SAFETY COMPLIANCE FACILITY SAMPLING AND TESTING INFORMATION

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This information is intended for Licensed Safety Compliance Facilities (SCF) regulated by the Bureau of Marijuana Regulation, a division of Michigan's Department of Licensing and Regulatory Affairs.

Version 2.0

This information does not constitute legal advice and is subject to change. Licensees are encouraged to seek legal counsel to ensure their operations comply with the Medical Marihuana Facilities Licensing Act and associated Administrative Rules.

INTRODUCTION

The sampling and analysis described in this guidance shall be conducted by a licensed safety compliance facility (SCF) accredited by the International Organization for Standardization (ISO) 17025 (Rule 47(9)(b) R 333.247).

Analytical testing of medical marijuana for safety and potency is increasingly recognized as a critical and necessary component of the industry for several reasons (Freeman et al. 2016):

- Laboratory testing minimizes the risk of pesticides, microbes, heavy metals, molds and residual solvents from being consumed by an immunocompromised population.
- Quantification of cannabinoid profiles and potency becomes available for the consumer and aids in determining appropriate dosing for individual use.
- Laboratory testing provides a sense of public safety and product quality for the tested medical marijuana.

Medical marijuana safety and potency is to be analyzed based on the most current version of the *Cannabis Inflorescence Monograph*, published by the American Herbal Pharmacopeia (AHP) or an alternative testing methodology approved by the department and validated by an independent third party that the methodology followed by the laboratory produces scientifically accurate results for each safety test it conducts. There are very few published standard methods for the analysis of marijuana. The purpose of this document is to provide guidance for the selection of applicable methodology pertaining to the testing of marijuana products. The references outlined in this document are not matrix specific methods and therefore lack complete matrix validation specific to marijuana products.

Rule 47 (R 333.247) of the Administrative Rules establishes testing and procedural requirements for Safety Compliance Facilities (SCFs).

The categories of contaminants identified in Rule 47 (R 333.247) of the Administrative Rules include:

- Potency
- Moisture content
- Water activity
- Chemical residue
- Heavy metals
- Residual solvents
- Microbial screening including foreign matter
- Mycotoxin (if requested by the department)

The potency methods referenced for the analysis of marijuana products are not derived from applicable standard methods as no proper standard method is available. Any method employed that was not derived from a standard method should be rigorously tested and validated prior to analysis of marijuana and marijuana product.

Note: The sources listed in this document are not exhaustive; other methodologies may be appropriate for use. Due to the constant evolution of scientific analytical methods, this reference document represents a living document that will be updated as needed.

Microbial Pathogens and Total Yeast and Mold

Concerning the testing of marijuana product for microbiological contaminants, there is a large pool of standard methods on which to draw. All microbiological methods employed should include applicable controls. Qualitative pathogen methods must confirm presumptive results as either positive or negative by the inclusion of a confirmation step. Confirmation of pathogens should not be addressed by simply rerunning positive sample enrichments or retesting remaining sample.

Methods applicable to *Salmonella spp*. and *E. coli* testing:

- Association of Analytical Communities (AOAC) 2016. “Salmonella in Foods, 967.25” http://www.eoma.aoac.org/methods/info.asp?ID=47595
- Food and Drug Administration (FDA), 2016. Bacteriological Analytical Manual (BAM). http://www.fda.gov/Food/FoodScienceResearch/LaboratoryMethods/ucm2006949.htm
- International Standards Organization (ISO), 2002. “ISO/TS 6579:2002.” http://www.iso.org/iso/catalogue_detail.htm?csnumber=29315
- International Standards Organization (ISO), 2012. “ISO/TS 13136:2012.” http://www.iso.org/iso/catalogue_detail.htm?csnumber=53328
- Salfinger, Yvonne and Tortorello, Mary Lou, 2015. Compendium of Methods for the Microbiological Examination of Foods, 5th Edition. American Public Health Association.
- United States Department of Agriculture: Food Safety and Inspection Service (USDA FSIS), 2016. Microbiology Laboratory Guidebook. http://www.fda.gov/Food/FoodScienceResearch/LaboratoryMethods/ucm2006949.htm

Methods applicable to total yeast and mold testing:

- Association of Analytical Communities (AOAC) 2016. “Yeast and Mold Counts in Foods, 997.02.” http://www.eoma.aoac.org/methods/info.asp?ID=46847
- Food and Drug Administration (FDA), 2016. Bacteriological Analytical Manual (BAM). http://www.fda.gov/Food/FoodScienceResearch/LaboratoryMethods/ucm2006949.htm

- Salfinger, Yvonne and Tortorello, Mary Lou, 2015. Compendium of Methods for the Microbiological Examination of Foods, 5th Edition. American Public Health Association.

Residual Solvent Testing

Concerning residual solvent testing, there is a large pool of standard methods from which to draw. All methods employed should include applicable controls.

Methods applicable to residual solvent testing:

- American Society for Testing Materials (ASTM), 2016. https://global.ihs.com/standards.cfm?publisher=ASTM&RID=Z56&MID=ASTM&gc lid=CJTImMLNosoCFQIHaQodhgoHkQ
- Environmental Protection Agency (EPA), 2016. “310B-Residual Solvents.” http://www3.epa.gov/ttn/emc/methods/method310b.html
- Lake, Rick., 2016. “RESTEK Revised USP 467 Residual Solvent Method.” RESTEK: http://www.restek.com/Technical-Resources/TechnicalLibrary/Pharmaceutical/pharm_A017
- United States Pharmacopeia (USP), 2008. “<467> Residual Solvents.” http://www.usp.org/usp-nf/official-text/accelerated-revisionprocess/accelerated-revision-history/general-chapter-organic-volatile

Pesticide Residue Testing

Concerning pesticide testing, there is a large pool of standard methods from which to draw. All methods employed should include applicable controls.

