Workshop on Cannabis Product Quality

Analytical Testing for the Cannabis Industry: Consumer Safety vs Regulatory Requirements

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ProVerde Laboratories, Inc.
Outline

- Increasing global acceptance for cannabis
  - Multiple regulatory jurisdictions (Country, State, Municipality)
  - Quality requirements vary greatly
- Regulations, contaminants, action limits and testing methods
  - Product sampling for laboratory submission
  - Cannabinoid potency
  - Pesticide testing
  - Microbial testing
  - Lack of harmonization (standardized methods or processes)
- Economic pressures on regulated market
  - Black market
  - Synthetic cannabinoids and analogs
Global Acceptance – Cannabis Regulatory Programs

US: 37 states

Global: 50 Countries

Medical use
Adult use

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By Jamesy0627144 - Derived from BlankMap-World.svg and BlankMap-World6-Subdivisions.svg., CC BY-SA 4.0, https://commons.wikimedia.org/w/index.php?curid=71821752
Laboratory Accreditation

Why is Accreditation Important to the Cannabis Industry?

- Most states require cannabis laboratories to be accredited
- ISO 17025 is most common, ORELAP accreditation required in Oregon
  - Confidence that products are tested by a competent laboratory
  - Confidence that laboratories have consistent processes and practices
  - Confidence that the laboratory is committed to good laboratory and ethical practices

- Calibrated Instruments
- Proficiency Testing
- Documentation

- Validated Methods
- Employee Training
- Routine Audits
United States – Specific Challenges

- Federally illegal
  - Restricts access to financial/legal services
    - Bank accounts, loans, leases/mortgages, tax incentives, insurance
    - Publically traded companies often will not provide services
    - Prevents access to federal assistance programs (e.g. during COVID)
  - Complicates a nationwide Proficiency Testing (PT) program

- Regulations established on a state by state basis
  - Large variance in requirements
  - May be influenced by industry lobbyists without regard to consumer safety

- Quality requirements vary by state
  - Testing for different contaminants
    - Utilization of different testing methodologies
  - Different acceptance levels
    - Samples that fail in one jurisdiction may pass in a different jurisdiction
United States – Range of Contaminant Action Limits

- **Residual Solvents**
  - Butane: not required -------- 12 ppm -------- 800 ppm -------- 5,000 ppm

- **Heavy Metals**
  - Lead: not required -------- 500 ppb -------- 10,000 ppb

- **Mycotoxins**
  - Aflatoxin: not required -------- 20 ppb

- **Pesticides**
  - Required poorly defined
  - 9 pesticides 10 ppb
  - 66 pesticides ND(?) to 10,000 ppb

- **Microorganisms**
  - Not Required
  - **E. coli/Salmonella**
    - Total aerobic
    - Total yeast & mold
  - **E. coli/Salmonella**
    - Aspergillus
  - **E. coli/Salmonella**
    - Aspergillus +7 other species
United States – Sample Collection

- Sample collection requirements varies by state
  - Some states utilize 3rd party or laboratory sample collection

- Several states permit producers to select and submit their own samples for testing
  - Samples may be cherry picked, not representative of bulk sample batch
  - Lab samples may be manipulated to increase potency measurements
    - Excessive drying, removal of moisture inflates %THC
    - Samples may be augmented with additional THC (kief)
  - Lab samples may be treated to kill microbial contaminants
    - Bulk sample batch may still contain harmful microorganisms
Cannabinoid Potency

- Highest potency brings the highest retail price
  - Less educated consumers driven by high THC content

- Has led to industry-wide potency inflation challenges
  - Producers may augment their samples prior to testing
  - Laboratories have significant incentive to manipulate samples and/or data
  - Some laboratories advertise “Highest Potency Results in the Market!”

- Most states keep cannabis testing data off-limits to public scrutiny
  - Often times little (if any) state-level review of data quality
  - Prevents independent review of collected data
Microbial Regulatory Approach

- Regulatory action limits may include “Total” counts
  - Total aerobic, total coliform, total bile-tolerant gram negative, total yeast & mold
  - Does not distinguish good from bad microorganisms
  - Product that does not pose risk to consumers may fail, presenting loss to producers

- Regulatory action limits may include only speciated microorganisms
  - Some states only require *E. coli, salmonella, aspergillus*
  - Assumes these are the only pathogens of concern
  - Does not include other pathogens: pseudomonas, penicillium, staphylococcus

- More recent regulatory limits include a broader combination of both
  - Total counts + several speciated microorganisms
  - Testing gets expensive for producers
## Microbial Testing Methods

- Measurement of microorganisms is impacted by choice of testing method

<table>
<thead>
<tr>
<th>Culture Based Assays</th>
<th>Pros</th>
<th>Cons</th>
</tr>
</thead>
</table>
| Relies on growth of microorganisms | - Long history of use in food safety  
- Detailed in the FDA Bacteriological Analytical Manual (BAM)  
- Has been certified for use in cannabis by AOAC  
- Low cost equipment | - Growth can be dependent on culture media selection  
- Non-selective growth  
- Longer turn-around times necessary to grow cultures  
- Not all microbes can be cultured (False Negatives) |
| - Culture Plates  
- PetriFilms  
- Most Probably Number | |

