LAB MATTERS

analysis|answers|action

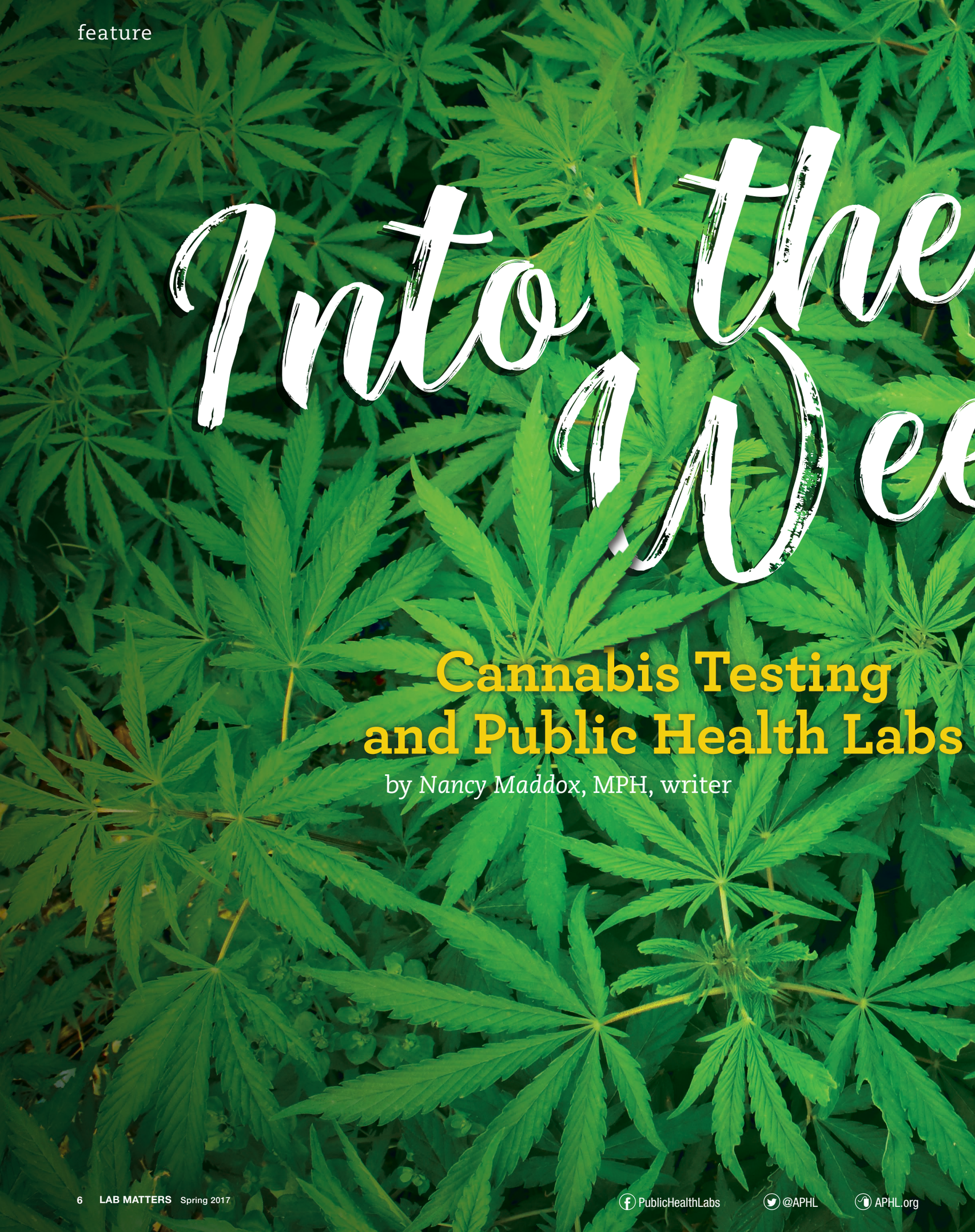
Spring 2017 Issue 2

Into the Weeds

Cannabis Testing and Public Health Labs

Inside:

ASSOCIATION OF PUBLIC HEALTH LABORATORIES



Into the Wee

Cannabis Testing and Public Health Labs

by *Nancy Maddox*, MPH, writer

eds

An ounce of recreational marijuana flower will set you back $125 at Buddy Boy, a Colorado cannabis retailer and medical marijuana dispensary with seven Denver locations and over 100 strains of weed, including Blue Magoo, Kush Master and Tangerine Haze.