Methods applicable to pesticide residue testing:

- Association of Analytical Communities (AOAC) 2016. “Pesticide Residues in Foods by Acetonitrile Extraction and Partitioning with Magnesium Sulfate, 2007.01” http://www.eoma.aoac.org/methods/info.asp?ID=48938
- Collaborative Validation of the QuEChERS Procedure for the Determination of Pesticide Residues in Food by LC-MS/MS. J.Agric.Food Chem, 2011,59,63836411.
- Determination of Pesticide Residues in Foods by Acetonitrile Extraction and Partitioning with Magnesium Sulfate: Collaborative Study LEHOTAY: Journal of AOAC International Vol.90,No.2,2007.
- Food and Drug Administration (FDA), 2016: Pesticide Analytical Manual (PAM). http://www.fda.gov/Food/FoodScienceResearch/LaboratoryMethods/ucm2006955.htm
- International Standards Organization (ISO), 2016. http://www.iso.org/iso/home.html
- United States Department of Agriculture: Food Safety and Inspection Service (USDA FSIS), 2016. Chemistry Laboratory Guidebook. http://www.fsis.usda.gov/wps/portal/fsis/topics/science/laboratories-andprocedures/guidebooks-and-methods/chemistry-laboratory-guidebook

Potency Determination

Concerning potency analysis, while several published methods exist, the available methods have not been validated to the level of a standard method. The following is a list of appropriate reference methods. Potency methods should be validated extensively to ensure they meet the requirements of testing.

Methods applicable to potency determination:

- Backer, Benjamin De., et al., 2009. Innovative development and validation of an HPLC/DAD method for the qualitative and quantitative determination of major cannabinoids in cannabis plant material. Journal of Chromatography B, 887 4115-4124.
- Bovens, Michael., et al., 2009. Recommended method for the identification and analysis of cannabis and cannabis products: manual for use by National drug analysis laboratories. United Nations. https://www.unodc.org/documents/scientific/ST-NAR-40-Ebook.pdf
- Gambaro, Veniero., et al., 2002. Determination of primary active constituents in Cannabis preparations by high-resolution gas chromatography/flame ionoization detection and high-performance liquid chromatography/UV detection. Analytica Chimica Acta 468, 245-254.
- L. Ambach, F. Penitschka, A. Broillet, S. König, W. Weinmann., 2014. Simultaneous quantification of delta-9-THC, THC-acid A, CBN and CBD in seized drugs using HPLC-DAD. Forensic Science International 243, 107-111.
- Stolker, A.A.M., et al., 2004. Determination of cannabinoids in cannabis products using liquid chromatography –ion trap mass spectrometry. Journal of Chromatography A, 1058, 143-151.
- Swift, Wendy., et al., 2013. Analysis of Cannabis Seizures in NSW, Australia: Cannabis Potency and Cannabinoid Profile, PLOS One v.8 i.7 e70052.
- Upton, Roy., et al., 2014. Cannabis Inflorescence Cannabis Spp.: Standards of Identity, Analysis, And Quality Control. American Herbal Pharmacopoeia.

Validation Guidelines

Any method derived from a standard method or literature method requires validation showing that the method is fit to purpose. In the absence of standard methods, a single laboratory validation or equivalent is required to show that the method is fit for purpose in the intended matrix and, if applicable, that any modifications to the original method do not negatively impact performance. Method validation should, at a minimum, verify accuracy, precision, analytical sensitivity, analytical specificity, limit of detection, limit of quantification, reportable range and the identification of interfering substances. For microbiological methods adopted from a standard method, inclusivity/exclusivity does not require complete reassessment, provided that the referenced media, primers, probes, antibodies, critical chemistries, etc., were not modified.

- Association of Analytical Communities (AOAC) 2012. “Methods Committee Guidelines for Validation of Microbiological Methods for Food and Environmental

Surfaces." AOAC: http://www.aoac.org/imis15_prod/AOAC_Docs/StandardsDevelopment/AOAC_Validation_Guidelines_for_Food_Microbiology-Prepub_version.pdf

- Association of Analytical Communities (AOAC) 2002. "Guidelines for Single Laboratory Validation of Chemical Methods for Dietary Supplements and Botanicals" AOAC: http://www.aoac.org/imis15_prod/AOAC_Docs/StandardsDevelopment/SLV_Guidelines_Dietary_Supplements.pdf
- Food and Drug Administration (FDA) 2015. "Analytical Procedures and Methods Validation for Drugs and Biologics: Guidance for Industry." FDA: http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm386366.pdf
- Food & Drug Administration Office of Foods and Veterinary Medicine (FDA) 2015. "Guidelines for the Validation of Analytical Methods for the Detection of Microbial Pathogens in Foods and Feeds 2nd Edition." FDA: http://www.fda.gov/downloads/ScienceResearch/FieldScience/UCM298730.pdf
- International Conference on Harmonization (ICH) 1996. "Harmonised Tripartite Guideline Validation of Analytical Procedures: Text and Methodology." ICH: http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Quality/Q2_R1/Step4/Q2_R1__Guideline.pdf
- United States Department of Agriculture Food Safety and Inspection Service (USDA FSIS) 2010. "Guidance for Test Kit Manufacturers, Laboratories: Evaluating the Performance of Pathogen Test Kit Methods." USDA: http://www.fsis.usda.gov/shared/PDF/Validation_Studies_Pathogen_Detection_Methods.pdf

In an effective testing program, standardized sampling procedures are an integral component to quality laboratory testing. The data generated from all analytical methods should be consistently reliable and legally defensible. To achieve this, method precision and accuracy measurements should be performed during the sample testing process. The guidance below will provide some best practices for the sample collection by the SCF.

