Department Of Cannabis Control
California Code of Regulations Title 4, Division 19

Initial Statement of Reasons

Subject Matter of Proposed Regulations: Standard cannabinoids test method and standardized operating procedures for all licensed commercial cannabis testing laboratories.

Section Affected: California Code of Regulations (CCR), title 4, section 15712.1 and 15712.2.

Background

On October 5, 2021, Governor Gavin Newsom signed California Senate Bill 544, which requires the Department of Cannabis Control (Department) to establish a standard cannabinoids test method, including standardized operating procedures, for use by all licensed testing laboratories. The law permits the development of the test method by the Department or through a reference laboratory. The law became effective January 1, 2022 and requires the establishment of one or more test methods by January 1, 2023.

Statement of Purpose, Problem, Rationale, and Benefits

The purpose of the proposed regulations is to implement and make specific Business and Professions Code section 26100(f)(2) pertaining to the establishment of a standard cannabinoids test method on or before January 1, 2023. Through the proposed regulations, the Department aims to ensure all licensed testing laboratories are using the same standardized cannabinoid test method which will ensure consumers receive accurate and consistent information regarding the cannabinoid content of the cannabis and cannabis product they use or consume.

An inherent challenge in regulating an industry that has not been federally regulated is the lack of standardized, generally accepted and validated methods for the testing of cannabis and cannabis products. If a standard test method is not available for an analysis, new methods must be developed and validated. Accordingly, section 15712 of the Department's existing regulations requires licensed laboratories to develop, validate and implement test methods for the required analyses and, to the extent practicable, requires the test methods developed to comport with established guidelines such as those from the U.S. Food and Drug Administration, the Association of Analytical Communities (AOAC) International, and United States Pharmacopeia. Due to the lack of generally accepted standardized methods, each licensed laboratory has developed and implemented its own test method for cannabinoid content analysis. The use of different methods by individual licensed laboratories can produce inconsistent analytical results between the laboratories, thus resulting in inconsistent reporting of cannabinoid content of cannabis and cannabis products among licensed laboratories.

The proposed regulations implement the requirement that the Department develop a standardized test method for cannabinoids for use by all licensed laboratories. The proposed regulations establish and make specific the standardized cannabinoids test method that all licensed laboratories must use. The proposed regulations inform the licensed laboratories of the standard operating procedures that they must follow and the instructions for the determination of cannabinoid concentrations using high performance liquid chromatography systems (HPLC). The proposed regulations also inform licensed laboratories of the timeline to commence utilizing the cannabinoid test method.

The proposed regulations are expected to benefit the health and welfare of California residents. The specific benefits anticipated are increased protection of the public from the harms associated with inconsistent laboratory testing methods for cannabinoids that can result in inconsistent reporting of the cannabinoid content of cannabis and cannabis products by licensed laboratories. The proposed regulations aim to provide uniformity and transparency for cannabinoid testing by establishing standard operating procedures and instructions for licensed laboratories to determine cannabinoids concentration. More specifically, the standard operating procedures provide instruction on sample preparation, sample extraction, proper dilution, necessary apparatus and materials, reagents, calibration standards, instrumental parameters, instrument analysis, method limit of quantification and reporting limit, quality control, acceptance criteria, and method verification. These factors can affect testing results, thus standardization of all these factors within a standard operating procedure will result in more accurate and consistent reporting of cannabinoid content by licensed laboratories.

The proposed regulations will also increase the Department's ability to effectively regulate licensed laboratories. A well organized, clearly written set of procedures will allow the Department to better educate licensees regarding the testing method as well as provide consistency in enforcement. Effective education and enforcement regarding the requirements found in the regulations are essential to the Department's goal of ensuring that California's licensed laboratories operate in a manner that benefits the state of California while reducing or eliminating the risks of harm to the people of the state. The increased clarity and efficiency obtained by the proposed regulation will further increase the Department's ability to carry out this mission.

Specific Purpose, Necessity, and Rationale for Adoption

The Department proposes adopting sections 15712.1 and 15712.2 of Division 19, of title 4, of the California Code of Regulations, as follows.

Section 15712.1. Test Method for Cannabinoids.

The Department proposes adopting section 15712.1 which requires licensed laboratories to use specified cannabinoid test methods and incorporates by reference the test method established by the Department that a licensed testing laboratory must use.

Proposed subsection (a) of section 15712.1 provides that notwithstanding section 15712, a licensed laboratory shall utilize the cannabinoids test method specified in this section. This is necessary in order to implement the requirements of Business and Professions Code section 26100, subdivision (f)(2), and to clarify that a licensed laboratory may no longer develop and implement its own test method for cannabinoid testing but must now utilize the cannabinoid test method specified by the Department. This proposed subsection ensures that all licensed laboratories will use the same standardized testing method in determining cannabinoid content to ensure accurate and consistent cannabinoid testing results by and amongst licensed laboratories.

Proposed subsection (b) of section 15712.1 provides that the licensed laboratory shall use the test method developed by the Department entitled Determination of Cannabinoids Concentration by HPLC, Standard Operating Procedures (New 05/15/2022) to perform the cannabinoid content analysis required by section 15724. This is necessary to make clear to licensed laboratories that the listed test method must be used when the laboratory performs the cannabinoid content analysis required by section 15724. This proposed subsection is necessary so that only the cannabinoid testing method established by the Department is used in determining cannabinoid content to ensure accurate and consistent cannabinoid testing results by and amongst licensed laboratories. The test method developed by the Department is incorporated by reference. This is necessary so that the lengthy and highly technical testing methodology is provided in a format that is recognizable and readily useable by a licensed laboratory to facilitate the laboratory's implementation of the method.

The test method developed by the Department utilizes High Performance Liquid Chromatography (HPLC). HPLC is an efficient and robust technique that is widely used in the industry to determine cannabinoid concentration. The cost of instrumentation, reagents and lab supplies needed for the HPLC method are economical compared to other techniques such as Liquid Chromatography Mass Spectrometry (LC-MS) and Gas Chromatography Mass Spectrometry (GC-MS). A majority of licensed laboratories currently utilize HPLC when performing the required cannabinoid testing. This proposed addition is necessary in order to provide the licensed laboratories with a standardized HPLC method.

