Comment on Proposed Regulation:
DPH-17-010E
Cannabis Manufacturing License
November 16, 2017

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November 28, 2017

Incorporating public health best practices from tobacco and alcohol regulation is necessary to protect public health by providing more information to consumers, restricting harmful formulations, and preventing abusive industry marketing tactics

GENERAL COMMENTS

Legalization of cannabis for medical and recreational use in California and other states represents a massive shift in the regulatory approach to the substance, even despite its continued illegality under federal law. Positive impacts of this change may include an end to enforcement practices that have disproportionately impacted many communities, particularly communities of color, as a result of criminalization. However, ***the creation and government endorsement of a legal cannabis industry that will span both medical and recreational use also presents risks that such an industry may seek to drive up demand, exploit abusive use to increase profit, and exert powerful influence over the regulatory environment as other industries have***

done, most notably tobacco [1], or that such other industries may seek to enter and dominate the new cannabis markets [2].

Evidence for cannabis's negative health effects (and medical efficacy) is underdeveloped, owing largely to longstanding barriers to research stemming from illegality [3, 4], but existing evidence supports a precautionary approach. Cannabis use is associated with development of substance use disorders [5, 6] and schizophrenia and other psychoses [4]. Cannabis smoking is associated with respiratory health harms [4], stroke [7], and cardiovascular disease [4, 7, 8], as well as secondhand smoke risks [9]. Cannabis and tobacco smoke share similar toxicity profiles [10], and California has identified cannabis smoke as a known human carcinogen since 2009 [11, 12].

Users may opt for manufactured cannabis products to avoid negative health effects associated with combustion [13, 14], but manufactured products also present risks. Some vaporized products (e.g., extracts and oils) are similar to e-cigarettes and sometimes use the same hardware [15], likely presenting similar risks, which for e-cigarettes include inhalation of ultrafine particles and chemical additives that can cause cardiovascular and pulmonary effects [16-19]. High-potency cannabis concentrates may increase risks for dependence, tolerance, and withdrawal [20], and heating these concentrates for inhalation ("dabbing," which can produce combustion at higher temperatures [21]) can release toxic chemicals including methacrolein and benzene [22]. Edibles can be unintentionally overconsumed by adults [23] and accidentally consumed by children [24].

California is the largest US medical cannabis market and will be the largest legal adult use market in the world, with the potential to influence national and global policy. It is critically important that the Department of Public Health model its cannabis regulations on best practices from established public health frameworks for regulating tobacco and alcohol [1, 25]. ***Public health objectives require that both cannabis markets be well controlled and designed to prevent diversion to illicit markets, abuse, increased prevalence, youth use, and the creation of a powerful industry that may encourage such outcomes using methods commonly employed by the tobacco and alcohol industries.***

Many elements of the proposed regulations are already consistent with public health best practices. This includes several elements which are likely to raise objections from the nascent cannabis industry but which are strongly grounded in evidence from tobacco and alcohol control models. These include:

- Implementing a sliding scale for licensure fees (§ 40150) to discourage dominance by larger and more powerful industry elements
- Requiring the use of a track and trace system (§ 40510 et seq.) to reduce diversion to illicit markets
- Prohibiting additives that increase potency or addictive potential (§ 40300) to moderate abuse risk
- Limiting THC content in manufactured products (§§ 40305, 40306) to reduce risks associated with accidental consumption and overconsumption
- Mandating labels and warnings with specific content (§§ 40408, 40410, 40412) that will counter the influence of abusive marketing practices.

Additionally, several proposed regulations include positive changes from earlier draft medical cannabis regulations that incorporate public health best practices. These include:

- Increasing license fees for the largest operators to discourage dominance by larger and more powerful industry elements (§ 40150(b))
- Clarifying the prohibition on caffeine as an additive with respect to naturally-occurring forms (§ 40300)
- Prohibiting products attractive to children or easily confused with non-cannabis foods, as well as products in the shape of humans, animals, insects, or fruit (§ 40300)
- Strengthening the prohibition on labels containing health-related statements that are not supported by evidence (§ 40410)
- Prohibiting persons tasked with cannabis enforcement from holding licenses (§ 40116).

