Title: Quality Assurance Program Plan for Analytical Testing Laboratories Performing Analyses of Finished Medical Marijuana Products and Marijuana-Infused Products in Massachusetts

The Protocol contains the following sections:

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Tables:

Acronym	Definition
AHP	American Herbal Pharmacopeia
ASTM	American Society for Testing and Materials
BAM	FDA Bacteriological Analytical Manual
CBI	Confidential Business Information
CCB	Continuing Calibration Blank
CCV	Continuing Calibration Verifications
cGMP	Current Good Manufacturing Practices
COC	Chain-of-Custody
DAD	Diode Array Detection
DOC	Demonstration of Capability
DOT	Department of Transportation
DQI	Data Quality Indicators
DQO	Data Quality Objectives
EDD	Electronic Data Deliverables
EPA	United States Environmental Protection Agency
FDA	United States Food and Drug Administration
ICH	International Conference for Harmonization
IR	Infrared
ISO	International Organization for Standardization
LCL	Lower Control Limit
LCS	Laboratory Control Sample
LIMS	Laboratory Information Management System
LOD	Limit of Detection
LOQ	The Limit of Quantitation
LWL	Lower Warning Limit
LOD	Limit of Detection
MDPH	Massachusetts Department of Public Health
MIP	Marijuana Infused Products
MMP	Medical Marijuana Products
NIST	National Institute of Standards and Technology
OOS	Out-of-Specification
PE	Performance Evaluation
POC	Point-of-Contact
PT	Proficiency Testing
QA	Quality Assurance
QAPP	Quality Assurance Program Plan
QC	Quality Control
QMS	Quality Management System
RMD	Registered Marijuana Dispensary
RPD	Relative Percent Difference
RSD	Relative Standard Deviation
SAP	Sampling and Analysis Plan
SOP	Standard Operating Procedures
TNI	The NELAC Institute
UCL	Upper Control Limit
USP	United States Pharmacopeia
VTSR	Validated Time of Sample Receipt
WHO	World Health Organization

1.0 SCOPE AND APPLICATION

This document serves as sub-regulatory guidance for all laboratories performing testing for the Massachusetts Department of Public Health (MDPH) Medical Use of Marijuana Program in order to provide data of known and appropriate quality when conducting the MDPH Protocol for Sampling and Analysis of Finished Medical Marijuana Products and Marijuana-Infused Products for Massachusetts Registered Medical Marijuana Dispensaries, and the Protocol for Sampling and Analysis of Environmental Media for Massachusetts Registered Medical Marijuana Dispensaries, with related Exhibits 4 through 7. The practices that are described in this Quality Assurance Program Plan (QAPP) are based upon the applicable guidance and regulations in 21 CFR Part 211, Subpart I (Current Good Manufacturing Practices [cGMP] for Finished Pharmaceutical Products, Laboratory Controls), relevant United States Pharmacopeia (USP) general chapters and methods, the International Conference for Harmonization (ICH) Guidelines, and the international standard requirements of ISO/IEC 17025:2005, The 2009 EL TNI (The NELAC Institute) Standard, Standard American Herbal Pharmacopeia (AHP), United States Food and Drug Administration (FDA) methods and guidance from relevant reference methods listed in the Appendix A Table 01 (Method Reference Table).

This document provides guidance on general procedures for laboratory operations including, for example, method validation, quality control (QC) sample analysis, and data review, reporting of results, as they relate to method compliance, laboratory systems, and overall good laboratory practices. In general, the document describes acceptable approaches for meeting the requirements of the existing MDPH protocols, incorporating best practices to the extent necessary for acceptable data. This document provides guidance within which the laboratories are to implement technical procedures to produce an objective account of reliable sample handling and analysis from the time of receipt of the sample, to the time analysis. Guidance is also provided for data reduction, data review, and final reporting of results. This document is meant to provide the Good Laboratory Practices for laboratory operations described in the attestation required by MDPH in the medical marijuana license application:

> "I, on behalf of the laboratory, attest that the laboratory will use Good Laboratory Practices for laboratory operations consistent with DPH guidance described in the Quality Assurance Program Plan for Analytical Testing Laboratories Performing Analyses of Finished Medical Marijuana Products and Marijuana-Infused Products in Massachusetts*."*

In order to outline the *required Good Practices* more clearly in this document, they are presented in italics. As compliance can be shown in a number of ways depending on the laboratory's processes, additional guidance on possible implementation approaches and suggestions for more robust compliance than the minimum is displayed in grey boxes. These grey boxes are not meant to be requirements and are only provided as assistance to the laboratories in their compliance efforts.

***Required Good Laboratory Practices* are presented in *italics* in this document.**

2.0 PROBLEM STATEMENT

A set of minimum standards for laboratory performance is required to assure that data submitted from the analysis of medical marijuana products and related matrices is of known and

appropriate quality. Within laboratory quality management systems such as ISO/IEC 17025:2005 and ISO-based standards such as the TNI Standard, USP, ICH and cGMP, critical references are made to client needs and specifications, and to the required level of confidence or method performance for the application of the testing method. Those requirements, including how method performance is to be validated, documented and communicated, and how the data are to be reported have not, prior to the issuance of this QAPP, been clearly defined.

3.0 DECISION RULE

Materials subject to analysis under the MDPH Protocol for Sampling and Analysis of Finished Medical Marijuana Products and Marijuana-Infused Products for Massachusetts Registered Medical Marijuana Dispensaries (MMJ_PR_3.0_020516) are to be analyzed using the current version of the MDPH protocols listed below:

- *Exhibit 4. Analysis Requirements and Recommended Limits for Metals in Finished Medical Marijuana Products*
- *Exhibit 5. Minimum Analysis Requirements for Residues of Pesticides and Plant Growth Regulators Commonly Used in Cannabis Cultivation*
- *Exhibit 6. Analysis Requirements for Microbiological Contaminants and Mycotoxins in Medical Marijuana Products*
- *Exhibit 7 (a). Concentration Limits for Residual Solvents*
- *Exhibit 7 (b). Concentration Limits for Residual Levels of Propane, n-Butane, or Iso-Butane, as Revised, November 23, 2016.*

Direction, on which materials are to be subjected to given protocol sections (Exhibits), is provided in Exhibit 8 (b). Laboratory Testing Flowchart.

The response to laboratory results is described and defined in Exhibit 8 (a). Actions in Response to Laboratory Analytical Results. The first decision point in the workflow depicted in Exhibit 8 (a) is the determination of whether the analytical results are valid with respect to the requirements. This is determined by evaluation of the validation and verification indicators and data quality indicators identified in this document.

4.0 MONITORING REQUIREMENTS

The protocols for the analysis of marijuana and marijuana products have requirements applicable to the different product types for contaminants as well as for the potency value of cannabinoids. These requirements are summarized by product type on Tables 1-4 with the established action limits prescribed in Exhibits 4-7 of the MDPH Protocol for Sampling and Analysis of Finished Medical Marijuana Products and Marijuana-Infused Products for Massachusetts Registered Medical Marijuana Dispensaries (MMJ_PR_3.0_020516). The data quality objectives are outlined in Appendix A and the specific requirements for the analysis by technology are described in Section 10.3 of this document.

Table 1 Monitoring Requirements of Finished Plant Material for Massachusetts Registered Medical Marijuana Dispensaries

Product Type	Analyte Class	Analyte(s)	Action Limit	Comment
Finished Plant Material **(all)**	Pesticides (MDPH Protocol MMJ_PR_3.0_020516, Exhibit 5)	Exhibit 5 List[1] and any additional pesticides analyzed	10 ppb or 5% of EPA established tolerance of residue	MDPH Protocol MMJ_PR_3.0_020516, Section 7.3
Finished Plant Material **(Final Point of Sale)**	Metals (MDPH Protocol MMJ_PR_3.0_020516, Exhibit 4)	As, Cd, Pb, Hg (total)	As: 1500[2]/200[3] µg/kg Cd: 500[2]/200[3] µg/kg Pb: 1000[2]/500[3] µg/kg Hg (total): 1500[2]/200[3] µg/kg	If passes limits for Exhibit 4(b) for ingestion only but not Exhibit 4(a) for all uses then refer to protocol Section 7.2 for labeling requirements
	Bacteriological contaminants (MDPH Protocol MMJ_PR_3.0_020516, Exhibit 6)	Aerobic Plate Count	$< 10^5$ CFU/g	
		Total Yeast and Mold	$< 10^4$ CFU/g	
		Total Coliform and E. Coli	$< 10^3$ CFU/g	
		Bile Tolerant Gram-Negative	$< 10^3$ CFU/g	
		Pathogenic E. Coli and Salmonella	Not Detected in 1 g	
		Mycotoxins[4]	< 20 µg of any mycotoxin per kg material	
	Cannabinoid Profile	Δ^9THC, CBD, THCa, CBDa	N/A (Report Results)	

[1] Pesticide compound as referenced in MMJ_PR_3.0_020516, Exhibit 5: bifenazate, bifenthrin, cyfluthrin, etoxazole, imazalil, imidacloprid, myclobutanil, spiromesifen, trifloxystrobin
[2] MMJ_PR_3.0_020516 Exhibit 4b – Ingestion Only
[3] MMJ_PR_3.0_020516 Exhibit 4a – All Use
[4] Mycotoxins is defined in the MDPH protocols as the sum of aflatoxin B_1 (AFB_1), B_2 (AFB_2), G_1 (AFG_1) and G_2 (AFG_2)

Table 2 Monitoring Requirements of Marijuana Resin and Concentrates for Massachusetts Registered Medical Marijuana Dispensaries

Product Type	Analyte Class	Analyte	Action Limit	Comment
Marijuana Resin and Concentrates **(All)**	Solvents (MDPH Protocol MMJ_PR_3.0_020516, Exhibit 7)	Exhibit 7(a) and 7(b) Butane	Exhibit 7(a) and 7(b) 12 mg/kg[5]	
	Metals (MDPH Protocol MMJ_PR_3.0_020516, Exhibit 4)	As, Cd, Pb, Hg (total)	As: 1500[6]/200[7] µg/kg Cd: 500[2]/200[3] µg/kg Pb: 1000[2]/500[3] µg/kg Hg (total): 1500[2]/200[3] µg/kg	If passes limits for Exhibit 4(b) for ingestion only but not Exhibit 4(a) for all uses then refer to protocol Section 7.2 for labeling requirements
Marijuana Resin and Concentrates **(Final Point of Sale)**	Bacteriological contaminants (MDPH Protocol MMJ_PR_3.0_020516, Exhibit 6)	Aerobic Plate Count	$< 10^5$ CFU/g	
		Total Yeast and Mold	$< 10^4$ CFU/g	
		Total Coliform and E. Coli	$< 10^3$ CFU/g	
		Bile Tolerant Gram-Negative	$< 10^3$ CFU/g	
		Pathogenic E. Coli and Salmonella	Not Detected in 1 g	
		Mycotoxins[1]	< 20 µg of any mycotoxin per kg material	
	Cannabinoid Profile	Δ^9THC, CBD, THCa, CBDa	N/A (Report Results)	

[5] Circulation letter: DHCQ 16-11-663, November 23, 2016. Analysis Requirements for Residual Solvents in Cannabis Oil.
[6] MMJ_PR_3.0_020516 Exhibit 4b – Ingestion Only
[7] MMJ_PR_3.0_020516 Exhibit 4a – All Use

Table 3 Monitoring Requirements of Marijuana Infused Products (MIPs) for Massachusetts Registered Medical Marijuana Dispensaries

Product Type	Analyte Class	Analyte	Action Limit	Comment
MIPS **(all)**	Bacteriological contaminants (MDPH Protocol MMJ_PR_3.0_020516, Exhibit 6)	Aerobic Plate Count	$< 10^5$ CFU/g	
		Total Yeast and Mold	$< 10^4$ CFU/g	
		Total Coliform and E. Coli	$< 10^3$ CFU/g	
		Bile Tolerant Gram-Negative	$< 10^3$ CFU/g	
		Pathogenic E. Coli and Salmonella	Not Detected in 1 g	
		Mycotoxins[8]	< 20 µg of any mycotoxin per kg material	
	Cannabinoid Profile	Δ^9THC, CBD, THCa, CBDa	N/A (Report Results)	

[8] Mycotoxins is defined in the MDPH protocols as the sum of aflatoxin B_1 (AFB_1), B_2 (AFB_2), G_1 (AFG_1) and G_2 (AFG_2)

Table 4 Monitoring Requirements of Environmental Media and Water Sources for Massachusetts Registered Medical Marijuana Dispensaries Product

Product Type	Analyte Class	Analyte	Action Limit	Comment
Soil and Growth Media, Water Sources	Pesticides (MDPH Protocol MMJ_PR_3.0_020516, Exhibit 5)	Exhibit 5[9] and any additional pesticides analyzed	10 ppb or 5% of EPA established tolerance of residue	Protocol Section 7.3
	Metals (MDPH Protocol MMJ_PR_3.0_020516, Exhibit 4)	As, Cd, Pb, Hg (total)	As: 1500[10]/200[11] µg/kg Cd: 500[2]/200[3] µg/kg Pb: 1000[2]/500[3] µg/kg Hg (total): 1500[2]/200[3] µg/kg	If passes limits for Exhibit 4(b) for ingestion only but not Exhibit 4(a) for all uses then refer to protocol Section 7.2 for labeling requirements
Water Sources	Bacteriological contaminants (MDPH Protocol MMJ_PR_3.0_020516, Exhibit 6)	Aerobic Plate Count	< 10^5 CFU/g	
		Total Yeast and Mold	< 10^4 CFU/g	
		Total Coliform and E. Coli	< 10^3 CFU/g	
		Bile Tolerant Gram-Negative	< 10^3 CFU/g	
		Pathogenic E. Coli and Salmonella	Not Detected in 1 g	
		Mycotoxins[12]	< 20 µg of any mycotoxin per kg material	

[9] Pesticide compound as referenced in MMJ_PR_3.0_020516, Exhibit 5: bifenazate, bifenthrin, cyfluthrin, etoxazole, imazalil, imidacloprid, myclobutanil, spiromesifen, trifloxystrobin
[10] MMJ_PR_3.0_020516 Exhibit 4b – Ingestion Only
[11] MMJ_PR_3.0_020516 Exhibit 4a – All Use
[12] Mycotoxins is defined in the MDPH protocols as the sum of aflatoxin B_1 (AFB_1), B_2 (AFB_2), G_1 (AFG_1) and G_2 (AFG_2)

5.0 QUALITY MANAGEMENT SYSTEM

The laboratory shall establish and maintain a quality management system based on the required elements contained in this section and the requirements set forth in the most current version of MDPH protocols and ISO/IEC 17025. The quality management system is to be appropriate for the type, range, and volume of medical marijuana testing activities undertaken by the laboratory. The elements of the QC system shall be documented in the laboratory's Quality Assurance Manual (QAM).

5.1 Laboratory Quality Assurance Manual

The Laboratory Quality Assurance Manual (QAM) and related quality documentation shall present the laboratory's quality management system (QMS) with the requirements contained in clause 4 of ISO 17025 and additional requirements addressing the guidance in this document and laboratory supplemental quality procedures that support the goal of continuous improvement.

A Laboratory QAM should address all elements that relate to the ISO 17025 Clause 4 requirements and any other activities that support compliance to these requirements; however, it does not need to contain all of the detail of each of these activities. For the ease of document revisions and approvals, the QAM may reference independent SOPs that contain the detailed procedures. In this way, one part of the lab QMS can be revised without necessitating a change to the entire manual.

The Quality Assurance Manual shall include the following information on the title page: document title, the laboratory's complete name and address, the name of the Quality Assurance Officer (however named), the identification of all major organizational units that are to be covered by the Laboratory Quality Assurance Manual, and the effective date of the version.

The most current ISO 17025 and this document are to be referenced for guidance when establishing a laboratory quality management system and preparing the Laboratory Quality Assurance Manual.

5.2 General Requirements and Responsibilities for Laboratory Staff

5.2.1 ***Laboratory Staff***

Laboratory staff members are responsible for the following activities:

- *Performing procedures in accordance with the SOPs, project-specific requirements, and policies set forth by the laboratory management. In this context, the requirements of this QAPP are referred to as project-specific requirements.*
- *Understanding and implementing the QA/QC requirements that pertain to their organizational/technical function.*

- *Each technical staff member is to have a combination of experience, education, and training to demonstrate adequately a specific knowledge and understanding of his/her individual responsibilities and a general knowledge of laboratory operations, test methods, QA/QC procedures, and records management.*

5.2.2 ***Laboratory Management***

The laboratory management is responsible for the following activities:

- *Appointing of a technical manager that has appropriate education and experience to have the ultimate responsibility over all decisions in the laboratory pertaining to technical issues, however defined by the laboratory, such as method development, staff technical training, stop and start work authorization, equipment maintenance and monitoring and evaluation of client requests pertaining to laboratory technical capabilities.*

- *Assuring that the laboratory has sufficient personnel with the appropriate education, training, technical knowledge, and experience to perform their assigned functions.*

- *Assuring that the laboratory has appropriate, secure, well-maintained facilities and equipment for the safe, successful conduct of analysis.*

- *Defining the minimum level of qualification, experience, and skills necessary for all positions in the laboratory. In addition to education and/or experience, basic laboratory skills such as using a balance, pipetting, and performing quantitative techniques are to be considered.*

- *Assuring that all technical laboratory staff members have demonstrated capability in the activities for which they are responsible. Such initial and ongoing demonstrations are to be documented in personnel training files.*

- *Assuring that all technical laboratory staff members understand, have access to, and conduct work in accordance with specific requirements provided by the Registered Marijuana Dispensary (RMD) and those requirements established in the MDPH protocols.*

- *Ensuring that thorough and accurate documentation of all analytical and operational activities of the laboratory is conducted and maintained.*

- *Providing supervision or providing for supervision of all personnel employed by the laboratory.*

- *Safety training and maintenance of safety records.*

5.2.3 ***Laboratory Quality Officer***

The laboratory shall appoint a staff member at management level as Laboratory Quality Officer and this person's duties shall be separate from production activities that may apply undue pressures to the decisions regarding compliance and data quality. This

Quality Officer shall have the responsibilities listed in ISO 17025:2005 Section 4.1.5 and authority in decisions where production and quality are in conflict.

In small laboratories, it may be necessary for one person to hold both technical manager and quality officer authorities and responsibilities. If this is the case, it should be clear in laboratory procedures which position holds ultimate responsibility and authority for decisions that relate to quality, technical, operational concerns. It is important that the QMS provides for the person to have direct access to the highest level of management.

5.2.4 ***Deputies and Points of Contact***

The laboratory management, however defined in the laboratory procedures, is to appoint deputies with the appropriate qualifications in the event of an extended absence of longer than one week. The responsibility for the technical data and quality decisions is to be clearly outline in the position descriptions to show authority when conflicts between production and quality arise.

The laboratory is to designate a single point of contact (POC) and an alternate to act as the primary RMD contact responsible for timely identification and resolution of any and all issues. The POC is responsible for the following activities:

- *Returning any phone calls initiated by the RMD or its designated consultant to the laboratory in a timely manner (i.e., within 1-2 hours) on a normal business day if the POC (or alternate) is not available at the initiation of the phone call.*

- *Initiating frequent communications with appropriate RMD personnel or the designated consultant during project activities that involve sampling and analysis.*

  ***Note**: If the POC shall be unavailable for more than 3-business days, the RMD and/or its designated consultants are to be notified. In this notification, the laboratory is to provide contact information for the appropriate alternate contact.*

- *Providing prompt verbal, text, or e-mail communication of any nonconformance observed during sample receipt to appropriate RMD personnel or the RMD's designated consultant as soon as possible but always within 24 hours (preferably 3 hours, beginning with the normal business day immediately following for problems noted during second shifts or weekends) of discovery. Problems may include, but are not limited to, broken bottles, errors, or ambiguities in paperwork, insufficient sample volume/weight, preservation checks outside of acceptance criteria, and elevated receipt and/or storage temperature. Nonconformance upon sample receipt that does not meet the laboratory sample acceptance policy is to result in the rejection of samples if the condition does not meet the criteria in* Appendix A*, Table 02.*

- *When sample receipt issues are discovered after hours, impacting samples with short holding times (< 24 hours remaining), the laboratory is to contact the RMD as soon as possible following discovery with follow-up during normal business hours.*

- *The POC is responsible for day-to-day activities associated with the management of the various analytical activities. These duties include scheduling analyses, oversight, and assignment of any activities related to client services.*

- *The laboratory is responsible for identifying associated QC failures that require decisions pertaining to resampling, repreparation, reanalysis, and report amendments and keeping records supporting the decisions.*

- *In the event that the laboratory becomes aware of any changes in local, state or federal regulations, state certification, analytical methodology, sampling regulation, Department of Transportation (DOT) regulations, or any other information that may affect the RMD sampling and/or analytical programs, the POC is to confirm the request for analysis with the RMD as soon as practical.*

5.3 Personnel Experience, Training and Qualifications

All sample analyses described in the MDPH protocols and governed by this QAPP are to be conducted by a laboratory that is either:

- *Accredited to International Organization for Standardization (ISO) 17025 by a third party accrediting body such as A2LA or ANAB, or PJLA; or*
- *Certified, registered, or accredited by an organization approved by the MDPH.*

Further requirements concerning the eligibility and responsibilities of analytical laboratories are provided in 105 CMR 725.105(C)(2). In addition to the regulatory qualifications and requirements referenced above, the laboratory is to have a demonstrated ability to perform the specific analytical methods required and to provide complete records and a robust quality assurance system.

5.3.1 ***Management Responsibility***

Laboratory management is to ensure the competence of all who operate specific equipment, perform tests and/or calibrations, evaluate results, and review and approve client reports. Appropriate supervision shall be provided to staff that are undergoing training. Personnel performing specific tasks are to be qualified based on appropriate education, training, experience, and/or demonstrated skills as required.

The laboratory management is to authorize specific personnel to perform particular types of sampling, testing, and/or equipment calibration, issue test reports, review, and interpret data, and to operate particular types of equipment. The laboratory is to maintain records of the relevant authorization(s), competence, educational and professional qualifications, training, skills, and experience of all technical personnel, including contracted personnel. This information is to be readily available and include the date on which authorization and/or competence is confirmed.

The laboratory management is responsible for the following personnel training activities:

- *Assuring that the training of each member of the technical staff is maintained up-to-date (ongoing).*

  - *Records are to be on file demonstrating that each employee has read, understand, and is using the latest version of the applicable SOPs and the laboratory's in-house quality documentation that relates to his/her job responsibilities.*

  - *Training courses or workshops on specific equipment, analytical techniques, or laboratory procedures are to be documented.*

  - *Training courses in ethical and legal responsibilities, including the potential disciplinary actions and penalties for improper, unethical, or illegal actions are to be documented.*

  - *Analyst training shall be considered up-to-date if his/her training file contains certifications that he/she has read and understands the most recent version of the test method (the approved method or standard operating procedure) and associated supporting procedural and guidance documents; documentation of continued proficiency for all parameters performed is to be demonstrated by at least one of the following once per year:*

  - *Records of at least four separately prepared, separately analyzed, non-consecutive laboratory control samples with acceptable levels of precision and accuracy. This is required for all initial demonstrations of capability. After initial demonstration of capability, acceptable analysis of an ISO 17043 proficiency test sample or four passing laboratory control sample (LCS) samples from routine analyses are valid as an ongoing demonstration of capability.*

  - *The laboratory's training procedures are to define clearly when an analyst is able to independently perform analyses and report data. There is to be a clear record of the completion of initial training and approval to work independently in the area of training.*

  - *An authorized technical staff member is to oversee work of a technical staff member in training and both staff members are to be identified in the analysis record to show that training was occurring.*

5.3.2 ***Training Goals***

Laboratory management is to communicate and establish goals with respect to education, training, and skills of the laboratory personnel. The laboratory is to have a procedure for identifying ongoing training needs and providing training of personnel. The training program is to be relevant to the present and anticipated tasks of the laboratory. The effectiveness of the training actions taken is to be evaluated and recorded as approved for the training to be considered complete.

5.3.3 *Contracted Personnel*

The laboratory is to use personnel who are employed by, or under contract to, the laboratory. Regardless of the type of employment contract, the personnel are to adhere to the requirements in the laboratory quality management system and the guidance provided herein.

5.3.4 *Job Descriptions*

The laboratory is to maintain current job descriptions for managerial, technical, and key support personnel involved in testing, data reduction and review and approval of reports.

The following elements are needed in job descriptions:

- *Responsibilities with respect to performing tests;*
- *Responsibilities with respect to the planning of testing and review of results;*
- *Responsibilities for reporting, review and approval of client reports;*
- *Responsibilities for performing method modification and method development and validation of new methods;*
- *Expertise and experience required;*
- *Qualifications and training needed to fulfill the responsibilities; and*
- *Managerial duties.*

5.4 Standard Operating Procedures (SOPs)

Standard Operating Procedures (SOPs) shall be developed by the laboratory for every activity performed during standard laboratory operation. This includes quality procedures, technical procedures, and any activities that support those activities including software, administrative, and calculation procedures. These procedures shall contain enough detail to perform the methods and shall be consistent with the current activities relevant to that SOP. In the instance where the procedures do not reflect current activities, they shall be revised according to a laboratory document control procedure, and this revision is to be tracked within the document for historical review purposes. SOPs detailing the laboratory's procedures are to be maintained under a formal document control system that includes a unique identification system and the retrieval/accounting of all outdated versions. SOPs are to be reviewed and updated when there is a change in the method, activity, or material such that the SOP is consistent with the method and laboratory procedures. A documented (including signoff) review of all SOPs is required at a frequency required by the laboratory's accreditation standards or own procedures. Laboratory SOPs are to be stored in a manner that provides protection from catastrophic loss (such as a fire).

The quality assurance (QA) department is to have a formal system for the distribution, tracking, and archiving of SOPs, logbooks, electronic logs, notebooks, and any other controlled documents. Periodic (monthly or quarterly, depending on usage) documented supervisory or peer review is to be performed on all logbooks and electronic logs utilized throughout the laboratory. The laboratory shall keep each SOP at the laboratory

premises and ensure that each SOP is accessible to laboratory employees during operating hours. The laboratory shall make each SOP, as well as any other SOPs associated with the licensee's ISO/IEC 17025 certificate of accreditation available for inspection upon request by MDPH.

5.4.1.1 **Components of Analytical SOPs**

References: ISO/IEC 17025:2005; The current adopted version and approved revision of the EL TNI Standard

Following the validation of a given method, generate analytical SOPs that shall be reviewed and approved by laboratory management. Critical sections of information to include in the analytical SOPs are listed below. It is important that the information in these sections be consistent with the method validation performed.

The following topics (where applicable) should be considered when determining critical components necessary for technical SOP:

- Clear Identification of the Method Name/Title;
- Scope and Application including applicable analytes and matrices;
- Method sensitivity statement and demonstration;
- Potential interferences with the analysis, if any;
- Measurement uncertainty (quantitative methods only);
- Description of type of item to be tested;
- Parameters or quantities and ranges to be determined;
- Apparatus, supplies, and equipment, including technical performance requirements and instrument operation parameters;
- Reference standards and reference materials required, including reagents;
- Instrument calibration procedures and acceptance criteria;
- Types, frequency, acceptance criteria and corrective actions for QC samples and calibration standards;
- Procedure for the preparation of test samples, QC samples, calibration standards, solutions, reagents and reference material preparation, including the following:
    - Sample identification and labeling requirements;
    - Sample Collection (specific to analytical methods used)
    - Sample Handling, Transport and Storage;
    - Sample Preservation;
    - Hold Time;
    - Sample homogenization and subsampling
    - Sample Preparation and Clean-up;
- Procedure for analyzing analytical batch samples;
- Data to be recorded, method of data analysis, primary and peer review, and data reporting/presentation requirements;
- The method of recording observations and results;
- Calculations performed;
- Environmental conditions required and any stabilization period needed;
- Waste management and waste disposal;
- References, and
- Health and safety precautions.

