Testimony of Lauren Vrabel, PharmD before the Pennsylvania Law & Justice Committee
March 14th, 2022

Introduction

Hello and thank you Sen. Regan and Sen. Brewster and all of the members of the Law & Justice Committee for your attention today. My name is Lauren Vrabel and I am a licensed pharmacist in Pennsylvania, Ohio, and Illinois. I earned my doctorate of pharmacy from Duquesne University and have been practicing in the Pennsylvania Medical Marijuana Program since 2018. Today I would like to address the ways in which the current Medical Marijuana Program has successfully mitigated public harm as well as identify areas for improvement. The topics are important considerations for the future Adult Use program as many can be adopted as best practices to reduce overall public harm, whether medical or recreational consumption. As the medical professional on duty at the dispensary, I offer a unique perspective.

Clinical Registrants & Academic Clinical Research Centers

I am proud to operate in Pennsylvania's Medical Marijuana Program for, in my opinion, it is very progressive compared to other states. The inclusion of Chapter 20 allows Clinical Registrants and Academic Clinical Research Centers to make progress on understanding cannabis as medicine. To my knowledge, Pennsylvania is the only state to include this legislation. While we have made significant strides in cannabis research over the past few years, there is still so much we need to discover and learn. Information on stability testing for dosage formulations as well as which combination of cannabinoids and terpenes provide the best patient outcomes is necessary. This information is used to establish clearer safety parameters and guidelines for specific medical conditions, similar to what we do with traditional pharmaceutical medications and over-the-counter supplements. Because of Chapter 20, this information will be more readily available to the cannabis community.

Medical Professionals Required for Dispensing

Another area that reduces public harm is the inclusion of medical professionals at the dispensaries. Several states such as Arizona, Maryland, and Ohio may require a medical professional to be on-call for permit holders, however the majority do not require any medical professional to be present or involved in the actual dispensing of medical marijuana. In Pennsylvania, a unique medical professional is required to be available, whether in person or via telemedicine, during hours of operation. This can be a physician, pharmacist, nurse practitioner, or physician assistant. The majority are pharmacists, as the role is very similar to traditional retail pharmacy.

In a study published by Thomas Jefferson University, one of the Pennsylvania ACRC's, medical patients identified that, "Dispensary pharmacists were considered reliable, consistent and expert sources of knowledge about cannabis characteristics. During certification, many clinicians referred patients to consult with pharmacists upon their first dispensary visit.

Participants indicated that they did so and considered information provided by pharmacists to be thorough and accurate. Within dispensaries, many participants expressed a preference to consult with pharmacists as opposed to counter dispensary staff when they wanted tailored guidance."[1]

As a pharmacist, my training prepared me to understand what drugs do to the body and what the body does to the drug. Working directly with the products allows me to have a greater understanding of the nuances of each, which is something not afforded to the certifying physicians in the program. In fact, the study indicated that between the dispensary staff, pharmacists, and certifying physicians, participants received the least guidance from their physicians. One participant in the study indicated that, "the people behind the counter [budtenders] have personal experience but often lack, I don't want to say that they lack anything, but it's not the same as you do with a pharmacist or someone with a broader working knowledge of it.."[1] Patients in the program qualify for one or more of the 23 pre-approved conditions that are deemed as debilitating or intractable, meaning that other therapies have not been successful at improving patient symptoms. Some patients have medication lists and unique conditions with multiple symptoms that require specific considerations and recommendations. The layman is not properly trained to accomplish this, so there is a need for a medical professional during the product selection process. Unlike traditional pharmaceutical practices, the certifying physician does not dictate a specific product or set dosing instructions. This may leave the patient vulnerable at the dispensary if it weren't for the inclusion of a medical professional.

Laboratory Testing

An additional area that Pennsylvania performs very well is ensuring that products are tested for safety parameters and strength of components. Products are tested for a range of microbiological impurities such as bacteria, mold, and pesticide residue, as well as heavy metals and foreign material. Batch testing is done at extraction and then again before the final product is packaged and distributed. During the curing process for flower, cannabis is dried to prevent bacteria and mold. It is necessary to test it again before packaging to ensure that the final moisture content is acceptable and that there were no significant losses of cannabinoids or terpenes. A sample of each testing batch is saved and retested after six months and one-year to validate expiration dates. Other states, like Illinois, do not require stability testing at all, whereas others like New York only re-test after 60 days. Stability testing is important not only to ensure there has not been any microbial growth, but also to ensure accurate strength of cannabinoids and terpenes on the package labeling. Overtime, cannabinoids and terpenes can degrade especially if products are not stored properly in a cool, dark place.[2] Research indicates that extracted products may be reasonably stable for one to two years.[3] Currently, the majority of products are given an expiration date one year after the date of packaging. If further stability studies are conducted by the laboratories, the shelf-life of several products could be increased.

