Cannabis Control Commission
COMMONWEALTH OF MASSACHUSETTS

Protocol for the Sampling and Analysis of Finished Marijuana Products and Marijuana Products for Marijuana Establishments, Medical Marijuana Treatment Centers and Colocated Marijuana Operations

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This document is issued by the Cannabis Control Commission. The applicable Marijuana laws, which include M.G.L. c. 94I, 94G 935 CMR 500.000 and 935 CMR 501.000, should be reviewed as they may provide or clarify the legal requirements related to this document. This protocol document should be checked periodically for revisions. Questions with regards to this document may be directed to Commission@CCCMass.com.

Summary of Edits/Changes:

- Change all references from Department of Public Health (DPH) to Cannabis Control Commission (Commission)
- Change all references from Registered Marijuana Dispensaries (RMDs) to "Licensees" (to refer to Marijuana Establishments (MEs), Medical Marijuana Treatment Centers (MTCs) and Colocated Marijuana Operations (CMOs) collectively).
- Updated 1.0 Purpose and Applicability
- Updated 2.0 Definitions and Acronyms – to reflect Commission regulatory definitions
- Updated 3.0 Applicable Regulations – to reflect Commission regulations
- Updated 4.0 Concentrate - Vaporizer Guidance
- Updated 7.0 Sample Analysis – Updated Pesticide, Heavy Metals and NEW Vape Section
- Updated 8.0 Data Evaluation – Added remediation language

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1.0 Purpose and Applicability

1.1 Purpose

The purpose of this Protocol is to provide Massachusetts Adult-use Marijuana Establishments, Medical Marijuana Treatment Centers and Colocated Marijuana Operations (herein referred to collectively as "Licensees") with required and recommended best practices for the collection and analysis of plant material and other finished adult-use and medical Marijuana products and Marijuana-infused products (MIPs) to comply with Massachusetts Cannabis Control Commission's (Commission) regulations: 935 CMR 500.000: *Adult Use of Marijuana* and 935 CMR 501.000: *Medical Use of Marijuana*.

This protocol is subject to revision based on evolving best practices, updated scientific information or standards/guidelines, or other information relevant to the contents of the protocol.

1.2 Applicability

This protocol applies only to Massachusetts Licensee operations, and not hardship cultivation operations. Testing requirements in the protocol apply only to the adult-use and medical-use Marijuana and Marijuana products dispensed by Massachusetts Licensees, including finished Marijuana and Marijuana products (i.e., plant material, resin, concentrates and MIPs) made with finished Marijuana ingredients. The protocol only addresses sampling and analysis to characterize cannabinoid identity and content profiles, and biological (microbial and fungal) and chemical (e.g., solvents, pesticides, growth enhancers, metals) contaminants introduced through cultivation of Marijuana plants and post-harvest processing and handling of Marijuana products and ingredients.

This protocol does not apply to nutritional product testing, allergen testing, or characterization of non-Marijuana ingredients in MIPs except as noted for vaporizer products. It does not address sampling and analysis to verify compliance with state regulations or best practices for production and handling of food products, pharmaceuticals, or dietary supplements, except for criteria for biological and chemical contaminants that may be introduced through inclusion of Marijuana as an ingredient.

Sampling and analysis of environmental media used for cultivation are addressed in a companion protocol, Protocol for Sampling and Analysis of Environmental Media for Massachusetts Registered Medical Marijuana Dispensaries.

2.0 Definitions and Acronyms

Terms listed in italic typeface are those defined in 935 CMR 500.002, 935 CMR and 501.002. Additional terms defined for this protocol are underlined and not in italic typeface. Capitalized terms not defined here are defined in 935 CMR 500.002 or 935 CMR 501.002.

Cannabinoid means any of several compounds produced by Marijuana plants that have medical and psychotropic effects.

Cannabinoid Profile means amounts, expressed as the dry-weight percentages, of delta-nine--tetrahydrocannnabinol, cannabidiol, tetrahydrocannabinolic acid (and cannabidiolic acid in a Marijuana Product. Amounts of other cannabinoids may be reported but are not required.

Marijuana (or Cannabis) means all parts of any plant of the *genus* Cannabis, not excepted in 935 CMR 500.002: *Marijuana* (a) through (c) and whether growing or not; the seeds thereof; and resin extracted from any part of the plant; Clones of the plant; and every compound, manufacture, salt, derivative, mixture or preparation of the plant, its seeds or resin including tetrahydrocannabinol as defined in M.G.L. c. 94G, § 1; provided that Cannabis shall not include:

(a) the mature stalks of the plant, fiber produced from the stalks, oil, or cake made from the seeds of the plant, any other compound, manufacture, salt, derivative, mixture or preparation of the mature stalks, fiber, oil, or cake made from the seeds of the plant or the sterilized seed of the plant that is incapable of germination;
(b) Hemp; or
(c) the weight of any other ingredient combined with Cannabis or Marijuana to prepare topical or oral administrations, food, drink or other products.

Certificate of Registration means a certificate formerly and validly issued by the Department of Public Health (DPH) or currently and validly issued by the Commission, that confirms an MTC, Independent Testing Laboratory, individual or entity has met all applicable requirements pursuant to M.G.L. c. 94I and 935 CMR 501.000 and is licensed by the Commission. An MTC or Independent Testing Laboratory may have been issued a provisional or final Certificate of Registration. After November 1, 2019, new or renewal Licenses, as applicable, may be issued to MTCs and Independent Testing Labs.

Commission means the Massachusetts Cannabis Control Commission as established by M.G.L. c. 10, § 76, or its representatives. The Commission has authority to implement the state Marijuana laws which include, but are not limited to, St. 2016, c. 334, The Regulation and Taxation of Marijuana Act, as amended by St. 2017, c. 55, An Act to Ensure Safe Access to Marijuana; M.G.L. 10, § 76, M.G.L. c. 94G; M.G.L. c. 94I; 935 CMR 500.000: *Adult Use of Marijuana*, and 935 CMR 501.000: *Medical Use of Marijuana*.

Consumer means a person who is 21 years of age or older.

Cultivation Batch means a collection of Cannabis or Marijuana plants from the same seed or plant stock and that are cultivated and harvested together, and receive an identical propagation and cultivation treatment including, but not limited to: growing media, ambient conditions, watering and light regimes, agricultural or hydroponic inputs. Clones that come from the same plant are one batch. The Licensee shall assign and record a unique, sequential alphanumeric

identifier to each Cultivation Batch for the purposes of production tracking, product labeling, and product recalls.

Department of Public Health (DPH*)* means the Massachusetts Department of Public Health, unless otherwise specified. DPH is the agency that administered the Medical Use of Marijuana Program prior to 2019.

Duplicate Samples means two samples taken from and representative of the same material that are carried through all steps of the sampling and analytical procedures in an identical manner. Duplicate samples may be used to evaluate variance in the assessment method, including sampling and analysis.

Edibles means a Marijuana Product that is to be consumed by humans by eating or drinking. These products, when created or sold by a Marijuana Establishment or an MTC, shall not be considered a food or a drug as defined in M.G.L. c. 94, § 1.

First Amended Quarantine Order means the *First Amended Quarantine Order Applying To Vaporizer Products With Conditions M.G.L. c.94I, M.G.L., c. 94G, § 4(a)(xix) and ($a^{1/2}$)(xxxi), 935 CMR 500.340: Quarantine Order, and 935 CMR 501.340: Quarantine Order* issued by the Massachusetts Cannabis Control Commission on December 12, 2019."

Finished Marijuana means Usable Marijuana, Cannabis resin, or Cannabis concentrate.