5.5 Laboratory Logbooks

All laboratory records are to be maintained in an organized manner. Logbooks themselves are to be uniquely identified and included in the laboratory document control system. Corrections to hardcopy records are to be made using a single strike-through and are to be initialed and dated by the individual making the correction. All corrections/changes/updates made to records in the laboratory information management system (LIMS) are to include an appropriate comment and be traceable via audit trail. All data recorded in logbooks, notebooks, and LIMS are to undergo routine periodic (e.g., monthly) documented supervisory review.

5.6 Instrument Data and Records

All instrument use (including rinses and diagnostic checks) is to be included in an analysis logbook or an electronic log. The data representing all such use is to be retained and archived in an organized manner whether reportable or not. The laboratory shall process instrument software chromatograms and data in a manner that allow for the historical reconstruction of the analysis. Instrument software is to track changes and chromatography changes with an audit trail and the laboratory shall have procedures for tracking changes in all other analytical records.

The records of the analysis that shall be retained include, but are not limited to:

- *Preparation records,*
- *Instrument conditions,*
- *Instrument method,*
- *Tunes,*
- *Check standards,*
- *Calibration records for each analyte (including a summary of any dropped points or change in reporting range),*
- *Instrument sequence,*
- *Chromatograms,*
- *Before and after records of manual integrations and any analyte deletion that includes a reason for the professional judgement decision,*
- *QC sample calculations,*
- *Dilutions and re-analysis samples of samples,*
- *Carryover reviews, and*
- *Data review.*

Analytical sequence logs (manually or electronically generated) are to contain every analysis/injection, regardless of the nature of the analysis/injection (i.e., reportable, non-reportable, or troubleshooting). Overwriting files is strictly prohibited. All QC components, including those samples from failed or unreported runs are to be maintained as part of laboratory records, as they shall be considered for use in laboratory control charts to generate limits unless determined to be a statistical outlier or result of an assignable cause.

Electronic files are not to be overwritten under any circumstance; documented training of staff on this issue is to be provided. Laboratory staff is to be trained to record actions

taken in the logbooks or electronic logs when any standard, tune, or QC sample initially fails and is repeated, such that the situation and action are fully documented and can be understood after-the-fact based on independent review of any logbook or electronic log.

5.7 Electronic Logging

Electronic logs are to be replicated to a separate medium (e.g., server, drive, or hard medium) daily at a minimum (more frequently is preferred). Electronic logs are to have a functional audit trail enabled and in use at all times. At a minimum, the audit trail function is to retain and retrieve the initial values in each field, updated values, the date, time, and operator identification for each update. Changes to analytical and compliance parameters are to be associated with a documented reason for the change, recorded by the identified operator.

Examples of analytical and compliance parameters include peak/signal intensity, peak area, normalizing parameters, time of analysis, response factors, weight and volume values, units, and dilution factors.

5.8 Maintenance Logs

Maintenance logs are to include records of all maintenance performed on an instrument (e.g., routine maintenance and external repairs) such that the maintenance performed can be historically traced (problem, solution, outcome format) with records documenting when instrument returned to control. It is recommended that the laboratory supplement the descriptions of problems, troubleshooting steps, and solutions with chromatograms or data showing the instrument response at each step. The author and date of entry are to be included for all log entries. *All instrument maintenance logbooks are to include the serial number(s) or permanently tagged identifier for the instrument and the associated peripherals such that the logbook is unambiguously associated with the instrument and the associated peripherals.*

5.9 Requests, Tenders, and Contracts

The laboratory is to determine whether the client is submitting samples for regulatory reporting. This is to be determined and recorded before sample receipt and log in through the request for analysis, chain of custody records and documented conversations with the client. This designation is to be included in project information and effectively communicated to laboratory staff who shall be involved in sample handling, analysis and reporting to ensure that the applicable ISO requirements, relevant guidance contained herein and the regulatory requirements are considered and applied to the samples at every point of the process.

If samples are not designated as regulatory, the sample report is to clearly state whether the analyses performed met the requirements of the regulatory analysis and accreditation to inform the Registered Marijuana Dispensary (RMD) and MDPH of the state of compliance to regulation if the data is to be reported to MDPH for any reason. If the analysis was not designated as regulatory and the client had specific requests that depart from ISO 17025 standard requirements, MDPH requirements, or documented laboratory procedures, these departures are to be clearly stated and the client report

narrative shall contain the language "this data is to be used for informational purposes only."

Data qualified as "Informational Purposes Only" when the sample was analyzed for purposes other than MPDH compliance reporting leaves a question as to whether the analysis was also performed to meet all of the requirements of the ISO accredited scope. In any event, where the requirements of the ISO accredited scope are not met, data should be separately qualified with language such as "Was not analyzed under ISO Scope of Accreditation" regardless of whether or not the samples are used for MDPH compliance.

5.10 Storage of Data

All data, instrument output (inclusive of electronic media), logbooks, electronic logs, reports, hardcopy and electronic copy of all data packages delivered, and applicable peripheral documentation, including, but not limited to, financial documents and invoices generated by each laboratory are to be stored in an organized, categorized, inventoried fashion for five (5) years after completion of the RMD request. At the RMD and/or MDPH's request, any and all data are to be submitted to the MDPH and/or RMD or their designated consultant/authorized representative upon request. Overwriting or disposal of any electronic media prior to this expiration period is strictly prohibited. All electronic and hardcopy data are to be stored in an easily accessible, climate-controlled environment. The laboratory is to exercise "best practices" in terms of frequent, redundant electronic backup procedures on proper long-term storage media and/or to remote servers to ensure that all raw data representing RMD sample analyses shall be maintained for the 5-year storage period. Electronic data are to be stored in a secure, limited access area with redundant copies stored in fireproof vaults and/or stored at an off-site facility. After the 5-year storage period, the laboratory is to contact the RMD to determine if data is to be properly disposed of, maintained for an extended period, or shipped to the RMD for storage. No data is to be disposed of without contacting the RMD for approval.

5.11 Software Control

Maintain an approved procedure for verifying the proper functioning of software implementations and measures to prevent loss of data integrity. This is to include documented procedures for data storage, back-up, archiving, and retrieval. This is also to include a set of procedures for capturing the unique identifier for a given QC sample (e.g., check standard, method blank, etc.) allowing for traceability back to the actual documentation supporting the preparation of that sample.

5.11.1 ***In-House Software Tools***

For in-house developed software tools such as spreadsheet formulae and macros, instrument upload files, and worksheets for calculations as well as any in-house developed databases, document the verification of proper functionality and security of each version and identify the version used to generate results. Implement databases with audit trails, registering each edit, the editor, date and time of edit.

Electronic records are to be protected by locking formula cells, locking worksheets upon completion of the analysis day, using locked and controlled templates as a source instead of a previous record, employing a unique identification system for files, and identifying personnel who create electronic records. Any changes to locked areas of macros, worksheets, and databases are to contain the initial record, the changed record, and the authorization and reason for change.

For original software, developed by, or under the direction of the laboratory, a lifecycle approach is to be incorporated into the validation procedure. Major steps of the lifecycle approach are listed below.

5.11.2 *In-House Developed Software and Tools*

For in-house developed software and tools, the laboratory is encouraged to establish a software lifecycle. For each piece of software, the software lifecycle should be defined by establishing the activities to assure quality and evidence of validation. This lifecycle is to include the following elements:

- Requirements – Intended performance and use of the software. Generate a functional requirement document.
- Design
- Source Code – create the source code needed for desired software functionality
- Test Plan – Develop a plan of the parameters and acceptance criteria to verifies proper software operation.
- Install – install the software onto the hardware
- Traceability – Generate reports and supporting documentation that maps the requirements of the Test Plan to the test actual results. This includes displaying the tested version number of the software on the output from the software.

Electronic uploads from software or to software that has not been validated by a known and reputable manufacturer are to be reviewed completely as though it were a manual transcription.

6.0 PROPER, LEGAL AND ETHICAL ACTIONS AND DATA INTEGRITY REPORTING - POLICIES, TRAINING, AND PROCEDURES

The laboratory shall have a process/procedure in place for educating and training personnel. Data integrity and ethics procedures in the laboratory include training, signed, and dated integrity documentation for all laboratory employees, periodic monitoring of data integrity, and documented data integrity procedures. Section managers uphold the spirit and intent by supporting integrity procedures, by enforcing data integrity procedures and ensuring staff participate in annual data integrity training.

Data integrity training is to be provided for all employees initially upon hire and annually thereafter. Attendance at an initial data integrity training (part of new employee orientation) and the annual refresher training are to be recorded with a signature attendance sheet. The data integrity training is to cover the difference between fraud and other data integrity issues defining intent and the correct documentation of errors immediately upon discovery.

A one-on-one session held between a new hire and the laboratory quality assurance manager accomplished within the first four (4) weeks of employment, preferably sooner, can be a major step assuring the employee has received needed initiation to quality system requirements. Discussion regarding the critical aspect of the role data integrity has with respect to the success of the laboratory cannot be understated. In addition to covering the systems by which to report suspected ethical violations, covering such basics as the importance of support equipment documentation, what constitutes a controlled document, policies regarding the treatment of raw data with respect to data obliteration/line-outs, are all basic examples that lead the new hire on the path that ultimately benefits both the lab and the staff member in the short and long term.

Specific integrity procedures for analyses involving chromatography (IC, GC, GCMS, HPLC, *etc.*) require the understanding and implementation of MDPH's Manual Integration Procedures (Section 6.1.2). *Training on these procedures is to be provided to all staff that performs chromatographic analyses.*

When contracted technical or support personnel are used laboratory management is responsible for ensuring that, they are trained to the laboratory's quality management system and data integrity procedures, competent to perform the assigned tasks, and appropriately supervised.

Employees shall report all violations to laboratory management or quality assurance. Failure to report an integrity violation is an act of condoning the activity and is seen by MDPH as equivalent to having actually committed the violation.

The mechanism for confidential reporting of ethics and data integrity issues is to contain (1) unrestricted access to laboratory management or QA officers, (2) an assurance that personnel shall not fear repercussion for reporting instances of ethics and data integrity breaches, and (3) anonymous reporting.

Laboratories can comply with the anonymous reporting structure in simple ways such as suggestion boxes or with intranet entry pages or a common "Data Integrity Report" email address that is accessible by all personnel. It should be noted to the staff during training that anonymous reporting may hinder the efforts to fully investigate the report.

Any potential data integrity issue is to be handled confidentially, to the extent possible, until a follow-up evaluation, full investigation, or other appropriate actions have been completed and the issues clarified. Inappropriate activities are documented, including disciplinary actions, corrective actions, and notifications of clients, if applicable. These documents are to be maintained according to the laboratory's records retention schedule.

Data integrity procedures are to be reviewed as part of the annual internal audit and periodically monitored through in-depth data review of audit trails or records review.

6.1.1 ***Data Integrity Requirements***

The laboratory is to be committed to ensuring the integrity of data, incorporating the highest appropriate standard of quality in all analytical programs.

- *Personnel shall not condone any accidental or intentional reporting of deceptive or misleading data. If laboratory management requests personnel to engage in an activity that compromises data integrity, they have the right to refuse compliance with the request and to appeal the action through the QA officer.*
- *Laboratory management shall not instruct subordinates to perform any practices that would violate this policy, nor shall laboratory management discourage, intimidate, or inhibit a staff member who may choose to appeal instruction under this agreement and shall not retaliate against those who do so.*
- *All work assigned to personnel shall be performed in compliance with the MDPH protocols, MDPH QAPP, laboratory QA manual and SOPs. It is the responsibility of staff to be aware of and compliant with current policies and procedure requirements for assigned duties.*
- *Personnel shall only report results or data that match the actual results observed or measured.*
- *Personnel shall not intentionally falsify any data in any manner. Data shall not be modified unless the modification is technically justified through a measurable analytical process approved by the QA officer. All such modifications shall be clearly documented.*
- *Recording of dates, times, and initials on data shall accurately reflect who and when the procedure was performed.*
- *Personnel shall not intentionally make false statements to, or seek to otherwise deceive data users, agency representatives, or auditors.*
- *Personnel shall not, through intentional acts of omission, commission, erasure, or destruction improperly report measurements, standard results, data, test results, or analytical conclusions.*
- *Personnel shall not destroy, or overwrite records of analyses or original observations. This includes, electronic files and instrument sequences, analytical reports, original recording of observations, etc.*
- *Personnel are required to understand, through training and review of quality systems documents, that any infractions of the laboratory data integrity procedures shall result in a detailed investigation that could lead to very serious consequences such as immediate termination, or civil/criminal prosecution.*

6.1.2 ***Manual Integration Procedures***

Manual Integration is the process performed by the data user when the automatic integration performed by the system is in error. *It is to be used when there is a misidentification or lack of identification of peaks due to retention time shifts, or when the software does not properly integrate split peaks, co-eluting peaks, peaks affected by baseline noise, negative baselines, rising or falling baselines, and excessive peak tailing.*

If manual integration is necessary, the analyst is to save the original file in paper or electronic format, record the reason for the integration, the analyst initials, and the date, and save the final file. All of these are to be available for review. This includes situations where an analyst has determined that the software has incorrectly identified a peak and has changed the identification to a non-detect.

All samples, standards, and QC samples are to be integrated in the same manner. Manual integrations shall never be performed in an attempt to meet acceptance criteria.

Any deviations from manual integration procedures that occur during data processing are to be documented in the final report. The SOPs are to include at least two levels of data review (primary and peer review) on each chromatogram in the analytical run that includes checks for improper software integration and consistent manual integration.

Manual integration may be necessary and appropriate when a slight shift in chromatographic retention times results in undetected peaks or false positive identification of compounds. Manual integration may also be necessary and appropriate when:

- Peak splitting resulting in the entire peak area not being integrated.
- Integration of closely eluting peaks or indistinguishable groups of peaks with the same quantitation signal, are integrated together as one peak.
- Baseline interference caused by highly contaminated samples, effect the integration of target and analytes.
- The target peak does not begin or end at baseline, but begins or ends on another peak or valley.

Examples of unacceptable manual integrations are peak shaving, peak enhancement, changing peak height, and shifting retention time windows without justification.

7.0 PROCEDURE GUIDANCE ON SAMPLE HANDLING AND STORAGE

Following established procedures for sample management is important in maintaining data quality. Strict custody procedures are necessary to maintain the integrity of the medical marijuana product samples. The subsections below detail the components of the sample handling and tracking system and address sample identification, packaging, shipping, and documentation

7.1 Sample Receipt and Sample Custody Requirements

The primary objective of sample custody procedures is to create an accurate written record that can be used to trace the possession and handling of all samples from collection, to shipment to the laboratory, to analysis, and to their final disposal. Documentation of proper custody by following Chain-of-Custody (COC) procedures is essential to establish sample integrity and validity of analytical results. COC procedures also serve to minimize loss or misidentification of samples and unauthorized tampering of collected samples. *Properly filled out COC records are to be part of the laboratory sample acceptance policy. If contracted couriers are used, the couriers are to be aware of the custody procedures to properly receive and relinquish custody.*

The integrity of samples after receipt by the laboratory is to be maintained through proper handling/storage procedures and preparation/analysis within applicable holding times. The laboratory is to refer to the specific method and regulation for applicable holding times. Documentation of appropriate sample handling/storage, and preparation/analytical procedures is to be maintained by the laboratory.

Laboratory custody of samples begins when samples are received by the laboratory. The laboratory is to have procedures in place to maintain the custody, security, and integrity of samples.

At a minimum, the Sample Custodian shall sign and record the date and time of sample receipt on the COC. The validated time of sample receipt (VTSR) is the time the samples are received at the laboratory from the RMD personnel or representative, or private courier; it is not the time the samples are opened or logged in at the laboratory. The laboratory is to have documented procedures for receipt of samples outside normal hours of operation.

Sample custody procedures are to be implemented to ensure that samples are not tampered with from the time of sample collection through time of transport to the independent testing laboratory. Custody of the samples by a given person is defined by:

- *Physical possession of the samples (i.e., carrying or holding the samples),*
- *Having the samples within clear view after having possession, or*
- *Having physical possession and leaving them in a secure location so that they cannot be tampered with. In addition, when samples are secured in a restricted area accessible only to authorized personnel, they shall be deemed to be in the custody of such authorized personnel.*

Sample custody documentation includes both laboratory notebooks and COC forms. Samples shall be accompanied by a properly completed COC form. The sample identifiers shall be listed on the COC form. When transferring the possession of samples, the individuals relinquishing and receiving shall sign, date, and note the time on the COC form. This record documents transfer of custody of samples from the sampler to another person, to the laboratory, and to any subcontracted laboratory.

7.1.1 ***Sample Temperature Measurement***

Samples requiring thermal preservation are not to be allowed to reach temperatures > 6.0°C during sample receipt/login procedures (prior to being placed in laboratory cold storage). Sample receipt temperatures are to be recorded on the COC or sample receipt form to the nearest 0.1°C using a thermometer or other appropriate temperature measurement device that is calibrated at least annually against a National Institute of Standards and Technology (NIST)-certified thermometer (see Section 10.3.1 for thermometer calibration requirements). The unique identifier for the thermometer or other device is to be recorded

Temperatures shall be taken using the temperature blank provided with the laboratory bottle shipment; if the temperature blank is broken, missing, or frozen, the temperatures of other sample bottles may be taken by non-invasive methods (e.g., uniquely identified, NIST-calibrated infrared [IR] gun). If temperatures are measured on sample bottles, this is to be noted in sample receipt documentation and on the COC. The IR thermometer is to be checked daily (or weekly at a minimum) when in use against a NIST-calibrated thermometer in the sample storage area. IR thermometer procedures are to contain consistent use between laboratory staff such as representative placement of bottle checked, type of bottle (glass, plastic, etc.) checked and distance from bottle and whether or not to include label of bottle according to manufacturer instruction. The laboratory procedures are to be specific as to whether a temperature blank or single IR

sample temperature failure indicates exceedance for the entire cooler or if individual sample temperatures shall be taken to assess compliance.

The laboratory is to maintain a record of samples that are received at temperatures outside of acceptance criterion (e.g., ≥ 6.0°C). (Please see the section below entitled, Communicating Sample Receipt Issues)

7.1.2 ***Chain-of-Custody Verification***

Following sample temperature measurement, the Sample Custodian shall examine the sample containers received and note any damage to sample containers/media. Sample container labels shall be compared to the COC Form, and any discrepancies (e.g., sample identification, preservation, sample matrix, requested analyses, etc.) shall be noted. Discrepancies between the samples received and the field COC Form are to be communicated to the RMD or its designee, who shall provide directions on how to proceed.

7.1.3 ***Sample Storage***

The laboratory is to maintain sample storage refrigerators at ≤ 6.0°C and sample storage freezers at < -10°C. The laboratory is to have adequate cold storage units to maintain temperature preservation as required by the requested analytical method. When sample storage cooler and freezer temperatures are outside of the acceptance range, the laboratory is to document corrective action, and any samples stored in the affected units shall be immediately moved to a cold storage unit within criterion and the impact on data quality is to be assessed and recorded. Samples are to be stored separately from performance evaluation (PE) samples, standards, spiking solutions, prepared reagents, and sample extracts or refrigerator blanks are to be run to assess contamination.

7.1.4 ***Communicating Sample Receipt Issues***

Any issues noted during sample receipt that may adversely impact data quality (including, but not limited to, loss of sample volume, samples with temperatures > 6.0°C; improper chemical preservation of samples; or documentation discrepancies) shall be communicated to the RMD or its designated consultant was soon as practical (via phone log or e-mail based on project personnel requirements) so that proper corrective action can be taken; documentation of this communication is to be preserved with the project records. If the sample receipt criteria are not met, the samples are to be rejected and the RMD is to be informed immediately of the need to resample.

All samples placed "on hold" because of sample receipt issues is to be stored in accordance with sample temperature preservation requirements (e.g., in sample refrigerators or freezers) until the issues have been resolved. When an issue requiring notification is discovered after normal business hours (i.e., between 0800 and 1700 Eastern Standard Time, Monday through Friday), the laboratory is to provide prompt verbal, text, or e-mail notification to the RMD or its designee. The laboratory is to maintain documentation detailing any sample receipt issues and the resolution directed by the RMD or its designee in the project files.

7.1.5 ***Holding Times***

Holding times shall be as specified in the tables presented in Appendix A, which are based on the most current MDPH protocols, USP monograph or general chapter, AHP, United States Environmental Protection Agency (EPA), and other MDPH-approved methods unless a shorter holding time is specifically requested by the RMD or the MDPH.

Holding time begins upon sample collection (the date/time the sample is collected as documented on the COC). The samples are to be in good condition and are to be received by the laboratory generally within 1-calendar day of sampling unless different arrangements have been made in advance with the laboratory. For shipments to be received by the laboratory after normal business hours (Monday-Friday, 0800-1700 hours), prior arrangements shall be made so that laboratory personnel are available to receive the samples. Samples with holding times of < 48 hours are to have documentation of the time they were set up for the short hold-time analysis. For all sample shipments, the primary laboratory contact, for the dispensary shipping the samples, is to notify all applicable laboratory personnel of the expected sample delivery so that laboratory personnel can prepare to receive the samples.

The laboratory is to adhere to the required holding times for the initial sample preparation/analyses. If samples are received with a significant portion of the holding time expired and the laboratory is concerned about meeting holding time requirements, RMD, or its designee is to be notified immediately upon sample receipt. If subsequent analysis/extraction becomes necessary due to method or technical requirements or failing QC, the laboratory is to make every effort to analyze these dilutions/re-extractions /reanalyses within the method holding time specified in Appendix A*.*

7.1.6 ***Subsampling and Homogenization***

Samples received by the laboratory are to be homogenized in full before subsampling for analysis or subcontracting takes place. The laboratory is to maintain procedures for homogenization and subsampling that include instructions on all matrices and how to handle samples that cannot be homogenized.

Homogenization and subsampling equipment and procedures are to be validated by laboratory-defined procedures that demonstrate the effectiveness of homogenization and subsampling through precision indicators (e.g., homogenization duplicates) and the effectiveness of the equipment cleaning through evaluation of blanks associated with the equipment.

A homogenization duplicate and a homogenization blank are to be assigned separately for flower and extract sample batches at defined intervals. The homogenization blank shall be randomly placed in the batch as to check all of the homogenization equipment for possible carryover rather than using a dedicated homogenization apparatus for the blank each time it is requested.

8.0 DATA QUALITY INDICATORS

Data Quality Objectives (DQOs) are listed below in Appendix A, Tables 03-09. Whenever possible, these objectives were set with the reference methods listed in the MDPH protocols. When additional information was needed for marijuana-specific, technology-specific, or analyte-specific objectives, other ancillary methods were utilized. Primary reference methods and ancillary reference methods used to develop data quality objectives for the required analytes are contained in Appendix A, Table 01. *If the laboratory employs methods other than those listed in* Appendix A*, Table 01, they shall be validated using the guidance in Section 9.0 of this document. Table 02 of* Appendix A *contains the sample handling, receipt, and storage requirements that are to be followed to ensure sample integrity for the required analyses.*

In order to assist in decision-making and to meet DQOs, measurement performance criteria have been established for the data that shall be generated under the guidance of this QAPP and have been determined by matrix, analytical group, and analyte. Measurement performance criteria are evaluated in relation to the five data quality indicators (DQIs) of: precision, accuracy/bias, representativeness, comparability, and sensitivity. The DQIs used in this QAPP are defined below in Sections 8.1 – 8.5. The DQOs are listed in the tables presented in Appendix A.

8.1 Precision

Precision is a measure of the agreement of independent sample results obtained under the same specified conditions. The goal is to maintain a level of analytical precision consistent with the objectives of the sampling activities. *Checks for analytical precision are to include the analysis of matrix spike and matrix spike duplicates, laboratory duplicates and medical marijuana product sample duplicates.*

8.2 Accuracy

Accuracy is a measure of how close a measured result is to the true value. When applied to test results, accuracy includes a combination of random and systematic error. When applied to a test procedure, accuracy refers to a combination of trueness and precision. *Analytical accuracy is to be monitored through initial and continuing calibration of instruments and the accuracy of the analytical data is to be assessed by the analysis of reference standards, matrix spikes, blank spikes, rinse blanks, and surrogate standards.*

8.3 Representativeness

Representativeness is the degree to which data accurately and precisely represent medical marijuana product quality, and is dependent on sampling and analytical variability and the variability of the product. The use of the prescribed laboratory analytical methods with associated holding times, preservation requirements, homogenization, subsampling, laboratory duplicates and DQOs are intended to provide representative data.

8.4 Comparability

Comparability is the degree of confidence with which one data set can be compared to another. *Comparability between product data collected over time is to be maintained through consistent use of the analytical methodologies set forth in this QAPP, using*

established quality assurance/quality control (QA/QC) procedures, and through utilization of appropriately trained personnel.

8.5 Sensitivity

Sensitivity is a quantitative measurement to determine if the independent testing laboratory's procedures/methodologies and their associated Limit of Detection (LOD) can satisfy the requirements, objectives and action limits established in the MDPH protocols. *LOD studies are required and are to be updated by the independent testing laboratory annually. The current LODs for the independent testing laboratory are to be maintained in a controlled document.*

The Limit of Quantitation (LOQ) is the minimum concentration of an analyte that can be routinely identified and quantified above the LOD by a laboratory with satisfactory accuracy and precision meeting the method requirements set forth in Appendix A of this document. Sensitivity can be measured either by performing an LOD study or by calculating the percent recovery of the analytes at the LOQ level. *In the event that data are to be reported in a range below the LOQ, LOD studies are to be performed as described in this QAPP.*

9.0 VALIDATION OF METHODS

9.1 References: ICH Q2 (R1), USP <1225>, ISO/IEC 17025:2005, and FDA OAR

Each independent testing laboratory is to implement an approved procedure for method validation for both quantitative chemical analyses and microbiological analyses. The objective of validation of an analytical procedure is to demonstrate that it is suitable for its intended purpose.

The objective of the analytical procedure is to be clearly understood and defined in a reviewed and approved validation protocol prior to performing the actual method validation. *The validation protocol shall govern the validation characteristics that need to be evaluated. The validation protocol and eventually, the analytical standard operating procedure (SOP), are to document clearly the manner in which the method is performed. It is to describe in detail the steps necessary to perform the analytical test, which includes (where applicable) but is not limited to: sample preparation, the equipment, reference standards and reagents used, preparation of reagents and buffers, equipment use and operation, instrument calibration, QC sample preparation and analysis frequency, QC sample acceptance criteria and corrective actions, calculations used.*

The independent testing laboratory is to validate all methods prior to sample analysis, including laboratory-designed or developed methods, commercially developed methods used outside their intended scope and methods that have been modified, in order to confirm that the methods are fit for the intended use.

Specifically, method validation is required for the following:

- *A new or original method;*
- *Expansion of the scope of an existing method to include additional analytes;*
- *Expansion of the scope of an existing method to include additional matrix types;*

- *Changes in the intended use of an existing method (e.g., screening vs. confirmatory); and*
- *Modifications to a method that may alter its performance specifications (e.g., modifications that could significantly affect the precision and accuracy, changes to the fundamental science of an existing method, significant changes to reagents, apparatus, instrumental parameters, sample preparation and/or extraction, or modification of a method's range beyond validated levels).*

The validation is to be as extensive as is necessary to meet the needs of the given application or field of application.

An example of a method that needs further validation would be Cannabinoid analysis. In this validation, it is important to demonstrate the ability to measure the major cannabinoids at multiple concentration ranges on the HPLC. In addition, selectivity may need to be further demonstrated pertaining to identification by providing confirmatory identification as a validation component using technologies such as NMR.