The purpose of the Standard Operating Procedures (SOP) for cannabinoid testing is to provide licensed laboratories with a validated test methodology to test the cannabinoid content of cannabis and cannabis products. The SOP provides licensed laboratories with universal procedures and criteria for the standardized testing of cannabinoids. This is necessary to provide consistency in cannabinoid testing across all licensed laboratories and to reduce the potential for misunderstandings regarding the relevant test method criteria and requirements. The SOP will ensure that licensed laboratories are testing for cannabinoids in the same manner with the same standards, thus making results more accurate and reliable amongst testing laboratories. This is necessary to achieve efficiency and uniformity of performance by licensed laboratories while also reducing disparities and deviations in laboratory practices among laboratories. The

proposed SOP will allow licensed laboratories to easily identify the requirements and processes for cannabinoids testing within the State of California.

The proposed SOP for the test method provides instructions for licensed laboratories to determine cannabinoids concentration. More specifically, the SOP provides instruction on sample preparation, sample extraction, proper dilution, necessary apparatus and materials, reagents, calibration standards, instrumental parameters, instrument analysis, method limit of quantification and reporting limit, quality control, acceptance criteria, and reporting results. The proposed SOP conforms to the requirements for SOPs established in section 15711. The proposed SOP includes a detailed description of all the SOP components specified in section 15711 as developed by the Department through validation of the test method.

The Scope section of the proposed SOP provides that the scope of the SOP includes the procedures and instructions for determination of cannabinoids using HPLC. This is necessary to inform the licensed laboratory of the scope of the analysis for which the SOP may be used.

The Application section of the proposed SOP provides that the method covers the determination of cannabinoid concentration in various cannabis product types. This is necessary to inform the licensed laboratory of the type of cannabis and cannabis products for which the test method has been validated and may be used.

The Introduction section of the proposed SOP provides a brief overview of the test procedure which includes sample extraction, dilution and analytical instrumentation. This is necessary so that the licensed laboratory can readily identify the basic requirements of the procedure.

The Definitions section of the proposed SOP provides a list of technical terms, their meaning, and their abbreviations that are used throughout the SOP. This is necessary so that the meaning of technical terms and their corresponding abbreviations are clear. Use of abbreviations throughout the SOP that are commonly used by laboratories is necessary to make the SOP easier to read rather than repeating the longer technical terms each time. Many of the defined terms are from the existing regulation section 15700 and are reiterated in the SOP for ease of reference by the licensed laboratory. This is necessary to ensure consistency in the use and meaning of the terms and for ease of reference by the licensed laboratory.

Proposed subsection 1 of the Definitions section provides “Acceptance criteria” means the specified limits placed on the characteristics of an item or method that are used to determine data quality. This reiterates the definition found in section 15700 and is included in the SOP for ease of reference by the licensed laboratory.

Proposed subsection 2 of the Definitions section provides “Continuing calibration verification” (CCV) means a type of quality control sample that includes each of the target method analytes that is a mid-range calibration standard which checks the continued validity of the initial calibration of the instrument. This reiterates the definition

found in section 15700 and is included in the SOP for ease of reference by the licensed laboratory.

Proposed subsection 3 of the Definitions section provides “Certified reference material” (CRM) means a reference material in cannabis or similar non-cannabis matrix prepared at a known concentration by a certifying body or a party independent of the laboratory with ISO/IEC 17034 accreditation and further provides for the calculation of percent recovery of the CRM. This definition is consistent with the one found in section 15700 and is included in the SOP for ease of reference by the licensed laboratory.

Proposed subsection 4 of the Definitions section provides “High Performance Liquid Chromatography” (HPLC) means the technique to separate, identify and quantify analytes in solution placed in a chromatography column at a high pressure, 500 psi or above. An HPLC system includes but not limited to, a solvent delivery module, a sample injection module, a column, and a detector. HPLC is a term commonly used and understood in the laboratory industry and this definition provides clarity for the regulated industry.

Proposed subsection 5 of the Definitions section provides “Initial Calibration Verification” (ICV) means a solution of each of the target method analytes of known concentration that is obtained from a source external to the laboratory and different from the source of calibration standards. This reiterates the definition found in section15700 and is included in the SOP for ease of reference by the licensed laboratory.

Proposed subsection 6 of the Definitions section provides “Liquid Chromatography” (LC) means the technique to separate, identify and quantify analytes in solution placed in a chromatography column. A LC system includes but not limited to, a solvent delivery module, a sample injection module, a column, and a detector. LC is a term commonly used and understood in the laboratory industry and this definition provides clarity for the regulated industry.

Proposed subsection 7 of the Definitions section provides “Laboratory Control Sample” (LCS) means a blank matrix to which known concentrations of each of the target method analytes are added. The spiked concentration must be at a mid-range concentration of the calibration curve for the target analytes. The LCS is analyzed in the same manner as the representative sample. This reiterates the definition found in section 15700 and is included in the SOP for ease of reference by the licensed laboratory.

Proposed subsection 8 of the Definitions section provides “Limit of detection” (LOD) means the lowest quantity of a substance or analyte that can be distinguished from the absence of that substance within a stated confidence limit. This reiterates the definition found in section 15700 and is included in the SOP for ease of reference by the licensed laboratory.

Proposed subsection 9 of the Definitions section provides “Limit of quantitation” (LOQ) means the minimum concentration of an analyte in a specific matrix that can be reliably

quantified while also meeting predefined goals for bias and imprecision. This reiterates the definition found in section 15700 and is included in the SOP for ease of reference by the licensed laboratory.

Proposed subsection 10 of the Definitions section provides “Method Verification” means the process of demonstrating that a laboratory is capable of replicating a validated test method with an acceptable level of performance. Use of verified testing methods by licensed laboratories is required by Business and Professions Code section 26100(g). Verification of test methods is a common practice in the laboratory industry to establish a laboratory’s competence in performing a specific method. This definition is necessary to provide clarity to the regulated industry.

Proposed subsection 11 of the Definitions section provides “Moisture content” means the percentage of water in a sample, by weight. This reiterates the definition found in section 15700 and is included in the SOP for ease of reference by the licensed laboratory.

Proposed subsection 12 of the Definitions section provides “Recovery” means measured concentration relative to the added (spiked) concentration in a reference material or matrix spike sample. This reiterates the definition found in section 15700 and is included in the SOP for ease of reference by the licensed laboratory.

Proposed subsection 13 of the Definitions section provides “Resolution” means a quantitative measure of how well two elution peaks can be differentiated in a chromatic separation. This subsection also specifies how resolution is measured. This definition is necessary to clarify the meaning of the term as used in the SOP and how it is measured. Resolution is the most important factor to demonstrate how peaks are separated from adjacent peaks. This ensures the accuracy of the quantitation results. Overlapping peaks indicate cannabinoids are not separated for quantitation and produce inaccuracy in analysis.