Finished Plant Material means usable Marijuana that has been trimmed and dried. Trimming includes removing the leaves immediately subtending the buds as well as any dead leaves or stems.

Flowering means the gametophytic or reproductive state of Cannabis or Marijuana in which the plant produces flowers, trichomes, and Cannabinoids characteristic of Marijuana.

Hardship Cultivation Registration means a registration issued to a Registered Qualifying Patient under the requirements of 935 CMR 501.027.

Independent Testing Laboratory means a laboratory that is licensed or registered by the Commission and is:

(a) Currently and validly licensed by the Commission;
(b) Accredited to ISO 17025:2017 or the *International Organization for Standardization* 17025 by a third-party accrediting body that is a signatory to the International Laboratory Accreditation Accrediting Cooperation mutual recognition arrangement or that is otherwise approved by the Commission;
(c) Independent financially from any MTC Marijuana Establishment or Licensee; and

(d) Qualified to test Marijuana and Marijuana Products, including MIPs, in compliance with M.G.L. c. 94C, § 34; M.G.L c. 94G, § 15; 935 CMR 500.000; and 935 CMR 501.000: *Medical Use of Marijuana*; and Commission protocol(s).

Licensee means a person or entity on the application and licensed by the Commission to operate a Marijuana Establishment or Independent Testing Laboratory under St. 2016, c. 334, as amended by St. 2017, c. 55, M.G.L. c. 94G, and 935 CMR 500.000. Any person or entity that solely provides initial capital to establish or operate the establishment and to whom, in return for the initial capital, requires only repayment of the loan and does not have any ownership or direct or indirect authority to control the Marijuana Establishment or Independent Testing Laboratory, will not be a Licensee. For the purposes of this Guidance Document, *Licensee* will be referred to as Marijuana Establishments, Marijuana Treatment Centers and Colocated Marijuana Operations collectively.

Marijuana Establishment (ME) means a Marijuana Cultivator (Indoor or Outdoor), Craft Marijuana Cooperative, Marijuana Product Manufacturer, Marijuana Microbusiness, Independent Testing Laboratory, Marijuana Retailer, Marijuana Transporter, Delivery Licensee, Marijuana Research Facility, Social Consumption Establishment or any other type of licensed Marijuana-related business, except a Medical Marijuana Treatment Center (MTC).

Marijuana-Infused Product (MIP) means a Marijuana Product infused with Marijuana that is intended for use or consumption, including but not limited to Edibles, ointments, aerosols, oils, and Tinctures. A MIP when created or sold by a Marijuana Establishment or MTC, shall not be considered a food or a drug as defined in M.G.L. c. 94, s. 1. MIPs are a type of Marijuana Product.

Medical Marijuana Treatment Center (MTC), (Formerly Known as a Registered Marijuana Dispensary (RMD)), means an entity licensed under 935 CMR 501.101 that acquires, cultivates, possesses, Processes (including development of related products such as Edibles, MIPs, Tinctures, aerosols, oils, or ointments), Repackages, transports, sells, distributes, delivers, dispenses, or administers Marijuana, products containing Marijuana, related supplies, or educational materials to Registered Qualifying Patients or their Personal Caregivers for medical use. Unless otherwise specified, MTC refers to the site(s) of dispensing, cultivation, and preparation of Marijuana for medical use.

Mycotoxin means a secondary metabolite of a micro-fungus that is capable of causing death or illness in humans and other animals. For the purposes 935 CMR 500.000 and 935 CMR 501.000, Mycotoxins shall include aflatoxin B1, aflatoxin B2, aflatoxin G1, aflatoxin G2, and ochratoxin A.

Pesticide means a substance or mixture of substances intended for preventing, destroying, repelling, or mitigating any pest, and any substance or mixture of substances intended for use as a plant regulator, defoliant, or desiccant; provided that Pesticide shall not include any article that

is a "new animal drug" within the meaning of § 201(v) of the Federal Food, Drug and Cosmetic Act (21 U.S.C. § 321(v)), or that has been determined by the Secretary of the United States Department of Health and Human Services not to be a new animal drug by a regulation establishing conditions of use for the article, or that is an animal feed within the meaning of § 201(w) of such act (21 U.S.C. § 321(w)).

Production Batch means a batch of finished plant material, Cannabis resin, Cannabis concentrate, or Marijuana-infused Product made at the same time, using the same methods, equipment, and ingredients. The Licensee shall assign and record a unique, sequential alphanumeric identifier to each Production Batch for the purposes of production tracking, product labeling, and product recalls. All Production Batches shall be traceable to one or more Cannabis or Marijuana Cultivation Batches.

Propagation means the reproduction of Cannabis or Marijuana plants by seeds, cuttings, or grafting.

Residual Solvent means a volatile organic chemical used in the manufacture of a Marijuana Product that is not completely removed by practical manufacturing techniques.

Seed-to-sale System of Record means the electronic tracking system designated and required by the Commission to perform a process (Metrc).

Tincture means a Cannabis-infused alcohol or oil concentrate administered orally in small amounts using a dropper or measuring spoon. Tinctures are not considered an Edible under 935 CMR 500.000 and 935 CMR 501.000 and are not subject to the dosing limitations applicable to Edibles under 935 CMR 500.150(4).

Trichome means a cannabinoid-producing glandular structure that grows on the plant surface of Marijuana plants, particularly on the buds of the female plant.

Usable Marijuana means the fresh or dried leaves and flowers of the female Marijuana plant and any mixture or preparation thereof, including Marijuana, Marijuana Products or MIPs, but does not include the seedlings, seeds, stalks, roots of the plant, or Marijuana rendered unusable in accordance with 935 CMR 500.105(12)(c).

Vegetation means the sporophytic state of the Cannabis or Marijuana plant, which is a form of asexual reproduction in plants during which plants do not produce resin or flowers and are bulking up to a desired production size for Flowering.

3.0 Applicable Regulations

This protocol was developed to provide Licensees with guidance on complying with the 935 CMR 500.000 and 935 CMR 501.000. In particular, the detailed steps outlined in this protocol

address requirements of the following sections of the regulations. Licensees should be familiar with the applicable regulations to ensure full compliance.

- 935 CMR 500.105(1)(h), 935 CMR 501.105(1)(h) - Plans for quality control, including Marijuana product testing for contaminants.

- 935 CMR 500.105(3), 935 CMR 501.105(3) - Handling of Marijuana

- 935 CMR 500.105(5), 935 CMR 501.105(5) - Labeling of Marijuana and Marijuana products.

- 935 CMR 500.120(6), 935 CMR 500.130(4), 935 CMR 501.120(6) and 935 CMR 501.130(4) - Marijuana and Marijuana products obtained from another Licensee.

- 935 CMR 500.160, 935 CMR 501.160 - Testing of Marijuana and Marijuana products.

4.0 Sampling and Analysis Requirements

Sampling and analysis requirements apply to all Marijuana-containing products dispensed by Massachusetts Licensees, which may include finished plant material, Cannabis resin, Cannabis concentrates (including vaporizer products), and MIPs. Because the nature and concentrations of contaminants and cannabinoid compounds may change throughout the production process, from cultivation through packaging, this section identifies the types of sampling and analysis that are required for each type of product. The results of the sampling and analysis are required for both quality control and labeling requirements (e.g., cannabinoid profile, testing certification). Licensees must ensure and be able to demonstrate to the Commission, that product label information complies with all applicable sections of 935 CMR 500.105(5)(a) and 935 CMR 501.105(5)(a).