The independent testing laboratory is to record the results obtained, the procedure used for the validation, and a statement as to whether the method is fit for the intended use. Each method shall be validated appropriately before use. The documentation maintained from the development and validation of new test methods is to contain at least the following information:

- *Clear Identification of the Method Title;*
- *Scope and Application;*
- *Description of type of item to be tested;*
- *Parameters or quantities and ranges to be determined;*
- *Apparatus and equipment, including technical performance requirements and instrument operation parameters;*
- *Reference standards and reference materials required;*
- *Environmental conditions required and any stabilization period needed;*

Typical validation characteristics, at a minimum, are to contain precision and accuracy studies and a demonstration of the quantitation limit to obtain an estimation of uncertainty. Characteristics to be evaluated, whenever practicable, are listed below and are described in the subsequent sections in further detail:

- Accuracy
  - Spike Recovery
- Precision
  - Repeatability/Reproducibility
  - Intermediate Precision
- Sensitivity
- Specificity
- Limit of Detection
- Limit of Quantitation
- Linearity
- Range
- Robustness

- Confirmation of Identity

When changes are made in the validated method, the influences of such changes are to be documented and, if appropriate, a new validation is to be carried out. The range and accuracy of the values obtainable from validated methods (e.g. the uncertainty of the results, detection limit, selectivity of the method, linearity, limit of repeatability and/or reproducibility, robustness against external influences and/or cross-sensitivity against interference from the matrix of the sample/test object), as assessed for the intended use, is to be relevant to the customers' needs.

9.2 Validation Guidance for Quantitative Chemical Analyses

For quantitative chemical analysis methods, validation is typically comprised of the following elements. Specific criteria for meeting the data quality objectives of this QAPP are presented in Appendix A of this document.

9.2.1 *System Suitability*

It is good practice to perform system suitability tests that are based on the concept that the equipment, electronics, analytical operations and samples to be analyzed constitute an integral system that can be evaluated as such. System suitability test parameters to be established for a particular procedure depend on the type of procedure being validated. These requirements typically include:

- injection repeatability,
- peak resolution,
- relative retention times for liquid chromatography analyses

9.2.2 *Determination of the Limit of Detection (LOD)*

The following method shall be performed if results are to be reported below the LOQ. The independent testing laboratory is to develop a procedure for the determination of a LOD for each analytical method for which the analyte can be spiked into a reference matrix. The general steps required for the procedure are described below: *When determining the LOD, prepare an adequate number of spikes of known amounts of analyte near, but above the instrument detection limit that are taken through the entire analytical method, including sample preparation (e.g., digestion, extraction, derivatizations, cleanups). From the variation in these measures, use the student t statistic to establish the upper confidence limit at p ≥ 0.99 for n-1 degrees of freedom. Compare this to a similar set of independent testing laboratory method blanks, applying the same statistic. Use the higher of the two calculated LOD values. Validate the LOD value by analyzing a suitable number of samples known to be near or prepared at the detection limit and perform a statistical evaluation on the associated results in order to determine the LOD value. Draft, review, and issue a written set of procedures detailing the procedures for the determination and verification of the LOD. Provide documented training to the procedures.*

Note: The LOD determination method accepted for compliance with this QAPP is based on the procedure for determining the Method Detection Limit presented in 40 CFR 136 Appendix B.

9.2.2.1 **Estimate the Initial LOD using one of the following:**

- The mean plus three times the standard deviation of a set of method blanks.
- The concentration value that corresponds to an instrument signal/noise ratio in the range of 3:1 to 2.5:1. This is performed preferably without smoothing of the analytical signal, but if smoothing is applied, it shall be the same smoothing method as is used for all sample and quality control sample analysis.
- The concentration equivalent of three times the standard deviation of replicate instrumental measurements of spiked blanks.
- That region of the standard curve where there is a significant change in sensitivity, i.e., a break in the slope of the standard curve.
- Instrumental limitations.
- Previously determined LOD obtained using the same instrument conditions.

It is recognized that the experience of the analyst is important to this process. However, the analyst is to include some or all of the above considerations in the initial estimate of the LOD.

9.2.2.2 **Determine the Initial LOD**

1. *Select a spiking level, typically 2 – 10 times the estimated LOD in the section above*

2. *Process a minimum of seven spiked blank samples and seven method blank samples through all steps of the method, including any sample preservation. Both preparation and analysis of these samples are to include at least three batches on three separate days' results in the method-reporting units.*

    a. *If there are multiple instruments that shall be assigned the same LOD, then the samples are to be distributed across all of the instruments.*

    b. *A minimum of two spiked samples and two method blank samples prepared and analyzed on different days is required for each instrument.*

    c. *Evaluate the spiking level: If any result for any individual analyte from the spiked blank samples does not meet the method qualitative identification criteria 2 or does not provide a numerical result greater than zero then repeat the spikes at a higher concentration.*

3. *Make all computations according to the defined method with final results in the method-reporting units.*

    a. *Calculate the sample standard deviation (S) of the replicate spiked blank measurements and the sample standard deviation of the replicate method blank measurements from all instruments.*
    b. *Compute the LODs (LOD based on spiked blanks) as follows:*

$$LOD_s = t_{(n-1,\ 1-\alpha=0.99)}S$$

Where:

LODs = the Limit of Detection
$t_{(n-1,\ 1-\alpha\ =\ 0.99)}$ = the students t value appropriate for a 99% confidence level [13] and a standard deviation estimate with n-1 degrees of freedom..
S = sample standard deviation of the replicate spiked blank sample analyses.

c. Compute the LOD_b (LOD based on method blanks) as follows:

i. If none of the method blanks give numerical results[3] for an individual analyte, the LOD_b does not apply.
ii. If some (but not all) of the method blanks for an individual analyte give numerical results, set the LOD_b equal to the highest method blank result.
iii. If all of the method blanks for an individual analyte give numerical results, calculate the LOD_b as:

$$LOD_b = \overline{X} + t_{(n-1,1-\alpha=0.99)}S_b$$

Where:
LOD_b = the LOD based on method blanks
$\overline{X}$= mean method blank
$t_{(n-1,\ 1-\alpha\ =\ 0.99)}$ = the students t value appropriate for a 99% confidence level and a standard deviation estimate with n-1 degrees of freedom.
S_b = sample standard deviation of the replicate blank sample analyses.

4. Set the greater of LODs or LOD_b as the initial LOD.

For qualitative measurements, determine the concentration threshold below which specificity becomes unreliable.

9.2.2.3 Ongoing LOD Data Collection

- *During any quarter in which samples are being analyzed, prepare, and analyze a minimum of two spiked samples on each instrument, in separate preparation batches, using the same spiking concentration level that was used to determine the LOD initially per the instructions in Section 9.2.2.2.*

- *Ensure that at least seven spiked samples and seven method blanks are completed for the annual verification that is described below in Section 9.2.2.2. If only one instrument is in use for a given method, then a minimum of seven spikes are still required, but they may be drawn from the last two years of data collection.*

[13] NIST/SEMATECH. 2013. E-Handbook of Statistical Methods. http://itl.nist.gov/div898/handbook/eda/section3/eda3672.htm

9.2.2.4 **Requirements for Re-determining the LOD**

- *Annually, at a minimum, the independent testing laboratory is to re-evaluate the spiking level used to determine the initial LOD. If more than 5% of the spiked samples analyzed, as part of the ongoing LOD data collection described in Section 9.2.2.2, do not return positive numerical results that meet all method qualitative identification criteria, then the spiking level shall be increased and the initial LOD re-determined following the procedure in Section 9.2.2.2.*

    - *If the method is altered in a way that can be reasonably expected to change its sensitivity, then re-determine the initial LOD according to Section 9.2.2.2 and restart the ongoing data collection described in Section 9.2.2.2.*[14]

    - *If a new instrument is added to a group of instruments whose data are being pooled to create a single LOD, analyze a minimum of two spiked replicates and two method blank replicates on the new instrument. If both method blank results are below the existing LOD, then the existing LOD_b is validated. Combine the new spiked sample results to the existing spiked sample results and recalculate the LOD_s as described in Section 9.2.2. If the recalculated LOD_s is within 0.5 to 2.0 times the existing LOD_s, and fewer than 3% of the method blank results (for the individual analyte) have numerical results above the existing LOD_s, then the existing LOD_s is validated and may optionally be left unchanged. If either of these two conditions is not met, then calculate a new LOD following the instructions in Section 9.2.2.*

9.2.2.5 **Annual Verification of LOD**

- *Annually, at a minimum, the independent testing laboratory is to re-calculate the LOD from the collected spiked samples and method blank results using the equations in Section 9.2.2.2*
- *When recalculating the LOD the independent testing laboratory is to include the ongoing data generated within the last twelve months which meet the following criteria for inclusion into the LOD calculation:*

    - *Data with the same spiking level used to determine the LOD previously. Only documented instances of gross failures (e.g., instrument malfunctions, mislabeled samples, cracked vials, formal statistical outlier testing) may be excluded from the calculations.*
    - *If outliers are removed, then the rationale for removal of specific outliers shall be tracked by matrix type, documented, and maintained by the independent testing laboratory with the results of the initial LOD determination.*
    - *If the independent testing laboratory believes the sensitivity of the method has changed significantly, then the most recent data available may be used, as long as compliance with the requirement for at least seven*

[14] A numerical result includes both positive and negative results, including results below the current LOD. Results do not include any value where a chromatographic peak is not present.

replicates in three separate batches on three separate days has been met (see Section 9.2.2).
- *If the method has been altered in a way that can be reasonably expected to change its sensitivity then use only data collected after the change.*
- *Include the initial LOD spiked samples, if the data were generated within 12 months.*
- *Only use data associated with acceptable calibrations and acceptable batch QC.*
- *Include all routine data, with the exception of batches that are rejected and the associated samples reanalyzed.*
- *Ideally, use all method blank results from the last 12 months for the LOD_b calculation. The independent testing laboratory has the option to use only the last six months of method blank data or the fifty most recent method blanks, whichever criteria yields the greater number of method blanks.*

- *The verified LOD is the greater of the LOD_s or LOD_b. If the verified LOD is within 0.5 to 2.0 times the existing LOD and fewer than 3% of the method blank, results (for the individual analyte) have numerical results above the existing LOD then the existing LOD may optionally be left unchanged. Otherwise, adjust the LOD to the new verification LOD.*

***Note**: The range of 0.5 to 2.0 approximates the 95th percentile confidence interval for the initial LOD determination with six degrees of freedom.*

9.2.3 *Limit of Quantitation (LOQ)*

The LOQ is to be determined for each analysis, using a documented standard procedure developed by the independent testing laboratory. The general steps required for the independent testing laboratory LOQ procedure are described below:

Determine the LOQ by preparing spikes of known amounts of analyte near the minimum level at which the analyte can be quantified with acceptable accuracy and precision. Experience and theory (e.g. Horwitz) holds that this is generally several multiples (e.g. three times) higher than the LOD (two times at a minimum). Take the LOQ spikes through the sample preparation steps of the method. Validate the LOQ value by analyzing a suitable number of samples (three spiked samples at a minimum) known to be near or prepared at the LOQ and evaluate the associated results in order to determine whether the results meet the DQOs for precision and percent recovery. It is required that the value also be supported by a calibration point at or below the LOQ for any given method and that method blanks be held to ½ the LOQ or less. On a periodic frequency, check samples that are taken through all method procedural steps are to be analyzed at the LOQ level in order to verify the method's accuracy near the LOQ value. Draft, review, and issue a written set of procedures detailing the procedures for the determination and verification of the LOQ. Provide documented training to the procedures.

9.2.3.1 **Ongoing Verification of the LOQ**

On a periodic frequency, check samples that are taken through all method procedural steps are to be analyzed at the LOQ level in order to verify the method's

accuracy near the LOQ value. The independent testing laboratory is to draft, review, and issue a written set of procedures detailing the procedures for the determination and verification of the LOQ. The default DQO for ongoing validation are to match those specified in the DQO Tables presented in Appendix A *or independent testing laboratory generated limits specific to LOQ verification can be established.*

9.2.4 ***Linear Range***

For quantitative measurements determine the linear calibration range if a standard curve is to be used or determine the target calibration standard and linearity if only a one calibration point is to be used.

As a general rule for a calibration curve, the mid-point is set at the target level (concentration) for quantitation of the analyte. Ideally, for the determination of contaminants in medical marijuana products (MMPs) and marijuana infused products (MIPs) the target LOQ is to be set at the contamination limits for each contaminant compound, where practical and achievable, as required by the MDPH Protocol for Sampling and Analysis of Finished Medical Marijuana Products and Marijuana-Infused Products for Massachusetts Registered Medical Marijuana Dispensaries, Protocol for Sampling and Analysis of Environmental Media for Massachusetts Registered Medical Marijuana Dispensaries.

For the establishment of linearity for chromatographic methods (*i.e.* GC and HPLC), the analysis of a minimum of five concentrations of analyte is recommended, with the low calibration standard being set at or below the LOQ. The coefficient of determination (r^2) for a calibration curve shall be ≥ 0.990.

The coefficient of determination (r^2), y-intercept, slope of the regression line and residual sum of squares are to be submitted as part of the validation results when determining the linear range of the method. A plot of the data is to be included. In addition, an analysis of the deviation of the actual data points from the regression line may also be helpful for evaluating linearity. Weighted linear calibrations using a $1/x^2$ weighting factor are encouraged if the relative error is thereby reduced at the critical concentration level.

For residual solvent analysis by gas chromatography and pesticide analysis by LC/MS/MS, higher order linear calibration models (*e.g.*, quadratic or cubic) may be used if performed frequently or verified throughout the range on an ongoing basis. Non-standard calibration fits for a specific analyte cannot be applied to arbitrarily to force a passing calibration. If an analyte shows to conform to a curve fit on a regular basis, the decision to change the calibration model is to be recorded along with justification such as change of column or decreased instrument performance.

In the event that support equipment calibration is limited to a single calibration point, the zero-point of the curve may be forced (i.e. set) to zero. If a multipoint calibration curve is analyzed, the intercept is not to be forced through zero, however the impact of a non-zero intercept may be diminished by use of a weighted calibration model.

The range of the method is typically derived from the linearity studies by confirming that the analytical procedure provides an acceptable degree of linearity, accuracy, and

precision when applied to samples containing known amounts of analyte within or at the extremes of the specified range of the analytical procedure.

The exact requirements for linearity are specified in the QAPP DQO Tables presented in Appendix A.

9.2.5 ***Accuracy***

For quantitative measurements, prepare and analyze spiked blanks in solvent or matrix samples with known concentration of analyte. Determine the accuracy of the method across the range of the method by utilizing at least three different concentration levels: low, middle, and high. Where the low concentration is the limit of quantitation and the high concentration is the highest concentration of the linear range. For the determination of accuracy a minimum of 9 determinations (*e.g.,* 3 concentrations /3 replicates each of the total analytical procedure). These samples are carried through the complete sample preparation procedure.

Matrix effects can also be assessed with these samples. Accuracy is to be reported as a percent recovery of the analyte that is calculated from the results.

The default DQOs for accuracy are specified in the TSM DQO Tables presented in Appendix A.

9.2.6 ***Precision (USP, ICH and ISO 17025)***

When determining the precision of the method, there are three primary elements: repeatability, reproducibility, and intermediate precision.

Repeatability can be assessed using the same procedure that was recommended for the determination of accuracy in the preceding section (*e.g.,* three concentrations /three replicates each). An alternative approach to determining repeatability would be a minimum of six determinations at a mid-level concentration or the target concentration for the method.

Reproducibility can be determined by participating in an interlaboratory study (*e.g.*, PE study, *etc.*). The objective of reproducibility is to verify that the method shall provide the same results in different laboratories. *Laboratories are expected to participate in interlaboratory studies that are become commercially available.*

Intermediate precision expresses the variation of a given method within the same laboratory. The extent to which intermediate precision is to be established depends on the circumstances under which the procedure is intended to be used. Intermediate precision is determined by comparing the results of a method run within a single laboratory over a number of days. A method's intermediate precision may reflect discrepancies in results obtained from the following:

- different analysts
- inconsistent working practice
- different instruments
- standards and reagents from different suppliers

- columns, reagents and media from different batches
- a combination of the parameters listed above

Precision shall be reported as the standard deviation or relative standard deviation (coefficient of variation). The confidence interval for which this precision is determined is to be reported for each type of precision investigated. The default DQOs are to match those specified in the DQO Tables presented in Appendix A *or those developed in accordance with the independent testing laboratory's technical procedure may be used in place the default DQOs. Where independent testing laboratory limits have been established, they are, at a minimum, to be used to identify trending and out of control events in order to inform continual improvement efforts. Repeatability shall be determined to be adequate so that reliable achievement of the method specific DQOs in* Appendix A *tables shall be supported.*

9.2.7 ***Selectivity/Specificity***

Evaluate potential interferences for each analyte under a given set of method conditions. For the evaluation of spectral, physical, or chemical interferences analyze a sample containing various suspected interferences in the presence of the measure. Spectral interference may be observed when an overlap of a spectral line from another element or background contribution occurs. Physical interference may occur from effects associated with sample transport processes on instruments. Chemical interferences are characterized by compound formation, ionization, or vaporization effects. Additional interference may occur from the contribution of signal from previous sample preparations which contaminate (or carry-over) into the next sample being tested.

Suitable identification tests are to be able to discriminate between compounds of closely related structures that are likely to be present (*e.g.*, cannabinoid profiles in the presence of terpenoids, flavonoids, and alkaloids). The discrimination of a procedure may be confirmed by obtaining positive results (perhaps by comparison with a known reference material) from samples containing the analyte, coupled with negative results from samples that do not contain the analyte. In addition, the identification test may be applied to materials structurally similar to or closely related to the analyte to confirm that a positive response is not obtained. The choice of such potentially interfering materials is to be based on sound scientific judgement with a consideration of the interferences that could occur.

9.3 Validation Requirements for Demonstrating Selectivity in Chromatographic Chemical Analysis

For chromatographic procedures, representative chromatograms are to be used to demonstrate selectivity and individual components are to be appropriately and qualitatively identified and labelled. Critical separations in chromatography are to be investigated at an appropriate level. For critical separations, selectivity can be demonstrated by the resolution of the two components, which elute closest to each other. Co-elution of peaks is to be monitored by monitoring retention times, applying peak symmetry criteria, and analyzing HPLC-UV peaks for peak purity using a diode-array detector (DAD).

Specific QC elements as they relate to chromatographic analyses are discussed below and a QC table summarizing those elements that are to be demonstrated when chromatographic methods are performed is presented in Appendix A.

9.3.1 ***Retention Times***

For chromatographic methods, all of the target analytes shall be retained on the column at a retention time that results in a minimum retention/capacity factor (k')[15] of > 2 and shall be resolved apart from any observed peaks and meet the peak identification requirements listed below shall be met.

For all initial calibration levels, the retention times for each target analyte shall be within ± 3 seconds of the midpoint standard for each target analyte. For CCV standards, the retention time of the CCV should not differ by > ± 6 seconds (0.2 minutes) or ± 0.04 relative retention time (RRT) units when internal standards are used, from the retention time established by the middle standard of the initial calibration. In MS methods, all internal standards retention times in the sample should not differ by > ± 6 seconds (0.2 minutes) or ± 0.04 RRT units (if applicable) from the retention time established by the associated CCV standard. For all target analytes reported in RMD samples and other method QC samples the retention time of the target analyte in the sample should not differ by ± 6 seconds (0.2 minutes) or ± 0.04 RRT units (if applicable) from the retention time established by the associated CCV standard. When retention time window criteria are not met, samples shall be reanalyzed within a new calibration or CCV to meet the retention time window criteria.

9.3.2 ***Peak Resolution***

For chromatographic peak resolution, a minimum acceptance criterion of ≤ 30% valley (that the valley between two adjacent peaks are not to exceed 30% of the peak height of the shorter peak) is required to provide for closely eluting compounds to be adequately resolved from each other. If resolution is determined to be insufficient, the independent testing laboratory shall modify method conditions where applicable in order to resolve co-eluting peaks from one another. Applicable components of validation of the modified method shall be completed successfully prior to sample analysis during method validation is described in Section 9.1.

9.3.3 ***Peak Symmetry (Tailing Factor, T)***

The accuracy of quantitation decreases with increase in peak tailing because of the difficulties encountered during peak integration when determining where/when the peak ends. As a result, the calculation of the area under the peak becomes less accurate. For all chromatographic peaks, the tailing factor is required to be ≤ 2, when calculated using the following calculation:

$$T = W_{0.05}/2f$$

Where $W_{0.05}$ is the width of the peak at 5% height and *f* is the distance from the peak maximum to the leading edge of the peak, the distance being measured at a point 5% of the peak height from the baseline. See example in figure below.

[15] k' = (Rt – t0)/t0; where: t0 is the column void volume (min) and Rt is the target analyte retention time (min).

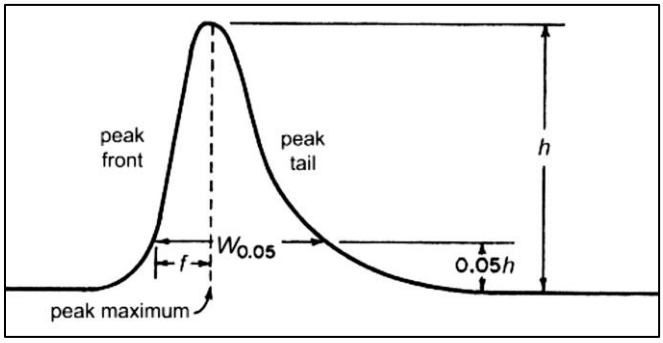

Figure 1. Determination of Tailing Factor on an Asymmetrical Peak [Reference: USP Chapter 621]

The independent testing laboratory is required to capture peak tailing for all chromatographic methods, where applicable. The independent testing laboratory is to provide the calculation used for determining peak tailing factor when requested by MDPH.

9.3.4 *Peak Purity (HPLC-UV Methods Only)*

Certain considerations are to be made when using instruments capable of calculating peak purity at multiple wavelengths, however named in the software, to determine the presence of co-eluting peaks in chromatographic methods. The HPLC method used the software settings and the parameters that independent testing laboratory selects within the peak purity software menu shall have an effect on the results that are obtained. The independent testing laboratory shall not use peak purity software to analyze peak, which elute at or near the column void volume.

The correct detector sample rate, signal wavelength, and bandwidths need to have been selected and used (*e.g.*, reference wavelength is to be turned OFF). Two spectral reference points are to be selected and placed at times before and after the peak of interest in clear baseline areas where no other peaks or spectra are seen. Select a minimum of seven spectra from the sample peak for comparison.

For all chromatographic peaks detected in HPLC-UV analyses, a DAD detector is to be used and the peak purity is to be monitored. When peaks have met the qualitative identification requirements presented in Section 9.1, and peak purity is calculated and no differences in the spectra are seen then the spectra are considered to be similar or homogeneous and no further action is required. When there is a difference between peak spectra and/or obvious co-elution during a chromatographic analysis and the peak resolution and/or tailing factor criteria established above are not met, then the independent testing laboratory is to modify method conditions in order to separate the two compounds from one another if detected during method development or validation. If the peak purity factor is below independent testing laboratory specifications for any sample, the RMD shall be contacted and the result shall be qualified if included in the report.

It is important to note that the absence of any spectral differences across a peak is not an indication of and should never be equated to actual chemical purity, as compounds similar to the target analyte may have similar absorbance profiles, the relative concentration of actual impurities may not be high enough to detect, the peaks are not resolved sufficiently (peak purity requires some resolution), or the compounds/impurities may not absorb light at the wavelengths scanned. To determine chemical purity, the sample may be analyzed using different analytical techniques such as liquid chromatography coupled with mass spectrometry (LC-MS), infrared spectroscopy (IR), nuclear magnetic resonance spectroscopy (NMR), or other wet chemistry techniques. Peak purity, as determined with DAD is used to help with the method development process and is used as an indication that a peak may not be composed of a single compound.

9.4 Validation Guidance for Microbiological Analyses

This section establishes method validation criteria for performing single-laboratory validation of methods that were developed to detect, identify, and quantify microbial analytes. This section applies when validating the performance of plate-count methods (*e.g.*, Petrifilm™, pour plates, spread plates, etc.), commercially-available microbiological diagnostic kits or automated instruments whose performance parameters were fully validated in multi-laboratory collaborative studies and evaluated by an independent accrediting body (*e.g.* AOAC, AFNOR, *etc*.) or validated by the USP, FDA, EPA or WHO.

Such applicable areas of methods development and evaluation include, but are not limited to, the following:

- Qualitative microbiological methods (*i.e*., detection assays)
- Quantitative microbiological methods (*i.e*., real-time polymerase chain reaction [PCR])
- Organism specific methods:
  - Bacteriological pathogens:
    - Salmonella spp.
    - Pathogenic Escherichia coli
    - Aspergillus
- Phenotypic Methods:
  - Biochemical characterization for identification
  - Antibiotic resistance traits for identification
  - Antigenic characterization for identification
- Genetic Based Methods:
  - Nucleic acid isolation/concentration/purification
  - Polymerase Chain Reaction
    - Conventional
    - Real-time
    - Reverse transcription
  - Sequencing:
    - Whole genome
    - Selective sequencing
    - Single nucleotide polymorphism (SNP) analysis
  - Strain-typing applications
- Immunological Methods:
  - Antibody capture
  - ELISA
  - Flow cytometry
- Plate-count methods (*e.g.*, Petrifilm™, pour plates, spread plates, *etc.*);
- Commercially-available microbiological diagnostic kits or automated instruments whose performance parameters were fully validated in multi-laboratory collaborative studies and evaluated by an independent accrediting body (*e.g.* AOAC, AFNOR, *etc*.) or validated by the USP, US FDA, US EPA or WHO.

Validation is the confirmation by examination and the provision of objective evidence that the particular requirements for a specific intended use are fulfilled. The independent testing laboratory shall validate non-standard methods, laboratory-designed/developed methods, standard methods used outside their intended scope, and amplifications and modifications of standard methods to confirm that the methods are fit for the intended use. Validation of microbiological methods is performed to demonstrate with adequate confidence that the results obtained by the in-house developed method are comparable to or exceed the precision and accuracy obtained relative to a validated reference method using a pre-determined statistical criteria contained in an approved validation protocol. When performing method verification, the independent testing laboratory is to confirm that the method can detect, identify, and quantitate an analyte while meeting the performance specifications established during method validation. *The independent testing laboratory*

shall record the results obtained, the procedure used for the validation, and a statement as to whether the method is fit for the intended use.

Each independent testing laboratory shall perform an in-house validation for the "first use" of such methods per the requirements prescribed in the subsequent sections below. For subsequent use(s) of the method, independent testing laboratory control samples are to be prepared for each lot of media and/or lot of diagnostic kits used to re-verify the method. For microbiological methods, typical validation would be comprised of the following elements:

9.4.1 ***Environmental Control Samples***

Controls for environmental conditions are to be used to assess biological sterility of the ambient independent testing laboratory environment. Acceptable environmental QC samples are to exhibit minimal total growth and growth of the target organisms are to be < LOD to demonstrate control. These controls are to be analyzed with each preparation batch (as defined in Section 1.1), and at a weekly frequency unless client samples are not analyzed for that method within the week. Environmental condition controls include, at a minimum, air settling plates and/or petri dishes utilizing every medium utilized in the method being evaluated. These controls are to be located in the immediate environment (e.g. hood, benchtop, instrument area, etc.) of client samples during sample set-up, enrichment, incubation, and analysis. The controls are to be left exposed to the sample environment from the start of the method (i.e. client sample set-up of the first sample) through the recording of the final raw result when the independent testing laboratory procedures indicate the associated client sample analysis is complete.

9.4.2 ***Negative Controls***

Prepare and analyze negative culture controls with each preparation batch of samples as defined in Section 1.1 to assess contamination associated with sterile technique and test sample handling and transport. Negative controls can be sterile dilution buffer (for non-selective media) or an organism for which growth is not supported by the selective medium; e.g., atypical or no growth. These controls are to be of a matrix similar to the batch of associated samples (when available) that is free of contamination and is processed simultaneously with and under the same conditions as samples through all steps of the analytical procedures and in which no contamination is present at concentrations that impact the analytical results for sample analyses.

