Scientific Data and Information About Products Containing Cannabis or Cannabis-Derived Compounds; Public Hearing; Request for Comments
Docket No. FDA-2019-N-1482

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We were pleased to learn about the FDA's diligence in addressing the safety of cannabis and cannabis-derived products, including by providing this opportunity for public comment. While we recognize that the FDA is seeking comments on scientific data and information regarding the safety, manufacturing, product quality, marketing, labeling, and sale of products containing cannabis or cannabis-derived compounds, we respectfully submit the following comments based on research we and our colleagues at UCSF have done pertaining to the need for clarification about regulatory requirements that apply to research as well as prompting FDA considering its role in the broader regulation of cannabis products and their marketing and promotion.

Reversing past decisions to regulate cannabis modeled on alcohol policies will likely become increasingly difficult once these processes are set in motion and a dominant policy framework and trajectory becomes established. **Designing future federal cannabis regulations to prioritize public health over business is an important policy decision that is necessary to develop and implement regulation of legal cannabis in a way that protects health.**[1]

Use of CBD Products in FDA-Regulated Research

CBD as a compound extracted from marijuana is currently classified as a Schedule I controlled substance by the Drug Enforcement Administration (DEA). Epidiolex, which is an FDA-approved drug that contains CBD derived from marijuana, is a Schedule V drug. However, when derived from hemp, CBD is no longer a scheduled substance pursuant to the 2018 Farm Bill. The FDA asserts that cannabis and cannabis-derived products are subject to the same authorities and requirements as FDA-regulated products containing any other substance, regardless of whether the products fall within the definition of 'hemp' under the 2018 Farm Bill.[2] **The FDA should further elaborate on and clarify its role in regulating research with hemp and hemp-derived products.**

Source of Hemp and Hemp-Derived Products for Research Use

As indicated in the Federal Register notice, the FDA is focused on how to better regulate food, drugs, and supplements, yet it is not clear where the FDA stands with respect to researchers'

[1] Barry RA, Glantz SA. Marijuana Regulatory Frameworks in Four US States: An Analysis Against a Public Health Standard. *American journal of public health.* 2018;108(7):914-923.
FDA Regulation of Cannabis and Cannabis-Derived Products: Questions and Answers, posted on FDA's website (https://www.fda.gov/news-events/public-health-focus/fda-regulation-cannabis-and-cannabis-derived-products-questions-and-answers), content current as of 4/20/2019.

ability to obtain hemp and hemp-derived products, including CBD, to (1) evaluate such products and their claims; and (2) conduct other types of research.

While the FDA makes clear that clinical research using marijuana involves "obtaining the marijuana for research from the National Institute on Drug Abuse (NIDA) within the National Institutes of Health or another Drug Enforcement Administration (DEA)-registered source,"[3] and while we recognize that clinical research requires filing of an Investigational New Drug (IND) application, **it is unclear what the FDA' position is regarding permissible sources from which researchers may obtain hemp and hemp-derived product for research use.**

FDA guidance addressing questions related to CBD states that it is not legal to sell a food, including animal feed, or an unapproved new drug, in interstate commerce.[4] The FDA seems to favor the position that researchers obtaining hemp products through interstate commerce violate its guidance. **This position ignores the fact that researchers can make important contributions to public knowledge and public health by conducting research and testing involving such products.**

Limiting the ability of researchers to obtain via interstate commerce hemp and products containing hemp-derived CBD, which are no longer defined as controlled substances, will impede important research. This would be problematic for researchers who already have strict limitations that do not allow for the use of routinely available cannabis and cannabis-derived compounds for use in research. **The FDA should permit researchers to obtain products containing hemp-derived CBD from a variety of sources, including via interstate commerce.**

Inability to Study Cannabis from All Available Sources, Including Products that Are Actually Being Consumed

Researchers are unable to study cannabis that is comparable in potency to what is currently available to the general public in states that have passed medical and recreational cannabis laws. Such a restriction hinders scientific understanding of cannabis use and its effects as it is actually used by people in the USA. Efforts should be made to expand the sources of cannabis that can be studied, allowing researchers to conduct research on cannabis that is in actual "real world" use (such as cannabis that is routinely available from dispensaries and retail outlets operating in states that have legalized certain cannabis use and sales), including research with the use of non-intoxicating cannabis extracts like CBD that are obtained from a variety of cannabis sources and sold at non-NIDA facilities.

Not only are clinicians and other members of the scientific and medical communities unable to study cannabis products that are routinely available in local retail shops and online, they are even barred from possessing samples to analyze for its constituents. This creates a problem because in some studies human subjects are permitted to come to

[3] https://www.fda.gov/news-events/public-health-focus/marijuana-research-human-subjects

[4]FDA Regulation of Cannabis and Cannabis-Derived Products: Questions and Answers, posted on FDA's website (https://www.fda.gov/news-events/public-health-focus/fda-regulation-cannabis-and-cannabis-derived-products-questions-and-answers), content current as of 4/20/2019.

research laboratories and use their own products for the purpose of the study; though scholars are allowed to collect blood and urine samples from subjects, they are paradoxically prohibited from analyzing the products that the participants are using.

For example, a UCSF laboratory is doing analytical chemistry work on NIDA marijuana products, is not allowed to possess even for chemical analysis any cannabis product without DEA approval, and DEA will approve only NIDA sourced cannabis. Others doing similar research have had to ask their research participants to deliver their personal products to a commercial laboratory, which in turn did cannabinoid assays and sent the results back to the academic researcher. This is a ridiculous way to do science.

As an example, UCSF researchers are very interested in the health effects of terpenes, which are present in high concentrations in marijuana smoke and in cannabis liquids that are vaped. They can measure terpene levels in urine of users, but cannot test their products to correlate urine levels with product levels. Thus, it is impossible to provide information that FDA could use as a basis to regulate products for potential toxicant exposure.

The FDA should indicate its support for expansion of the sources of cannabis available to researchers, as increased research on the health effects of the types of cannabis products that are in "real world" use would support the overall FDA mission of protecting public health.

The FDA, Working with Other Appropriate Agencies, Should De-Schedule or Re-Schedule Cannabis

Rapid commercialization is outpacing state and federal regulatory rulemaking, with myriad permutations of novel and traditional cannabis products quickly becoming available to the public in spite of cannabis' Schedule I status. Descheduling or rescheduling would allow research to be performed more efficiently and on a wider array of cannabis products that are actually in the market, so that claims regarding risks and benefits could be fully vetted by the scientific community, the FDA, and the states. While the Farm Bill legalized hemp, Congress explicitly reserved the FDA's authority and jurisdiction to regulate all cannabis broadly, under its food and drug authorities.[31] **The expansion of state legalization of medical and adult-use cannabis has bypassed the federal regulatory scheduling structure, making it more important for health advocates to press the federal government to reverse or modify cannabis' Schedule I designation and facilitate needed research and product regulation, particularly for therapeutic claims.**

Federal action to reschedule cannabis in a way that facilitates research on health and therapeutic effects is urgently needed to provide accurate evidence that will allow public health authorities, regulators, policy makers, and health professionals to respond to questions from their patients and their families regarding cannabis.