SAMPLING RECOMMENDATIONS

According to Rule 47(9)(c) (R 333.247) of the Administrative Rules an SCF shall maintain internal standard operating procedures (SOPs). It is the responsibility of the SCF to define a standard operating procedure that minimizes both imprecision and bias and lists chronological steps that ensure a consistent and repeatable method.

The objective of a sampling procedure is to ensure the proper collection, clear labeling, proper preservation, careful transportation and storage of samples by trained personnel for laboratory analyses. Collection of the sample is critical as it must be truly representative of the material being analyzed or the results will not be meaningful.

SCFs should develop a statistically valid sampling method to collect a representative sample from each batch of product.

The sample should be adequate to perform the required testing. The amount of sample required for testing may vary due to the sample matrix, analytical method and laboratory specific procedures, but a minimum sample volume of 0.5% of the batch is required to achieve a representative sample for analysis according to Rule 48(2)(b) (R 333.248) of the Administrative Rules**.** The department may publish recommendations for this subdivision based on the type of marihuana product being tested. For concentrates, extracts and marijuana-infused products, the sample volume should follow the guidelines in this document.

An example collection procedure is included in this document, but each SCF is required by rule R 333.247 9(c) to maintain internal standard operating procedures, which includes having their own collection procedure. For detailed information regarding sample collection, please refer to “Good Samples: Guidance on Obtaining Defensible Samples” (Thiex 2015), or “Sampling Cannabis for Analytical Purposes” (Sexton 2013).

(See Appendix A for information regarding required testing for each sample matrix).

EXAMPLE COLLECTION PROCEDURE

Representative Sampling

When sampling a harvest batch, the sampler should check for signs of non-uniformity such as different types or sizes of containers, variations in marks and labels, or mixed batch numbers. During sampling, the sampler should look for differences in the usable marijuana being sampled such as color, shape, size and treatment. The batch should be uniform for all factors that appear on the label; hence, variations in the product may indicate nonuniformity in the batch and that any sample drawn may not be representative for testing. The sampler should document anomalies on the SCF’s sampling form and in the statewide monitoring system.

General guidelines for sampling include:

1. Gaining access to the entire batch and in addition, ensuring that the package has the correct METRC RFID tag.
2. Use of appropriate sampling equipment and consistently following procedures.
3. Taking equal portions for each sample increment.
4. Randomly or systematically taking sample increments throughout the batch.
5. Obtaining a minimum number of sample increments, which will be based on batch size.
6. Recording all observations and procedures used while collecting the sample increments on an appropriate sampling form.
7. Samplers should ask the facility to show the source package for derivative packages to ensure that all required tests are selected by the facility at the time of the sampling event.

8. Questions about required testing should be referred to the department.

Random Sampling

Prior to beginning the sampling procedure, the sampler should survey the site to identify the conditions under which the marijuana is being kept. All sampling must be performed by personnel employed by the SCF and must be in accordance with the SCF's internal SOP. The requirements for sampling and sample size are provided in Rule 48(2)(b) (R 333.248) of the Administrative Rules. If the SCF will perform additional testing in addition to the required testing this must be part of the planning process. To ensure representativeness, the sampling plan must be designed such that each increment within the batch has an equal chance of being selected.

Note: The sample size must be enough to complete all analyses required but shall in no case be less than 0.5% of the weight of the batch. The maximum batch size shall be 15 pounds.

Sample increments should be randomly selected from different locations within a container or set of containers. The SOP should include how to do the following:

1. Assign location numbers within containers.
2. Use a random number generator to determine which location to sample.
3. Document where each sample increment was sampled, and the volume collected from each increment.

Assign divisions based on the type of container in the site-specific sampling plan. Use a random number generator with the higher number equal to the number of divisions for the container. When there are multiple containers use existing or arbitrary order of containers to assign numbers to the total of "divisions multiplied by total number of containers" (divisions x # containers = total number of random increments) and record in the sampling report. The SCF should have details in its SOP, on how it will achieve random sampling in an unclear decision unit.

Equipment and Supplies

Below is a list of equipment and supplies that may be necessary for collecting marijuana samples:

- Sampling equipment such as spoons, spatulas, transfer pipettes, or other matrix specific tools
- Tongs
- Teri-wipes, or equivalent
- Field balance (Capable of 0.01 g measurements)
- Calibrated Verification Weights appropriate to verify accuracy of field balance
- Cleaning supplies – solvent, bleach, 70% ethanol
- Gloves (powder-free, nitrile, sterile)

- Mylar bags (for final sample transport and storage) and/or amber glass jars (for final sample transport and storage)

Records and Documentation

The sampling SOP should be readily accessible to all pertinent personnel, should use these guidelines as minimum requirements, and must include additional detail specific to the SCF's procedures. Deviations from, or additions to, the SOP must be documented in detail and included on the final report.

Sampling Records/Field Data

In addition to collecting the sample, a sampling report form should be created for the batch sampled and should include any observations made while taking the sample. Examples on information that should be included:

- Name and address of producer including licensee number
- Product type
- Total mass of batch
- Unique SCF batch ID#, METRC batch ID #, as designated
- Total container number
- Number of sample increments
- Number of containers sampled
- Number of sample containers collected
- Total mass sampled
- Sampling Procedure ID and revision date
- Description of equipment used
- Place where sampled
- Date sampled
- SCF license number
- Sampler's identification and/or signature
- Name of responsible party for the batch and transport information
- Receiving SCF and types of tests required or requested

If any of the above information requested on the sampling report form is unavailable, indicate "N/A" in the appropriate space. All sampling report forms should be signed by the sampler.