For validation studies, six replicates of the sterile matrix (non-selective media) or six replicates of non-target organisms (selective media) are to be prepared, tested, and confirmed by the method. The default acceptance criterion for negative controls are <1 CFU/g of matrix being tested. If the independent testing laboratory negative control(s) fail to meet acceptance criteria, then the associated samples that were prepared in the independent testing laboratory since the last acceptable independent testing laboratory blank are considered suspect and reanalyzed.

9.4.3 ***Positive Culture Controls***

The independent testing laboratory shall prepare and analyze positive culture controls in order to assess and demonstrate method accuracy. A positive culture control shall exhibit positive growth or exhibit expected characteristics to assure the system is

working. For example, turbidity in a tube filled with enrichment broth showing growth or a characteristic physical (phenotypic) colony for the bacterial culture showing a positive test result.

For validation studies, six replicates are to be prepared in the inoculated matrix, tested, and confirmed by the method. The default acceptance criterion for accuracy, reported as percent recovery of the spiked amount, is 80-120%.

9.4.4 ***Precision***

Sample duplicates are not required but are recommended for microbiological sample analyses. *When the precision is expressed as relative percent difference (RPD) between duplicate samples, the RPD is to be ≤ 20% unless otherwise specified in the QAPP or by a control limit determined in accordance with the technical procedure*. For results expressed as Most Probable Number (MPN), both results should be within the 95% confidence interval (if available) for at least one of the results.

Six replicates each are to be prepared in the inoculated matrix, tested, and confirmed by the method. When samples are not analyzed in duplicate, control can be demonstrated by maintaining false positives or false negatives at a rate of ≤ 5%.

9.4.5 ***Specificity***

Evaluate potential interferences for each analyte under a given set of method conditions. For the evaluation of microbial interferences, analyze a sample containing various suspected interferences in the presence of the measure.

- *All growth and recovery media shall be checked to assure that the target organism(s) respond in an acceptable and predictable manner.*

- *To ensure that analysis results are accurate, target organism identity shall be verified as specified in the method (e.g., by use of the completed test) or by use of secondary verification tests.*

- *In order to ensure identity and traceability, reference cultures used for positive and negative controls shall be obtained under an ISO Guide 34 accreditation. Microorganisms may be single-use preparations or exist as cultures that are maintained. Cultures that are maintained shall be verified for their intended use (e.g., acceptable purity, stability, and viability of the organism) using documented procedures and acceptance criteria.*

- *Reference cultures may be revived (if freeze-dried) or transferred from slants and sub-cultured one time, in order to provide stock reference material. The reference material shall be preserved by a technique that maintains the characteristics of the strain/organism. Characterized reference materials shall be used to prepare working standards for routine work. If reference materials have been thawed, they shall not be refrozen and re-used.*

- *Working standards shall not be sequentially cultured more than five times and shall not be sub-cultured to replace the original stock reference material.*

9.4.6 ***Assay Ruggedness***

Demonstrate the ruggedness of the assay by adjusting critical parameters such as incubation time, incubation temperature and waiting time before incubation.

9.4.7 ***Re-Validation***

When the testing procedure is modified from the existing SOP/protocol in such a way that does not meet the criteria in Section 9.0, the independent testing laboratory is to demonstrate that the modifications do not adversely affect the precision and accuracy of the method. If the results are acceptable then re-validation of the test method is not necessary. However, if the accuracy and precision of the method is not acceptable following a modification to the method then validation is to be performed using the new conditions, prior to sample analysis.

10.0 QUALITY CONTROL SAMPLES AND PROCEDURES

The independent testing laboratory is to implement an approved procedure defining warning limits, control limits, analysis frequency, acceptance criteria, and corrective actions for QC samples or for calibrations in the SOPs for metals, cannabinoid profile, pesticides, residual solvents, mycotoxins, and microbiological methods.

10.1 General

QC includes all technical activities that measure the characteristics and performance of a MDPH approved independent testing laboratory process or procedure against defined standards. The MDPH QAPP and associated technical procedures are to provide those standards and procedures for identifying those standards. *In order to monitor and control data quality, independent testing laboratories are to apply MDPH-provided guidance in addition to approved methods and good laboratory practices to define QC samples and establish performance indicators. Such indicators include instrument- or protocol-related parameters that are routinely monitored in order to evaluate the independent testing laboratory's performance and to provide information needed for estimating measurement uncertainty (i.e., precision, bias, etc.). QC samples are used to demonstrate control over the analytical process and are to be tracked by appropriate personnel. If the QC sample control limits are exceeded, independent testing laboratory management is to be informed and corrective action is to be initiated.*

The independent testing laboratory is to define method QC sample preparation, warning limits, control limits, sample analysis frequency, acceptance criteria, and corrective actions for QC samples or for calibrations in each analytical SOP. In the absence of method-specified limits, apply a defined procedure for determining warning limits and control limits, involving outlier testing, and statistical process control principles.

Within each written SOP/protocol, establish the following QC procedures in order to monitor method performance and QC:

- *Positive and negative controls, chemical or microbiological as applicable to the test type, to monitor tests such as blanks, matrix spikes, etc.;*
- *Tests to define the variability and/or repeatability of the independent testing laboratory results such as replicates;*
- *Measures to assure the accuracy of the method including calibration and/or continuing calibrations, use of certified reference materials, proficiency test samples, or other measures;*
- *Measures to evaluate method capability, such as Limit of Detection and limit of quantitation or range of applicability such as linearity;*
- *Selection of appropriate formulae to reduce raw data to final results such as regression analysis, comparison to internal/external standard calculations, and statistical analyses;*
- *Selection and use of reagents and standards of appropriate quality;*
- *Measures to assure the selectivity of the test for its intended purpose; and*
- *Measures to assure constant and consistent test conditions (both instrumental and environmental) where required by the method such as temperature, humidity, light or specific instrument conditions.*

Method performance is typically monitored by evaluating certain QC samples along with each batch of samples under study. A batch is defined as samples prepared and/or analyzed together with the same process and personnel, using the same lot(s) of reagents. *A **preparation batch** is composed of 1-20 sample(s) of the same quality systems matrix, meeting the above-mentioned criteria and with a maximum time between the start of processing of the first and last sample in the batch to be 24 hours. An **analytical batch** is composed of prepared samples (extracts, digestates, or concentrates) which are analyzed together as a group.* An analytical batch can include prepared samples originating from various quality management system matrices and can exceed 20 samples. The QC samples included in each batch measure performance characteristics of the entire process on an ongoing basis.

When preparing QC samples, any piece of equipment that comes in contact with the product under analysis (e.g. forceps, syringes, scalpels, scissors, swabs, pipettes, membranes, or other special items that may be required by a specific test, etc.) along with any manipulations performed by the analysts, are to be controlled and tested throughout each analysis. Thus, all equipment, fluids, and culture media used to prepare quality control samples shall be handled in a manner that duplicates, as closely as possible, the manipulations of the actual sample being analyzed.

For microbiological assays, all materials used as laboratory controls are to be sterilized by the independent testing laboratory. However, the method of sterilization need not be the same as that used for the product sample, but shall render the material sterile. When products are tested by direct inoculation (e.g. non-filterable materials, insoluble solids, etc.) the independent testing laboratory shall use uncontaminated products for laboratory controls that are similar in size, shape, and texture as the product being tested. As part of daily verification of method performance,

10.2 Batch Quality Control Samples

The default set of batch QC samples are as follows:

- *Laboratory/Method blanks (Negative Controls): A sample of a matrix similar to the batch of associated samples (when available) that is free from the analytes of interest and is processed simultaneously with and under the same conditions as samples through all steps of the analytical procedures (e.g., homogenization, subsampling, digestion, extraction, cleanup and analysis), and in which no target analytes or interferences are present at concentrations that impact the analytical results for sample analyses.*

- *Laboratory Control Samples: A spiked sample for chemistry or positive culture control for microbiology analyses that is generally used to establish intra-laboratory or analyst specific precision and bias or to assess the performance of all or a portion of the measurement system.*

- *Matrix Spike (spiked sample or fortified sample): A sample prepared, taken through all sample preparation and analytical steps of the procedure unless otherwise noted in a referenced method, by adding a known amount of target analyte to a specified amount of sample for which an independent test result of target analyte concentration is available. Matrix spikes are used, for example, to determine the effect of the matrix on a method's recovery efficiency.*

- *Laboratory Duplicates/Matrix Spike Duplicates: Two aliquots of the sample used to assess precision of the analytical process.*

The independent testing laboratory should determine, based on the objectives and confines of the method, whether laboratory duplicates or matrix spike duplicates will make a more useful comment on precision. If the target analytes are assumed to be mostly non-detect, as in a contaminant analysis, it is prudent to choose the Matrix Spike Duplicates so that actual numbers are compared. If the target analytes are expected to present in concentrations above the method LOQ, a laboratory duplicate is very useful, especially in the case of an investigation of a data request or an evaluation of whether re-analysis is necessary.

The QC samples listed above are in addition to required instrument-specific checks such as calibrations and Calibration Verification Samples: (Calibration check standards analyzed periodically in the analytical batch for quantitative analyses), instrument blanks and interference checks.

10.2.1 ***Establishing Control Limits***

The default advisory limits for accuracy (Appendix A) are to be used until such time as 20 or more data points are obtained under a set procedure. After that time, the data are to be examined for statistical outliers, or failures from a known, assignable cause. Both types of values are to be removed from the data set, and then summary statistics are to be calculated to determine mean and standard deviation for the purpose of setting warning and control limits. The independent testing laboratory is to use these

laboratory-developed control limits, unless they exceed the limits in the DQO tables, in which case the DQO limits are to be applied.

The upper and lower warning limits (UWL, LWL) are to be set at 2 σ from the mean and the upper and lower control limits (UCL, LCL) are to be set at 3 σ from the mean.

For example, when a QC sample data point is outside of ± 3σ this is considered a rare event, which indicates that there is only a 0.3% chance that this was caused by the normal laboratory process. Since this data was outside of the warning limits, the data would typically be rejected and an investigation shall typically be conducted. The investigation is a planned action to correct the problem and to prevent the reporting of incorrect results. Sometimes the investigation shall reveal a recording or computational mistake that can be revised to obtain the correct value. *If the investigation reveals an assignable cause, i.e. deterioration of reagents, improperly prepared reagents, inadequate storage of reagents or standards, then the analysis is to be repeated. When outliers are found, all analytical results for that analytical batch are inspected to ensure that erroneous results are not reported.*

Additional detail should be provided in the independent testing laboratory's technical procedures for establishing and updating normality testing, skewness correction, proper exclusion of for-cause outliers and statistical outliers.

10.2.2 ***QC Sample Data Review***

Implement an approved procedure for review of data supporting reported sample results and associated QC data. This is to include an independent review of data supporting sample results and associated QC data.

Data that is determined to be a statistical outlier shall be flagged as such and is excluded from the data set before statistical calculations are made. Control limits calculated from data sets containing outliers are not valid.

Each suspected outlier is evaluated and rejected if found to be unrepresentative, or to have a high probability of being unrepresentative. Rejection for a reason is referred to as rejection for assignable cause.

An outlier is a data point that is different from the main data pattern, and/or is not representative of the data set. Outliers are extreme cases of one variable, or a combination of variables, which have a strong influence on the calculation or statistics. The primary protections against obtaining or using an outlier are awareness during all operations and visual inspection of data before performing statistical analyses. Formal outlier testing or assignable causes shall be the only basis for point exclusion.

Control charts are typically used for detecting shifts of the monitored variable than charts based on individual observations. The chart shall disclose trends and shifts from assignable causes that can be corrected. A trend shall show a tendency or movement in a particular direction. If a series of consecutive data points move steadily either upward or downward, a trend is indicated. If a series of consecutive data points fall either above or below the centerline, a shift is indicated. When a trend or shift is detected, it is annotated as such on the chart and reviewed to the extent possible to identify if a

significant concern is indicated regarding the QC sample results and overall method performance. If the review indicates a significant concern, a corrective action is initiated to determine the cause.

The following rules should be considered when conducting trend analysis:

1. A data point is greater than three standard deviations from the mean.
2. Nine points in a row are all on the same side of the mean.
3. Six points in a row are all either increasing or decreasing.
4. Fourteen points in a row alternating up and down.
5. Two out of the last three points are greater than two standard deviations away from the mean on the same side.
6. Four out of the last four points are greater than one standard deviation from the mean on the same side.
7. Fifteen points in a row are less than one standard deviation from the mean on either side.
8. Eight points in a row are greater than one standard deviation from the mean on either side.

10.2.3 *QC Sample Documentation and Review*

Implement the following QC procedures:

- *Document an unbroken chain of QC procedures tracing the final preparation to the initial lot of materials (e.g., equipment, standards and reagents);*
- *Identify QC samples that are prepared and analyzed with a given sample analysis sequence in the instrument software for an analytical sequence and/or on the work instruction sheets;*
- *Document a review of independent testing laboratory notebooks at a specified frequency.*

The independent testing laboratory shall, upon request, provide all supporting data and information to demonstrate that the laboratory is in compliance with these requirements.

This information may include, but is not limited to the following:

- Data verifying the training of the analyst performing the analyses;
- Data pertaining to the sample preparation and cleanup that is material to the sample result and associated quality control sample results.
- Data verifying that the analytical system was properly calibrated and in control at the time of analysis, including:
    - Calibration and verification method and frequency,
    - Source of standards,
    - Concentrations of standards,
    - Response factors,
    - Instrument linear ranges,
    - Check standards,
    - Control limits,
    - Logbooks,
    - SOPs,

- Sample preparation records,
- LOQ verifications, and
- LOD studies

10.3 Equipment

10.3.1 *Testing, Inspection, Maintenance and Calibration of Support Equipment*

All quantitative apparatus used as part of sample preparation (including, but not limited to, thermometers, micropipettes, microsyringes, auto dispensers, balances, and weights) are to undergo frequent, documented calibration/tuning checks inclusive of meeting a reasonable acceptance criterion (e.g., ± 2% of the true value for volumetrics) and documented corrective action when acceptance criteria are not met. Certification information (cleanliness and volume precision) for all quantitative apparatus are to be maintained with complete traceability. All volumetric labware shall be Class A. Disposable labware used for volumetric measurements shall be demonstrated on a production lot basis to have accuracy and precision meeting Class A specifications. Extracts for the analysis of organic compounds are to be stored in the same type of vials (amber or clear) as the associated standards and at the appropriate storage temperatures. Sample preparation is to be fully documented and inclusive of sample preparation conditions (e.g., digestion, extraction, cleanup, etc.) and documentation that allows traceability of analytical data back to all prepared and purchased reagents, acids/solvents, filters, digestion tubes, and reference solutions, and their certificates of analysis or statements of purity (e.g., lot numbers of solvents and acids recorded in preparation logs). Wherever practicable, support equipment is to be labeled with a unique ID and a calibration expiration date. If an expiration date of calibration cannot be directly labeled, it is the responsibility of the staff member who utilizes that piece of equipment to ensure it remains in calibration.

10.3.1.1 **Thermometer Calibration**

Thermometers or other appropriate temperature measurement devices are to be calibrated at least annually against a NIST-certified thermometer. All thermometers are to be labeled with a unique identification number, the date of calibration, the date that the next calibration is required, and the correction factor (even if "0.0°C"). The independent testing laboratory NIST-certified thermometer is to be re-certified at a minimum of every 3 years. Recorded temperatures are to include the identifier for the thermometer used, the actual thermometer measurement and corrected thermometer measurement.

10.3.1.2 **Balance Calibration and Verification**

Balances and weights shall be checked by an ISO 17025 accredited outside vendor on an annual basis, and inspection stickers are to be available for examination. Logbooks and electronic logs are to contain the unique IDs of the balance and the weights, the acceptance criteria and are to include periodic documented peer or supervisory review. The review period for this review is to be at least quarterly.

If the independent testing laboratory wishes to verify the linearity of the balances on a daily basis in addition to bracketing the use range then include a protocol for

testing a minimum of three weights for linearity checks, and include additional weights needed to bracket the current use range. When performing balance verification use ASTM Class 1 weights (or equivalent). Incorporate the acceptance criteria listed in the DQO tables in Appendix A

Laboratory top-loading balances shall be capable of 0.1-gram accuracy for sampling. Analytical balances shall be capable of accuracy to 0.001 mg. All balances and their records shall be inspected at minimum by an accredited vendor performing calibration and certification in compliance with ISO/IEC 17025. The independent testing laboratory QA department is accountable for verifying a label is placed on each calibrated balance and that a calibration certificate is obtained.

10.3.2 ***Testing, Inspection, Maintenance and Calibration of Analytical Equipment***

10.3.2.1 **HPLC (UV-Vis or DAD)**

Note: Additional details on the following requirements appear in Appendix A.

Instrument stability and performance are to be monitored on an ongoing basis to determine if there are conditions that affected the data quality of client samples. The independent testing laboratory is to, as part of the data review record, document this evaluation for each analytical batch. If it is determined from this evaluation that the data quality was possibly affected, it shall be documented in the client report narrative.

This is achieved by evaluating baselines, chromatographic peak shape, retention times, interferences, or reduced sensitivity on each analysis of standards, samples, dilutions, and QC samples.

Evaluation in chromatography methods includes the monitoring of surrogates that closely match the behavior of the target analyte. If the lab deems there is an appropriate mix of surrogates for the target analytes or there are suggested surrogates listed in accepted reference methods for chromatography analysis of the target analytes in marijuana matrices, it is recommended the independent testing laboratory use these surrogates to monitor extraction efficiency and instrument performance to the criteria found in Appendix A, Table 6.

10.3.2.2 **ICP-MS**

Note: Additional details on the following requirements appear in Appendix A.

The ICP-MS method validation is to include a Linear Dynamic Range study that exceeds the daily working linear range to determine the initial instrument linearity. This range is to be verified annually or as need to identify any possible degradation of the instrument components that would affect data quality. Interelement correction factors shall be measured and updated at least semi-annually. Interelement and isobaric interferences shall by monitored daily and collision cell or reaction cell technology shall be used to suppress such interferences.

A minimum of four measures of intensity are to be used and averaged in determining signal intensity. Downward trending of the individual measures is to be used in assessing whether carryover is affecting the measurement.

Internal Standards are available and required when analyzing for metals in marijuana matrices.

10.3.2.3 **GC-FID**

Note: Additional details on the following requirements appear in Appendix A.

Instrument stability and performance are to be monitored on an ongoing basis to determine if there are conditions that affected the data quality of client samples. The independent testing laboratory is to, as part of the data review record, document this evaluation for each analytical batch. If it is determined from this evaluation that the data quality was possibly affected, it shall be documented in the client report narrative. If large differences are noted between two columns or between GC/FID and GC/MS analysis, GC/MS analysis shall be used to report the result of the target analyte

This is achieved by evaluating baselines, chromatographic peak shape, interferences, or reduced sensitivity on each analysis of standards, samples, dilutions, and QC samples.

Gas chromatography requires confirmation of result on a column of different polarity or an MS detector. When sample results are confirmed using two dissimilar columns or with two dissimilar detectors, the agreement between the quantitative results should be evaluated after the identification has been confirmed. Large differences in the numerical results from the two analyses may be indicative of positive interferences with the higher of the results, which could result from poor separation of target analytes, or the presence of a non-target compound.

Evaluation in chromatography methods includes the monitoring of surrogates that closely match the behavior of the target analyte. If the lab deems there is an appropriate mix of surrogates for the target analytes or there are suggested surrogates listed in accepted reference methods for chromatography analysis of the target analytes in marijuana matrices, it is recommended the independent testing laboratory use these surrogates to monitor extraction efficiency and instrument performance to the criteria found in Appendix A, Table 03b.

10.3.2.4 **GC-MS**

Note: Additional details on the following requirements appear in Appendix A.

Instrument stability and performance is to be monitored on an ongoing basis to determine if there are conditions that affected the data quality of client samples. The independent testing laboratory is to, as part of the data review record, document this evaluation for each analytical batch. If it is determined from this evaluation that the data quality was possibly affected, it shall be documented in the client report narrative.

Due to the nature of mass spectrometry, if the lab deems that there is an appropriate mix of internal standards is available or there are lists of internal standards listed in an accepted reference method for MS detection in the analysis of the target analytes in marijuana matrices, the independent testing laboratory is to utilize these internal standards to monitor instrument performance to the criteria found in Appendix A, Table 3a.

Monitoring instrument stability and performance is achieved by evaluating baselines, chromatographic peak shape, interferences, or reduced sensitivity on each analysis of standards, samples, dilutions, and QC samples. Evaluation in chromatography methods includes the monitoring of surrogates that closely match the behavior of the target analyte. If the lab deems there is an appropriate mix of surrogates for the target analytes or there are suggested surrogates listed in accepted reference methods for chromatography analysis of the target analytes in marijuana matrices, it is recommended the independent testing laboratory use these surrogates to monitor extraction efficiency and instrument performance to the criteria found in Appendix A, Table 3a.

10.3.2.5 **LC-MS-MS**

Note: Additional details on the following requirements appear in Appendix A.

Instrument stability and performance is to be monitored on an ongoing basis to determine if there are conditions that affected the data quality of client samples. The independent testing laboratory is to, as part of the data review record, document this evaluation for each analytical batch. If it is determined from this evaluation that the data quality was possibly affected, it shall be documented in the client report narrative.

Due to the nature of mass spectrometry, if the lab deems that there is an appropriate mix of internal standards is available or there are lists of internal standards listed in an accepted reference method for MS detection in the analysis of the target analytes in marijuana matrices, the independent testing laboratory is to utilize these internal standards to monitor instrument performance to the criteria found in Appendix A*, Table 4.*

Monitoring instrument stability and performance is achieved by evaluating baselines, chromatographic peak shape, interferences, or reduced sensitivity on each analysis of standards, samples, dilutions, and QC samples. Evaluation in chromatography methods includes the monitoring of surrogates that closely match the behavior of the target analyte. If the lab deems there is an appropriate mix of surrogates for the target analytes or there are suggested surrogates listed in accepted reference methods for chromatography analysis of the target analytes in marijuana matrices, it is recommended the independent testing laboratory use these surrogates to monitor extraction efficiency and instrument performance to the criteria found in Appendix A, Table 4.

10.3.3 *Testing, Inspection, Maintenance and Calibration of Microbiological Equipment and Support Equipment*

10.3.3.1 **PCR/Fluorescence Systems**

QC samples included in the instrument procedure provide feedback on the functioning of PCR/Fluorescence instrumentation. *The microbiology procedures in the laboratory shall include record keeping that traces each QC check in Appendix A, Table 09 to a result.*

10.3.3.2 **Temperature Measuring Devices**

Temperature measuring devices such as liquid-in-glass thermometers, thermocouples, and platinum resistance thermometers used in incubators, autoclaves and other equipment used during microbiological analyses shall have the appropriate graduation and quality to meet specification(s) in the method. These devices shall be verified to national or international standards for temperature. Verification shall be done at least annually.

10.3.3.3 **Incubators**

Temperature of the incubator should be verified twice a day when in use, with the time of each verification separated by at least four hours. If temperature windows are exceeded, catalog contents of incubator and re-prepare. If there is not enough sample mass to reanalyze, qualify the results on the client report.

The surfaces within the incubator that come into direct contact with sample plates or films (i.e. trays or racks) should be cleaned using a lint free cloth and disinfectant after each use, or daily at a minimum. The remaining surfaces and other components of the incubator should be cleaned with a lint-free cloth and disinfectant on a weekly basis.

10.3.3.4 **Autoclaves**

The performance of each autoclave is to be initially evaluated by establishing its functional properties and performance, for example heat distribution characteristics with respect to typical uses. Demonstration of sterilization temperature is to be provided by use of a continuous temperature-recording device or by use of a maximum registering thermometer with every cycle. At least once during each month that the autoclave is used, appropriate biological indicators shall be used to determine effective sterilization. The selected biological indicator shall be effective at the sterilization temperature and time needed to sterilize lactose-based media. Temperature sensitive tape shall be used with the contents of each autoclave run to indicate that the autoclave contents have been processed. Autoclave maintenance (either internally or by service contract) shall be performed annually and shall include a pressure check and verification of the temperature device performance. The autoclave mechanical timing device shall be verified quarterly against a stopwatch and the actual time elapsed documented.

Records of autoclave operations shall be maintained for every cycle. Records shall include: date, contents, maximum temperature reached, pressure, time in sterilization mode, total run time (may be recorded as time in and time out) and analyst's initials.

10.3.3.5 **UV Instruments used for Sterilization**

UV instruments, used for sanitization, shall be tested quarterly for effectiveness with an appropriate UV light meter, by plate count agar spread plates or other methods providing equivalent results such as UVCide® *strips. If the output is less than 70% of original for light tests or if count reduction is less than 99% for a plate containing 200 to 300 organisms, the bulbs of the UV instrument are to be replaced.*

10.3.3.6 **Labware**

The independent testing laboratory shall have a documented procedure for washing labware used for microbiological analysis, if applicable. Detergents designed for independent testing laboratory use shall be used. Glassware shall be made of borosilicate or other non-corrosive material, free of chips and cracks, and shall have readable measurement marks. Washed labware shall be tested at least once daily, each day of washing, for possible acid or alkaline residue by testing at least one piece of labware with a suitable pH indicator such as bromothymol blue. Records of testing of washed labware shall be maintained.

10.4 Water for Analysis

Water specifications have been described by ASTM (American Society for Testing and Materials) D1193, ASTM D5196, ISO 3696, and USP <1231> Water for Pharmaceutical Purposes. Historically waters of the highest purities have often been described as "Type I" to designate ultrapure waters, and Type II, Type III or Type IV to designate lower grades (Table 5).

Resistivity and conductivity are concepts to be familiar with when it comes to water purity. Resistivity is the tendency of water without ions to resist conducting electricity. The unit of measure is megaohm-centimeter (MΩ-cm), and varies with temperature. The theoretical maximum is 18.2 to 18.3 MΩ-cm at 25°C. The higher the ionic content, the lower the resistivity and conversely, the lower the ionic content, the higher the resistivity.

Conductivity is the tendency of water that contains ions to conduct electricity. The unit of measure is the Siemen(S), microsiemens/centimeter (µS/cm) or micro-ohms/cm. Conductivity increases with temperature so values are reported as compensated at 25 °C whereas resistivity is the inverse of conductivity and is expressed in 18.2 MΩ-cm @ 25 °C.

The ASTM establishes specifications for Types I, II, III, and IV reagent grade water (D1193-06-2011) as shown on Table 5. The water quality is further classified as Type A, Type B, or Type C depending on the applicable bacteriological and endotoxin quality (Table 6). ASTM D1193-06 Type I water (or equivalent) is to be used for all chemical analyses performed under the guidance provided in this QAPP.

The conductivity of the deionizing water systems shall be monitored and recorded in a log or logbook on each working day. Additionally, the cell constant of each resistivity meter shall be checked on an annual basis. Proper indication of corrective actions shall be recorded as comments in the logbook when the resistivity does not meet the lower acceptance limits. For ongoing checks of water used for microbiological analyses the criteria for Type I water and those presented on Table 6 should be met. Additionally, for microbiological analyses, the established DQO criteria for specific pathogens in dilution water and buffers presented within the DQO Tables presented on Tables 8 and 9 of Appendix A*, should be established per lot or batch of water or buffer used.*

Table 5 American Society for Testing and Materials Reagent Grade Water Specifications ASTM D1193-06 (2011)

Parameter	Type I	Type II	Type III	Type IV
Resistivity, min. MΩ-cm (@ 25°C)	18.0	1.0	4.0	0.2
pH, SU (@ 25°C)	NA	NA	NA	5 to 8
TOC, max. (µg/L)	50	50	200	NS
Sodium, max. (µg/L)	1	5	10	50
Chloride, max. (µg/L)	1	5	10	50
Total Silica, max. (µg/L)	3	3	500	NA

Table 6 American Society for Testing and Materials ASTM D1193-06 (2011)

Parameter	Type A	Type B	Type C
Bacteria, max. (CFU/100 mL)	1	10	1000
Endotoxin (EU/mL)	< 0.03	0.25	NA

10.5 Preventative measures

Specific procedures for maintaining a sterile workspace and preventing cross-contamination are to be written in to each SOP as appropriate for the target organisms. Floors and work surfaces shall be non-absorbent and easy to clean and disinfect. Work surfaces shall be adequately sealed. Laboratories shall provide sufficient storage space, and shall be clean and free from dust accumulation. Plants, food, and drink are prohibited from the laboratory work area.

