

National Institute on Drug Abuse

RECOMMENDATIONS FOR
NIDA'S CANNABIS POLICY
RESEARCH AGENDA

REPORT FROM THE
CANNABIS POLICY RESEARCH WORKGROUP

February 6, 2018



NATIONAL ADVISORY COUNCIL ON DRUG ABUSE

February 6, 2018

Nora D. Volkow, M.D.
Director, National Institute on Drug Abuse
6001 Executive Boulevard
Bethesda, MD 20892

Dear Dr. Volkow:

I am pleased to transmit *Recommendations for NIDA's Cannabis Policy Research Agenda* from the National Advisory Council on Drug Abuse Workgroup. The Workgroup was formed in January 2017 at your request to provide a policy research agenda to respond to the changing landscape and growing challenges surrounding the liberalization of cannabis laws. In approaching our charge, we were agnostic on the issue of cannabis reform. Instead, we focused purposefully on identifying a policy research agenda that will advance science on the causes and consequences of drug use and addiction. We also focused on how to apply that knowledge to improve individual and public health in whatever legal regime the states decide to pursue, whether or not more policy liberalization occurs. This report and its recommendations reflect the consensus view of the Workgroup members, and we take full responsibility for the contents.

Owing to the complexity of cannabis reform and to the range of challenges facing the researchers, policymakers, and regulators seeking to develop scientifically based responses to it, our recommendations fall into five areas, each with priorities presented in order of importance. As you will see, some of the recommendations identified as being the most important may indeed be the most difficult to implement, but the Workgroup felt strongly that these priorities must be addressed. In addition, the Workgroup identified some priorities that may be more closely aligned with the missions of other federal agencies. Nevertheless, these are included in recognition of the NIDA's leadership role in substance misuse research and your personal dedication to ensuring that science serves the public health.

The members of the Workgroup and I thank Susan Weiss, Ph.D., for her critical support throughout the process. Her knowledge of the research challenges surrounding cannabis proved invaluable throughout our deliberations. In addition, we thank Katia D. Howlett, Ph.D., Steve Gust, Ph.D., Marsha Lopez, Ph.D., and Eric Wargo, Ph.D., for their unwavering support of our effort. Finally, we thank Lori Whitten, Ph.D., Senior Science Writer with Synergy Enterprises, Inc., for her expertise in accurately capturing various Workgroup discussions and deliberations to support the development of this report.

Sincerely yours,

A handwritten signature in cursive script that reads "John Carnevale".

John Carnevale, Ph.D.
Member,
NIDA National Advisory Council on Drug Abuse

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EXECUTIVE SUMMARY

The mission of the National Institute on Drug Abuse (NIDA) is to advance science on the causes and consequences of drug use and addiction and to apply that knowledge to improve individual and public health. In support of its mission, Nora D. Volkow, Ph.D., created the Cannabis Workgroup to advise the NIDA on a policy research agenda to respond to the rapidly changing landscape and dearth of science related to these cannabis reforms. Its charge included identifying research priorities related to the consumption of psychoactive cannabis in all its forms, both for perceived medical benefits (medical use) and for nonmedical use (often colloquially referred to as recreational use). The Workgroup was deliberately agnostic on the wisdom of cannabis reform, focusing its efforts instead on identifying the knowledge gap between science and policy.

Throughout a 1-year period, the Workgroup addressed numerous important questions: What are the most important questions that the NIDA should address as a funding agency? What policies are likely to be the most effective at reducing the adverse effects of cannabis use? What research programs could inform us of the possible positive and negative effects that cannabis policies might have? The Workgroup addressed these questions by developing a set of guiding principles to focus the discussions and eventual formation of recommendations for the NIDA's policy research agenda. These principles were:

1. The NIDA's research mission is understood to be inclusive, flexible, and public health-oriented.
2. Research must be neutral about actions, laws, and policies set by any jurisdiction regarding cannabis.
3. Priority should be given to research that will remain germane under a wide range of policy frameworks.
4. Research should focus on behaviors and consequences that are associated with the greatest harms or benefits and the policies that ameliorate or exacerbate those harms.
5. Research should consider both short- and long-term effects.
6. Research should be sensitive to the realities of cannabis laws and policies.
7. Research should be sensitive to the realities of cannabis production, marketing, and use.
8. Research should acknowledge that, sometimes, large gaps can emerge between a law or policy as written and its implementation.

Guided by these eight principles, the Workgroup initially identified lists of research ideas that fell into five broad topic areas: (1) Cannabis Use; (2) Epidemiology; (3) Health and Social Consequences; (4) The Structure, Behavior, and Conduct of the Industry; and (5) Prevention and Treatment. The Workgroup did not believe it was possible to create a single list of research priorities because it is difficult to compare the value of projects across topic areas.

This report presents 28 recommendations for policy research in the five topic areas. The Executive Summary identifies the top two priorities in each area.

Cannabis Use

The Workgroup identified seven policy research priorities for the NIDA's consideration. Regarding the top priority, the Workgroup recognized that standardized measures of cannabis use frequency, amount, product form, administration method, and dose are needed to gain a more complete understanding of use and its outcomes. Standardized measures have proved useful for alcohol (and other substances). It helps people to be able to think in terms of a standard drink or dose for the purposes of measurement as well as for self-monitoring, diagnosis, and conversations between physicians and patients who may or may not be struggling with misuse. However, the Workgroup also recognized that, because of the range of different cannabis products, formulations, and forms, there is no comparable concept or measure for cannabis. Nevertheless, the Workgroup viewed exploratory research on the feasibility of establishing a standardized dose as a necessary endeavor, which resulted in the following recommendation:

- *Explore the possibility of constructing a standardized dose similar to that for alcohol (the standard drink), tobacco (a cigarette), or opioids (morphine milligram equivalents) for researchers to employ in analyzing use and for users to understand their consumption.*

The Workgroup members were concerned about the public's perception about the lack of health risks for cannabis use. This perception may translate into serious problems related to driving, the workplace, and academic achievement. Based on this consideration, the Workgroup determined that a better understanding of impairment is necessary to protect public health and safety. This became the second priority for cannabis use research:

- *Establish standards for measuring cannabis intoxication and impairment.*

Epidemiology

The Workgroup identified three research priorities. More knowledge is needed on trends, determinants of use, and the potential adverse or beneficial health and psychosocial consequences. The Workgroup identified the top priority for this area to be:

- *Conduct research to understand better the epidemiology and trends in cannabis use, frequent use, and cannabis use disorder and its criteria (also called abuse, dependence, or addiction). Currently, these criteria include tolerance, withdrawal, craving, use patterns reflecting impaired control, and continuing use regardless of potential or actual adverse psychological or medical consequences.*

The Workgroup also discussed the need for better epidemiological tools to detect use and consequences. In particular, researchers should refine and improve self-report tools on use, impairment, and consequences, as well as examine the use of social media to track emerging trends. The second priority for Epidemiology is:

- *Expand information sources about use, impairment, and its consequences.*

Health and Social Consequences

The Workgroup identified six research priorities in this topic area. More research is needed on how cannabis reform may affect cannabis use and vehicle crashes, accidents, and risky behaviors. The Workgroup identified the following top two priorities:

- *Develop effective roadside tests for cannabis impairment that can be practically deployed by law enforcement. This priority is urgent. It should be pursued in a way that gets useful devices or strategies deployed in the field as rapidly as possible.*
- *Determine the prevalence of and factors related to cannabis use (in its various forms and potency) and cannabis-involved crashes, other types of injury or property damage, adverse health events requiring medical attention, and other risky behaviors. This priority would include, but not be limited to, topics such as the simultaneous use of cannabis and alcohol or of cannabis and tobacco, and how cannabis use modifies or is modified by other demonstrated risk factors.*

The Structure, Behavior, and Conduct of the Industry

The Workgroup identified four research priority subareas, each containing their own prioritization. The Workgroup believes that much more research is needed on how industry behavior can be expected to affect use and misuse. In this regard, the top priority recommended by the Workgroup centers on industry structure.

- *Research retail sales, promotion, and marketing (how products are sold and how they get marketed)—The state-legalized cannabis industry is new and evolving, and regulators lack evidence to guide how its many products and practices should best be regulated to protect the public health.*

The Workgroup also determined that an important tool for affecting use pertains to pricing of cannabis products as well as the effects of alternative taxes on use. Accordingly, it identified the following as the second priority for this topic area:

- *Research taxes and prices—excise taxes are arguably the single most important lever in tobacco and alcohol policy. It is already known that consumption falls when prices rise, although the extent of price responsiveness is not fully clear.*

Prevention and Treatment

The Workgroup identified eight research priorities. The Workgroup recognized the importance for research about innovative strategies to address cannabis misuse. In particular, different tactics and messaging strategies may be needed for a substance that is increasingly seen as not risky and that is widely described as being useful for its perceived medicinal purposes. The Workgroup believes that prevention science about topics such as risk and protective factors will need to be refined to account for changes in cannabis laws—that is, new research on prevention approaches to complement community strategies that speak to both local conditions and broader population health considerations. Similarly, the changing cannabis policy environment

will also likely impact our treatment needs, and there are three recommendations on this topic. However, the top two priorities recommended by the Workgroup pertain to prevention:

- *Design and develop the most effective prevention strategies, messages, and materials suitable for cannabis in this new context for all audiences.*
- *Design and develop more effective broader community/environmental prevention approaches through public policy (e.g., limiting outlet density or limiting use in public, higher taxes).*

INTRODUCTION

Since California began permitting medical use of cannabis in 1996, 28 other states and the District of Columbia have legalized medical use, and eight states plus the District of Columbia have legalized use for nonmedical purposes.^{1,2} The change in laws means that most Americans now live in states permitting cannabis use for its perceived medical value. In fact, over 63 percent of Americans live in states or territories that permit medical cannabis, and over 21 percent live in parts of the country that have legalized cannabis for nonmedical use (often colloquially referred to as recreational use).

In recent years, potentially as a result of this widespread legalization of use and the debate surrounding it, all age groups have seen declines in many factors limiting cannabis use, including perceptions of harm and perceptions of parental disapproval (among youth). While rates of cannabis use and initiation of use among youth ages 12-17 did not significantly change from 2002 to 2016, such increases were found among every other age group. Increased frequency of use among users also occurred over that time frame. As a consequence of this use, almost 4 million U.S. residents meet the diagnostic criteria for a cannabis use disorder in 2016; however, only 747,000 U.S. residents received substance use treatment services for cannabis use. Additionally, possibly as a result of legalization only taking effect for those age 21 and older, the mean age of first use has also increased.³

Legal changes have occurred as public support for the legalization of nonmedical cannabis use is on the rise. Indeed, if state liberalization trends continue, millions of additional Americans may have access to legal cannabis, even while the federal government maintains its prohibition. This increased access may lead to increases in rates of use, disorders, addiction, and demand for treatment services.