Streamlining Federal Approvals for Cannabis Research

The pathways for conducting cannabis research are complex and involve numerous federal agencies. **Federal agencies involved in granting approvals for cannabis research - including the FDA, DEA, and NIDA - should streamline the process and enhance research opportunities.**

To that end, anything the FDA can do to partner with other federal agencies to ease barriers to research would be of significant value.

Cannabis has shown evidence of a therapeutic value for a several conditions, but restrictions in access have hindered the conduct of rigorous clinical research needed to adequately define what conditions respond to cannabis, what components of cannabis account for these beneficial effects, and what the appropriate dosing regimen is. As a result, individuals are currently using cannabis and cannabis-derived products to manage medical conditions in ways that may not be supported by the evidence or without the informed recommendations of their healthcare providers. **Given the increasing need for scientific knowledge about cannabis and its potential medicinal or therapeutic effects, researchers are eager to conduct research that addresses the key priorities noted in the 2017 National Academies report, "The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research,"[5] removing barriers to conducting this research is critical to answering the specific questions posed by the FDA in its request for comments.**

Bidirectional Gateway Effect between Cannabis and Tobacco among Youth

As social norms have shifted toward acceptance of cannabis use, highlighting potential synergy between the tobacco and cannabis. While high school student cigarette smoking declined (from 20.0% 30 day prevalence in 2007 to 8.8% in 2017), cannabis use remained stable (19.7% vs. 19.8%).[6] The historic patterns of tobacco serving as a gateway to cannabis is reversing, with adolescent cannabis often now preceding tobacco use. Weekly cannabis use among teen non-tobacco smokers is associated with increases in subsequent tobacco initiation (OR = 8.3; 95% CI 1.9-3.6) and 21-year old daily cannabis smokers that were not nicotine dependent (based on the Fagerström Test for Nicotine Dependence) have triple the odds of developing nicotine dependence by age 24 compared with non-nicotine dependent cannabis nonusers.[7] These findings are consistent with the tobacco companies' early understanding that cannabinoids and nicotine could be complementary products.[8]

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[5] National Academies. 2017. The Health Effects of Cannabisand Cannabinoids: The Current State of Evidence and Recommendations for Research. Washington, DC: The National Academies Press.
[6] Centers for Disease Control. High School Youth Risk Behavior Surveillance System 2017; https://nccd.cdc.gov/Youthonline/App/Default.aspx. Accessed September 20, 2018.
[7] Patton GC, Coffey C, Carlin JB, Sawyer SM, Lynskey M. Reverse gateways? Frequent cannabis use as a predictor of tobacco initiation and nicotine dependence. *Addiction (Abingdon, England).* 2005;100(10):1518-1525.
[8] Barry RA, Hiilamo H, Glantz SA. Waiting for the opportune moment: the tobacco industry and marijuana legalization. The Milbank quarterly. 2014;92(2):207-242.

FDA should regulate cannabis in such a manner in a manner that prevents unvetted health claims in the media

The Media's Role in Changing Perceptions of Risk[9]

The public relies on popular media for health information about cannabis.[10] Halverson et al assessed the accuracy of reporting on health effects of cannabis use in *GreenState*, a specialty publication on cannabis published by the San Francisco Chronicle and the main newspaper using the Index of Scientific Quality for Health Related News Reports.[11] Seventeen *GreenState* articles and four San Francisco Chronicle articles were identified for analysis. Health articles in *GreenState* scored 2.9 (±1.1 [SD]) Global, with the highest scoring category Applicability (4.5 ± 0.4) and the lowest Precision (2.4 ± 1.0) on a scale of 1–5. In contrast, the San Francisco Chronicle articles received a Global rating of 4.6 (±0.2), ranging from Applicability (5.0 ± 0) to Benefits (3.8 ± 0.9). Articles in the San Francisco Chronicle scored significantly higher in all categories but Benefits which was not significantly different for the *San Francisco Chronicle* compared with *GreenState* (3.8 vs. 3.6, p = 0.77). **The public, clinicians, and policymakers need to be aware of this pattern and treat information in specialty cannabis publications like *GreenState* with an appropriate level of skepticism until the quality of reporting improves to general journalistic standards.**

The perception of "great risk" from weekly cannabis use dropped from about 50% in 2002 to about 34% in 2014.[12, 13] In 2017, 81% of US adults believed cannabis had at least one medical benefit, most commonly pain management (66%), followed by treatment of epilepsy and multiple sclerosis (48%), and relief from anxiety, stress, and depression (47%), with 29.2% agreeing that smoking marijuana prevents health problems.[14] Eighteen percent believed exposure to secondhand cannabis smoke is somewhat or completely safe for adults, 8% indicated it was somewhat or completely safe for children, and 7% agreed that marijuana use is somewhat or completely safe during pregnancy. Consistent with these changing perceptions, cannabis use among US adults more than doubled between 2001 and 2013.[15] Despite increased legalization and use, conclusive evidence regarding the health effects of cannabis remains limited. **Because more Americans are using cannabis and legalization is influenced by popular media, it is**

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[9] *Id.*

[10] Ryan T. Halvorson, Christopher C. Stewart, Aishwarya Thakur & Stanton A. Glantz (2018): Scientific Quality of Health-Related Articles in Specialty Cannabis and General Newspapers in San Francisco, Journal of Health Communication, DOI: 10.1080/10810730.2018.1534906

[11] *Id.*

[12] Azofeifa, A., Mattson, M. E., Schauer, G., McAfee, T., Grant, A., &Lyerla, R. (2016). National estimates of marijuana use and related indicators - national survey on drug use and health, United States,2002-2014. MMWR Surveill Summ, 65(11), 1–28. doi:10.15585/mmwr.ss6511a1

[13] Compton, W. M., Han, B., Jones, C. M., Blanco, C., & Hughes, A. (2016).Marijuana use and use disorders in adults in the USA, 2002-14: Analysis of annual cross-sectional surveys. Lancet Psychiatry, 3, 954–964. doi:10.1016/S2215-0366(16)30208-5

[14] Keyhani, S., Steigerwald, S., Ishida, J., Vali, M., Cerda, M., Hasin, D., . . Cohen, B. E. (2018). Risks and benefits of marijuana use: A national survey of U.S. Adults. Annals International Medica. doi:10.7326/m18-0810

[15] Hasin, D. S., Saha, T. D., Kerridge, B. T., Goldstein, R. B., Chou, S. P.,Zhang, H., . . . Grant, B. F. (2015). Prevalence of marijuana usedisorders in the United States Between 2001-2002 and 2012-2013. JAMA Psychiatry, 72(12), 1235–1242. doi:10.1001/jamapsychiatry.2015.1858

important for the FDA to facilitate research so that people will be able to obtain reliable information about the health effects of cannabis.