Proposed subsection 14 of the Definitions section provides “Reporting Limit” (RL) means the lowest concentration at which an analyte can be detected in a sample in each analytical batch and specifies how the RL is determined. This definition is necessary to clarify the meaning of the term as used in the SOP and how it is determined. Specifying the method to determine the RL is necessary because when a sample has to be diluted before analysis, either because of matrix problems or to get the instrument response within the linear dynamic range, the RL is raised by a factor corresponding to the dilution factor.

Proposed subsection 15 of the Definitions section provides “Relative percent difference” (RPD) means the comparative statistic that is used to calculate precision or random error and provides the formular for calculation of the RPD. This reiterates the definition found in section 15700 and is included in the SOP for ease of reference by the licensed laboratory.

Proposed subsection 16 of the Definitions section provides “Retention Time” (RT) means the time take for a solute to pass through a chromatography column. This definition is necessary to clarify the meaning of the term as used in the SOP. RT is used to identify the cannabinoid associated with a specific peak. Comparing the retention time of the sample to the calibration standards, enables the licensed laboratory to identify which cannabinoids the sample have.

Section I of the proposed SOP, Safety, provides information regarding the potential health effects of the chemicals used in the SOP and advises the adherence to general laboratory safety precautions, use of personal protective equipment, and the handling of chemicals in accordance with federal, state and local requirements. This is necessary to provide the licensed laboratories with information regarding appropriate safety precautions when performing the test method. Laboratory work poses risks to workers due to potential exposure to toxic chemicals, flammable solvents, and other materials. Management of these risks in a safety program and the general guidance presented in the SOP reduce the risk of harm to laboratory workers. The proposed provision advises that the toxicity and carcinogenicity of each chemical used in this method have not been thoroughly investigated and therefore each chemical compound must be treated as a potential health hazard and exposure must be limited to the lowest possible level. This advisement is the same as the safety advisement used by federal agencies such as the Environmental Protection Agency with their testing methodologies. The advisement is generally applicable to the use of chemicals by laboratories and is appropriate to include in the establishment of new test methodology. The provision also refers licensed laboratories to the Laboratory Safety Guidance by the Occupational Safety and Health Administration (OSHA)[1] for detailed laboratory safety requirements. This is a requirement for industry and chemical laboratories which the licensed testing laboratories are already required to follow, thus these are not new requirements. Including this information in the SOP is necessary to ensure the licensed laboratories and laboratory personnel utilizing the method are aware of the safety considerations associated with the test method.

Section II of the proposed SOP, Apparatus and Materials, provides a list of equipment and materials that are required in the performance of the test method. This is necessary so that the licensed laboratory is aware and can easily find a list of the equipment and materials that is required to perform test method.

The list of equipment includes an HPLC system. HPLC is utilized to separate and quantify cannabinoids based on the use of a column module, solvent delivery module, detector module, sampling module, and associated computer with software for control of the instrument and data analysis. The column module contains the column used for separation of cannabinoids and controls temperature during chromatography. The

[1] Occupational Safety and Health Administration (OSHA), Laboratory Safety Guidance, (OSHA 3404-11R) (2011).

solvent delivery module is required to control stable accurate solvent flow through the column, separating the cannabinoids. The detector module detects the cannabinoids with wavelength of 220nm which was optimized on the system used to develop the method to achieve strong consistent signal. The sampling module loads samples for analysis and injects precise volumes into the HPLC system. The computer data system controls all parts of the HPLC during chromatography, stores data, and performs calculations to quantify cannabinoids. These items are all necessary so that the licensed laboratory understands the specific requirements that are needed in order to achieve accurate and reliable results using the HPLC method. Testing methods are developed using particular instruments and equipment with specific performance characteristics and deviation from specifications can result in inaccurate and unreliable test results. The ultimate requirement for the performance of the HPLC system is that it can separate the cannabinoids to achieve a minimum resolution of 1.3.

The list of equipment also includes a tissue homogenizer and a cryogenic grinder capable of grinding samples to less than 1 mm. The tissue homogenizer is required to grind samples such as cannabis flower to a uniform particle size. The cryogenic grinder is required to grind difficult samples to a uniform particle size. Freezing is necessary for some samples such as gummy edibles, chocolates prior to grinding, otherwise the unfrozen samples will not grind to a uniform homogenate for testing. For the extraction of cannabinoids, particle size will affect extraction efficiency. A tissue homogenizer and cryogenic grinder meeting the specified grinding capabilities obtain efficient extracts from cannabis and cannabis products so that they can be accurately quantified. Both the tissue homogenizer and cryogenic grinder should be capable of grinding multiple samples without cross contamination so that the laboratory has capability of analyzing a larger number of samples.

Additional equipment includes an analytical balance capable of weighing to the nearest 0.1 mg and a top loading balance capable of weighing to the nearest 0.1 g. This is necessary to ensure weighing devices are accurate in order to minimize errors associated with sample weights. The method also requires disposable glass Pasteur pipettes; pipettes and pipet tips; conical polypropylene centrifuge tubes (50ml); a centrifuge that can effectively separate solids or particles from the extraction solvents by centrifugal force; sonicator; ice bucket; HPLC vials (amber); HPLC caps; LC Column that can work with the HPLC system to separate the cannabinoids of interest to achieve a minimum resolution of 1.3; disposable syringes with Luer-Lok tips, 3 ml; syringe filter disk, 0.2 µm Polytetrafluoroethylene (PTFE); HPLC solvent bottles, 1 L; vortex mixer (analog vortex mixer or equivalent); Griffin glass beakers; and a graduated cylinder. This additional equipment is required to perform the method and accurately weigh samples, measure or weigh solvents, extract cannabinoids effectively for analysis, handle liquids; correctly dilute solutions; contain solvents, and not contaminate samples or in any way interfere with the method. Without this listed equipment the laboratories would be producing inaccurate results and have potential variation from the standard reference method that would bring nonuniformity to cannabinoid analysis.

Section III of the proposed SOP, Reagents, provides a list of reagents that are required in the performance of the test method. The reagents are water, methanol, acetonitrile, and formic acid, and are listed at HPLC grade or above. This list is necessary so that the licensed laboratory is aware and can easily find a list of the reagents that is required to perform test method. The specific reagents are chosen to function in the extraction, dilution, separation and quantification of cannabinoids. The list also specifies the grade for the particular reagents which is necessary so that the licensed laboratory understands the specific requirements that are needed in order to achieve accurate and reliable results. HPLC grade is required because it reduces the detector noise, baseline drifts, enhances the quality of data, and assures reproducibility between laboratories.