4.1 Overview of Marijuana Products and their Production

Marijuana products that may be dispensed by Licensees in Massachusetts include finished plant material, Cannabis resin, Cannabis concentrates, and a variety of MIPs. Marijuana for all of these product categories must originate with plants cultivated by a Licensee and all product labeling must include a batch number to identify the batch associated with manufacturing and processing (935 CMR 500.105(5), 935 CMR 501.105(5)). Therefore, Licensees are responsible for carefully tracking Marijuana throughout the production cycle, from cultivation through dispensing to consumers and patients. Marijuana and Marijuana Products procured by a Licensee from another Licensee pursuant to 935 CMR 500. must be tested by the supplying Licensee and documentation of testing consistent with this protocol must be provided to the receiving Licensee by the supplying Licensee, along with chain-of-custody documentation.

Exhibit 1 provides an overview of the adult use and medical-use Marijuana production process as regulated in Massachusetts by the Commission. During cultivation, plants are typically grown from seed, cuttings, or through a tissue culture method called micropropagation (AHP 2013). Plants may be grown in soil, other solid growth media, or in hydroponic systems. All cultivation methods place the plants in contact with environmental media and other inputs, such as soil or agricultural products, which have the potential to introduce chemical or biological contaminants.[1] Because medically-active compounds are at their highest concentration on the inflorescences of the female plant, Marijuana plants are harvested when the plants reach peak maturity. Post-harvest handling steps include drying and trimming, which should be managed carefully to avoid mold and bacterial growth and to preserve medicinally-active compounds. For further details on medical Marijuana cultivation and post-harvest handling methods, refer to AHP (2013).

Harvested and dried Marijuana plants can be used directly to produce any of the three finished Marijuana types:

1. Dried and trimmed usable Marijuana, the inflorescences (i.e., "buds"), may be used directly (e.g., smoked) without further processing. It also may be used as a source material for other finished Marijuana products or as an ingredient in MIPs.
2. Cannabis resin, commonly referred to as "hashish" or "hash," is formed by collecting and compressing cannabinoid-containing resin glands (i.e., trichomes). Cannabis resin also includes "bubble hash," which is made by extracting the resin glands using cold water and physical separation (Colorado Pot Guide, 2014).
3. Concentrates, which include various oils, waxes, and solids, are produced with solvent extraction methods. Vape products that heat Cannabis oils fall under this classification. Concentrates have higher cannabinoid concentrations than other finished Marijuana products, but also may contain residuals of potentially harmful solvents if not manufactured properly. In addition, any contaminants present in the source plant material may be concentrated in a resin or concentrate product.

Exhibit 1. Overview of Marijuana Production

Under 935 CMR 500.002 and 935 CMR 501.002, an MIP is defined as a Marijuana Product infused with Marijuana that is intended for use or consumption, including but not limited to Edible Marijuana-infused Products, ointments, aerosols, oils, and Tinctures. A Marijuana-infused Product (MIP) when created or sold by a Marijuana Establishment or MTC, shall not be considered a food or a drug as defined in M.G.L. c. 94, §. 1.

[1] Testing for media used in Marijuana cultivation is discussed in the companion *Protocol for Sampling and Analysis of Environmental Media for Massachusetts Registered Medical Marijuana Dispensaries*.

4.2 Commission Marijuana Testing Requirements

Testing for finished Marijuana and Marijuana products includes screening for chemical and biological contaminants (Section 4.2.1) and cannabinoid profile testing (Section 4.2.2). Section 4.2.3 discusses methods for determining the amount of usable Marijuana contained within a dispensed product, as required for product labeling. Sections 5.0 through 7.0 further describe the detailed sampling frequency, sample collection procedures, and analyses required for contaminant and cannabinoid profile testing.

This protocol defines the minimum testing required to conform with 935 CMR 500.000 and 935 CMR 501.000. Licensees have discretion to perform analysis beyond these requirements.

Product problems should be reported to the Commission when there is a concern about the quality, authenticity, performance, or safety of any finished Marijuana or Marijuana product. Problems with product quality may occur during manufacturing, shipping, or storage. These may include:

- suspect counterfeit product;
- product contamination;
- defective components;
- poor packaging or product mix-up;
- questionable stability;
- labeling concerns; and
- unknown fillers and cutting agents

Testing laboratories and Licensees are often the first to recognize a product quality problem. Individuals shall report any concerns to the Commission by phone: (774) 415-0200; email: Commission@CCCMass.com; or via Mail to: Cannabis Control Commission
ATTN: DIRECTOR OF INVESTIGATIONS
2 Washington Square
Union Station 2nd Floor
Worcester, MA 01604

4.2.1 Contaminant Testing

Contaminant testing requirements are based on the contaminants potentially introduced at each stage of production. Exhibit 2 identifies the potential contaminants of concern during each stage of Marijuana production and the testing requirements for each product type.

<u>Cultivation</u>

Cultivation is not in the scope of testing of this protocol, but is included in Exhibit 2 to identify the contaminants of concern potentially introduced during cultivation. These include non-organic

pesticides, metals, and other synthetic organic compounds in environmental media or other cultivation inputs (e.g., soil amendments, hydroponic products), as well as fungal and bacterial growth on the plants. Environmental media must be tested, as described in the Protocol for Sampling and Analysis of Environmental Media for Massachusetts Registered Medical Marijuana Dispensaries, to reduce the introduction of chemical contaminants during cultivation. However, this testing will not necessarily ensure that the Marijuana plants are free of chemical contaminants, and does not address fungal/bacterial infestation. Therefore, Marijuana products must be tested for chemical contamination before they can be distributed, sold and consumed.

Marijuana should be cultivated and harvested in traceable "cultivation batches," such that all Marijuana within a cultivation batch has been produced with the same seed or plant stock, soil or other solid growing media, water, other agricultural/hydroponic inputs, and growing conditions. Cultivation batches should be sequentially numbered and traced throughout post- harvest production steps, and manufacturing/processing batch numbers must be included on the labels of all products to facilitate product recalls.

Finished Plant Material

Finished plant material dispensed to consumers and patients consists of usable Marijuana that has been trimmed and dried. Trimming includes removing the leaves immediately subtending the buds as well as any dead leaves or stems (AHP 2013). A "production batch" of finished plant material must be traceable to one or more cultivation batch(es). All production batches of finished plant material must be tested for pesticides and metals, which may be introduced during cultivation. Production batches intended for dispensing and direct use as adult use or medical product must also be tested for biological contaminants (bacteria, fungi, and mycotoxins), as shown in Exhibit 2.

Finished plant material is tested instead of living or freshly harvested plants because drying and trimming may affect the concentrations of contaminants and because fungal/bacterial growth may occur during finishing.

Finished plant material that exceeds a limit (see Section 7.0) for any contaminant included in the required testing cannot be distributed as finished Marijuana without first being reanalyzed and/or remediated pursuant to 935 CMR 500.160(12) and 935 CMR 501.160(11). The Commission may require additional contaminant screenings to ensure compliance.

Cannabis Resins and Concentrates

Cannabis resins and concentrates may be produced from the finished plant material of one or more cultivation batches. If the finished plant material fails to meet a required testing requirement, but the finished plant material is not dispensed to a consumer or patient, then it may be used to derive resins and concentrates. The resins and concentrates may be dispensed as long as they meet the respective concentration limit identified in Section 7.0. Each production batch

of Cannabis resin or concentrate must be given a sequential identifier for product tracking and labeling. The Licensee must keep records of the Marijuana cultivation batch(es) used for each production batch, and include the manufacturing/processing batch number on product labels.

Testing requirements for Cannabis resins and concentrates are summarized in Exhibit 2. Because these products may be made only from plant material that has already tested below limits for pesticides, testing for these contaminants is not required again. However, Cannabis concentrates must be tested for metals, as well as residual solvents if solvents were used in their production. If Cannabis concentrates are produced or extracted with solvent free processes, a solvent screening is not required. Specifically, testing is required for any solvent used to make a Cannabis concentrate production batch.