In particular, most patients overestimate benefits and underestimate harm of medical treatments.[16] **For this reason, the FDA should assume jurisdiction and create regulations that prohibit the use of unvetted, anecdotal health claims regarding cannabis products that have played a role in shifting public opinion toward normalization.**

Demand Reduction Policies

Advertising and marketing

The alcohol and tobacco industries promote ineffective self-regulation through voluntary codes to avoid effective legal restrictions. In particular, the US alcohol industry's voluntary advertising code commits companies not to advertise in outlets (i.e., print, television, radio, and the Internet) in which more than 30% (roughly the proportion of the population aged 2 to 20 years) of the audience is "reasonably" expected to be aged younger than 21 years. In 2013, the Colorado Department of Revenue codified the alcohol industry's voluntary code into its regulations for marijuana marketing, permitting advertising and marketing, including event sponsorship (e.g., sporting events and concerts) at which less than 30% of the audience is aged younger than 21 years. Consistent with public health best practices, in 2016, the Oregon Retail Marijuana Scientific Advisory Committee (formed by the Oregon Public Health Division) recommended that regulators broaden marketing restrictions to include sports and other sponsorships. [17,18] The Committee also recommended using an audience threshold for minors of less than 15% (the fraction of the US adolescent population) for all marketing to avoid "programming for the general population [reaching] most teens." Despite this recommendation, the Oregon Liquor Control Commission adopted the same marketing regulations as Colorado.

Instead of deferring to voluntary self-policing policies regarding the marketing and advertising of cannabis determined by the cannabis industry, the FDA should impose restrictions on the messaging the cannabis industry may use when creating new products for consumption.

Packaging and warning labels

In 2016, Colorado, Washington, and Oregon passed laws requiring marijuana companies to include a THC warning symbol on the principal display area of a marijuana product package to indicate that the product contained marijuana. As of December 2017, none of the states required

[16] Hoffmann, T. C., & Del Mar, C. (2015). Patients' expectations of the benefits and harms of treatments, screening, and tests: A systematic review. JAMA International Medicine, 175(2), 274–286. doi:10.1001/jamainternmed.2014.6016

[17] Marijuana Enforcement Division, Colorado Department of Revenue. Permanent rules related to the Colorado Retail Marijuana Code 1 CCR 212-2. 2013. Available at: https://www. colorado.gov/pacific/sites/default/files/ Retail%20Marijuana%20Rules,% 20Adopted%20090913,%20Effective%20101513%5B1%5D_0.pdf. Accessed August 25, 2017.

[18] State of Oregon. Oregon HB 3400.2016. Available at https://www.oregonlegislature.gov/bills_laws/ors/ors475B.html. Accessed August 25, 2017.

pictorial warnings or standardized packaging based on international tobacco health warning label best practice to deter use.[19] The Oregon Public Health Division developed rules for marijuana labeling and warning labels, providing an opportunity to propose alternative policies to those adopted in Colorado and Washington, where state liquor control boards developed labeling rules. Although all 4 states prohibit marijuana companies from making false or misleading claims on marijuana packages, only Oregon requires health claims to be

> . . . supported by the totality of publicly available scientific evidence (including evidence from well-designed studies conducted in a manner which is consistent with generally recognized scientific procedures and principles), and for which there is significant scientific agreement, among experts qualified by scientific training and experience to evaluate such claims.[20]

In addition to false or misleading health claims, the Oregon labeling law specifically prohibits labels that are "attractive to minors," including

> . . . cartoons, designs, brands, or names resembling non-cannabis products typically marketed to minors, symbols or celebrities used to market products to minors, images of minors, and words that refer to products commonly associate with or marketed by minors.[21]

Colorado, Washington, and Alaska use vague health risk statements, age restriction (i.e., legal for those aged 21 years and older), risks to pregnant women, risks of driving under the influence, and activation time for marijuana edibles. **These state-level warnings are modeled on the alcohol industry's voluntary code, which current research suggests is not effective in preventing problematic alcohol use.**

The National Institutes of Health recommends health warnings be no more than 10 to 15 words long and use language at a sixth-grade reading level or lower to ensure readability across a wide array of socioeconomic backgrounds. Only Oregon designed warning statements suitable for low-literacy children and adults. None of the states require health message content to rotate or be regularly updated as new scientific evidence becomes available to prevent "burn out" of outdated warning labels.

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[19] Rachel A. Barry and Stanton A. Glantz, 2018: Marijuana Regulatory Frameworks in Four US States: An Analysis Against a Public Health Standard. American Journal of Public Health 108, 914_923, https://doi.org/10.2105/AJPH.2018.304401

[20] Secretary of State. Oregon Health Authority. Public Health Division - Chapter 333, Division 7, Section 333-007-0090 General Label Requirements; Prohibitions; Exceptions. Available at: https://secure.sos.state.or.us/oard/viewSingleRule.action;JSESSIONID_OARD=vDpvX2QcO DGZnimDKDiPekqoxRqRGmgMFeUvqKdeTJKg2RMtBgX!-1740555568?ruleVrsnRsn=52229. Accessed May 17, 2018. Google Scholar

[21] Secretary of State. Oregon Health Authority. Public Health Division - Chapter 333, Division 7, Section 333-007-0090 General Label Requirements; Prohibitions; Exceptions. Available at: https://secure.sos.state.or.us/oard/viewSingleRule.action;JSESSIONID_OARD=vDpvX2QcO DGZnimDKDiPekqoxRqRGmgMFeUvqKdeTJKg2RMtBgX!-1740555568?ruleVrsnRsn=52229. Accessed May 17, 2018.

To follow public health best practices when regulating cannabis or cannabis-derivatives, the FDA should require health message content to rotate or be regularly updated as new scientific evidence becomes available to prevent "burn out" of outdated warning labels.

Best Practices from Tobacco & State-level Cannabis Labelling Requirements

Inform and educate consumers through on-package labeling

Effective on-package labeling informs consumers and discourages initiation and use.[22]

Modern labeling requirements are essential components of effective tobacco control [23] that should guide cannabis policy. The size, prominence, position, and design of health warning labels influence their impact on risk perceptions [24,25]). The Family Smoking Prevention and Tobacco Control Act (Tobacco Control Act)[26] amended the Federal Cigarette Labeling and Advertising Act[27] to require nine rotating warning statements on labeling and advertisements. Each label statement is required to cover the top 50% of the front and rear panels of the package and at least 20% of the area of the advertisement. Similarly, the WHO Framework Convention on Tobacco Control (FCTC), an evidence-based global tobacco control treaty adopted by 181 parties that prioritizes public health[28], requires tobacco health warnings cover at least 30% and ideally 50% or more of a package's principal display area, a standard associated with higher health knowledge and motivation to quit.[29,30] Increasing label size also improves effectiveness among youth.[31] . Some countries' warnings occupy 90% of the package[32], and the tobacco industry has opposed larger, more effective warnings.[33] **Based on the Tobacco Control Act's mandate for tobacco labeling, as well as the best practices enunciated by the FCTC, the FDA should implement a 50% (or at minimum 30%) coverage requirement for cannabis warnings that would eliminate ambiguity and likely produce gains in health knowledge and warning effectiveness, potentially reducing demand.**

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[22] Daniel G. Orenstein & Stanton A. Glantz (2018) Regulating Cannabis Manufacturing: Applying Public Health Best Practices from Tobacco Control, Journal of Psychoactive Drugs, 50:1, 19-32

[23] World Health Organization. 2013. WHO Framework Convention on Tobacco Control: Guidelines for implementation. Geneva, Switzerland: WHO Press.