The Department should maintain or strengthen these regulations even if industry and its allies object to them or seek to weaken them.

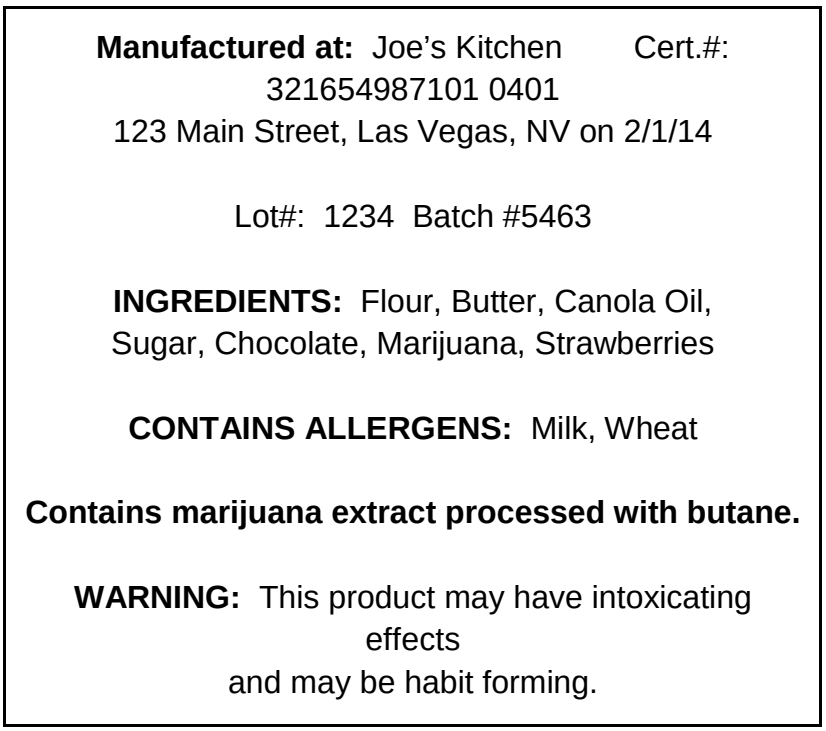
Building on these positive elements of the proposed regulations, the following specific changes are needed to ensure that the proposed regulations are fully consistent with evidence-based best practices from tobacco and alcohol control in order to create a well-regulated legal market for cannabis in California that will minimize adverse effects on the health of Californians.

SPECIFIC RECOMMENDATIONS

1. Increase visibility of warning labels (§§ 40405, 40408)

The proposed regulations (§ 40405) require a primary panel label and a separate informational panel label that includes mandatory warnings (§ 40408), both with a miniscule minimum 6-point font. The size, prominence, position, and design of health warning labels influence their impact on risk perceptions [26, 27]. Tobacco health warnings that cover at least 30% and ideally 50% or more of the package's principal display area, as required under the WHO Framework Convention on Tobacco Control (FCTC) [28] are associated with higher health knowledge and motivation to quit [26, 27]. Increasing label size also improves effectiveness among youth [29]. Some countries' tobacco warnings occupy up to 90% of the package [30], and the tobacco industry has intensely opposed larger and more effective warnings [31]. The proposed regulations' standard is vulnerable to industry manipulation. **Requiring warnings on the primary panel and covering a minimum 30% (ideally 50%) of the principal display area would eliminate ambiguity and likely produce gains in health knowledge and warning effectiveness.**

The proposed minimum 6-point font is consistent with Oregon [32], but considerably smaller than Nevada [33], which requires front and rear labels with minimum 12-point font. A 6-point font is challenging to read, as illustrated in the comparison below:



Manufactured at: Joe's Kitchen Cert.#: 321654987101 0401
123 Main Street, Las Vegas, NV on 2/1/14

Lot#: 1234 Batch #5463

INGREDIENTS: Flour, Butter, Canola Oil,
Sugar, Chocolate, Marijuana, Strawberries

CONTAINS ALLERGENS: Milk, Wheat

Contains marijuana extract processed with butane.

