To: Senate Judiciary Committee
From: Kalev Freeman M.D. Ph.D., Medical Director Vermont Patients Alliance
Date: January 20, 2016

Thank you for the opportunity to testify. I am an emergency physician and professor at the medical school, the Governor's physician appointee to the Vermont Alcohol and Drug Abuse Council, and medical director of the Vermont patience alliance non-profit medical cannabis dispensary in Montpelier. This testimony represents only my own opinions and not those of the University or any other entity.

My testimony will focus on *Cannabis* testing for public safety, and the best practices for analytic laboratories in Vermont. I was also asked to comment on the Health Impact Assessment

A. Review of Health Impact Assessment

First, I would like to commend the Health Department in its Health in All Policies approach. Health impact assessments (HIAs) are a strong tool in investigating the effects of policy and planning decisions on health outcomes, and making recommendations to optimize potential positive health impacts and mitigate potential negative health impacts. I appreciate having the opportunity to carefully review the HIA, entitled "Marijuana Regulation in Vermont", and furthermore, I appreciate the challenges inherent in producing such a document given the rapid and exponential increase in data that needs to be considered. I hope that I can provide some constructive feedback.

The HIA clearly represents a tremendous effort, and the committee has reviewed a large amount of data. While there is some valuable material here, the HIA unfortunately also has significant limitations. I would challenge specifically the section on page 39, "What might change in other substance use disorders and treatment if Vermont regulated and taxed marijuana?" The HIA authors suggest that "early and persistent use of marijuana is significantly related to both later cannabis dependence diagnosis and an increased risk of using other illicit drugs, including opioids" and provide two citations: Ferguson et al., 2015, Silins et al., 2014. I was surprised to read this because it is not consistent with the current literature. I'm a scientist, and I like to review original data whenever possible, so I sought out the references provided. One of these (Silins et al., 2014) is cited 5 additional times in the HIA; the source is not provided in the reference list but I was able to track it down. These references are both from a long-running study in Australia and New Zealand.

This lead me to look more closely at the references and citations. Unfortunately, the HIA lacks appropriate references and citations throughout; many of those provided are incorrect; and many recent citations from the US are ignored in favor of obscure reports from remote parts of the world. *Of particular concern, the "Executive Summary" on page 3 presents a table intended to serve as a "Literature Review" - with summary assessments of putative impacts of cannabis on specific health indicators – but it is presented without a single citation or reference.* This is confusing and completely out of the ordinary for academic work. When expert panels make consensus recommendations, the specific clinical trials, case reports, or other evidence used to weigh the "strength of the evidence", are carefully presented, reviewed and cited. Here, we see "very strong evidence" but have no way to find that evidence. If this HIA was an assignment for one of my medical students, it would receive an "incomplete" grade.

In more general terms, I would completely turn this HIA on its head, and suggest that we look at Cannabis regulation in VT from a completely different perspective – in the context of our opioid epidemic. We need to understand what is going on right here in VT and New England, and not in Australia.

Could Cannabis be part of the solution to Vermont's opioid epidemic? My primary suggestion is that the Dept of Health should completely revise the Health Impact Assessment of Cannabis regulation, taking into account the substitution effect on opioids, muscle relaxants and alcohol. The HIA as currently written does not adequately address the realities of Vermont's prescription and illicit drug problems.

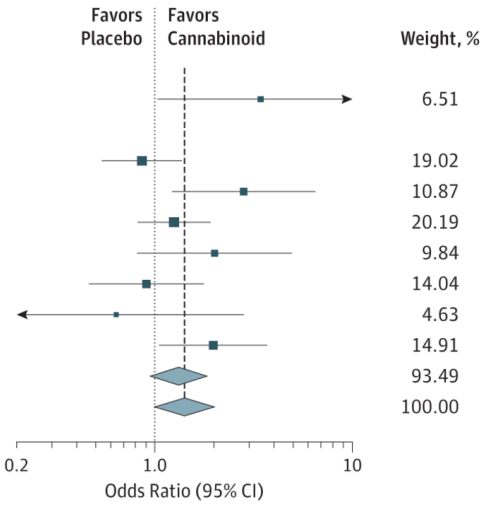
Vermont has an opportunity to take a new, different and progressive approach to the regulation of *Cannabis*. Look, we can all agree that the problem here in VT is not with *Cannabis*, but opioid and other prescription drug abuse. I think we all want to do the right thing - protect our youth and promote the public health. The Dept of Health should be jumping at *Cannabis* as a truly remarkable opportunity to address the opioid epidemic.