[24] Surgeon General. 2012. Preventing tobacco use among youth and young adults: A report of the Surgeon General. Atlanta. GA: Department of Health and Human Services.

[25] World Health Organization. 2013. WHO Framework Convention on Tobacco Control: Guidelines for implementation. Geneva, Switzerland: WHO Press.

[26] Family Smoking Prevention and Tobacco Control Act, Pub. L. 111-31 (2009), Section 201(a)

[27] Federal Cigarette Labeling and Advertising Act, 15 U.S.C. 1333 (1966)

[28] World Health Organization. 2005.WHO Framework Convention on Tobacco Control. Geneva, Switzerland: WHO Press. Available at https://www.who.int/fctc/text_download/en/

[29]World Health Organization. 2013. WHO Framework Convention on Tobacco Control: Guidelines for implementation. Geneva, Switzerland: WHO Press.

[30] Surgeon General. 2012. Preventing tobacco use among youth and young adults: A report of the Surgeon General. Atlanta. GA: Department of Health and Human Services.

[31] Hammond, D. 2012. Tobacco packaging and labeling policies under the U.S. Tobacco Control Act: Research needs and priorities. Nicotine Tob Res 14 (1):62–74.

[32] World Health Organization. 2017a. WHO Report on the Global Tobacco Epidemic, 2017: Monitoring Tobacco Use and Prevention Policies. Geneva, Switzerland: World Health Organization.

[33] Hiilamo, H., E. Crosbie, and S. A. Glantz. 2014. The evolution of health warning labels on cigarette packs: The role of precedents, and tobacco industry strategies to block diffusion. Tob Control 23 (1):e2.

A larger warning label would also permit more prominent font. California's minimum six-point font is consistent with Oregon's requirement (Oregon Administrative Rules 333-007-0220 (2017)-b), but considerably smaller than Nevada's warning label (Nevada Administrative Code § 453A.512 (2017)), which requires front and rear labels with minimum 12-point font. A six-point font is challenging to read and even smaller than the approximately 10-point font suggested by a cannabis industry white paper.[34]

The Tobacco Control Act[35] requires cigarette warning labels to be "in conspicuous and legible 17-point type…in a manner that contrasts, by typography, layout, or color, with al other printed material on the package" and parallels the FCTC's requirement that tobacco health warnings be "large, clear, visible and legible."[36] FDA should adopt these best practices and require cannabis warning labels to use 17-point type that is conspicuous and legible and that contrasts with other package elements.

Include rotating health warnings and pictorial warnings

Like the tobacco industry,[37] cannabis industry stakeholders oppose strong health warnings, deeming them "speculative" and based on "insufficient information" .[38] Tobacco warning labels are more effective when changed periodically[39,40,41] **To educate consumers and reduce perceptions of harmlessness, FDA-approved cannabis labels should include rotating health warnings consistent with current risk information, just as rotating health warnings are required for cigarettes.[42]**

The National Academies Report provides one source for warnings and a corresponding standard for evaluating products' health-related statements, which must be "supported by the totality of publicly available scientific evidence."[43] On this basis, warnings would include at minimum associations meeting the Report's "Substantial Evidence" standard, including worse respiratory symptoms, problem use and dependence, motor vehicle accidents, lower birth weight, and

[34] Grossman, C., A. Livingston, J. Wellington, and C. Barnes. 2017. Cannabis packaging and labeling: Regulatory recommendations for states and nations. Denver, CO: Council for Responsible Cannabis Regulation.
[35] Family Smoking Prevention and Tobacco Control Act, Pub. L. 111-31 (2009), Section 201(a)(2)
[36] World Health Organization. 2003.WHO Framework Convention on Tobacco Control. Geneva, Switzerland: WHO Press.
[37] Hiilamo, H., E. Crosbie, and S. A. Glantz. 2014. The evolution of health warning labels on cigarette packs: The role of precedents, and tobacco industry strategies to block diffusion. Tob Control 23 (1):e2.
[38] Daniel G. Orenstein & Stanton A. Glantz (2018) Regulating Cannabis Manufacturing: Applying Public Health Best Practices from Tobacco Control, Journal of Psychoactive Drugs, 50:1, 19-32,
[39] Crawford, M. A., G. I. Balch, R. Mermelstein, and Tobacco Control Network Writing. 2002. Responses to tobacco control policies among youth. Tob Control 11 (1):14–9.
[40] Hitchman, S. C., P. Driezen, C. Logel, D. Hammond, and G.T. Fong. 2014. Changes in effectiveness of cigarette health warnings over time in Canada and the United States, 2002–2011. Nicotine Tob Res 16 (5):536–43.
[41] World Health Organization. 2003.WHO Framework Convention on Tobacco Control. Geneva, Switzerland: WHO Press.
[42] Family Smoking Prevention and Tobacco Control Act, Pub. L. 111-31 (2009), Section 201(c)
[43] National Academies. 2017. The Health Effects of Cannabisand Cannabinoids: The Current State of Evidence and Recommendations for Research. Washington, DC: The National Academies Press..

development of schizophrenia and other psychoses.[44] A single standard may be more easily defended against industry pushback. I**deal warnings would additionally consider evidence from more recent studies, animal studies, and comparable tobacco products to provide more comprehensive risk information regarding secondhand exposure,[45] respiratory disease[46], neuropsychological decline[47] and cancer [48, 49] based on product type**.

Text-only tobacco labels (currently used in the U.S.) are poorly recalled and have low impact on use.[50] While not yet implemented by the FDA,[51] the 2009 Tobacco Control Act requires pictorial health warnings,[52] which are more impactful and informative than text-only warnings.[53, 54, 55, 56] and decrease tobacco product attractiveness to youth.[57, 58] **Based on demonstrated effectiveness for tobacco, pictorial warnings would likely improve the impact and effectiveness of cannabis labels.**

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[44] National Academies. 2017. The Health Effects of Cannabisand Cannabinoids: The Current State of Evidence and Recommendations for Research. Washington, DC: The National Academies Press..

[45] Wang, X., R.Derakhshandeh, J. Liu, S. Narayan, P. Nabavizadeh, S. Le, O. M. Danforth, K. Pinnamaneni, H. J. Rodriguez, E. Luu, R. E. Sievers, S. F. Schick, S. A. Glantz, and M. L. Springer. 2016b. One minute of marijuana secondhand smoke exposure substantially impairs vascular endothelial function. J Am Heart Assoc 5 (8): e003858.

[46] Owen, K. P. M. E. Sutter, and T. E. Albertson. 2014. Marijuana: Respiratory tract effects. Clin Rev Allergy Immunol 46 (1):65–81.

[47] Meier, M. H., A. Caspi, A. Ambler, H. Harrington, R. Houts, R. S. Keefe, K. McDonald, A. Ward, R. Poulton, and T. E. Moffitt. 2012. Persistent cannabis users show neuropsychological decline from childhood to midlife. Proc Natl Acad Sci U S A 109 (40):E2657–64.