Section IV of the proposed SOP, Calibration Standard, provides a list of standard solutions that are required in the performance of the test method. This is necessary so that the licensed laboratory is aware and can easily find a list of the standard solutions that are required to perform test method. Proposed subsection A provides a list of cannabinoid stock standard solutions. The list includes stock solutions for those cannabinoids that are required to be tested pursuant to section 15724 as well as additional cannabinoids that are not specifically listed in section 15724, but were analyzed for and validated using the test method. Including these stock standard solutions in the SOP allows a licensed laboratory to identify these cannabinoids if they are present in a sample during regulatory compliance testing. The ability to identify all cannabinoids in a sample, in is critical to accurate reporting of cannabinoid content of cannabis and cannabis products. The current state of the cannabis testing industry is that additional cannabinoids are voluntarily being tested for and reported Pursuant to Business and Professions Code section 26120(c), cannabis and cannabis products must be labeled with pharmacologically active ingredients including THC, CBD and other cannabinoids, thus testing methods should be able to identify additional cannabinoids to allow licensees to meet this requirement.

Proposed subsections B and C of the Calibration Standard section provides a list of cannabinoid mix working standard solutions and calibration standard solutions, respectively, and instruction on how to prepare and store the solutions. This is necessary to provide the licensed laboratory with specific instructions in the preparation of the solutions to ensure that all licensed laboratories are using uniform and consistent standards with the testing methodology and to ensure licensed laboratories are storing standard solutions in a manner to avoid degradation. These standards were chosen to give a useful linear calibration range for the instrument to accurately quantify cannabinoids. These standards have been evaluated and determined by the Department to be optimal for the accuracy, precision and overall quality of results for the cannabinoid testing method.

Section V of the proposed SOP, Procedure, provides the procedures for conducting the cannabinoids analysis including moisture content analysis, sample preparation, sample extraction, instrumental parameters, and analysis. This is necessary so that licensed laboratories have the specific step by step instructions to conduct the analysis and to

ensure all licensed laboratories are performing the analysis in the same manner. The steps specified are given in logical order for the licensed laboratory to accurately perform the method and meet the requirements for accurately reporting. Before samples can be tested, they need to be ground, extracted, and diluted accurately into a solvent for analysis. Other steps included are instrument configuration and equilibration of the instrument which need to be done prior to analyzing samples. Instrumentation for analysis needs calibration prior to analysis and reporting.

Proposed subsection A of the Procedure section provides that the licensed laboratory shall test and report the moisture content of dried flower including pre-rolls as required by section 15717 and requires the percentage moisture content be used to calculate the dry-weight percent cannabinoid. This is necessary because section 15724 requires the reporting of results for harvest batches on a dry-weight basis.

Proposed subsection B.1, Sample Preparation, of the Procedure section provides the procedures for homogenization of specific types of samples. This is necessary so that licensed laboratories have the specific instructions for homogenization of the various types of samples. Homogenization is a critical step in the preparation of a sample for analysis and is required by section 15714(a). The method of homogenization varies based on the sample type and includes grinding for plant material and freeze/grinding for edibles. Specification of homogenization procedures is necessary in order to achieve a uniform sample that will be amenable to extraction of cannabinoids in the sample for analysis by the method. Through validation, the Department has determined the listed methods for homogenization to be the most effective in obtaining accurate and reliable test results based on sample type.

Proposed subsection B.2 provides instructions regarding the sample size to be used in the analysis and varies based on the specific sample matrix being analyzed. This is necessary because section 15724(a) sets a 0.5 gram sample size for all cannabinoid matrices. The Department has determined however, through validation of the method, that the 0.5 gram sample size is not optimal for all cannabinoid matrices and has determined that the sample sizes specified in the SOP will yield the most accurate test results for the various matrices.

Proposed subsection C, Sample Extraction, of the Procedure section provides the specific instructions for sample extraction, including specifying the extraction solvent and dilution based on the sample matrix. The Department has determined through method validation that the specified extraction solvent and dilution provide optimal results. This is necessary in order to achieve the most accurate test results for the various matrices.

Proposed subsection D, Instrumental Parameters, of the Procedure section provides the instrumental parameters for the instruments used in the test method. The instrumental parameters listed are those specific to the Perkin Elmer Altus A-30 liquid chromatography instrument and Restek Raptor ARC-18 column used by the Department in performing and validating the test method. This is necessary so that the

SOP accurately reflects the parameters of the instrument used for performing the test method and to inform licensed laboratories of the specific instrumentation used and its specifications to be able to separate and accurately quantify cannabinoids. The provision clarifies that the instrumental parameters will be specific to the column and LC system used by a licensed laboratory, thus the system used by a licensed laboratory may have different parameters to include in its specific SOP. The provision clarifies that an equivalent HPLC system is one that separates the cannabinoids tested with a minimum resolution of 1.3. This gives laboratories flexibility in utilizing a variety of HPLC systems with a clear requirement to guide them. The Department has determined that the instrumental parameters are optimal for the accuracy, precision and overall quality of results for the cannabinoid testing method.

Proposed subsection E, Instrument Analysis, of the Procedure section provides the step by step instructions for running the samples, including quality control samples, using the HPLC. This is necessary so that licensed laboratories have clear instructions on running the samples using HPLC in order to obtain accurate and reliable test results. The licensed laboratory has requirements to meet in section 15729, Laboratory Quality Assurance (LQA) Program, and section 15730, Laboratory Quality Control (LQC) Samples. The step by step instructions in this provision are given to aid licensed laboratories to meet these requirements. These requirements for instrumental analysis have been evaluated and determined by the Department to be optimal for the accuracy, precision and overall quality of results for the cannabinoid testing method.

Section VI of the proposed SOP, Method Limit of Quantification and Reporting Limit (RL), provides the limits of detection (LOD) and limits of quantification (LOQ) for the various cannabinoids tested by the method. The LOD and LOQ are important performance characteristics of a test method and are required by section 15731. This proposed provision clarifies that LOQ and LOD should be calculated and established by the licensed laboratory in accordance with section 15731 as part of the method verification that is required by section 15712.2. This is necessary because LOD and LOQ are system and method specific and may change based on changes in operational parameter changes or use of a different system. This provision also provides the method for determining the Reporting Limit for each batch of samples. This is necessary to accommodate the change in the smallest amount of an analyte that can be reported in analysis by the licensed laboratory in a particular batch of samples. Dilution of samples is routinely done to correctly quantify cannabinoids within the calibrated range of the instrument. After dilution, the amount that can be effectively reported is no longer directly determined by the method LOD or LOQ. Dilution must be accounted for in the final result and the mechanism to accurately reflect this change in the reported final result is with a Reporting Limit.

