A growing concern: Quality control in the cannabis industry

The cannabis industry is rapidly changing, offering significant opportunity for those companies willing to navigate its regulatory and scientific complexities and uncertainties. For most of the 20th century, the plant *Cannabis sativa* was classified in the US as a Schedule 1 drug—that is, one with no acceptable medical use.

People have long turned to cannabis to treat ailments, including pain, inflammation, and depression, when other therapeutics failed. Because of cannabis’s classification, however, they have typically had to get it through illicit, unregulated sources. As the market expands to legitimacy, there is increasing focus on the need for quality control.

In just the past few years, the regulatory landscape and industry parlance around cannabis has begun to shift (see sidebar *Cannabis by many names* on next page). In all 50 states, cannabis varieties classified as hemp are no longer considered controlled substances. That means these plants and their extracts are legal as long as they contain less than 0.3% by dry weight of the intoxicating component of cannabis, Δ9-THC. And while THC itself remains a Schedule 1 drug according to federal law, several states have decriminalized all *C. sativa* varieties for medicinal or recreational use, regardless of THC content. The US Food and Drug Administration has also approved some cannabis-based pharmaceuticals, and Canada has legalized cannabis for medical and recreational use by adults.

For the cannabis industry, the surges in legal supply, consumer demand, and medical research are starting to converge. Dozens of clinical trials are exploring non-intoxicating cannabidiol, CBD, as a treatment for a variety of disorders. The US CBD market alone is expected to reach $20 billion by 2025 in some scenarios. The key for the industry is to maintain quality amid rapid expansion.
The growing challenge is consistency. Growers supplying manufacturers of CBD and other hemp-derived products depend on measuring the THC content of their crops to ensure that they stay within legal limits. Data from state-certified labs performing quality testing could inform efforts to standardize cannabis-based products. And attention to chemicals used during cannabis processing can reduce impurities from manufacturing and maintain quality from the field through to a finished product. “The higher the chemical grade, the higher the confidence in final product quality among manufacturers and consumers,” says Matthew Szap, scientist and technical communications manager at Spectrum Chemical.

**CROP TESTING FOR CANNABINOIDS**

“The big question in hemp production right now is how to reduce the risk of a growers’ crop testing ‘hot,’” says Larry Smart, a professor of horticulture at Cornell University. “Hot” crops have a delta-9-THC content higher than 0.3% by dry weight. If plants have delta-9-THC concentrations above this regulated amount, growers could face crop destruction or legal consequences.

One of the current quantification standards for delta-9-THC in *C. sativa* is to examine samples using high-performance liquid chromatography (HPLC) and...
detect molecules after separation with ultraviolet light. Growers can send samples to dedicated laboratories for preparation and analysis. They can also do testing on the farm using conventional instruments, like those used in industrial and academic labs, or with a portable HPLC system and disposable equipment.

Start-up Mariposa Technology is working to bring testing directly into hemp fields using existing handheld Raman spectrometers. Raman spectroscopy is a nondestructive technique that uses laser light to provide structural information about molecules in a sample, such as a flower or bud on a hemp plant.

“In thirty seconds after the button is pressed, you get a result on the screen, so the analysis can be done anywhere in the field,” says Dmitry Kurouski, a plant biophysicist at Texas A&M University who studies how Raman spectroscopy can be used to diagnose plant disease. Kurouski is partnering with Mariposa on the hemp analysis system.

Mariposa is developing a proprietary database of spectral signatures from cannabinoids. “Raman spectroscopy provides a molecular fingerprint, and the uses are almost limitless once a good, strong database has been developed,” says Michael Dalle Molle, the firm’s chief operating officer.

Using that database of molecular signatures from hemp plants, machine learning algorithms can be trained to quantify THC and CBD content. Farmers will be able to apply this technology to monitor THC levels in growing plants and determine when to harvest for optimum CBD yield, Dalle Molle says.

**CULTIVATION FOR COMPLIANCE**

Plant cultivation has been underground for so long that the chemical profiles for *C. sativa* flowers labeled with the same cultivar name have been found to have widely varying cannabinoid content. Larry Smart, a plant scientist at Cornell University, and his colleagues have identified genetic markers to distinguish *C. sativa* plants that will produce CBD at high levels from those that will produce THC at levels above legal limits.

These genes are the instructions for proteins that produce molecular precursors to THC and CBD. A plant that contains two copies of the gene for THC production will primarily produce THC and very little CBD. Plants containing both the THC genetic marker and CBD genetic marker are very likely to test hot, Smart says. Plants containing two copies of the CBD genetic marker, and no active genes for THC production, are cultivars with only low-THC plants, he adds.

Smart’s research paves the way for companies looking to source CBD products to ensure a constant supply of high-quality materials that are reliably low in THC.
SUPPLYING THE MARKET
Not all cannabis-based products come from the farm. As of this writing, three of the four cannabinoids approved by the US Food and Drug Administration are made in the lab because it is still illegal to grow cannabis with delta-9-THC content above 0.3% by dry weight—colloquially described as “high THC.” Dronabinol, available in capsules as Marinol and in a liquid as Syndros, is synthetic delta-9-THC. It is approved to treat nausea caused by chemotherapy, as well as weight loss and anorexia associated with AIDS.