[48] California Environmental Protection Agency. 2017. Chemicals known to the state to cause cancer or reproductive toxicity. Office of Environmental Health Hazard Assessment. https://oehha.ca.gov/media/downloads/proposition-65/p65single01272017.pdf.

[49] Tomar, R. S., J. Beaumont, and J. C. Y. Hsieh. 2009. Evidence on the carcinogenicity of marijuana smoke. California Environmental Protection Agency Office of Environmental Health Hazard Assessment Reproductive and Cancer Hazard Assessment Branch. Sacramento, CA.

[50] Hammond, D. 2012. Tobacco packaging and labeling policies under the U.S. Tobacco Control Act: Research needs and priorities. Nicotine Tob Res 14 (1):62–74.

[51] In response to a lawsuit filed in October 2016 by eight public health and medical groups and several individual pediatricians, in March 2019 a U.S. District Court ordered FDA to issue a final rule mandating graphic health warnings on cigarette packs and advertising by March 15, 2020. AAP et al. v. FDA, Civil Action No. 1:16-cv-11985-IT, Memorandum And Order Granting Injunctive Relief (D. Mass., March 5, 2019). Available at https://www.tobaccofreekids.org/press-releases/2019_03_06_us_warning_labels.

[52] Family Smoking Prevention and Tobacco Control Act, Pub. L. 111-31 (2009), Section 201(d)

[53] Hammond, D., G. T. Fong, R. Borland, K. M. Cummings, A. McNeill, and P. Driezen. 2007. Text and graphic warnings on cigarette packages: Findings from the international tobacco control four country study. Am J Prev Med 32 (3):202–9.

[54] Hitchman, S. C., P. Driezen, C. Logel, D. Hammond, and G.T. Fong. 2014. Changes in effectiveness of cigarette health warnings over time in Canada and the United States, 2002–2011. Nicotine Tob Res 16 (5):536–43.

[55] World Health Organization. 2003.WHO Framework Convention on Tobacco Control. Geneva, Switzerland: WHO Press.

[56] Campaign for Tobacco Free Kids, Tobacco Health Warnings: Evidence of Effectiveness. Available at: https://www.tobaccofreekids.org/press-releases/2018_09_06_warninglabels

[57] Hammond, D. 2012. Tobacco packaging and labeling policies under the U.S. Tobacco Control Act: Research needs and priorities. Nicotine Tob Res 14 (1):62–74.

[58] McCool, J., L. Webb, L. D. Cameron, and J. Hoek. 2012.Graphic warning labels on plain cigarette packs: Will they make a difference to adolescents? Soc Sci Med 74 (8):1269–73.

The FDA should implement regulations requiring pictorial warnings, as they are likelier to be seen by low-literacy adults and children and to reach those who cannot read the text language.

Adopt a highly visible and salient cannabis product symbol

Tobacco companies' research on packaging color and consumer perceptions indicates that black is most visually prominent, particularly black text on a lighter background .[59] Red was specified in California's proposed regulations (also Colorado, Oregon, and Washington regulations[60] and cannabis industry recommendations,[61] **but yellow more effectively gains and keeps attention, is perceived as less attractive, and signals a warning, especially with black text as in road signs. [62]A cannabis warning symbol emulating road warning style, color, and shape[63] (Figure 1) would more effectively attract and maintain consumer attention.** A cannabis leaf, as opposed to the more technical "THC," is likelier to be understood by most consumers. Similar visuals appear in Oregon's framework and in industry recommendations.[64].

Figure 1. Comparison of THC/cannabis warning symbols. (left) Original California THC warning symbol as proposed in CDPH regulation § 40412(a)[65]. (center) Revised California cannabis warning symbol in emergency CDPH regulations § 40412(a)[66]. (right) Recommended alternative cannabis warning symbol.

Packaging variation among cannabis products supports 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's size should be considered part of mandatory primary panel warning coverage (at least 30% and ideally

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[59] Lempert, L. K., and S. A. Glantz. 2016. Implications of tobacco industry research on packaging colors for designing health warning labels. Nicotine Tob Res 18 (9):1910–4.
[60] Rachel A. Barry and Stanton A. Glantz, 2018: Marijuana Regulatory Frameworks in Four US States: An Analysis Against a Public Health Standard. American Journal of Public Health 108, 914_923, https://doi.org/10.2105/AJPH.2018.304401
[61] Grossman, C., A. Livingston, J. Wellington, and C. Barnes. 2017. Cannabis packaging and labeling: Regulatory recommendations for states and nations. Denver, CO: Council for Responsible Cannabis Regulation.
[62] Lempert, L. K., and S. A. Glantz. 2016. Implications of tobacco industry research on packaging colors for designing health warning labels. Nicotine Tob Res 18 (9):1910–4.
[63] U.S. Department of Transportation. 2002. Manual on Uniform Traffic Control Devices. Washington, DC: F.H. Administration.
[64] Grossman, C., A. Livingston, J. Wellington, and C. Barnes. 2017. Cannabis packaging and labeling: Regulatory recommendations for states and nations. Denver, CO: Council for Responsible Cannabis Regulation.
[65] California Department of Food and Agriculture. 2017b. Emergency regulations for cannabis cultivation.
[66] California Department of Public Health. 2017c. DPH-17-010E: Cannabis manufacturing licensing. https://www.cdph.ca.gov/Programs/OLS/CDPH%20Document%20Library/DPH-17-010E_ER_RegText_Application.pdf

50% of the principal display area based on FCTC tobacco label requirements discussed earlier).[67]

Require plain packaging

Tobacco companies use packaging as a marketing tool to bypass other marketing restrictions, [68] establishing brand identification among youth, young adults, and other target populations.[69, 70] The youth marketing effect of package branding is powerful at in-store displays[71], 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[72] fully standardized "plain packaging" free of logos, colors, and branding, allowing only plain text brand and variant information in specified size, font, and position.[73, 74, 75]

Plain cigarette packaging is associated with reduced brand awareness and identification[76] and reduced cigarette appeal among adolescents and young adults[77, 78, 79, 80] Plain