Sampling a Batch of Marijuana

1. Physically locate the batch to be sampled as well as the package and tag information from the statewide monitoring system.
2. Review the container label information for harvest lot number, producer, and other pertinent information. Each harvest lot should be separated into batches of 15 lbs. or less and must be assigned a unique batch number by the grower. Do not sample if a unique batch number is not available.

3. Determine the number of containers in the batch and the batch size. Visually verify the batch size for each container. Do not sample if the batch size is unavailable or exceeds 15 lbs. for a container or if the batch weight does not match the information entered into the statewide monitoring system.
4. Determine the number of containers from which sample increments must be collected using a random number generator.
5. Select the appropriate sampling tool to ensure that it reaches all portions of the container.
6. Collection instruments should be clean prior to use to prevent cross-contamination of sample increments. Sampling tools which appear to be dirty or otherwise compromised should not be used.
7. To prevent contamination, sampling tools should be cleaned and sealed at the SCF prior to use or may be cleaned in the field between batches using an appropriate solvent and decontaminant to prevent cross contamination of batches during sampling.
8. Results from cleaning procedure tests should be below the reporting limit of the target analyte(s) for the associated analyses.
   Note: Samplers should take extreme care if sampling from multiple sites in one day to ensure contaminants, pathogens, or organisms are not transferred between facilities. The sampler may clean sampling equipment in the field between samplings at a single facility. However, the sampler should bring enough sets of sampling equipment to use a new set at each facility. All field equipment should be returned to the SCF following sampling and cleaned according to the SCF's procedures. Where aseptic technique is required, please refer to the FDA Aseptic Sample guidelines (Investigations Operations Manual Subchapter 4.3.6) for information.
9. Visually inspect each test sample increment to assess uniformity;
10. If non-uniformity is identified, record observation in the sampling report. It is expected with marijuana to have variable sizes of flowers. When drawing sample increments, approximately equal amounts of product are to be taken with each probing and from each container. Care must be taken by the sampler to not damage the portion of the product which is not being collected.
11. Combine all sample increments to form the composite sample.
12. Ensure enough sample increments are taken to meet sample size requirements for all analytical method(s) being performed.
13. Seal and label the composite sample with the following minimum requirements:

    - SCF license number
    - Unique identifier for sampling event
    - Sampling date and name of sampler
    - Producer's license or registration number
    - Harvest batch numbers
    - Label "PRODUCT NOT TESTED" in bold capital letters in minimum 12-point font.

14. Apply a custody seal to the sample container in a manner which prevents the product from being tampered with or transferred prior to testing. This seal may contain the SCF sample identification number.
15. Complete the sampling report while at the sampling location as well as an appropriate chain of custody form and data entry into the statewide monitoring system.
16. The sample, sampling report and manifest from the statewide monitoring system should be transported to the SCF using packaging appropriate for secure and timely transport.

Preparation of the Sample

1. The SCF must have detailed procedures on maintaining custody and sample integrity during transport. These procedures should take into consideration controlling temperature and other environmental factors.
2. Submit the composite sample to the SCF in its entirety.
3. Composite samples must always be identified by labeling or marking the sample container to associate them with the batch from which they originated and with the sampling report. Containers for sample transport must be designed to prevent damage, contamination, spillage, or commingling of the sample during transport. Examples of sampling containers include: glass, amber jar with a PTFE-lined lid or a Mylar bag. A tamper-proof seal is should be marked with the sampler's name, date, and sample number.

Preparing a sample for Retesting

1. As prescribed in Rule 46 (R 333.246), a safety compliance facility may test or retest a sample to validate the results of a failed safety test except as indicated under subrule (2) of this rule.
2. A failed test sample must pass 2 separate retests consecutively to be eligible to proceed to sale or transfer. If both retests pass, the batch is out of quarantine and eligible for sale or transfer. If 1 or both retests fail, the marihuana product must be destroyed as provided in these rules. A failed safety test must include documentation detailing the initial failure and the corrective action in the statewide monitoring system.
3. Rule 48(2)(f) (R 333.248) A safety compliance facility may request additional sample material from the same licensee from which the sample was collected for the purposes of completing the required safety tests as long as the requirements of this rule are met. Each retest will be a new sample and the sample must be enough in volume to perform the testing for the required parameter and must be chosen at random from the harvest batch.
4. A marihuana product is prohibited from being retested in all the following circumstances:

    a) The marihuana product is in a final package.

b) A final test for chemical residue failed pursuant to these rules. If the amount of chemical residue or chemical residue active ingredient found is not permissible by the department, the marijuana product is ineligible for retesting and the product must be destroyed.

c) A final failed test for microbials on marihuana-infused product is ineligible for retesting and the product must be destroyed.

Quality Assurance/Quality Control

Representative sampling should meet a 95% confidence level and limit sampling error. Increasing the number of sample increments to compensate for normal batch heterogeneity is the simplest means to achieve a representative sample. Typically, a minimum of ten (10) sample increments is considered a representative decision unit for marijuana. The sampler should be prepared to collect adequate sample mass for all analyses requested by the producer.

Field Quality Control

Field sampling equipment should be certified clean prior to use by the SCF. Cleaning techniques will vary depending upon the desired analysis. In general, sampling equipment should be sterile for microbiology samples and clean for chemistry samples. The SCF should perform cleanliness checks on each batch of sampling equipment prior to taking that equipment into the field. Results from cleaning procedure tests must be below the reporting limit of the target analyte(s) for the associated analyses. If cleanliness checks fail, the sampling equipment must be re-cleaned, sterilized and retested.

Field Duplicates

Field duplicates are recommended for any marijuana sampling event, but not required. The field duplicate should be collected using the same procedure and contain the same number of sample increments as the primary sample. The SCF must have documentation of the client request for a field duplicate with any client specified quality objectives and precision limits should meet the client’s need.

