Massachusetts Department of Public Health

Bureau of Healthcare Safety and Quality
Medical Use of Marijuana Program

Response to Public Comments

February 12, 2016

This document provides the Massachusetts Department of Public Health (DPH) response to public comments received as part of the open comment period on the *Protocol for Sampling and Analysis of Finished Medical Marijuana Products and Marijuana Infused Products for Massachusetts Registered Medical Marijuana Dispensaries* that was released as a Revised Draft for Public Comment on November 20, 2015 ("Revised Protocol").

The Revised Protocol provides regulatory guidance for Registered Marijuana Dispensaries (RMD) and/or analytical testing laboratories conducting product testing in compliance with the Department of Public Health (DPH) Regulations regarding the medical use of marijuana, 105 CMR 725.000 et seq.

The following 18 comments or questions were drawn from approximately 185 comments submitted on the Revised Protocol. As many individuals submitted similar or identical comments or questions, the 18 comments or questions below may represent the combination of similar comments or questions by one or more individuals.

1) **The new DPH Protocol on hydrocarbon extraction (e.g., using butane to produce cannabis concentrate), will restrict dispensaries from serving patients and limit patients' access to their preferred form of medical marijuana.**

   The Revised Protocol does not restrict the use of butane when extracting oils from cannabis flower. The Revised Protocol requires that when butane is used in the extraction process, the levels of butane may only be present at safe levels in the finished product.

2) **The strict set of standards proposed by DPH will force patients to pursue marijuana products from the expensive and unregulated grey/black market. Support of the grey/black market may endanger the health of patients and the suppliers who make the products, since chemicals can be dangerous if they are used incorrectly or remain in finished product. Less restrictive regulations will help eliminate the risks associated with the grey/black market and encourage the development of a better quality product.**

   DPH is committed to ensuring that patients have access to the safest form of medical marijuana. The Revised Protocol is based on the standards used in the manufacturing of pharmaceutical products. DPH recognizes the hazard potential of chemical contaminants and has based the current standards on established best practices. The contaminant limits have been established to be health protective and are comparable to standards used for over-the-

counter drugs, rather than illegal narcotics. DPH is committed to ensuring patient access to products that are free of contamination.

3) **Using hydrocarbons for the production of marijuana concentrates and other products is essential to the health and well-being of patients and allows patients to explore more options for methods of use other than smoking (e.g., vaping and edibles). Hydrocarbons are safe if they are used correctly and are removed from the final product. Strict hydrocarbon standards are limiting research and development of improved marijuana products for patients.**

   The Revised Protocol allows for the use of hydrocarbons. DPH agrees that hydrocarbons are safe if used correctly and removed from the final product.

4) **Other states with medical marijuana laws already have established limits for hydrocarbons in finished products. The limits in other states are far less restrictive than those proposed by DPH (e.g., 800 ppm). DPH allows the use of chemicals that are carcinogens, while other states do not. How did DPH develop its levels?**

   The marijuana regulations in various states are constantly evolving. Each state program has been established with different laws, and the legal use of marijuana differs in each state. For example, some states do not allow some forms of marijuana (e.g., dried flower). Therefore, direct state-by-state comparisons are difficult.

   Comments submitted on the DPH Draft Protocol appear to recommend the use of an inhalation (air) standard of 800 ppm for a healthy adult worker to establish a residual solvent standard for a medical marijuana patient. This is not a health-protective approach. Exposure standards developed for healthy adult workers are not the same as standards developed for potentially very ill patients. In addition, an air concentration of 800 ppm of butane is not the same as 800 mg/kg of butane in an edible marijuana product. Air concentrations described in ppm refer to a volume-based ratio of a volume of gas mixed in a million volumes of air.

   The DPH upper limits for residual solvents are drawn from the limits described in US Pharmacopoeia (USP) (Chapter <467>). The USP has established standards for over 50 residual solvents that are used in the manufacturing of chemical and biological drug substances, dosage forms, compounded preparations, excipients, medical devices, and dietary supplements sold in the United States.