WARNING: This product may have intoxicating effects
and may be habit forming.

A 6-point font standard is also smaller than the approximately 10-point font a 2017 cannabis industry white paper suggests [34]. **Requiring minimum 12-point font would be consistent with FDA's requirements for most tobacco warnings [35] and ensure cannabis warnings are readable and salient**, paralleling the FCTC's requirement that tobacco health warnings to be "large, clear, visible and legible" [28]. A larger warning label would also permit a larger, more prominent font size.

2. Include rotating health warnings and pictorial warnings (§ 40408)

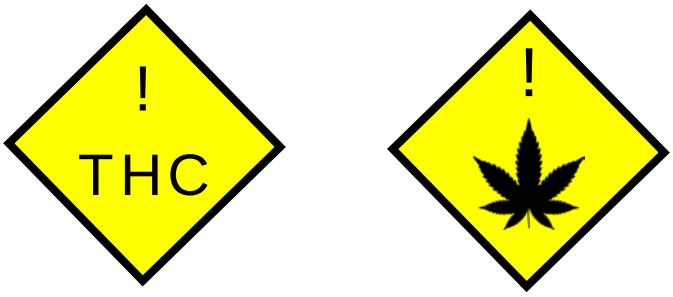
The proposed regulations (§ 40408) mandate textual warnings of hazards for children and animals, use while pregnant or breastfeeding, delayed intoxication, and impaired driving. Tobacco warning labels are more effective when changed periodically. To better educate consumers and reduce perceptions of harmlessness, cannabis labels should include comprehensive and rotating health warnings consistent with current risk information, including secondhand exposure [9], chemical additives [17, 18], dependence [20, 36], cardiovascular disease [9, 36-38], respiratory disease [39], neurological disease [40], and cancer [11, 12] based on product type.

Text-only labels, as currently used for tobacco in the US, are poorly recalled and have low impact on use [41]. **Pictorial health warnings are more impactful and informative [28, 42, 43] and decrease product attractiveness to youth [29, 44]. Pictorial warnings are also more likely to be seen by low-literacy adults and children and to reach those who cannot read the language used for text [27].** Based on their effectiveness for tobacco, pictorial warnings are likely to improve the impact and effectiveness of cannabis warning labels.

3. Adopt a highly visible and salient cannabis product symbol (§ 40412)

The proposed regulations (§ 40412(a)) require a warning symbol denoting the presence of cannabis. Tobacco companies' research on packaging color and consumer perceptions indicates that black is most visually prominent, particularly black text on a lighter background [45]. The color required under the proposed regulations appears to

be black text on white background based on the document available on the Department's website. Yellow is more effective for quickly gaining and keeping attention, is perceived as less attractive, and signals a warning, especially paired with black text as in road sign warnings [45]. **A warning symbol using black text and yellow background that emulates road warning style and shape [46], as in two options illustrated below, would more effectively attract and maintain consumer attention.**



The proposed regulations (§ 40412(b)) require the symbol be at least ½ inch by ½ inch and "printed legibly and conspicuously." Likely packaging variation among cannabis products supports also mandating coverage of a minimum percentage of the product's primary panel to prevent companies from using large package size, colors, or other markings to render the symbol ineffective. **The symbol should be incorporated into warnings covering at least 30% and ideally more than 50% of the principal display area.**

4. Require plain packaging (§ 40415)

The proposed regulations (§ 40415) require cannabis product packaging to be tamper-evident, child-resistant, opaque (for edibles), and re-sealable (for multi-serving products), but do not restrict colors, logos, or branding. Tobacco companies use packaging as a marketing tool to bypass other marketing restrictions [47], establishing brand identification among youth, young adults, and other target populations [48]. The youth marketing effect of package branding is powerful at in-store displays [49], but extends beyond retailers. **For example, when an adult purchases a product, children at home will likely see the branded package.** For tobacco, WHO recommends [28] fully standardized "plain packaging" free of logos, colors, and branding, allowing only plain text brand and variant information in specified size, font, and position [47, 50, 51].