10.6 Lock Out and Tag Out Procedures

If any piece of laboratory equipment is not functioning properly, proper tag out or lock out procedures are to be followed according to established written procedures. No piece of equipment that is properly locked out or tagged out is to be used for analytical purposes.

11.0 QUALITY ASSURANCE ACTIVITIES

Several assessment and oversight activities are to be conducted in order to prevent and correct non-conformities and other quality management system issues. These include preventative actions; identifying and tracking non-conformities; implementing and monitoring informal and formal corrective actions, internal auditing and external oversight; performance testing; performing root cause analysis; management review. The following sections provide details on implementing good practice for these activities.

11.1 Preventative Actions

Preventative actions and corrective actions are often thought to be synonymous. Although they can be handled with the same process preventative action by definition occurs prior to non-conformity. Preventative action often occurs informally by independent testing laboratory staff involved with the quality management system. If an independent testing laboratory can foresee an event or a process at risk, the laboratory management often takes action to avert the potential loss of control and avert disruption to operations.

Preventative actions applied may include training on upcoming new methods, hiring back-ups, and training them before employee turnover, maintenance on an instrument that is known to decline in performance during a certain timeframe etc.

This practice is to be recorded to show the effectiveness of client feedback, management review, and staff engagement in the independent testing laboratory quality management system. The concern of potential nonconformance and supporting information can be entered into the same tracking and use the same forms as corrective action with an examination of potential nonconformance based on the observed possible root cause.

All employees are to be trained in recording potential causes of nonconformance, whether in a separate tracking system or in the same system as the Corrective Action Tracking System and these are to be discussed at management review meetings.

An effective procedure to involve staff in the recognition of causes at the root of nonconformances requires setting aside roughly 10 minutes of regularly conducted department meetings to allow the quality manager to address nonconformances and client complaints. Developing this communication between the QA department and individual departments, explaining the importance to the continual improvement of independent testing laboratory operations and procedures, explaining the importance of tracking the corrective and preventative actions as a tool that is both a best practice and a certification requirement all serve to meet data integrity requirements. Feedback at such meetings of successful corrective actions taken as a result of nonconformances and preventative actions succeed in bolstering the quality assurance procedures in place.

11.2 Complaints

The independent testing laboratory is to demonstrate a commitment to continuous improvement and service to the client in all of its documentation of communication with clients.

The independent testing laboratory shall have a detailed definition of a client compliant in its procedures and these procedures shall apply to all staff of the independent testing laboratory in order to capture complaints regardless of the method through which they are received. The independent testing laboratory shall track all complaints for evaluation during the Management Review and shall outline in the procedures which types of complaints are to be elevated to the proper independent testing laboratory personnel member in order to be included in the formal Corrective Action system. The types of complaints that shall be elevated to require formal corrective action include, but are not limited to:

- *Data/report amendments,*
- *Non-Conformance affecting data quality,*
- *Non-Conformance to lab procedures,*
- *Non-Conformance to MDPH Protocols and QAPP*
- *Sampling Non-Conformance,*
- *Request for Raw Data pertaining to report that is unavailable,*
- *Requests for Re-Runs not met, and*
- *Re-Sampling and Re-analysis results differ.*

The independent testing laboratory personnel that are responsible for investigation of any corrective actions are to have documented training on root cause analysis. Laboratory investigation records are to include an assigned corrective action that follows from the root cause analysis and are to include records of follow-up on the corrective action to ensure effectiveness. Follow-up records are to include date of follow-up, person performing the follow-up, records reviewed, and an evaluation of whether the corrective action, and therefore the root cause analysis, was sound enough to correct the problem and prevent recurrence.

It is helpful to define clearly complaints that need to be recorded in order to track client feedback that pertains to quality. These procedures should be required in the training plans of all staff as the staff members who most often receive complaints, such as sample receipt personnel, are sometimes unaware that it is necessary to record these and have them investigated.

11.3 Identifying and Recording Non-Conformances

The independent testing laboratory is to have procedures describing the process by which non-conformances are identified and recorded and the formal Corrective Action process is to be used if these nonconformances are defined in the laboratory procedures as requiring formal Corrective Action.

All employees are to be trained to identify non-conformance and to document the occurrence according to independent testing laboratory procedure. When nonconformance is detected or suspected within independent testing laboratory operations, the laboratory management is notified and is to evaluate the situation and proceed in accordance with the laboratory procedure for nonconformances. An evaluation of the significance of the nonconformance is to be made by authorized individuals within the independent testing laboratory management.

A nonconformance is a result, condition, or action that falls outside procedural or quality management system requirements.

Nonconformance may consist of any of the following:

- Nonconforming Laboratory Analyses:
  - Invalid test results;
  - Incomplete test reports;
  - Incorrect equipment information;
  - Incorrect data reduction and calculation of sample results;

    - Late test reports;
    - Deviation from laboratory standard operating procedures;
    - Other
- Deviations from laboratory quality management system policies and procedures (*e.g.*, Quality Manual, SOPs);
- Analytical and/or general equipment issues;
- Software issues;
- Third-party Vendor services or products that do not meet the requirements of the laboratory quality management system
    - Reagents or standards which are expired or do not meet laboratory specifications;
    - Nonconforming service (*i.e.* contract laboratory analysis);
    - Damaged materials or client samples; and
    - Other.
- Client error:
    - Incomplete or failure to provide comprehensive testing specifications
    - Inappropriately preserved, transported or documented materials or samples;
- Other as applicable.

A major nonconformance is a situation that affects critical laboratory processes and operations and requires immediate attention and action, a situation that may cause significant impact to data quality or utility. A minor nonconformance is a situation that affects laboratory operations and could become a major nonconformance if it recurs frequently. With frequent recurrence, it becomes a threat to the laboratory operations or is a situation that may cause changes to laboratory environments if not controlled. Minor nonconformances are to be tracked to ensure they are random and not systemic.

Each identified nonconformance requires prompt action and may require additional action, including the suspension of a particular independent testing laboratory process until an investigation can be performed. The quality manager (or designee) has the authority and responsibility to lead the investigation of a nonconformance, to determine root cause and to identify the corrective action needed.

When a nonconformance is recognized as major nonconformance, an investigation is to be initiated by the independent testing laboratory as described in Section 11.5.1. When a nonconformance is recognized as a minor nonconformance the independent testing laboratory shall determine whether an investigation is to be initiated and whether formal corrective action is warranted. Each identified nonconformance is to be recorded by the independent testing laboratory and the record is to indicate the nature of the nonconformance and the action taken.

The RMD is to be notified when analytical testing requests do not have sufficient information regarding testing specifications or when sample receipt issues are encountered. Nonconforming or out-of-specification (OOS) samples are to be identified, segregated and quarantined (whenever possible) to a designated hold area.

Nonconformance reports shall be analyzed for trends during the management review meetings and a determination shall be made as to whether an investigation and/or additional action(s) are required.

11.4 Informal Corrective Actions

Informal Corrective actions are comprised of activities defined in the procedures in response to minor, nonsystematic non-conformances, which can be corrected in order to avoid data impact but do not require the full process of formal corrective action.

The independent testing laboratory may choose to perform informal corrective action when a nonconformance is identified but does not impact the client data or the effectiveness of the laboratory quality management system in a significant manner provided that the departure from procedure is random and does not consistently recur. *These are to be defined in the independent testing laboratory SOPs with simple corrective actions assigned and they shall be tracked to identify any patterns or reoccurrence which would indicate they required formal corrective action. Informal corrective actions are to be reviewed, approved, recorded, and reviewed by appropriate personnel designated in the associated procedures.*

Departures that can be handled with informal corrective action include but are not limited to single QC failures, instrument performance that exceeds warning limits, a missed entry in a support record such as a balance verification and other events that are due to human error but upon investigation are found to not impact the sample or data integrity.

11.5 Performing Formal Corrective Action

Formal Corrective Actions are comprised of activities designed to address quality management system failure. Formal corrective action shall be performed for the following events:

- *External audit findings (Client or regulatory);*
- *Internal audit findings;*
- *Management review findings;*
- *Recurring technical analysis departures such as calibration failures, qc failures, decreased instrument performance, and missed components in primary or secondary data review;*
- *Proficiency test failures;*
- *Client complaints pertaining to issues other than administrative or unavoidable circumstances;*
- *Recurring sample rejection due to laboratory container shipment errors;*
- *Records that cause breaks in traceability;*
- *Data recalls or amended reports;*
- *Failure to maintain schedules effectively for document review, internal audits, demonstrations of capability, or training.*

11.5.1 ***Root Cause Analysis***

The procedure for corrective action shall start with an investigation to determine the root cause(s) of the problem. Root cause analysis is the key and sometimes the most difficult part in the corrective action procedure. Staff that are designated and authorized to investigate major nonconformances are to be provided documented root cause analysis training. Investigation and root cause analysis records are to be kept including

data packages that identify the nonconformance so that corrective action effectiveness can be monitored on an ongoing basis.

Often the root cause is not obvious and thus a careful analysis of all potential causes of the problem is required. Potential causes could include customer requirement training, consumables, or equipment and its calibration. It is recommended that root cause analysis be performed by two methods or two individuals to examine several possible causes. If the root cause is not clear, an individual not involved in the day-to-day operation under study can be a valuable addition to the team.

11.5.2 ***Assignment of Corrective Actions***

Corrective action is the action taken to eliminate the causes of an existing non-conformity, defect, or other undesirable situation in order to prevent recurrence. *The independent testing laboratory is to select, document and implement corrective actions in a timely manner. The corrective actions selected by the independent testing laboratory are to be congruent with the result of the root cause analysis, the address the problem and prevention of problem recurrence. The degree of corrective action is to be appropriate to the magnitude and the risk of the problem. The independent testing laboratory is to set a goal date for the completion of the corrective action and identify in the records the individuals responsible for implementation and the components to be tracked to ensure effectiveness.*

11.5.3 ***Monitoring of Corrective Actions***

The independent testing laboratory is to monitor the results to ensure that the corrective actions taken have been effective. The independent testing laboratory is to assign an appropriate goal date for the completion of the corrective actions upon implementation. The independent testing laboratory is to record the follow-up activities and records of effectiveness over an appropriate time period. Closed corrective actions are to be included as a detailed component in the next internal audit. If the departure was severe enough, the corrective action is not to be considered closed until an internal audit of the affected parts of the system has been performed. (ISO/IEC 17025:2005 Section 4.11.5)

11.6 Internal Audits

Annually, the independent testing laboratory is to prepare a schedule of internal audits to be performed during the year. These audits verify compliance with the requirements of the MDPH protocols, and the requirements of the laboratory QMS, including analytical methods, SOPs, the Quality Manual, ethics policies, data integrity, other laboratory policies, and the ISO 17025 Standard. These audits are to be performed by trained and qualified personnel who are, wherever resources permit, independent of the activity to be audited. While the Quality Manager is responsible for scheduling of the Internal Audit, it is recommended that Supervisors and Staff are included in this process in order to promote ownership and engagement in the laboratory's activities.

In addition to the scheduled internal audits, it may sometimes be necessary to conduct special audits as a follow-up to corrective actions, PT results, complaints, regulatory audits or alleged data integrity issues. These audits address specific issues.

The area audited, the audit findings, and corrective actions are to be recorded. Audit results are to be reviewed after completion to assure that corrective actions were implemented and effective. Records are to be kept pertaining to the scheduling of internal audits, the timely completion of audit activities, the number of findings arising from audit activities, and the timely resolution of the corrective actions implemented as a result of audit activities. These metrics are to be included in the Management Review meeting(s).

While the ISO 17025 requirement is for the entire Internal Audit to be completed annually, it is often scheduled in a staggered manner to avoid the bottleneck of such a large undertaking. In addition, although the standard states that the auditor must be "independent of the activity performed", this does not preclude supervisors and backups auditing analytical work that is performed by the primary analyst within the same department or by the same methodology as the auditor performs. There are other schemes that should be considered in order to engage all independent testing laboratory staff further in the internal audit activities and resulting corrective actions. This assignment of audits can actually encourage cooperation and consistency throughout the department or technology.

11.7 External Oversight

Laboratories performing analysis of medical marijuana products for regulatory reporting to MDPH shall participate in the accreditation activities of the ISO accreditation body (AB), including compliance to the requirements addressing client or RMD audits, and monitoring, auditing, and on-going examination as required by MDPH. Laboratories are to make staff and records available to the RMD, MDPH, and the ISO AB upon request for audits, desk reviews, and investigation of complaints at all times. The laboratories are to be prepared for these activities by maintaining a clear and organized records management system and procedures to compile data in simplified formats.

The MDPH program may employ a variety of methods to assess the ongoing quality produced by laboratories. These activities may be conducted to address events such as complaints, product failures, or recalls, the potential for litigation, and rule changes or implementations. They shall also address on-going efforts of MDPH such as gathering data and information for education, reporting, research, or standardization with other state health programs.

Deliverables that may be requested by MDPH may include independent testing laboratory SOPs, full data packages, including all QC and raw data associated with samples, requests for specific reports or electronic data deliverables (EDD) formats that compile data differently than a standard client report. MDPH or its agents may conduct unannounced onsite inspections. These activities may result in suggestions by MDPH of opportunities for improvement and are encouraged to maintain open dialogues and participate in cooperative efforts outside of the scope of the activities defined here.

11.7.1 ***Confidential Business Information (CBI) Considerations***

During on-site audits, on-site auditors may come into possession of information claimed as business confidential. A business confidentiality claim is defined as "a claim or allegation that business information is entitled to confidential treatment for reasons of

business confidentiality or a request for a determination that such information is entitled to such treatment."

When information is claimed as business confidential, the independent testing laboratory is to place on (or attach to) the information at the time it is submitted to the auditor, a cover sheet, stamped or typed legend or other suitable form of notice, employing language such as "trade secret", "proprietary", "business confidential" or "company confidential". Confidential portions of documents otherwise non-confidential shall be clearly identified. CBI may be redacted or edited to eliminate references to client identity by the responsible independent testing laboratory official at the time of removal from the laboratory. However, sample identifiers or other components necessary to the nature of the review, may not be obscured from the information. Alternate numbering systems and crosswalks may be employed if sample identifiers jeopardize the client confidential information.

11.7.2 ***Corrective Actions for Internal Audits and External Oversight***

The independent testing laboratory is identify who is responsible for initiating corrective action where a nonconformance is found that could reccur (beyond expected random QC failures) or where there is doubt about the compliance of the independent testing laboratory to its own policies and procedures. In addition, the independent testing laboratory shall identify the personnel responsible for monitoring and recording the corrective action

Internal or external audit findings are responded to within the time frame agreed to at the time of the audit. The response may include action plans that could not be completed within the response time frame. A completion date is established by independent testing laboratory management for each action item and included in the response.

Audit findings that cast doubt on the effectiveness of the independent testing laboratory operation to produce data of known and documented quality or that question the correctness or validity of sample results shall be investigated. Corrective action procedures above are to be followed. The RMD is to be notified in writing if the investigation shows the independent testing laboratory results have been negatively affected and the MDPH testing requirements have not been met. The RMD is to be notified as soon as practical after the independent testing laboratory discovers the issue. Independent testing laboratory management shall ensure that this notification is carried out within the specified time frame.

11.8 Proficiency Test Samples

11.8.1 ***PT Sample Handling, Analysis and Reporting***

Proficiency Testing (PT) samples are a pillar of ISO accreditation in that they are meant to demonstrate the independent testing laboratory's ability to report accredited analysis data of unknown client samples within a defined accuracy window. They are samples spiked with known concentration levels of target analytes prepared by a third-party organization accredited to ISO 17043.

At a minimum, the independent testing laboratory is to complete the requirements of their accrediting body, which includes one successful PT for each method and matrix included in Massachusetts regulation, if available, prior to reporting samples for compliance and one additional PT for each method and matrix combination annually.

Although a double-blind PT is not currently available, the independent testing laboratory is to make every effort to treat the PT according to their procedures. Also, in order to make an effective statement as to the independent testing laboratory's capability of accurately analyzing an unknown client sample, the independent testing laboratory shall not treat the PT sample in any way that differs from the handling of a client sample. This is demonstrated by the records relating to the PT sample from sample receipt through to reporting.

This includes the following instructions but can also include any handling of the PT that would give the independent testing laboratory additional assurance of the result that would not be available for client samples.

To demonstrate independent testing laboratory proficiency, PT samples are to be treated as and analyzed with typical samples in the normal production process where possible, including the same sample log-in procedures analysts, maintenance triggers, preparation, calibration, QC and acceptance criteria, sequence of analytical steps, number of replicates, data analysis, manual integrations, identification, and confirmation procedures. PT samples are not analyzed multiple times unless routine samples are analyzed multiple times. When PT samples present data analysis challenges such as high concentrations or coelutions, those challenges are to be addressed as they would with a client sample.

The type, composition, concentration, and frequency of QC samples analyzed with the PT samples are the same as with typical samples.

Whenever possible, the PT sample is to be prepared and analyzed with other samples to avoid having a QC set unique to the PT. The PT cannot be chosen for spiking or duplication within a batch consistently, but if there are no other samples in-house for the analysis, the required QC for a batch is to be performed.

Prior to the closing date of a study, independent testing laboratory personnel are not to:

- *Subcontract analysis of a PT sample to another laboratory that is to be reported for accreditation purposes.*
- *Knowingly receive and analyze a PT for another laboratory that is to be reported.*
- *Communicate with an individual from another laboratory concerning the analysis of the PT sample.*
- *Attempt to find out the assigned value of a PT from the PT Provider.*
- *Perform maintenance or calibration on an instrument when the data quality samples or instrument performance data would not normally necessitate such actions.*
- *Provide additional verification, validation, or review.*
- *Analyze the sample in multiple batches, on multiple instruments, or by multiple analysts.*

11.9 Management Review

Independent testing laboratory management is to review the laboratory quality management system (QMS) and technical operations annually, and may perform these reviews on a more frequent basis at the discretion of the laboratory management.

All employees are to be trained in entering potential causes of nonconformance and these are to be discussed at regular intervals and summarized at management review meetings. The effectiveness of the participation and documentation of nonconformances shall be evaluated along with the effectiveness of the corrective actions that were implemented.

Management review is intended as a resource for help in other areas of the quality management system but is not a substitute for performing internal audits.
It is recommended that the independent testing laboratory management meet more frequently and review sections of the quality management system and technical operations on a rotating basis to cover all sections within a year. A process by which more frequent section review with respect to the quality management system can be achieved with success and acceptance from independent testing laboratory operations should involve the QAM and independent testing laboratory director/manager scheduling and performing department specific quarterly meetings. It is beneficial that these meetings discuss the successes of completing corrective actions, encouraging the continual feedback from staff regarding department operations and throughput, successful response to any audit findings and client complaints, and any ideas to improving overall processes and procedures.

11.9.1 ***Management Review Topics***

The following are to be reviewed to ensure their suitability and effectiveness:

- *The suitability of policies and procedures;*
- *Reports from managerial and supervisory personnel;*
- *The outcome of recent internal audits;*
- *Prior, ongoing and aging corrective and preventive actions;*
- *Effectiveness of previous corrective and preventive actions taken;*
- *Changes in external and internal conditions relevant to the quality management system;*
- *Assessments by external bodies;*
- *The results of interlaboratory comparisons or proficiency tests;*
- *Changes in the volume and type of the work;*
- *Customer feedback;*
- *Complaints;*
- *Recommendations for improvement; and*
- *Other relevant factors, such as QC activities, resources, and staff training.*

Findings from management reviews and the actions that arise are to be recorded. Independent testing laboratory management is to verify that the actions are discharged within an appropriate and agreed upon timeline. If needed, a corrective or preventive action shall be initiated for identified action items examined during the management review. The laboratory is to follow their corrective or preventative action items until they

are declared closed and informal (i.e., the results of the investigation are implemented and follow-up has been completed).

11.10 Data Review, Verification, Validation and Reconciliation with DQOs

The independent testing laboratory shall have procedures that include two levels of full data review of every component of the analysis. The primary review is typically performed by the analyst and the secondary review by someone trained in the independent testing laboratory quality management system and, if possible, with a demonstration of capability (DOC) in the analysis. If the independent testing laboratory staff is limited, the second level of review is to be performed by someone who has demonstrated technical knowledge of the analysis according to the independent testing laboratory training procedures.

The independent testing laboratory training standard operating procedure, (and/or the data review procedure should such exist), should state qualification procedures needed for adequate secondary review of data from a primary analyst. Basic training requirements as documentation of a read/understood of the SOP, a knowledge of the instrumentation used to produce the result, and established competency in the quality assessment of data are minimum requirements an independent testing laboratory establishes in order to obtain the required integrity of the result reported.

The following elements are required when reviewing data in addition to any elements contained in the reference methods, laboratory SOPs, and relevant state and federal regulation:

- *Technical data review records are to contain associated preparation and batch IDs and references to controlled versions of the SOPs used in preparing and analyzing the samples.*
- *Chemistry analyses review is to include a review of all required data elements such as sample prep conditions, chromatograms, identification of peaks, manual integrations, calibration criteria, QC samples, sample preservation and hold times, reporting ranges, and data upload or transcription.*
- *Microbiology analysis review is to include a review of the method requirements such as incubator temperature ranges and minimum times of incubation, and acceptability of the criteria contained in the DQO tables.*
- *Review of microbiological data shall also include the times of analysis, the temperatures of the support equipment and a periodic review of the physical count (as marked on a plate or re-counted from a saved plate) against the written record.*
- *For microbiological data, regardless of schedule, all QC checks such as air checks, media checks, dilution water checks, equipment-cleaning checks and any other checks pertinent to the analysis are to be traceable to results and are to be treated as bracketing checks if a failure occurs.*

For all analyses, periodic review of support equipment calibration and verification records, standard and reagent preparation records, and sample receipt records are to be performed.

This review is to be performed on a frequency defined by independent testing laboratory management, based on the amount of data the independent testing laboratory is prepared to recall and reissue and the amount of clients they are willing to notify based on the timeframe.

It is recommended that the reviews happen frequently enough to notify clients of any possible error before it is too late to re-sample and re-analyze the batch before it is sold by the client.

The independent testing laboratory is to have procedures for a full review by the quality assurance manager (or designee) of a minimum of 10% of client sample events from sample receipt to sample reporting.

The independent testing laboratory is to have procedures that outline verification of data in cases where the analytical result may be in doubt due to historical inconsistency, possible contamination, or carryover, and other possible causes of inaccuracy as identified by the professional judgement of competent personnel and procedural triggers based on the evaluation of quality control sample results and other DQIs.

- *Carryover procedures are to be developed and are to identify steps in the analysis that contain risk of carryover of target analytes to the subsequent samples and provide detail on verification that sample detections are not caused by contamination from other sources during primary and secondary data review. They are to include the reanalysis of samples following a sample of unknown matrix that have significant detections at levels determined by the independent testing laboratory based on observed carryover per analyte in the method development stages. If a sample has detections above this concentration, the independent testing laboratory shall re-analyze any samples following any samples with significant detections in the same target analytes. If the independent testing laboratory places instrument blanks before or after QC samples, the carryover procedures shall match the concentration of those samples. These evaluations shall be documented. Samples associated with visual detections in blanks or rinses, even if values are below the LOQ are to be considered for reanalysis if the same target analytes are detected.*

In the event that the instrument can be programmed to add additional rinse times when a certain concentration is reached, the method shall apply to both QC and samples and the samples are to be evaluated as above for carryover if the rinse is extended

- *Verification of sample results that fall close to the action limits shall be performed. A sample is considered close to the action limit if the result exceeds the precision criteria for the method.*

- *If sample verification is performed and the results do not agree with the initial analysis and there is not an assignable cause, such as a misinjection, the sample shall be evaluated a third time. A favorable sample result, whether from an initial run or a verification run cannot be arbitrarily chosen and verification shall include at a minimum, a third confirmation analysis.*

- *Data verification is performed by assessing the combined data quality indicators such as results of the data review and the review of support documentation as well as an understanding of expected data results such as the expected cannabinoid amounts in known matrices. Data validation is performed on an ongoing basis by the independent testing laboratory staff as defined in these procedures to ensure that the reported result meets the criteria of the independent testing laboratory and is of known and appropriate quality according to the independent testing laboratory's quality management system and the relevant standards and regulations.*

11.11 Treatment of Out-of-Specification (OOS) results

The independent testing laboratory is to implement an approved procedure for investigating OOS test results, including RMD samples that fail to meet current MDPH Protocol limits for regulated contaminants and QC sample failures.

The procedure(s) are to detail the circumstances, criteria, and documentation required to conduct and complete an investigation of OOS results. The independent testing laboratory is to provide documented training to the procedures. Include in the procedure the assessment of independent testing laboratory practices associated with the OOS result and include details for retesting samples. The specifications for whether to retest are to be based on the objectives of the testing and clearly defined decision rules.

The independent testing laboratory is to specify the maximum number of retests to be performed on a sample in advance in the written SOP. The number may vary depending upon the variability of the particular test method employed, but shall be based on scientifically sound principles. In the predetermined retesting procedure, the independent testing laboratory is to determine a point at which the additional testing ends and the batch of product are statistically evaluated. In addition, the independent testing laboratory is to develop a corrective action procedure for the review of unsatisfactory data.

The independent testing laboratory is to establish criteria with instructions for reporting of results in this procedure. In the case of a clearly identified laboratory error, the retest results would substitute for the original test result. The independent testing laboratory is to retain all original data and record an explanation of the error. The records shall include the initials of all personnel involved in the review or the investigation, date, a discussion of the error and supervisory comments. If no laboratory or calculation errors are identified in the first analysis, there is no scientific basis for invalidating initial OOS results in favor of passing retest results. All test results, both passing and suspect, are to be reported and the report shall contain all of the information necessary for the client or regulatory authority to interpret the result and understand the related factors of uncertainty.

12.0 REPORTING OF RESULTS

12.1 Significant Figures

Unless directed otherwise in writing by MDPH or its designated consultant, or unless conflicting state or regulatory agency requirements exist, analytical results for chemical analyses are to be reported as if three digits were significant. For analyses with regulatory action limits, the independent testing laboratory shall report in the state tracking system with

the amount of significant figures in the action limit with one additional significant figures, if achievable based by the method. For plate counts, round results to two significant figures. Application of significant figures is not to result in decimal places added to any value as it approaches a method LOQ/reporting limit (RL). In the event that a discrepancy exists between the guidelines provided above and project-specific requirements, the RMD and/or MDPH are to be contacted for resolution.

12.2 Reporting Results Obtained from Subcontractors

When the test report contains results of tests performed by subcontractors, these results are to be clearly identified. The subcontractor is to report the results in compliance with the requirements of RMD, ISO 17025 and relevant state and federal regulation. The independent testing laboratory is responsible for the results of the subcontractor, and is to have procedures detailing the review of the subcontractor results for conformance and known data quality.

The independent testing laboratory may reproduce these reports in full within the laboratory official report. This is recommended as it is easy to identify the subcontracted laboratory, the subcontracted results. In addition, the primary laboratory takes responsibility for the subcontracted laboratory results as it pertains to data review and reports. If the report is reproduced in full, this mitigates the risk of transcription errors, LOQ differences, and missing narratives.

12.3 Reporting Not-Detected and Low-Level Results

Generally, results that are not detected above the LOQ are to be reported as "<" followed by the numerical value of the sample-specific LOQ. The sample specific LOQ value is the default LOQ value determined in accordance with this QAPP, adjusted for any variations in sample size analyzed and final volume of the extract or digestate (i.e., dilution factor).