Not interested in flower buds? Not a problem. Buddy Boy will be happy to sell you a Jungle Roast chocolate bar ($4.50), Sons of Sativa canna punch ($7.00 and up), Mountain High Suckers lozenges ($6.08) or any of dozens of other edibles, concentrates, tinctures or topicals. Buddy Boy even has its own "Bud Club" rewards program and a discount for military veterans.

Yet, in 2017, the most remarkable thing about Buddy Boy is not its broad array of wares, but rather the mere fact that they are so openly advertised on the Internet. As it stands today, cannabis is a Schedule I narcotic, on the same US government list as heroin, ecstasy and other illicit drugs deemed to have high abuse potential, "lack of accepted safety" for medicinal use and "no currently accepted medical use in the United States."

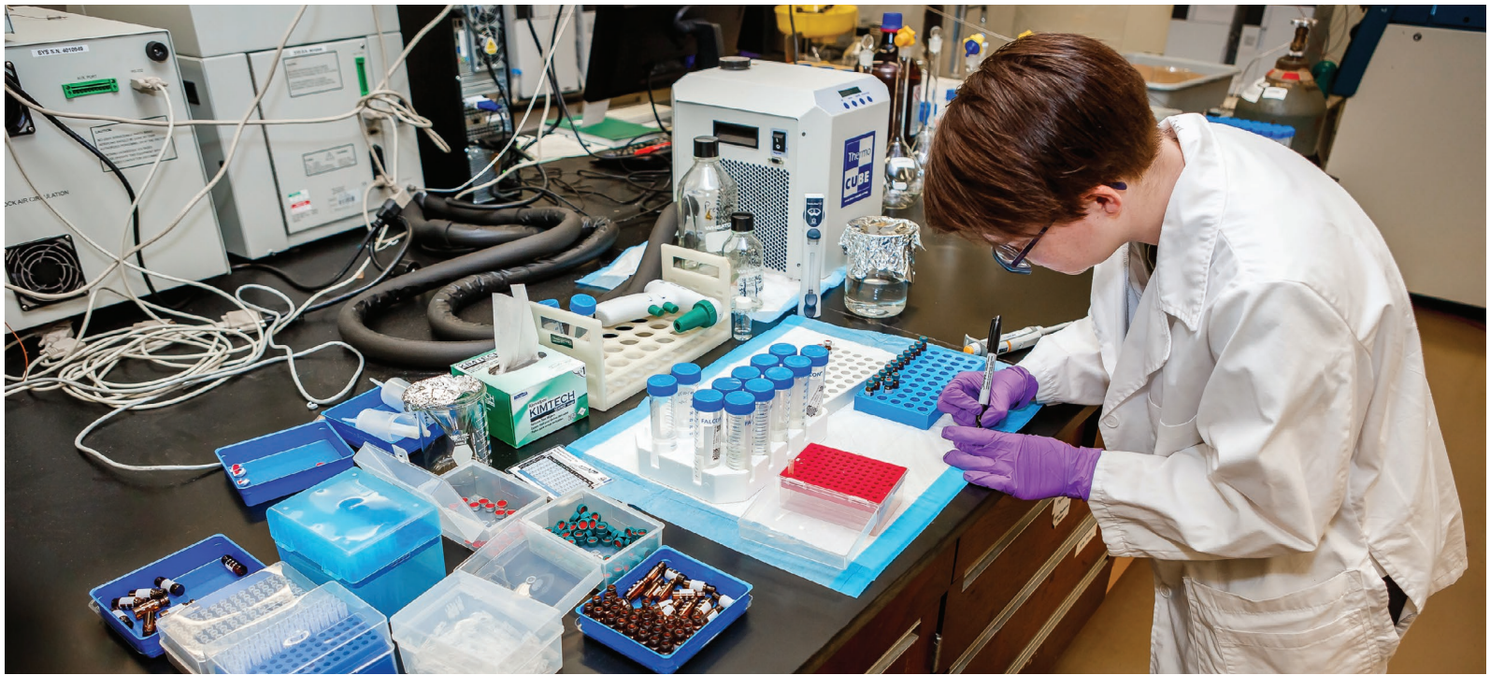
This discrepancy—between cannabis's ready availability and its federal classification—is a problem. It is a problem for the District of Columbia and 28 states that have legalized cannabis for medical and/or recreational adult use. It is a problem for cannabis vendors and users, who operate in a largely cash-only, legal gray zone. And it is a problem for state agencies and laboratories tasked with regulatory oversight and public health surveillance of cannabis safety.