Equipment Blanks

Equipment rinse blank samples provide a Quality Control check on the potential for cross contamination by measuring the effectiveness of the decontamination procedures on the sampling equipment. An equipment blank is required to validate equipment cleaning procedures for all required analyses. It is recommended but not required that an equipment blank is collected upon each sampling event to demonstrate the equipment was not introduced to contamination after cleaning. The equipment rinse blank samples consist of analyte-free matrix, as applicable, rinsed across sample

collection and processing equipment. If the analytes of interest are detected in the equipment rinse blank samples, the detected concentrations will be compared to the associated sample results to evaluate the potential for contamination.

The equipment blank should pass the required analysis at <LOQ for cleaning validation. If the equipment blank is collected at the sampling event, the lab should have acceptability guidelines listed in their SOP and what actions to take if the evaluation demonstrates unacceptable results.

Demonstration of Capability

Prior to testing samples, a satisfactory initial demonstration of capability (IDOC) or competency assessment should be used. The SCF should have a documented procedure for performing the IDOC.

The IDOC should be repeated:

1. Every time there is a change in personnel or method and
2. When the method has not been performed by the SCF or sampler within a 12-month period.

This procedure should employ one of the following approaches to demonstrating capability:

1. Comparison of replicate samples within a defined Relative Standard Deviation (%RSD)[1].
2. Comparison of a sample collected to that of one collected by personnel with an existing IDOC within a defined Relative Percent Difference (RPD).

Thereafter, ongoing continuing demonstration of capability (CDOC) as per the quality control requirements referenced in the SOP should be done at least annually. The SCF should have a documented procedure for performing the CDOC. The SCF should retain documentation verifying CDOC for each sampler and make this documentation available upon request.

Sampler Qualifications

Model qualifications for samplers of marijuana are:

- Physically able to perform the duties of a sampler
- No conflict of interest
- Employed by the SCF
- Pass initial and ongoing demonstrations of capability

Education and Training for Samplers

Initial documented training – including principles, procedures, and policies of sampling – should be performed by an instructor that has demonstrated competency in performing and instructing on the sampling methods referenced or equivalent.

Field Audits

The SCF should adopt an ongoing system for performing audits of field activities. Field audits should be conducted periodically and in accordance with a predetermined schedule and procedure. The goal of the field audit is to verify that the sampling operation continues to comply with the requirements of the regulations and is being performed according to the SCF's sampling SOP. Audits are to be carried out by trained and qualified personnel who are, wherever resources permit, independent of the activity to be audited. The field audit shall address all elements of the sampling activities and shall be documented.

When field audit findings cast doubt on the effectiveness of the operations or on the correctness or validity of the field sampling activities, the associated SCF should take timely corrective action and notify customers in writing if investigations show that test results may have been affected.

Auditing Checks

1. Using audit checklists:
   - Review sampling and performance records from the preceding year for deficiencies in the application of sampling protocol
   - Observe the sampler conducting sampling procedures
   - Have the auditor and sampler collect samples from the same harvest lot for evaluation and comparison of results
2. Record any deficiencies and initiate corrective action.

Sample size

As stated in Rule 48(2)(b) (R 333.248), the sample size must be sufficient to complete all analyses required but shall in no case be less than 0.5% of the weight of the batch. The maximum batch size is 15 pounds. The required sample size for a given batch size varies depending upon the size of the batch. Please refer to Table 1, below.

Table 1- Example Sample size requirements based on size of batch

Batch size in Pounds (lbs.)	Required sample size		
	Pounds (lbs.)	Ounces (oz)	Grams (g)
≤1	0.005	0.08	2.3

1.01 ≤2	0.010	0.16	4.5
2.01 ≤3	0.015	0.24	6.8
3.01 ≤4	0.020	0.32	9.1
4.01 ≤5	0.025	0.40	11.3
5.01 ≤6	0.030	0.48	13.6
6.01 ≤7	0.035	0.56	15.9
7.01 ≤8	0.040	0.64	18.1
8.01 ≤9	0.045	0.72	20.4
9.01 ≤10.	0.050	0.80	22.7
10.01≤11	0.055	0.88	25.0
11.01≤12	0.060	0.96	27.3
12.01≤13	0.065	1.04	29.6
13.01≤14	0.070	1.12	31.9
14.01≤15	0.075	1.20	34.2

Sampling a batch

1. When collecting a primary sample from a batch, a minimum of ten (10) sample increments should be collected. Collect the sample increments by following different paths through the batch container or by taking the sample increments systematically at well-separated points along a heptagonal pattern.
2. As the batch increases in size, it is necessary to collect additional sample increments to make primary sample (Table 2).

Table 2 – Minimum number of sample increments for the primary sample based on batch size.

Batch Size (lbs.)	≤ 2	≤ 4	≤ 6	≤ 8	≤ 10	≤ 12	≤ 14	≤ 15
# of increments	7	7	8	8	9	9	10	10

Concentrate & Extract Sample Increment Specifications

Process Lot Weight (grams)	Sample Increments (3-gram increments)
0-230	4
231-680	8
681-1360	12
1361-2720	16
2721-4540	20
4541+	32

Marijuana Infused Product Sampling Size Specifications

Process Lot (units)	Sample Size (units)
2-15	2
16-50	3
51-150	5
151-500	8
501-3200	13
3201-35000	20

Required Safety Tests and Limits

Potency

Cannabinoid potency data quantifies levels of plant cannabinoids present in cannabis products. Producers are required by Rule 47 (R 333.247) of the Administrative Rules to obtain potency levels for THC and CBD, the two most common cannabinoids.

It is important for patients to know THC and CBD levels as these will have a strong influence on the effects of the product. For example, some patients may want a strain with a high CBD:THC ratio. The required cannabinoid tests include Tetrahydrocannabinol level (THC), Tetrahydrocannabinol acid level (THC-A), Cannabidiol (CBD) and Cannabidiol acid levels (CBD-A).

