Cannabis Laboratory Challenges
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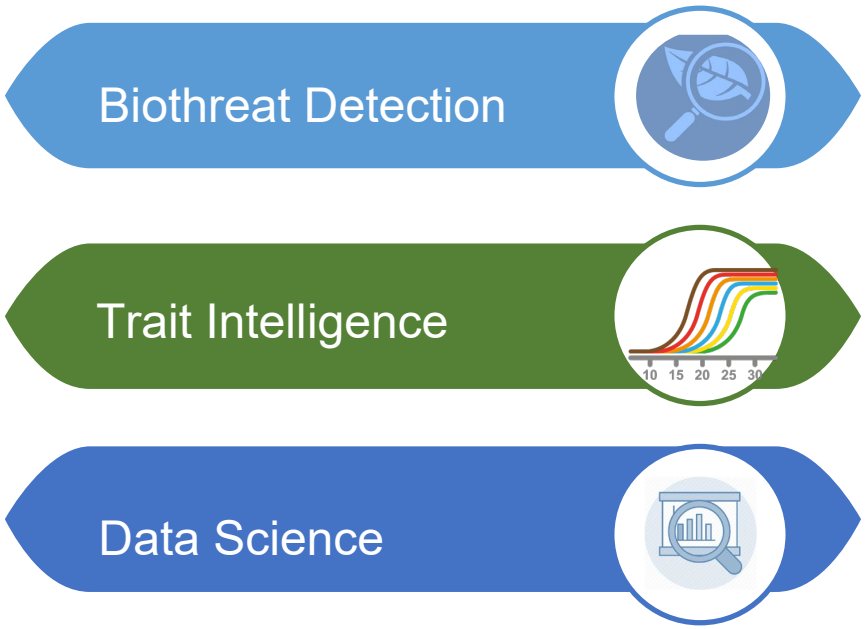
Medicinal Genomics

Medicinal Genomics is a leader in cannabis safety testing, cannabis genetics, and point-of-grow testing solutions. Medicinal Genomics' tests ensure patients have access to safe, quality cannabis, while also helping growers and producers detect harmful microbes, identify desirable plant traits, and increase yields.



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Agenda

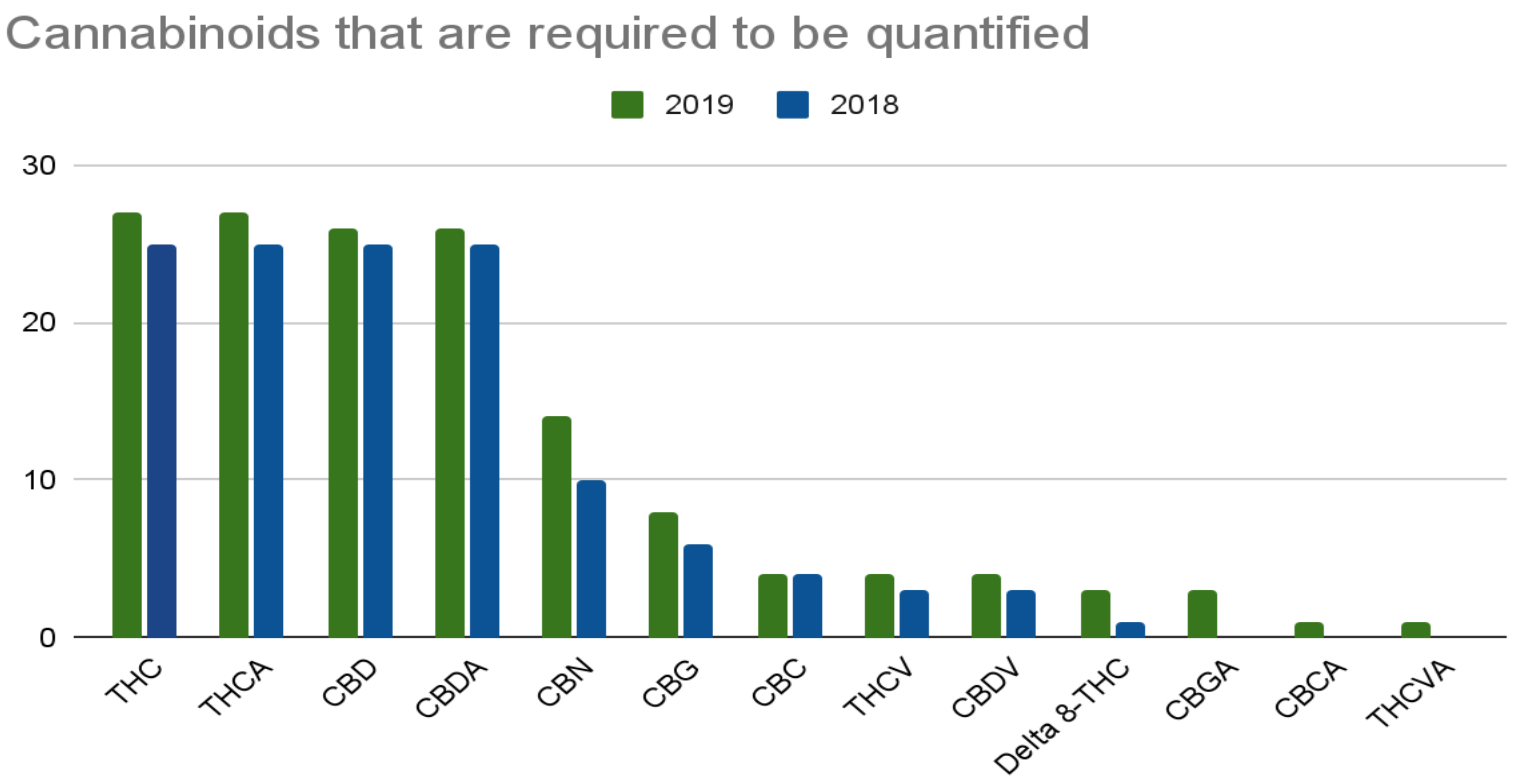
- Diversity of State Medical Cannabis Program Required Testing Rules
- Lack of Accreditation Standards & Challenges w/Reference Methods
- Challenges of Testing the Cannabis Matrix
- Additional Laboratory Specific Challenges
- Lab Shopping
- Solutions to Alleviate Laboratory Challenges