Regulatory Standards

Although Pennsylvania's program is robust and thriving, there are certain aspects that impede additional success. The largest area of improvement needed encompasses the implementation of proper regulatory standards. There is a lack of regulation across dispensaries, grower-processors, laboratories, and the medical professionals who operate within the industry.

This void leads to confusion and misinformation that is spread to the general public which can, not only reduce positive outcomes for patients, but also cause harm.

Terminology

At the utmost importance is the standardization of terminology or nomenclature utilized within the program. Word choice can greatly affect the meaning or sway the understanding of a rule and regulation and must be clear, concise, and appropriate. For example, the list of dosage formulations approved for dispensing includes the following: pill, oil, topical forms including gel, creams, or ointments, a form medically appropriate for administration by vaporization or nebulization, including dry leaf or plant form for administration by vaporization, tincture, and liquid. This list is extensive, but can lead to confusion. The term "oil" can be used to describe Rick Simpson Oil, the oil contained in the cartridges, tinctures, and liquids. The intended definition of oil gets lost in translation between the certifying physician, what is recommended to the patient, and what is considered an oil at the dispensary. Clarification of terminology will prevent confusion.

A tincture is an example of a liquid dosage formulation, but by definition is unique because it contains at least 20% alcohol by volume. When examining products offered by grower-processors, several liquids are labeled as tinctures yet do not identify alcohol in the ingredient list nor provide the alcohol content. This misleads the medical professionals as well as the general public, for a tincture that contains alcohol may be absorbed sublingually, or under the tongue, whereas one that does not cannot. Correctly categorizing products will prevent misinformation. Additionally, two dosage formulations were approved for dispensing but not included in the rules and regulations or the medical professional certification portal: transdermal products and suppositories. Although both seem to loosely fall under topically administered products, the distribution, metabolism, and excretion of these routes of administration differ in comparison. The differences require a separate approach to counseling points and monitoring parameters, as both may cause intoxication.

Additionally, word choice affects the interpretation of the rules and regulations when considering the adoption of the COVID-19 statutory and regulatory provisions permanently. Prior, the rules and regulations stated "a dispensary shall ensure that a physician or a pharmacist is present at the facility at all times during the hours the facility is open to dispense or to offer to dispense medical marijuana products to patients and caregivers."(§ 1161.25.) This indicates that the medical professional must be physically present at the dispensary during operating hours.

During the state of emergency, the following was stated regarding the suspension of this section of the act:

> "The requirement in 35 P.S. §10321.801(b) and 28 Pa Code §1161.25(a) and (b) that a medical professional (physician, pharmacist, physician assistant or nurse practitioner) be onsite at the facility at all times during dispensing hours. The medical professional must remain available for remote patient consultations and must continue to verify each patient certification prior to the patient being dispensed medication at the facility."[4]

With permanently adopting telemedicine, the medical professional at the dispensary can operate remotely and does not need to physically be present at the dispensary for dispensing to occur. Unfortunately, this has led to confusion. The update does not indicate that the remote medical professional is still required to be unique, meaning a different medical professional per operating

dispensary. It is my understanding that permit holders may be utilizing one medical professional to perform their duties at multiple locations simultaneously. This not only presents inappropriate pharmacist burden, but also limits the ability to effectively and safely respond to patient concerns.