[67] Daniel G. Orenstein & Stanton A. Glantz (2018) Regulating Cannabis Manufacturing: Applying Public Health Best Practices from Tobacco Control, Journal of Psychoactive Drugs, 50:1, 19-32,
[68] Freeman, B., S. Chapman, and M. Rimmer. 2008. The case for the plain packaging of tobacco products. Addiction 103 (4):580–90.
[69] Daniel G. Orenstein & Stanton A. Glantz (2018) Regulating Cannabis Manufacturing: Applying Public Health Best Practices from Tobacco Control, Journal of Psychoactive Drugs, 50:1, 19-32,
[70] Wakefield, M., C. Morley, J. K. Horan, and K. M. Cummings.2002. The cigarette pack as image: New evidence from tobacco industry documents. Tob Control 11 Suppl 1:I73–80.
[71] Robertson, L., C. Cameron, R. McGee, L. Marsh, and J. Hoek. 2016. Point-of-sale tobacco promotion and youth smoking: A meta-analysis. Tob Control 25 (e2):e83–e89.
[72] World Health Organization. 2003.WHO Framework Convention on Tobacco Control. Geneva, Switzerland: WHO Press
[73] Freeman, B., S. Chapman, and M. Rimmer. 2008. The case for the plain packaging of tobacco products. Addiction 103 (4):580–90.
[74] Hammond, D. 2014. Standardized Packaging of Tobacco Products: Evidence Review. Irish Department of Health. Dublin, Ireland.
[75] Tobacco Labelling Resource Centre. 2017. Plain packaging. http://www.tobaccolabels.ca/plain-packaging/.
[76] Balmford, J., R. Borland, and H. H. Yong. 2016. Impact of the introduction of standardised packaging on smokers' brand awareness and identification in Australia. Drug Alcohol Rev. 35 (1):102–109.
[77] Germain, D., M. A. Wakefield, and S. J. Durkin. 2010. Adolescents' perceptions of cigarette brand image: Does plain packaging make a difference? J Adolesc Health 46 (4):385–92.
[78] Lund, I., and J. Scheffels. 2013. Young smokers and nonsmokers perceptions of typical users of plain vs. branded cigarette packs: A between-subjects experimental survey. BMC Public Health 13:1005.
[79] Moodie, C., A. M. Mackintosh, G. Hastings, and A. Ford. 2011. Young adult smokers' perceptions of plain packaging: A pilot naturalistic study. Tob Control 20 (5):367–73.
[80] White, V., T. Williams, and M. Wakefield. 2015. Has the introduction of plain packaging with larger graphic health warnings changed adolescents' perceptions of cigarette packs and brands? Tob Control 24 (Suppl 2): ii42–ii49.

packaging also makes health warnings more noticeable and effective[81, 82, 83] and reduces the impact of misleading branding on perceived harmfulness [84, 85]

The FDA should create regulations that combine precepts of plain packaging and large graphic labels in order to diminishe cannabis's appeal to adolescents by increasing attention and perceptions of harm and reducing social appeal.

Eliminate all packaging that appeals to children or imitates non-cannabis products

A broad prohibition on packaging attractive to children would better prevent industry targeting of youth.[86] For example, a proposed Canadian recreational cannabis law prohibits packaging and labeling associating a product with "a way of life such as one that includes glamour, recreation, excitement, vitality, risk or daring" or "if there are reasonable grounds to believe that the package or label could be appealing to young persons" (C-45). Even this broader language remains subjective (e.g., defining "glamour**"). A plain packaging requirement avoids interpretive problems and removes opportunities to mislead consumers and unlawfully market to youth using packaging.**

Absent plain packaging, regulations must anticipate and counter numerous industry tactics. Imitative packaging (copying the appearance of non-cannabis products) is an issue that cannabis industry stakeholders recognize requires regulation.[87] **Regulations should prohibit imitating the packaging of any non-cannabis product to reduce accidental consumption risks and prevent marketing to youth.**

[81] Beede, P., and R. Lawson. 1992. The effect of plain packages on the perception of cigarette health warnings. Public Health 106 (4):315–22.
[82] Surgeon General. 2012. Preventing tobacco use among youth and young adults: A report of the Surgeon General. Atlanta. GA: Department of Health and Human Services.
[83] Wakefield, M., K. Coomber, M. Zacher, S. Durkin, E. Brennan, and M. Scollo. 2015. Australian adult smokers' responses to plain packaging with larger graphic health warnings 1 year after implementation: Results from a national cross-sectional tracking survey. Tob Control 24 (Suppl 2): ii17–ii25.
[84] Wakefield, M., K. Coomber, M. Zacher, S. Durkin, E. Brennan, and M. Scollo. 2015. Australian adult smokers' responses to plain packaging with larger graphic health warnings 1 year after implementation: Results from a national cross-sectional tracking survey. Tob Control 24 (Suppl 2): ii17–ii25.
[85] White, V., T. Williams, and M. Wakefield. 2015. Has the introduction of plain packaging with larger graphic health warnings changed adolescents' perceptions of cigarette packs and brands? Tob Control 24 (Suppl 2): ii42–ii49.
[86] Daniel G. Orenstein & Stanton A. Glantz (2018) Regulating Cannabis Manufacturing: Applying Public Health Best Practices from Tobacco Control, Journal of Psychoactive Drugs, 50:1, 19-32,
[87] Grossman, C., A. Livingston, J. Wellington, and C. Barnes. 2017. Cannabis packaging and labeling: Regulatory recommendations for states and nations. Denver, CO: Council for Responsible Cannabis Regulation.

Prohibit product formulations that may increase health risks

Evidence of health effects for manufactured cannabis products is even more limited than for cannabis generally.[88] **Manufactured products also introduce concerns, including additives,**[89] increased **potency,**[90] **and similarity to non-cannabis products**.[91,92, 93]

The FDA should also mandate THC dose labeling. There are cases in which people took an overdose resulting in serious medical consequence because they did not know they were taking a high dose of THC. California regulations require reporting of potency and dosage, but the FDA should regulate all cannabis products in a similar manner to ensure quality control and consumer safety. **The medical and scientific communities still do not have enough information on pharmacokinetics, precisely due to the difficulty in gaining approval to perform compliant research given cannabis' confounding research-limiting Schedule I designation.**

Clearly prohibit additives that promote addictiveness or initiation, including nicotine, caffeine, menthol, and characterizing flavors

Combinations of cannabis products with additives, such as caffeine or nicotine should be prohibited in all forms, regardless of source**.**[94] **Specifically, nicotine in all forms, including tobacco, e-liquids, and similar products, should be prohibited from being added to a cannabis product**

Crucially, regulations should prohibit harmful additives in all forms of manufactured cannabis products.

Regulations should prohibit adding menthol to non-topical cannabis products.[95] In tobacco products, menthol is more than a flavoring agent, affecting nicotine dependence through behavioral reinforcement[96] and encouraging breath holding, which increases nicotine exposure.[97] Stimulated by direct and indirect tobacco industry marketing, younger and newer smokers

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[88] National Academies. 2017. The Health Effects of Cannabisand Cannabinoids: The Current State of Evidence and Recommendations for Research. Washington, DC: The National Academies Press..

[89] California Department of Public Health. 2017a. DPH-17-004: Medical cannabis manufacturing: Initial statement of reasons. https://www.cdph.ca.gov/Documents/OMCS_ISOR_DPH-17-004.pdf.

[90] Raber, J. C., S. Elzinga, and C. Kaplan. 2015. Understanding dabs: Contamination concerns of cannabis concentrates and cannabinoid transfer during the act of dabbing. J Toxicol Sci 40 (6):797–803.

[91] Daniel G. Orenstein & Stanton A. Glantz (2018) Regulating Cannabis Manufacturing: Applying Public Health Best Practices from Tobacco Control, Journal of Psychoactive Drugs, 50:1, 19-32,

[92] Coffman, K. 2014. Hershey settles infringement lawsuits with two edible pot companies. Reuters. https://www.reuters.com/article/usa-hershey-marijuana/hersheysettles-infringem e n t - l a w s u i t s - w i t h - t w o - e d i b l e - p o t -companiesidUSL2N0SD03620141018

[93] Leafly. 2017. Topicals. https://www.leafly.com/products/topicals.

