Howard L. Bost Memorial Health Policy Forum

Who can grow and sell, what kinds of products, and where?

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Hemp vs. Medical Marijuana

- **Hemp**
  - Fiber, Seed and Cannabinoid Production
  - High CBD/Low THC
  - According to current federal law: Cannabis is considered hemp – not marijuana – no part of the plant (including the leaves and flowers) exceeds a THC concentration of “more than 0.3 percent on a dry weight basis.”

- **Medical Marijuana**
  - Higher THC Levels
  - >0.3% THC allows for more optimal genetics for product formulation
  - Additional secondary cannabinoids and terpenes for added therapeutic effect

- Benefits and products?
Current Landscape

- Industrial Hemp Federally Legal as of 2018
- Kentucky Hemp Program: 2018
  - KDA approved 1,035 applications to cultivate, 41 processor/handler applications
  - Processors reported $57.75 million in gross product sales ($16.7 million in 2017)
  - Processors spent $23.4 million in capital improvements
  - Employed a total of 459 people in 2018
- 3 Legal Medical Marijuana States & DC
- 11 Legal Recreational Marijuana States & DC
- Massachusetts
  - 50 RMDs approved for sales
  - 59,288 active patients
  - 7,005 active caregivers
  - 293 registered healthcare providers
  - 66,945 active healthcare provider certifications
- Oregon
  - 24 Laboratories
  - 196 Processors
  - 1094 Producers (Growers)
  - 591 Retailers
  - 133 Wholesalers
- CBD projecting the market to grow by 700% to $2.1 billion by 2020, according to Forbes and Hemp Business Journal

The Endocannabinoid System: The Basis for Medical Cannabis

- Regulates our physiology, mood, and everyday experience
- Brain receptors respond pharmacologically to cannabis and cannabis extracted biomolecules
- Over 100 cannabinoids and several hundred more terpenes in cannabis plant
  - CBD and THC studied most extensively
- Endogenous cannabinoids (such as anandamide and 2AG) that occur naturally in the mammalian brain and body
- Synthetic cannabinoids created by pharmaceutical researchers
- CBD and THC have been demonstrated (clinically and pre-clinically) to have
  - Anti-tumoral, antioxidant, anti-spasmodic, anti-psychotic, anti-convulsive, and neuroprotective properties.
  - CBD directly activates serotonin receptors, causing an anti-anxiety effect

Source: Project CBD, 2019.
Cannabis Supply Chain: Who’s Involved?

- Licensed by individual states for both hemp and medical marijuana
- State programs and regulations vary
  - Regulations for growing
  - Regulations for production
  - Regulations for final products – potency and contaminants
  - Regulations for analytical laboratories – sampling and analysis

Source: Twitter.com/GovCanHealth
Current Problems and Risks: New Industry Growing Pains

- Limited and inconsistent federal and state regulations
- Lack of quality control and traceability throughout supply chain
- Quality of lab data, TAT
- Additional clinical and pre-clinical data needed and being acquired
- Farmers and producers: variable genetics, inconsistent product valuations
- Products are unsafe and inconsistent
The Cannabis Industry: How long can it stay the Wild West?

- The Industry Drive for Quality, Transparency and Accountability is here.
  - Investor expectations
  - Customer Base and Dispensary demand
  - FDA and USDA regulations and guidelines to be issued on hemp and CBD
  - Focus on Consistency and Uniformity as a challenge in:
    - Determining the right product for different medical conditions or varying desired effects
    - Obtaining regular medicine that was effective for a medical condition
    - Perception and trust issues in states considering legalization
  - Risk:
    - Failed/Lost Product due to Compliance Testing
    - Litigation
    - Recalls
    - Public Health
    - Public Perception

- Quality control minimizes risks and optimizes value
cGMP: Controlling Product Quality in Cannabis Production

Good Manufacturing Practices

- Requirements used by the FDA to ensure products are produced consistently and meet quality standards
- Pharmaceutical, Food, Nutritional Supplements
- Non-Cannabis cGMP testing often happens in-house.
- In-house testing or contract testing with an ISO 17025 accredited laboratory until regulatory testing is considered good practice.

Other industry-parallel GxP

- GLP – Good Laboratory Practices
- GAP- Good Agricultural Practices
- FDA and USDA guidelines for hemp and CBD products will shed light
ISO: Voluntary Standardization

- International Organization of Standards
  - Business Standard that provides Quality System requirements with freedom to demonstrate compliance in various ways
  - Often voluntary-comment on credibility

- ISO Standards
  - ISO 9001 Quality Management Systems (Manufacturing)
  - ISO 17025 Testing Laboratories
  - ISO 22000 Food Safety Management
Cannabis Production: An Overview

- Cultivation
  - Indoor vs. Outdoor

- Extraction
  - CO2 (GRAS)
  - EtOH/Cryo-EtOH
  - Hydrocarbon
  - Cold-Press/Hydraulic Press
  - Aqueous (Cold Water Extraction)
  - Newer Production Technologies

- Post-Processing
  - Winterization
  - Decarboxylation
  - Distillation
  - Chromatography

- Final Product Development
  - Several Delivery Mechanisms
  - Whole Flower
  - Sublingual
  - Transdermal - lotions, creams, salves, patches
  - Oral – capsules, edibles
  - Suppositories
  - Vapes
  - Animal/Pet Products