All Cannabis resin or concentrate production batches intended for distribution to consumers and patients as finished Marijuana products must be tested for bacteria, fungi, and mycotoxins. Testing for these biological contaminants is not required for Cannabis resin or concentrate production batches that will be used only to manufacture MIPs.

If required testing finds that a production batch of Cannabis resin or concentrate exceeds any applicable contaminant limit (see Section 7.0), the production batch cannot be dispensed as a finished Marijuana product without first being reanalyzed and/or remediated followed by additional required contaminant screening to ensure compliance .

Marijuana Vaporizer Products
The provisions set forth in this Guidance Protocol, in conjunction with 935 CMR 500.105(5)(c) and 500.160(1) and (2) and 935 CMR 501.105(5)(c) and 160(1) and (2), aim to mitigate the known risks associated with Marijuana vaporizer products that utilize concentrated marijuana oils (vape products). At the time of adoption of this protocol there remain many unknown factors and variables regarding the long-term use and overall effects of using vape products. This section of the guidance protocol addresses several issues and challenges faced when regulating legal vape products in the Commonwealth.
The Commission will continue to facilitate the availability of regulated, legal vape products while also taking steps toward mitigating potential health risks associated with vape products. The Commission understands the need to continue to develop and implement regulations and guidance informed by scientific research that will reflect additional studies into the health effects of utilizing vape products. This Guidance Protocol document shall be updated as new information becomes available to the Commission through its ongoing investigations and findings, as well as through industry research and scientific studies.

<u>MIPs</u>

The Commission assumes that all MIP production batches will be destined for dispensation and consumer or patient use. Therefore, all MIP production batches must be tested for biological

contaminants (bacteria, fungi, and mycotoxins). Production batches must be discarded and not dispensed to patients if any biological contaminant limit is exceeded.

MIPs may be made only with finished Marijuana products that have passed applicable metals, pesticide, and solvent testing requirements. For this reason, testing MIPs for metals, pesticide, and solvent contaminants is not required. However, Licensees have discretion to perform this testing of MIPs voluntarily.

Each MIP production batch must be given a sequential identifier (ID) for product tracking and labeling. Records must be kept that identify the cultivation batch(es) and finished Marijuana production batches associated with each MIP production batch. The manufacturing/processing batch number must be included on product labels to aid in product tracking and recalls.

4.2.2 Cannabinoid Profile Testing

All Marijuana products, shown in Exhibit 1, including any finished Marijuana or MIP, must bear a label that identifies the list of ingredients, including the cannabinoid profile of the Marijuana contained within the product, including the THC level (935 CMR 500.105(5), 935 CMR 501.105(5)). Therefore, for the purposes of labeling Marijuana products in Massachusetts, the cannabinoid profile must include, at a minimum, the percentage by dry weight (i.e., the weight of the material remaining after it has been thoroughly dried) of D9- tetrahydrocannnabinol (D9-THC), cannabidiol (CBD), tetrahydrocannabinolic acid (THCa), and cannabidiolic Acid (CBDa). Medicinal benefits have been attributed to other cannabinoids, and these compounds may be included in the cannabinoid profile at the discretion of the Licensee

It is important to note that heat (including combustion) can cause chemical reactions that convert cannabinoids to more or less potent forms. For example, combustion (e.g., during smoking) causes non- psychotropic cannabinoid acids, abundant in the plant material, to be converted to psychotropic forms. However, medical users report health benefits from products that do not require high temperatures or combustion for production or use (AHP 2013).

Because production of finished Marijuana products and MIPs may affect cannabinoid chemistry, as well as the concentration or dilution of active ingredients, each product type must be tested to characterize the cannabinoid content and profile.

4.2.3 Usable Marijuana Content

105 CMR 725.105(E)(2)(c) and 725.105(E)(3)(d) require labels of Marijuana products to identify the quantity of usable Marijuana contained within the product, as measured in ounces. For finished plant material and products containing finished plant material, the quantity of usable Marijuana is simply the weight in ounces of the plant material in the product. Massachusetts has determined that 10 ounces of finished plant material is the maximum 60-day supply allowed for

medical Marijuana patients. This is the largest amount of usable medical Marijuana that may be dispensed by any RMD in Massachusetts.

When finished plant material is used to derive Cannabis resin or concentrates, processing alters the physical form and quantity (i.e., weight and volume) of the usable Marijuana. To enable the comparison of usable Marijuana in the various product types, DPH originally developed assumptions that should be used to express the quantity of usable Marijuana in Cannabis resins or concentrates in terms of the equivalent ounces of plant material. Based on Colorado Department of Revenue (2015) sources previously reviewed by DPH, it can be assumed that the yield of a Cannabis resin or concentrate is 19 percent of the starting weight of plant material. This is based on the assumption that a typical butane extraction from 28.4 g (1 oz.) of flower will yield 5.5 g of oil.

When the weight of Cannabis resin or concentrate in a dispensed product is known, the quantity of usable Marijuana, expressed in equivalent plant material weight, should be calculated by multiplying the resin or concentrate weight by 5.3 (i.e., 1 ÷ 0.19). For example, the quantity of usable Marijuana in 1.9 ounces of Cannabis oil is 10 ounces (1.9 ounces of Cannabis oil x 5.3 = 10 ounces of usable Marijuana). Therefore, 1.9 ounces of Cannabis oil is equivalent to the maximum 60-day supply of useable plant material.

The amount of usable Marijuana in a MIP is equal to the amount of usable Marijuana included in the product ingredients, measured before mixing, baking, or other processing or manufacturing steps. If more than one type of finished Marijuana ingredient is used to prepare a MIP, the amount of usable Marijuana in the MIP is the sum of the usable Marijuana in the ingredients.

5.0 Sampling Program Design

Under 935 CMR 500.160(2) AND 935 CMR 501.160(2), Marijuana must be tested for the cannabinoid profile and contaminants. The Marijuana products to be tested include: finished plant material (i.e., inflorescences or “buds”), Cannabis resin, Cannabis concentrates, and various types of MIPs. The purpose of testing is to ensure product quality and safety, and to provide information needed for product labeling requirements.

Because it is not possible to test all Marijuana, Licensees must collect representative samples to provide to one of the Commission’s licensed ITLs. Specifically, each medical Marijuana production batch must be sampled and analyzed, and the samples collected for a production batch must be representative of all of the medical Marijuana in the batch. The protocol provides the following definition of production batch:

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 Licensee must 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 must be traceable to one or more Marijuana cultivation batch(es).

Samples from each production batch must be collected in a ready-to-use condition. For production batches that will be dispensed to patients, ready-to-use means ready for packaging or post-packaging. For other production batches, ready-to use means ready for use as an intermediate or ingredient in making other products. After samples are collected, the entire production batch must be stored in a secure, cool, and dry location until analytical results are returned by the laboratory.

Sampling frequency is dictated by the production schedules, which may vary among Licensees due to scale, product types dispensed, and consumer and patient demand. The Licensee is responsible for implementing a production batch tracking approach that meets the regulatory needs and definitions as well as ensuring representative sample collection and analysis of those batches. The Licensees must be able to demonstrate to the Commission that the production tracking, sampling, and analysis procedures are capable of obtaining representative samples. The guidelines below are provided to aid Licensees in developing an approach that meets Commission requirements for representativeness.