State Medical Cannabis Program Required Testing Rules

Background

- Cannabis is illegal at the federal level
  - Controlled Substance Act of 1970
- Cannabis is classified as a Schedule 1 controlled substance
  - No FDA-approved medical use, a high potential for abuse or addiction
- Cannabis legalization
  - CA was first to legalize medical cannabis in 1996
  - CO and WA were first to legalize adult-use cannabis in 2012
  - Today, 36 states and 4 territories have legalized medical cannabis,
  - And, 17 states, 2 territories, and DC have legalized adult use
- **Each state has a unique set of required testing rules**

Cannabinoid Potency



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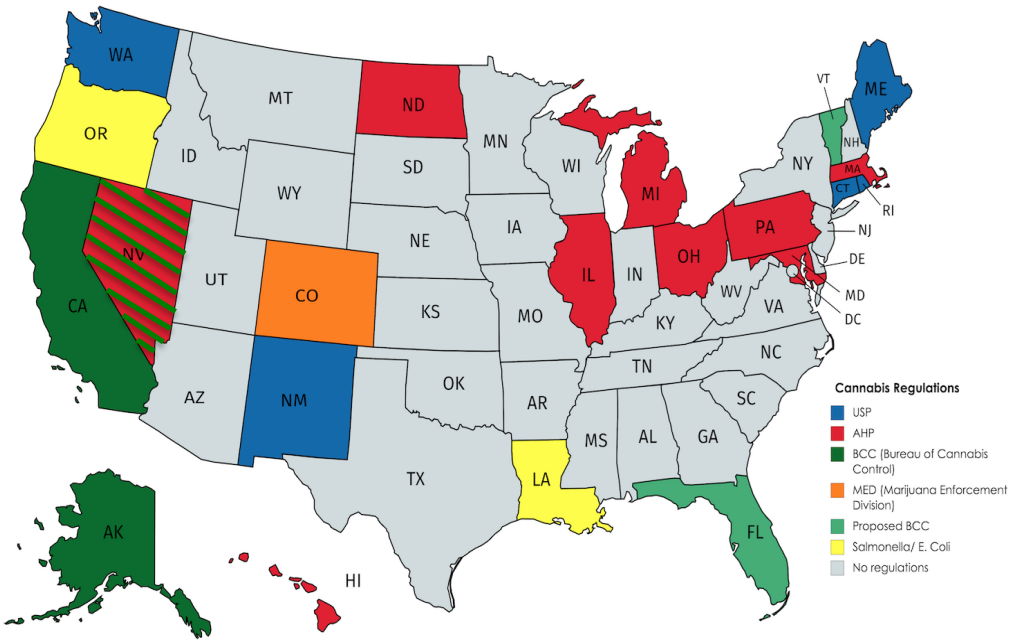
Microbial Testing Regulations

AHP

- Total Aerobic Count
- Total Yeasts & Molds
- Total Coliforms
- Total Bile Tolerant Gram Negative Bacteri
- *E.coli*
- *Salmonella* spp.