Likewise, nabilone, sold under the brand name Cesamet, is a synthetic derivative of delta-9-THC. It is approved to treat nausea resulting from cancer therapy.

Epidiolex, which contains CBD, originates differently. Manufacturers grow cultivars of *C. sativa* that produce high amounts of CBD and low amounts of THC. Scientists extract CBD from those greenhouse plants using a multistep process that includes checks for potency and contaminants. Epidiolex is used to treat seizures associated with tuberous sclerosis complex as well as two rare forms of epilepsy, Dravet syndrome and Lennox-Gastaut syndrome. While Epidiolex is the first FDA-approved CBD drug, it is unlikely to be the last, as clinical trials continue on CBD’s health benefits.

Beyond FDA-approved medications, CBD extracted from hemp is popping up in dietary supplements, cosmetics, and beverages. “Extracting a kilogram of CBD can be done for a quarter of the price of synthesizing it in the lab,” says Peter Sampson, the president of IntrinsiChem Consulting. The potential benefits of

Hemp growers need to be able to test their plants in the field to harvest at the highest cannabidiol (CBD) concentration, while also ensuring their crop is within legal limits for Δ9-tetrahydrocannabinol (delta-9-THC) levels.

*Credit: Shutterstock*
CBD—it is touted as a remedy for insomnia, anxiety, and pain, among other disorders—are under active investigation.

Regardless of claims, CBD is and will most likely remain a strong market. For companies extracting CBD from hemp for consumers, turning out a quality product comes down to using quality ingredients throughout growing and production, as well as quality testing the final product.

Szap at Spectrum says that, because medical cannabis and hemp-derived products are ingested by humans, “manufacturers should pay close attention to the grades of chemicals they use because the quality of those grades can affect the quality and consistency of the final product.” Ingredients can include ethanol for crude product extraction and product flavoring agents such as vanillin.

The quality of chemicals used also impacts testing results. “Using food-grade chemicals for consumables should be a priority,” says Todd Griffin, the CEO and chief scientist at the testing lab G2 Analytical. “Lower-quality solvents can also mean that testing is less accurate as impurities interfere with the analysis,” he adds.

**STANDARDIZING PRODUCT TESTING**

All but two states in the US have laws that let people get medical cannabis via a recommendation from a medical provider or allow for limited use of CBD products containing no or little THC.¹ In most states, cannabis products including oil extracts and food products must undergo testing at state-certified labs for cannabinoid potency and for contaminants like molds, pesticides, and heavy metals.

“Standardization in testing of *C. sativa* products is a challenge because each state has different regulations,” says Stephen Goldman, the chief scientific officer at Kaycha Labs, which operates hemp and cannabis testing labs in nine states.

US Pharmacopeia, an independent nonprofit health organization, has issued quality guidance regarding cannabis and cannabis-related products.² Federal guidance for cannabis quality testing is being developed.³
Quality testing datasets could be a key source of data for regulators navigating the rapidly changing cannabis industry, Goldman says. For example, one emerging concern is the practice of converting CBD extracted legally from hemp into intoxicating molecules such as Δ8-THC (delta-8-THC). Delta-8-THC differs from the structure of delta-9-THC, regulated as a Schedule 1 drug, in only the position of one bond.

Multiple websites provide kitchen recipes for the conversion; the delta-8-THC product, however, exists in a legally ambiguous area between controlled substance and legal hemp-derived product.

The FDA and the American Society for Testing and Materials have warned consumers about potentially unsafe ingredients or unsanitary conditions for delta-8-THC production. "There will always be synthetic chemists in the world. They make a compound, regulators figure out what’s going on and they shut it down, as they did with delta-8 in Colorado," Goldman says.

GROWTH AHEAD
The cannabis industry is still in its infancy and there is much still to learn about this storied plant. It’s not all about CBD and THC either—C. sativa contains more than 100 cannabinoids. Research into these myriad components is ongoing as scientists attempt to learn how they interact with each other and the body. For example, researchers studying cannabis pharmacology are increasingly looking at potential synergistic effects of cannabinoid combinations. The process by which cannabinoids are extracted, purified, and packaged are also being evaluated for their impact on the final product. In one recent study, cannabinoids in extracts from the same high-CBD cultivar varied depending on the solvents used during extraction.

To move the cannabis industry toward maturity, producers and scientists still have many questions to answer. How does chemical quality affect production and analysis of cannabis products? Do cannabis products have additional therapeutic uses beyond what is currently known? How will advances in field testing drive the industry forward? What does the future hold for federal standards and compliance? Staying informed will be key to growers, processors, and manufacturers as the cannabis industry continues to transform and blossom.

REFERENCES:
3. Lee Sanchez et al., “Confirmatory non-invasive and non-destructive differentiation between hemp and cannabis using a hand-held Raman


7. US Food and Drug Administration, 5 Things to Know about Delta-8 Tetrahydrocannabinol – Delta-8 THC, March 18, 2022, https://www.fda.gov/consumers/consumer-updates/5-things-know-about-delta-8-tetrahydrocannabinol-delta-8-thc.