To perform required testing, Licensees will collect samples to be analyzed by licensed and appropriately certified ITLs, as noted in Section 7 of this protocol. The amounts of sample required for cannabinoid or contaminant testing may vary by analytical method and laboratory-specific procedures, therefore the Licensee should confer with the ITL to determine the minimum sample size required for evaluation. In all cases, the amount of sample supplied to the laboratory should be large enough and sufficiently homogenized to provide a representative sample of the production batch but not in excess to raise issues with possible diversion or waste disposal.

5.1 Representative Sampling

Specific procedures for collecting representative samples of Marijuana production batches are likely to vary depending on several attributes of the products and production methods:

Homogeneity – A sample is more likely to accurately represent the production batch if the material is homogenous (i.e., well mixed). Mixing or other homogenization steps help to homogenize the product before sample collection.

Physical Form – Production batches will vary in physical form (e.g., liquids, solids), density, and viscosity. Physical form can affect homogeneity, homogenization steps, and sample collection methods. For example, liquid products can be homogenized by stirring. Grinding and other methods described further below can be used to homogenize solid products.

Quantity – Because production batches may vary in scale (i.e., volume or weight), varying numbers or sizes of samples may be required to promote representativeness.

In addition, sample representativeness can be affected by the timing and frequency of sample collection. Because of variation among production schedules (e.g., due to product type, production scale, patient demand), sampling frequencies will vary among Licensees and production batches. However, representativeness will be ensured by the requirement that all production batches are tested.

5.2 Representative Sampling by Physical Form and Quantity

Exhibit 3 provides instructions for representative sampling of Marijuana production batches, including finished Marijuana products and MIPs. These instructions were developed based on sampling guidance for food products and herbal medicines developed by the Codex Alimentarius Commission (1999) and the United States Pharmacopeia Chapter 561 (USP, Undated-b), respectively, and account for differences in the physical forms of the production batches as they relate to homogeneity and quantity. If application of these guidelines is impractical for specific products, it is the responsibility of the Licensee to develop and document a scientifically defensible sampling approach.

Homogeneity plays an important role in methods for representative sampling. While liquid products such as Cannabis oil and liquid MIPs can be stirred or mixed to homogenize the product before sampling, other products such as Cannabis resin, baked goods, or hard candies cannot. Homogenization of some solid products, such as ground plant material or semi-solid resin is possible. Because of its importance, further guidance on homogenization methods is provided in Section 5.3.

5.3 Sampling Guidance by Matrix

Finished Marijuana products and MIPs can be in varied physical states or matrix (e.g., liquids to hard solids). To better understand the specific requirements the following guidance is provided based on the matrix of the material to be characterized.

<u>Liquids (Cannabis Oil and Some MIPs)</u>

Liquid products such as Cannabis oil or liquid MIPs should be thoroughly stirred or mixed before sampling to ensure homogenization of the sample. Cannabis oil or other liquid Cannabis from each production batch should be sampled using units of volume. Samples of concentrates or oils should be collected following each production batch if they are to be sold, and before any further processing into MIPs.

Finished Plant Material or Friable MIPs

Sampling shall be performed such that the dried and trimmed inflorescences, or buds, of the Marijuana plant that are collected are representative in maturity and composition of the entire production batch of finished plant material. The sampling timeframe for Marijuana buds should be after the completion of the finishing (i.e., drying and trimming) of the plant material production batch.

Homogenization of the finished plant material may be difficult to accomplish prior to sampling due to the heterogeneous nature of the finished plant material. Recommendations from ISO 1839-1980 guidelines for sampling loose leaf tea (i.e., a material similar in nature to Cannabis plant material) state that in most cases it is "impracticable and purposeless" to re-blend the contents of a large container of tea in order to obtain a representative sample. USP guidance for sampling articles of botanical origin (USP Chapter <561>) recommends that, for items with component parts larger than 1 cm in any dimension, samples should be withdrawn by hand, then combined and mixed prior to analysis. ISO 1839-1980 also states that if the primary samples consist of loose material, they should be combined to constitute the bulk sample for evaluation.

Quartering is a method to promote the representativeness of a homogenized Marijuana sample. Quartering involves heaping the adequately mixed and homogenized ground product into a square shape, dividing the heap into four equal quarters, and selecting samples from two of the opposite quarters, which are mixed and sampled (Sexton and Ziskind, 2013; USP Chapter <561>; WHO, 2007). The remaining quarters may then be combined and mixed, then used for microbiological and contaminant testing (Sexton and Ziskind, 2013; USP Chapter <561>; WHO, 2007). The quartering process may be repeated until the required quantity is obtained, and the remaining material may be returned to the batch if possible (USP Chapter <561>; WHO, 2007).

Solids and semi-solids (Cannabis Resin and Some MIPs)

Solid and semi-solid products such as resin should be ground and thoroughly mixed, if possible, to be homogenized (USP Chapter <561>; WHO, 2007). A grinding device that minimizes loss (e.g., leaching of resins from finished plant material) should be used, and the grinding device should be cleaned thoroughly after each use. Once ground, quartering, as described above, can be used to collect the sample.

If grinding is impracticable, subsamples of the product should be taken from different areas of the product mass. For example, it might be possible to slice the product mass in sections prior to collection of subsamples or take the subsamples directly from different locations on the product surface (e.g., lower, middle, and upper).

Resin and other solids should not be melted as a means of homogenization. Heating the product may alter the cannabinoid profile or contaminant levels (WHO, 2005) thereby rendering the sample unrepresentative of the source product.

When subsamples are required, subsamples should be composited (combined), if possible, and mixed to obtain a quantity sufficient for evaluation. The quantity sufficient for evaluation may vary by analytical method and laboratory-specific procedures, therefore the Licensee should confer with the ITL l to determine the minimum sample quantity required for evaluation.

Compositing subsamples may be impractical for some product types (e.g., hard candies or other products in discrete solid units). In these cases, individual product units can be provided to the ITL as samples for analysis. In some cases, the ITL l may combine extracts or digestates prepared from the solid subsamples and analyze the volumetrically combined extract/digestate as a composite.

5.4 Quality Control (QC) Samples

Duplicate samples shall be collected to provide verification of sampling and laboratory procedures. Specifically, a duplicate should be collected for 5 percent (1 per 20) of the samples collected for each Marijuana product type. Duplicate samples shall not be identified to the ITL (this is considered blind quality control). Duplicate samples are used to evaluate any variance in the sampling and analysis procedures. To ensure authenticity, it should be noted that QC samples should be taken on the same day, be derived from the same batch and documented on the Commission test results tracking sheet.

6.0 Sample Collection Procedures

This section describes sample collection procedures that are generally applicable to any Marijuana product that Licensees may dispense, including, but not limited to, finished plant material; liquid concentrates or MIPs; resins, waxes, creams, or other semi-solid products; or solid concentrates or MIPs; or vape products. Because of the wide range of Marijuana products that Licensees may offer, particularly MIPs, these sample collection procedures may require adaptation in some cases.

In all cases, sample collection must be conducted in a manner that provides analytically sound and representative samples so that all Marijuana products dispensed are safe, effective, and accurately labeled. The Licensee must document every sampling event and provide this documentation to the Commission upon request.

Prior to Sample Collection. The Licensee should assemble all equipment and information needed before beginning. Items to assemble before sampling include, but are not limited to, the following:

- Sample collection plan for each product type;
- Logbook or sample collection forms;
- Chain-of-custody forms (COCs);

- Disposable gloves;
- Decontaminated tool(s), such as a spatula, knife, sampling spear, or pipette;
- Stainless steel bowl and implement to homogenize the product (e.g., by stirring, chopping, or grinding);
- Clean, decontaminated surface for sample processing;
- Sample containers appropriate for the analyses required;
- Container labels and pen with indelible ink;
- Supplies to thoroughly clean, decontaminated and dry sampling equipment between samples; and
- A cooler with ice to keep samples cool until refrigeration or shipment to the laboratory.