USP

- Total Aerobic Count
- Total Yeasts & Molds
- Total Coliforms
- Total Bile Tolerant Gram Negative (BTGN)
- *E.coli*
- *Salmonella* spp.
- *Pseudomonas aeruginosa*
- *Staphylococcus aureus*



BCC (California)

- Shiga toxin producing *E. coli*
- *Salmonella* spp.
- *Aspergillus flavus, A. fumigatus, A. niger, & A. terreus*

AOAC

AOAC developed SMPRs for *Aspergillus*, *Salmonella* spp., STEC and TYM. MI, MD and AZ moving towards mandating AOAC accredited methods

Source - https://www.medicinalgenomics.com/cannabis-microbial-testing-regulations-by-state/

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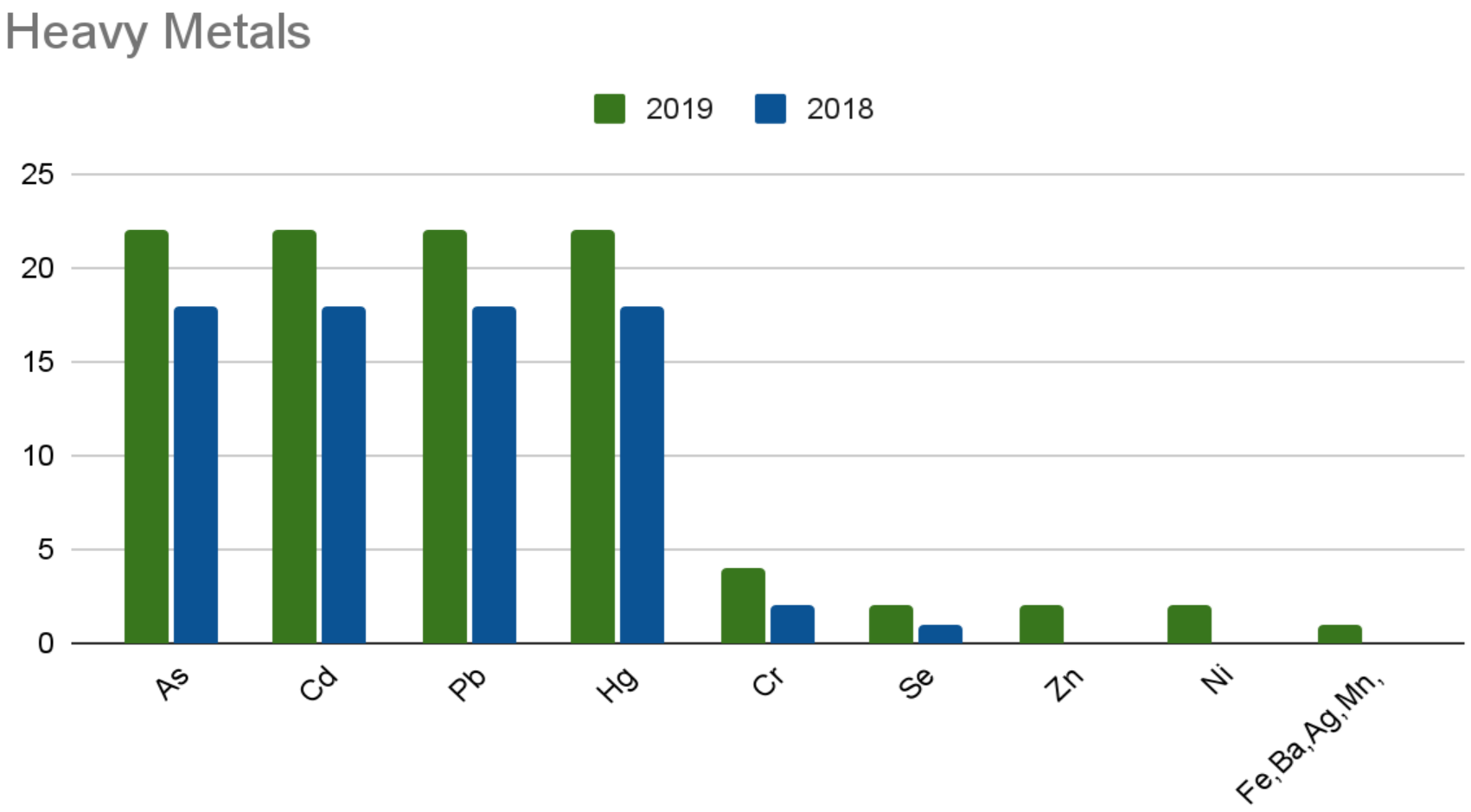
Pesticide Testing