<table>
<thead>
<tr>
<th>Molecular Based Assays</th>
<th>Pros</th>
<th>Cons</th>
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</table>
| Identification of species specific molecules (DNA) | - Best approach for species identification (specificity)  
- High sensitivity  
- Rapid turn-around times  
- High throughput  
- Automation | - Primer choice is critical  
- False positives from DNA of non-viable microorganisms  
- False negatives from use of inappropriate primer  
- High risk of cross contamination  
- Instrument and supplies can be expensive |
| - PCR  
- qPCR  
- MicroArray  
- ELISA | |
Economic Pressures

- Regulated cannabis production is expensive
  - Licensing fees, real-estate, insurance, production supplies, testing requirements, HR requirements, taxes, financial services, municipality payments

- Black market
  - Many expenses detailed above don’t apply. Low overhead leads to lower prices
  - Pervasive use of pesticides
  - Synthetic cannabinoids and analogs
  - No quality requirements means highly contaminated consumer supply
  - High risk to consumer safety (EVALI, contaminants, synthetic cannabinoids)

- Puts financial infrastructure of regulated market at risk
  - Oversupply and black market push retail prices and margins down
  - In Massachusetts, retail flower price dropped 42% in last year
    - Good for consumers, until regulated market collapses
Pesticides in Vape Cartridges

<table>
<thead>
<tr>
<th>Residue</th>
<th>Level (ng/g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bifenazate</td>
<td>32,920</td>
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<tr>
<td>Bifenthrin</td>
<td>296,663</td>
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<tr>
<td>Cyfluthrin</td>
<td>19,422</td>
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<tr>
<td>Etoxazole</td>
<td>463</td>
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<tr>
<td>Imidacloprid</td>
<td>809</td>
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<tr>
<td>Myclobutanil</td>
<td>22,277</td>
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<tr>
<td>Paclobutrazol</td>
<td>769</td>
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<tr>
<td>Piperonyl Butoxide</td>
<td>934</td>
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<tr>
<td>Spiromesifen</td>
<td>744</td>
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<tr>
<td>Spirotetramat</td>
<td>75</td>
</tr>
<tr>
<td>Carbaryl</td>
<td>8,024</td>
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<tr>
<td>Carbofuran</td>
<td>6,009</td>
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<tr>
<td>Metalaxyl</td>
<td>5,205</td>
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<tr>
<td>Diazinon</td>
<td>578</td>
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<tr>
<td>Tebuconazole</td>
<td>16,163</td>
</tr>
<tr>
<td>Malathion</td>
<td>58,086</td>
</tr>
<tr>
<td>Chlorantraniliprole</td>
<td>950</td>
</tr>
</tbody>
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Additives in Vape Cartridges

- α-tocopherol
- α-tocopherol acetate
- Vitamin E acetate

Vitamin E Standards

Believed to be responsible for EVALI crisis
The term “synthetic” refers to chemical compounds created through a chemical process by human agency, as opposed to those of natural origin. These compounds can be synthesized to imitate a natural product (e.g. $\Delta 9$-THC), or they can be synthesized to create a compound not found naturally (e.g. $\Delta 9$-THCPO).
Synthetic Cannabinoids – in Vape Products

Significant concentrations of un-natural isomers and synthetic byproducts.

* No toxicity information available *
Synthetic Cannabinoids – in Edibles

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Synthetic Cannabinoids – New analogs

Not found naturally
No toxicity information
Synthetic Cannabinoids – Mixtures

INGREDIENTS: 1000 MG Total Extracts. HHC, D8THC, THCo, CBG, CBN & Live Resin Terpenes.

This product contains a custom blend of hemp-derived 5 active cannabinoids:
- THCo
- CBG
- CBN
- Δ8 THC
- HHC

and contains < .3% Δ9 THC

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Synthetic Cannabinoids – Widely Available

- Available on Amazon.com
- No mention of THC
- No mention of Δ8
- No warning on psychoactivity
- No age restriction for purchase
Δ8-THC Legal Status
Four Dead After Using Synthetic Cannabis Containing Rat Poison

There were a total of 52 cases of people affected with coagulopathy, a bleeding disorder.

By – Ben Munson, Editor, Cannabis Equipment News, Unit 202 Productions, Eric Sorensen
Oct 11, 2022

Child’s death attributed to delta-8 THC is another blow to CBD sector

Published 7:47 PM EDT, Fri October 21, 2022
Summary

- Cannabis safety is complicated by jurisdictional variance
  - Contaminants to be evaluated and tolerance limits vary significantly
- Challenges can be exacerbated by weak/ineffective regulations
  - Product sampling, potency inflation, pesticide testing, microbial contaminants
- Black market poses multiple threats to the regulated cannabis industry
  - Undercutting prices drives consumers to the unregulated market
  - Absence of quality standards poses significant risk to consumer safety
  - Prevalence of synthetic products on the market presents unknown hazards
- Standardized methods and proficiency testing will help to address many of these challenges
- Ultimate goal would be for global harmonization of standards!
Thank You!

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