Product Labeling

A lack of standardization with respect to product labeling can lead to confusion over administration techniques or inappropriate dosages, possibly causing adverse effects. In 2019, the University of the Sciences held meetings to discuss recommendations for medical cannabis labeling in the Commonwealth of Pennsylvania and presented their suggestions.[5] Currently, solids that are single unit dosage formulations, such as capsules, are often labeled by total cannabinoid content. For example, the package indicates 1000mg THC on a container of 20 capsules. As a comparison, this would be similar to labeling a 30-count bottle of ibuprofen 200mg as "Ibuprofen 6,000mg" which is confusing. The Summit recommends labeling these products in terms of mg per unit of product (mg/capsule) as opposed to by mg contained in the entire package. Labels for oral liquid dosage formulations will often tout an expected mg/ml of components, but not indicate that the actual testing results may vary within a certain percentage. Currently, oral liquid products are dispensed in opaque vials that contain a dropper in the lid that is demarcated up to 1 milliliter (1 ml). Package labeling indicates total milligrams per total volume of container, a milligram per milliliter strength, or percentage strength and total volume. Unfortunately, this is not consistent from grower-processor to grower-processor. Additionally, labeling sometimes specifies a target dose that the formula is anticipated to produce within a certain percentage of variability, however this is not clearly communicated to the patient. The lack of standardization can cause confusion when substituting products due to inconsistent supply, which may cause adverse events. The Summit recommends that liquids should be labeled with the strength per container volume followed by the strength per 1 milliliter. They do not comment on target doses, however one suggestion is to caution that the actual dose may vary on the package. Topical products currently are only labeled with total milligrams of cannabinoids per container; the Summit recommends to also include the percent concentration as well. One final recommendation from the Summit was to provide a detailed list of all active and inactive ingredients and to specify any allergens. "A complete list is important due to factors such as patient safety, drug-drug interactions, efficacy of the product, and disease states being treated."[5] A specific concern is avoiding products that contain ingredients that are known to cause an allergic reaction in a patient.

By providing the entirety of this information in a clear and consistent manner, the labeling would resemble the drug facts labeling used in everyday over-the-counter (OTC) products. The FDA established the OTC Drug Facts regulation in order to make it easier for consumers to read and understand OTC drug product labeling and use OTC drug products safely and effectively. The patients and future adult-use consumers deserve the same readability.

Marketing

Improved standardization with respect to marketing can easily reduce public harm, as the intended audience is the patient. If marketing is not appropriately scrutinized, patients may be misled by false information that impacts their purchases and ultimately outcomes. For example, a cartridge that is marketed as a Sativa is expected to produce effects that are uplifting, energizing, and suitable for daytime use. Often those words or similar are used on packaging, handouts, and even branding. This can be misleading if the product contains cannabinoids and/or terpenes that, anecdotally and through animal studies, promote sedation or sleep.

As addressed previously, if an oral liquid is marketed as a tincture but does not contain alcohol, it will not be absorbed underneath the tongue. Sublingual preparations are expected to have an onset of action in about 15 minutes.[6] This is significantly faster than oral administration, which takes about 30 minutes to one hour.[7,8] Dose stacking is a common error that occurs when patients take a second dose of a product before waiting to assess the effects. Once the effects are felt, they are much stronger or even unpleasant if the additive dose is greater than the patient's tolerance. This occurs commonly with oral preparations due to the longer onset of action. Because a false tincture is marketed to have a quicker onset of action, patients are at a greater risk for dose stacking.

Product Availability and Consistency

In the research published by Thomas Jefferson University, patients indicated an area of concern and frustration is product availability and consistency. Many participants commented that when they found a product that worked well to treat their symptoms, it could be difficult to find at subsequent visits or at other dispensaries.[1]

We are at the mercy of growing and harvesting a plant that is suitable for extraction which can be the rate-limiting factor for product availability and consistency. Measures have been taken to expand the variety of products available by allowing a yearly increase period for acquiring additional seeds and clones, however no significant measures have been taken to ensure product consistency. Currently, not every grower-processor provides CBD-dominant products, which are perceived as more medical by nature. A possible solution would be to require grower-processors to produce certain products, specifically those with cannabidiol (CBD), at specific ratios in comparison to other products. Similar to states such as Illinois and Vermont, it is pertinent that Pennsylvania medical patients receive priority access to products. Priority should be placed not only when there is a shortage in products but also during the cultivation and extraction processes to ensure that the products that they rely on for relief are available.

Education

A lack of standardized education is a common theme regarding cannabis and the cannabis industry. Because research has been limited until recent years, we have not been able to fully

understand the plant. This is why it is largely not taught in schools, leading laymen and scientists alike to search for information and play "catch up" while the industry expands. When one misinterprets the information or promotes anecdotal evidence as facts, misinformation spreads and can be detrimental to public safety and health.