Sample collection personnel should create a new entry for each sampling event in a sample collection logbook or prepare sample collection forms for documentation of sample collection. Sample collection documentation should identify the sample collection date and start time, participating personnel, a general description of the product type and batch number sampled, a description of the sampling procedures used, and a record of batches that would potentially be impacted should analysis results indicate unacceptable contamination levels.

Sample collection personnel shall identify or determine the cultivation batch number, production batch, and number of samples to be collected based on the guidance provided in Section 5, as well as further guidance obtained in consultation with the ITLs. The number of samples taken from each cultivation and/or production batch must be recorded in the sample collection logbook or forms. Record the sample cultivation and production batch identifiers (ID) for each sample. The batch IDs will be included on sample labels. In addition to the batch ID, create a unique sample ID for each sample. Sample identifiers should be unique for a given sample event. Record the batch and sample IDs in the sample collection logbook.

Any tools that contact the samples should be made of stainless steel or other inert material to avoid potential contamination of the sample. Appropriate sample containers should be made of suitable materials.

Preparing sample labels and affixing them to sample containers immediately before sampling is recommended. Information to include on the label includes at a minimum the batch and sample IDs and date/time of collection and by whom. Additional information that must be recorded in documentation, if not on the label, includes sample collector's name, product type, collection method, and other details about the product, such as MIP type or production method.

Sample Collection. Collect the planned samples from each cultivation or production batch one at a time. Follow these basic steps for each sample:

1. Wear disposable gloves to mitigate potential for contamination of samples.
2. Ensure that the sampling area is clean and decontaminated and lay out any tools and equipment needed.

3. Collect the sample using an appropriate tool. Do not touch the sample with your hands or allow the sample to touch anything that might cause cross contamination.
4. If necessary, place the sample in the stainless steel bowl or on a decontaminated cutting surface for homogenizing the sample using either the sample collection tool or separate clean, decontaminated implement.
5. Record the time each sample was collected and record any difficulties, inconsistencies with the sampling plan, or other remarks (e.g., environmental conditions) that might be relevant to data analysis or quality assurance.
6. To avoid cross contamination of samples, any tools or equipment that comes in contact with the finished plant material or other Marijuana products should be cleaned before collecting the next sample.
7. All samples should be placed in clean, airtight sample containers that are large enough to hold the prescribed sample quantity with minimal headspace. Sample containers must be firmly closed and appropriately labeled.
8. To preserve the chemical and biological composition of the samples, they should be refrigerated or maintained on ice until shipped to the analytical laboratory.
9. Chain-of-custody paperwork should be completed immediately prior to shipment to the analytical laboratory.

Marijuana products and MIPs, especially solids or semi-solids such as finished plant material, may be heterogeneous with respect to distribution of cannabinoids or contaminants. To obtain a representative sample, liquid products should be thoroughly stirred or mixed before sampling. Solid and semi-solid products must be ground and thoroughly mixed. A grinding device that minimizes loss (e.g., leaching of resins) should be used, and the grinding device should be cleaned thoroughly after each use.

Another method to promote the representativeness of a ground Marijuana product is quartering. Quartering involves heaping the ground product, dividing the heap into four equal quarters, and selecting samples from two of the quarters, which are combined and mixed (Sexton and Ziskind, 2013). The remaining quarters may then be combined and mixed, then used for microbiological and contaminant testing (Sexton and Ziskind, 2013).

Resin and other solids should not be melted as a means of homogenization. Heating the product may alter the cannabinoid profile or contamination levels (WHO, 2005) thereby rendering the sample unrepresentative of the source product.

Edible products tend to be relatively homogeneous (Sexton and Ziskind, 2013), so a selection of packaged or ready-to-dispense MIPs may be provided to the analytical laboratory to represent a given production batch (Sexton and Ziskind, 2013). MIPs may be either liquid or solid, and the solid MIPs may be of varying density (e.g., baked goods and candies). Laboratory samples of MIPs shall be homogenized prior to testing such that the sample is representative of the whole product. Homogenized samples should be mixed and quartered similar to the procedure described above. If production batches of individually packaged MIPs are sampled, multiple

packaged products should be sampled such that they are representative of the production batch size.

7.0 Sample Analysis

All sample analyses described in this protocol shall be conducted by an independent laboratory that is either:

1. Accredited to International Organization for Standardization (ISO) 17025 by a third-party accrediting body such as A2LA or ACLASS, or
2. Certified, registered, or accredited by an organization approved by the Massachusetts Department of Public Health.
3. Licensed with the Commission pursuant to 935 CMR 500.050(7) and 935 CMR 501.052.

Further requirements concerning the eligibility and responsibilities of analytical laboratories are provided in 935 CMR 500.029 and 935 CMR 501.029.

In addition to the regulatory qualifications and requirements referenced above, the independent laboratory should have a demonstrated ability to perform the specific analytical methods required and to provide defensible documentation and quality assurance.

The sections below identify the analytical methods and analyses required for characterizing the cannabinoid profile of Marijuana products, as well as the presence and levels of potential contaminants, including metals, pesticides and plant growth regulators, microbiological contaminants and mycotoxins, and residual solvents.

7.1 Cannabinoid Profile

Although many cannabinoids and related compounds are present in the Cannabis plant, characterization of the cannabinoid profile should include, at a minimum, the dry-weight percentage of delta-nine-tetrahydrocannnabinol (D9-THC) and cannabidiol (CBD).

Because target cannabinoid contents and ratios may vary depending on the desired dosage, medical condition, and other use considerations, minimum profile standards are not mandated. However, the cannabinoid profile must be included in product labeling under 935 CMR 500.105(5) and 935 CMR 501.105(5). Analytical procedures for determining cannabinoid profiles are available in AHP (2013).

7.2 Metals

Finished Marijuana products must be tested for the four metals listed in Exhibit 4. Quantification of metals must be performed with a validated method such as those provided by USP (Chapter <233>) or FDA (2011). A production batch of finished Marijuana products (e.g., finished plant

material, Cannabis resin, or Cannabis concentrate) may only be dispensed to patients if all four of the metals are below the upper limits for the respective product and intended use specified in Exhibit 4 (e.g., ingestion only or all other uses). These limits are in micrograms (µg) of contaminant per kilogram (kg) of product.

Once a production batch of finished Marijuana has been determined to meet the limits in Exhibit 4, it must bear the following label:

This product has been evaluated for environmental contamination (impurities) assuming that no more than 10 grams (0.35 ounces) of finished plant material (or the equivalent amount of concentrate) will be consumed per day.

In addition to the above labeling requirement for all production batches of finished Marijuana, if the quantification of metals is below the upper limits specified for "Ingestion Use Only", as described in Exhibit 4 (b), the production batch of finished Marijuana must bear the additional label:

THIS PRODUCT HAS BEEN EVALUATED FOR IMPURITIES BASED ON ORAL CONSUMPTION ONLY.
DO NOT INHALE THIS PRODUCT.

7.2.1 Metals and Marijuana Vape Products

Heavy metal accumulations are an issue of particular concern when analyzing and assessing the potential health impacts associated with the use of vape products. Instances of elevated levels of heavy metals have been identified in vape products tested by the Commission that have been subject to quarantine in accordance with the *First Amended Quarantine Order Applying to Vaporizer Products with Conditions* ("First Amended Quarantine Order"), issued on December 12, 2019. In some cases, the sampled vape product(s) failed testing due to heavy metal concentrations in excess of allowable limits. The upper allowable limit for heavy metals in marijuana and marijuana products is 500 parts per billion (ppb) for all uses and 1,000 ppb for ingestion only as stated in Exhibit 4.