- All 28 states test for pesticides
- In 2019, 24 pesticides have been found in at least 1 cannabis product
- 9 of 24 pesticides are not tested by any states
- 5 of 9 are fungicides

Powdery mildew, a fungus, is prevalent pest in cannabis cultivation

Metals that are Required to be Quantified



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Lack of Accreditation Standards & Challenges with Reference Methods

Limited Method Validation Option

	SMPRs	Approved Method
Microbial	**Sal./STEC** **Aspergillus** **TYM**	• Sal./STEC-flower • Asp.-Flower & MIPs • TYM flower
Heavy Metals	**Cadmium** **Lead** **Mercury**	• Cd, Pb, Hg-latter 2021
Pesticides	**124 Pesticides**	• Pesticides-latter 2021

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Reference Standard Fit for Purpose

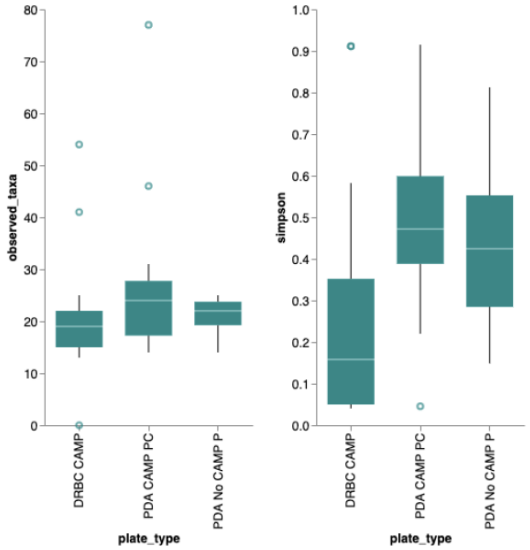
The problem with Culture Based Methods for TY&M

The recent AOAC ERV TY&M study found that media, such as DRBC, containing antibiotics significantly impacts the diversity of microbes that grow, and as a result, the CFU values vary by orders of magnitude. Antibiotic selections are utilized to reduce background bacteria but many of these antibiotics (chloramphenicol) inhibit growth of most pathogenic fungi found on cannabis.

1. *Fusarium*
2. *Pythium*
3. *Aspergillus*

In addition, **PDA with chloramphenicol demonstrated the highest diversity and the highest concordance** with whole genome sequencing. **DRBC plating demonstrated the lowest diversity**. DRBC was selected as a reference method for TY&M. **DRBC is missing 5 fold more yeast and molds than PDA +CAMP or molecular methods.**

Sample	DRBC						
	10^{-2} CFU/g	10^{-2} CFU/g	10^{-2} CFU/g	10^{-3} CFU/g	10^{-3} CFU/g	10^{-3} CFU/g	Final Result CFU/g
Low A	0	4	1	1	0	0	170
Low B	0	3	1	1	1	0	130
Low C	2	1	0	0	0	0	100
Low D	2	5	2	0	2	0	300
Low E	2	0	2	0	0	0	130
	Average CFU/g						170
	PDA with Chloramphenicol						
	10^{-2} CFU/g	10^{-2} CFU/g	10^{-2} CFU/g	10^{-3} CFU/g	10^{-3} CFU/g	10^{-3} CFU/g	Final Result CFU/g
Low A	8	16	12	1	3	2	1200
Low B	8	12	8	1	0	3	930
Low C	13	19	13	1	2	1	1500
Low D	3	12	21	2	0	1	1200
Low E	9	7	4	0	3	3	670
	Average CFU/g						1100
	PDA						
	10^{-2} CFU/g	10^{-2} CFU/g	10^{-2} CFU/g	10^{-3} CFU/g	10^{-3} CFU/g	10^{-3} CFU/g	Final Result CFU/g
Low A	127	133	124	32	32	21	14000
Low B	151	157	101	26	20	28	15000
Low C	TNTC	TNTC	TNTC	41	45	37	41000
Low D	147	141	123	32	26	26	15000
Low E	138	102	119	23	15	24	13000
	Average CFU/g						20000