Legal and attitudinal changes regarding cannabis are not limited to the United States. Other nations are liberalizing their cannabis laws as well—with some considering or pursuing more robust legalization. Uruguay famously became the first country to legalize the production and sale of marijuana in 2013, although pharmacies did not begin selling the product until summer 2017. Canada is also pursuing cannabis legalization that is expected to be implemented in 2018, which, because of its proximity, may have substantial effects on this country. Jamaica has taken steps to liberalize its cannabis laws, as have many South American countries, including Colombia, Ecuador, and Mexico. Portugal has liberalized its policy on all drugs, including cannabis. The

¹ As used here, cannabis is a broad term intended to encompass all psychoactive products and chemical compounds (e.g., marijuana, cannabinoids) derived from the cannabis plant.

² In January 2018, the Vermont Legislature approved a bill legalizing nonmedical use; although it does not establish a regulatory system allowing commercial sales or purchases.

³ Substance Abuse and Mental Health Administration, 2016 National Survey on Drug Use and Health.

liberalization trend appears to broadly span Europe and the Western Hemisphere, but not Africa or Asia.

The cannabis that Americans are using is also becoming more potent, and the ways that the drug is consumed have become more diverse. Historically, the levels of delta-9-tetrahydrocannabinol (THC; the main psychoactive chemical in cannabis) in cannabis supplied for research purposes have been approximately 2-4 percent, but the THC levels in most commercial cannabis today are much higher, in some cases as high as 24 percent (see below).

The combination of these trends is creating challenges for researchers, policymakers, and regulators to develop scientifically based responses. To be clear, the rapidity of changing cannabis policy has far outpaced the knowledge base, data infrastructure, and regulatory capacity needed to formulate effective implementation strategies informed by science to protect public health and safety. Many of the individuals and institutions charged with developing and implementing cannabis regulations complain that their questions largely go unanswered. Moreover, stakeholders across the Nation—particularly those who live in states and municipalities that have legalized nonmedical use—are rapidly learning valuable lessons about cannabis, the impacts that policy changes may have on individuals and communities, and strategies to safeguard public health in the age of cannabis legalization. However, what they are learning has not been subject to scientific scrutiny; thus, best practices to inform the public and protect public health and safety have not been determined. Research is needed to quantify how well implementation is working to learn about the effectiveness of decisions made to accommodate the rapidly changing landscape in cannabis laws.

It is also the case that the basic vernacular of cannabis laws remains too broad to support the nuanced discussion that should accompany this policy change. Labels such as “decriminalization,” “medical marijuana,” and even “legalization” obscure substantial variation in implementation and practical effect. And those differences matter.⁴ Consider the difference between “legalization” as it currently functions in Washington, DC (where sales remain illegal) and “legalization” in Colorado or Washington state (where 2,900 and 1,800, respectively, retail outlets exist).⁵ The issue is not simply semantic, as alcohol and tobacco researchers have extensively evaluated and demonstrated the impact of outlet proximity and density on use of these substances as well as related harms. Cannabis policy must be studied with the same level of attention to detail.

⁴ Several public data sets, including the National Institute on Alcohol Abuse and Alcoholism’s APIS and NIDA-supported Law Atlas, track many elements of these laws and policies, but very little research has explored the implications of this marijuana policy variation to date.

⁵ The number of outlets for Washington state is from Rick Garza, the director of the Washington State Liquor Control Board; the number of outlets for Colorado is from the Department of Revenue 2016 Annual Report, (https://www.colorado.gov/pacific/sites/default/files/2016%20MED%20Annual%20Report_Final.pdf).

This report presents recommended research priorities prepared by the NIDA National Advisory Council on Drug Abuse Cannabis Workgroup (the Workgroup). It aims to respond to the changing landscape and growing challenges created by the liberalization of cannabis laws.

The Workgroup notes that the multiple subjects discussed within the body of this report require differentiation. There is the cannabis plant as a whole, which itself can be bred so as to increase or decrease concentration levels of various components. Then there are derivatives of the cannabis plant, such as oils and waxes. And, finally, there are specific individual components of cannabis, which can be either synthesized independently of the plant or derived chemically from whole cannabis. Each of these subjects have differing effects. Some are used by individuals for the intoxicating effects. Some are used for perceived medical effects. And some are used as prescribed for demonstrated medical benefits.

The document is organized into multiple topic areas, not all of which seemingly map neatly into the NIDA’s traditional mission. The Workgroup determined early on that it would not be possible to develop a single consolidated list of policy research priorities across topic areas. Instead, the Workgroup decided that it would be more productive to state priorities within each topic area. The Workgroup also decided early on not to let budget constraints—congressional appropriations to the NIDA—limit its thinking on policy research priorities, opting instead to identify research priorities independently of the question of resources to fund research—that is, policy should drive budget decisions, and not vice versa.⁶

WORKGROUP CHARGE

The Workgroup was formed in January 2017 to provide advice to Dr. Volkow and the NIDA on a policy research agenda to respond to the changing landscape and growing challenges surrounding the liberalization of cannabis laws. For purposes herein, the scope was taken to include research priorities related to the consumption of psychoactive cannabis in all its forms, both for perceived medical benefits (medical use) and for nonmedical use, but not the use of hemp for fiber, seed, oil, or other purposes that do not relate to the plant’s psychoactive effects.

The Workgroup charge includes being agnostic on the wisdom of efforts to liberalize cannabis laws. The intent is to inform the NIDA of the policy research gap it might seek to close and to advise on its perception of priorities pertinent to the NIDA’s mission to advance science on the causes and consequences of drug use and addiction and to apply that knowledge to improve individual and public health.⁷ The Workgroup’s charge permitted it to identify research priorities that might be more under the purview of other federal agencies.

⁶ Of course, the Workgroup understands that sometimes the congressional appropriations process will override an agency’s discretionary funding choices by “earmarking” or directing that certain resources be used for specific purposes.

⁷ See “NIDA’s Mission” at <https://www.drugabuse.gov/about-nida/strategic-plan/nidas-mission>.

Because cannabis policies are changing rapidly in many jurisdictions, the NIDA has an opportunity to set a research agenda to determine the effects (both positive and negative) of the psychoactive chemicals contained in the cannabis plant, the industry that produces it, and associated policies. As the Nation’s lead federal agency supporting scientific research on substance use and its consequences, the NIDA is well positioned to inform other federal agencies of the research gap that could be closed from a collaborative effort.

Workgroup members believe that the NIDA should collaborate with its federal partners—including the White House Office of National Drug Control Policy (ONDCP), the Substance Abuse and Mental Health Services Administration (SAMHSA), the Department of Veterans Affairs, and others—to support research that promotes public understanding of the necessity for an expanded cannabis policy research agenda. The goal of this collaboration would be to develop a federal research agenda that would prompt a range of public health studies to address all of the high-priority policy research gaps related to use and its consequences, industry structure, supply or availability, and policy. To be clear, the policy research gap is not just about matters affecting use (consumption) and its consequences. The research gap includes matters related to the effect of how the industry is organized (e.g., for profit firms versus state-owned monopolies), product type and availability, impact on public health, efforts to adapt prevention and treatment programs to address public health concerns, and other serious areas of consequences such as educational achievement, workplace productivity, and family and community stability.

The Workgroup’s charge provided it one year to complete its work.

Workgroup members undertook this endeavor with the perspective that many people do not believe cannabis is addictive or harmful. This means that the NIDA and its federal partners need to engage in a public education effort to better inform people about the risks of cannabis based on current scientific knowledge. This effort includes educating the public on the various types of cannabis products now available and on the likelihood that the effects (both positive and negative) will vary based on the type of product used, its route of administration, and the specific mix of cannabinoids found in the product.

WORKGROUP PARTICIPANTS

The Workgroup is composed of eight members, selected by the NIDA based on their extensive research experience on cannabis and familiarity with the NIDA’s research on the topic.

Workgroup members include:

Chair: John Carnevale, Ph.D.—Dr. Carnevale has over 35 years of experience in drug policy, criminal justice, and health care policy and program evaluation work with the U.S. government and in the private sector. He served for over 11 years at the ONDCP, where he directed the formulation of the National Drug Control Strategy and the federal drug control budget to implement it. Dr. Carnevale also conducted research at the Office of Management and Budget on drug policy budgeting and, together with his work in the White House, has served three administrations and four drug czars. Since forming his firm in 2000, Dr. Carnevale has developed

and managed an extensive portfolio of projects involving policy research and evaluation, public budgeting, strategic planning, performance measurement, economic impact evaluations, and local law enforcement agency reform. Dr. Carnevale has also worked as a public finance economist in the U.S. Department of the Treasury in the Office of State and Local Affairs. Dr. Carnevale holds a bachelor's degree in economics from the University of Maine and a doctorate in public finance economics from the Maxwell School at Syracuse University. Dr. Carnevale is currently a member of the NIDA Drug Policy Advisory Council.

Ken Mackie, M.D.—Dr. Mackie is a professor of psychological and brain sciences at Indiana University, Bloomington, Indiana (IUB) and an adjunct professor of anesthesiology at Indiana University School of Medicine. He is also the Linda and Jack Gill Chair of Neuroscience and the director of the Gill Center for Biomolecular Science at IUB. He received his M.D. from Yale University and completed his internal medicine internship in the Yale system and anesthesiology residency at the University of Washington. He did postdoctoral work at Rockefeller University and the University of Washington. For 15 years he combined an active laboratory research program with clinical care in anesthesiology at the University of Washington. In 2007 he was recruited to IUB as a Gill Chair. Dr. Mackie's research interests focus on understanding the relationships between cannabinoids (such as THC) and endocannabinoids and the pharmacological and physiological responses to both. Dr. Mackie is a member of several professional societies including the Society for Neuroscience, the American Society for Pharmacology and Experimental Therapeutics, the International Cannabinoid Research Society, and the American Society of Anesthesiologists. Dr. Mackie is currently a member of the NIDA Drug Policy Advisory Council.

Rosalie Liccardo Pacula, Ph.D.—Dr. Pacula is a senior economist at the RAND Corporation and a professor at the Pardee RAND Graduate School. She serves as director of RAND's BING Center for Health Economics and codirector of the RAND Drug Policy Research Center. Her research at RAND over the past 20 years has largely focused on issues related to illegal or imperfect markets (health care markets, insurance markets, illicit drug markets), measurement of the size of these markets, the impact they have on behavior (suppliers and consumers), and the effectiveness of policy interventions at targeting behavior within these markets. She was the lead investigator of several NIDA-funded studies examining the impact of marijuana liberalization policies (decriminalization, medicalization, and legalization) on marijuana use and public health. Dr. Pacula has been a member of the National Bureau of Economic Research since 1997, is the current vice president of the International Society for the Study of Drug Policy, is an assistant editor of *Addiction*, serves on the editorial board of several journals, and is a scientific reviewer for the National Institutes of Health's (NIH) Health Services Organization and Delivery committee.

Jonathan Caulkins, Ph.D.—Dr. Caulkins is a member of the National Academy of Engineering and has served on the faculty of Carnegie Mellon's Heinz College since 1990, with leaves of absence to be codirector of RAND's Drug Policy Research Center in Santa Monica (1994-1996), to found RAND's Pittsburgh Office (1999-2001), and to teach at Carnegie Mellon's campus in Doha, Qatar (2005-2011). He specializes in building systems models of aggregate societal outcomes related to

drugs, crime, violence, and terror and how policy changes may affect those outcomes. He has published over 150 journal articles and 11 books and monographs, including most recently a second edition of *Marijuana Legalization* (Oxford University Press).