Section VII of the proposed SOP, Quality Control, provides that quality control samples should be analyzed in accordance with the requirements of section 15730. This is necessary to clarify that licensed laboratories are required to meet existing requirements regarding use of quality control samples. Quality control samples are used

to measure method accuracy, precision, contamination, and matrix effects. Quality control samples are necessary because quality control sample results are used to ensure that data released by the licensed laboratory is valid, reliable and reproducible.

Proposed subsections A and B of the Quality Control section provides a detailed explanation and instructions on the use of quality control samples with sample batches, including solvent blanks, ICV, CCV, method blanks, sample duplicates, post-dilution matrix spikes and laboratory control samples. This is necessary in order for the licensed laboratories to have step by step instructions regarding the use of quality control samples, understand their purpose, and meet requirements of section 15730 for the use of laboratory quality control samples. The levels chosen are consistent with section 15730 and based on standards from the FDA. This is necessary to ensure all licensed laboratories are following the same quality control procedures in order to consistently produce valid and reliable results.

Proposed subsection C, Integration, of the Quality Control section provides that all chromatograms should be processed by automatic detection and integration of peaks using instrument software. This is necessary to ensure consistency of results and to minimize the manual manipulation of chromatographic data files. Integration is a key component of chromatographic data interpretation and is the subject of regulatory scrutiny in International Organization for Standardization (ISO) 17025 audits. This provision also requires that laboratories that perform manual integration, shall have an integration policy that includes justification, documentation and managerial review and approval of manual integration. This is necessary to ensure that if manual integration occurs, there is sound justification for the process and that laboratory management personnel is responsible for reviewing and approving the data, justification and validity of the results. This provision specifies that the manual integration policy is required to outline the proper way to integrate chromatographic peaks, the preference of automatic integration for consistency, and if manual integration is needed, documentation of the justification and supporting documentation including chromatograms showing both automatic and manual integration. This is necessary to clearly outline the requirements for the integration policy if a licensed laboratory will perform manual integration and to establish that automatic integration is the preferred method to ensure data integrity and consistency. This is also necessary to ensure that if manual integration is done, it should only be done if there is sound scientific justification and should be well documented. Excessive manual integration indicates there may be a problem with the instrument requiring investigation and preventative maintenance. This extra requirement for a policy for manual integration is a standard requirement for laboratory quality control and oversight. Shifting integration to meet quality control requirements is the subject of scrutiny during audits by ISO 17025 accrediting bodies and inspections. Laboratories are required to conduct internal audits in accordance with ISO/IEC 17025 standards pursuant to section 15735. The Food and Drug Administration also provides guidance for bioanalytical methods to include an SOP or guideline for the re-integration of data including criteria, performance, rationale and documentation including the original and re-integrated data. (U.S. Food and Drug Administration, Center for Drug

Evaluation and Research, *Bioanalytical Method Validation Guidance for Industry*, section III.C., Validated Methods: Expectations of In-Study Analysis and Reporting) (May 2018)).

Proposed subsection D, Retention Time (RT) Acceptance Window, of the Quality Control section requires and provides instructions for the calculation of the retention time acceptance window of each cannabinoid. This is necessary to make sure that the peak identification of each cannabinoid is accurate because a peak is identified to be a specific cannabinoid by the retention time. If a peak is out of the retention time acceptance window, there may be a problem with the instrumentation not properly separating compounds, it is not that cannabinoid, or it may be another cannabinoid or impurity. Retention times are used in conjunction with other Quality Controls to give an indication of validity of the method. (US Food and Drug Administration, Guidelines for the Validation of Chemical Methods in Food, Feed, Cosmetics, and Veterinary Products, 3rd Edition (October 2019).

Proposed subsection E, UV-Visible Spectrum, of the Quality Control section provides instructions for the determination of a sample analyte peak when identification of the peak is in question. This is necessary to make sure that the peak identification of each cannabinoid is accurate. This provision requires the further identification of the cannabinoid by comparison of the UV-Visible spectrum of the sample peak to the UV-Visible spectrum of the cannabinoid standard peak. This is necessary because a peak on a chromatograph is identified to be a specific cannabinoid by the retention time and verified by the match to the UV-Visible spectrum for the cannabinoid. If a sample peak UV-Visible spectrum does not match the UV-Visible spectrum of the cannabinoid standard, there may be a problem with the instrumentation not properly separating compounds, it is not that cannabinoid, or it may be another cannabinoid or an impurity. This provision provides that if UV-Visible spectrum of the sample peak and the cannabinoid standard peak do not match, then the sample peak shall not be reported as the cannabinoid. This is necessary to ensure that the results are accurately reported. This provision also provides instructions if there is evidence of a cannabinoid and an impurity. This provision provides if the impurity and the cannabinoid spectrums are mixed, the spectra may be deconvolved and reported following the requirements for manual integration set forth in section VII.C. This is necessary to ensure that cannabinoid test results are accurately reported. Peak purity used in conjunction with other Quality Controls is used to give an indication of validity of the method.

Section VIII of the proposed SOP, Acceptance Criteria For Quality Control Samples, provides the acceptance criteria for quality control samples. This acceptance criteria is required by section 15730 and is necessary for the determination of data quality. The requirement is duplicated here for ease of reference by the licensed laboratories.

Section IX of the proposed SOP, Reporting Results, provides the requirements for reporting test results. Proposed subsection A requires results to be calculated and reported in accordance with the cannabinoid reporting requirements in section 15724

and the data package requirements in section 15732. This is necessary to make clear that laboratories must report results in accordance with existing regulatory requirements.

Proposed subsection B of the Reporting Results section requires that the results for all samples are reported with 3 significant figures. Three significant figures are chosen as it reflects the resolution of the measurement of cannabinoids by the method. This is necessary to establish a standardized reporting format for use by all licensed laboratories.

Proposed subsection C of the Reporting Results section requires that results that are below the reporting limit determined in Section VI of the SOP are reported as "<RL". This is necessary to provide licensed laboratories with a standardized format for reporting results that are below the reporting limit. Reporting limit is the lowest concentration at which an analyte can be detected in a sample in each analytical batch and is necessary for the accuracy of the results report so that the customer can better understand the results.

Proposed subsection (c) of section 15712.1 provides that the cannabinoid test method identified in subsection (b) shall not be altered by the licensed laboratory. This is necessary in order to maintain the uniformity of the procedure used by testing laboratories and to prevent changes to the procedure that may render it less accurate and reliable.