   As the USP does not have a standard for butane (propane, n-butane and iso-butane), DPH based the residual solvent limit on the Commission of the European Communities, Scientific Committee on Food Recommendations (SCF). SCF has evaluated propane, n-butane and iso-butane as extraction solvents and determined that a residue level of 1 mg of residual hydrocarbon per kg of food consumed is safe. The SCF evaluation suggests that these hydrocarbons are typically present in prepared foods in amounts less than 0.1 mg/kg. After careful review of the SCF assessment, DPH has adopted a level of 1 mg/kg (or 10 times the background level of 0.1 mg/kg) as a health-protective residual solvent limit for cannabis oils.

DPH is continuing to engage stakeholders on opportunities to refine the interim guidance on butane informed by (a) laboratory reports and data packages describing the measurement of butane in medical marijuana products sold in Massachusetts; and (b) analyses prepared by consultants describing a proposed health-based standard.

5) **The scientific evidence supporting the proposed DPH Protocol is unclear or nonexistent. No specific level (ppm) has been proven as unsafe. People inhale higher levels of the regulated chemicals from the lighter used to smoke the marijuana, or even from the air in the environment. DPH should postpone the establishment of restrictive levels until there is more scientific evidence.**

DPH is required by law to develop a regulatory framework to ensure that qualified patients have timely access to *safe* marijuana for medical use. The Revised Protocol has been established using specific levels that are published in authoritative sources such as the United States Pharmacopeia and the European Union Commission of the European Communities, Scientific Committee on Food. For example, the USP-based approach is the international standard for all manufactured pharmaceutical products.

The USP approach has the added advantage of utilizing an established system where all stakeholders have the opportunity for input. This is because the USP standards are developed and changed in an open and collaborative process, seeking informed input from independent experts with a wide variety of backgrounds – healthcare, regulatory, industry, academia, and others. By adopting this approach, we are ensuring that the process is credible, rigorous, and provides a high level of public assurance that the standard has been developed using a broadly representative body of science.

6) **DPH should clarify the difference between the amount that a patient can be prescribed and the amount that can be purchased.**

A physician "certifies" instead of "prescribes" a qualifying patient for marijuana. A physician may certify a patient for marijuana for no less than 15 days and up to a year, but within the period of time that certification is valid, a qualifying patient may only be dispensed a 60 day supply at a time. A physician may certify a patient for 10 ounces of marijuana for that 60 days or another amount, if the physician documents the rationale for doing so in compliance with the Regulations. A patient may be dispensed up to that certified amount within that 60 days and may not be dispensed more until the 60 days has expired. Due to the limitations of the testing capacity on the laboratories currently operating within Massachusetts, RMDs have sought waivers from testing requirements for certain contaminants. To protect patient safety until the laboratories are able to test for the required contaminants, the waivers are conditioned upon RMDs selling no more than 4.23 ounces to a qualifying patient over a 60 day period.

7) **The current cost of medical marijuana is a problem for patients. Eliminating the strict regulations proposed by DPH will lower the cost. Dispensaries have spent a lot of money to treat patients effectively, an effort which will go to waste if the strict regulations are maintained.**

DPH is committed to ensuring that patients have access to the safest form of medical marijuana. The Revised Protocol is based on the standards used in the manufacturing of pharmaceutical products.

8) **It seems like DPH is establishing strict regulations to slow the progress of the medical marijuana business and restrict access to patients who need it. There are further actions that DPH should take to support the medical marijuana market and the patients in Massachusetts:**

   a. **DPH should open a state-run facility to test for chemicals like those in fertilizers and in final marijuana products sold to patients.**

DPH does not regulate or operate laboratories that test marijuana for medical use. The Regulations state that all testing must be conducted by an independent laboratory that is accredited to International Organization for Standardization (ISO) 17025 by a third party accrediting body such as A2LA or ACLASS, or certified, registered, or accredited by an organization approved by the Department.

   b. **DPH should require that medical marijuana products be prescribed like pharmaceuticals. Physicians should be required to learn about the features of medical marijuana, such as the different strains, routes of administration, etc.**