[94] Daniel G. Orenstein & Stanton A. Glantz (2018) Regulating Cannabis Manufacturing: Applying Public Health Best Practices from Tobacco Control, Journal of Psychoactive Drugs, 50:1, 19-32,

[95] Daniel G. Orenstein & Stanton A. Glantz (2018) Regulating Cannabis Manufacturing: Applying Public Health Best Practices from Tobacco Control, Journal of Psychoactive Drugs, 50:1, 19-32,

[96] Ahijevych, K., and B. E. Garrett. 2010. The role of menthol in cigarettes as a reinforcer of smoking behavior. Nicotine Tob Res 12 Suppl 2:S110–6.

[97] Garten, S., and R. V. Falkner. 2004. Role of mentholated cigarettes in increased nicotine dependence and greater risk of tobacco-attributable disease. Prev Med 38 (6):793–8.

disproportionately use menthol cigarettes, owing to the reduced harshness menthol contributes as a local anesthetic.[98,99] 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.[100, 101] Menthol use is more common among tobacco industry-targeted groups, including youth of color, women, and LGBTQ populations.[102] Menthol smokers, especially persons of color and younger smokers, also experience more difficulty quitting.[103]

While not direct evidence on the relationship between menthol and cannabis dependence, menthol cigarette smokers are likelier than non-menthol smokers to report past-30-day cannabis use[104]. Dual use of menthol cigarettes and cannabis also increased from 2005–14.[105] Manufactured cannabis products incorporating menthol already exist.[106] Menthol's sensory effects may contribute similar behavioral reinforcement for cannabis as for tobacco, 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 associations with cannabis use support a cautious policy prohibiting menthol in non-topical cannabis products to prevent repeating harms attributable to mentholated tobacco products.**

Beyond menthol, **a prohibition on characterizing flavors in nonedible products is necessary to discourage inappropriate use of medical products and deter youth use. Flavored**

[98] Rath, J. M., A. C. Villanti, V. F. Williams, A. Richardson, J. L. Pearson, and D. M. Vallone. 2016. Correlates of current menthol cigarette and flavored other tobacco product use among U.S. young adults. Addict Behav 62:35–41.
[99] Surgeon General. 2012. Preventing tobacco use among youth and young adults: A report of the Surgeon General. Atlanta. GA: Department of Health and Human Services.
[100] Alexander, L. A., D. R. Trinidad, K. L. K. Sakuma, P. Pokhrel, T. A. Herzog, M. S. Clanton, E. T. Moolchan, and P. Fagan. 2016. Why we must continue to investigate menthol's role in the African American smoking paradox. Nicotine & Tobacco Research 18:S91–S101.
[101] Yerger, V. B. 2011. Menthol's potential effects on nicotine dependence: A tobacco industry perspective. Tob Control 20 Suppl 2: ii29–36.
[102] Giovino, G. A., A. C. Villanti, P. D. Mowery, V. Sevilimedu, R. S. Niaura, D. M. Vallone, and D. B. Abrams. 2015. Differential trends in cigarette smoking in the USA: Is menthol slowing progress? Tob Control 24 (1):28–37.
[103] Foulds, J., M. W. Hooper, M. J. Pletcher, and K. S. Okuyemi. 2010. Do smokers of menthol cigarettes find it harder to quit smoking? Nicotine Tob Res 12 Suppl 2:S102–9.
[104] Kong, G., M. E. Morean, D. A. Cavallo, D. R. Camenga, and S. Krishnan-Sarin. 2015. Reasons for electronic cigarette experimentation and discontinuation among adolescents and young adults. Nicotine Tob Res 17 (7):847–54.
[105] Schauer, G. L., E. N. Peters, Z. Rosenberry, and H. Kim. 2017. Trends in and characteristics of marijuana and menthol cigarette use among current cigarette smokers, 2005–2014. Nicotine Tob Res, p. ntw394.
[106] Hughes, Z. 2016. Review: PURE vapor pen. http://www.dopemagazine.com/pure-vapor-pen/.

products attract young smokers to tobacco[107, 108, 109] **and e-cigarettes.**[110,111] **Most adolescent tobacco and e-cigarette users' use is initiated with flavored products.**[112] **Disguising unpleasant tastes with flavors to attract young users is a tobacco industry strategy the cannabis industry could employ, absent strong regulations by the FDA.**

The FDA's 2009 ban on cigarettes with characterizing flavors in cigarettes precipitated a decrease in adolescent tobacco use and substantial reductions in the probability of being a cigarette smoker and in cigarettes smoked among adolescents.[113] Because the final 2009 ban failed to include menthol cigarettes or flavored non-cigarette tobacco, increased use of cigars, pipes, and menthol cigarettes (implying substitution for flavored cigarettes) limited the impact on adolescent tobacco use.[114] **Cannabis regulations should prevent similar effects by prohibiting characterizing flavors in nonedible products.**[115]

Flavored edibles present similar concerns requiring further research on impacts on use and initiation. Regarding medical cannabis products, any therapeutic effect is likely unrelated to flavorings, and alternative formulations should remain available.

The tobacco industry has opposed effective and innovative public health policies to prevent regulatory diffusion.[116] Cannabis is not tobacco, and the cannabis industry is not, for now,[117] the tobacco industry. Nevertheless, cannabis has health risks, many analogous to tobacco, and much remains unknown about the health effects of manufactured cannabis products. **A precautionary approach by the FDA, informed by evidence-based tobacco control best practices, will minimize potential population health harms and avoid repetition of dangerous tobacco industry behavior by the cannabis industry.**

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[107] Carpenter, C. M., G. F. Wayne, J. L. Pauly, H. K. Koh, and G.N. Connolly. 2005. New cigarette brands with flavors that appeal to youth: Tobacco marketing strategies. Health Aff (Millwood) 24 (6):1601–10.
[108] Surgeon General. 2012. Preventing tobacco use among youth and young adults: A report of the Surgeon General. Atlanta. GA: Department of Health and Human Services.
[109] Villanti, A. C., A. L. Johnson, B. K. Ambrose, K. M. Cummings, C. A. Stanton, S. W. Rose, S. P. Feirman, C. Tworek, A. M. Glasser, J. L. Pearson, A. M. Cohn, K. P. Conway, R. S. Niaura, M. Bansal-Travers, and A. Hyland. 2017. Flavored tobacco product use in youth and adults: Findings From the first wave of the PATH study (2013–2014). Am J Prev Med 53 (2):139–151.
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[111] McDonald, E. A., and P. M. Ling. 2015. One of several "toys"for smoking: Young adult experiences with electronic cigarettes in New York City. Tob Control 24 (6):588–93.
[112] Ambrose, B. K., H. R. Day, B. Rostron, K. P. Conway, N.Borek, A. Hyland, and A. C. Villanti. 2015. Flavored tobacco product use among US youth aged 12–17 years, 2013–2014. JAMA 314 (17):1871–3.
[113] Courtemanche, C. J., M. K. Palmer, and M. F. Pesko. 2017. Influence of the flavored cigarette ban on adolescent tobacco use. Am J Prev Med 52 (5):e139–e146.
[114] Courtemanche, C. J., M. K. Palmer, and M. F. Pesko. 2017. Influence of the flavored cigarette ban on adolescent tobacco use. Am J Prev Med 52 (5):e139–e146.
[115] Daniel G. Orenstein & Stanton A. Glantz (2018) Regulating Cannabis Manufacturing: Applying Public Health Best Practices from Tobacco Control, Journal of Psychoactive Drugs, 50:1, 19-32,
[116] Hiilamo, H., E. Crosbie, and S. A. Glantz. 2014. The evolution of health warning labels on cigarette packs: The role of precedents, and tobacco industry strategies to block diffusion. Tob Control 23 (1):e2.
[117] Barry RA, Hiilamo H, Glantz SA. Waiting for the opportune moment: the tobacco industry and marijuana legalization. The Milbank quarterly. 2014;92(2):207-242.

