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Good morning, Senator Ingwersen, Representative Pluecker, distinguished members of the Committee On Agriculture, Conservation and Forestry. I would like to express my sincere gratitude for the opportunity to speak before this esteemed committee today. My name is Gary Ickes, and I am a resident of Smithfield, Maine. I am a scientific formulator within the industry, the manager of a medical-facing cannabinoid company, Plant & Flask, and a shaper participant of Seed2Health Learning Health Alliance. I am here today to discuss LD 1996 and share my perspective on its implications.

Re: Sec. 3. 7 MRSA §2231, sub-§1-A, ¶G is enacted to read:

> "Synthetic hemp-derived cannabinoid" means any cannabinoid that is not naturally occurring in hemp or a cannabinoid, whether naturally occurring in hemp or not, that is produced by manufacturing a hemp-derived cannabinoid in a manner that modifies the molecular structure."

Introduction

This bill aims to improve consumer safety by prohibiting synthetic cannabinoid additives in hemp products. However, an unintended consequence is also the blanket banning of numerous minor cannabinoids with promising health benefits backed by scientific research. As outlined below, compounds like THCV, CBDV, CBG, CBC, and CBN may serve important medical purposes and offer alternatives to CBD without psychoactivity. Banning them wholesale goes too far without nuance or exemptions, depriving consumers and patients of access to potentially beneficial cannabinoids simply because they occur naturally in only low concentrations.

Evidence for Therapeutic Potential of Proposed Banned Cannabinoids

- THCV: Known for its appetite suppressant effects, THCV has shown promise in pre-clinical models for increasing energy expenditure and reducing glucose intolerance, potentially supporting weight loss and metabolic health. Its

antagonistic effects on THC suggest it may offer therapeutic benefits without the risk of intoxication, relevant for conditions like impulse control and obsessive-compulsive disorders (Salami et al., 2020).

- CBDV: Demonstrating efficacy in raising seizure thresholds in animal models, CBDV is highlighted as a novel anticonvulsant, particularly for hard-to-treat forms of epilepsy. This aligns with the evidence that certain cannabinoids can be combined for optimal seizure reduction, necessitating the GPR55 receptor for the anticonvulsant effects of CBD (Roshni Kollipara et al., 2023).
- CBG: Research in the Journal of Cellular and Molecular Medicine indicates CBG's potential as a therapy for inflammatory bowel diseases like Crohn's and colitis, due to its interaction with endocannabinoid receptors regulating inflammation. Additionally, CBG has shown specific antiviral properties that could contribute to COVID-19 therapeutic development (Romano et al., 2014; Salami et al., 2020).
- CBC: CBC has been found to strongly suppress pain and swelling in animal models of inflammatory pain by enhancing anandamide signaling, establishing its potential as an anti-inflammatory and painkiller. Its ability to elevate mood-regulating endocannabinoids without causing sedation suggests rapid-onset antidepressant and anti-stress effects (Salami et al., 2020).
- CBN: In participant-blinded, placebo-controlled human trials, CBN improved sleep quality ratings for over 50% of individuals with sleep disturbances. Its notable antibacterial properties against antibiotic-resistant MRSA bacteria in skin wound infection models underline its potential as a novel treatment (Salami et al., 2020).

Naturally Occurring THC Isomers - THC Happens, in Nature, in many forms

Delta-9-tetrahydrocannabinol (THC) as the Primary Psychoactive Component:

- Delta-9-tetrahydrocannabinol (THC) is recognized as the primary psychoactive component of cannabis. A study comparing the pharmacokinetic and behavioral effects of inhaled THC versus intraperitoneal injection in female rats highlights the central role of Delta-9 THC in cannabis's psychoactive effects. This research contributes to understanding how Delta-9 THC's pharmacological properties translate into its psychoactive effects, underscoring its significance as the main psychoactive constituent in cannabis (Penman et al., 2023).

Δ8-Tetrahydrocannabinol (Δ8-THC) - A Naturally Occurring Minor Constituent:

- The presence of Δ8-THC as a minor naturally occurring isomer in cannabis was highlighted in the study by L. A. Ciolino et al., which identified multiple THC isomers in vaping liquids, including Δ8-THC, alongside the predominant Δ9-THC. This study underscores the diversity of THC isomers present in cannabis products (L. A. Ciolino et al., 2021).

Δ10-Tetrahydrocannabinol (Δ10-THC) - Identification and Characteristics:

- The identification and receptor binding characteristics of Δ10-THC isomers were discussed in the study by Mehdi Haghdoost et al. Although this study does not explicitly focus on the natural occurrence of Δ10-THC in cannabis, it provides valuable insights into this less common THC isomer (Mehdi Haghdoost et al., 2023).

