, and CBL. Under the conditions of the experiment, neutral cannabinoids (top) such as  $\Delta^9$ -THC, CBD, and CBL are ionized in positive mode while their respective acidic cannabinoids (bottom) are ionized in negative mode. For the full application, request Shimadzu's Application News No. HPLC-028.

Analysis of 16 Cannabinoids with the Shimadzu LC-2040C 3D with mass spectrometer (LCMS-2020)

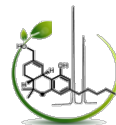


## LC-MS/MS Analysis

LC-MS/MS compared with LCMS (described above) provides a higher level of sensitivity (S/N), selectivity, and confirmation of the compounds. UHPLC instead of HPLC can be used for faster analysis time. Also, full baseline resolution of the cannabinoids is not required because of the selectivity of the triple quadrupole mass spectrometer. The data includes MRM transitions for a quantifier ion and at least one qualifier ion. For the full application, request Shimadzu's Application News No. LCMS-108 for 16 cannabinoids.



Analysis of 16 Cannabinoids with Shimadzu's Nexera UHPLC and LCMS-8050

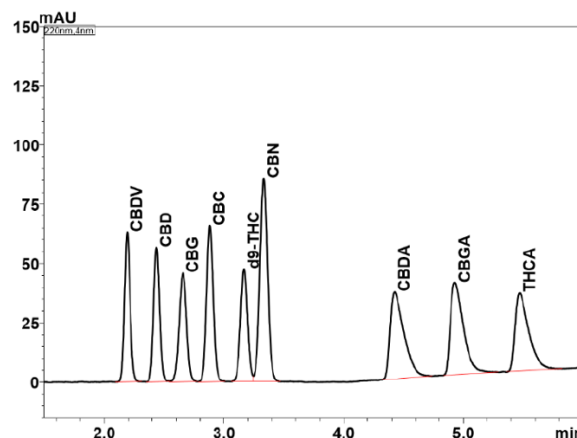


# Potency Testing Alternatives

## SFC Analysis

HPLC has long been considered the gold standard for the quantitative analysis of cannabinoids in cannabis and hemp growing for its robust methods, efficacy for both acid and neutral forms, and its simple sample preparation. A lesser known technique is supercritical fluid chromatography (SFC) which uses supercritical CO<sub>2</sub> as the primary mobile phase.

SFC offers advantages over HPLC. First, the use of CO<sub>2</sub> allows for increased flow rates due to the lower viscosity and backpressure compared to aqueous solvents. In addition, SFC is generally regarded as a “green” technique due to the minimization of organic solvents and reduced generation of hazardous waste. This has the added advantage of reducing the operating cost of the instrument as far less hazardous waste is produced. For the full application, request Shimadzu’s Application News No. HPLC-034 for analysis of 9 cannabinoids.

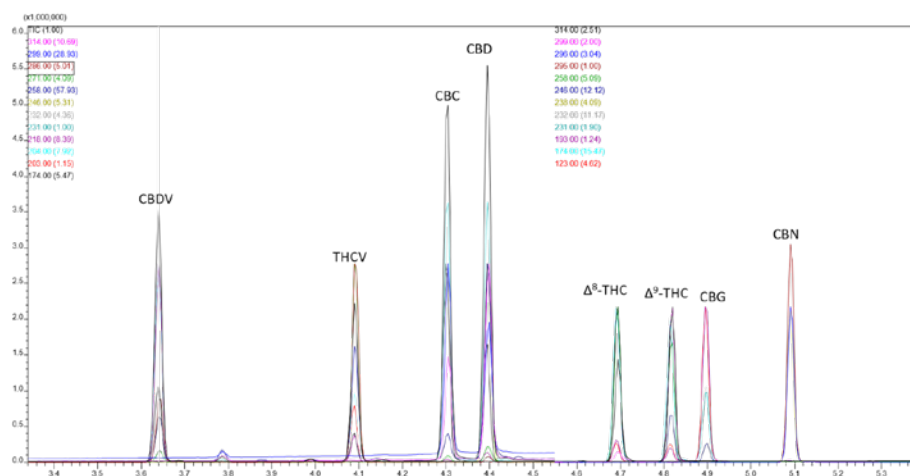


Analysis of 9 cannabinoids with Shimadzu’s Nexera UC Supercritical Fluid Chromatograph (SFC)

## GC or GCMS Analysis

Gas Chromatography with a Flame Ionization Detector (GC-FID) is a lower cost alternative for cannabinoid analysis; however, the acidic compounds, such as THCA, CBDA, and CBGA, are converted to the neutral forms of THC, CBD, and CBG, respectively. The result is Total delta-9-THC = delta-9 THC + delta-9-THCA, and similarly for Total CBD and Total CBG because of the hot injector port. The addition of an FID to any GCMS can offer a wider dynamic range.