Mark Ware, MRCP (UK)—Dr. Ware is a tenured associate professor of family medicine and anesthesia at McGill University and practices pain medicine at the McGill University Health Centre in Montreal, Quebec, Canada, where he is the director of clinical research at the Alan Edwards Pain Management Unit. He recently served as the vice chair of the Federal Task Force on the Legalization and Regulation of Cannabis in Canada. His research focuses on the safety, efficacy and effectiveness of cannabis and cannabinoids in pain and symptom management, and he has published over 90 peer-reviewed papers and six book chapters. He is the executive director of the nonprofit Canadian Consortium for the Investigation of Cannabinoids.

Stuart Gitlow, M.D.—Dr. Gitlow, immediate past president of the American Society of Addiction Medicine (ASAM) Board of Directors, is the executive director of the Annenberg Physician Training Program in Addictive Disease, which he started in 2005 to ensure medical student access to training that stimulates them to develop and maintain interest in working with patients with addiction. He served in the past as chair of the American Medical Association's (AMA's) Council on Science and Public Health. Dr. Gitlow serves as ASAM's delegate to the AMA. Board certified in general, addiction, and forensic psychiatry, Dr. Gitlow has an active addiction medicine practice. A graduate of the Massachusetts Institute of Technology and Mount Sinai School of Medicine, Dr. Gitlow's psychiatric and public health training took place in Pittsburgh, following which he went to Harvard for his forensic fellowship. Dr. Gitlow is on faculty at the University of Florida.

Deborah Hasin, Ph.D.—Dr. Hasin is professor of epidemiology at Columbia University. She directs the NIDA T32 Substance Abuse Epidemiology Training Program in the Department of Epidemiology in Mailman, and she directs the Substance Dependence Research Group at New York State Psychiatric Institute. Dr. Hasin conducts research on drug and alcohol use and substance use disorders in the general population and in specialized vulnerable groups. She has published over 400 papers. Dr. Hasin's current studies include the relationship of state marijuana laws to marijuana and other substances; time trends in drug and alcohol disorders in the United States; the validity of DSM-5 definitions of substance and psychiatric disorders in national and clinical populations; and randomized trials of the efficacy of interactive voice response and smartphone enhancements of brief interventions to reduce drinking and drug use. Dr. Hasin has participated in World Health Organization studies, served on the National Advisory Council to the National Institute on Alcohol Abuse and Alcoholism, and been a member of the American Psychiatric Association's DSM-5 Substance Use Disorders Workgroup.

Albert Terrillion, D.P.H.—Dr. Terrillion is the deputy director for Evaluation and Research for the Community Anti-Drug Coalitions of America's (CADCA's) federally funded National Coalition Institute. Dr. Terrillion is a health professional with over 20 years of experience at the local, state, and national levels. He has worked both in and with rural and urban communities in Louisiana, Virginia, and other states and territories. His work has included building partnerships

between health systems and community groups and supporting community use of data and evidence-based practices to improve health outcomes. He is originally from New Orleans, where he worked in academic translational research, community improvement, and health workforce training and prevention education. Dr. Terrillion led several local initiatives to support New Orleans' recovery from Hurricane Katrina. He holds a Doctor of Public Health from Tulane University's School of Public Health and Tropical Medicine and graduate degrees in education and organizational development.

The Workgroup received invaluable support from several NIDA staffers whose expertise and understanding of the NIDA's mission and programs greatly facilitated the Workgroup's process and progress. NIDA staffers include Dr. Susan Weiss, director of the Division of Extramural Research; Dr. Katia Howlett, deputy director of the Division of Extramural Research; Dr. Steve Gust, director of International Programs; Dr. Marsha Lopez, chief of the Epidemiology Research Branch within the Division of Epidemiology, Services and Prevention Research; and Dr. Eric Wargo, science writer in the Science Policy Branch within the Office of Science Policy and Communications. In addition, the workgroup would like to thank Dr. Lori Whitten, senior science writer with Synergy Enterprises, Inc., for her expertise in accurately capturing various workgroup discussions and deliberations to support the development of this report.

WORKGROUP PROCESS

The Workgroup process included multiple telephonic conference meetings and one in-person meeting, along with an ongoing discussion on several topics via email. The objective of the effort was to complete a report that would be presented to the Council, at which time Dr. Volkow and Council members would respond to the recommendations.

The first meeting occurred via telephone conference on February 16, 2017. At the beginning of the meeting, Dr. Volkow charged the group to try to answer the following questions: What are the most important questions that we should be addressing from a funding agency perspective? What are the policies that are likely to be the most effective at reducing adverse effects of cannabis use? What research programs could inform us of possible positive and negative effects that these policies might have?

The Workgroup decided that it would be constructive to start with a set of guiding principles to engage the process of developing a policy research agenda for the NIDA. These principles are outlined in the next section. These guiding principles were then used as the basis for the Workgroup's effort to identify research priorities.

Additional information to inform the Workgroup's priority-making recommendations was acquired through an in-person meeting in June at the NIDA. The group wanted to hear from individuals with real-world experience in implementing new cannabis policies to ascertain what information was needed to inform policy (and what knowledge gaps they felt were important to fill). Specifics about the insights and advice gleaned from the outside experts attending the in-person meeting are summarized in Appendix A in this report.

PRINCIPLES ADOPTED BY THE CANNABIS WORKGROUP

The NIDA Strategic Plan for 2016 to 2020 states that its mission is to advance science on the causes and consequences of drug use and addiction and to apply that knowledge to improve individual and public health care and its utilization. Mindful of this strategic mission, the Workgroup adopted principles to guide its deliberations to form recommendations for the NIDA's policy research agenda.

THE EIGHT PRINCIPLES

1. The NIDA's research mission is understood to be inclusive, flexible, and public health-oriented.
2. Research must be neutral about actions, laws, and policies set by any jurisdiction regarding cannabis.
3. Priority should be given to research that will remain germane under a wide range of policy frameworks.
4. Research should focus on behaviors and consequences that are associated with the greatest harms or benefits and the policies that ameliorate or exacerbate those harms.
5. Research should consider both short- and long-term effects.
6. Research should be sensitive to the realities of cannabis laws and policies.
7. Research should be sensitive to the realities of cannabis production, marketing, and use.
8. Research should acknowledge that, sometimes, large gaps can emerge between a law or policy as written and its implementation.

DISCUSSION

1. The NIDA's research mission is understood to be inclusive, flexible, and public health-oriented.

- The NIDA should interpret its mandate broadly to avoid leaving important topics unexplored if other relevant agencies are not stepping forward in time to inform the decisions that need to be made.
- Inclusivity means setting research priorities to understand how cannabis use, availability, and consequences affect public health and well-being across diverse populations.

For health research more generally, there is an expected division of labor, with NIH efforts being complemented by those of foundations, other agencies (e.g., Centers for Disease Control and Prevention [CDC], SAMHSA, and the National Highway Traffic Safety Administration—vis-à-vis drug-impaired driving) and multiple Institutes within NIH; however, not all these agencies have fully embraced their research responsibilities occasioned by the rapid changes in cannabis policy, products, production methods, marketing, and use.

2. Research must be neutral about actions, laws, and policies set by any jurisdiction regarding cannabis.

- Research should inform policy, programs, and practices at the local, state, and national levels concerning the rapidly changing patterns of supply,⁸ use, and legal status. The goal is not to produce evidence to make a case for or against any particular cannabis policy (medical, decriminalization, nonmedical, etc.). Right now, science is lagging far behind policy innovation.
- The most obvious form of policy research is evaluation of the effects of a jurisdiction having changed its policies; however, it would be a mistake to limit NIDA cannabis policy research to this one methodology, since no jurisdiction has yet implemented full commercial legalization at the national level; the effects of actions in one jurisdiction spill over on other jurisdictions, and the total effects likely will not fully manifest for at least a generation after implementation.
- Legalization, as the term is understood in the colloquial sense, is *not* assumed to be the Nation's policy moving forward. Indeed, there is enormous uncertainty at present as to what will be the nature of national cannabis policies a decade hence.
- Research should be sensitive to the public health impact of differing regulatory approaches, industry practices, and market models.

3. Priority should be given to research that will remain germane under a wide range of policy frameworks.

- Fundamental aspects of cannabis policy and laws are in flux, both domestically and internationally.
- The peculiar situation in the United States today of state-legalized systems operating in violation of federal law is not likely to be stable in the long run. Limiting research to today's policies will be of little value if the policies of tomorrow will be entirely different. Priority should go instead to uncovering insights that are likely to remain relevant even as the state and/or national policies evolve.

4. Research should focus on behaviors and consequences that are associated with the greatest harms or benefits and the policies that ameliorate or exacerbate those harms.

- Harms considered should include short-term consequences of acute intoxication as well as long-term consequences of sustained use. Harms should include those suffered by friends and family members, as well as the general public, not just those suffered by the user.

5. Research should consider both short- and long-term effects.

⁸ Workgroup members felt that it was very important for NIH and their partners to keep in mind all aspects of cannabis supply—cultivation, processing, disposal, distribution, warehousing, and retail sale, in addition to the products that different people in the supply chain are allowed to bring to market. Policies and regulations might develop targeting some parts of the supply chain, but not others, and that has implications on these markets. Product innovation, for example, has been particularly rapid in this industry, not unlike the alcohol and tobacco industry, but devoid of much regulation.

- Legalization can come in many “flavors,” and its long-term effects may not be fully observed for a generation or more.
- The possibility of long-term consequences does not take away from the need to know what happens in the short term that could lead to policy adjustments or modifications.

6. Research should be sensitive to the realities of cannabis laws and policies.

- Policy as implemented often differs from the letter of proposition, statute, and/or regulation in matter and timing. Looking at relationships between policy as written and outcomes can create model misspecification when implementation departs from written policy.
- Proper policy evaluation requires development of measures relevant for understanding policy implementation (e.g., interpretation of a policy by actors the policy targets).
- Passage of a law does not mean that the law is implemented the next day: time lags exist between passage of law and its implementation, and research on policy effects must be cognizant of this reality.
- Cannabis laws and policies are changing rapidly, so priority should be given to research that is unlikely to be rendered moot by those changes.
- When state policies allow for local discretion on implementation, then studies that assess local variation should be given greater weight than those that take the state as the unit of analysis.

7. Research should be sensitive to the realities of cannabis production, marketing, and use.

- Cannabis is consumed via multiple modalities including vaping, dabs, edibles, tinctures, and lotions, not just smoking (i.e., combusting).
- Prices have been falling and potency rising as policies have liberalized.
- Cannabis is often consumed with alcohol and/or tobacco, among other intoxicants.
- Like most legal and illegal intoxicants, the bulk of cannabis is consumed by the minority of past-year users who consume daily or near-daily. This, of course, can be the case for medical and nonmedical use. Harms are likely to be similarly concentrated in that subset of users, while benefits, if any, might be concentrated in other groups.
- Research questions can differ as a function of the motivation for use.

8. Research should acknowledge that, sometimes, large gaps can emerge between a law or policy as written and its implementation.