The safety issue is not insignificant. The Mountain High Suckers lozenges sold at stores like Buddy Boy, for example, were voluntarily recalled in 2015 after testing positive for imidacloprid and myclobutanil—two pesticide chemicals banned for use on Colorado-grown cannabis. At the time, it was the 16th cannabis-related recall in Denver in 16 weeks, according to *The Cannabist*, an online, Denver-based news outlet.

Yet, even if unsprayed, *Cannabis sativa* carries risks. For one thing, the plant's proclivity for concentrating dangerous heavy metals in its tissues is so well known that industrial hemp is sometimes used for phytoremediation of heavy metal polluted soils, including around the abandoned Chernobyl nuclear power plant in Ukraine.

And earlier this year, researchers at the University of California at Davis announced that they had detected potentially dangerous microbes on 90% of cannabis samples purchased from 20 Northern California growers and dispensaries. The study was prompted by the unexpected death of a California cancer patient and medical marijuana user who was killed by a fungal infection.

Anne Walsh, PhD, MD—who oversees medical marijuana testing at the New York state public health laboratory (PHL), the Wadsworth Center—stressed the necessity of laboratory testing to verify dosage and protect vulnerable populations: "Many of the patients who will be using this will be immune-compromised or very young children with seizure disorders who, if they get a good response, will be taking this product long term."



A technician in the Wadsworth Center labels cannabis sample vials in preparation for the autosampler

"Much more than dry flower testing"

The problems for state laboratories stem from both legal constraints and their limited, collective experience with cannabis testing. "So much of this issue is anecdotal; it would be good to have some hard data," said Julianne Nassif, MS, APHL's environmental health director. Nassif noted that, in the absence of federal guidance and regulations, "states have had to figure this out on their own and they have very different approaches."

The issue is further complicated by the grassroots origin (no pun intended) of virtually all state cannabis laws, which tend to be based on voter initiatives crafted by pro-cannabis groups. For example, the 2010 ballot initiative legalizing medical marijuana in Arizona was silent on matters pertaining to public health. Thus, The Grand Canyon State has no product testing requirements, and no state entity has regulatory authority over the private labs offering cannabis-testing services, such as potency analysis.

> **Patients have a right to have access to medicine of known purity and quality.**

Of six state PHLs surveyed for this article, only one, New York's Wadsworth Center, performs routine cannabis testing, and only for medical marijuana, as nonmedical "adult use" is illegal in New York. Two others—the Colorado Department of Public Health & Environment (CDPHE) laboratory and the Massachusetts Department of Public Health (MDPH)—provide oversight and guidance to commercial cannabis-testing laboratories in their states. And the remaining three—the Alaska State Public Health Laboratories, Arizona Department of Health Services Laboratory and the Washington State Department of Health Public Health Laboratories—perform no cannabis testing and have no oversight of their states' cannabis industries.

Dave Verbrugge, manager of analytical toxicology at the state PHL in Alaska—which legalized "adult use" in 2014—said he would like the state to have "a technical presence" overseeing private laboratories that perform required quality control testing for Alaska's cannabis growers and processors. That responsibility lies with the Alaska Marijuana Control Board in the state department of commerce. So far, the health agency has received no cannabis tax revenue to support laboratory oversight and neither the PHL nor the state food safety laboratory (housed in a separate agency) has volunteered to bring up a cannabis-testing program.

Said Verbrugge, "Neither one of us really has capacity. Plus, we felt it wasn't a good fit for the PHL to be testing marijuana plants for an intoxicating agent and certifying that."

Marijuana's status as a Schedule I narcotic was also an issue: "At least half of our funding is federal. I definitely had some concerns about the potential for changes in the [federal] administration and enforcement of federal grant requirements regarding a drug-free workplace." Although the US Drug Enforcement Agency (DEA) registers qualifying analytical laboratories to work with controlled substances, Verbrugge said it is unclear "whether testing marijuana for recreational use would be a violation of a DEA license."

Of course, even without the DEA looking over scientists' shoulders, any marijuana testing program requires analytical methods. And a ripple effect of the federal stance on cannabis has been a lack of laboratory guidance from any US government agency, other than a CDC protocol developed to monitor children's exposure to secondhand cannabis smoke.

This void is being filled by both nongovernmental organizations and the state laboratories tasked with cannabis oversight.