The Revised Protocol describes a process to evaluate marijuana for medical use to ensure that contaminants such as residual solvents, heavy metals, and microbial contamination are not present. The Revised Protocol does not place any restrictions or establish guidelines for the prescription of marijuana for medical use. Physicians who certify marijuana for medical use are required to undergo continuing education regarding the medical use of marijuana, including side effects, dosage, and contraindications, including with psychotropic drugs, as well as on substance abuse recognition, diagnosis, and treatment related to marijuana.

   c. **DPH should regulate medical marijuana in a way similar to the regulation of alcohol and prescriptions.**

The Revised Protocol has been established using procedures drawn from the United States Pharmacopeia. The USP has established standards for chemical and biological drug substances, dosage forms, compounded preparations, excipients, medical devices, and dietary supplements for any products sold in the United States. These standards are the same standards that are applied to prescription drugs sold in the United States.

d. DPH should clearly explain its regulation decisions to the public.

Detailed information regarding DPH regulations decisions may be found at the following website:

http://www.mass.gov/eohhs/gov/departments/dph/programs/hcq/medical-marijuana/

e. DPH should conduct ongoing research on medical marijuana.

DPH is evaluating ways to support research into the medical use of marijuana and will provide further information when it is available.

9) A different profile of pharmacologically active compounds results when using hydrocarbons for extraction than when CO2 is used. Marijuana products made from hydrocarbon extraction processes should be available to patients if desired.

The Revised Protocol describes a process to evaluate medical marijuana to ensure that contaminants such as residual solvents, heavy metals, and microbial contamination are not present. The Revised Protocol does not describe an evaluation of the pharmacologically active compounds in cannabis. The Revised Protocol does not restrict the use of the hydrocarbon butane when extracting oils from cannabis flower. The protocols require that when butane is used in the extraction process, the levels of butane are present at safe levels.

10) It appears from the November 20th presentation that DPH proposes 10/g day of medical marijuana - that would make the 60 day supply 600g or 21 oz?

DPH regulations allow a physician to certify a patient for 10 ounces of marijuana for 60 days, or another amount, if the physician documents the rationale for doing so in compliance with the Regulations. In the Revised Protocol, the heavy metal limits are based on United States Pharmacopeia (USP) standards applicable for pharmaceuticals that have a maximum use of 10 g/day. In the November 20th presentation, we wanted to illustrate that this is the maximum amount of product that should be consumed in any given day. This is not the same as saying that the regulations allow a patient to obtain 10 g of marijuana every day.

11) The 10 ppb level for Pesticides and Plant Growth Regulators in Exhibit 5 seems low in comparison to the USDA maximum allowed samples, which ranges from 10-fold to 1000-fold higher than the recommended ppb. Consider changing this pesticide screening approach, and eliminate some of the pesticides that DPH requires to be evaluated.

The USDA (2012a) Laboratory Selection Criteria for Pesticide Residue Testing that is referenced in the Revised Protocol is useful as a guide for analytical testing laboratories to ensure that any pesticides and plant growth regulators that are used in the cultivation of marijuana (e.g., nutrient solutions, fertilizer, grow media, soil amendment, etc.) that would be prohibited under the USDA Organic Agriculture Program, would also be prohibited for use in the cultivation of marijuana in Massachusetts.

Since the November 2015 release of the draft Revised Protocol, DPH has made interim revisions to the "Minimum Analysis Requirements for Residues of Pesticides and Plant Growth Regulators Commonly Used in Cannabis Cultivation," and will be developing Final Guidance over the next year.

The interim guidance allows a laboratory that is unable to perform the required testing of pesticide residues at or below the 10 parts per billion (ppb) criteria to 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). The interim guidance has also removed 9 pesticides from the list of required analytes on Exhibit 5 (i.e., Abamectin, Acequinocyl, Chlormequat chloride, Daminozide, Fenoxycarb, Paclobutrazol, Natural Pyrethrins, Spinosad, Spirotetramat).

Over the next year a revised approach for the testing and analysis of pesticides/plant growth regulators will be developed. DPH is working with stakeholders as well as local, state and national experts to refine this approach. The current strategy is to develop a list of pesticides and plant growth regulators that are being specifically applied to finished marijuana plants or products. This list will be informed by the continually evolving best practices of state agencies charged with the ensuring the safety of medical use of marijuana programs, and the state-of-the-science on available analytical laboratory methods to measure pesticide residues on cannabis plants.