- Research must be sensitive to distinctions among federal, state, and local state laws— what is the domain of each of these jurisdictions and how might inconsistencies between them influence implementation in one. For example, the letter of a law in a state allowing a cannabis industry might be restrained by the federal government’s policies related to banking and large-scale cultivation. Similarly, local jurisdictions adopting a policy of nonenforcement or bans independent of the state influence the implementation of the state policy.

- Priority should be given to those areas of policy where there is a clear understanding of how a law is implemented and where the ability to effectively measure the impact of a specific policy within a given jurisdiction is relatively high.
- Policies do get refined and modified over time, and research needs to consider the extent to which these refinements and modifications influence the behavior, products, and outcomes being studied.

RESEARCH PRIORITIES IDENTIFIED BY THE CANNABIS WORKGOU P

This section of the report presents research priorities identified by the Cannabis Workgroup for the NIDA's consideration. It is important to note that the Workgroup did not feel it was possible to create one consolidated list of research priorities because of the difficulty in comparing the value of projects across topic areas. Instead, we found it more practical to state priorities within each topic area.

Guided by the eight principles discussed earlier, the Workgroup initially identified lists of ideas that fell into five broad areas: (1) Cannabis Use; (2) Epidemiology; (3) Health and Social Consequences; (4) The Structure, Behavior, and Conduct of the Industry; and (5) Prevention and Treatment.

The Workgroup notes that the following lists are not exhaustive, but are instead meant to provide advice, to prompt thinking and to further discussion on what we perceive to be the most pressing policy research topics. Also, these lists deliberately avoid proposing an agenda/role for the Food and Drug Administration (FDA), which does not conduct research and whose mission clearly differs from the NIDA's. However, given that so many states and individuals consider and treat cannabis as a drug and that the FDA also plays a key role in regulating tobacco, nicotine, and the safety of alcoholic beverages, we note that important and pressing questions about cannabis safety and (if considered a medicine) efficacy might potentially be addressed by the FDA. There are, however, enormously important and pressing questions about what the FDA's posture should be toward cannabis if it were legalized federally and, indeed even today, given that so many states have already chosen to legalize it for its perceived medical and recreational purposes.

Cannabis is a drug, so it ought logically to be governed by the Food, Drug, and Cosmetics Act. If the Controlled Substances Act is not being enforced, then there should be some other federal oversight and control, whether through the Federal Food, Drug, and Cosmetic Act or some other mechanism. There could be scope within the NIDA's research portfolio to fund research (e.g., international historical and policy comparisons) that would help inform those crucially important FDA decisions, but we judged that to be within the FDA domain and so did not address them here.

CANNABIS USE

The Workgroup quickly recognized that standardized measures of cannabis use frequency, amount, product form, administration method, and dose are most needed to gain a more complete understanding of use and its outcomes. It has proved useful for alcohol (and other substances). It helps people to be able to think in terms of a standard drink or dose, for purposes of measurement but also for self-monitoring, diagnosis, and conversations between physicians and patients who may or may not be struggling with misuse. Standardized measures for light, moderate, regular, heavy, and chronic use are needed that consider not just the recentness and frequency of use but also the form, amount, and, in particular, amount per use episode.

Measures of a standardized dose of cannabis in its various product forms (e.g., flower, edible, or extract) and modes of administration (smoking, eating, topical, vaping, or dabbing), and the extent to which a user might use multiple forms or products, are necessary to better understand exposure, intoxication, and impairment. However, owing to the range of different cannabis products, formulations, and forms, there is no comparable concept or measure for cannabis, and this lack seems increasingly problematic. Responding to that gap is a research priority.

The Cannabis Workgroup noted that past and present laboratory research is most often conducted using relatively low-THC cannabis.⁹ Yet, the cannabis products now emerging in markets include many items with much higher potency (flower products labeled as being up to 25 percent THC are routinely sold) and types with newer methods of administration (e.g., edibles and extracts, which can be vaped or dabbed as opposed to traditional smoking) that have the potential to deliver much higher doses of THC and other cannabis components than were available in the past. The Workgroup believes that research is needed to understand the continuum and the public health impact of these newly emerging products. The problem domain is no longer limited to a single drug (marijuana), but now includes a range of products derived from the cannabis plant. Likewise, the active chemicals of interest extend beyond THC, now including cannabidiol (CBD), terpenoids, and flavonoids.

The Workgroup discussed findings on the prevalence of youth cannabis use across a period of liberalization of cannabis laws. It noted that published studies of national data show that since 1991, youth marijuana use did not increase after the passage of medical marijuana laws compared to contemporaneous national trends derived from remaining states. In addition, over the past several years, youth cannabis use prevalence has not changed when viewed in the aggregate. Recent work published in *Pediatrics* demonstrates, however, that when youth are disaggregated into groups of those who ever tried cigarettes, ever drank alcohol, or never done both, cannabis use appeared to rise in all three groups over the same time period in which no rise is found when all youth are aggregated together. An explanation of the paradox of these apparent inconsistent trends was a point of much discussion, suggesting an area clearly worthy of additional research, which is highlighted below. The fact that such aggregate trends in use deviate from historical trends in perceived harmfulness and disapproval was also highlighted as a subject in need of more work. Ongoing monitoring of youth cannabis use and its influences is clearly an important research topic.

Workgroup participants agreed that generational or cohort effects regarding cannabis policy changes should be studied, as there is reason to believe that short-term effects of a policy may differ from long-term effects. Moreover, it may take time for some policy impacts to become manifest. Importantly, participants agreed that the health impacts on adults (apart from health impacts of driving under the influence of alcohol [DUI]), including older adults, are largely and mistakenly ignored. Currently, an increasing proportion of the public incorrectly perceives that

⁹ The NIDA cannabis supply has expanded in recent years to provide greater diversity and higher potency (either THC or CBD) products, but this still does not compare with what is already available through dispensaries and other state-legalized distributors.

there are no health concerns about cannabis use among adult users, even though adults are clearly at risk for cannabis use disorder/addiction, and the average age of onset for cannabis use disorder (21.7 years) is during young adulthood. Furthermore, many members of the public see cannabis as medicine and believe that it has positive effects not only for pain relief (which has a reasonable evidence base for efficacy of cannabinoids) but also for many other problems (e.g., to self-manage depression or anxiety) for which existing evidence on efficacy is either lacking or suggests potential harms rather than benefit.

The Workgroup noted that methods to study the impact of cannabis use on driving and in the workplace (and schools) and potential impairment are needed. This issue is complex, as it intersects with medical cannabis use. For example, researchers do not know if medical use affects work performance, how this varies by THC or CBD content, or how prior use affects current performance (productivity). Workplace performance issues include military recruitment and are particularly important for safety-sensitive professions where the safety of others is at stake (e.g., pilots, truck drivers, other drivers [e.g., taxi, Lyft, Über], train conductors, and airplane mechanics).

The Workgroup felt that one of the clearest opportunities for the NIDA to lead in research is in an effort to define standardized measures of cannabis use frequency, amount, product form, administration method, and dose. The feasibility of harmonizing measures within the international research community was discussed, and many agreed that it could be beneficial for expanding our shared knowledge on the public health and public safety concerns related to cannabis consumption. The Workgroup recognized the difficulty of developing such harmonized measures at this early stage given the disparate products and modes of consumption across nations. However, if harmonization is feasible, research on cannabis policy and the knowledge gleaned from policy experiments would be more generalizable and less confined to one nation's unique experience. Therefore, the Workgroup determined that the importance to policy research of developing standardized measures outweighed the difficulty associated with a successful outcome. It is simply too important a topic to be ignored.

The Workgroup offers the following recommendations presented in priority order for the NIDA's consideration regarding cannabis use:

1. Explore the possibility of constructing a standardized dose similar to that for alcohol (the standard drink), tobacco (a cigarette), or opioids (morphine milligram equivalents) for researchers to employ in analyzing use and for users to understand their consumption:
 - a) To what extent does potency (THC), mix of other cannabinoids present (e.g., CBD), amount consumed, form consumed (plant material, concentrate, wax, edible) and method of ingestion influence the notion of a standardized dose?
 - b) Can reasonable standards be developed to define standardized dose for a range of different cannabis products?
2. Establish standards for measuring cannabis intoxication and impairment:

- a) Society needs both objective and subjective measures of intoxication and impairment in order to assess policy effects, so early funding for their proper measurement is necessary:
 - i. Understanding whether there are clear dose-response relationships, or without such relationships, how to use standardized quantities of known products containing specific mixes of cannabinoids to measure intoxication and impairment for light and heavy users.
 - ii. Understanding how potency influences health and behavioral outcomes and may be modified by route of administration.
 - iii. Considering differences in these measured values and/or effects by gender, adult/youth status, polysubstance use/cannabis-only use, new user/existing user, and weight/body mass index.
 - iv. Understanding whether impairment is essentially a unidimensional construct, or whether cannabis can degrade one type of performance significantly, but not others, depending on the dose, mixture of cannabinoids consumed, time since use, duration and pattern of cannabis use, etc.
 - b) Research is needed on whether those who use cannabis only for medical purposes, those who use only for nonmedical purposes, and those who use for both purposes differ, including their quantity per occasion and frequency of use. Further, if possible, measures tailored to differentiate between medical and nonmedical use could be useful.
3. Conduct research on the relationship between cannabis and other drug use, such as alcohol, tobacco, or opioids (e.g., polydrug use, sequence of use, sequence of use sufficient to qualify as a substance use disorder), including:
- a) Understanding of concurrent use (same week or month), simultaneous use (same use session), and bundled (mixed within same product) use of cannabis, including blunts and vape pens (containing nicotine and cannabis extracts blended together).
 - b) The extent to which substitution or complementarity occurs at the individual and market levels in the short and long run, and its health and economic impacts.
 - c) The relative health harmfulness of cannabis compared to other substances along multiple dimensions.
 - d) Investigation of how policy changes influence use of cannabis and other substances.
4. Develop better ways of measuring levels and types of consumption (e.g., moderate versus heavy use). For example, while asking about number of days people used in the past month offers a more refined understanding than just asking about whether there was use in the past month, now that there are many types of cannabis products and most consumption is concentrated in people who report using daily or near-daily, additional questions should be developed, tested, and deployed to better characterize contemporary use patterns:

- a) Need to consider measurement in terms of amount per use episode and frequency of use episodes (per day, per week, per month).
 - b) How do these alternative levels of consumption change with amount and duration of use?
- 5. Determine whether there is a specific dose, i.e., a threshold, under which functional impairment does not occur and no detectable health risk is imposed for adults to use cannabis, and, if so, establishing that threshold and determining how this threshold can effectively be communicated to the public:
 - a) Is there a specific threshold in terms of acute use/effects, and is there a safe dose in terms of chronic use/health effects?
 - b) Is there a specific threshold/product for pregnant women or nursing mothers?
 - c) Is there a specific threshold/product for drivers?
 - d) Is there a specific threshold/product for people who operate machinery, or work in higher-risk workplace environments, and/or people whose work ultimately may affect the safety of others, and what *employer* rights or powers are needed (if any) in order for the employers to be able to guarantee nonusing co-workers a safe workplace environment and guarantee the public a lack of downstream harm?
- 6. Identify factors influencing product choice and mode of administration:
 - a) Identifying market, environmental, social, and individual factors correlated with current product choice/demand.
 - b) Understanding the prevalence of cannabis use modalities, including vaping, dabs, edibles, lotions, and others; methods of consumption; and the relative risk profiles (health and public safety) of each.
 - c) Understanding long-term relationships related to product choice; that is, is one form of cannabis product a “gateway” to others, perhaps others with greater health risks? Can vaping cannabis be a gateway to vaping nicotine, which could then escalate to tobacco smoking with all its health harms?
 - d) Evaluating the impact of policies that influence measurement of use of different products (singular use of specific products, use of multiple cannabis products, various modes of administration, self-reported use where use is legal).
- 7. Investigate what motivates people to use different cannabis products or specific modes of administration (e.g., high/low THC products, specific types of products):
 - a) What drives individuals toward different modalities, including vaping, dabs, edibles, tinctures, lotions, and others, and what are the relative risk profiles of each? What are the influences of perceived health risks, levels of intoxication, marketing, availability, age, social networks, or other motivations on cannabis use patterns?
 - b) Understanding differential use across demographic groups and for medical and recreational users and mixed-purpose users.
 - c) Are certain user profiles (e.g., medical users, recreational users, and mixed-purpose users) correlated with preference for a particular product type?