The first cannabis-specific guidance document published in the United States—*Cannabis Inflorescence*, Cannabis spp., *Standards of Identity, Analysis and Quality Control*—is a monograph released in 2013 by the American Herbal Pharmacopoeia, a nonprofit organization that promotes "the responsible use of herbal medicines." Jahan Marcu, PhD, one of more than 30 contributors to the monograph, said it is "intensely peer-reviewed" and cited in the cannabis laws of 19 states, including California.

Last May, APHL released its own cannabis document, *Guidance for State Medical Cannabis Testing Programs,* developed by a committee of experts drawn from PHLs, academia and the private sector. It cites some of the same source material as the American Herbal Pharmacopoeia monograph. However, this guidance is geared toward governmental testing programs and covers, among other things, product sampling, microbial and heavy metal testing, toxicity scoring, risk assessment and criteria for determining acceptable risk.

A few states, including Massachusetts and New York, have developed their own methods, either created *de novo* or based on existing testing protocols for foods, drugs and other consumer products. MDPH, for example, has

relied heavily on methods developed by the US Pharmacopeial Convention, a nonprofit organization whose pharmaceutical standards are enforceable by the US Food and Drug Administration (FDA).

"The truth is, there is no single guidance that works," said Marc A. Nascarella, PhD, chief toxicologist at MDPH and a contributor to the APHL cannabis guidance. "Cannabis is now being put into oils, resins, food products, suppositories, tinctures, creams, lotions, vape pens and, of course, cigarettes. It is much more than dry flower/plant testing."

MDPH conducts no cannabis testing itself, but is a resource for the four private labs doing quality control testing for Massachusetts's registered medical dispensaries. MDPH also reviews the ISO-compliant laboratory reports the dispensaries are required to submit for a representative sample of their products.

> **At least half of our funding is federal. I definitely had some concerns about the potential for changes in the [federal] administration and enforcement of federal grant requirements regarding a drug-free workplace.**

Based on those reports, Nascarella said that levels of detection and levels of quantitation have gone down over the past two years or so. He said, "The labs are improving their methods; I think their techniques are getting better."

CDPHE is now populating a reference library with marijuana testing methods, relevant scientific literature and standard food and pharmaceutical test methods that can serve as a starting point for cannabis-related method development. Earlier this year, the agency asked the Colorado legislature to fund a marijuana reference laboratory in the state PHL, and that request has received preliminary approval. If okayed, "that would set us up to do health investigations and to be a technical resource to private laboratories," said Heather Krug, MS, who coordinates the CDPHE marijuana laboratory inspection program.

The Proficiency Testing Conundrum

Yet another hurdle stemming from US cannabis policy is the federal ban on transporting Schedule I substances across state lines. That means the laboratory reference materials used to validate testing protocols, conduct quality control checks and assure technicians' testing proficiency must come from in-state.

In Colorado, where "adult use" marijuana sales began January 2014, proficiency testing (PT) has been a complicated issue. Krug said that, from the beginning, Colorado's 14 commercial cannabis-testing laboratories were required to participate in PT as soon as practicable or risk losing their state certifications. Then, two years ago, with no acceptable program yet available, the legislature handed CDPHE responsibility for cannabis PT.

She said, "We basically set up a process where CDPHE oversees the production of PT samples and does the statistical analysis of all the results labs submit to us, but we use a private marijuana testing facility [that implements a CDPHE-developed protocol under CDPHE supervision] for the sample production and distribution."

The program initially focused on potency testing for cannabis flowers and is now working on developing PT samples for edibles and concentrates.

"It's a pretty good system," Krug said. "We're creating the samples from real marijuana. Each commercial lab tests the PT samples, and we use the robust mean of their results as the assigned PT value we grade the results against."

In the meantime, at least one commercial enterprise, Emerald Scientific, has begun offering cannabis PT samples and reference standards for sale. But to comply with interstate transport restrictions, the California-based company

Weighing and pooling a medical cannabis sample in the Wadsworth Center

A sample tray of cannabis samples is loaded into the liquid chromatography-mass spectrometer at the Wadsworth Center

has had to devise an elaborate system in which it functions mostly as an intermediary: Laboratories order products through Emerald, but the products are created and evaluated by third-party accredited PT providers located in the customer's own state. Moreover, products must have a sufficiently low concentration of tetrahydrocannabinol—the principle euphoria-inducing cannabis ingredient—to be exempt from DEA regulations.