Proposed subsection (d) of section 15712.1 provides that, notwithstanding the requirements of section 15724(a), the licensed laboratory shall analyze the sample size of a representative sample that is indicated in the cannabinoid test method identified in subsection (b). This is necessary so that the licensed laboratory uses the appropriate sample size designated by the specific test method. The sample size established in section 15724(a) was established as a general standard and was not established based on a particular test method. The sample sizes designated in the approved test method are specific to the test method and have been determined and established in order to achieve the most accurate test results.

Proposed subsection (e) of section 15712.1 provides that prior to using a cannabinoid test method identified in subsection (b), the licensed laboratory shall perform verification of the test method to demonstrate that the laboratory is capable of meeting test method's performance specifications. Verification of test methods is required by Business and Professions Code section 26100(g) and is necessary so that the testing laboratory can demonstrate that it is capable of performing the standardized test method. Verification ensures that the laboratory can obtain comparable results on the same matrix, using equivalent equipment and circumstances, as the standard validated method.

Proposed subsection (f) of section 15712.1 provides that the licensed laboratory using the cannabinoid test method identified in subsection (b) need not provide the Department with a validation report of the cannabinoid test method as required by

sections 15702(c)(1) and 15713. This is necessary because the Department has already performed the work to validate the test method and duplication by the licensed laboratory is unnecessary. Method validation is a process by which a non-standard test method is developed and standardized to ensure it is capable of producing valid and consistent results. Validation is a key step in the process of developing the standardized test methods listed in subsection (b). Because the Department has already performed the validation work, duplication by the licensed laboratory is unnecessary.

Proposed subsection (g) of section 15712.1 provides that the licensed laboratory shall provide the Department with its standard operating procedures implementing the cannabinoid test method identified in subsection (b) in accordance with the requirements of section 15702(b) and 15711(a). This is necessary to clarify that, although the laboratory is required to utilize a standard operating procedure and test method identified by the Department, the licensed laboratory must still adapt those procedures to its own laboratory and analytical instrumentation and must submit its SOP to the Department as required for all testing procedures. The proposed section further provides that the SOP shall be submitted with the verification report required by section 15712.2 prior to use of the method for regulatory compliance testing. This is necessary to clarify when a licensed laboratory that is currently in operation must submit its SOP.

Proposed subsection (h) of section 15712.1 provides that the licensed laboratory shall commence utilizing the cannabinoid test method specified in subsection (b) no later July 1, 2023. This is necessary in order to provide a licensed laboratory with sufficient time to implement the methodology, including the purchase of any additional equipment and reagents necessitated by the test method. The phase-in period will also allow a licensed laboratory to deplete supplies that may not be compatible with the new methodology. The Department has determined with their internal use of the method on various products that a six-month lead time is sufficient to allow implementation of the new method without undue financial hardship on the licensed laboratory. The current methods being used by licensed testing laboratories have been reviewed and approved by the Department. The issue of inconsistent results amongst laboratories is being addressed by this specified cannabinoid test method. During the phase-in period, licensed laboratories will continue to use methods approved by the Department to protect public safety. will continue to be under the oversight of current approved testing methodologies, review by the Department, and monitoring by the Department for public safety.

<u>Section 15712.1. Verification of Test Method for Cannabinoids.</u>

The Department proposes adopting section 15712.2 which sets forth the method verification requirements for use of the cannabinoid test method identified in section 15712.1. Proposed subsection (a) requires that each licensed laboratory perform verification of the cannabinoid test method in its own laboratory prior to using the test method for regulatory compliance testing in order to demonstrate that the licensed

laboratory is capable of meeting test method's performance specifications. This is necessary so that the licensed laboratory can demonstrate its ability to perform the test method prior to its use to ensure the accuracy of testing results. Verification of test methods is a common practice in the laboratory industry to establish a laboratory's competence in performing a specific method. Use of verified testing methods by licensed laboratories is required by Business and Professions Code section 26100(g).

Proposed subsection (b) defines "Method Verification" to mean the process of demonstrating that a laboratory is capable of replicating a validated test method with an acceptable level of performance. This definition is necessary to provide clarity to the regulated industry and duplicates the definition of method verification included in the SOP. Verification of test methods is a common practice in the laboratory industry to establish a laboratory's competence in performing a specific method. Use of verified testing methods by licensed laboratories is required by Business and Professions Code section 26100(g).

Proposed subsection (c) provides that method verification by the licensed laboratory must address the criteria listed in the table below:

Criteria	Number Required	Notes
Sample matrices	≥1	A single matrix can be selected even if the original method is applicable to multiple matrices
Matrix blanks	≥1	
Method blanks	≥1	
Spike concentration levels	≥2	
Spike replicates	≥3	

This is necessary so that the laboratory can demonstrate, and the Department can confirm, the laboratory's capability in performing the test method. The criteria listed in the table is taken from FDA's Guidelines for the Validation of Chemical Methods Food, Feed, Cosmetics, and Veterinary Products, 3rd Edition (October 2019). The Department has determined that it is appropriate to utilize the criteria from the FDA's guidelines because they are widely accepted as an appropriate scientific standard.

Proposed subsection (d) provides that the licensed laboratory shall calculate and establish the Limit of Detection and Limit of Quantification for all analytes in accordance with section 15731 as part of the method verification. This is necessary because the LOD and LOQ are important performance characteristics of a test method and are required by section 15731 which specifies the method for calculating and establishing LOD and LOQ. LOD and LOQ are required to be established as part of the method verification process because LOD and LOQ are system and method specific and may change based on changes in operational parameters or use of a different system.

Proposed subsection (e) provides the licensed laboratory shall evaluate the linear dynamic range for all analytes to ensure they meet the needs for the method. Linear dynamic range is the region over which the signal emission is directly proportional to the concentration of the sample and is important for the accuracy of quantitative analysis. Licensed laboratories are required to evaluate linear dynamic range pursuant to section 15713 which is necessary to ensure the accuracy of quantitative analysis.

Proposed subsection (f) requires a licensed laboratory to generate a verification report for the cannabinoid test method and specifies the information to be included in the report. This is necessary so that the licensed laboratory understands the information and documentation that must be part of the verification report. The required information and documentation will allow the Department to assess the laboratory's ability to perform the test method. The verification report is required to include instrument calibration data. A calibration curve is a mathematical tool used in analytical chemistry that provides a set of reference points that unknown chemical substances can be compared to. This requirement is necessary because it enables the Department to ensure the accuracy of the test method. The verification report is also required to include raw data, including instrument raw data. This requirement is necessary because it enables the Department to trace the integrity of the data and to hold licensed laboratories accountable for testing, thus deterring testing laboratories from producing fictitious data in lieu of performing the actual analysis.