Imagine if we could cut the number of prescription pills for pain and muscle spasm in the homes and medicine cabinets of Vermonters, by 1/3 to 1/2. This could happen with a successful, progressive *Cannabis* experiment. The Health Impact Assessment of Cannabis regulation needs to take into account the situation in Vermont, and assess the public health impact of large-scale reduction in pain medications that might be achieved with a successful *Cannabis* program.

I would call on Vermonters to ask that their physicians offer medical marijuana as an alternative to opioids. To be clear, I am using the word opioid and not opiate, because the prescription pills are the source of the problem Every heroin addict I meet in the ER, tells me they became hooked on pills, first, before moving to heroin. We have to do something about getting these pills out of our system. The most common reason that doctors prescribe opioids is for pain control. We have more and more data showing that *Cannabis* is highly effective for pain. The most recent meta-analysis in JAMA showed that cannabinoids produce a 30% improvement in pain odds (Figure).

Figure. Cannabinoids Produce a 30% Improvement in Pain Odds. Recent review (*JAMA* 2015;313(24):2456-2473. doi:10.1001/jama.2015.6358.) identified 28 studies assessing chronic pain (63 reports, 2454 participants). One compared cannabinoids to amitriptyline; the others were all placebo controlled. Some studies were considered at high risk of bias. A meta-analysis of 8 trials (685 total participants, below) shows 30% or greater improvement in pain with cannabinoid compared with placebo, stratified according to cannabinoid. The square data markers indicate odds ratios (ORs) from primary studies, with sizes reflecting the statistical weight of the study using random-effects meta-analysis. The horizontal lines indicate 95% CIs. The blue diamond data markers represent the subtotal and overall OR and 95% CI. The vertical dashed line shows the summary effect estimate, the dotted shows the line of no effect (OR = 1).

Improvement in Pain With Cannabinoid vs Placebo by Study	Cannabinoid Events No.	Cannabinoid Events Total No.	Placebo Events No.	Placebo Events Total No.	Odds Ratio (95% CI)	Weight, %
Tetrahydrocannabinol (smoked)						
Abrams et al,[77] 2007	13	25	6	25	3.43 (1.03-11.48)	6.51
Nabiximols						
GW Pharmaceuticals,[22] 2005	54	149	59	148	0.86 (0.54-1.37)	19.02
Johnson et al,[69] 2010	23	53	12	56	2.81 (1.22-6.50)	10.87
Langford et al,[65] 2013	84	167	77	172	1.25 (0.81-1.91)	20.19
Nurmikko et al,[76] 2007	16	63	9	62	2.00 (0.81-4.96)	9.84
Portenoy et al,[67] 2012	22	90	24	91	0.90 (0.46-1.76)	14.04
Selvarajah et al,[70] 2010	8	15	9	14	0.63 (0.14-2.82)	4.63
Serpell et al,[88] 2014	34	123	19	117	1.97 (1.05-3.70)	14.91
Subtotal $I^2 = 44.5\%$, ($P = .0.94$)	241	660	209	660	1.32 (0.94-1.86)	93.49
Overall $I^2 = 47.6\%$, ($P = .0.64$)	254	685	215	685	1.41 (0.99-2.00)	100.00



Not only does *Cannabis* decrease opioid requirements, but also, it appears that patients are using it as a substitute for other more toxic, substances. I recently reviewed a medical survey of nearly 500 medical *Cannabis* patients in Maine, showing reported significant reductions in benzodiazepines and alcohol use, along with opioid reductions. There is another group in Iowa surveying dispensaries, focusing specifically on opioid reduction in patients over 60 years old. Elderly patients are finding significant reductions or even complete elimination of their need for opioid medications, with access to the Vermont medical *Cannabis* program. They feel better without the opioids – more energy, less constipation, and better sleep. And there have been zero overdoses. Imagine the health impact, if we could reduce pain pills and muscle relaxants in the medicine cabinets of patients over 60. Or, if we could cut ½ or 1/3 of the pills completely out of Vermont by substituting *Cannabis*.