Plain cigarette packaging is associated with reduced brand awareness and identification [52] and reduced appeal of cigarettes to adolescents and young adults [53-

56]. Plain packaging also makes health warnings more noticeable and effective [26, 57, 58] and reduces the impact of misleading branding on beliefs about harmfulness [56, 58]. Combining plain packaging and large graphic labels extends the reach and impact of public health media campaigns [59] and diminishes tobacco's appeal to adolescents by increasing attention and perceptions of harm and reducing social appeal [44].

Cannabis plain packaging examples are limited. Oregon permits cannabis companies using generic packaging and labels to bypass the state's label preapproval process and fee [60, 61]. Uruguay prohibits the two private companies supplying cannabis to the recreational market from including company labels on packaging [62]. **Mandatory plain packaging would eliminate a promotional avenue used routinely by the tobacco industry, with likely positive impacts on cannabis use and perceptions of harmfulness.**

5. Broaden packaging restrictions to eliminate appeals to children and imitation of other non-cannabis products (§§ 40410, 40415)

The proposed regulations (§ 40410(c)) prohibit packaging with cartoons, "images, characters, or phrases that are popularly used to advertise to children," or "imitation of candy packaging or labeling." However, elements not "popularly used to advertise to children" often remain appealing to children and teens, including themes of glamour, beauty, sex, or adventure. A broader prohibition on such elements is necessary to prevent industry targeting of youth, but still invites subjectivity as to what constitutes glamour, for example. The current proposed prohibition on the imitation of "candy" packaging in § 40410(c) and "products typically marketed to children" in § 40415 do not account for the wide variety of products that may be attractive to children. For example, the proposed language would not prohibit imitation of common snack foods that children would frequently encounter that are marketed to adults (e.g., granola bars). A complete prohibition on the imitation of all non-cannabis products would more effectively reduce the risk of accidental consumption. **Adoption of a plain packaging standard avoids interpretive problems and undermines the opportunity to use packaging to mislead consumers and unlawfully market to youth.**

6. Prohibit the addition of menthol and other characterizing flavors in non-topical and non-edible products (§ 40300)

The proposed regulations (§ 40300(b)) prohibit additives that "increase potency, toxicity or addictive potential." In tobacco products, menthol is more than a flavoring agent. Menthol affects nicotine dependence through behavioral reinforcement [63] and encouragement of breath holding, which increases nicotine exposure [64]. Stimulated by industry marketing, younger and newer smokers disproportionately use menthol

cigarettes, drawn to the reduced harshness menthol contributes as a local anesthetic [26, 65]. Menthol contributes to the inequitable tobacco burden on the health of African-American smokers, who disproportionately smoke menthol cigarettes and have higher rates of tobacco-related diseases despite smoking fewer cigarettes per day and initiating smoking later [66, 67]. Menthol use is more common among groups targeted by the tobacco industry, including youth of color, women, and LGBTQ populations [68]. Menthol smokers, especially persons of color and younger smokers, also experience more difficulty quitting [69].

Menthol cigarette smokers are more likely than non-menthol smokers to report past 30-day cannabis use [70]. Dual use of menthol cigarettes and cannabis also increased from 2005-2014 [71]. Manufactured cannabis products incorporating menthol are already available [72]. Menthol's sensory effects potentially contribute similar behavioral reinforcement for cannabis use as for tobacco use, and menthol likely produces similar anesthetizing and cooling effects for inhaled cannabis products as for tobacco. **Menthol's links to nicotine addiction and health inequities and its existing associations with cannabis use support a cautious policy prohibiting menthol in non-topical cannabis products to prevent repetition of harms attributable to mentholated tobacco products.**