Using GC-MS(/MS) has advantages over the FID detector due to the same discussions from before about mass spectrometers over other detectors. As expected, the cost of MS increases the price of the instrumentation. Shown is an example of using Shimadzu’s 11-part cannabinoid mix (220-91239-21), but only 8 peaks appear because the acid to neutral conversion applies to GC-MS(/MS) as well. There are GC-based methods for measuring the acidic compounds using a chemical process called derivatization.<sup>1</sup>



Analysis of 11 Cannabinoids with Shimadzu’s GCMS

<sup>1</sup>Journal of Food and Drug Analysis (2018) 1283 -1292, Vladimiro Cardenia et al.

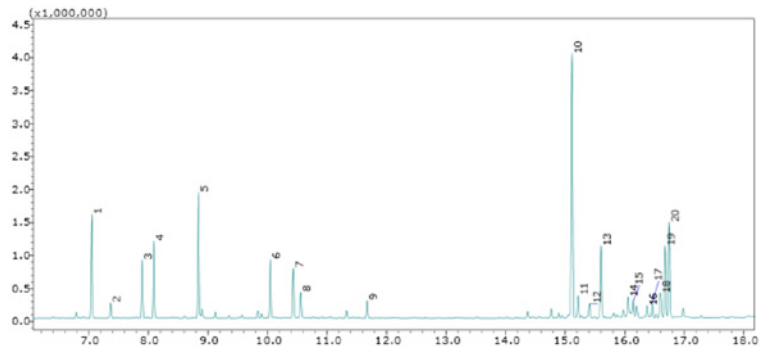


# Terpene Profiling

Terpenes are produced in trichomes (where THC is produced) and give cannabis its distinctive flavor and aroma. Terpenes also act as essential, medicinal hydrocarbon building blocks, influencing the overall homeopathic effect. From the pine odor of pinene to the citrus-like smell of limonene, the characterization of terpenes and their synergistic effect with cannabinoids is easily achieved using Shimadzu gas chromatography.

For the ultimate in terpene analysis, Shimadzu offers both the GCMS-TQ8050 NX and the GCMS-QP2020 NX coupled with either the HS-20 (for headspace only) or the AOC-6000 (for headspace, liquid, or SPME). With either instrument and the included Wiley/NIST library, these systems can easily identify more than 3,000 flavor and fragrance compounds to meet your terpene profiling needs. For those looking for standard terpenes, a GC-2030 with an FID or the addition of an FID to any GCMS can offer a wider dynamic range. This may be helpful depending on the concentration ranges of the samples. It should be noted that for heavier, less volatile terpenes, liquid injection has been used.

If residual solvents (page 11) or pesticides (page 9) are also of interest, consider starting your lab with the GCMS-TQ8050 NX with HS-20 to maximize the functionality of the instrumentation.



Terpenes in Butane Hash Oil (BHO)