Results below the LOQ may only be reported if authorized in writing by MDPH. Results below the LOD are never to be reported. For guidance on the determination of LOD and LOQ, refer to Sections 9.2.2 and 9.2.3 of this document.

12.4 Amendments to Reports

Material amendments to a report after issue shall be made only in the form of a further document, or data transfer, which includes the statement:

"Supplement to Test Report number...[or as otherwise identified]", or an equivalent form of wording. Such amendments are to meet all the requirements of ISO 17025:2005E. When it is necessary to issue a complete new report, the report is to be uniquely identified and is to contain a reference to the original report that it replaces.

12.5 MDPH-specific Reporting Requirements

The results of each test, or series of tests carried out by all laboratories performing analyses for the MDPH Medical Marijuana Program are to be reported accurately, clearly, unambiguously and objectively, and in accordance with any specific instructions in the MDPH Protocol for Sampling and Analysis of Finished Medical Marijuana Products and

Marijuana-Infused Products for Massachusetts Registered Medical Marijuana Dispensaries (Section 8.0), Protocol for Sampling and Analysis of Environmental Media for Massachusetts Registered Medical Marijuana Dispensaries, as well as ISO/IEC 17025:2005(E), Section 5.10.

Specific operational requirements from the MDPH Protocols and ISO 17025 standard with regard to results reporting are combined and summarized below.

The accurate reporting of results is an important aspect of gathering information in a way that is consistent and appropriate for the assessment of the quality of medical marijuana products. The MDPH may require data to be reported in certain formats that are not specified in this QAPP, with specific compounds and quantitation or limits of detection for reporting. Without written permission provided by the MDPH, data are not to be reported as a quantitative estimate below the method LOQs.

Data may only be reported as quantitative estimates or with data qualifiers if a QC sample failure occurs during reanalysis after the corrective actions described in Appendix A, Tables 03-09 have been implemented and documented. Only the following QC sample failures may result in the reporting of qualified data:

- *Contamination observed in the method blank at concentration levels that exceed the criteria listed in Appendix A, Tables 03-08 for chemical analyses.*
- *The recovery of target analytes in the LCS/LCSD or MS/MSD fail to meet the criteria established in Appendix A, Tables 03-08 for chemical analyses.*
- *The recovery of surrogate and/or internal standard compounds fails to meet the criteria established in Appendix A, Tables 03-08 for chemical analyses.*
- *Water bath and/or incubator temperature exceeds temperature window during microbial analysis and insufficient sample exists to repeat analysis.*
- *Ambient air checks fail to meet acceptance criteria for microbial analyses as prescribed on Table 09, Appendix A.*
- *QC sample (e.g. laboratory duplicates, negative controls, positive controls, etc.) failures during microbial analyses as prescribed on*
- *Table 09, Appendix A, but insufficient sample is available to repeat analysis.*

*Data **are not to be** reported with instrument calibration and/or continuing calibration failures. The corrective actions described in Appendix A, Tables 03-09 shall be followed if the instrument calibration or continuing calibration check fails. Data **are not to be** reported with sample receipt, holding time or other documented sampling issues that may affect sample integrity as described in Appendix A, Table 02.*

*When reporting qualified results, the qualifier (e.g., J, *, etc.) shall be presented immediately adjacent to the reported result and/or as a footnote reference and an explanation of the qualifier shall be included within the client report. If a QC sample fails then the corrective actions presented in the DQO tables presented in Appendix A are to be followed.*

12.5.1 ***Report Template***

Each independent testing laboratory is to enter results into the MDPH standardized results report template presented in Appendix C*. This reporting template is intended to*

eliminate reporting differences between laboratories, while capturing comprehensive and complete laboratory records across all laboratories within the MDPH Medical Marijuana testing program. The template offers a common ISO/IEC 17025 compliant reporting format that shall be used to unify and standardize the information and tools being provided to patients and providers of healthcare.

The template contains two major sections: (1) a cover page, which contains information about the sample being tested and the lab authorization of the reported results, and (2) the analytical results of the sample testing. Many fields in the template display notes when selected that provide instruction for data entry. Some fields are restricted to a list of options; this is portrayed in the template using drop-down lists. Fields with data restrictions and fields that apply to particular types of samples are noted within the data dictionary. As the template is refined, some fields may be optional or even removed if deemed non-essential. The report template includes the following sections to document the information described below:

COVER PAGE

The cover page contains fields that are included within several different "boxes" or sections.

Box A: Report Heading

Box A contains basic descriptive information about the independent testing laboratory report.

A1. Lab Name: Name of the independent testing laboratory issuing the report.

A2. Lab Address: Address and other contact information of the independent testing laboratory.

A3. Lab Sample ID: Sample identification number assigned by the independent testing laboratory. Each lab report should contain information about one sample, and the sample ID number should be unique from all other reports from that laboratory (except for revised versions of previously submitted reports).

A4. Report Title: Title of the report.

A5. Revision number (if necessary): To be included if report is a revision of previously submitted report.

A6. Report Date: Date on which the laboratory report is finalized and submitted/published (mm/dd/yy).

BOX B: RMD Info

Box B includes information about the client transaction.

B1. RMD Name (List - unrestricted): Name of the Registered Marijuana Dispensary (RMD) that submitted the sample, using a 2-5 letter code associated with that RMD.

B2. RMD Address: Address and other contact information of the RMD, specifically the cultivation/production location from which the sample was collected and shipped.

B3. Manifest/COC Number: Identifier of the Manifest or Chain-of-Custody form used when sample was relinquished to the independent testing laboratory.

B4. Date Received: Date the sample was delivered to the independent testing laboratory.

BOX C. Sample Identification

Box C contains the various RMD identifiers relevant to the sample. Identifiers are assigned by the RMD following the guidelines in Section 5.0 of Protocol for Sampling and Analysis of Finished Medical Marijuana Products and Marijuana-Infused Products for Massachusetts Registered Medical Marijuana Dispensaries (henceforth referred to as "MDPH Protocols").

C1. RMD Sample ID: Sample identifier assigned by the RMD. An RMD sample ID is unique to each sampling event. An RMD Sample ID may be associated with one or more laboratory reports, as the sample could be split after collection and sent to multiple labs for testing, or could be re-tested. Multiple RMD sample IDs may be associated with one Batch ID if the production batch was sampled on multiple distinct occasions.

C2. Batch ID: Unique alphanumeric ID of the production batch from which the sample was collected. Production batch is defined in Section 5.0 of the MDPH Protocols as:

"Production Batch means a batch of finished plant material, cannabis resin, cannabis concentrate, or MIP made at the same time, using the same methods, equipment, and ingredients. The RMD shall assign and record a unique, sequential alphanumeric identifier to each production batch for the purpose of production tracking, product labeling, and product recalls. All production batches shall be traceable to one or more marijuana cultivation batch(es)."

C3. Parent Batch ID: The production or cultivation batch ID(s) of the parent product used in the production of the sample. For resin and concentrate samples, the parent batch ID shall be the batch ID(s) of the flower/plant material used to produce the resin or concentrate. For MIP samples, the parent batch ID shall be the batch ID(s) of the concentrate/oil used to produce the MIP. For flower samples, the parent batch ID shall be the ID of the cultivation batch(es) that produced the finished plant material.

BOX D: Picture of Sample

D. Sample Picture: Picture of delivered sample prior to laboratory analyses.

BOX E: Sample Properties

Box E describes physical properties of the delivered sample.

E1. Sample Size: Weight or volume of the sample upon receipt. Must be reported in weight or volume units, such as grams or milliliters; "number of units" is not permitted for this field (see E2).

E2. Number of servings/units: The number of "servings" or units present in the submitted sample. This field is required for marijuana-infused-product samples only.

E3. Matrix (list): Sample matrix. The field is limited to a list of the matrix categories described in Section 5.3 of the MDPH Protocols (Liquid; Plant Material or Friable Solid; Solid or Semi-Solid) and an option for "other," which should be specified in adjoining cell.

E4. Sample Condition: The condition of the sample upon receipt. This includes any notable observations (e.g., presence of moisture).

E5. Re-test: Indicate if the laboratory report represents a re-test of an RMD sample (i.e., Yes or No).

E6. Remediated Sample: Indicate if the RMD sample comes from a remediated batch (i.e., Yes or No). If "Yes" is selected, a description of the batch remediation should be provided.

BOX F: Product Characterization

Box F includes several fields used for characterizing the tested product.

F1. Production Stage (list - restricted): Stage of medical marijuana production from which sample was collected and includes: (1) Plant Material; (2) Cannabis Resins and Concentrates; and (3) Marijuana-Infused Product (MIP). All products must be placed into one of the three categories because the production stage determines the contaminant tests required for the sample (see Exhibit 8b of the MDPH Protocols).

F2. Product Class (list): Second tier of product categorization. Each production stage classification (F1) is divided into one or more product class categories, as displayed on Table 7 below.

Table 7 Production Stage Classification for Medical Marijuana Products

Production Stage	Product Class
Finished Plant Material	Flower
Cannabis Resin & Concentrates	Oil Resin Shatter Wax
Marijuana-Infused Product (MIP)	Edible (Food, Drink, Capsule) Suppository Tincture Topical Other

F3. Product Type: Description of the product type. Examples of a product type description include: plant material (e.g., flower); cannabis resin and concentrates (e.g., kief, bubble hash, rosin, wax, shatter, vape oil, RSO, etc.); MIPs (edibles) (e.g., beverage, capsule, brownie, bar, cookie, gummy, lozenge, nugget, etc.); and MIPs (non-edibles) (e.g., tincture, spray, lotion, patch, suppository, etc.).

F4. Retail Name: Retail name of the finished product. The retail name is included primarily to provide supplemental descriptive information, and to help understand how products are being presented to patients. Some product sample may not be intended for sale (e.g., oil intended to be used in the production of a MIP) and therefore this field may be left blank. Include in the

specify field the species of flower (e.g., C. sativa, C. indica, hybrid), as well as the cultivar or strain name (e.g., Bruce Banner).

F5. Grow Material: For flower samples only; the type of grow material used during the cultivation of the marijuana plant from which the finished plant material was harvested from.

F6. Intended Route of Consumption: The consumption method intended for the product, as determined by the RMD. This field lists options "all uses" and "ingestion only," as well as options for inhalation and various absorption pathways (i.e., dermal, sublingual, rectal), and includes an "other" option with an opportunity to specify additional consumption routes.

F7. Extraction Solvent: The type of solvent used for cannabinoid extraction in the production of the sample. Solvent types commonly used for cannabinoid extraction include: Hydrocarbons, which includes n-Butane, iso-butane, and Propane; CO2 (supercritical fluid); alcohols, which includes ethanol; and lipids, which includes butter and vegetable oils.

BOX G. Test Types Run

This field includes a checkbox indicating which tests were performed on the sample. Each option in the check box corresponds to an individual subsection in the analytical results section of the template. The test types included in the checkbox represent all required tests for product samples, as outlined in Section 7.0 of *Protocol for Sampling and Analysis of Finished Medical Marijuana Products and Marijuana-Infused Products for Massachusetts Registered Medical Marijuana Dispensaries*, with an additional option to describe Terpene Profile.

BOX H: Authorization

Box H provides the independent testing laboratory's interpretations of the laboratory results and authorization of the report.

H1. Case Narrative, Laboratory Notes, and Statement: Write-up of case narrative including data interpretations. Any accreditations of certifications the laboratory wishes to report, any additional notes from the laboratory on the sample analysis, and any statements (i.e., "results relate only to the samples tested," "report may not be reproduced except in its entirety," etc.) are to be included in this field.

H2. Product Approval: Check box indicating interpretation of the results. Enter an "X" in a box to denote whether the product may be dispensed for all uses, may be dispensed as an ingestion only product, or may not be dispensed, based on the interpretation of the laboratory analyses as compared to the MDPH standard limits.

H3. Authorization signature: Signature from the independent testing laboratory authorizing the report and certifying the results.

ANALYTICAL RESULTS

The analytical results section is split into subsections representing each possible type of test that may be reported by the independent testing laboratory. Tests that are not run may be left blank. Each section includes the following general information in addition to the analytical results-specific sections:

Lab Sample ID: Sample identification number assigned by the independent testing laboratory. Each laboratory report should contain information about one sample, and the sample ID number should be unique from all other reports from that laboratory (except for revised versions of previously submitted reports); also reported in A3.

Analysis Date: Date(s) when the analysis was performed.

Analytical Method: The analytical method used (*e.g.*, GC-MS/MS, GC-FID, HPLC-MS/MS, HPLC-UV-Vis, ELISA, MPN with cultured enrichments, etc.).

Lab SOP #: Laboratory-specific standard operating procedure (SOP) used for sample preparation and all analyses (i.e., cannabinoid profile, heavy metals, microbiological contaminants, pathogenic bacteria, mycotoxins, residual solvents, pesticides, and terpene profile).

Analyst: Initials of the independent testing laboratory analyst who performed the analysis.

Narrative: Written narrative summary of the analysis, including relevant instrumentation and standard methods.

Test ID: Unique identifier given to each specific test run (i.e., cannabinoid profile, heavy metals, microbiological contaminants, pathogenic bacteria, mycotoxins, residual solvents, pesticides, terpene profile).

TABLE I. CANNABINOID PROFILE

Analyte: MDPH requires that products are tested for, at minimum, Δ9-THC, THCa, CBD, and CBDa. The cannabinoid profile table includes several rows without a defined analyte for the independent testing laboratory to enter additional cannabinoids that are tested beyond those that are required.

Result (Concentration): The measured concentration for each cannabinoid. Percentage dry weight (%wt) is the preferred unit of measurement, though any mass(cannabinoid)-to-mass(sample) can be used.

Result ("Dose" weight): Optional field – may be used for MIP samples. The calculated amount of cannabinoid in a single serving of a MIP. Requested units are mg/serving.

LOD: Limit of Detection.

LOQ: Limit of Quantitation.

TABLE J. HEAVY METALS ANALYSIS

Analyte: MDPH requires that heavy metal testing of MMJ product samples includes testing of Arsenic (inorganic) (As), Cadmium (Cd), Lead (Pb), and total Mercury (Hg).

Result (Concentration): The measured concentration for each analyte. Results are to be reported in parts-per-billion (ppb) units (or the equivalent µg/kg).

LOD: Limit of Detection.

LOQ: Limit of Quantitation.

Limits (All Uses): The MDPH standard limit of each analyte for products intended for all uses.

Limit Test (All Uses): Pass/Fail field for the "all uses" standard limits.

Limits (Ingestion Only): The MDPH standard limit of each analyte for products intended for ingestion only.

Limit Test (Ingestion Only): Pass/Fail field for the ingestion only standard limits.

TABLE K. MICROBIOLOGICAL CONTAMINANTS TEST

Analyte Symbol: Symbol for analyte test as described below on Table 8.

Test Analysis: Name of the analyte test as described below on Table 8.

Table 8 Microbiological Contaminant Analysis Symbol

Analyte Symbol	Test Analysis
AC	Total Viable Aerobic Bacteria
YM	Total Yeast & Mold
CC	Total Coliforms
EB	Total Bile-Tolerant Gram Negative Bacteria

Result: Reported result of the microbial test analysis.

Unit: Unit of measurement associated with the reported result.

Standard Limits: The MDPH standard limit of each analyte. The standard limits differ based on product characteristics (see Exhibit 6 of the MDPH Protocols), and shall have to be selected and entered into the table by the independent testing laboratory.

Limit Test: Sample pass/fail for the analyte standard limit test.

TABLE L. PATHOGENIC BACTERIA SCREEN

Analyte Symbol: Symbol for analyte test as described below on Table 9.

Test Analysis: Name of the analyte test as described above on Table 9.

Table 9 Pathogenic Bacteria Contaminant Analysis Symbol

Analyte Symbol	Test Analysis
ECPT	*E. coli* (O157)
SPT	*Salmonella*

Result: Reported result of the pathogen screen. As these analyses are usually indicator tests, result shall be "positive" or "negative," rather than a quantitative result.

Unit: Unit of measurement associated with the reported result.

Standard Limits: The MDPH standard limit of each analyte.

Limit Test: Sample pass/fail for the analyte standard limit test.

TABLE M. MYCOTOXIN TEST

Analyte Symbol: Symbol for analyte test.

Test Analysis: Name of the analyte test.

Result (Concentration): The measured concentration for each analyte. A cell in the table heading can be used to report the unit of measurement of the reported results. Parts-per-billion (ppb) units are preferred.

LOD: Limit of Detection.

LOQ: Limit of Quantitation.

Standard Limits: The MDPH standard limit for total mycotoxins.

Limit Test: Sample pass/fail for the analyte standard limit test.

TABLE N. RESIDUAL SOLVENTS TEST

Analyte: Analyte tested

Result (Concentration): The measured concentration for each analyte. A cell in the table heading can be used to report the unit of measurement of the reported results. Parts-per-million (ppm) units are preferred. When hydrocarbon analysis are reported, a "Total Hydrocarbons" row should be included which sums the results of n-butane, iso-butane, and propane. The total hydrocarbons value is to be evaluated against the 12 ppm standard limit.

LOD: Limit of Detection.

LOQ: Limit of Quantitation.

Standard Limits: The MDPH standard limit for residual solvent parameters.

Limit Test: Sample pass/fail for the analyte standard limit test.

TABLE O. PESTICIDE SCREEN

Analyte: Analyte tested

Result (Concentration): The measured concentration for each analyte. A cell in the table heading can be used to report the unit of measurement of the reported results. Parts-per-billion (ppb) units are preferred.

LOD: Limit of Detection.

LOQ: Limit of Quantitation.

Standard Limits: The MDPH standard limit for pesticides

Limit Test: Sample pass/fail for the analyte standard limit test.

Method QA/QC Test: Due to ongoing method development and validation for pesticides testing at the analytical laboratories, analytical tests have occasionally failed laboratory QA/QC tests for particular pesticides. Including this field in the results table shall enable the reviewer to make a quick determination on the reliability of the reported result.

TABLE P. TERPENE PROFILE

Analyte: Analyte tested.

CAS Number: CAS Number of the analyte being tested.

Result (Concentration): The measured concentration for each analyte. Percent weight (wt%) units are preferred.

LOD: Limit of Detection.

LOQ: Limit of Quantitation.

13.0 REFERENCES

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Appendix A
Data Quality Objective (DQO) Tables

Appendix A - Table 01
Method Reference Table

Analysis	Technology	Primary Reference(s)	Ancillary Reference(s)	Comment
Residual Solvents	GC/MS	• USP <467> Residual Solvents • USP <621> Chromatography • USP <736> Mass Spectrometry	• EPA 8260C*	*Consulted for additional GC-MS and Headspace specific objectives and details on quantitation
Residual Solvents	GC/FID	• USP <467> Residual Solvents • USP <621> Chromatography • USP <736> Mass Spectrometry	• EPA 8000D* • EPA 8015D	*Consulted for additional chromatography confirmation requirements
Pesticides	LC/MS/MS	• AHP (2013) • EPA 1694*		*The AHP does not discuss methodology for the most current limits of pesticides set by MDPH. EPA 1694 was consulted for LC/MS/MS specific objectives of contaminants
Metals	ICP/MS	• USP <233> • USP <232> • USP <2232>	• EPA 6020A*	*Consulted for additional ICP-MS specific objectives
Cannabinoids	HPLC (UV-Vis or DAD)	• AHP (2013) • UNODC (2009)	• EPA 548.1*	*Consulted for additional HPLC specific objectives

Appendix A - Table 01
Method Reference Table

Analysis	Technology	Primary Reference(s)	Ancillary Reference(s)	Comment
% Moisture	Gravimetric	• USP <921> • ASTM Method D2216 – 98		
Microbiology 1. Viable Aerobic Bacteria 2. Total Yeast and Mold 3. Total Coliforms 4. Bile-tolerant Gram-negative Bacteria	Plates and Films	• AHP (2013) • FDA Bacteriological Analytical Manual (BAM) • USP <62>	1. BAM Chapter 3 Aerobic Plate Count 2. BAM Chapter 18, 3. BAM Chapter 4 4. USP <62>	
Microbiology 1. Pathogenic *E.coli* *2. Salmonella* 3. Mycotoxins	PCR, ELISA	• AHP (2013) • USP <561> • FDA BAM	1. BAM Chapter 4a 2. BAM Chapter 5 3. BAM Chapter 18	
Sample Handling and Storage	Sample Collection	• USP <561> • EPA 8000D • FDA BAM		

Appendix A - Table 02
MDPH Sample Handling and Receipt Requirements
Quality Control Requirements

Item	Requirement	Acceptance Condition	Corrective Action
Sample Containers	Sample vessels/media shall be appropriate for the type analytical parameters for which the bottle type is to be used for collection. Pesticides, solvents, and cannabinoids analyses require amber glass containers with PTFE-lined lids and metals analyses may come from the amber glass containers if only the target analytes are being analyzed. If other metals besides those required in the protocols are analyzed or metals speciation is to be performed, a representative sample shall be contained in high density polyethylene containers. Sample vessel/media and preservative lot numbers shall be recorded for each outgoing bottleware shipment to maintain traceability.	Sample containers that are one-use only shall be lot tested to show the level of target analytes are < ½ LOQ. There shall be an SOP outlining the validation of bottle lots and the cleaning of any sample containers that are used more than once. This SOP shall contain a validation of the cleaning procedure that includes an equipment blank analyzed at least monthly for the target analytes to validate the on-going acceptability of the cleaning procedure. Results from these samples shall be < ½ LOQ for each relevant target analyte. Records of frequency of sample container cleaning shall be maintained and available for inspection.	Samples associated with a contaminated blank may not be re-prepared and re-analyzed. Samples shall be resampled and reanalyzed. The contamination (including a list of affected samples) shall be documented and formal corrective action shall be performed. Trip blanks, field blanks, rinse blanks, and equipment blanks shall not be reanalyzed solely for the purpose of reporting "not-detected" results. Blanks may only be reanalyzed if there is a valid technical reason for reanalysis (*e.g.,* injection failure or QC failure) If the validation of cleaning procedure analysis has hits > ½ LOQ, the samples bracketed by the failed study that were placed in that batch of containers shall be catalogued as affected by contamination, resampling, repreparation, and reanalysis of the samples shall be performed.

Appendix A - Table 02
MDPH Sample Handling and Receipt Requirements
Quality Control Requirements

Item	Requirement	Acceptance Condition	Corrective Action
Sample Size	Sufficient sample vessels shall be provided for the collection of the required increments if they are to be composited at the laboratory. The protocols indicate the number of increments that shall be taken for analysis. These amounts are to be received by the laboratory regardless of the particular analytes to be tested. The representative sample shall provide enough mass for all relevant laboratory analyses and required QC as defined in the laboratory sample receipt policy. Sufficient sample mass for reanalysis and duplicate analyses is to be considered in determining the minimum sample mass required.	The laboratory verifies that the mass required for each analysis, including QC samples and validation procedures contained in its sample acceptance policy.	The samplers shall be advised that the sample mass is insufficient. The determination on whether additional sample collection is needed or would be compliant may only be made with concurrence from MDPH.
Holding Time	The amount of time from sample collection to sample preparation and analysis shall be limited based on the known stability of the analytes in a given matrix.	Microbiology parameters – 48 hours (if micro DQOs are not met a second analysis may be performed within 96 hours of sample collection) Metals parameters – 14 days (if Mercury is not analyzed, 6 months) Pesticides – 7 days to extraction, 40 days from extraction to analysis Residual Solvents – 7 days Cannabinoids – 7 days to extraction, 7 days from extraction to analysis	Samples received outside of the holding time shall be rejected by the laboratory for the appropriate analyses and resampled. If some analyses are within hold time, the laboratory shall confirm with the client that they want these analyzed or if the entire suite of analyses shall be resampled.

Appendix A - Table 02
MDPH Sample Handling and Receipt Requirements
Quality Control Requirements

Item	Requirement	Acceptance Condition	Corrective Action
Preservative and Storage	Temperature preservation between 0°C < 6.0°C is required for all analyses. If Mercury is not to be analyzed, metals samples collected separately do not require temperature preservation.	The laboratory shall document a received temperature of 0°C - ≤ 6.0°C for all samples unless sampled same day. If sampled same day, the temperature and evidence of cooling shall be documented upon receipt.	The RMD shall be held responsible for any resampling/reanalysis resulting from samples not shipped and stored at appropriate temperatures. Samples that were not sampled same-day that are received by the laboratory out of temperature shall be rejected by the laboratory and resampled. Samples that arrive the same day of sampling without evidence of cooling shall be rejected by the laboratory and resampled.
Trip Blanks/ Field Blanks/ Rinse Blanks/ Equipment Blanks	Trip blanks, field blanks, rinse blanks, and equipment blanks are recommended to be included with each sampling event and strongly recommended for sampling events that include residual solvent analysis to ensure that contamination was not introduced at the sampling site or by the sampling equipment. The laboratory shall prepare blanks the same day as the sampling event or of the preparation of sample containers (not days or weeks in advance). Ultra-pure, deionized/distilled water shall be provided for use when field personnel collect field, rinse, or equipment blanks.	Target compounds/analytes shall not be present at concentrations > ½ LOQ. All blanks shall meet QC criteria (*e.g.*, surrogates, internal standards).	Samples associated with a contaminated blank shall not be reprepared and reanalyzed. The contamination (including a list of affected samples) shall be documented in the client report. Trip blanks, field blanks, rinse blanks, and equipment blanks shall not be reanalyzed solely for the purpose of reporting "not-detected" results. Blanks may only be reanalyzed if there is a valid technical reason for reanalysis (*e.g.,* injection failure or QC failure).

Appendix A - Table 02
MDPH Sample Handling and Receipt Requirements
Quality Control Requirements

Item	Requirement	Acceptance Condition	Corrective Action
Sample Documentation	The laboratory shall have in its procedures and available to all sample collectors and couriers a sample acceptance policy that includes the requirements contained in this table. Sample container labels and COC forms shall include the following information at a minimum: site location, sample date and time, initials of sampler, licensee number, batch number, location within facility, increment location within batch, sample number, analytical method, and preservative. The laboratory shall provide enough blank labels and containers to allow for the maximum amount of samples that may be collected from the site.	The laboratory has delivered the current sample acceptance criteria, shipping requirements, blank sample labels, and COC forms that meet MDPH sampling protocol requirements.	The laboratory shall contact the client if there are questions on the sample documentation. The client conversation shall be documented by the laboratory. If the client does not have the information required for the sample, the sample shall be rejected and resampled.
Sample Documentation	The lab shall receive a request for analysis. This can be a standalone document or in the form of a COC or a sampling and analysis plan (SAP). The lab shall receive a sampling field record that has the information required in the sampling protocols such as the location and mass of increments that were combined in the field from the RMD.	The laboratory shall include the applicable request for analysis, COC, sampling records, and/or SAP in the final report.	If the RMD does not have an official sampling and analysis plan and the COC is unclear, the laboratory shall confirm a request for analysis with the RMD. If the request for the analysis is for standard compliance testing as confirmed by the RMD and the sample field records have enough information to confirm the required sampling from the protocols was performed, the laboratory should note the lack of documentation and the confirmation with the RMD in the report narrative.

Appendix A - Table 02
MDPH Sample Handling and Receipt Requirements
Quality Control Requirements

Item	Requirement	Acceptance Condition	Corrective Action
Chain-of-Custody	All bottleware shipments shall be documented under COC procedures.	The laboratory shall place sample containers in appropriate custody-sealed sample coolers for outgoing shipment. The laboratory shall have custody procedures consistent with state regulation and that define custody as it pertains to times when the sample is not in immediate sight of the person who holds custody. Custody seals, locked coolers and containers, locked vehicles, and other precautions shall be discussed in the custody procedures if not explicitly stated in the state regulation.	When tampering with bottleware shipments is evident, the client and MDPH shall be notified immediately for instructions on how to proceed.