Epidemiology is the study of the distributions and determinants of health conditions in populations. Epidemiologic research on cannabis, therefore, includes understanding its current status and trends as well as the factors leading to its use and how its use leads to adverse or beneficial health and psychosocial consequences.

1. Conduct research to understand better the epidemiology and trends in cannabis use, frequent use, and cannabis use disorders and its criteria (also called abuse, dependence, or addiction). Currently, these criteria include tolerance, withdrawal, craving, use patterns reflecting impaired control, and continuing use regardless of potential or actual adverse psychological or medical consequences:
 - a) Develop a knowledge base on the risks for cannabis use disorders overall and among diverse populations is crucial to determining the potential impacts of policy on cannabis use and cannabis use disorders:
 - i. Research is needed on factors associated with the development of tolerance and withdrawal, on whether development of tolerance differs depending on route of administration, which cannabis effect is examined, and the relationship of tolerance and withdrawal to patterns of use of cannabis and other substances, and to other consequences of use.
 - ii. Research is needed to determine whether tolerance plays a role in transition from occasional use to long-term frequent or heavy use.
 - iii. Research is needed on experimental users, relatively naïve users, long-term frequent users, and those falling between these extremes on multiple types of harmful outcomes, including motor vehicle crashes, workplace accidents, etc.
 - iv. Research is needed to develop a better understanding of the relationship between cannabis use and cannabis use disorders, other substance use disorders, and other psychiatric disorders (including affective, anxiety, and psychotic disorders).
 - v. Research is needed to determine whether new products that become available in legal markets influence the epidemiology and risk of cannabis use disorders (e.g., high versus low THC products, and vaping or dabbing versus smoking).
2. Expand information sources about use, impairment, and its consequences:
 - a) Building epidemiological tools to better detect use and consequences (e.g., to include health records, prescription drug monitoring program data,¹⁰ registries, databases).

¹⁰ Prescription drug monitoring programs are state-run electronic databases used to track the prescribing and dispensing of controlled prescription drugs to patients. They are designed to monitor this information for suspected misuse or diversion (i.e., channeling drugs into illegal

- b) In light of the federal prohibition on use, refining and improving self-report tools on use, impairment, and consequences (e.g., drug DUI, including cannabis; better ways of enabling users to accurately report quantities consumed per day of use).
 - c) Using social media to track emerging trends in use, patterns of use, product forms and brands, and sales, including addressing privacy concerns in social media research.
3. Study differences in patterns of use across jurisdictions with different policies and the effect of greater availability in one jurisdiction (including Canada) on use in adjoining jurisdictions.

HEALTH AND SOCIAL CONSEQUENCES

Very little is known about the health and social impacts of the changing landscape around cannabis reform. The Workgroup noted that there is more research to be done on how cannabis reform may affect cannabis use and vehicle crashes, accidents, and other risky behaviors given limited information on, and useful metrics for, cannabis intoxication and impairment. Similarly, more work is needed to understand how cannabis reform affects workplace performance, health, and safety.

The Workgroup also was concerned that the public's perception about the lack of health concerns could translate into a serious problem with regard to driving and impairment. There was agreement among Workgroup members that individuals impaired from cannabis use should not drive—however, the public does not have an understanding of what impairment entails and what it means for DUI. A better understanding of impairment is necessary to protect the public health and safety from cannabis DUI. State regulators are in immediate need of information about the relationship between cannabis impairment and vehicle crashes and injuries, as well as injury involving pedestrians, including the relative success of various laws and policies designed to limit such risks.

Where legalization is occurring, regulators are also being pressed for policy guidance regarding the workplace, particularly as it pertains to critical safety positions. The Workgroup identified the following areas where research is most needed to inform policy:

1. Develop effective roadside tests for cannabis impairment that can be practically deployed by law enforcement. This priority is urgent. It should be pursued in a way that gets useful devices or strategies deployed in the field as rapidly as possible.
2. Determine the prevalence of and factors related to cannabis use (in its various forms and potency) and cannabis-involved crashes, other types of injury or property damage, adverse health events requiring medical attention, and other risky behaviors. This priority would include, but not be limited to, topics such as the simultaneous use of cannabis and

use), and they can give a prescriber or pharmacist critical information regarding a patient's controlled substance prescription history. This information can help prescribers and pharmacists identify patients at high risk who would benefit from early interventions.

- alcohol or of cannabis and tobacco, and how cannabis use modifies or is modified by other demonstrated risk factors.
3. Assess the impact of cannabis use on human capital development. There is a critical need to develop more knowledge on:
 - a) Effects of different patterns of short- and long-term use on brain development, educational attainment, grades, test scores, high school completion, and typical transition from school to work (done at a younger age/after college).
 - b) Presenteeism/absenteeism/tardiness (school and work).
 4. Understand the effects within the family, including:
 - a) The effects of maternal cannabis consumption during pregnancy and breastfeeding.
 - b) Neonatal and birth (perinatal) outcomes.
 - c) How cannabis initiation and use, youth and adult, affect family sustainability (neglect, need for foster care, family stability).
 5. Expand information sources on neurological, cognitive, and physical health impacts:
 - a) Development of information systems to capture adverse events associated with medical use (e.g., side effects) and nonmedical use (e.g., poisonings). (See Epidemiology.)
 - b) Research is needed to understand dose-response (and route and form of administration) relationships between consumption of specific products and specific physical health (e.g., respiratory illnesses, cardiovascular, cancers, immune system issues), mental health (depression, psychoses, schizophrenia), and behavioral health effects (apathy, motivation, etc.):
 - i. Tying neurological and cognitive assessments to use of components contained within cannabis (THC, CBN, CBD, etc.), focusing on most common combinations consumed/sold.
 - ii. Examining confounding variables on cannabis use and outcomes.
 - c) Effects associated with increased victimization (impaired individuals are more likely to be victims of crime, sexual abuse, and so on).
 6. Research health consequences of cannabis use above and beyond those caused by the cannabis itself—it is widely understood that tobacco smoking causes health harms in ancillary ways, such as fires. Likewise, injecting drugs can cause harms (such as spread of HIV/AIDS and hepatitis) that do not directly involve the drug per se. There are parallel concerns with cannabis that have been neglected and should be a research priority:
 - a) Cannabis production usually involves the use of pesticides and, at present, there are no federal guidelines as to which, if any, are safe. What are the toxic effects of ingestion of these pesticides or the pyrolyzation byproducts of burning pesticides?
 - b) Should there be differential quality control standards for different subpopulations (e.g., cannabis is used for perceived medicinal benefits by people with HIV/AIDS—inhaling molds can have different effects on people who are immunocompromised than on healthy subjects).

- c) What risks are posed by the manufacturing processes used to create extracts, such as residual butane left in butane hash oil extraction products?¹¹ Is supercritical carbon dioxide extraction sufficiently safe so that regulations should require carbon dioxide extraction?
- d) What risks are posed by vaping pens, (e.g., exposure to heavy metals that can be inhaled when parts of the pen are heated to high temperatures during their use)?

THE STRUCTURE, BEHAVIOR, AND CONDUCT OF THE INDUSTRY

It is generally understood that a comprehensive research program addressing tobacco-related health harms should extend beyond tobacco use, epidemiology, and social consequences to encompass research on the tobacco industry itself. This same understanding applies to the alcohol industry. Therefore, it stands to reason that cannabis research should include the study of the cannabis industry, as well.

Industry behavior can be expected to affect use and misuse. That is most obvious for pricing, since price is known to affect use, but also pertains to myriad other aspects of industry behavior. For example, the number and type of retail outlets have been found to affect consumption of other goods, including alcohol, so it may likewise affect cannabis sales and use.

These effects make studying industry practices important in their own right, to help regulators make prudent decisions to protect public health. For example, if the marketing of certain types of cannabis products is associated with greater incidence of problems (such as dependence, impaired driving, or child poisonings), that would be a basis for regulating or restricting those types of products or practices.

Documenting industry practices and assessing their effects are also necessary because any attempt to understand trends in cannabis use should seek to control for changes over time and across space in modes of distribution and other industry practices. It is important to disentangle whether changes in incidence or prevalence represent fundamental shifts in demand or if they are the byproducts of industry actions.

It would be very inefficient to expect every health researcher interested in studying the industry to develop systematic information on retail availability, marketing, product mix, and price—among other industry behaviors—in all jurisdictions over time just as a prestep to their ultimate analysis of, for example, how prevention messages do or do not affect use. The measurement of these controls would be better done as a concerted effort, with the results made available to all in a convenient format rather than having each research team reinvent that wheel (and perhaps do so in slightly different ways that undermine comparability across studies).

¹¹ Butane hash oil extraction refers to a type of cannabis extraction that produces products that have names such as wax, shatter, honey, whip, and budder.

Customarily, attention focuses on what might be termed “tactical questions.” But they can also be raised and are perhaps even more important with respect to structural decisions concerning who is allowed to play what roles in supplying cannabis legally. So far, all the U.S. states that have launched state-level production for nonmedical use have adopted just one model, namely, entrusting production, marketing, and distribution to a for-profit industry. There are many other models, including restricting supply to nonprofits, co-ops (“cannabis clubs”), for-benefit corporations, and government or government-controlled authorities. The choice of “architecture” could matter for various outcomes, has largely been ignored, and yet could be studied, both by making comparisons across countries that follow different models and by drawing comparisons with other substances (e.g., alcohol and tobacco) and behaviors (e.g., gambling).

For convenience, we divide recommendations within this broad area into four categories.