GCMS-TQ8050 NX Triple Quadrupole Gas Chromatograph Mass Spectrometer

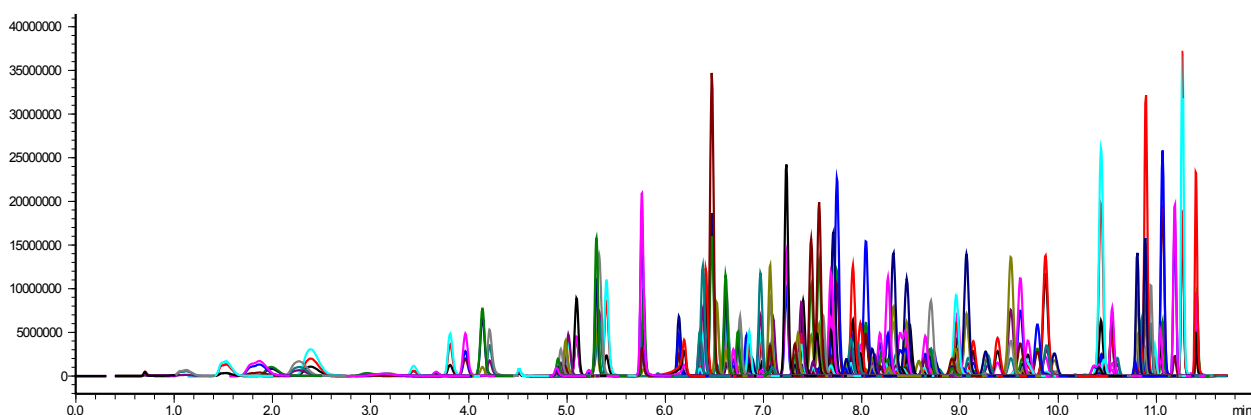




# Pesticide Analysis

Pesticides are used in commercial cannabis grow operations to kill insects and spiders that thrive on cannabis plants. Pesticides are carcinogenic and mutagenic, causing serious harm to cannabis consumers, especially immunocompromised medicinal cannabis users. Shimadzu offers the most sensitive and comprehensive pesticide analysis and confirmation available utilizing Liquid Chromatography-Triple Quadrupole Mass Spectrometry (LC-MS/MS). While most pesticides are analyzed using Electro-Spray Ionization (ESI) with LC-MS/MS, many labs use atmospheric pressure chemical ionization (APCI) for the difficult-to-analyze pesticides. For related applications, request Shimadzu's Application News No. SSI-LCMS 104 and SSI-LCMS 105.

Offering excellent sensitivity and throughput, the ultra-low detection limits provided by Shimadzu LC-MS/MS make this technique ideal for the analysis of pesticides commonly employed during cannabis cultivation.



High-sensitivity LC-MS/MS analysis of 211 pesticides in cannabis dry product in less than 12 minutes using a Shimadzu LCMS-8060 triple quadrupole mass spectrometer



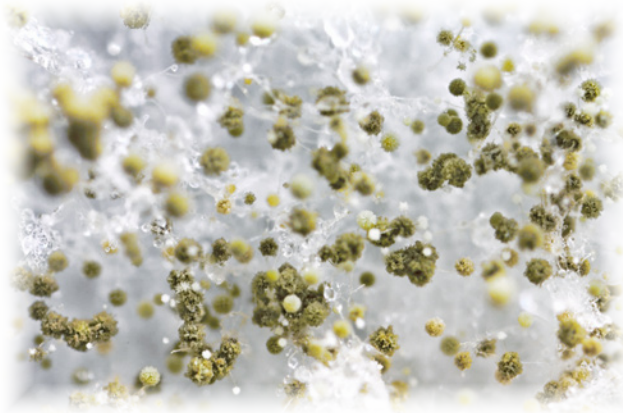
LCMS-8060 Triple Quadrupole Mass Spectrometer

Because the pesticide list varies from state to state and country to country, and is subject to change, the addition of a GC-MS/MS may be required for complete pesticide analysis. Choose the triple quadrupole GCMS-TQ8050 NX with AOC-20i or AOC-6000 for volatile pesticides, pesticides that are difficult to analyze by electrospray ionization (ESI), and other problematic pesticides that are difficult to analyze by LC-MS/MS. The GCMS-TQ8050 NX, with the proper configuration, can also be used for terpene profiling (page 8) and residual solvents analysis (page 11).





# Mycotoxins Analysis



Since cannabis has a high moisture content, long term storage of the material can allow for fungal growth known as mold. Mycotoxins are a toxic secondary metabolite of mold. Aflatoxins are a subset of mycotoxins which are found in soils and decaying vegetation. Regulatory bodies have placed restrictions on the allowable limits present in food.

An LCMS-8060 offers the cannabis lab the ability to rapidly test for mycotoxins achieving the ultralow levels of detection needed.