Potential Direct Effects if LD1996 Passes

1. Lesser-known cannabinoids like CBG, CBC, and CBN have shown promising therapeutic potential in research studies for conditions from seizures to arthritis without causing intoxication. Banning them contradicts consumer health and wellness interests.
2. Compounds subject to an outright ban such as THCV do frequently occur naturally, albeit more minorly, in certain cannabis strains. Concentration methods are needed to unlock efficacy for disorders like uncontrolled appetite or OCD behaviors. This ban could deprive responsible access without cause.
3. Establishing cannabinoid concentration thresholds scaled to safety data enables low-risk access to cannabis' intricate pharmacopoeia, upholding choice and accountability together. Subjective cutoffs serve neither consumer nor industry. Proportional, evidence-based limits forestall dangers while nurturing innovation.
4. Not all definitions properly distinguish between enrichment of native cannabis compounds using selective physical techniques versus artificial addition of foreign lab-devised cannabinoids. Ambiguity around extractions from rare "hemp" strains further mires issues. Definitional rigor enables regulatory clarity.
5. Whether truly arising from limited natural biosynthesis or human manipulation of naturally abundant precursors, discrepancies like permissible delta-9-THC alongside prohibited delta-8-THC reveal inconsistencies in banning rationales

requiring redress.

6. Supply-side prohibition historically channels demand towards uncontrolled black market vectors rather than abating it, propagating risks including contaminated products, unsafe practices, and crime. We must learn from past policy failures.

Potential Unintended Consequences of Passing LD1996

1. Differentiating between natural and synthetic compound origins may demand sophisticated analytical testing beyond current infrastructure scalability, necessitating costly instrumentation investments. Combined with interpreting manifold novel regulatory requirements, disproportionate administrative and operational burdens could strain producers, especially smaller entities.
2. Codifying 0.5 milligram per package THC limits may heavily restrict the diversity of ingestible and inhalable products readily available to general consumers. Resultant market narrowing clouds legal supply channels while dwelling demand seeks fulfillment through unlawful alternatives, repeating public dangers of the opioid and ensuing vaping crises.
3. Mandating sweeping criminal history checks on workers irrespective of temporality or relevance risks denying livelihoods based on past unrelated misdeeds rather than present qualifications. Such lifetime consequences confronting those trying to build legitimate careers only drive recurrence of offenses and recidivism.
4. Micro enterprises lacking sizable capital reserves and integrated supply infrastructure may fold under the weight of freshly minted regulatory burdens stacked onto licensing, production, testing, and distribution processes. Market capture by deeper-pocketed corporations reduces overall industrial innovation alongside equitability.
5. Confining products to inherently occurring compounds with minute toxicology risk profiles can foster consumer trust, differentiating lawful offerings clearly from black market ones potentially contaminated with dangerous adulterants. Still, enforcement based on unrealistic testing standards or legal ambiguities introduces uncertainty undermining confidence.
6. Attempting to legislate away supply and demand grounded in wider social permissiveness instead breeds unauthorized networks Insufficiently regulated products then pose higher threats to individuals and communities than pragmatic standards-based oversight of existing commercial channels.
7. Constraints on established or investigational cannabinoids beyond predominant

ones stunt product development trajectories as researchers must either shift focus or continue work without commercialization pathways. This slows therapeutic pipeline outputs, depriving patients of timely access to prospectively beneficial medicines.

Conclusion & Policy Recommendations

There exists substantial and growing evidence that THCV, CBDV, CBG, CBC, CBN and other rare cannabinoids hold promise as specialized medicines and health supplements. However, due to only naturally low occurrence, they require concentration from raw extracts to provide therapeutic benefit. An overly broad ban on cannabinoid isomerization and synthesis would essentially prohibit these compounds without just cause.

I propose allowing cannabinoids present in any amount naturally in the cannabis plant, while regulating maximal concentrations based on safety data for final products.

Definitions should differentiate between enrichment of intrinsic compounds using physical methods like chromatography versus adding artificially devised cannabinoids. With refined policy language and practice standards, access can be preserved responsibly.

This bill, as written, is too broad without nuance or exemptions, banning beneficial minor cannabinoids and introducing issues that could be avoided with evidence-based concentration thresholds, definitional clarity, and responsible access allowances. Refinements are needed to align with consumer health interests.

Final Questions

If delta-9-THC legally acquired by a Maine consumer degrades through natural processes over time into other cannabinoids like delta-8-THC or CBN, does this chemical conversion via environmental factors like heat, air, and light count as "synthesis" of new cannabinoid compounds? Or is synthesis understood to mean artificial laboratory production of cannabinoids, while natural degradation causes changes without external intervention or introduction of novel reactants? Could prohibitions on compounds derived through natural degradation processes essentially restrict access to cannabinoids arising innately but in vanishingly small amounts if not concentrated or accumulated through degradation of more abundant precursors?

In summary:

- Does natural degradation over time count as "synthesis" or is that term reserved for artificial lab production?
- Do restrictions apply equally to rare cannabinoids arising from natural degradation pathways versus naturally occurring cannabinoids synthesized in a lab from due to low accumulation rates in *cannabis sativa L*?

References

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