1. Research retail sales, promotion, and marketing (how products are sold and how they get marketed)—The state-legalized cannabis industry is new and evolving, and regulators lack evidence to guide how its many products and practices should best be regulated to protect the public health. The Workgroup identified a list of research areas where more knowledge could be of immediate benefit to regulators:
 - a) Viability and effectiveness of efforts to restrict industry’s marketing efforts in ways that shield youth and other vulnerable populations from being targeted.
 - b) Feasibility and implications of allowing or banning certain forms of promotions:
 - i. Promotion of products at events (e.g., sports, concerts), in movies, via celebrity endorsements, etc.
 - ii. Product placement in stores (e.g., analogs to “power walls” of tobacco products, whether THC-infused candies can be sold near traditional candies, when and where cannabis can be sold outside cannabis-only stores).
 - c) The implications of restrictions on packaging (limiting products to plain packaging to avoid glamorizing brands, requiring products to be sold in child-safe containers, imposing maximums or minimums on quantities in a package (e.g., limiting the amount of THC in a single candy bar to reduce the risk of overdose).
 - d) The implications of imposing various rules concerning labeling of potency and other aspects of cannabinoid content.
 - e) Implications of where products can be consumed (i.e., on-site consumption versus off-site consumption; in public view or only in private spaces; in places with only adults or adults plus youth, such as restaurants).
 - f) Implications of where products can be sold (grocery stores, liquor stores, convenience stores), retail sales outlet density, allowance of delivery services to home.
2. Research taxes and prices:
 - a) Excise taxes are arguably the single most important lever in tobacco and alcohol policy. It is already known that consumption falls when prices rise, although the extent of price responsiveness is not fully clear. That implies interest in:

- i. Measuring the price of cannabis products, even in illegal markets.
 - ii. Estimating the elasticity of demand (by market segment and product type).
 - iii. Understanding how much tax evasion and/or purely black market supply would accompany different rates and types of taxes (e.g., it might be easier to collect a given tax at the producer than at the retailer level). Tax avoidance is an important issue with tobacco, and cannabis may be even easier to source from distant, low-tax locations because it has a much higher value-to-weight ratio.
 - b) There are many ways of taxing cannabis production and sales (e.g., ad valorem versus weight-based or THC-based taxes), and taxes create incentives that can distort sales and use patterns. For example, a weight-based tax (e.g., \$100 per ounce) might encourage sale of higher-potency products to reduce the effective tax per hour of intoxication or per unit of THC consumed.
 - c) Minimum pricing rules are another way to limit price declines and ensuing effects on consumption that merits study.
 - d) Studying the effects and possible regulation of coupons, sales, give-away promotions, happy hours, etc.
 - e) Industry adapts to taxes; that is part and parcel of the notion that taxes can distort market outcomes. There are many ways that this could happen with cannabis, including selling it as a loss leader, bundling it with other products (e.g., cannabars charging a high cover charge but then selling cannabis below cost), and frequent buyer clubs with membership fees, etc.
3. Research the effects of alternative business models for retail distribution for both medical and nonmedical products:
- a) Most states that have legalized cannabis allow brick-and-mortar stores for medical and for recreational products, but deciding who gets to sell is a (potentially very important) policy option, not a requirement for legalization.¹² Canadian provinces will default to a mail-order delivery model in provinces that do not design a brick-and-mortar distribution system by July 2018. And stores can be stand-alone (as at present), or sales can be in general-purpose grocery, convenience, and other stores (as with beer in many states). There is likely to be considerable variation in retail models between Canadian provinces and territories, which may present a sort of “natural experiment.” There are likely very important public health consequences of those choices, and they have not been adequately investigated.
 - b) Given existing results for other substances, including alcohol, one might expect that the existence and number of outlets, density of outlets, and location and types of outlets (cannabis only, cannabis plus other products; on-premise versus

¹² Early drafts of Canada’s law allow mail-order delivery and provincial retail options; Uruguay will permit sales through pharmacies, but not stand-alone stores.

off-premise consumption, etc.) will affect patterns of use and misuse, but research on those effects is not sufficient to provide solid guidance to regulators.

4. Research the effectiveness of alternative regulatory models for public health and public safety, to include topics such as:
 - a) The markets for medical cannabis vary markedly across states. It is unclear which model(s) are most consistent with the public health interest or how the viability of these models might be affected by legalization of production for nonmedical use.
 - b) What are the benefits, risks, and other consequences of combining regulatory authority over medical and recreational cannabis into a single regime?
 - c) The FDA has not been enforcing provisions of the Food Drug and Cosmetics Act (FDCA) against state-legalized cannabis industries, perhaps because all such activities remain illegal under federal law. What are possible implications for the FDA, the industry and public health if the FDCA was enforced?
 - d) What lessons can be learned/best practices adopted from alcohol and tobacco regulatory models in order to promote public health and safety?
 - e) What barriers exist to importing those lessons (e.g., the absence of a parallel to the 21st Amendment’s granting states special powers over alcohol commerce relative to general limitations under the Interstate Commerce Clause, or the difficulty negotiating something like tobacco’s Master Settlement Agreement given the fragmentation of the cannabis industry)?
 - f) What are model regulatory frameworks and practices? Much of the cannabis policy literature lives at a fairly high level of abstraction, contrasting, for example, legalization with decriminalization, or it delves into tactical matters (how far stores should be from schools). Yet there are an enormous range of different “architectures” for legalization, and within any given architecture there are myriad regulatory decisions that collectively may be of great consequence.
 - g) What are necessary and effective steps to prevent industry-capture of regulatory bodies and processes?
 - h) The implications of monitoring medical cannabis “recommendations,” perhaps in a manner similar to prescription drug monitoring programs. Possible research issues include:
 - i. Document and describe the types and quantities of cannabis that budtenders or others recommend for various patients and conditions.
 - ii. Study such data to shed light on what products/forms are frequently recommended for particular medical conditions, and where data become available, to include products/forms recommended by physicians and dispensary clerks.

PREVENTION AND TREATMENT

The changing landscape concerning the legal and regulatory status of cannabis increases the need for research about innovative strategies to address cannabis misuse. In particular, different tactics and messaging strategies may be needed for a substance that is increasingly seen as not

risky and that is widely described as being useful for its perceived medicinal purposes. Likewise, to the extent that cannabis transitions to a legal drug, the government will have to decide whether the prevention message for adults is don't use (as with tobacco) or use prudently (as with alcohol) and how to ensure that use by youth is discouraged. In addition, the government will have to decide how best to manage the possibility of a growing demand for treatment of cannabis use disorders. At present, limitations in the research make it difficult to approach these crucial choices in an evidence-based manner.

The Workgroup believes that prevention science about topics such as risk and protective factors will need to be refined to account for changes in cannabis laws—that is, new research on prevention approaches to complement community strategies that speak both to local conditions and broader population health considerations. Perhaps more fundamentally, the tactics and curricula that proved effective in the past, when cannabis was uniformly illegal and more stigmatized, may no longer work, and new approaches may need to be tested and developed. Additionally, policy itself can be a prevention intervention, depending on its structure and implementation, which means that disparities in laws and regulations must be studied to learn how they impact initiation and problem use.

Similarly, the changing cannabis policy environment will also likely impact our treatment needs, as research has clearly documented a rise in near-daily use of cannabis over the past two decades. In addition to a potential rise in problematic use, there will be other system impacts on our treatment infrastructure. Because of prohibition in the states, many people have been channeled to treatment through the criminal justice system for simple possession offenses, some of whom have no real underlying cannabis use disorder. Cannabis liberalization policies at the state level will change the composition of those who are referred to treatment within the state, and might suggest the need for new treatment programs to better address the population now gaining access to treatment. Treatment of cannabis use disorder remains a challenge, though research has demonstrated that behavioral interventions, such as motivational enhancement therapy, cognitive behavioral therapy, and contingency management, may help reduce use and the negative consequences associated with use.

With all of this in mind, the Workgroup identified the following areas as priorities:

1. Design and develop the most effective prevention strategies, messages, and materials suitable for cannabis in this new context for all audiences that are:
 - a) Cognizant of cannabis products/methods of consumption with differing levels of potency and components (e.g., CBD), effects on tolerance, risks of misuse and use disorders, and other health and safety consequences.
 - b) Cognizant of what we still do not know about cannabis and its harms.
2. Design and develop more effective, broader community/environmental prevention approaches through public policy (e.g., limiting outlet density, limiting use in public, higher taxes).
3. Develop an evidence base for treating cannabis use disorders and addiction, and develop recovery support that encompasses behavioral and pharmacological interventions.

4. Invent and assess the effectiveness of prevention strategies that target social norms and accidents/risky behaviors, such as media education and other broad research information dissemination strategies (e.g., Lower Risk Cannabis Use Guidelines, *American Journal of Public Health*, 2017). For example, is there an effective cannabis analog to “Friends don’t let friends drive drunk”?
5. Develop effective regulations that limit the impact of cannabis advertising on use, particularly among children and other vulnerable populations:
 - a) Types of advertisement allowed (print, billboards, newspapers, radio, television, the internet).
 - b) Exposure through social media.
 - c) Visible in public places (public transportation, malls, parks, etc.).
 - d) Content allowed/requirements (warning labels).
 - e) The value of enhanced enforcement of laws prohibiting sales and dissemination to minors.
6. Improve the efficacy of cessation efforts that occur outside of the formal treatment system to curtail the progression of drug use from light use to problem drug use.
7. Explore the effect of higher-potency cannabis and increased availability of (and exposure to) cannabis on treatment need, models, and outcomes.
8. Assess the extent to which our current cannabis treatment programs meet the needs of and effectively treat the changing population entering treatment.

CONCLUSIONS

The Workgroup believes that scientists and public health experts need to determine how to galvanize interest among the federal government and Congress for funding cannabis research. There is a great need for scientific research on cannabis that informs policy and regulation of the drug, as regulators have to make many decisions about cannabis, and, by their own testimony, they are currently “winging it.”

In addressing the research priorities identified above, the Workgroup understands that building public support for research may be difficult, because most people believe cannabis is safe for adults. For example, while it appears that there is widespread agreement on the negative consequences of cannabis use during adolescence, most people do not see health or social problems with adult use (apart from DUI). It is critical for the public to have plain-language and accurate information on the addictiveness of cannabis. It is also important for the public to have access to knowledge about both the short- and long-term effects of policy changes. Legalization can come in many flavors, and its long-term effects may not be fully observed for a generation or more. The possibility of long-term consequences does not take away from the need to know what happens in the short term.

Mechanisms are needed to study the longitudinal effects of cannabis on health and public safety. Research priorities in this area should have value over the long run and should include the following areas of focus: the biological effects of chemicals in cannabis, the ways that the industry acts to influence policy, and patterns of use among heavy users (those roughly 20 percent of users who use the majority of cannabis) and light users (those remaining individuals whose use is infrequent and seemingly much less problematic). And there is a need for more knowledge about cannabis consumption methods, especially potency and dosing.

As is the view of the state’s regulators, the Workgroup views research on cannabis as a federal government task to fill the national knowledge void around cannabis reform. The Workgroup understands that states and consumers need objective information on the effects of medical cannabis. Patients need to know that cannabis includes a wide range of products, with various cannabinoid ratios. Internationally, there is a paucity of randomized controlled trials on medical cannabis (which can be challenging to conduct, given the difficulties with administrative requirements, complex formulations, placebos, and blinding). Researchers need to test high-CBD products for medical use. Given its standing in the federal research community, the NIDA can lead a national research agenda that will inform policymakers, the public, and consumers about the effectiveness of reform and its social and economic impacts.