Total THC and CBD values should be calculated and reported as follows:

Total THC= (THCa * 0.877) + d9-THC

Total CBD= (CBDa * 0.877) + CBD

The department recommends potency results be reported “as is” and not corrected for moisture content. Using dry-weight results, the weight of a sample if it was completely dried out with no moisture left present higher values. If potency results are reported based on dry-weight, a comment should be added to the report.

Chemical Residue

BMR published a list of approved chemicals for use on medical marijuana. To assure the safety of the public the department published a list of banned chemical ingredients

that cannot be used on medical marijuana products in accordance with Rule 47(12). The rule states, “the list for acceptable action limits must meet those set forth in legal regulations for tolerances and exemptions for chemical residues in food, 40 CFR part 180, subpart C, or the federal insecticide fungicide, and rodenticide act, 7 USC 136 to 136y, whichever is more stringent.” Since there are no federally recognized and published limits for marijuana in 40 CFR part 180, subpart C, or the federal insecticide fungicide, and rodenticide act, 7 USC 136 to 136y; the department published the below list.

Chemical residue testing will be performed for the published list of banned chemical ingredients, the action limits are provided in the table below. If a sample exceeds the published action limit, the sample will be documented as a fail in the statewide monitoring system. Action limits will be updated based on the limits of quantitation (LOQ) achievable by the SCFs. The list will be continually evaluated and updated based on available scientific and industry information, or if the federal government adds marijuana to 40 CFR part 180, subpart C, or the federal insecticide fungicide, and rodenticide act, 7 USC 136 to 136y.

Table 3- List of Banned ingredients Parts Per Million (PPM)

Analyte	Chemical Abstract Services (CAS) Registry number	Action Limit (ppm)
Abamectin	71751-41-2	0.5
Acephate	30560-19-1	0.4
Acequinocyl	57960-19-7	2
Acetamiprid	135410-20-7	0.2
Aldicarb	116-06-3	0.4
Azoxystrobin	131860-33-8	0.2
Bifenazate	149877-41-8	0.2
Bifenthrin	82657-04-3	0.2
Boscalid	188425-85-6	0.4
Carbaryl	63-25-2	0.2
Carbofuran	1563-66-2	0.2
Chlorantraniliprole	500008-45-7	0.2
Chlorfenapyr	122453-73-0	1
Chlorpyrifos	2921-88-2	0.2
Clofentezine	74115-24-5	0.2
Cyfluthrin	68359-37-5	1
Cypermethrin	52315-07-8	1
Daminozide	1596-84-5	1
DDVP (Dichlorvos)	62-73-7	1
Diazinon	333-41-5	0.2
Dimethoate	60-51-5	0.2
Ethoprophos	13194-48-4	0.2

Etofenprox	80844-07-1	0.4
Etoxazole	153233-91-1	0.2
Fenoxycarb	72490-01-8	0.2
Fenpyroximate	134098-61-6	0.4
Fipronil	120068-37-3	0.4
Flonicamid	158062-67-0	1
Fludioxonil	131341-86-1	0.4
Hexythiazox	78587-05-0	1
Imazalil	35554-44-0	0.2
Imidacloprid	138261-41-3	0.4
Kresoxim-methyl	143390-89-0	0.4
Malathion	121-75-5	0.2
Metalaxyl	57837-19-1	0.2
Methiocarb	2032-65-7	0.2
Methomyl	16752-77-5	0.4
Methyl parathion	298-00-0	0.2
MGK-264	113-48-4	0.2
Myclobutanil	88671-89-0	0.2
Naled	300-76-5	0.5
Oxamyl	23135-22-0	1
Paclobutrazol	76738-62-0	0.4
Permethrins*	52645-53-1	0.2
Prallethrin	23031-36-9	0.2
Phosmet	732-11-6	0.2
Piperonyl_butoxide	51-03-6	2
Propiconazole	60207-90-1	0.4
Propoxur	114-26-1	0.2
Pyridaben	96489-71-3	0.2
Pyrethrins+	8003-34-7	1
Spinosad	168316-95-8	0.2
Spiromesifen	283594-90-1	0.2
Spirotetramat	203313-25-1	0.2
Spiroxamine	118134-30-8	0.4
Tebuconazole	80443-41-0	0.4
Thiacloprid	111988-49-9	0.2
Thiamethoxam	153719-23-4	0.2
Trifloxystrobin	141517-21-7	0.2

* Permethrins should be measured as cumulative residue of cis- and trans-permethrin isomers (cas numbers 54774-45-7 and 51877-74-8).
+ Pyrethrins should be measured as the cumulative residues of pyrethrin 1, cinerin 1 and jasmolin 1 (cas numbers 121-21-1, 25402-06-6, and 4466-14-2 respectively).

Residual Solvents

Some producers of marijuana products use solvents and other chemicals to extract and/or concentrate active ingredients. BMR has adopted a list of action limits for solvent based products based on a literature review of common extraction and concentration techniques in the industry. Action limits are based on the "International Conference for Harmonisation (ICH) Guideline Q3C (R5) on Impurities: Guidelines for residual solvents" and information provided by states with current medical marijuana programs.