If *Cannabis* is a safe and effective alternative to opioids for pain control, as the peer-reviewed medical literature strongly supports, then it seems that all conditions for which opioids are acceptable should be qualifying conditions for medical *Cannabis*. Even more, medical providers should be able to recommend marijuana to adult patients at their own discretion and not based on symptoms or qualify conditions determined by legislative action. A recent study in JAMA internal medicine showed that on a state-by-state basis, medical cannabis laws had a significant effect on decreasing opioid analgesic overdose mortality; this effect exceeded that of prescription drug monitoring programs or pharmacist ID laws (Table).

Table. Association Between Medical Cannabis Laws and State-Level Opioid Analgesic Overdose Mortality Rates in the United States, 1999-2010

	Percentage Difference in Age-Adjusted Opioid Analgesic Overdose Mortality in States With vs Without a Law		
	Primary Analysis	Secondary Analyses	
Independent Variable[a]	Estimate (95% CI)[b]	Estimate (95% CI)[c]	Estimate (95% CI)[d]
Medical cannabis law	−24.8 (−37.5 to −9.5)[e]	−31.0 (−42.2 to −17.6)[f]	−23.1 (−37.1 to −5.9)[e]
Prescription drug monitoring program	3.7 (−12.7 to 23.3)	3.5 (−13.4 to 23.7)	7.7 (−11.0 to 30.3)
Law requiring or allowing pharmacists to request patient identification	5.0 (−10.4 to 23.1)	4.1 (−11.4 to 22.5)	2.3 (−15.4 to 23.7)
Increased state oversight of pain management clinics	−7.6 (−19.1 to 5.6)	−11.7 (−20.7 to −1.7)[e]	−3.9 (−21.7 to 18.0)
Annual state unemployment rate[g]	4.4 (−0.3 to 9.3)	5.2 (0.1 to 10.6)[e]	2.5 (−2.3 to 7.5)

[a] All models adjusted for state and year (fixed effects).

[b] R^2 = 0.876.

[c] All intentional (suicide) overdose deaths were excluded from the dependent variable; opioid analgesic overdose mortality is therefore deaths that are unintentional or of undetermined intent. All covariates were the same as in the primary analysis; R^2 = 0.873.

[d] Findings include all heroin overdose deaths, even if no opioid analgesic was involved. All covariates were the same as in the primary analysis. R^2 = 0.842.

[e] $P \leq .05$.

[f] $P \leq .001$.

[g] An association was calculated for a 1-percentage-point increase in the state unemployment rate.

JAMA Intern Med. 2014;174(10):1668-1673. doi:10.1001/jamainternmed.2014.4005.

Unfortunately, we have not seen this effect in Vermont. One could argue that this is because Vermont has one of the most restrictive, tightly regulated, and smallest medical *Cannabis* programs in the US.

While many physicians remain steadfast against the sale of Cannabis as an intoxicant or for recreational use, perhaps we can come together and approach taxation and regulation of *Cannabis* from a Vermont perspective. We can take this unique opportunity to promote *Cannabis* as an organic, nutraceutical product, that is effective for pain. Increasing availability of high-quality medical *Cannabis* to adults, either through the medical program or through over-the-counter sales in pharmacies and health food stores, would likely cause a significant substitution effect in Vermont, reducing dependence and abuse of opioids, muscle relaxants and alcohol.

B. *Cannabis* testing for public safety – best practices for analytic laboratories in Vermont.

Working with Bia Diagnostics, an internationally recognized leader in food safety testing, we produced a white paper to define the best practices for analytical laboratories that perform testing of *Cannabis* and *Cannabis*-derived products intended for human consumption. Specifically, we address the following questions for regulators and policy makers interested in ensuring safety as the Vermont *Cannabis* industry evolves: How should *Cannabis* products be tested for public safety? How should the testing laboratories be regulated and accredited? What will it cost to do the recommended testing?