In New York, where the Wadsworth Center performed potency testing on roughly 25 to 30 lots of medical marijuana per month last year—the first year of legal medical marijuana sales in the state—there are no commercial cannabis PT providers. Walsh said Wadsworth relies on internal demonstrations of competency and obtains good concordance with manufacturers' reported potency values. So far, no private laboratories have applied for approval to conduct cannabis testing in New York. If they did, Walsh said various PT options have been discussed, but no definitive solution identified. (In addition to potency, Wadsworth tests medical cannabis for nine types of bacteria, three types of fungus, five mycotoxins and nine metals or metalloids. It also screens for over 100 pesticides.)

According to *The Economist*, the entire US cannabis industry was worth about $6 billion in 2016 and is expected to grow substantially when recreational sales begin in California in 2018.

"The future is looking really good for the cannabis industry"

Despite rumblings from the Trump administration about stricter enforcement of federal drug policies, several of those interviewed for this article said it is hard to envision a rollback of the looser, new cannabis laws. In fact, the very election that propelled Donald Trump to the presidency saw the legalization of recreational marijuana in four additional states—California, Nevada, Maine and Massachusetts.

Last year, Colorado's roughly 2,600 licensed cannabis businesses moved a billion dollars worth of recreational and medicinal products and paid the state $50 million in taxes. According to *The Economist*, the entire US cannabis industry was worth about $6 billion in 2016 and is expected to grow substantially when recreational sales begin in California in 2018.

Even the US government has shown a schizophrenic attitude toward marijuana, with FDA's approval of Syndros® cannabis oral solution as a Schedule II drug in March and the agency's ongoing review of a second cannabinoid drug, Sativex®, which is already legal in more than a dozen countries outside the US.

According to a study reported in *JAMA Internal Medicine*, the 13 states with medical cannabis laws in effect before October 2010 experienced a 25% lower mean annual opioid overdose rate during 1999-2010 than states without such laws.

While there are still health and safety concerns associated with cannabis, a new National Academies of Sciences, Engineering and Medicine report found "conclusive or substantial evidence" that cannabis or cannabinoids are an effective treatment for chronic pain, chemotherapy-induced nausea and vomiting, and multiple sclerosis spasticity symptoms.

The same report, released in January, recommends that CDC, APHL, state and local health agencies and assorted partners "fund and support improvements" to federal and state-based public health surveillance efforts to monitor the health effects of cannabis use. It explicitly calls for the development of novel diagnostic technologies to rapidly assess cannabis exposure and for state-based programs to analyze the chemical composition of cannabis and related products.

Given that almost 20 million Americans aged 12 and up reported marijuana use in 2013 (7.5% of this population group)—and that one in five Americans now lives in a state that has legalized recreational cannabis—it seems likely that more state and local laboratories will be tasked with some form of cannabis oversight and will need supplemental funding to accommodate this work.

Jahan Marcu, PhD, chief science officer for Americans for Safe Access—an advocacy group pushing for greater availability of cannabis for therapeutic use and research—said, "Patients have a right to have medicine of known purity and quality."

Marcu, who is also chief auditor for a nonprofit, third party certification program for the medical cannabis industry, said, "It is time for us to look at all available research and to have an adult conversation about cannabis as a medicine. We have the standards documents and we have the ability to regulate this product."

In 2014, the American Herbal Products Association published its own standards for cannabis business operations. And in February, the American Society for Testing and Materials (ASTM) announced that it would be developing voluntary, international standards for cannabis farming, quality management systems, laboratory testing, processing, security and personnel practices. Already, many accrediting groups, including A2LA and the ANSI-ASQ National Accreditation Board, offer external assessments of medical marijuana-testing laboratories to ISO/IEC 17025 standards.

Jeremy Applen, vice chair of the ASTM Cannabis Standards Committee, said, "I think it would be very difficult for the US to try to take away this industry." He noted that Israel is already a global leader in medical cannabis research and that Canada, Germany, Uruguay, Australia and Chile either have a cannabis program or are in the process of developing one.

Applen said, "I think the future is looking really good for the cannabis industry, and as that growth occurs, I think there will be big changes around cannabis testing. … Labs providing testing for pharmaceutical or dietary supplement companies will start to bring cannabis testing on-line as well. That speaks to the need for standardization across the industry."

Last August, the DEA denied a petition to remove cannabis from the list of Schedule I drugs. It was the fourth denial.