Larger, more effective warnings, plain packaging, and stricter limits on product constituents and potency would help inform consumers, inhibit harmful marketing practices, and improve product safety.

Creation of Regulations Avoiding Revolving Door, Conflicts of Interest, and Regulatory Capture

Government employees in states that have legalized medical or adult use cannabis have come under increasing scrutiny for holding private interests in the cannabis industry, highlighting the problem of conflicts of interest (COIs) and demonstrating the need for robust regulation to prevent public employees from having COIs in the cannabis industry.[118, 119] Such provisions recognize the current reality facing cannabis regulation arising from cannabis' continued illegality coincides with a robust legal state-level market existing side by side with a residual illicit market that operates outside of a federal oversight scheme.[120,121]

Lack of attention to ethical precepts may augment cynicism about the integrity and efficacy of governance among the citizenry.[122, 123, 124]

On the basis of this case study of the California's Bureau of Cannabis Control–proposed COI rules for public employees,[125, 126] we collected comprehensive data on how states that legalized medical cannabis or that legalized adult use cannabis regulated public employees' private commercial interaction with the cannabis markets. **As of April 2018, only 20% (6/30) of states (including Washington, DC as a state) that legalized medical cannabis had COI provisions in their medical cannabis codes, whereas 88% (7/8) of states that legalized adult use cannabis had COI provisions in their cannabis codes.** The remaining states' codes possessed no cannabis-specific conflict of interest as it pertains to public employees, instead falling back on subject-matter general codes that are little more than "toothless tigers."

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[118] Candice M. Bowling and Stanton A. Glantz, 2019: Conflict of Interest Provisions in State Laws Governing Medical and Adult Use Cannabis, American Journal of Public Health 109,

[119] Bowling, Candice & A. Glantz, Stanton. (2019). Civic Engagement in California Cannabis Policy Development. Journal of Psychoactive Drugs. 10.1080/02791072.2019.1627444.

[120] Candice M. Bowling and Stanton A. Glantz, 2019: Conflict of Interest Provisions in State Laws Governing Medical and Adult Use Cannabis, American Journal of Public Health 109, 423_426,https://doi.org/10.2105/AJPH.2018.304862

[121] Bowling, Candice & A. Glantz, Stanton. (2019). Civic Engagement in California Cannabis Policy Development. Journal of Psychoactive Drugs. 10.1080/02791072.2019.1627444.

[122] Organisation for Economic Co- Operation and Development. Managing conflict of interest in the public sector: a toolkit. 2005. Available at: http://www.sourceoecd.org/governance/ 9264018220. Accessed June 15, 2018.

[123] Blake R, Grob JA, Potenski DH, Reed P, Walsh P. The nature and score of state government ethics codes. Public Prod Manage Rev. 1998;21(4):453–459.

[124] Gilman SC, Lewis CW. Public service ethics: global dialogue. Public Adm Rev. 1996;56(6):517–524.)

[125] Candice M. Bowling and Stanton A. Glantz, 2019: Conflict of Interest Provisions in State Laws Governing Medical and Adult Use Cannabis, American Journal of Public Health 109, 423_426,https://doi.org/10.2105/AJPH.2018.304862

[126] Bowling, Candice & A. Glantz, Stanton. (2019). Civic Engagement in California Cannabis Policy Development. Journal of Psychoactive Drugs. 10.1080/02791072.2019.1627444.

Public faith in regulatory systems and in the regulators themselves justifies the implementation of cannabis-specific COI rules to allow the government to focus on efficient policymaking, efficient service provision, and moving the cannabis trade from the illicit to licit market, rather than on the ethical failings of public employees. Governmental ethics codes are often perceived to be little more than symbolic, lacking buy-in, strong enforcement mechanisms, funding, and administrative priority. [127]

Unique aspects of the cannabis market that need to be explicitly recognized by the FDA when preparing COI rules.[128,129] Provisions and regulations relating to COIs that are specific to the FDA's regulation of cannabis are preferable to subject-matter general ethics codes as they apply to any government employee, given the fluid nature of cannabis policy and the ever-evolving market. Further, the lack of federal regulations and legislation relating to cannabis has created a void wherein state-level government employees may, and, have, exploited COIs while retaining government employ. Short of suggesting an explicit prohibition on former law enforcement officers or former legislators with records staunchly opposing cannabis legalization from entering the cannabis trade, it poses many of the same ethical concerns as an allowance for currently employed governmental employees or law enforcement officers from obtaining license to cultivate, produce, or sell, or otherwise profit from the cannabis trade while simultaneously engaging in regulatory-creation or enforcement.

In order to avoid glaring COIs that damage public faith and avoid regulatory capture that has impeded other areas of federal regulation, such as the revolving door between the FCC and Wall Street preceding the 2007 subprime economic meltdown, **the FDA should recognize that cannabis, being a previously illicit substance, is a novel area of regulation that presents ethical conundrums that could be diffused by drafting of conscientious conflict of interest rules for governing actively-employed government employees working in the area of cannabis licensure, regulation, and enforcement.**

Conclusion

We appreciate the opportunity to comment on this notice and commend the FDA's efforts in overseeing the challenging task of regulating the safety and efficacy of cannabis and cannabis-derived products. The FDA should immediately take steps to lower barriers to medical research on the health effects of cannabis broadly. Over the longer term, the FDA should develop a comprehensive regulatory regime for cannabis based on best practices from tobacco control.

[127] Thompson DF. Paradoxes of government ethics. Public Adm Rev. 1992; 52(3):254–259.
[128] Candice M. Bowling and Stanton A. Glantz, 2019: Conflict of Interest Provisions in State Laws Governing Medical and Adult Use Cannabis, American Journal of Public Health 109, 423_426, https://doi.org/10.2105/AJPH.2018.304862
[129] Bowling, Candice & A. Glantz, Stanton. (2019). Civic Engagement in California Cannabis Policy Development. Journal of Psychoactive Drugs. 10.1080/02791072.2019.1627444.