CALIFORNIA CANNABIS MANUFACTURERS ASSOCIATION

August 1, 2022

Ms. Nicole Elliott
Director, Department of Cannabis Control
Legal Affairs Division
2920 Kilgore Road
Rancho Cordova, CA 95670
Submitted via E-mail: publiccomment@cannabis.ca.gov

Re: Implementation of SB 544 and Proposed §15712.1 and 15712.2 Additions to Title 4, Division 19 broadly related to a single standardized, cannabinoid test method

Dear Ms. Elliott:

On behalf of the California Cannabis Manufacturers Association, (CCMA) we appreciate the opportunity to comment on the proposed additions to the Department of Cannabis Control (DCC) Regulations (Title 4, Division 19). We support and align our comments below with the comments prepared by Dr. Jeffrey Raber, Ph.D and CEO of the Werc Shop Laboratory.

As leaders and business owners in California's cannabis industry, CCMA knows it is imperative for cannabis statutes and regulations to provide strong public health safety standards while encouraging achievable and business-friendly practices that foster a robust, regulated marketplace. We pride ourselves on being leaders in product safety and industry standards through our implementation of protocols aligning with long standing mainstream industries to create trustworthy brands, products, and processes.

The proposed new additions to the DCC Regulations (Title 4, Division 19) would limit cannabis testing laboratories in California to the use of a *single*, DCC-defined cannabinoid analysis method and a *single*, sample preparation method. Senate Bill 544 (SB 544) mandated that DCC "establish one **or more** standardized cannabinoids test methods." Presumably, the Legislature intended that more than one should be developed, if necessary. Sound science demands that there be more than one sample preparation and extraction method for all of the various product matrices present on the cannabis market today.

Overall, CCMA commends your Agency on the forethought and technical research that went into these proposed regulations and we support the goal to communicate accurate information to cannabis consumers. However, we believe that permitting **only one** method will not solve the problem of high THC numbers and will likely make the problem worse. Mandating one single method will inevitably *and counterintuitively* lead to inaccurate labeling and quite possibly adverse events due to inadvertently ingesting more THC than expected.

In the comments that follow, we offer suggestions about how to further refine the approaches proposed in the draft rules with reference to analogous approaches used in botanical analysis along with cautionary tales. We believe our suggestions may help prevent the Agency from traveling down a blind-alley and hampering diversity and innovation.

The overall summary of the below is: 1) the proposed proscriptive methods for HPLC analysis and sample preparation will create more problems than they will solve and 2) alternative methods should be permitted if equivalence can be demonstrated with the official method, as is common in the analytical sciences.

We urge you to strongly consider the second point if you are committed to moving forward on the first point.

DCC Mistaken Summary of Existing Law

In the Notice of Proposed Rulemaking (dated June 17, 2022), the summary of subsection (f)(2) of section 26100 of the Business and Professions Code as revised by SB 544 is misstated multiple times throughout the document beginning on page 3. The Notice of Proposed Rulemaking and the Initial Statement of Reasons makes multiple references to "a standardized method" or "the method" when section 26100 clearly states "one or more" methods. As such, the summary of existing law should make use of the descriptive phrase "at least one" to accurately describe the scope of the Legislative mandate.

Will the Proposed Single Method Solve the Problem?

Simply stated, the problem that SB 544 sought to address is that some laboratories consistently report higher THC numbers than others. In fact, labs that do this garner more business because cannabis flower and flower products (e.g. pre-rolls) are priced at retail stores according to THC content as was demonstrated in Washington state in 2018.[1] This is due to the widely held, but mistaken, consumer belief that products with a higher labeled THC content: 1) will have more THC per gram, 2) will be of greater quality or 3) are a better value. Even a small difference in THC concentration, for example 25% THC vs. 20% THC, can make the difference between having a salable product and not, or having a product with greater sales velocity. The economic incentives for cheating are high.

By proposing that all licensed California cannabis labs must use the same DCC-proposed methods for sample preparation and HPLC analysis down to specific parameters such as, wavelength of detection and solvent systems, the assumption is that the elevated THC reporting is a technical problem and that the proposed DCC methods are the technical solution. As described in the previous paragraph, we disagree that the problem is technical in nature. Rather, the economic incentives of reporting high THC numbers are significant and are currently left unchecked by enforcement mechanisms, such as fines and license suspensions.

Even if we assume the problem is technical in nature, the proposed technical solution will not solve the stated problem. One need look no further than the 70-130% acceptable recoveries permitted in the Acceptance Criteria for Quality Control Samples (Section VIII) in the proposed analysis method.[2] This allows one lab that tests the THC content perfectly (i.e. 100% recovery) and a second lab that tests it 30% higher to both be "right" and both be in compliance. This is the difference between cannabis labelled as 20% THC vs. 26% THC or 25% THC vs. 32.5% THC. The former difference is enough to prevent some stores from even stocking the product, while the latter difference is enough to command both greater demand and willingness to pay higher prices from consumers.

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[1] MacRae J. (2018, MARCH 14). Paying for Potency? HI-Blog. Straight Line Analytics. Retrieved July 26, 2022, from https://straightlineanalytics.biz/2018/03/paying-for-potency/

[2] Department of Cannabis Control, Cannabis Testing Laboratory Branch Determination of Cannabinoids Concentration by UPLC, Standard Operating Procedures CM-002 (Final 3/29/2022).