As a final thought, the Workgroup believes that it would be valuable to have the NIDA work in concert with the CDC, SAMHSA, ONDCP, and others to support a systematic effort to inform and be informed by state policymakers and regulators about their experiences in implementing policy reforms. This would include meeting with states that are now addressing cannabis law reform for purposes of delineating challenges, lessons learned, and unintended consequences from their experiences thus far.

APPENDIX A: THE JUNE 5, 2017, IN-PERSON MEETING

The in-person meeting occurred on June 5 at the NIDA. In selecting presenters for the in-person meeting, Workgroup members wanted to hear from individuals from states with experience in having to establish cannabis regulations. Such individuals have dealt with the challenge of implementing regulations using the limited knowledge that research has to offer thus far. Thus, they would be sensitive to research gaps. The two states with the most experience with both medical and nonmedical (or recreational) cannabis were Washington and Colorado.

Given that the liberalization of cannabis policy is not confined just to the United States, the Workgroup sought an international perspective and asked Dr. Mark Ware to discuss Canada's experience. Developments in Canada are of particular importance given the long shared border and extensive cross-border commerce and transit.

In addition, the Workgroup received written information from a list of research questions relevant to cannabis policy developed by Karen Smith, director of the California Department of Public Health, who was invited to present but could not attend the meeting.

The two individuals external to the Workgroup who made presentations were Rick Garza, director of the Washington State Liquor and Cannabis Board, who leads the development and implementation of cannabis regulations in Washington state, and Andrew Freedman, now with his J.D. and with Freedman & Koski, Inc., Colorado's director of Marijuana Coordination for Governor John Hickenlooper. As was previously noted, Dr. Ware, from McGill University, is a member of the Workgroup and background information on him is presented above.

WASHINGTON STATE PERSPECTIVE AND LESSONS LEARNED

Mr. Garza described the historical context for cannabis policy in Washington state. He noted that the author of the initiative to legalize cannabis production and use did not confer with the Washington State Liquor Board (which eventually was given the authority to regulate the drug) when developing the initiative (I-502), which meant his office could not begin its work until after the initiative was approved by voters.

Mr. Garza reviewed the timeline of cannabis-related policies in Washington state. I-502 passed in November 2012. Adult use and possession of amounts suitable for personal consumption became legal on December 1, 2012. Commercial production and sale required licenses, and the Liquor and Cannabis Board had until December 1, 2013, to establish the licensure system. The first producer license was issued in 2013. Retail stores opened in July 2014, and the medical and recreational cannabis markets were integrated starting July 1, 2016. The number of retail outlets and the hours of operation are limited, as is the advertising for cannabis products. Retail cannabis outlets may sell only that drug (alcohol co-sale is not permitted). For consumer safety, there are some restrictions on edible cannabis products that would especially appeal to children. Mr. Garza noted that Colorado also passed its law permitting recreational use at the same time

as Washington state did and that his office often looked to Colorado for guidance. Mr. Garza also stated his surprise that his office could not find regulation models for cannabis in Europe.

Mr. Garza reported his surprise that youth prevalence in Washington state so far seems unaffected by the changing landscape. He reported it as a paradox about what research would predict for prevalence in light of a deterioration of risk factors that correlate with increased use. He indicated Washington state's 2016 survey data show that among high school students, past-30-day cannabis use is static or has fallen from previous years. Yet, perception of cannabis risk has decreased. These data counter historic relationships between these two variables. Perhaps the paradox is explained by the fact that underage users have always been able to easily obtain cannabis if it is illegal. National data from Monitoring the Future show that cannabis use among high school students is flat, perceived harmfulness has fallen, and perceived availability has reached a plateau.

Regarding the charge of the Workgroup, Mr. Garza offered insight into gaps in policy research that complicated his work and remain of critical importance. The following topic areas were highlighted:

- *Cannabis use*—Research is needed about cannabis consumption methods, particularly in regard to the potency and dosing of extracts and concentrates.
- *Cannabis product potency (particularly for concentrates)*—Should there be a limit on cannabis product potency? This question is particularly important given reports of increased emergency department visits and psychological and behavioral consequences (e.g., panic attacks).
- *Pesticide use when growing cannabis*—What are safe levels of pesticide use? Mr. Garza thinks that safe pesticide use should be a federal public good; in other words, the U.S. Environmental Protection Agency should provide guidance on this topic, but such guidance is unavailable. Eventually, Washington used Oregon's list of prohibited pesticides. Issues have emerged with the standards and independence of Washington state laboratories that test cannabis for pesticides. Recently, Washington state decided to conduct its own pesticide testing through a contract with its Department of Agriculture, rather than using independent laboratories, because those facilities were being scrutinized by the industry for lack of consistency in their testing. The Department of Agriculture will do the testing and certify laboratories. Now that there is random testing of all cannabis producers, Washington state is finding pesticides that are not on its approved list, along with others that should not be used.
- *Blood levels for driving under the influence (DUI)*—How does cannabis use affect driving? Currently, the DUI threshold in Washington state is 5 nanograms/milliliter. Medical cannabis patients have testified about the level being too low. Washington (and other states) do not know how to recommend safe use, because they do not know the definition of safe use. More information is needed about the appropriate level for cannabis DUI; and there are no standard units of cannabis (akin to the "standard drink"), which compounds the problem.
- *Cannabis possession limits*—Are possession limits too high for various types of cannabis products? Should there be different limits for recreational versus medical use? In Washington state, medical users can purchase three times the upper limit for recreational

use, which is 1 ounce at a time per retail outlet. However, recreational users can continue buying from multiple stores to exceed 1 ounce.

- *Cannabinoids besides THC and CBD*—Research thus far has focused on THC and CBD. Are there other cannabinoids that states should be aware of, and, if so, what limits should there be on these?
- *Edibles and concentrates*—How should states handle edibles and concentrates? In Washington state, cannabis edibles or infusions cannot be given or marketed to children. No more than 10 milligrams of active THC per serving in edible cannabis products can be sold. Cannabis packaging must bear warnings about the product. Washington state has a committee (comprising a public health officer, enforcement officer, licensing director, and rules coordinator) that looks at cannabis product marketing and does not allow packaging that is especially appealing to children. Resealable packaging standards were developed with the poison control center.
- *Health effects (positive and negative) of cannabis*—A balanced research approach is needed on the health effects of cannabis, with attention to both the potential benefits and the negative consequences. Organizations can lose credibility when they present only one side. Regulators need to know the potential benefits of cannabis (e.g., for pain relief). It is critical for the public to have plain-language information on the addictiveness of cannabis, because, currently, most people do not believe it is addictive.
- *Social consequences of cannabis use*—More research is needed on the impact of cannabis on diverse populations. In Washington state, the prevalence of cannabis use among high school students with differing race/ethnicities (Hispanics, Blacks, and Native Americans) is higher than that of alcohol. The cigarette and alcohol industries target ethnic populations. Is this also true for cannabis?
- *Home growing of cannabis*—Are home grows a good idea? Washington state does not allow home growing, and it is the only state to implement this policy. There is demand for home growing for personal use among the public, but many issues arise from this policy (e.g., diversion into the black market). Medical patients can grow cannabis for themselves or in a cooperative. (Mr. Freedman, whose presentation is discussed next, noted that Colorado is rolling back home growing (from a limit of 99 to only 12 plants), as it was associated with crime and violence.) There is concern that homegrown cannabis is being diverted out of state for sale on the black market.
- *Advertising restrictions and prevention*—How effective are restrictions that prohibit advertising close to places where children are present (e.g., schools and playgrounds)? How can such effectiveness be measured? Currently, enforcement of this regulation is random. The public was upset about cannabis advertisements, so Washington state recently passed a bill to limit billboards to advertising of the cannabis business only (not its product). The impact of this law warrants study.
- *Taxes, pricing, and sales*—How should states structure tax regimes? And should those tax regimes be structured to ensure competition with the illegal market? In Washington state, the specific tax on cannabis is 37 percent. Other standard taxes (e.g., sales tax and local excise taxes) also pertain, so that the total level of taxation is 47 to 50 percent. A gram of

cannabis sells for about \$8, compared with the current black market price of \$9 to \$11/gram. People predicted that this high level of taxation for the legal product would have no impact on the black market. Mr. Garza reported that those predictions were incorrect. The cannabis industry argues that the tax is too high. Sales figures in the state have been higher than expected (about \$1.3 billion). Mr. Garza asked if there should be pricing minimums, as there are for alcohol?

Mr. Garza added that Washington state conducts compliance checks to ensure that its cannabis retail outlets (1,800) do not sell to underage individuals, as it does with alcohol licensees (18,000). The compliance rate for cannabis (92 percent) is better than that for alcohol outlets.

As a final note, Mr. Garza noted that the Washington State Liquor and Cannabis Board is funded at \$8.7 million this year, and it has 140 officers statewide to check alcohol, tobacco, and cannabis retailers' compliance with policies. This is a relatively high level of staffing, but there are not enough resources to do the job. States will need to know optimal staffing levels to make their jobs (enforcement of regulations) more meaningful and effective as this new industry emerges.

COLORADO PERSPECTIVE AND LESSONS LEARNED

Mr. Freedman reviewed key contextual information regarding cannabis policy and made some assertions about the state perspective on the credibility of research to inform state regulatory policy. He began his presentation by discussing two major challenges facing the federal research agenda for it to become a credible resource or knowledge base if it is to influence state cannabis policy.

1. *"Anecdotes trump science on every level of discussion"* in the cannabis policy conversation, as people do not consider federally funded research to be credible, particularly with respect to medical use. The testimony of medical cannabis patients about the benefits of the drug is more powerful than any science report. Adding to this mistrust is the fact that predictions of deleterious outcomes from legalization did not materialize. At this point, the challenge for the research community is overcoming public opinion that perceives the plural of "anecdote" to constitute evidence-based research.
2. *"Everything is innocent until proven guilty, except pesticides."* When it comes to cannabis products, it is assumed that if there is no evidence that something is harmful, then it is presumed to be harmless. Because the federal government has not revised cannabis policy, states innovated. Pesticides for growing cannabis are a different matter, and the assumption should be that they are harmful until proven safe for humans.

In addressing the charge to the Workgroup, Mr. Freedman stated that states would benefit from research on the different types of cannabis and cannabis products and the effects of dose levels. Although they are difficult to determine, variety and dose are critical components to consider. In addition, he noted that in Colorado, there is much more concern about obtaining knowledge

about the impact of cannabis use on naïve users and youth than on long-term adult users. Legislators are simply not focused on long-term adult users.

Mr. Freedman also reported that, as is the case in Washington state, youth cannabis use after legalization has not changed. Mr. Freedman presented survey data indicating that there has not been a statistically significant increase in youth cannabis use since Colorado legalized recreational cannabis for adults. However, there is a credibility gap, as shown by criticism of the state when it did not report *nonstatistically significant* increases in youth use. Demands to report nonstatistically significant increases put states in a difficult position, as releasing this information might reduce public attention to actual rises in youth cannabis use prevalence in the future. There will undoubtedly be generational effects on youth cannabis use that depend on advertising regulations, normalization of use, and other factors. Participants agreed that these issues have been perennial in the area of youth substance use.