12) The drying of marijuana products may alter the potency profile (cannabinoid) content of the product. As THC and CBD molecules are recognized by some patients and physicians as being important in treatment, DPH should encourage the testing of THC-A and CBD-A in cannabinoid profiles of unheated materials.

The Revised Protocol describes testing medical marijuana to ensure that contaminants are not present and patients have access to safe product. In general, the Revised Protocol describes "Minimum Analysis Requirements" and do not describe a comprehensive evaluation of the pharmacologically active compounds in cannabis. While the Revised Protocol does not place any restrictions or establish guidelines for the prescription of certain types of marijuana for medical use, or analysis that may be performed in addition to the minimum requirements, it should be noted that THC-A and CBD-A have been added to the cannabinoid profile testing requirements

13) DPH should raise the maximum allowable levels of Cd and Pb to match the USDA standards for ingestible products.

The Revised Protocol adopts upper limits for heavy metal contaminants that have been established by the United States Pharmacopeia (USP). These standards have been developed specifically for drugs sold in the United States. The USP standards in the National Formulary (NF) are also the official enforceable standards for pharmaceutical product strength, quality and purity by the FDA.

14) DPH should only require the testing for the individual solvents if the solvent has been used in the processing of the plant for that product.

The Revised Protocol states that cannabis concentrates must only be tested for residual solvents if the solvents were used in their production. Specifically, testing is required for a solvent if that solvent was used to manufacture a concentrate.

15) Laboratories performing MMJ testing should follow the guidelines for personnel similar to CLIA and DPH regulations for clinical laboratories.

While DPH has developed a process to provide an evaluation of laboratory capability, DPH does not regulate or operate laboratories that test marijuana for medical use. The Regulations state that all testing must be conducted by an independent laboratory that is accredited to International Organization for Standardization (ISO) 17025 by a third party accrediting body such as A2LA or ACLASS, or certified, registered, or accredited by an organization approved by the Department.

16) Regulations require medical cannabis to be grown organically. Organic soil and organic nutrients may contain higher levels of arsenic and heavy metals. Tests could result in higher levels because of it.

The Revised Protocol references the USDA Organic Program as a guide to ensure that any pesticides that are prohibited under the USDA Organic Agriculture program, are also prohibited for use in the cultivation of marijuana in Massachusetts. The Revised Protocol requires the testing of finished plant material to ensure that pesticides and plant growth regulators have not been used.

Both soil and soil amendments must be tested for heavy metals long before they are ever used in the cultivation of cannabis plants. This testing is covered in the "Protocol for Sampling and Analysis of Environmental Media for Massachusetts Registered Medical Marijuana Dispensaries."

17) The heavy metal standards are based on two different routes of exposure (e.g., ingestion or inhalation). Why was this approach not taken for residual solvent levels?

The Revised Protocol refers to an approach to evaluate heavy metal contaminants and residual solvents that have been established by the United States Pharmacopeia. This is a significant point as this approach *adopts* USP standards and did not develop them. While the USP has a different heavy metal standard for inhalation and ingestion, respectively, it does not have two different standards for residual solvents.

18) DPH should explain the "10 gram/day" assumption described in the derivation of the Heavy Metal Standards.

In the Revised Protocol, the heavy metal limits are based on concentrations listed in the United States Pharmacopeia (USP) document describing Elemental Impurities (i.e., metals). The Recommended Limits for Metals (Protocol Exhibit 4) have been adopted by DPH based on USP

calculations of concentration limits for components (drug substances and excipients), that assume products will be used at any dose up to a *maximum* daily dose of 10 grams per day. These values are default concentration limits that are set by USP for manufacturers and suppliers of drug products. The 10 g/day value was not used quantitatively by DPH to calculate a concentration limit. As the USP limit is applicable for any use up to a maximum of 10 g/day, we wanted to ensure that patients understand that this is the maximum amount of product that should be consumed in any given day. We recognize that most patients will use much less than this amount.