We provide specific recommendations that can serve as a roadmap for policy makers seeking direction in the uncharted territory of *Cannabis* in public health and safety considerations. We review the legal requirements for laboratory testing in 23 states and the District of Columbia, and provide details and references that support the following specific recommendations:

1. Testing for public safety. We recommend that Cannabis and Cannabis-derived products intended for human consumption, must be sampled, tested, and labeled prior to retail sale.
(a) Sampling. A licensed laboratory, medical dispensary, or third-party body must certify that the samples are representative of the lot or batch and were obtained according to standardized procedures.
(b) Testing. Laboratory testing must include measurement of potency and levels of contaminants by a laboratory operation accredited according to criteria for competence set by the International Organization for Standardization (ISO) 17025. All lots must be tested for potency; acceptance sampling of at least 10% of lots must be tested for contaminants.
(c) Labels. Consumer labels must at minimum list the potency of the primary active ingredients, delta-9 tetrahydracannabinoid (THC) and cannabidiol (CBD), as 95% confidence interval around the measured point estimate; they must also provide warning of the risk of exposure to children.

2. Laboratory Regulation. We recommend that laboratories must follow licensing, accreditation, and management protocols established by the State of Vermont.
(a) Laboratory operations that perform testing of Cannabis for public safety must be licensed by the State either as a medical marijuana dispensary or independent laboratory and must be accredited to the ISO 17025 standard; the assessment and accreditation process must be carried out by an International Laboratory Accreditation Cooperation (ILAC) third-party body that is itself accredited to the ISO 17011 standard.
(b) Laboratory operations must be housed in secure facilities fulfilling the same security requirements defined by the State for retail, production, and cultivation.
(c) Laboratories must be supervised by a qualified scientist with a PhD or equivalent industry experience (i.e., 3 or more years), in quantitative testing of Cannabis, agricultural, food, or pharmaceutical products.
(d) Laboratory operations may be associated with cultivators, producers, wholesalers, retail stores or medical dispensaries as long as they are licensed by the State and accredited to the ISO 17025 standard by an International Laboratory Accreditation Cooperation (ILAC) third-party body.

3. Financial considerations. Individuals will be willing to pay a premium for certified consumer-safe products, and that this premium will be equal or greater than the costs associated with quality control. To explore this hypothesis, we produced a financial model that calculates the total costs for a commercial cultivator or producer of Cannabis-based products to perform our recommended safety testing (See supplemental material). This model shows that - given the stated assumptions - the costs of testing for potency and quality range from less than 1% (i.e., 0.87%) of the total value of the product when the product is priced at $18/gram to 2.53% of the total value of the product when the product is priced at $5/gram. The recommended testing strategy would therefore add very little in cost to the producer.

4. Regulatory guidance. As the industry matures and scientific data accumulates, we recommend that regulatory guidelines should be revised. The State should establish a Cannabis Scientific Advisory Council to set thresholds for contaminants, make decisions on product recalls, and oversee the allocation of State funds for Cannabis research from sales tax revenues. Specifically, the Council should provide policy guidance in the creation and implementation of a Cannabis Science Research Grant Program to the Vermont State Colleges and Universities for scientific research on the basic science and clinical effects of Cannabis and its derivatives.

C. Conclusions

Vermont has an opportunity to take a new, different and progressive approach to the regulation of *Cannabis*. Look, we can all agree that the problem here in VT is not with *Cannabis*, but opioid and other prescription drug abuse. I think we all want to do the right thing - protect our youth and promote the public health. The Dept. of Health should be jumping at *Cannabis* as a truly remarkable opportunity to address the opioid epidemic.

Imagine if we could cut the number of prescription pills for pain and muscle spasm in the homes and medicine cabinets of Vermonters, by 1/3 to 1/2. This could happen with a successful, progressive *Cannabis* experiment. The Health Impact Assessment of Cannabis regulation needs to take into account the situation here in Vermont, and assess the public health impact of large-scale reduction in pain medications that might be achieved with a successful *Cannabis* program.

Cannabis should be legally available to adult Vermonters, but let's make it a nutraceutical product and not a recreational one. Vermont can lead the nation in *Cannabis* regulation, focused on the plant's use as a nutraceutical product that is available in licensed health food stores and pharmacies - not in smoking lounges and recreational bars that encourage intoxication. Products must be tested for quality and potency, and the State should allocate a portion of tax revenue obtained from sales, to medical and scientific research. Such a progressive, compassionate and rational approach to *Cannabis* regulation could benefit Vermonters, giving the next generation better and safer alternatives to current medications for pain, muscle spasm, and insomnia, thereby decreasing opioids and other frequently abused pharmaceuticals.