In terms of specific research questions that would be of value to states, Mr. Freedman highlighted the following areas:

- *Is cannabis a substitute for or complement to other drugs?* It is important to determine this scientifically, as legalization advocates argue persuasively that opioids, alcohol, and tobacco are much worse than cannabis. They also claim, without data, that cannabis is a substitute for alcohol. Whether this is true or not should be answered empirically.
- *What is the best way to detect and enforce prohibitions on polydrug use while driving?* In Colorado, 5 nanograms/milliliter of cannabis is the legal limit for driving. To be charged with DUI, drivers also must fail an on-street sobriety test. This method of determining DUI works at the moment, but polydrug use is more problematic. Policymakers need research on how to enforce DUI in the case of polydrug use. Any technology developed to identify impaired drivers must be easy to use on the roads and be able to withstand court scrutiny.
- *What are the relationships among cannabis taxation, advertising, price points, and use disorder?* Currently, policymakers are guessing about the effects of these factors on cannabis use disorder. Legislators are persuaded by the argument that problematic use is equivalent to functional impairment. Of course, there is a need to define functional impairment and determine how to measure it in a standardized way.
- *Are current advertising restrictions sufficient?* Cannabis advertising restrictions are sufficient for prevention of use among children, as policies from tobacco are readily transferrable. However, more legislators need to understand that there is a relationship between advertising and youth cannabis use.
- *Is it possible to limit potency?* Mr. Freedman commented that limiting the potency of cannabis concentrates for dabbing is the “winnable battle” in states that are considering legalization. Many people are appalled when they see videos of people dabbing, and the argument that the potency of concentrates should be lower than the current 22 percent will probably resonate among the public. Others would counter that cannabis concentrate users will simply double their intake if potency is lowered. It is important to note that most people who present at hospitals for cannabis use are naïve users who

have tried edibles or dabbing. Therefore, one can make the argument to policymakers that the high potency of these products (particularly concentrates) is an immediate public safety risk. It would be helpful to show policymakers images of people dabbing.

- *What are the effects of maternal cannabis consumption during pregnancy and breastfeeding?* Cannabis advocates argue that the drug is safer for pain relief than using opioids during pregnancy. Similarly, they say it is safer to use cannabis as an appetite stimulant than to refrain from eating in cases of severe morning sickness. Social media comments on this topic are informative and, again, anecdotes are trumping research.
- *What are the trends in heavy cannabis use?* Data are needed on this topic, and Colorado started collecting this information last year. Participants commented that a reasonable definition of “heavy cannabis use” is consuming the drug three to four times daily, but agreed that the research community needs to standardized definitions of use for purposes of conducting research with comparative value.

Linking back to his opening challenge for research, *the use of pesticides to grow cannabis is the only place to maintain a “guilty until proven innocent” approach*, Mr. Freedman stated that state regulatory systems cannot keep up with this issue. The Colorado Department of Agriculture has issued an exhaustive list of pesticides approved for use on “leafy greens” that it applies to cannabis. It also applies the tolerance exemption for pesticides that are not dangerous to humans, no matter how much is used. The upshot of these policies is that Colorado has a small list of pesticides that are acceptable to use on cannabis. Cannabis growers must produce evidence that the pesticides they use are not harmful to consumers, but there is clearly room for a federal role in informing this topic.

CANADIAN PERSPECTIVE AND LESSONS LEARNED

Dr. Ware provided background about recent cannabis regulatory reform in Canada and added substantially to the discussion about domestic and international research needs. He began by noting that Canada had only recently reviewed and proposed a revision to its policies regarding nonmedical cannabis use, so it is too early to share information about lessons learned other than the need to consult widely and to prepare and proceed carefully. He offered his perspective on cannabis-related issues as a family physician and pain specialist who recently served as vice chair of the Federal Task Force on Cannabis Legalization and Regulation in Canada. This nine-member Task Force consulted with international jurisdictions and Canadian citizens from across the country in 2016 about their hopes and concerns related to proposed new legislation on cannabis. There was great interest from multiple sectors, and a wide range of views were presented including those of law enforcement, patients and consumers, youth, health and safety experts, and several branches of the Canadian government. The Task Force presented its report to the Canadian government in December 2016.

In 2017 the Canadian Parliament concluded its reading of the proposed cannabis legislation, Bill C-45 (“The Cannabis Act”). This federal legislation incorporated many of the Task Force report’s findings, and the bill is now (at the time of writing) under review in the Canadian Senate. The

legislation remains in flux and will continue to be considered by Parliament and the Senate in early 2018. Prime Minister Justin Trudeau is in favor of Bill C-45, and there is a general feeling that a change in the cannabis law is long overdue. Similar discussions around cannabis policy occurred in Canada in 1971 and again in 2001. Dr. Ware noted that Canadian provinces and territories, municipalities, and communities are already developing and announcing their strategies and responses.

Some important elements of the proposed cannabis legislation in Canada include:

- Minimizing harms by limiting the legal age to 18 (provinces will be permitted to adjust the legal age upward but not downward, as is the case with alcohol). Eighteen is the age of majority in Canada for various aspects of life (not 21, which is used mostly in the United States).
- Marketing restrictions to require plain packaging for cannabis and prohibit advertising outside retail outlets. Cannabis packaging and labeling should specify cannabinoid content.
- There is currently no proposed regulation concerning cannabis product potency.
- Considerations for taxation and pricing, with early funding commitments (CDN \$9.6 million in 2017) for public education.
- Emphasis on prevention and treatment of cannabis use disorders.
- Workplace safety is a big concern, with specific issues identified around how to regulate cannabis use (including medical use) among workers and determine impairment.
- Supply and distribution of cannabis—including its production, extraction, and distribution and sale. Although the Task Force discussed cannabis derivatives, it opted to not recommend the legal sale of edible products. However, cannabis extracted into food-grade oils for oral consumption is permitted (and is often used for medical purposes). (Note: these proposed restrictions have subsequently been amended during the parliamentary review process.)
- Avoiding the co-sale of cannabis with alcohol.
- Personal cultivation to be permitted (limited to four plants per household) for nonmedical use.
- Provinces and territories will decide about distribution regulations; selling cannabis through self-service displays or vending machines to be prohibited to prevent youth access.
- Personal cannabis possession limits set at 30 grams, which is about 1.06 ounces. The provinces would determine permitted places to use cannabis.
- Heavy criminal penalties proposed for selling cannabis to minors.
- As is the case in the United States, the public and lawmakers are concerned about impaired driving and further research is needed.

Dr. Ware also provided background about medical cannabis use in Canada. Medical cannabis access has been permitted in Canada since 1999, and the law has evolved due to repeated court challenges from patients. Over 80 federally licensed cannabis producers are now permitted to

sell dried or fresh herbal cannabis or oils. There is no list of approved conditions; physicians can authorize cannabis for any medical condition. Producers sell medical cannabis directly to patients (i.e., there is no dispensary or pharmacy system). As of June 2017, over 250,000 patients were registered for medical cannabis. Companies produce many different products (more than 400), fulfilling orders and shipping them directly to patients via mail or courier. The Task Force discussed whether this medical cannabis program would be necessary upon legalization of nonmedical use and finally recommended keeping it in place for 5 years, with reconsideration at the end of that period. Patients argued that they did not want to buy medicine in retail outlets, preferring to continue consultations with physicians about cannabis use for their conditions. Medical cannabis regulations in Canada continue to evolve.

The Task Force recognized that understanding the true health effects of cannabis is a complex research undertaking that needs to recognize tremendous variability within individuals, plants, doses, delivery systems, contexts, and research questions. There is no capacity to determine which cannabis chemovars (“strains”) to recommend to patients with different conditions. The Workgroup inquired whether patients order cannabis strains that are high in CBD. (Mr. Freedman noted that Colorado’s hemp program is growing strains for CBD use.¹³) Dr. Ware added that Canada has had a hemp industry since 1996, but currently regulates it separately from medical cannabis. This approach may change under the new proposed Cannabis Act. Canadian regulations for the cultivation of medical cannabis are strict.

Crucial topics related to cannabis legalization in Canada include impaired driving, the age restriction, marketing limitations, and retail options. Home cultivation and use of pesticides when growing cannabis are also of great interest. High-use patterns require scientific study. The Task Force identified many areas where research on cannabis is needed. These include the following:

- *What are the risks of cannabis use on the developing brain?*
- *How are those risks influenced by age, potency, and frequency?*
- *What are the effects of cannabis use on adolescent development?*
- *In the area of the workplace, what is the risk of impairment with cannabis use?*
- *What is the relationship between THC levels and impairment?*
- *In the area of surveillance, what is the best way to monitor availability, THC/CBD content, use, misuse, and the pharmacological effects of derivatives (including edibles and concentrates)?*
- *What are the effects of vaping (e.g., pharmacology and product safety, including constituents), lung and airway health, and effects on smoking (e.g., comparing tobacco and cannabis)?*
- *What is the impact of cannabis use on teenage use patterns and health consequences (e.g., misuse and driving)?*
- *What is the prevalence of cannabis use and driving risk/outcomes (need baseline and follow-up measures)? Researchers need to develop and validate roadside oral fluid testing*

¹³ Hemp is cannabis with low THC.

devices. There needs to be international coordination of cannabis use surveillance methods, capacity, and reporting.

- *What is the economic impact of cannabis regulation (e.g., a comprehensive evaluation that includes medical care costs, medication use, and job creation)?*

Research in these areas will inform the education of retail outlet staff, cannabis producers, law enforcement, health care professionals, and the general public and patients.

Dr. Ware added that Canada will engage in a public education campaign on cannabis that will target topics such as DUI, safe and responsible use (e.g., low-risk use guidelines¹⁴), and information for parents regarding cannabis discussions with children.

On the topic of medical use, Dr. Ware stated that the impact of CBD on THC's effects (medical and nonmedical) is unknown. Research is needed on the therapeutic benefits and risks of cannabis use for medical purposes, including novel delivery systems (e.g., topical, suppositories, and inhaled). Researchers need to develop a consensus on the quantifiers of use and prevalence parameters (e.g., amount, frequency, potency, and product characteristics). Information is needed on the effects of pricing (including taxation) on cannabis use patterns. More information is needed on medical cannabis dosing, and people are discussing limits or ranges on the daily dose for medical use. Ongoing medical research on the health and medicinal effects of cannabis is greatly needed.

Dr. Ware reminded the Workgroup that scientists must consider various issues related to cannabis research. Because cannabis is a controlled substance, research facilities must be licensed, and the regulating authority for natural health products for sale in Canada cannot currently consider it. There are regulations related to research access to cannabis materials. Burgeoning areas of cannabis research include pharmacogenomics, pharmacosurveillance, and qualitative research (e.g., the narratives and experiences of users).

As a final point, Dr. Ware also identified the importance in studying the structure of the industry itself. As with other legal substances, researchers will need to consider the role of industry in the development of drugs, devices, and technologies (e.g., sequencing, extraction, isolation, and big data).

¹⁴ For more information about Canada's low-risk guidelines, see Fischer, B., Jeffries, V., Hall, W., Room, R., Goldner, E., & Rehm, J. (2011). Lower Risk Cannabis Use Guidelines for Canada (LRCUG): a narrative review of evidence and recommendations. *Canadian Journal of Public Health/Revue Canadienne de Sante'e Publique*, 324-327.