PHARM CBD (WWW.PHARM-CBD.COM)
Current Market Values

- **Flower**
  - Smokeable
    - High CBD $100 - $500/lb
    - High THC >$1000/lb
  - Biomass for Processing
    - $2-$4/CBD % Point/lb

- **Isolates**
  - CBD: $3K-$5K/kilogram
  - CBG: $10K-$20K/kilogram
  - CBN: $15K-$30K/kilogram

- **Full Spectrum**
  - High CBD (>60% CBD) Winterized Crude – $1000 - $2000/kilogram
  - High CBD Distillate - $4000+

- **Broad Spectrum (THC Free)**
  - $5000 - $6000/kilogram

- **Final Products** $0.05 - $1.00/mg
Cannabis Cultivation: Controlling Contamination and Optimizing Product Quality

- Quality and Consistent Genetics
  - Feminization
    - Minimizes cross-pollination
    - Consistent biochemical profiles
    - More robust plants

- Grow in Controlled Environments where possible
  - Soil
  - Nutrients
  - Chemicals
  - Temperature
  - Humidity
  - Lighting
  - Ventilation

- GAPs and SOPs
  - Process marijuana in a safe and sanitary manner
  - Leaves and flowers of the female cannabis plants
    - Well cured and free of seeds and stems
    - Free of dirt, sand, debris, and other foreign matter
    - Free of contamination by mold, rot, other fungus, pests and bacterial diseases
    - Prepared and handled on food-grade environment no contact with bare hands
    - Packaged in a secure area.
    - Stored in proper temperature, humidity, protected from light and oxidation
Trichomes: What are they and why we need to preserve them

• Defense for plants
• Produce important biochemicals
• Volatile and risk destruction
  • Physical contact
  • Heat
  • Light
  • Oxygen
• Proper trimming, drying, and curing techniques can help keep trichomes viable for longer, which in turn will preserve the cannabinoids and terpenoids contained within.
cGMP in Cannabis Production

Identify Critical Quality Attributes and Critical Process Parameters for each Product/Process

Establish Product Specifications/Quality Limits

Source and Intermediate Material Testing

Critical Control Points
  • Controlling introduction points of contaminants during processing and production

End-Product Uniformity Testing

Product Control
  • Increases consistency and efficiency
  • Entire process designed, evaluated, and continuously improved.

Done at the scale necessary to ensure product consistency, quality and safety.

Risk and process/product improvement drives testing choices.

Beginning/Middle/End Testing
  • Testing for desired attributes (Cannabinoids, Terpenoids) and contaminants alike
  • Source Material - Ingredients
  • Equipment – Carryover, consistent operation
  • Final Product – Desired attributes, uniformity, contaminants
Non-Regulatory Testing in Cannabis

Paradigm change: One-Time Compliance Testing is moving towards GMP Testing for the entire process.

Regulatory compliance is not enough and for a different purpose. GMP Testing is starting to become a regulator practice to enhance product and process control and optimization efforts.

Industry Challenge: Product Variability

Variability is reduced by having specifications for each step of the process.

Industry Challenge: Addressing Contaminant Introduction Points

Testing source material through final product, verifying equipment cleaning and carry-over prevention procedures. Cannabis product development and manufacturing has to be improved and controlled.

Improvement in the industry by mirroring other cGMP industries:

Get it right the first time with careful planning. Continuous improvement.
Laboratory Selection is Critical

Is the Laboratory Accredited
- ISO 17025 Accredited
- State Certified
- FDA/USDA Recognized

What are your initial and end products?
- Laboratories should be able to demonstrate proficiency in each matrix to be tested

Can the laboratory meet your needs?
- Hemp methods: low THC and high CBD
- Sensitive instrumentation: catch pesticides in source material
- Quality Control
  - Can the lab achieve the precision and accuracy in data that will drive your GMP/QbD decisions?
cGMP/QbD production will depend on your state, your process, and your products.

Product and business decisions are based on consistent data on an ongoing basis.

Laboratory data of known and appropriate quality is key to any GMP/QbD system.

Choosing a laboratory to evaluate your system before regulatory testing is crucial to success.

Consistent and safe user experience

Consistent products of known quality and uniformity based on accurate data

Controlling product quality, drives costs down for our operations and ultimately our consumers

Risks identified and mitigated in timely fashion

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Data and customer feedback used to drive targeted therapies for humans and animals

Local economies and farmers benefit from new sustainable crop

Escaping the Wild West and entering Legitimacy
Extra Slides
Process Control in Cannabis

QUALITY AND TRACEABILITY FROM “SEED TO SHELF”

- Production method should be safe and avoid introducing unwanted contamination into products
- FDA recognizes CO2 and Cold-Press as GRAS
- Traceability throughout supply chain
- Production conducted in ISO Certified and cGMP Compliant Laboratory
- Quality by Design (QbD)
- Manufacturing performed under cGMP principles
- Quality Assurance System
- Standard Operating Procedures
- Documentation
- Continual Improvement throughout product lifecycle

- Test, Test, Test!
  - Raw material testing
  - Intermediate Testing
  - Final Product Testing
  - Representative Samples to Characterize Complete Batch
- Establish product specifications for release
- Labeling and Packaging Standards
- Contaminant remediation
- Clean extractions – removal of contaminants and unwanted constituents
- High throughput and efficiency
- Optimize yield
- Isolation of new/novel cannabinoids