Table 4- Action Limits for Residual Solvents in Parts Per Million (PPM)

Solvent	CAS No.	Action Limit for Products Meant for Inhalation (ppm)	Action Limit for All Other Products (ppm)
1,2-Dichloroethane	107-06-2	2	5
Acetone	67-64-1	750	5000
Acetonitrile	75-05-8	60	410
Benzene	71-43-2	1	2
Butanes (all isomers)	106-97-8	800	5000
Chloroform	67-66-3	2	60
Ethanol	64-17-5	1000	5000
Ethyl acetate	141-78-6	400	5000
Ethyl ether	60-29-7	500	5000
Ethylene oxide	75-21-8	5	50
Heptane	142-82-5	500	5000

Hexanes (all isomers)	110-54-3	50	290
Isopropyl alcohol	67-63-0	500	5000
Methanol	67-56-1	250	3000
Methylene chloride	75-09-2	125	600
Pentanes (all isomers)	109-66-0	750	5000
Propane	74-98-6	2100	5000
Trichloroethylene	79-01-6	25	80
Toluene	108-88-3	150	890
Total xylenes (ortho-, meta-, para-)	1330-20-7	150	2170

Microbiological Impurities

The presence of microbes is common in natural products. It is important to distinguish between organisms ubiquitous in nature and those that are known pathogens. “Indicator tests” do not directly test for pathogens but serve as quality tests or indications that follow-up pathogen testing should be performed (Holmes et al. 2015). The criteria for acceptability are in Table 5 (below). The table lists the microbiological impurities and the detection limits associated with each organism to be tested.

In addition, Aspergillus has been added to the organisms which will require identification. Aspergillus is a mold that produces extremely hardy spores and is capable of replication at much lower water activity levels compared to other organisms. Under normal conditions, the human immune system removes these from the lungs. In the immunocompromised, however, certain Aspergillus species can cause invasive lung disease. BMR has established detection limits based on the literature available.

Water activity (Aw)

Water activity (Aw) is a measure of the available water that can be utilized for microbiological growth. Aw ranges from 0 to 1 with microbial growth unlikely below Aw 0.6. Most marijuana is dried and cured to a final water activity level of Aw 0.3-0.6, most

pathogens cannot grow below Aw 0.9 (Holmes et al. 2015). Water activity, or the moisture of the marijuana flower in units, measured below Aw 0.65 will safeguard marijuana products against microbial growth during storage and before sale. A solid or semi-solid edible marijuana product shall be deemed to have passed water activity testing if the water activity does not exceed 0.85 Aw.

Foreign Matter Test

This is a pass/fail test that examines the material for the presence of sand, soil, cinders, dirt, insect fragments, hair, mammalian excreta and mold, also for the presence of foreign matter of inorganic origin, such as metal or plastic shavings, particles of rubber, packaging contaminants, etc. Failures should be documented photographically.

Table 5- Microbial Screening, Foreign Matter, Water Activity and Moisture Content Limits

Total Viable Aerobic Bacteria CFU/g
Unprocessed materials 10^5 Processed material 10^5 CO2 and solvent-based extracts 10^4
Total Yeast and Mold CFU/g
Unprocessed materials 10^4 Processed material 10^4 CO2 and solvent-based extracts 10^3
Total Coliforms CFU/g
Unprocessed materials 10^3 Processed material 10^3 CO2 and solvent-based extracts 10^2
E. coli* (pathogenic strains) and *Salmonella spp.
Unprocessed materials not detected in 1 gram Processed material not detected in 1 gram CO2 and solvent-based extracts not detected in 1 gram
Bile-tolerant gram-negative bacteria CFU/g
Unprocessed materials 10^3 Processed material 10^3 CO2 and solvent-based extracts 10^2
Aspergillus flavus, Aspergillus fumigatus, Aspergillus niger and Aspergillus terreus
This is a pass/fail test. If the Aspergillus spp. are detected, the sample fails.
Foreign Matter
Not more than 5.0% of stems 3mm or more in diameter; not more than 2.0% of other foreign matter (mites, hair, mold, etc.).
Water Activity
A marijuana sample shall be deemed to have passed water activity testing if the water activity does not exceed 0.65 Aw A solid or semi-solid edible marijuana product shall be deemed to have passed water activity testing if the water activity does not exceed 0.85 Aw

Moisture Content of dry material (crude marijuana after packaging)
Not more than 15%

Heavy Metals

Elemental impurities do not provide any therapeutic benefit to the medical marijuana patient. Because of their high degree of toxicity, arsenic, cadmium, lead, chromium and mercury rank among the priority metals that are of public health significance (Tchounwou P et al. 2012). The BMR requires an SCF to test for the presence of heavy metals in medical marijuana.

Table 6 lists the heavy metals required and their associated concentration limits based on a 10 gram/day consumption of medical marijuana.

Table 6: Heavy Metals Concentration Limits

Heavy metal	Action Limit for all Inhaled Marijuana (ppm)	Action Limit for other Marijuana products (ppm)
Lead	< 0.5	< 0.5
Inorganic Arsenic	< 0.2	< 1.5
Mercury	< 0.1	< 3.0
Cadmium	< 0.2	< 0.5
Total Chromium	< 0.6	2.0

Homogeneity Test

Ensuring that THC is distributed uniformly throughout a batch of a marijuana-infused product provides users with the assurance of a consistently prepared edible. A user who may be accustomed to a chocolate bar containing 50mg of THC will know what effect to expect when he/she consumes that bar.

A packaged unit of infused product cannot contain more than 200 mg of THC and should be divided into distinct and easily identifiable dosages. Each dose should contain no more than 50 mg of THC. Testing for homogeneity is not required on every batch every time. The test is required on the **initial batch** and **every six months** as verification, if the manufacturing process does not change. The processor should attest that there are no changes to the manufacturing process prior to the SCF taking a sample. The SCF should include this attestation on the chain of custody form.

Rule 61 (2) (R 333.261) A processor shall have a process in place to test homogeneity of marijuana-infused products. The allowable variation for weight and delta-9 tetrahydrocannabinol (THC) potency between the actual results and the intended serving is to be + or – 15%. Although processors are not required to have homogeneity testing completed on cannabinoids aside from delta-9 THC, accurate dosing is important, and the processor may request this testing. Homogeneity testing only applies to marijuana-infused products in accordance with Rule 61.