In a second study performed by Thomas Jefferson University, clinicians in Pennsylvania were surveyed about their attitudes, training, and experiences regarding medical cannabis and patient consumption of medical cannabis.[9] Only 51% of participants reported completing any formal cannabis training and of the participants, physicians were significantly more comfortable with their knowledge and recommending it to patients. This may be because the majority of physicians who completed the survey were certifying physicians, however the disparity in training across all disciplines creates an urgent need to expand training opportunities.

As current information becomes available, it is pertinent that those working in the industry, regardless of their role, maintain their understanding of cannabis. In order to be employed by a permit holder, all employees must take a 2-hour course and pass a knowledge test. The medical professionals, including certifying physicians, must take a 4-hour continuing education course. These courses are only required to be completed once, with no further requirement for continuing education. It is my recommendation that evidence-based education standards be implemented and required for all industry professionals on an annual basis in order to maintain a comparable understanding of the science behind cannabis as a medicine. Additionally, the medical professionals should be required to complete cannabis-related continuing education as a part of maintaining their professional license. This will prevent gaps in knowledge between those who interact with patients or consumers on a daily basis which ultimately will prevent public harm.

To exemplify how education prevents public harm, I interviewed a patient who experienced an extreme case of overmedication. The patient explained that she went to the dispensary for the first time and asked the person at the counter for the strongest thing for sleep. She had been struggling with nighttime symptoms that kept her up at night. The attendant did not ask any additional questions and dispensed Rick Simpson Oil (RSO), recommending a starting dose no larger than the head of a pin. RSO is a viscous product that is supplied in oral syringes. Because of the viscosity, it is difficult to plunge precise doses from the syringe. If too much is plunged, it is easy to consume too large of a dose because RSO is extremely potent. Colloquially, the recommended starting dose is approximately the size of half of a grain of rice. Although extremely small, this amount can be as strong as 40mg. Recommended doses for cannabis naive patients are between 2.5-5mg.[6] When the patient consumed the RSO, she admitted to plunging more than what was recommended and experienced an extreme case of over-medication. Her symptoms included dizziness, increased heart rate, labored breathing, anxiety, and extreme sedation. Believing her symptoms were life-threatening, she took an ambulance to the emergency room to receive treatment. It took approximately three days for the symptoms to fully resolve. This adverse event could have been prevented if proper education had been implemented at the dispensary level and passed on to the patient. It is recommended that first time patients meet with the medical professional on duty so that they are educated about the different dosage formulations and provided a personalized recommendation based upon symptoms and medical history. In the instance that the patient refuses consultation from the medical professional, appropriate counseling methods should be utilized at the point of sale. Common methods include asking questions to gauge patient experience and tolerance level, cautioning on side effects and adverse events, and informing on duration of effects.

Inspections

Although dispensaries and grower-processor facilities are inspected by the Department of Health, it is unclear whether laboratories, certifying physicians, or the medical professionals within the program are held to the same scrutiny. This creates a gap in standardization that has the potential to allow room for public harm. Laboratories should be inspected for retention of records, following procedures, accuracy of testing, and anything else that the Department deems necessary to ensure appropriate business is conducted. Over the past several years, the FDA has issued warning letters to firms that market unapproved products that contain CBD. As part of their actions, they tested for the chemical content of cannabinoids and found that several did not contain the amount of CBD that they claimed to contain.[10] A study published in January 2022 examined 27 delta-8-THC products sold over-the-counter in New York. Of the products, none contained accurate labeling for delta-8-THC, 11 contained unlabeled cutting agents, and all contained reaction side-products from the chemical manipulation of CBD to delta-8-THC. The samples also contained heavy metals that were hypothesized to have leached from the hardware of the cartridge, as well as elevated levels of silica which is used during purification processes.[11] Although several factors may have contributed to the aforementioned findings, this information is relevant as the accuracy of testing facilities is paramount to patient health and success.

Certifying physicians should be audited for maintaining patient records including proof that prior diagnosis has taken place before the certification appointment. They should also provide proof that appropriate counseling has occurred per the rules and regulations. Although the non-certifying physicians who are part of the medical marijuana program are subject to inspection at the dispensary, they too should be inspected. Inspection for this group would include ensuring that patient certifications were checked prior to dispensing so that any limitations or restrictions were followed. All those who participate in the Pennsylvania Medical Marijuana Program should be held to a similar standard when it comes to ensuring that they are compliant with the rules and regulations. The simplest way to enforce the rules and regulations is to require inspections and follow-up inspections to ensure that the parties have made changes to reflect the integrity of the program.