Appendix A - Table 03a
MDPH Residual Solvents by GC/MS
Quality Control Requirements

Quality Control Item	Frequency	Acceptance Criteria	Corrective Action
GC/MS Tuning	Every 12 hours.	Ensure correct mass assignment. Ion abundances shall meet the instrument manufacturer tuning criteria.	Retune instrument. Do not proceed with calibration until tune criteria are met.
Initial Calibration	Each time the instrument is set up and when calibration verification criteria are not met. A minimum of five calibration standards is required for first order linear (at least six standards are required for higher order calibration). The low-level calibration standard shall be at or below the LOQ. Weighting should be utilized to minimize Relative Standard Error (RSE) at the protocol action limit.	A calibration curve shall be generated with all target compounds and surrogate compounds if used with an $R^2 \geq 0.990$. For all initial calibration levels, the retention times shall be within ± 3 seconds of the midpoint standard.	If the calibration curve is $R^2 \leq 0.990$, perform corrective action and recalibrate the instrument. When retention -time -window -criteria are not met, samples shall be reanalyzed within a new calibration or CCV to meet the retention time window criteria.
Initial Calibration Verification (ICV)	A second-source calibration verification standard, when commercially available, shall be analyzed after every initial calibration within the same tune as the initial calibration	Recovery of all target compounds and surrogates should be 70-130%.	Correct system and reanalyze ICV. If second ICV fails, recalibrate system.

Appendix A - Table 03a
MDPH Residual Solvents by GC/MS
Quality Control Requirements

Quality Control Item	Frequency	Acceptance Criteria	Corrective Action
Continuing Calibration Verification (CCV)	Initially, after each set of 10 sample analyses, and at the end of each sequence. The final CCV shall be prepared at the same time as the other standards in order to assess the stability of the light gasses.	Recovery of all target compounds and surrogates should be 70-130%. Retention time of the CCV should not differ by ± 6 seconds or ±0.04 RRT units from the retention time established by the middle standard of the initial calibration.	Correct system and reanalyze CCV. If second CCV fails, recalibrate system and reanalyze all samples since last successful CCV.
Internal Standards	If used, the IS shall be added to every standard, sample, and QC sample. For all samples and QC samples, sample internal standard area counts and RTs shall be compared to the internal standard area counts and RTs of the associated CCV standard. CCV internal standard area counts and RTs shall be compared to the area counts and RTs of the ICV standard.	Area counts of the internal standard peaks shall be 50-150% of the internal standard area observed in the associated CCV. The RT of the internal standard shall not vary more than ± 6 seconds from the RT or ±0.04 RRT units of the internal standards observed in associated CCV standard.	Reanalyze affected samples at dilution to check for matrix interference. If internal standard still fails, perform corrective action, recalibrate the instrument, and reanalyze sample.
Method Blank	One per preparation batch of up to 20 samples.	All target compounds for which there is a detection in associated samples, ≤½ the LOQ or < 10% of associated positive sample results (whichever is higher).	If positive results for contaminant compounds are not observed in the associated samples, record the failure in the client narrative. If positive results for contaminant compounds are observed in the associated samples, re-prepare and reanalyze associated samples.

Appendix A - Table 03a
MDPH Residual Solvents by GC/MS
Quality Control Requirements

Quality Control Item	Frequency	Acceptance Criteria	Corrective Action
Surrogate Recovery	If used, added to all calibration standards, blanks, samples, and QC samples.	All surrogates shall meet laboratory-generated acceptance limits and fall within the retention time windows.	Check instrument performance. Correct the problem and reanalyze the sample if a problem is identified. If the problem is suspected to be matrix interference, dilute and reanalyze the samples. If surrogate recovery criteria are met upon reanalysis, report the reanalysis results. If the observed retention time of a surrogate is outside of the established retention time window, corrective action shall be performed and the affected samples and QC shall be reanalyzed.
Laboratory Control Sample (LCS)	One LCS per preparation batch of up to 20 samples.	% Recoveries within laboratory-generated limits. Laboratory generated acceptance criteria recovery windows cannot be set at ≤ 15% at the low end and cannot be set at ≥ 150% at the high end.	Reanalyze LCS to confirm results. If LCS results are outside of acceptance criteria upon reanalysis, re-prepare the preparation batch and reanalyze samples. If the LCS results are still outside of acceptance criteria, recalibrate and reanalyze associated project samples. If high recoveries are observed and “not-detected” results are reported for the associated samples, reanalysis is not necessary. Record the failure in the client report narrative.

Appendix A - Table 03a
MDPH Residual Solvents by GC/MS
Quality Control Requirements

Quality Control Item	Frequency	Acceptance Criteria	Corrective Action
Matrix Spike/Matrix Spike Duplicate (MS/MSD)	One per matrix per preparation batch of up to 20 samples. All requested target compounds shall be included in the spiking solution.	% Recoveries and RPDs within laboratory-generated limits. Laboratory generated acceptance criteria recovery windows cannot be set at ≤ 15% at the low end and cannot be set at ≥ 150% at the high end. Laboratory generated limits for precision cannot exceed %RPD ≤ 40%	Reprepare or reanalyze the affected sample (s) at a dilution or with additional cleanups to examine matrix affects. If LCS results meet acceptance criteria and the MS/MSD still exceed criteria, note the nonconformance in the client report narrative with information on matrix interference if apparent in the reanalysis at a dilution.
Medical Marijuana or MIP Field Duplicate	Duplicate of a sample taken at a frequency of once per medical marijuana or marijuana-infused product batch.	%RPD ≤ 30% until enough points are collected for laboratory generated acceptance limits to be statistically derived. Laboratory generated limits for precision cannot exceed %RPD ≤ 40%	If the field duplicate exceeds precision criteria, RMD shall be informed and the batch shall be resampled and reanalyzed. If the field duplicate exceeds precision criteria upon resampling and reanalysis, the laboratory shall note this on the report.
Qualitative/ Quantitative Issues	Each target analyte.	The instrument level of all target compounds shall be below the upper calibration level.	Dilute the sample to bring the target compound level within the instrument calibration range.

Appendix A - Table 03b
MDPH Residual Solvents by GC-FID
Quality Control Requirements

Quality Control Item	Frequency	Acceptance Criteria	Corrective Action
Initial Calibration	Each time the instrument is set up and when calibration verification criteria are not met. A minimum of five calibration standards is required for first order linear (at least six standards are required for higher order calibration). The low-level calibration standard shall be at or below the LOQ. Weighting should be utilized to minimize Relative Standard Error (RSE) at the protocol action limit.	A calibration curve shall be generated with all target compounds and surrogate compounds if used with an $R^2 \geq 0.990$. For all initial calibration levels, the retention times shall be within ± 3 seconds of the midpoint standard.	If the calibration curve is $R^2 \leq 0.990$, perform corrective action and recalibrate the instrument. When retention time window criteria are not met, samples shall be reanalyzed within a new calibration or CCV to meet the retention time window criteria.
Initial Calibration Verification (ICV)	A second-source calibration verification standard, when commercially available, shall be analyzed after every initial calibration within the same tune as the initial calibration	Recovery of all target compounds and surrogates should be 70-130%.	Correct system and reanalyze ICV. If second ICV fails, recalibrate system.

Appendix A - Table 03b
MDPH Residual Solvents by GC-FID
Quality Control Requirements

Quality Control Item	Frequency	Acceptance Criteria	Corrective Action
Continuing Calibration Verification (CCV)	Initially, after each set of 10 sample analyses, and at the end of each sequence. The final CCV shall be prepared at the same time as the other standards in order to assess the stability of the light gasses.	Recovery of all target compounds and surrogates should be 70-130%. Retention time of the CCV should not differ by ± 6 seconds from the retention time established by the middle standard of the initial calibration.	Correct system and reanalyze CCV. If second CCV fails, recalibrate system and reanalyze all samples since last successful CCV.
Retention Time (RT) Window	Each analyte within each sample analysis.	Retention time of each analyte should not differ by > 3 seconds of the retention time established for that analytes in the last CCV analyzed.	1.) Reject the identification of the analyte. 2.) Apply analyst judgement on the basis of chromatographic data to make the identification with confirmation and concurrence from a second analyst.
Method Blank	One per preparation batch of up to 20 samples.	All target compounds for which there is a detection in associated samples, ≤½ the LOQ or < 10% of associated positive sample results (whichever is higher).	If positive results for contaminant compounds are not observed in the associated samples, record the failure in the client narrative. If positive results for contaminant compounds are observed in the associated samples, re-prepare and reanalyze associated samples.

Appendix A - Table 03b
MDPH Residual Solvents by GC-FID
Quality Control Requirements

Quality Control Item	Frequency	Acceptance Criteria	Corrective Action
Surrogate Recovery	If used, added to all calibration standards, blanks, samples, and QC samples.	All surrogates shall meet laboratory-generated acceptance limits and fall within the retention time windows.	Check instrument performance. Correct the problem and reanalyze the sample if a problem is identified. If the problem is suspected to be matrix interference, dilute and reanalyze the samples. If surrogate recovery criteria are met upon reanalysis, report the reanalysis results. If the observed retention time of a surrogate is outside of the established retention time window, corrective action shall be performed and the affected samples and QC shall be reanalyzed.
Laboratory Control Sample (LCS)	One LCS per preparation batch of up to 20 samples.	% Recoveries within laboratory-generated limits. Laboratory generated acceptance criteria recovery windows cannot be set at ≤ 15% at the low end and cannot be set at ≥ 150% at the high end.	Reanalyze LCS to confirm results. If LCS results are outside of acceptance criteria upon reanalysis, re-prepare the preparation batch and reanalyze samples. If the LCS results are still outside of acceptance criteria, recalibrate and reanalyze associated project samples. If high recoveries are observed and “not-detected” results are reported for the associated samples, reanalysis is not necessary. Record the failure in the client report narrative.

Appendix A - Table 03b
MDPH Residual Solvents by GC-FID
Quality Control Requirements

Quality Control Item	Frequency	Acceptance Criteria	Corrective Action
Matrix Spike/Matrix Spike Duplicate (MS/MSD)	One per matrix per preparation batch of up to 20 samples. All requested target compounds shall be included in the spiking solution.	% Recoveries and RPDs within laboratory-generated limits. Laboratory generated acceptance criteria recovery windows cannot be set at ≤ 15% at the low end and cannot be set at ≥ 150% at the high end. Laboratory generated limits for precision cannot exceed %RPD ≤ 40%	Reprepare or reanalyze the affected sample (s) at a dilution or with additional cleanups to examine matrix affects. If LCS results meet acceptance criteria and the MS/MSD still exceed criteria, note the nonconformance in the client report narrative with information on matrix interference if apparent in the reanalysis at a dilution.
Confirmation	Tentative identification of an analyte occurs when a peak from a sample extract falls within the daily retention time window. Confirmation techniques include analysis using a second column with dissimilar stationary phase, GC/MS, or by other recognized confirmation techniques.	All confirmation techniques: QC requirements (listed on Tables 3a and 3b) shall pass on both initial and confirmation analyses. If two dissimilar columns are used for confirmation, the results shall be confirmed with an RPD ≤ 40%.	If a peak is not confirmed, the sample is reported as < LOQ on the client report. If QC such as an LCS, surrogate, or method blank fails high on a column but all of the hits are ND, the results may be reported with a note in the client report narrative. If the QC does not pass on a column or the RPD > 40%, and the analyte is detected, the sample shall be reprepared and reanalyzed. Dilution or additional cleanups are recommended if chromatographic interference is noted. If QC on one or both columns fails upon reanalysis or if the two columns again produce an RPD > 40%, the analyte detection shall be confirmed using a recognized confirmatory technique.

Appendix A - Table 03b
MDPH Residual Solvents by GC-FID
Quality Control Requirements

Quality Control Item	Frequency	Acceptance Criteria	Corrective Action
Qualitative/ Quantitative Issues	Each target analyte. Professional judgement of highly experienced individuals is required for a dual-column analysis. There are some situations where the quantitative result may be reported off the secondary column.	The instrument level of all target compounds shall be below the upper calibration level. If there is obvious interference on the primary column, the secondary column may be chosen as the primary reporting column as long as the secondary column still confirms the detected peaks both qualitatively (retention time) and quantitatively (QC passes and RPD < 40%).	Dilute the sample to bring the target compound level within the instrument calibration range. If secondary column is used for reporting and primary column is used for confirmation, this shall be noted in the client narrative.

Appendix A - Table 04
MDPH Pesticides by LC-MS/MS
Quality Control Requirements

Quality Control Item	Frequency	Acceptance Criteria	Corrective Action
Mass Calibration and Optimization	Annually and upon any major maintenance or procedural changes	Mass calibrate to ensure accurate assignments of mass to charge ratios (m/z). Optimize to best mass assignment, retention time, transition ion assignment, and ratio abundance of transition ions for each target analyte.	If optimization shifts, perform troubleshooting corrective action as noted in maintenance procedures and record in maintenance log until optimization is achieved.
Initial calibration	Each time the instrument is set up and when calibration verification criteria are not met. A minimum of five calibration standards is required for first order linear (at least six standards are required for higher order calibration). The low-level calibration standard shall be at or below the LOQ. Weighting should be utilized to minimize Relative Standard Error (RSE) at the protocol action limit.	A calibration curve shall be generated with all target compounds and surrogate compounds if used with an $R^2 \geq 0.990$. For all initial calibration levels, the retention times shall be within ± 3 seconds of the midpoint standard.	If the calibration curve is $R^2 \leq 0.990$, perform corrective action and recalibrate the instrument. When retention time window criteria are not met, samples shall be reanalyzed within a new calibration or CCV to meet the retention time window criteria.
Initial Calibration Verification (ICV)	A second-source calibration verification standard, when commercially available, shall be analyzed after every initial calibration within the same tune as the initial calibration	Recovery of all target compounds and surrogates should be 70-130%.	Correct system and reanalyze ICV. If second ICV fails, recalibrate system.

Appendix A - Table 04
MDPH Pesticides by LC-MS/MS
Quality Control Requirements

Quality Control Item	Frequency	Acceptance Criteria	Corrective Action
Continuing Calibration Verification	Initially, after each set of 10 sample analyses, and at the end of each sequence. The final CCV shall be prepared at the same time as the other standards in order to assess the stability of the light gasses.	Recovery of all target compounds and surrogates should be 70-130%. Retention time of the CCV should not differ ± 6 seconds from the retention time or ±0.04 RRT units established by the middle standard of the initial calibration.	Correct system and reanalyze CCV. If second CCV fails, recalibrate system and reanalyze all samples since last successful CCV.
Internal standards	When used, Internal Standards are added to all blanks, standards, QC samples, and samples. Sample internal standard area counts and RTs shall be compared to the internal standard area counts and RTs of the associated CCV standard. CCV internal standard area counts and RTs shall be compared to the area counts and RTs of the ICV standard.	Internal standards shall meet laboratory generated limits of a minimum of 30 samples Express the assessment as a percent recovery interval of ± two standard deviations. ± 6 seconds from the retention time or ±0.04 RRT units established by the associated continuing calibration standard.	Reanalyze affected samples at dilution to check for matrix interference. If internal standard still fails, perform corrective action, recalibrate the instrument, and reanalyze sample.
Method Blank	One per preparation batch of up to 20 samples.	All target compounds for which there is a detection in associated samples, ≤ ½ the LOQ or < 10% of associated positive sample results (whichever is higher).	If positive results for contaminant compounds are not observed in the associated samples, record the failure in the client narrative. If positive results for contaminant compounds are observed in the associated samples, re-prepare and reanalyze associated samples.

Appendix A - Table 04
MDPH Pesticides by LC-MS/MS
Quality Control Requirements

Quality Control Item	Frequency	Acceptance Criteria	Corrective Action
Laboratory Control Sample (LCS)	One LCS per preparation batch of up to 20 samples.	% Recoveries within laboratory-generated limits. Laboratory generated acceptance criteria recovery windows cannot be set at ≤ 15% at the low end and cannot be set at ≥ 150% at the high end.	Reanalyze LCS to confirm results. If LCS results are outside of acceptance criteria upon reanalysis, re-prepare the preparation batch and reanalyze samples. If the LCS results are still outside of acceptance criteria, recalibrate and reanalyze associated project samples. If high recoveries are observed and "not-detected" results are reported for the associated samples, reanalysis is not necessary. Record the failure in the client report narrative.
Matrix Spike/Matrix Spike Duplicate	One per matrix per preparation batch of up to 20 samples. All requested target compounds shall be included in the spiking solution.	% Recoveries and RPDs within laboratory-generated limits. Laboratory generated acceptance criteria recovery windows cannot be set at ≤ 15% at the low end and cannot be set at ≥ 150% at the high end. Laboratory generated limits for precision cannot exceed %RPD ≤ 40%	Reprepare or reanalyze the affected sample (s) at a dilution or with additional cleanups to examine matrix affects. If LCS results meet acceptance criteria and the MS/MSD still exceed criteria, note the nonconformance in the client report narrative with information on matrix interference if apparent in the reanalysis at a dilution.
Qualitative/Quantitative Issues	Each target analyte.	The instrument level of all target compounds shall be below the upper calibration level.	Dilute the sample to bring the target compound level within the instrument calibration range.

Appendix A - Table 04
MDPH Pesticides by LC-MS/MS
Quality Control Requirements

Quality Control Item	Frequency	Acceptance Criteria	Corrective Action
Surrogate Compounds	If used, added to all calibration standards, blanks, samples, and QC samples.	All surrogates shall meet laboratory-generated acceptance limits.	Check instrument performance. Correct the problem and reanalyze the sample if a problem is identified. If the problem is suspected to be matrix interference, dilute and reanalyze the samples. If surrogate recovery criteria are met upon reanalysis, report the reanalysis results. If the observed retention time of a surrogate is outside of the established retention time window, corrective action shall be performed and the affected samples and QC shall be reanalyzed.

Appendix A - Table 05
MDPH Metals by ICP/MS
Quality Control Requirements

Quality Control Item	Frequency	Acceptance Criteria	Corrective Action
Tune and Optimization	Daily, before analysis.	According to instrument manufacturer specifications.	Perform instrument maintenance and reanalyze tune solution until criteria are met.
Initial Calibration	Daily. The laboratory may draw a calibration curve using a four-point curve and a blank with the lowest non-zero standard being at or below 0.5 of the Target analyte action limit and the top standard being at or above 1.5 of the Target analyte action limit).	The correlation coefficient (r) for a four-point calibration curve shall be ≥ 0.995.	Any single standard may be rerun once, however repeated failure requires that the standards be reprepared and the instrument calibration shall be rerun.
Initial Calibration Verification/Blanks (ICV/ICB)	Each time the instrument is calibrated. Immediately after instrument calibration, the ICV and ICB are analyzed.	ICV is within 90-110% of the true value. ICB All targets < ½ the LOQ.	Reanalyze ICV or ICB once, if ICV or ICB is still out, terminate analysis, correct problem, and recalibrate instrument.
Linear Dynamic Range determination	LDR may be > the standard solution at 1.5 target analyte action limit. LDR shall be determined initially for each target analyte and whenever major instrument maintenance is performed.	LDR standard shall be within 10% of true value.	Reprepare and reanalyze once. If LDR standard is still out, the full linear dynamic range determination shall be rerun.

Appendix A - Table 05
MDPH Metals by ICP/MS
Quality Control Requirements

Quality Control Item	Frequency	Acceptance Criteria	Corrective Action
Continuing Calibration Verifications/Continuing Calibration Blank (CCV/CCB)	After a passing ICV and ICB, the CCV/CCB shall be analyzed initially, after each set of 10 sample analyses, and at the end of each sequence.	CCV is within 90-110% recovery. CCB contains all target compounds for which there is a detection in associated samples, ≤ ½ the LOQ or < 10% of associated positive sample results (whichever is higher).	Reanalyze CCV or CCB. If CCV or CCB is still out, terminate analysis, correct problem, and recalibrate instrument. Reanalyze all analytical samples since the last compliant CCV/CCB. For CCB failures, if positive results for contaminant compounds are not observed in the associated samples, record the failure in the client narrative. If positive results for contaminant compounds are observed in the associated samples, re-prepare and reanalyze associated samples.
Method Blank	One per preparation batch of up to 20 samples.	All target compounds for which there is a detection in associated samples, ≤ ½ the LOQ or < 10% of associated positive sample results (whichever is higher).	If positive results for contaminant compounds are not observed in the associated samples, record the failure in the client narrative. If positive results for contaminant compounds are observed in the associated samples, re-prepare and reanalyze associated samples.
Laboratory Control Sample (LCS)	One LCS per digestion batch of up to 20 samples.	80-120% recovery .	Reanalyze LCS to confirm results. If LCS results are outside of acceptance criteria upon reanalysis, re-prepare the preparation batch and reanalyze samples. If the LCS results are still outside of acceptance criteria, recalibrate and reanalyze associated project samples. If high recoveries are observed and “not-detected” results are reported for the associated samples, reanalysis is not necessary. Record the failure in the client report narrative.

Appendix A - Table 05
MDPH Metals by ICP/MS
Quality Control Requirements

Quality Control Item	Frequency	Acceptance Criteria	Corrective Action
Matrix Spike/Matrix Spike Duplicate (MS/MSD; pre-digestion)	One LCS per digestion batch of up to 20 samples.	80-120% recovery. RPD ± 20%.	Reprepare or reanalyze the affected sample (s) at a dilution to examine matrix affects. If LCS results meet acceptance criteria and the MS/MSD still exceed criteria, note the nonconformance in the client report narrative with information on matrix interference if apparent in the reanalysis at a dilution.
Internal Standards (ISs)	All internal standards for analysis used for reporting are evaluated against the mid-level standard of the initial calibration.	The internal standard intensity recovery shall be within 70% to 125% of the corresponding internal standard in the mid-level standard of the initial calibration.	If the exceedance is in a CCV or CCB, the analysis should be stopped and the instrument recalibrated. If the exceedance is only observed in field sample analysis, matrix effect is indicated and the affected samples should be diluted 5× (successively) until the IS(s) pass criteria and the reason for the dilution should be noted in the client report narrative.
Qualitative/ Quantitative Issues	Each target analyte.	The instrument level of all target compounds shall be below the upper calibration level.	Dilute the sample to bring the target compound level within the instrument calibration range.

Appendix A - Table 06
Cannabinoids by HPLC
Quality Control Requirements

Quality Control Item	Frequency	Acceptance Criteria	Corrective Action
Initial Calibration	Each time the instrument is set up and when calibration verification standard acceptance criteria are not met. A minimum of five calibration standards is required for first order linear (at least six standards are required for higher order calibration). The low-level calibration standard shall be at or below the LOQ. Weighting should be utilized to minimize Relative Standard Error (RSE) at the protocol action limit.	The calibration curve shall have a correlation coefficient $R^2 \geq 0.990$ For all initial calibration levels, the retention times shall be within ± 3 seconds of the midpoint standard.	If the calibration curve is $R^2 \leq 0.990$, perform corrective action and recalibrate the instrument. When retention time window criteria are not met, samples shall be reanalyzed within a new calibration or CCV to meet the retention time window criteria.
Initial Calibration Verification (ICV)	A second-source calibration verification standard shall be analyzed after every initial calibration.	Recovery of all target compounds and surrogates should be 70-130%.	Correct system and reanalyze ICV. If second ICV fails, recalibrate system.
Continuing Calibration Verification (CCV)	Initially, after each set of 10 sample analyses, and at the end of each sequence.	Recovery of all target compounds and surrogates should be 70-130%. Retention time of the CCV should not differ by ± 6 seconds from the retention time or ±0.04 RRT units the established by the middle standard of the initial calibration.	Correct system and reanalyze CCV. If second CCV fails, recalibrate system and reanalyze all samples since last successful CCV.

Appendix A - Table 06
Cannabinoids by HPLC
Quality Control Requirements

Quality Control Item	Frequency	Acceptance Criteria	Corrective Action
Laboratory Control Sample (LCS)	The surrogate in the method blank shall serve as the LCS unless an approved reference material of appropriate concentration is available. When an approved reference material of appropriate concentration is available, prepare one LCS from that material per preparation batch of up to 20 samples.	Surrogate recoveries should be within laboratory-generated limits. % Recoveries within 70-130% when the LCS is prepared from an approved reference material.	Reanalyze LCS to confirm results. If LCS results are outside of acceptance criteria upon reanalysis, re-prepare the preparation batch and reanalyze samples. If the LCS results are still outside of acceptance criteria, recalibrate and reanalyze associated project samples. If high recoveries are observed and "not-detected" results are reported for the associated samples, reanalysis is not necessary but the failure shall be noted in the client report narrative.
Matrix Spike	The Matrix Spike is required if there is an approved reference material of appropriate concentration to fall within calibration range after extraction available under an ISO Guide 34 accreditation available. One per preparation batch of up to 20 samples. All requested target compounds shall be included in the spiking solution.	% Recoveries within laboratory generated limits. Laboratory generated acceptance criteria recovery windows cannot be set at ≤ 15% at the low end and cannot be set at ≥ 150% at the high end.	Reprepare or reanalyze the affected sample (s) at a dilution or with additional cleanups to examine matrix affects. If LCS results meet acceptance criteria and the MS/MSD still exceed criteria, note the nonconformance in the client report narrative with information on matrix interference if apparent in the reanalysis at a dilution.

Appendix A - Table 06
Cannabinoids by HPLC
Quality Control Requirements

Quality Control Item	Frequency	Acceptance Criteria	Corrective Action
Matrix Sample Duplicate	One per extraction batch per matrix per concentration level ≤ 20 samples per day. Shall undergo all sample preparative procedures.	≤ 20% RPD	Reprepare and reanalyze the affected sample with an LCS and an LCS duplicate to show that the precision of the analysis is still within criteria. If sample results still exceed criteria and LCS/LCS duplicate were within laboratory generated precision criteria, note the nonconformance in the client report narrative as possible matrix interference or non-uniform product.
Retention Time (RT) Window	Each analyte within each sample analysis.	Retention time of each analyte should not differ by > 3 seconds of the retention time established for that analytes in the last CCV analyzed.	3.) Reject the identification of the analyte. 4.) Apply analyst judgement on the basis of chromatographic data to make the identification with confirmation and concurrence from a second analyst.
Surrogate	If used, added to all calibration standards, blanks, samples, and QC samples.	All surrogates shall meet laboratory-generated acceptance limits and fall within the retention time windows.	Check instrument performance. Correct the problem and reanalyze the sample if a problem is identified. If the problem is suspected to be matrix interference, dilute and reanalyze the samples. If surrogate recovery criteria are met upon reanalysis, report the reanalysis results. If the observed retention time of a surrogate is outside of the established retention time window, corrective action shall be performed and the affected samples and QC shall be reanalyzed.

Appendix A - Table 06
Cannabinoids by HPLC
Quality Control Requirements

Quality Control Item	Frequency	Acceptance Criteria	Corrective Action
Qualitative/ Quantitative Issues	Each target analyte.	The instrument level of all target compounds shall be below the upper calibration level.	Dilute the sample to bring the target compound level within the instrument calibration range.

Appendix A - Table 07
MDPH % Moisture by Gravimetric Analysis
Quality Control Requirements

Quality Control Item	Frequency	Acceptance Criteria	Corrective Action
Balance Calibration and Verification	Calibration annually under ISO 17025 calibration. Verified daily, prior to sample analysis. Weight range shall bracket the measured sample weights and their tared containers.	± 0.1% of certified mass for weights > 1.0 g. ± 0.2% of certified mass for weights < 1.0 g.	Balances outside of the acceptance criteria shall be taken out of service and serviced by a technician. Balances shall not be used until the acceptance criteria can be met.
Preparation Blank	One per preparation batch up to 20 samples.	Blanks ≤ 0.01 g	Reanalyze all associated samples displaying positive results ≤ 10× the blank level. Corrective action is not required if sample concentration is > 10× the blank level.
Laboratory Duplicate	One per 10 analyses.	≤ 20% RPD	Flag data and report unacceptable precision as a qualifier for all associated results that are required to be reported in dry weight.
Constant Weight	Each Sample	The laboratory shall perform two measurements between heating to ensure that a constant weight has been established. These two masses shall agree within ± 0.2%.	If a constant weight is not reached, the laboratory shall repeat the heating and measuring procedural steps until a constant weight is achieved. If a continuous loss of weight is occurring, it is possible that the laboratory is losing analytes that are volatile at the oven temperature and the laboratory should consider other methods or lower temperatures that allow for loss of water but not the constituent analytes of the product.