LCMS-8060 Triple Quadrupole Mass Spectrometer

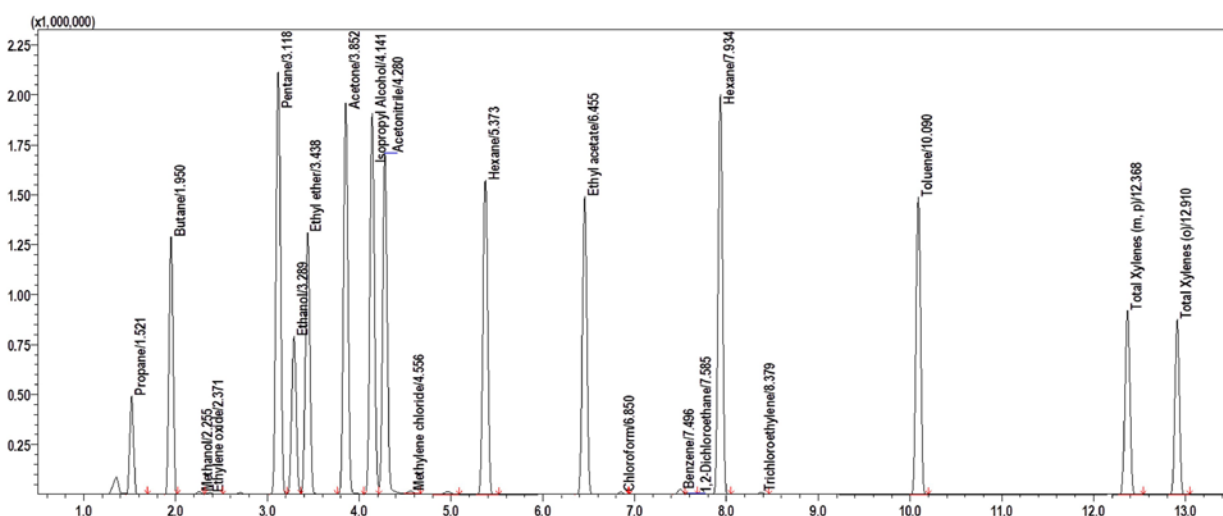




# Residual Solvents

Residual solvents are leftover chemicals from the process used to extract cannabinoids and terpenes from the plant. The solvents are evaporated to prepare high-concentration oils and waxes. Sometimes, the evaporation process does not remove all of the solvent. Since these solvents are not safe for human consumption, it is important to verify their absence so you can guarantee you are providing a safe, chemical-free product.

The Shimadzu GCMS-QP2020 NX with HS-20 Headspace Sampler enables rapid identification and quantitation of very low concentrations of residual solvents. However, if one plans to purchase the GCMS-TQ8050 NX or GC-2030 with headspace for terpene profiling (page 8) or the GCMS-TQ8050 NX for pesticide analysis (page 9), then any one of these platforms is capable of measuring residual solvents analysis but will provide different levels of identification confirmation.



TIC chromatogram of 20 Residual Solvent standards (required in CA)



Shimadzu GCMS-QP2020 NX with HS-20 Headspace Sampler



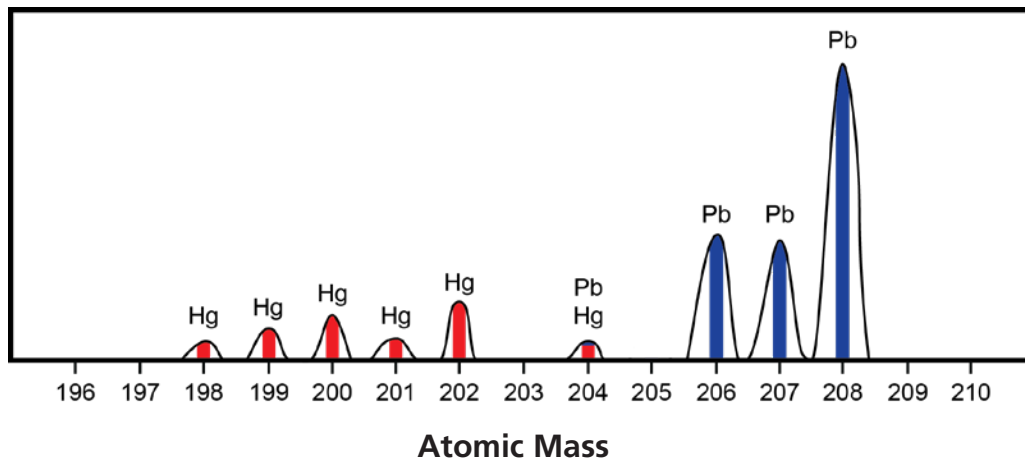


# Heavy Metals Testing



Metals can be found in soil and fertilizer. As cannabis plants grow, they take up metals from the soil. 'Heavy metals' are a group of metals considered to be toxic and include lead, cadmium, arsenic and mercury. Laboratory testing helps to ensure that your products are free from toxic concentrations of these hazardous metals. Additional toxic and nutritional elements are easily added to the analysis list as needed.