The leaching of heavy metals into vape products may be due to a number of factors including time, device composition, temperature and usage. The factor of time is particularly concerning because it is not known how long leaching occurs after vape devices are filled with cannabis oil. In the absence of sufficient information developed over the course of long-term studies regarding vape devices that all potential contributing factors that impact the leaching of metals into vape products will continue to be monitored and investigated by the Commission. Accordingly, Licensees shall continue to conduct a second heavy metal screening requirement on all finished vape products subject to the First Amended Quarantine Order.

Every vape product sold must be accompanied with a written insert at the point of sale which identifies the manufacturer of the device and its known components, including the battery, and discloses materials used in the device's atomizer coil (e.g. titanium, titanium alloy, quartz, copper, nichrome, kanthal, or other specified materials). Specific additives used in the production of the vape product, including thickening agents, thinning agents and terpenes, shall also be disclosed along with their Certificates of Analysis. The Commission will continue to gather information regarding the manufacturing and design specifications of the vape cartridge and devices and will update this Guidance Protocol regarding heavy metal accumulations in vape products accordingly.

7.3 Pesticides Residues and Plant Growth Regulators

Non-organic pesticides may not be used to cultivate Marijuana in Massachusetts (935 CMR 500.120(5) and 935 CMR 501.120(5). As discussed in Section 5, all production batches of finished plant material must be tested for residues of prohibited pesticides. At a minimum, samples of finished plant material must be tested for the pesticides, including plant growth regulators, listed in Exhibits 5 and 5 a. Exhibits 5 and 5a identifies appropriate analytical methods for each of the listed pesticides.

A production batch of finished plant material may be dispensed to consumers, patients or be used to make other Marijuana products if no individual pesticide or plant growth regulator is detected above 10 ppb. A laboratory that is unable to perform the required testing of pesticide residues at or below the 10 parts per billion (ppb) criteria may determine compliance by ensuring that any pesticide residues are present at a level less than or equal to 5 percent of the US EPA tolerance for the specific residue. EPA pesticide tolerances are available from Title 40 of the Code of Federal Regulations (CFR). In such circumstances, DPH should be notified regarding the specific pesticides to which this method is being applied.

Marijuana and Marijuana products shall be tested for contaminants specified by the Commission but not limited to any plant growth regulators and the presence of pesticide. State law prohibits use of pesticides on marijuana cultivation. The Commission applies a 10 parts per billion (10 ppb) threshold to determine detection of pesticides for purposes of compliance with pre-market testing requirements. Any product that obtains a true value at the limit of detection (LOD) concentration means there is at least a 99% probability of reporting a detection. Pesticide detection above the LOD but below the quantification limit (BQL) is also considered out of compliance.

The ITL's shall report the pesticide levels in Marijuana products that are detected in the certificate of analysis. If a sample is found to contain pesticides or is above the permissible limits in the pesticides table (exhibit 5), it is considered out of compliance and or a failure. Under 935 CMR 500.120(5) and 935 CMR 501.120(5) licensees are required to immediately report to the Commission any test result indicating pesticide noncompliance. The associated product batch may not be released for retail sale and may not be remediated

Exhibit 5 requires Marijuana and Marijuana products to be tested for the following pesticides:

1. Bifenazate (Miticide)
2. Bifenthrin (Insecticide)
3. Cyfluthrin (In
4. Extoxazole (Insecticide/Insect Growth Regulator)
5. Imazalil (Fungicide)
6. Imidacloprid (Insecticide)
7. Myclobutanil (Fungicide)
8. Spiromesifen (Insecticide)
9. Trifloxystrobin (Fungicide)

Exhibit 5a requires Marijuana and Marijuana products to be tested for the following pesticides (in addition to those specified in Exhibit 5):

1. Abamectin
2. Azadirachtin
3. Azoxystrobin
4. Boscalid
5. Carbaryl
6. Chlorfenapyr
7. Dinotefuran
8. Lambda-Cyhalothrin
9. Paclobutrazol
10. Permethrin
11. Piperonylbutoxide
12. Pyrethrin
13. Spinosad
14. Spirotetramat

Acknowledging that no method currently exists that analyzes all registered pesticides efficiently (USDA, 2012a), USDA developed a "target" analyte list of 195 prohibited pesticides (USDA, 2011). Under USDA procedures for pesticide residue testing in organic food (USDA, 2013; USDA, 2014), Specifically, pesticide testing should be performed consistent with the following sections of National Organic Program Handbook: Guidance and Instructions for Accredited Certifying Agents and Certified Operations (USDA, 2014):

NOP 2611: Laboratory Selection Criteria for Pesticide Residue Testing NOP 2611-1: Prohibited Pesticides for NOP Residue Testing
NOP 2613: Responding to Results from Pesticide Residue Testing

A further discussion of the application of this testing approach is available in USDA's 2010 - 2011 Pilot Study Pesticide Residue Testing of Organic Produce (USDA, 2012b).

7.4 Microbiological Contaminants and Mycotoxins

Analytical requirements for microbiological contaminants and mycotoxins are listed in Exhibit 6. Requirements for total viable aerobic bacteria, total yeast and mold, total coliforms, and bile-tolerant gram-negative bacteria are given in colony forming unit (CFU) counts per mass of product sample. The requirement for pathogenic E. coli and Salmonella spp. is based on detection in a one-gram sample, and the requirement for mycotoxins is based on the concentration per kilogram of sample. Analytical methods for enumerating and identifying specific microbiological contaminants must be consistent with the following United States Pharmacopeia (USP) chapters:

- USP Chapter <61>: Microbiological Examination of Nonsterile Products: Microbial Enumeration Tests. USP 36, Chapter <61>
- USP Chapter <62>: Microbiological Examination of Nonsterile Products: Tests for specified Microorganisms. USP 36, Chapter <62>

Analytical methods for mycotoxins must be consistent with USP chapter:

- USP Chapter <561>: Articles of Botanical Origin. USP 36, Chapter <561>

7.5 Residual Solvents

As discussed in Section 4.2.1, residual solvents testing is required only for Cannabis resins and concentrates where solvents have been used in the production process. In particular, a production batch of Cannabis oil may be dispensed as a finished Marijuana product or used to make another Marijuana product only if:

- Laboratory analysis verifies that all solvents used at any stage of Cannabis oil production, except in cleaning equipment, are below the limits provided in Exhibit 6; and
- The production batch passes all other applicable testing requirements.

Only solvents listed in Exhibit 7 may be used in the production of Cannabis oil. A Licensee is required to test only for those solvents used, and it is not required to test for any residual solvents if it can document that no solvents were used in the Cannabis oil production process.
The upper limits for residual solvents in Exhibit 7 are given as milligrams of residual solvent per kilogram of Cannabis oil. The upper limits are based on residual solvent standards provided by the United States Pharmacopeia (USP Chapter <467>), the International Conference on Harmonization (ICH, 2011), and AHP (2013). Consistent with the standards provided by these sources, “Class 1” solvents including benzene, carbon tetrachloride, 1,2- dichloroethane, 1,1-dichloroethene, and 1,1,1-trichloroethane may not be used in the production of any Marijuana product.

Analyses to determine residual solvent concentrations in Marijuana products must be performed in accordance with the methods identified in USP Chapter <467>.

7.6 Vitamin E Acetate

Vitamin E Acetate (VEA) is a contaminant of concern that has been linked to unregulated, vape products acquired on the illicit market. The Center for Disease Control and Prevention has previously identified VEA as a potential contributor to the 2019 EVALI (e-cigarette or vaping product use associated lung injury) outbreak. While results from tests ordered by the Commission show that no licensed vape product tested positive for VEA, the Commission will continue to require mandatory VEA testing on final, ready-to-sell vape products until a final determination between VEA and EVALI has been reached by the CDC or until the Commission amends its First Amended Quarantine Order and issues any further administrative order apply to vaporizer products.