Regardless of whether a single method or more than one method is mandated for use by all laboratories, the recovery tolerances should be tightened significantly. This will avoid the "compliant" over-labeling of THC issues that persists today and that actually penalizes labs that report accurate results. Narrow the allowable recovery range and DCC will have a more powerful tool to enforce against lab shopping and intentionally elevated THC test results. Whatever else is done, making this single change will lead to improved label accuracy and improved consumer protections.

Are the Proposed Methods Ideal or Even Robust?

The DCC-proposed methods for both HPLC analysis and sample preparation each have limitations. For example, the required analysis wavelength of 220 nm is a region where matrix interference often occurs since many more analytes beyond cannabinoids absorb at this wavelength. Furthermore, the required running solvent systems preclude the use of buffered aqueous phases, which generally are preferred to avoid peak shifting and to help ensure proper peak shape. Even if buffers were permitted, the requirement to analyze at 220 nm would create interference and baseline homogeneity issues with buffer salts, such as ammonium formate and ammonium acetate. There are other issues that we will not go into here, but suffice it to say that the HPLC analysis method currently presented is far from perfect.

The sample preparation methods are also lacking. For example, requiring cryogenic grinding for all chocolate, hard candy, gummy and cookies samples and then extracting with only a specified extraction solvent is neither effective nor cost-effective. There are other means to ensure homogeneity of samples that do not involve costly and time-consuming cryogenic grinding. Furthermore, products within the broad categories listed can vary widely in their matrix elements. For example, not all cookies use the same ingredients. These different ingredients yield different matrices that behave differently and sometimes create different sources of interference as has been described in the scientific literature for cannabinoid-containing chocolate samples.[3] The currently proposed extraction solvent was found to be highly ineffective at extraction of cannabinoids from chocolate matrices, which if implemented, would ultimately lead to under-reporting THC content and could lead to an unexpected THC-overdosing experience.

By tying the hands of laboratories to use only very specific sample preparation methods, the DCC and the people of California will have to learn to accept inaccurate results for some products. At best, consistently inaccurate results will be achieved. At worst, labs will be absolved of all responsibility to get the right answer because they are "just following directions."

The Concept of Compendial Methods and Applicability to Cannabis Products

Compendial methods are typically created for single active pharmaceutical ingredients (APIs) and often for analysis in the same or very similar matrices. The wide-range of product types that contain cannabinoids and the extreme diversity of matrices precludes the use of a single compendial method that does not permit amendments.

When a compendial method identifies more than one analyte, it is common to define a critical pair (two compounds that elute close to each other) and to establish a minimal resolution for those compounds. If the method, as implemented using a specific instrument or peripherals (e.g. C18 HPLC column) does not achieve the pre-defined minimal resolution, one is allowed to slightly modify the mobile phase. We would encourage the DCC to proactively consider this if proceeding with a single HPLC analysis method.

[3] Dawson DD and Martin RW. Investigation of Chocolate Matrix Interference on Cannabinoid Analytes. Journal of Agricultural and Food Chemistry 2020 68 (20), 5699-5706DOI: 10.1021/acs.jafc.0c01161

Common and Valid Practice of Demonstrating Equivalence to Compendial Methods

As detailed in USP 621 on Chromatography, "allowable adjustments" are common for modifying even compendial methods.[4] This is often necessary because it is impractical to expect everyone to run the method on the same instrumentation platform, with the same configuration and the same disposables. "Allowable adjustments" help define a range of permitted variations for key components of the system (cf. system suitability) to allow flexibility in implementation and to allow the method to evolve with technological innovation.

In addition, USP General Notices and Requirements section 6.30 (Alternative and Harmonized Methods and Procedures) states, "Alternative methods and/or procedures may be used if they provide advantages in terms of accuracy, sensitivity, precision, selectivity or adaptability in automation of computerized data reduction or in any other special circumstances" as long as method *validation* is performed.[5]

Furthermore, the academic literature is replete with publications that demonstrate how a non-compendial or newly developed method is equivalent to a compendial method. This process demands a full validation package, not simply verification. Nevertheless, this is generally accepted practice, especially for broad-based methods that assess a multitude of analytes in a plethora of product matrices.

Overall, it is difficult for individuals and firms that are accustomed to working with compendial methods and standards-setting organizations to understand the logic of attempting to force a single HPLC column and sample preparation method on an industry without permitting "allowable adjustments" to the method(s), at the very least, or the ability to demonstrate equivalence to the "official" method. In fact, the statutory language seems to acknowledge this when the plain text directs the DCC to develop "one or more" methods. Persisting with a single, unalterable and inflexible method approach might give industry the wrong idea that DCC is more concerned with making the implementation of SB 544 easy on the Agency rather than doing what is best for the industry and the consuming public.

If you have any questions about our comments, please contact Alicia Priego at aliciap@strategies360.com. Thank you for your time.

Respectfully,

Kenny Morrison,
CCMA President

[4] USP. Chromatography General Chapter <621>. In: USP–NF. Rockville, MD: USP; Aug 1, 2014.
[5] USP. General Notices and Requirements. In: USP 32–NF 27. Rockville, MD: USP; May 1, 2009.