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Challenges of Testing the Cannabis Matrix

Each Cannabis Matrix is Unique

Flower

- Lipid rich
- Trichomes
- Terpenes
- Cannabinoids
- Endophytes

Extracts & Concentrates

- Oils
- Tinctures (alcohol based)
- Whole plant extract

Marijunna Infused Products

- Gummies (gelatin)
- Chocolate (fat)
- Candy (sugar)
- Just about anything

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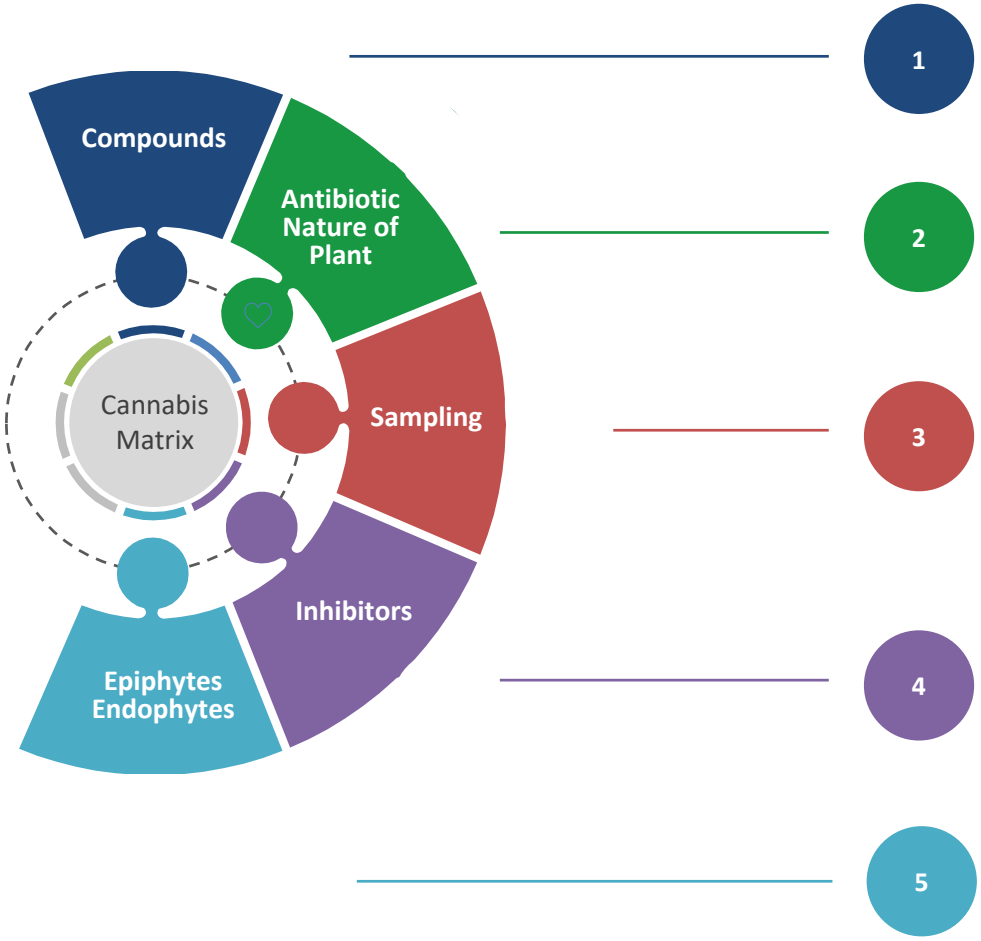
Very Complex Cannabis Matrix



- Over 900 analytical aspects for Cannabis
  - Cannabinoids, Terpenes, Flavonoids
  - Contaminants
  - Pesticides
  - Heavy Metals
  - Solvents
  - Mycotoxins/microorganisms
- Cannabis is 15-20% by weight an antibiotic. Each cultivar could have a different antibiotic library, which will alter what pathogens grow on culture bases systems
- No testing can fix improper sampling. Is the sample representative of the batch? When is the sample taken? Who takes the sample?
- Citrus in MIPs inhibit pathogen growth on culture based systems
- Detergents are used to dissolve lipids that break down pathogen cell walls - lower counts in culture
- Plants antibiotics properties are diverse and can be different from different types of cannabis cultivars.
- Pathogenic species live inside the cannabis plant such as Aspergillus. These organisms cannot be detected with culture based system without destroying viability

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Other Cannabis Laboratory Challenges

- Lab result variations between labs are due to different testing methods
- Use of non-validated methods when testing another sample type
- Lack of trained laboratory technical staff with cannabis experience
- Lab accreditation not required in some states (ISO 17025)
- Growers/processors/manufacturers allowed to perform sampling
- Lack of state-run proficiency testing programs with cannabis matrix
- Underfunded regulatory agencies unable to enforce testing rules
- **LAB SHOPPING**

Why is Lab Shopping a Problem?