Electronic Tracking System

The Electronic Tracking System is required to be utilized to record all transactions from seed-to-sale and back. It is one component of the program that is standardized, but does not meet expectations. When the program went live in February 2018, MJ Freeway was not ready to be used in Pennsylvania. This led to undocumented patient purchases until approximately May 2018. This still affects dispensaries today that are unable to return products back to the grower-processors. Additionally, the platform experiences frequent outages which requires dispensary employees to deny sales to patients. Occasionally these outages led to computational errors that forced dispensary employees to track down potential human errors that did not exist. Adding to frustration, the medical professionals, including certifying physicians, are required to utilize a separate platform to document patient interactions. This is because the Electronic Tracking System lacks the features to separately indicate physician recommendations as well as pharmacist notations. A platform that includes these features will allow for better continuity of care between the certifying physicians and the dispensary.

In Summary

Thank you for allowing me the opportunity to present my testimony as a pharmacist working in the Pennsylvania Medical Marijuana Program. Although the Commonwealth of Pennsylvania does not want to sit idly as surrounding states introduce their Adult Use programs, it is important to learn from the progress and hurdles of the current Medical Program. It is important to pay attention to details. And it is important to prevent public harm to the best of our abilities.

References:

1. Reed, Megan K., et al. "A Failure to Guide: Patient Experiences within a State-Run Cannabis Program in Pennsylvania, United States." *Substance Use & Misuse*, vol. 57, no. 4, 27 Dec. 2021, pp. 516–521., https://doi.org/10.1080/10826084.2021.2019780.
2. Sannikova, Natalia. "The Effect of Storage Conditions on Cannabinoid Stability." *Ascension Technical Artciles*, June 2020, pp. 1–7.
3. Fairbairn, J W, et al. "The Stability of Cannabis and Its Preparations on Storage." *Journal of Pharmacy and Pharmacology*, vol. 28, no. 1, 28 Jan. 1976, pp. 1–7., https://doi.org/10.1111/j.2042-7158.1976.tb04014.x.
4. Pennsylvania, Office of Medical Marijuana. *Medical Marijuana Coronavirus (COVID-19) Notice - June 15, 2021*, 15 June 2021.https://bit.ly/3I7XmkG. Accessed 9 Mar. 2022.
5. "Sudi Recommends Additional Labeling for Medical Cannabis Products Sold in Pa." *University of the Sciences Substance Use Disorders Institute*, https://www.usciences.edu/news/2019/sudi-recommends-additional-labeling-for-medical-cannabis-products-sold-in-pa.html.
6. MacCallum, Caroline A., and Ethan B. Russo. "Practical Considerations in Medical Cannabis Administration and Dosing." *European Journal of Internal Medicine*, vol. 49, 4 Jan. 2018, pp. 12–19., https://doi.org/10.1016/j.ejim.2018.01.004.
7. Grotenhermen, Franjo. "Pharmacokinetics and Pharmacodynamics of Cannabinoids." *Clinical Pharmacokinetics*, vol. 42, no. 4, 2003, pp. 327–360., https://doi.org/10.2165/00003088-200342040-00003.
8. Huestis, Marilyn A. "Human Cannabinoid Pharmacokinetics." *Chemistry & Biodiversity*, vol. 4, no. 8, Aug. 2007, pp. 1770–1804., https://doi.org/10.1002/cbdv.200790152.
9. Worster, Brooke, et al. "Clinician Attitudes, Training, and Beliefs about Cannabis: An Interprofessional Assessment." *Cannabis and Cannabinoid Research*, 31 Dec. 2021, https://doi.org/10.1089/can.2021.0022.
10. Office of the Commissioner. "Warning Letters and Test Results for Cannabidiol-Related Products." *U.S. Food and Drug Administration*, FDA, 5 Aug. 2021, https://www.fda.gov/news-events/public-health-focus/warning-letters-and-test-results-cannabidiol-related-products.
11. Meehan-Atrash, Jiries, and Irfan Rahman. "Novel Δ8-Tetrahydrocannabinol Vaporizers Contain Unlabeled Adulterants, Unintended Byproducts of Chemical Synthesis, and

Heavy Metals." *Chemical Research in Toxicology*, vol. 35, no. 1, 10 Dec. 2021, pp. 73–76., https://doi.org/10.1021/acs.chemrestox.1c00388.