Notes:
- Method-specific requirements supersede the QC requirements in this table. The more stringent of the method requirements and requirements provided herein shall be followed.
- Sample weights shall be bracketed by the balance calibration range.

Appendix A - Table 07
MDPH % Moisture by Gravimetric Analysis
Quality Control Requirements

Appendix A - Table 08
MDPH Microbiology by Plates and Films

Quality Control Item	Frequency	Acceptance Criteria	Corrective Action
Media 1. APC 2. Yeast and Mold 3. Total Coliforms 4. Bile-tolerant Gram-negative Bacteria	Every lot, before use	Negative Control < 1 CFU/g	Reject Lot. Check other variables such as positive and negative controls and media with fresh lot of media. Catalog any affected samples and reanalyze.
Plates/Bottles/Films 1. APC 2. Yeast and Mold 3. Total Coliforms 4. Bile-tolerant Gram-negative Bacteria	Every lot, before use	Negative Control < 1 CFU/g	Reject Lot. Check other variables such as positive and negative controls and media with new plates/bottles/films. Catalog any affected samples and reanalyze.
Dilution Water or Buffer • All methods where dilutions are applicable	Every lot, before use or monthly if system is in-house.	Meet all ongoing criteria prescribed in Section 10.3.3 of the QAPP. Negative Control < 1 CFU/g	Reject lot of water. If system is in-house, perform maintenance and a series of checks before putting back in service. Catalog any affected samples and reanalyze.
Water Baths 1. APC 2. Total Coliforms 3. Bile-tolerant Gram-negative Bacteria	Temperature checked twice a day separated by 4 hours when in use.	45°C ± 1°C or test temperature ± 1°C	If temperature windows are exceeded, catalog contents of incubator and re-prepare. If there is not enough sample mass to reanalyze, qualify the results on the client report.
Incubator 1. APC 2. Yeast and Mold 3. Total Coliforms 4. Bile-tolerant Gram-negative Bacteria	Temperature checked twice a day separated by 4 hours when in use.	1. 35°C ± 2°C 2. 25°C ± 2°C 3. 20°C -25°C (pre-incubation) 4. 30°C -35°C (test for absence and quantitative)	If temperature windows are exceeded, catalog contents of incubator and re-prepare. If there is not enough sample mass to reanalyze, qualify the results on the client report.

Appendix A - Table 08
MDPH Microbiology by Plates and Films

Quality Control Item	Frequency	Acceptance Criteria	Corrective Action
Autoclave • Method requirements pertaining to pressure, temperature, autoclave time at temperature, and total time.	Every batch	Content Defined Criteria • Media • Waste • Plates/Bottles Consider running weekly spore ampule to assess sterility.	If maximum pressure and/or temperature are not reached or not held for the required amount of time, perform maintenance on the autoclave and use indicators to ensure effectiveness before re-sterilizing contents.
Ambient Air Checks • General media plate (HPC) exposed for 15 minutes	Weekly	Not to exceed 15 CFU/plate	Catalogue samples analyzed since last check. Investigate source of contamination and assess data quality on affected samples by examining negative control records. Qualify samples that had affected data quality on client report.
Lab Duplicates	1 per preparation batch up to 20 samples. For MPN, one per 10 samples	For results expressed as MPN, both results should be within the 95% confidence interval (if available) for at least one of the results.	Inform the client. If possible, reanalyze associated samples. If reanalysis is not possible due to available sample, quality the affected sample in the batch on the client report.
Duplicate Count	Every 10% of samples	Same person < 5% RPD Different person < 10% RPD	Both analysts should repeat their counts. If the results are still outside of control, assess the counting procedures and perform corrective action as necessary in the form of procedural change and/or training, as indicated by the root cause analysis.
Positive Controls 1. APC 2. Yeast and Mold 3. Total Coliforms 4. Bile-tolerant Gram-negative	Every batch	Detected	Perform checks on quality control indicators to assign source of contamination or inhibition. Reanalyze associated samples after appropriate corrective action is taken.

Appendix A - Table 08
MDPH Microbiology by Plates and Films

Quality Control Item	Frequency	Acceptance Criteria	Corrective Action
Bacteria			
Negative Controls 1. APC 2. Yeast and Mold 3. Total Coliforms 4. Bile-tolerant Gram-negative Bacteria	Every batch	Negative Control < 1 CFU/g	Perform checks on quality control indicators to assign source of contamination. Reanalyze associated samples after appropriate corrective action is taken.

Appendix A - Table 09
MDPH Microbiology by PCR and ELISA

Quality Control Item	Frequency	Acceptance Criteria	Corrective Action
Dilution Water or Buffer • All methods where dilutions are applicable 1. Pathogenic E.coli 2. Salmonella 3. Mycotoxins	Ongoing checks Every lot or batch	Meet all ongoing criteria prescribed in Section 9.1 of the QAPP. Negative Control 1. Not detected in 1 g 2. Not detected in 1 g 3. > 20 ppb of sum of aflatoxin B_1 (AFB_1) B_2 (AFB_2), G_1 (AFG_1) and G_2 (AFG_2)	Reject lot of water. If system is in-house, perform maintenance and a series of checks before putting back in service. Catalog any affected samples and reanalyze.
Water Baths 1. Pathogenic E.coli 2. Salmonella 3. Mycotoxins	Twice a day separated by 4 hours when in use	1. N/A 2. 49 ± 1°C; 43 ± 0.2 °C; 42 ± 0.2°C 3. N/A	If temperature windows are exceeded during the relevant step of the method, catalog contents of incubator and re-prepare. If there is not enough sample mass to reanalyze, qualify the results on the client report.
Incubator 1. Pathogenic E.coli 2. Salmonella 3. Mycotoxins	Twice a day separated by 4 hours when in use	1. 35 ± 1.0°C and 44 ± 1.0°C 2. 35.0°C ± 2 °C 3. N/A	If temperature windows are exceeded during the relevant steps of the method, catalog contents of incubator and re-prepare. If there is not enough sample mass to reanalyze, qualify the results on the client report.
Autoclave • Method requirements pertaining to pressure, temperature, autoclave time at temperature, and total time.	Every batch	Content Defined Criteria • Media • Waste • Plates/Bottles Consider running weekly spore ampule to assess sterility	If maximum pressure and/or temperature are not reached or not held for the required amount of time, perform maintenance on the autoclave and use indicators to ensure effectiveness before re-sterilizing contents.

Appendix A - Table 09
MDPH Microbiology by PCR and ELISA

Quality Control Item	Frequency	Acceptance Criteria	Corrective Action
Ambient Air Checks • General media plate exposed for 15 minutes	Monthly	Not to exceed 15 CFU/plate	Catalogue samples analyzed since last check. Investigate source of contamination and assess data quality on affected samples by examining negative control records. Qualify samples that had affected data quality on client report.
Lab Duplicates	Every Batch	<20% RPD	Inform the client. Reanalyze associated samples. If reanalysis is not possible due to available sample, quality the affected sample in the batch on the client report.
Positive Controls 1. Pathogenic E.coli 2. Salmonella 3. Mycotoxins	Every batch	1. Detected 2. Detected 3. 90-110% recovery for aflatoxin B_1 (AFB_1) B_2 (AFB_2), G_1 (AFG_1) and G_2 (AFG_2)	Perform checks on quality control indicators to assign source of contamination or inhibition. Reanalyze associated samples after appropriate corrective action is taken.
Negative Controls 1. Pathogenic E.coli 2. Salmonella 3. Mycotoxins	Every Batch	1. Not Detectable in 1 g and IC, if applicable, is positive 2. Not Detectable in 1 g and IC, if applicable, is positive 3. < 5ppm of each individual aflatoxin or < 20 ppb of sum of aflatoxin B_1 (AFB_1) B_2 (AFB_2), G_1 (AFG_1) and G_2 (AFG_2)	Perform checks on quality control indicators to assign source of contamination. Reanalyze associated samples after appropriate corrective action is taken.

Appendix B
Data Review Instructions and Checklists

Chemistry Data Review Checklist Template Instruction

1) Data Review Templates are examples that can be used for method data review or internal audits.
2) Each checklist should be customized to the analysis requirements and criteria set out in the MDPH protocols, the text of this document, the MDPH QAPP DQO tables (Appendix A of this document), or laboratory generated limits.
3) Reference SOP section should be supplemented with any additional requirements for the relevant samples.
4) Checks that may be considered for addition include but are not limited to interference checks, dilution checks, dual column checks, varying CCV concentrations, historical agreement, or data agreement such as MeHg<Total Hg.
5) Font in red indicates areas of example only and should be replaced with parallel or additional QC checks.
6) Delete any QC checks that are not performed in method.
7) Client Sample sections can be simplified by Project ID, Preparation Batch IDs or Analytical Batch IDs if all are included in the method review.
8) Sample IDs used for QC samples such as matrix spikes or matrix duplicates should be recorded in the comment sections.
9) Standard and Traceability records should include the record reviewed that contained the traceability to standards and reagents. The identification should be contained in batch records and preparation logbooks. If not included in other review procedures, such as logbook review, this review should include a review traceability back to the specific Certificate of Analysis on file for each standard and reagent used in the analysis.
10) For use as an internal audit checklist, specific supporting elements should be added from the quality management system and supporting technical SOPs. These include but are not limited to current analyst DOC record references, support equipment logbook reviews, and, record of training records reviewed.

Insert Organic Method Name

I. Analytical Batch Information — **Analytical**

SOP: | Sequence/s:
Version: | Date: | Instrument ID:
Method File(s): | Analysis Date: | Analyst:
Electronic Filename(s): | Analyte Group:
**Review sheet includes current QAO & Manager instruction; SOP revsn pending date | Reference SOP ❑ ( ) ❑ (())

II. Client Samples (items) listed by Prep Batch

P Batch: | P Batch: | P Batch:

III. Standards & Reagents

Traceability Record (()) | Preparation Logbook ID:

		Analyst			Analyst Comments (see below as well)	Reviewer		Review notes
IV. Calibrations		**Pass**	**Fail***	**N/A**		**Agree**	**C.A.R****	
Corr. Coef. (all analytes	≥ 0.990	❑	❑			❑	❑	
(())	Analytes all within RE%?	❑	❑	❑		❑	❑	
	<LOQ (or are a verified impurity)	❑	❑	❑		❑	❑	
Retention Time of Mid-Standard Int. Std.?		❑	❑	❑		❑	❑	
ICV (2nd Source)	Recovery: 70%-130%	❑	❑			❑	❑	
ICB/CCB	Conc < ½LOQ or <LOD	❑	❑			❑	❑	
CCV	Recovery: 70%-130%	❑	❑			❑	❑	
((CCV concentration 2))	Recovery: 70%-130%	❑	❑			❑	❑	
((CCV low concentration)	**70-130%**	❑	❑	❑		❑	❑	
Internal Standards	50%-150%	❑	❑	❑		❑	❑	
Instrument Replicate %RPD	<%%	❑	❑	❑		❑	❑	
RT of all Surrogates within 6 secs or 0.4 RRT of MidStanda		❑	❑	❑		❑	❑	
V. Analytical Quality Control		**Pass**	**Fail***			**Agree**	**C.A.R****	
Batch Size	≤ 20 samples	❑	❑			❑	❑	
Method Blank (BLK,LRB	Conc < ½LOQ or <LOD	❑	❑			❑	❑	
LCS (BS,LFB)	**Matrix1:** 85-115% **Matrix 2** 80-120%							
Surrogate(s)	**Matrix1:** 85-115% **Matrix 2** 80-120%	❑	❑			❑	❑	
VI. Sample QC		**Pass**	**Fail***			**Agree**	**C.A.R****	
MS/MSD	RPD: ± 30%	❑	❑			❑	❑	
Matrix Spikes ††	**Matrix 1 :** 70-130% **Matrix 2:** 75-125%	❑	❑			❑	❑	
(())	**Matrix 1 : 70-130% Matrix 2: 75-125%**	❑	❑	❑		❑	❑	
†† (unless spike < 30% background)								
VII. Field QC		**Pass**	**Fail***	**Verified**	**N/A**	**Agree**	**C.A.R****	
Field/Equipment Blank(s)	Conc < ½LOQ or <LOD	❑	❑	❑	❑	❑	❑	
Field Duplicates	RPD: ±40% (±2LOQ if <5LOQ)	❑	❑	❑	❑	❑	❑	
Data Agreement	(within 20%RPD or LOQ)	❑	❑	❑	❑	❑	❑	
VIII. Data Management		**Yes**	**N/A**			**Agree**	**C.A.R****	
Manual Integrations Reviewed and Recorded?		❑	❑			❑	❑	
Data Calculations/Entry/Upload Complete & Accurate		❑	❑			❑	❑	
LIMS: Chemist initials; Instrument ID; Update status		❑	❑			❑	❑	
Is optional batch narrative attached?		❑	❑			❑	❑	

IX. Follow up after initial review — **Yes** **N/A**

Corrective actions that were required (C.A.R.) by the reviewer have been completed: ❑ ❑

Signatures & Dates

Analyst | Date | Ma | Reviewer | Date: 3-3

See back for additional comments

Additional Analyst Comments	Reviewer Comments

Analyst	Date	Reviewer	Date:

See back for additional comments

Additional Analyst Comments	Reviewer Comments

The batch was selected for an internal audit: ❑

-4

* If a QC element fails and data is reported with a qualifier, include in the comments the QC result value, the qualifier code, and the grade. If data is not reported, comment "Affected data not reported"

Insert Inorganic/Metals Method Name

I. Analytical Batch Information — **Analytical**

SOP: | Sequence/s:
Version: | Date: | Instrument ID:
Method File(s): | Analysis Date: | Analyst:
Electronic Filename(s): | Analyte Group:
**Review sheet includes current QAO & Manager instruction; SOP revsn pending date | Reference SOP ❑ ( ) ❑ (())

II. Client Samples (items) listed by Prep Batch

P Batch: | P Batch: | P Batch:

III. Standards & Reagents

Traceability Record (()) | Preparation Logbook ID:

IV. Calibrations		Analyst Pass	Fail*	N/A	Analyst Comments (see below as well)	Reviewer Agree	C.A.R**	Review notes
Corr. Coef. (all analytes	≥ 0.998	❑	❑			❑	❑	
(())	Analytes ±20% of true or ± LOQ	❑	❑	❑		❑	❑	
((Interference Check))	<LOQ (or are a verified impurity)	❑	❑	❑		❑	❑	
	not<LOQ, but interf's low so data not affected	❑	❑	❑		❑	❑	
ICV (2nd Source)	Recovery: 90-110%	❑	❑			❑	❑	
ICB/CCB	Conc < ½LOQ or <LOD	❑	❑			❑	❑	
CCV	Recovery: 90-110%	❑	❑			❑	❑	
((CCV concentration 2))	Recovery: 90-110%	❑	❑			❑	❑	
((CCV low concentration)	**90-110%**,	❑	❑	❑		❑	❑	
Internal Standards	50%-150%	❑	❑	❑		❑	❑	
Instrument Replicate %RPD	<%%	❑	❑	❑		❑	❑	
		❑	❑	❑		❑	❑	

V. Analytical Quality Control		Pass	Fail*			Agree	C.A.R**	
Batch Size	≤ 20 samples	❑	❑			❑	❑	
Method Blank (BLK,LRB	Conc < ½LOQ	❑	❑			❑	❑	
LCS (BS,LFB)	**Matrix1:** 85-115% **Matrix 2** 80-120%	❑	❑			❑	❑	

VI. Sample QC		Pass	Fail*			Agree	C.A.R**	
MS/MSD	RPD: ± 20%	❑	❑			❑	❑	
Matrix Spikes ††	**Matrix 1 :** 70-130% **Matrix 2:** 75-125%	❑	❑			❑	❑	
(())	**Matrix 1 : 70-130% Matrix 2: 75-125%**	❑	❑	❑		❑	❑	

†† (unless spike < 30% background)

VII. Field QC		Pass	Fail*	Verified	N/A		Agree	C.A.R**	
Field/Equipment Blank(s)	Conc < ½LOQ	❑	❑	❑	❑		❑	❑	
Field Duplicates	RPD: ±40% (±2LOQ if <5LOQ)	❑	❑	❑	❑		❑	❑	
Data Agreement	(within 20%RPD or LOQ)	❑	❑	❑	❑		❑	❑	

VIII. Data Management	Yes	N/A		Agree	*	
Data Calculations/Entry/Upload Complete & Accurate	❑			❑	❑	
LIMS: Chemist initials; Instrument ID; Update status	❑			❑	❑	
Is optional batch narrative attached?	❑	❑				

IX. Follow up after initial review	Yes	N/A
Corrective actions that were required (C.A.R.) by the reviewer have been completed:	❑	❑

Signatures & Dates

Analyst | Date | Reviewer | Date:

See back for additional comments

Additional Analyst Comments	Reviewer Comments

Additional Analyst Comments	Reviewer Comments

The batch was selected for an internal audit: ❑

* If a QC element fails and data is reported with a qualifier, include in the comments the QC result value, the qualifier code, and the grade. If data is not reported, comment "Affected data not reported".
** C.A.R = Corrective Actions Required--Comment should state if a "green sheet" or "issue" was created.

Appendix C
Report Template

A. REPORT HEADING					
LAB NAME		LAB SAMPLE ID		REPORT TITLE	
LAB ADDRESS				REVISION #	
				REPORT DATE	

B. RMD INFO	
RMD NAME	
RMD ADDRESS	
MANIFEST/CoC NUMBER	
DATE RECEIVED	

C. SAMPLE IDENTIFICATION	
RMD SAMPLE ID	
BATCH ID	
PARENT BATCH ID	

D. PICTURE OF SAMPLE

OPTIONAL
(not required at this time)

E. SAMPLE PROPERTIES	
SAMPLE SIZE *Units=*	
NUMBER of SERVINGS **MIP only*	
MATRIX *Other:*	
SAMPLE CONDITION	
RE-TEST	YES/NO
REMEDIATED	YES/NO
Description	

F. PRODUCT CHARACTERIZATION			PRODUCTION STAGE	
PRODUCT CLASS	*For Plant Material:*	*Other:*		
	For Conc. & Resin:	*Other:*		
	For MIP:	*Other:*		
PRODUCT TYPE			INTENDED ROUTE OF CONSUMPTION	
RETAIL NAME			*Other:*	
Specify:			EXTRACTION SOLVENT	
GROW MATERIAL **flower only*				

G. TEST TYPES RUN

- ☐ (CN) Cannabinoid Profile
- ☐ (HM) Heavy Metals Analysis
- ☐ (MB) Microbiological Test
- ☐ (PT) Pathogen Screen
- ☐ (MY) Mycotoxin Test
- ☐ (VC) Residual Solvents Test
- ☐ (PS) Pesticide Screen
- ☐ (TP) Terpene Profile

H. AUTHORIZATION

CASE NARRATIVE, LABORATORY NOTES, and STATEMENTS

THIS PRODUCT:		
		MAY be dispensed
		MAY be dispensed as <u>INGESTION ONLY</u> product
		MAY <u>NOT</u> be dispensed

LAB AUTHORIZATION SIGNATURE

TABLE I. CANNABINOID PROFILE **Analysis Date:**

Lab Sample ID: *<equal to heading>* Analytical Method: Lab SOP #: Analyst:

Narrative Summary of Analysis

Test ID	Analyte	Concentration *unit=* %wt	"Dose" weight *unit=* mg/serving		LOD *unit=* %wt	LOQ *unit=* %wt
	Δ9-THC					
	THCa					
	CBD					
	CBDa					
	<to add>					
	<to add>					
	<to add>					
	<to add>					
	<to add>					
	<to add>					
	<to add>					
-	**MAX THC**					
-	**MAX CBD**					
-	**CBD:THC RATIO**					

TABLE J. HEAVY METALS **Analysis Date:**

Lab Sample ID: *<equal to heading>* Analytical Method: Lab SOP #: Analyst:

Narrative Summary of Analysis

Test ID	Analyte	Concentration *unit=* ppb	LOD *unit=* ppb	LOQ *unit=* ppb		Limits - All Use		imits - Ingestion Onl	
						Limits (ppb)	Test	Limits (ppb)	Test
	As					200	PASS/FAIL	1500	PASS/FAIL
	Cd					200	PASS/FAIL	500	PASS/FAIL
	Hg					100	PASS/FAIL	1500	PASS/FAIL
	Pb					500	PASS/FAIL	1000	PASS/FAIL

TABLE K. MICROBIOLOGICAL CONTAMINANTS **Analysis Date:**

Lab Sample ID: *<equal to heading>* Analytical Method: Lab SOP #: Analyst:

Narrative Summary of Analysis

Test ID	Analyte Symbol	Test Analysis	Result	Unit		Standard Limits *unit=* CFU/g	Limit Test
	AC	Total Viable Aerobic Bacter		CFU/g			PASS/FAIL
	YM	Total Yeast & Mold		CFU/g			PASS/FAIL
	CC	Total Coliforms		CFU/g			PASS/FAIL
	EB	Total Bile-Tolerant Gram Negative Bacteria		CFU/g			PASS/FAIL

TABLE L. PATHOGENIC BACTERIA **Analysis Date:**

Lab Sample ID: *<equal to heading>* Analytical Method: Lab SOP #: Analyst:

Narrative Summary of Analysis

Test ID	Analyte Symbol	Test Analysis	Result		Standard Limits	Limit Test
	ECPT	*E. coli (O157)*			Not detected in 1g	PASS/FAIL
	SPT	*Salmonella*			Not detected in 1g	PASS/FAIL

TABLE M. MYCOTOXINS **Analysis Date:**

Lab Sample ID: *<equal to heading>* Analytical Method: Lab SOP #: Analyst:

Narrative Summary of Analysis

Test ID	Analyte Symbol	Test Analysis	Result *unit=* ppb	LOD *unit=* ppb	LOQ *unit=* ppb	Standard Limits *unit=* ppb	Limit Test
						<20	PASS/FAIL
						<20	PASS/FAIL
						<20	PASS/FAIL
						<20	PASS/FAIL
						<20	PASS/FAIL

TABLE N. RESIDUAL SOLVENTS **Analysis Date:**

Lab Sample ID: *<equal to heading>* Analytical Method: Lab SOP #: Analyst:

Narrative Summary of Analysis

Test ID	Analyte	Result *unit=* ppm	LOD *unit=* ppm	LOQ *unit=* ppm		Standard Limits *unit=* ppm	Limit Test
	n-Butane					-	-
	Iso-Butane					-	-
	Propane					-	-
	<to add if necessary>						PASS/FAIL
	<to add if necessary>						PASS/FAIL
	<to add if necessary>						PASS/FAIL
	<to add if necessary>						PASS/FAIL
-	**Total Hydrocarbons (Sum)**	**0**	**-**	**-**		**12**	**PASS/FAIL**

TABLE O. PESTICIDES **Analysis Date:**

Lab Sample ID: *<equal to heading>* Analytical Method: Lab SOP #: Analyst:

Narrative Summary of Analysis

Test ID	Analyte	Result *unit=* ppb	LOD *unit=* ppb	LOQ *unit=* ppb	Standard Limits *unit= ppb*	Test		Method QA/QC Test
	Bifenazate				10	PASS/FAIL		
	Bifenthrin				10	PASS/FAIL		
	Cyfluthrin				10	PASS/FAIL		
	Etoxazole				10	PASS/FAIL		
	Imazalil				10	PASS/FAIL		
	Imidacloprid				10	PASS/FAIL		
	Myclobutanil				10	PASS/FAIL		
	Spiromesifen				10	PASS/FAIL		
	Trifloxystrobin				10	PASS/FAIL		
	<to add if necessary>				10	PASS/FAIL		
	<to add if necessary>				10	PASS/FAIL		
	<to add if necessary>				10	PASS/FAIL		
	<to add if necessary>				10	PASS/FAIL		
	<to add if necessary>				10	PASS/FAIL		
	<to add if necessary>				10	PASS/FAIL		
	<to add if necessary>				10	PASS/FAIL		
	<to add if necessary>				10	PASS/FAIL		
	<to add if necessary>				10	PASS/FAIL		
	<to add if necessary>				10	PASS/FAIL		

TABLE P. TERPENE PROFILE **Analysis Date:**

Lab Sample ID: *<equal to heading>* Analytical Method: Lab SOP #: Analyst:

Narrative Summary of Analysis

Test ID	Analyte	CAS Number	Concentration *unit=* %wt	LOD *unit=* wt%	LOQ *unit=* wt%
	<to add>				
	<to add>				
	<to add>				
	<to add>				
	<to add>				
	<to add>				
	<to add>				
	<to add>				
	<to add>				
	<to add>				
	<to add>				
	<to add>				
	<to add>				
	<to add>				
	<to add>				
	<to add>				
	<to add>				
	<to add>				
	<to add>				
	<to add>				
	<to add>				

QA / QC RESULTS

TABLE Q. QC RESULTS - CANNABINOID PROFILE **Analysis Date:**

Analytical Method:	Lab SOP #:	Analyst:
Notes describing QC test		

Analyte	Prep Concentration *unit=*	Measured Concentration *unit=*	RECOVERY (%)
Δ9-THC			
THCa			
CBD			
CBDa			
<to add>			
<to add>			
<to add>			
<to add>			
<to add>			
<to add>			
<to add>			

TABLE R. QC RESULTS - HEAVY METALS **Analysis Date:**

Analytical Method:	Lab SOP #:	Analyst:
Notes describing QC test		

Analyte	Prep Concentration *unit=*	Measured Concentration *unit=*	RECOVERY (%)
As			
Cd			
Hg			
Pb			

TABLE S. QC RESULTS - MICROBIOLOGICAL CONTAMINANTS **Analysis Date:**

Analytical Method:	Lab SOP #:	Analyst:
Notes describing QC test		
Date of most recent QC check:		
Status:		

TABLE T. QC RESULTS - PATHOGENIC BACTERIA

Analytical Method:	Lab SOP #:	Analyst:
Notes describing QC test		

DATE	QC CHECK	PATHOGEN	RESULT	STATUS
	Control (+)	*E. coli (O157)*		
	Control (-)	*E. coli (O157)*		
	Standard 1	*E. coli (O157)*		
	Standard 2	*E. coli (O157)*		
	Control (+)	*Salmonella*		
	Control (-)	*Salmonella*		
	Standard 1	*Salmonella*		
	Standard 2	*Salmonella*		

TABLE U. QC RESULTS - MYCOTOXINS **Analysis Date:**

Analytical Method: Lab SOP #: Analyst:

Notes describing QC test

Analyte	Reference Concentration *unit=*	Measured Concentration *unit=*	STATUS
<to add>			
<to add>			
<to add>			
<to add>			

TABLE V. QC RESULTS - RESIDUAL SOLVENTS **Analysis Date:**

Analytical Method: Lab SOP #: Analyst:

Notes describing QC test

Analyte	Prep Concentration *unit=*	Measured Concentration *unit=*	RECOVERY (%)
<to add>			
<to add>			
<to add>			
<to add>			
<to add>			
<to add>			

TABLE W. QC RESULTS - PESTICIDES **Analysis Date:**

Analytical Method: Lab SOP #: Analyst:

Notes describing QC test

Analyte	Prep Concentration *unit=*	Measured Concentration *unit=*	RECOVERY (%)	STATUS
Bifenazate				
Bifenthrin				
Cyfluthrin				
Etoxazole				
Imazalil				
Imidacloprid				
Myclobutanil				
Spiromesifen				
Trifloxystrobin				
<to add>				
<to add>				
<to add>				
<to add>				
<to add>				
<to add>				
<to add>				
<to add>				
<to add>				
<to add>				