There are several ways to determine trace metals in plant material, all requiring an acid digestion. However, the Inductively Coupled Plasma Mass Spectrometry (ICP-MS) method provides the sensitivity to measure low levels of these toxic metals without the need for additional sample preparation or purchase of additional expensive sample introduction accessories.



Portion of ICP-MS mass spectrum showing presence of mercury and lead in a contaminated sample



ICPMS-2030 Inductively Coupled Plasma Mass Spectrometer



# Moisture Content & Precision Weighing



Moisture can be extremely detrimental to the quality of stored cannabis products. Dried cannabis typically has a moisture content of 10-12%. A moisture content above 12% is prone to mold growth.

The moisture content of a variety of cannabis samples can be measured using Shimadzu MOC63u (and MOC-120H) balances. The MOC63u is applicable to a variety of cannabis products and its long-life and high-power halogen heater provides quick and accurate measurement.

We offer a complete line of balances, from top-loading to analytical.





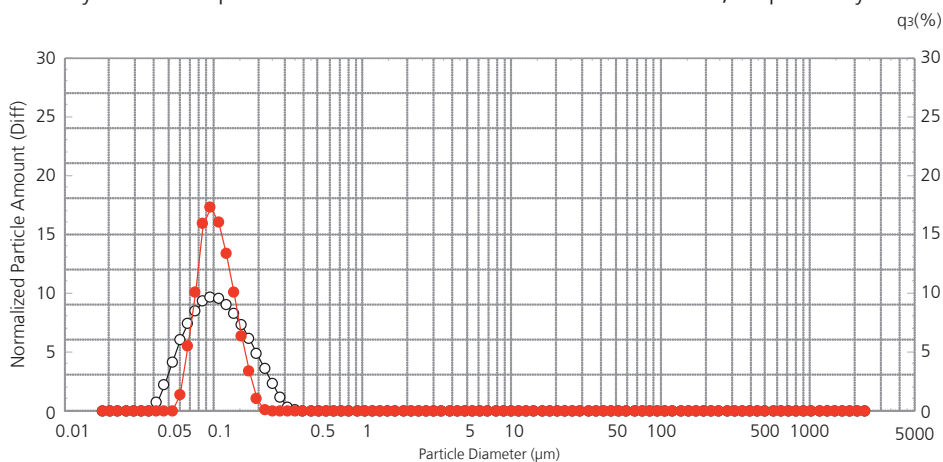


# Particle Size Testing

Cannabinoids such as TCH and CBD are lipophilic (fat-loving) while many foods, beverages, and cosmetic products are lipophobic (fat-hating). As scientist know, "like dissolves like," so the problem of incorporating cannabinoids into a wide range of products is mixing oil (non-polar) and water (polar). With water-based lotions, creams, and beverages oil is mixed in using an emulsifier. Emulsifiers are surface-active agents that act as a border between two immiscible liquids, enabling them to blend together in an emulsion, creating a suspension of oil particles within the water. Examples of emulsifiers are lecithin, xanthan gum, and Quillaja Saponario. Additional carrier oils, such as coconut oil and triglycerides, may also be used to improve emulsion stability and absorption.

As a general rule, smaller particle size emulsions are more stable, have higher bioavailability, and can be incorporated into a wide range of products. Nano-emulsions, which contain nanometer (nm) sized particles, are the ideal product. The distribution of the particles should have a narrow, nanometer, monomodal distribution. Less stable, multimodal distributions can occur from an insufficient emulsification process or during formulation or from storage as aggregates form. Further, emulsions below 100nm are transparent and useful for clear liquid products.

Shimadzu's SALD-2300 Laser Diffraction Particle Size Analyzer is ideal for measuring particles from 17-nanometers to 2500-microns. Aqueous emulsions can be analyzed with the SALD-MS23 flow cell accessory, while lotions and creams can be analyzed with little sample preparation using the SALD-HC23 High Concentration sample measurement accessory. Dry powder samples can also be analyzed using the SALD-DS5 Cyclone Injection accessory. The SALD-2300 used in conjunction with Shimadzu's Cannabis Analyzer (Page 4) is the ideal solution for stability studies of particle size and cannabinoid concentrations, respectively.