Definition

- Some cannabis growers, processors, and product manufacturers look for a facility that will provide favorable results

- In extreme cases, “Tell me what you want it to say, and I will put it in the certificate of analysis”

Potency Inflation

- Too much emphasis on THC concentration

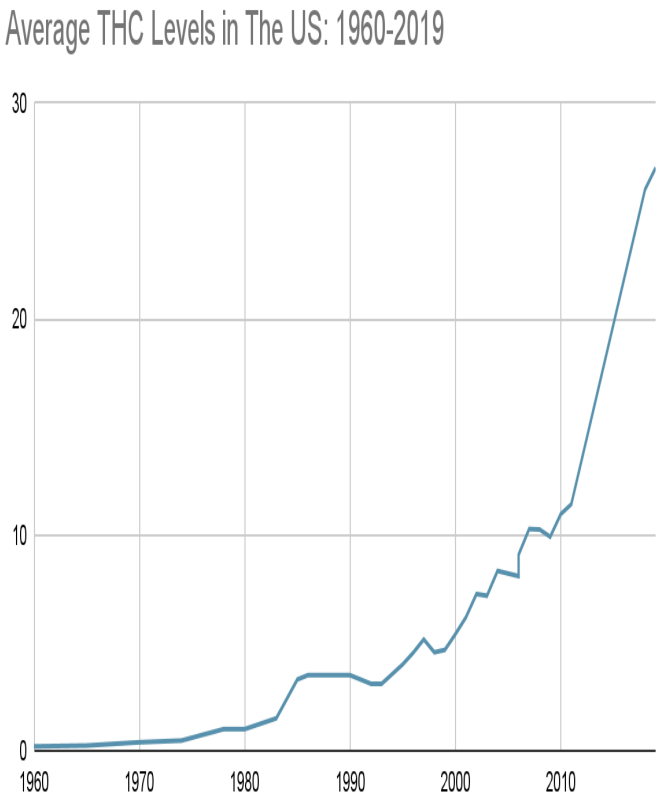
  - In other words, consumers will pay more for higher THC products, which affects the entire supply chain

  - Leads to some labs that consistently report higher THC concentrations

  - Leads some sample submitters to adulterate samples

    - spray THC oil on flowers

    - sprinkle THC crystals on flowers



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Pass on Contaminant Testing

- Pass on pesticide testing
  - In one state, due to non-detect/detect for 21 Category 1 pesticides- labs required to achieve LOQ of 0.1ppm

    - labs using LC/MS/MS, validated method, and highly trained chemists achieve a lower LOQ (*e.g.* <0.01ppm)

    - Wrong action: take samples to a lab with a higher LOQ (*e.g.* 0.1ppm), which may lead to false negative results

    - Right action: rule modification to set an action level

Real World Examples

- In 1 state, a scientist examined 14 months of results from 10 labs
  - 6 labs had a sample failure rate of 10-15%
  - 1 lab had a 0% failure rate
  - 3 labs had a <10% failure rate
  - A lower failure rate correlated with higher THC concentrations
  - 3 labs had 5% higher THC concentrations
  - Some growers data showed increased THC upon switching labs
- In another state, an audit found that a lab falsified 1200 THC results
- 30 Blue Dream samples brought from different growers w/16-38% THC
  - 2nd lab determined that all samples had between 16-20%
- In another state, an investigation found that a lab falsified 700 pesticide results over a 4 month period

Solutions

Suggested Solutions For Cannabis Regulatory Agencies

- Increase funding for lab and required testing rules enforcement
- Hire multiple scientific SMEs from different disciplines
- Have a lab accreditation program with annual lab audits conducted by trained regulators
- Establish a state-run proficiency testing program using cannabis samples
- Create standardized action levels for the different types of contaminants
- Require a set of instrument capabilities
- Require lab training program for technical staff with maintenance of training and competency records for each staff
- Should not use a historical gold standard test from other industries (*e.g.* plating method) as the reference standard test for this complex matrix

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Questions?

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