Proficiency Testing

The Medical Marihuana Facilities Licensing Act (MMFLA) and the Administrative Rules, Rule 47(8) (R 333.247) require the Department of Licensing and Regulatory Affairs to establish a proficiency testing program and designate safety compliance facility participation. A safety compliance facility shall analyze proficiency test (PT) samples using the same procedures with the same number of replicate analyses, standards, testing analysts and equipment as used for marijuana product testing.

The following proficiency testing must be performed by Safety Compliance Facilities (SCFs) annually:

- SCFs will need to complete one set of PT samples for all tests on their scope of accreditation from an approved third-party vendor.
- Proficiency test results must be conveyed as numerical accuracy percentages, not simply as PASS/FAIL results. Actual PASS/FAIL results must be calculated based on accuracy thresholds generated by reproducibility studies specific to each assay.
- Safety Compliance Facilities should use any ISO 17043 accredited laboratory for their testing needs. There are several ISO 17043 accredited laboratories where samples can be purchased, including The Emerald Test, NSI Lab Solutions, Sigma-Aldrich and Absolute Standards Inc.
- For parameters where there are currently no commercially available PT samples, SCFs should send samples (as blind samples) to another licensed SCF who performs testing by the same or similar methodology. The results should then be compared. A passing grade for the PT requires a score of at least 80%.
- At least annually the department will require unscheduled random testing of matrix matched samples to evaluate the overall performance of the SCF's.
- Copies of all proficiency testing (both acceptable and unacceptable) results should be sent to the department for review via email: LARA-BMR-Enforcement@michigan.gov. Please indicate in the subject line "Proficiency Testing Results for Review-SCF Name."

ADDITIONAL TESTING

BMR is committed to evidence-based decision-making when implementing technical guidance for licensed SCFs. As research into marijuana use and safety advances, this report will be revised and updated to reflect the state of science as it pertains to the medical marijuana industry.

Medical Marijuana Testing Requirements

	Bud, shake/trim from Harvest Batch	Marijuana Extract non-solvent & non-CO_2*	Marijuana Concentrate solvent based**	Marijuana Concentrate (Supercritical $C0_2$) no additional solvent used***	Marijuana-Infused Product
Moisture Content	√				
Homogeneity					√
Potency Analysis	√	√	√	√	√
Foreign Matter Inspection	√	√			√
Microbial Screen	√	√			√ **Failed tests cannot be repeated**
Water Activity	√				√
Heavy Metal Screen	√	√	√	√	√ (If Extract or concentrate not previously tested)
Residual Solvents			√		√ (If Extract or concentrate not previously tested
Chemical Residue Analysis	√ **Failed tests cannot be repeated**	√ **Failed tests cannot be repeated**	√ **Failed tests cannot be repeated**	√ **Failed tests cannot be repeated**	√ (If Extract or concentrate not previously tested) **Failed tests cannot be repeated**

*Extraction using ice water, rosin press or dry ice.

**Solvents are used in the extraction process including Butane, Ethanol/Isopropyl alcohol, etc.

***Extraction process without winterization where a solvent is used. This abbreviated testing ONLY applies to products created without the use of a solvent. Products that are winterized MUST follow the solvent based testing requirements.

APPENDIX A-DEFINITIONS

Batch- means all marijuana product of the same variety that has been processed together and exposed to substantially similar conditions throughout processing.

Chain of Custody- The chronological documentation showing the collection, custody, control, transfer, analysis, and disposition of a sample.

CFU/g- Colony forming units per gram. Refers to a measure of the amount of bacteria per given amount (1 gram) of a sample.

Edible Marijuana Product-means any marijuana-infused product containing marijuana that is intended for human consumption in a manner other than smoke inhalation.

Harvest batch- means a designated quantity of harvested marijuana, all of which is identical in strain and has been grown and harvested together and exposed to substantially similar conditions throughout cultivation.

Safety Compliance Facility- A facility that is licensed to perform tests of medical marijuana and products containing medical marijuana that is:

(a) Accredited as operating to ISO standard 17025 by an accreditation body that is: (i) Operating in accordance with the International Organization for Standardization (ISO) standard ISO/IEC 17011; and (ii) A signatory to the International Laboratory Accreditation Cooperation (ILAC) Mutual Recognition Arrangement (MRA);

(b) Independent from all other persons involved in the Michigan Medical Marihuana industry; and

(c) Licensed with the Bureau of Medical Marihuana.

Limit of Quantification (LOQ)- The lowest concentration at which the analyte can not only be reliably detected but at which some predefined goals for bias and imprecision are met.

Marijuana Product- means marijuana or a marijuana-infused product, or both, as those terms are defined in the act unless otherwise provided for in these rules.

Medical Marijuana Concentrate- A product derived from medical marijuana that is kief, hashish, bubble hash, oil, wax, or other product, derived from marijuana or that includes cannabinoids extracted from the plant by any means.

Representative Sample- A sample obtained according to a sampling procedure designed to ensure that the different parts of a batch or lot or the different properties of a batch or lot are proportionally represented.

Sample- An amount of medical marijuana collected by laboratory personnel from a licensee and provided to a safety compliance facility for testing.

Solvent- A substance that can dissolve another substance, or in which another substance is dissolved, forming a solution. Examples of solvents include water, acetone, turpentine and ethanol.

Statewide Monitoring System- Compliance statewide monitoring system.

Target Analyte- A chemical the lab must test for to see if it is present in medical marijuana.

Usable Marijuana-

(a) The dried leaves and flowers of the marijuana plant.
(b) Does not include seedlings, seeds, stems, stalks or roots of the plant.

Water Activity- The partial vapor pressure of water in a substance divided by the standard state partial vapor pressure of water.

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