Beyond menthol, a broad prohibition on characterizing flavors in nonedible products is necessary to deter youth use. Flavored products are a key tool for attracting young smokers to tobacco [26, 73, 74] and e-cigarettes [75, 76]. Most adolescent tobacco and e-cigarette users currently use and initiated with flavored products [77]. Disguising unpleasant tastes with flavors to attract young users is a tobacco industry strategy that could easily repeat for manufactured cannabis products absent strong regulations. The FDA's 2009 ban on cigarettes with characterizing flavors (authorized by the Family Smoking Prevention and Tobacco Control Act) was followed by a decrease in adolescent tobacco use and substantial reductions in the probability of being a cigarette smoker and in cigarettes smoked among adolescents [78]. Because the final 2009 ban controversially failed to include menthol cigarettes or flavored non-cigarette tobacco, increased use of cigars, pipes, and menthol cigarettes limited the impact on adolescent tobacco use.

Cannabis regulations should prevent similar effects by prohibiting characterizing flavors in nonedible products. Flavored edible products present similar concerns that require further research on how they may impact use and initiation. While some patients prefer flavored products, any therapeutic effect is likely unrelated to flavorings, and alternative formulations (e.g., tinctures) are available.

7. Set lower THC limits for inhaled products and products likely to be accidentally consumed (§ 40306)

The proposed regulations (§ 40306) limit nonedible manufactured medical cannabis products to 2000 mg THC per package and adult use products to 1000 mg per package, both far higher than the 100 mg permitted for edibles (§ 40305). In the Initial Statement of Reasons for earlier draft medical cannabis regulations, the Department noted that that "capsules, tinctures, and topicals" are "more traditional medical delivery mechanisms" [79, p. 102]; however, nonedible products is a broad category that includes highly potent concentrates that can be heated and quickly inhaled [80], providing the THC equivalent of several joints in one breath [81]. Such products potentially present increased dependence risks [20] and have been linked to psychosis in case reports [82].

Other inhalable manufactured products in the "nonedible" category that are less concentrated or consumed more slowly also present potential risks. Vaporizing liquid extracts, for example, causes inhalation of ultrafine particles, which present cardiovascular and respiratory risks in e-cigarettes [16-19] and likely have similar risks for vaporized cannabis products. **Inhaled cannabis products present specific risks distinct from other forms of consumption, and the Department should reduce allowable THC content of these products relative to forms such as capsules and tinctures.** A 100 mg THC per unit limit on all inhaled manufactured cannabis products (matching that for edibles) would better protect public health and denormalization of smoking behavior.

Edible products present clear accidental consumption risks due to similarity to non-cannabis products and were responsible for approximately half of pediatric cannabis exposures in a two-year Colorado study [24]. **Nonedible products also present accidental consumption risks.** Non-cannabis topical products account for 5.3% of pediatric exposure calls to poison centers nationally [83], and cannabis-infused products add additional risks, especially those resembling products children commonly encounter, such as lotions [84]. While most cannabis topicals are not psychoactive when used as directed (because few cannabinoids reach the brain via this pathway), accidental ingestion remains concerning. Many concentrates and extracts also resemble food (e.g., honey [85]) or trade on food-like flavors or aromas (e.g., "Pineapple Dream Concentrate" [86]). Harmful pediatric exposures to e-cigarette and nicotine liquids are increasingly frequent [87], and similar preparations of cannabis extracts could present related risks. Therefore, **we recommend extending the 100 mg THC per package limit for edibles to nonedible manufactured medical cannabis**

products with significant accidental consumption risks, including concentrates, extracts, and topicals.

CONCLUSION

The science surrounding the potential harms and benefits of medical cannabis is evolving, but known risks of dependence, cardiovascular and pulmonary disease, and other concerns justify a precautionary approach. The Department's proposed regulations reflect many public health best practices, but fall short in other areas. Incorporating additional best practices from tobacco and alcohol control to improve the size and clarity of labels, restrict on-package marketing, limit total THC content, and prevent the addition of additives that increase risks of addiction and youth use will ensure a functional and well-regulated cannabis system that prioritizes protection of public health over business interests in the State of California.

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