Example of a narrow, nanometer, monomodal distribution of particles

Shimadzu's SALD-2300 Laser Diffraction Particle Size Analyzer





# Software Compliance

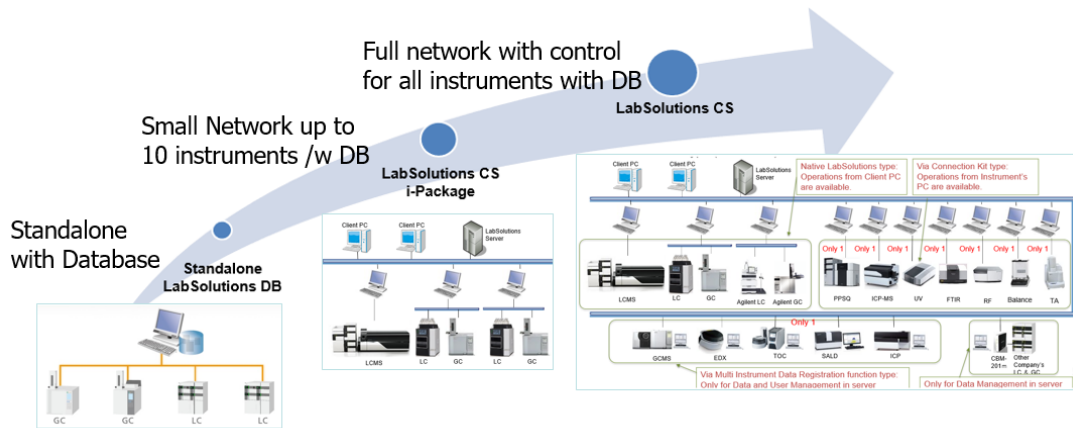
LabSolutions DB/CS provides comprehensive features, controls and functionality that assure data integrity in your cannabis laboratory. The broad nature of these controls allows a compliant data management environment to be quickly and easily established whether working with a small number of instruments within a single laboratory or with multiple instruments across a large number of laboratories.

This also includes the ability to:

- Manage additional, non-analytical instruments in a compliant manner (e.g. balances / weigh scales)
- Capture additional laboratory data in a compliant and integrated manner
- Integrate common third-party instruments from multiple vendors into a single compliant data management environment
- Step up from folder/file management to database management for FDA 21 CFR Part 11 Compliance

LabSolutions DB/CS provides multiple features and functions which support data integrity and electronic records/electronic signatures compliance.

These features can be mapped against the FDA's 21 CFR Part 11 (Electronic Records, Electronic Signatures), EU Eudralex 4, Annex 11, PIC/S and Computerized Systems and data integrity ALCOA+ requirements.



# Research Platforms

Does your facility need capabilities beyond the standard quality control lab? Shimadzu offers a wide variety of research instrumentation that allows you to be at the forefront of cannabis research. Having these advanced tools at your fingertips gives you access to the most advanced technology available.

Instrumentation includes:

- Online SFE-SFC-LC-MS/MS – reduces sample preparation and detects isomeric and chiral compounds
- MALDI-TOF MS – detection of microorganisms and cultivar typing
- High-resolution Q-TOF LCMS – accurate mass measurements

# Cannabinoid Standards

Shimadzu manufactures two cannabinoid mixtures to reduce the time of your sample preparation. Each standard has a concentration of 250ug/mL housed in a flame-sealed ampule. All Shimadzu standards are manufactured to ISO-17025 Guide 34 requirements.

- 10-part mix contains: THC-A,  $\Delta$ 8-THC,  $\Delta$  9-THC, CBD, CBD-A, CBD-V, CBN, CBG, CBG-A, CBC
- 11-part mix contains: THC-A, THC-V,  $\Delta$ 8-THC,  $\Delta$  9-THC, CBD, CBD-A, CBD-V, CBN, CBG, CBG-A, CBC

Part Number	Description
220-91239-20	Certified Cannabinoids Standards Mixture - 10 Components 1mL x 250ug/mL
220-91239-21	Certified Cannabinoids Standards Mixture - 11 Components 1mL x 250ug/mL



## Columns and Vials

Shimadzu specifically engineered a superficially porous liquid chromatography analytical and guard column for the analysis of cannabinoids. Ensure the ultimate in resolution and sensitivity for cannabis analysis by using the NexLeaf™ brand.

Part Number	Description
220-91525-70	NexLeaf™ CBX™ for Potency, LC Column 2.7 $\mu$ m 150 mm, 4.6 mm ID
220-91525-72	NexLeaf™ CBX™ Guard Column 2.7 $\mu$ m, pack of 3
220-91525-73	NexLeaf™ Guard Column Holder
227-34001-01	LabTotal Vial Kit, 100/pk
220-90631-01	Vial, 40mL, EPA Clear, 72/pk



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