The verification report must also include cannabis reference materials or certified reference material results. This is necessary because it enables the Department to evaluate the quality of data produced by the licensed laboratory. Including this allows traceability or the clear relationship between results and the samples by using appropriate standards. This is included to verify analytical measurement methods, including the calibration of instrument.

Data and calculations pertaining to LOD and LOQ determinations must also be included in the verification report. This is necessary because it enables the Department to determine the level at which the laboratory can confidently report an accurate value for an analyte in a particular matrix, using a specific method.

The verification report must also include a Laboratory Quality Control (LQC) report, as described in section 15730(j). The LQC report as described in section 15730(j) include LQC acceptance criteria, measurements, analysis dates and matrix types. This is necessary because it enables the Department to evaluate how the laboratory achieves accurate results while ensuring the data from the quality control samples are precise.

Proposed subsection (g) requires a supervisory or management employee of the laboratory to review, approve, sign, and date the verification report. This is necessary because it enables the department to ensure that laboratory supervisory or management personnel is reviewing the data and approving the method verification report while also placing responsibility of this approval on the head of the laboratory. This is also necessary to show that the laboratory has properly followed the steps within

ISO 17025 to review and approve tests before utilizing them. Laboratories are required to conduct internal audits in accordance with ISO/IEC 17025 standards pursuant to section 15735. Use of methods that are not reviewed and approved could lead to inaccurate results in testing cannabis and cannabis products, which will negatively impact the public health and fail to provide the consumer with accurate information.

Proposed subsection (h) requires the licensed laboratory to provide the Department with a verification report demonstrating verification of the cannabinoid test method prior to use of the method for regulatory compliance testing of cannabis goods. This is necessary so that Department can confirm the testing laboratory's capability in performing the test method prior to the laboratory's utilization for testing of cannabis goods.

Incorporation by Reference

The following documents are incorporated into the regulations by reference:

Determination of Cannabinoids Concentration by HPLC, Standard Operating Procedures (New 05/15/2022)

Technical, Theoretical, and/or Empirical Study, Reports, or Documents

The following documents were relied on for this rulemaking process:

1. Department of Cannabis Control, Cannabis Testing Laboratory Branch

Determination of Cannabinoids Concentration by UPLC, Standard Operating Procedures CM-002 (Final 3/29/2022).

2. Department of Cannabis Control, Cannabis Testing Laboratory Branch

Flower Sample Grinding on Geno/Grinder, Standard Operating Procedures GM-002 (Sept. 24, 2021).

3. Department of Cannabis Control, Cannabis Testing Laboratory Branch

Edible Sample Grinding on Freezer/Mill, Standard Operating Procedures GM-001 (Sept. 24, 2021).

4. Department of Cannabis Control, Cannabis Testing Laboratory Branch, *Validation of a UPLC Method for Cannabinoids Concentration Quantification in Cannabis Flower* (March 2022).

5. University of California, San Diego, Center for Medicinal Cannabis Research, *Method Validation Cannabinoid Potency (9 Cannabinoids by UPLC-PDA)* (April 18, 2022).

6. US Food and Drug Administration, *Guidelines for the Validation of Chemical Methods in Food, Feed, Cosmetics, and Veterinary Products, 3rd Edition* (October 2019).

7. Occupational Safety and Health Administration (OSHA), U.S. Department of Labor, *Laboratory Safety Guidance* (OSHA 3404-11R) (2011).

8. Barkovich, *High Performance Liquid Chromatography*, LibreTexts, Inc. (April 24, 2022).

9. Restek, *Fast, Low-Solvent Analysis of Cannabinoids Increases Lab Productivity and Decreases Solvent Costs* (Lit. Cat. #FFFA3123-UNV) (2020).

10. U.S. Food and Drug Administration, Center for Drug Evaluation and Research, *Bioanalytical Method Validation Guidance for Industry* (May 2018).

Economic Impact and Fiscal Impact Assessment

Business Impact

The Department of Cannabis Control has 48 licensed laboratories as of May 13, 2022. The businesses impacted by the regulation are all licensed testing laboratories.

Economic Impact Assessment

The proposed regulations require licensees to commence utilizing the Department established cannabinoid test method no later than six months following the Department's adoption of the test method through these proposed regulations. Many of the licensed laboratories currently use an HPLC system consisting of a column module, solvent delivery module, photodiode-array detection module and sampling module that is capable of separating the cannabinoids of interest to achieve a minimum resolution of 1.3 because the system is a basic instrument that is used to separate cannabinoids effectively and efficiently. The cost of a an HPLC system that meets the proposed regulatory requirements is approximately $60,000. Additionally, the grinding and homogenization procedures in the proposed regulations would require licensed laboratories to have a grinder capable of grinding samples to less than 1 mm. If the licensees do not have an existing grinder that is sufficient, the cost of a grinder would range from approximately $20,000 to $35,000. Further, the proposed regulations would also require the licensed testing laboratories to freeze grind edible samples and the associated cost for the liquid cryogens is approximately $10,000 per year. Licensed laboratories also purchase solvents and standards in the ordinary course of business, but in varying quantities depending on the volume of samples being processed. On average, a licensed laboratory may spend $800 for standards and $500 for solvents in a year and $2,000 for a column. However, the costs of standards, solvents, and columns would be incurred even if the proposed regulations were not in effect as they are necessary supplies to operate a licensed laboratory.

It is anticipated that the cost for most licensed laboratories to comply with the proposed regulations are minimal as most laboratories currently use similar testing methods and are in possession of all relevant apparatus and materials necessary to comply with the proposed regulations. The lowest range of initial costs for a licensed testing laboratory

to comply with the proposed regulations would be approximately $1,300.00 reflective of purchasing $800 for standards and $500 for solvents, assuming the licensed laboratory already possessed a LC column, adequate grinder, and HPLC system.

However, if a licensed laboratory needed to purchase the required equipment and supplies the approximate costs are as follows: a new HPLC system for $60,000, a grinder for $35,000, liquid cryogens for $10,000, standards at $800, solvents for $500, and a LC column for $2,000.00, the upper range of initial costs would be $108,300. The annual ongoing costs would amount to approximately $11,300 including $800 for standards, $500 for solvents, and $10,000 for liquid cryogens though costs may vary depending on the volume of samples a particular licensed laboratory processes each year.