The Marijuana vape product guidance protocol recommends that for a final, ready-to-sell vape product, a test sample of the finished product containing at least one (1) gram of marijuana oil must be sent to one of the Commission's licensed ITLs for heavy metal and VEA testing. A one (1) gram test sample will provide the ITLs with enough source material to run the required tests in addition to any duplicative screenings if needed. The one (1) gram sample size amount takes into consideration the inherent challenges and difficulties with extracting marijuana oil from final, ready-to-sell vape products.

Marijuana vape products will continue to receive all required contaminant testing for concentrates as required under 935 CMR 500.160 and 935 CMR 501.160. Additionally, per the Commission's First Amended Vape Order and 935 CMR 500.160 and 501.160, final ready-to-sell vape products must also pass a second heavy metal screen in addition to a Vitamin E Acetate (VEA) screen.

To date, a standardized method for opening Marijuana vape products and extracting the oil contents has not been developed by any of the Commission's licensed ITLs. The Marijuana oil from the pre-filled vape products must first be carefully extracted from the device or cartridge before conducting the heavy metal and VEA tests to prevent introducing contaminants. Many of the vaporizer product devices are not constructed in a manner that easily allows them to be reopened after being sealed. These vaporizer products are not easily opened once sealed partly due to concerns with tampering of finished devices. Care must be taken during the extraction process such as not to introduce metal fragments that may inadvertently become lose from tools or instruments. The Commission will continue to work with the ITLs and vape product device manufacturers in efforts to eventually create standardized instructions for extracting marijuana oils from final, ready-to-sell vape products.

8.0 Data Evaluation

Licensees are required to reanalyze or remediate failed Marijuana and Marijuana products pursuant to 935 CMR 500.160(12) and 935 CMR 501.160(11). Upon receiving notification that Marijuana or Marijuana product has failed any test for contaminants, the Licensee shall either reanalyze the Marijuana or Marijuana product, shall take steps to remediate the Marijuana or Marijuana product or destroy the Marijuana and Marijuana product. Licensees must ensure that any failed Marijuana and Marijuana product are properly remediated through the Commission's Seed-to-sale System of Record (Metrc).

Reanalysis

If the Licensee chooses to reanalyze the sample, the same sample shall be submitted for reanalysis at the ITL that provided the initial failed result. If the sample passes all previously failed tests at the original ITL, an additional sample representing the same sample set previously tested shall be submitted to an ITL other than the original ITL for a Second Confirmatory Test. To be considered passing and therefore safe for sale, the sample shall have passed the Second Confirmatory Test at an ITL other than the ITL that provided the initial failed result. Any Marijuana and Marijuana product that fails the Second Confirmatory Test shall not be sold, transferred or otherwise dispensed to consumers, patients or Licensees. Any such product is subject to an Order of Destruction to be issued by the Commission at its discretion.

Remediation

If the Licensee chooses to remediate, a new test sample shall be submitted to any licensed ITL, which may include the ITL that provided the initial failed result, for a full-panel test. Any failing Marijuana or Marijuana product may be remediated a maximum of two times. Any Marijuana or Marijuana product that fails any test after the second remediation attempt shall not be sold, transferred or otherwise dispensed to consumers, patients or Licensees. Any such product is subject to an Order of Destruction to be issued by the Commission at its discretion.

Destruction

If the Licensee chooses to destroy the failed Marijuana and Marijuana product it shall do so in accordance with 935 CMR 500.105(12) and 935 CMR 501.105(11).
Licensees are required under 935 CMR 500.160(4) and 935 CMR 501.160(4) to "have a written policy for responding to laboratory results that indicate contaminant levels are above acceptable limits established in the protocols." The analytical results provided by the ITLs, including those for finished Marijuana and Marijuana products discussed in this protocol, will be a primary means for Licensees to ensure compliance with this requirement.

The ITL results must include, at a minimum, the following in the laboratory data package:

- Case Narrative:
    - The narrative, written on laboratory letterhead, shall describe any sample receipt, preparation, or analytical issues encountered as well as any method non- conformances or exceedance of QA/QC criteria used by the laboratory.
    - The narrative shall identify the preparation and analytical methods utilized by the laboratory.
    - The narrative shall include a signed statement by an authorized laboratory representative as to the accuracy, completeness, and compliance with the methods of the results presented.

- Chains-of-custody (COC) information or other paperwork indicating requested analyses and documentation of sample collection and receipt.
- Summary of analytical results including sample identifier, methods performed, target analytes analyzed for, result or reporting limit, proper qualifier according to laboratory standard procedures, units of measure, preparation date(s), where applicable, and analysis date(s).

It is highly recommended that the laboratory data package also includes sufficient data to evaluate the laboratory results, including a summary of laboratory QA/QC results. The type of applicable QA/QC results differ by analysis method, but can include surrogates or deuterated monitoring compounds, laboratory QC samples such as spikes, blanks, and duplicates, and calibration summaries. It is the responsibility of the Licensee to provide information sufficient to demonstrate that the results are accurate and precise, and in line with method capabilities and project data quality objectives (DQOs).

Depending on the outcome of the analysis, the Licensee may need to take action to address unacceptable levels of contamination or to perform follow-up investigation. Exhibit 8 is a flowchart Licensees should use to determine the correct course of action in response to each laboratory analytical data package. As discussed above, if any analysis fails to meet all applicable DQOs, then the finished Marijuana product or MIP cannot be dispensed. In this case, the production batch may be resampled for follow-up testing. A production batch may be retested once and records of the original analysis must be retained. If applicable DQOs are not met, the production batch cannot be dispensed to consumers or patients, or used in the production of MIPs.

If a batch of finished plant material fails to meet a metal or a bacteria/fungi/mycotoxin standard described in Exhibits 4 and 6, the finished plant material cannot be dispensed to a consumer or patient as finished Marijuana without first being reanalyzed and/or remediated pursuant to 935 CMR 500.160(13) or 935 CMR 501.160(12). Finished plant material that fails to meet a metal or a bacteria/fungi/mycotoxin standard may be used to derive other finished Marijuana products (e.g., resins, concentrates). While the finished plant material or finished Marijuana product may be treated in a manner to reduce the concentration of metals or bacteria/fungi/mycotoxin

contaminants, the finished plant material or finished Marijuana product may not be treated to bind or restrict the availability of the metals or bacteria/fungi/mycotoxin in an analysis without reducing the total contaminant content.

If a batch of finished plant material fails to meet a pesticide residue and plant growth regulator limit described in Exhibit 5, Exhibit 5a and Section 7.3, cannot be dispensed to consumers or patients or used to derive other products. Marijuana and Marijuana products that fail for pesticides or plant growth regulators may not be remediated and the associated batch will be subject to an Order of Destruction issued by the Commission at its discretion.

If a concentrate or resin exceeds the residual solvent requirements described in Exhibit 7 and Section 7.5 it cannot be dispensed to consumers or patients without first being reanalyzed and/or remediated pursuant to 935 CMR 500.160(12) and/or 935 CMR 501.160(11). If upon reanalysis and/or remediation the concentrate/resin meets the residual solvent standard, the ultimate finished Marijuana product may be dispensed to consumers and patients as long as all applicable limits are met.

As required by 935 CMR 500.160(5) and 935 CMR 501.160(5), the Licensee must maintain the results of all testing for no less than one year. These records must be available for inspection by the Commission upon request.

9.0 References

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