To calculate the approximate total statewide costs a business may incur to comply with this regulation over its lifetime, the upper range of costs is approximately $108,300 added to the annual ongoing costs of $11,300 yields a sum of $119,600.00. $119,600 multiplied by ten years results in a grand total of $1,196,000.00

The proposed regulations will not have a significant adverse economic impact on businesses.

The Department does not anticipate the creation or elimination of jobs or licensed businesses, or the expansion of existing businesses, as a result of the proposal. The proposed regulations are standardizing an HPLC cannabinoid test method which is already used by a majority of licensed laboratories, thus it is anticipated that existing laboratory personnel can perform the procedure proposed by the regulation and there will be no creation or elimination of jobs. The proposed regulation does not add or increase testing requirements, thus it is anticipated the regulation will not result in the creation, expansion, or elimination of businesses.

The total statewide economic benefit of this regulation is difficult to quantify in dollars because many of the benefits are fiscally intangible. The primary benefit of the proposed regulations is to protect the health and welfare of California residents by ensuring that licensed laboratories are properly testing cannabis and cannabis products and reporting accurate results. This will allow consumers to receive accurate information regarding the level of cannabinoids in cannabis and cannabis products, while ensuring that the labeling of cannabis and cannabis products is accurate. Additionally, the proposed regulations reduce the ability to select licensed laboratories to achieve more favorable testing results.

The proposal does not benefit or negatively impact worker safety or the State's environment because the proposed regulatory action does not involve any topic that induces harm or benefit to worker safety or the environment in the State.

Fiscal Effect on State Government

The proposed regulations govern licensed laboratories while implementing the statutory requirement for the Department, on or before January 1, 2023, to establish a standard cannabinoids test method, including standardized operating procedures that shall be utilized by all testing laboratories. There is no impact on the Department's workload created by the proposed regulations. Thus, there is no fiscal impact on state government resulting from the proposed regulations.

Disclosures Regarding the Proposed Action

The Department has made the following initial determinations:

Local mandate: There will be no local mandate.

Cost to any local agency or school district requiring reimbursement pursuant to Gov. Code section 17500, et seq: None.

Any other non-discretionary cost or savings imposed upon local agencies: None.

Cost or savings to any state agency: None.

Cost or savings in federal funding to the state: None.

Effect upon housing: There is no effect on housing.

Specific Technologies or Equipment

The proposed regulations require the following equipment necessary to perform the test method established by the Department as required by statute.

1) HPLC equipment consisting of a column module, solvent delivery module, photodiode-array detection module and sampling module that is capable of separating the cannabinoids of interest to achieve a minimum resolution of 1.3.
2) Tissue homogenizer capable of grinding samples to less than 1 mm.
3) Cryogenic grinder capable of grinding samples to less than 1 mm.

The HPLC equipment consisting of a column module, solvent delivery module, photodiode-array detection module and sampling module that is capable of separating the cannabinoids of interest to achieve a minimum resolution of 1.3 is required because the HPLC equipment's purpose is to separate and analyze compounds such as cannabinoids. A measure of how well separated cannabinoids are is resolution. The HPLC is able to clearly separate the cannabinoids to accurately determine their concentration. Lower resolution will indicate that the cannabinoids are not uniquely separated and cannot be accurately quantified. HPLC is an established technology that has been used for the separation and analysis of chemical compounds. HPLC is utilized in the analysis of compounds by internationally recognized bodies such as the Food and

Drug Administration, the Association of Analytical Communities (AOAC), the United States Pharmacopeia, and the European Chemicals Agency.

The tissue homogenizer capable of grinding samples to less than 1 mm, is required to grind samples to a uniform particle size. For the extraction of cannabinoids, particle size will affect extraction efficiency. A tissue homogenizer meeting the grinding capabilities specified in this section obtain efficient extracts from cannabis and cannabis products so that they can be accurately quantified. The tissue homogenizer must be capable of grinding multiple samples without cross contamination so that the laboratory has capability of analyzing a larger number of samples.

The cryogenic grinder capable of grinding samples to less than 1 mm, is required to grind difficult samples to a uniform particle size. Freezing is necessary for some samples such as gummy edibles, chocolates prior to grinding, otherwise the unfrozen samples will not grind to a uniform homogenate for testing. For the extraction of cannabinoids, particle size will affect extraction efficiency. A cryogenic grinder meeting the grinding capabilities specified in this section obtain efficient extracts from cannabis and cannabis products so that they can be accurately quantified. The cryogenic grinder must be capable of grinding multiple samples without cross contamination so that the laboratory has capability of analyzing a larger number of samples.

Consideration of Alternatives

No reasonable alternative to the regulatory proposal would be either more effective in carrying out the purpose for which the action is proposed or would be as effective or less burdensome to affected private persons and equally effective in achieving the purposes of the regulations in a manner that ensures full compliance with the law being implemented or made specific.

Set forth below are the alternatives which were considered and the reasons each alternative was rejected:

1. Alternative No. 1: Not adopt the proposed regulations. This alternative was rejected because SB 544, as codified in Business and Professions Code section 26100(f)(2), requires the Department to establish a standard cannabinoids test method, including standardized operating procedures, that shall be utilized by all testing laboratories. If the Department does not adopt the proposed regulations, there will be no standardized test method for licensees to follow to test cannabinoids and the Department will not have complied with its statutory mandate.
2. Alternative No. 2: Liquid Chromatography/ Mass Spectrometry (LCMS or LCMSMS). These methods use the separating power of liquid chromatography but use a different detector called mass spectrometry that is highly sensitive. The LC method specified in the reference method can be used with the LCMS or LCMSMS method. The advantage to this method is that it can uniquely identify

compounds by mass or a mass fragment spectrum. The disadvantage is the cost as these instruments are approximately $200,000 to $800,000. The Department did not adopt this method because only a small number of licensed laboratories currently utilize this method and it would be very costly for licensees.

3. Alternative No. 3: Gas Chromatography/Mass Spectrometry (GCMS). This method is rarely used for cannabinoids as the heating routine used by GCMS causes chemical changes of the cannabinoids. These chemical changes will give inaccurate results for cannabinoid analysis. There are variations to this method that allow derivatization of the sample to protect it from degradation in analysis. However, licensed laboratories that have undergone method validations do not use this method, and the additional cost of a GCMS instrument, slower analysis time, and added steps of derivatization make it unfeasible for routine testing. Additionally, the Gas Chromatography Mass Spectrometry instruments cost approximately $170,000. The Department did not adopt this method as it is rarely used for cannabinoids testing and costly.