Development of Medicinal Marijuana Testing in New Jersey

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DEPARTMENT OF AGRICULTURE

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NJ Medicinal Marijuana Program (MMP)

- The *New Jersey Compassionate Use Medical Marijuana Act* (Senate Bill, No. 119, *the Act*, N.J.S.A. 26:6I-1 et seq) was signed into law on January 18, 2010.
- The NJ Department of Health (NJDOH) Medicinal Marijuana Program was established to implement the law, develop and enforce the regulations.
- NJ PHEL-ECLS started the Marijuana Testing Project in June 2012.

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Project Goals

- **To comply with the Law**
  - Potency compliance of < 10 % Delta-9-Tetrahydrocannabinol (Δ-9-THC)
    - Free of pesticides, toxic heavy metals, and mycotoxins

- **To establish reliable test methods**
  - Establish an accurate, sensitive, cost effective, rugged, defensible test method for medicinal marijuana with a shortest specimen turn around time.

Implementation Protocols for a Test Method

- Select target analytes
- Select analytical instrument
  - HPLC-DAD, ICPMS, and HPLC-Fluorescence Detection
- Provide personnel training
- Develop the test method
- Validate the test method
  - Selectivity, Precision Accuracy, Representation (sample size), Completeness, Comparability, Sensitivity
- Establish SOPs
- Establish reporting system
- Implement the test method

Analysis of Marijuana for Cannabinoids Using HPLC-DAD* Method

Target Analytes

- Cannabidiol (CBD)
- Cannabidiolic acid (CBDA)
- Cannabigerollic acid (CBGA)
- Cannabigerol (CBG)
- Cannabinol (CBN)
- Delta-8-terahydrocannabinol (Δ-8-THC)
- ***Delta-9-Tetrahydrocannabinol (Δ-9-THC)***
- ***Tetrahydocannabinolic acid (THCA)***

HEAT

Note: THCA ------>Δ-9-THC

*High Pressure Liquid Chromatography – Diode Array Detector

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Sample Processing and Analysis Method for Cannabinoids

0.2 gram MM Ground individual or a composite cultivar

↓

Extraction and centrifugation

↓

Filtration and preparation of appropriate dilutions

↓

Evaporation, reconstitution, addition of internal standard, mix and inject

↓

Analysis by High Pressure Liquid Chromatography – Diode Array Detector

Note: % of batch weight per cultivar: 1-5%; ~2.5 g/sample

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Summary of Method Evaluation Results for Cannabinoids Analysis

- **Calibration range :** 0.25 – 50 µg/mL (v) (0.005 – 1% by sample wt)
- **Coefficient of Determination (R^2):** ≥ 0.995
- **Method Precision (%RSD) :** 5-12 %
- **Accuracy (%Recovery for % Δ-9-THC):** 105 ± 12.5% (spiked Medical Marijuana samples)

  Note: Allowable RSDs on sample duplicates : <30%

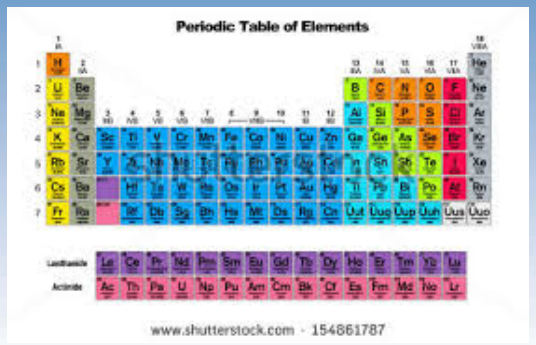
  Allowable Matrix Spikes Recoveries: 70% - 130%

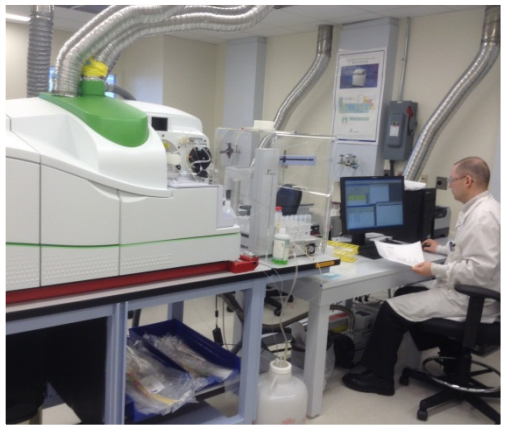
- **Detection Limit :** 0.25 µg/mL (v) (50 µg/g by wt)

Elemental Analysis on Medicinal Marijuana

Target Analytes

- Arsenic
- Cadmium
- Chromium
- Iron
- Lead
- Manganese
- Mercury
- Nickel
- Selenium
- Zinc





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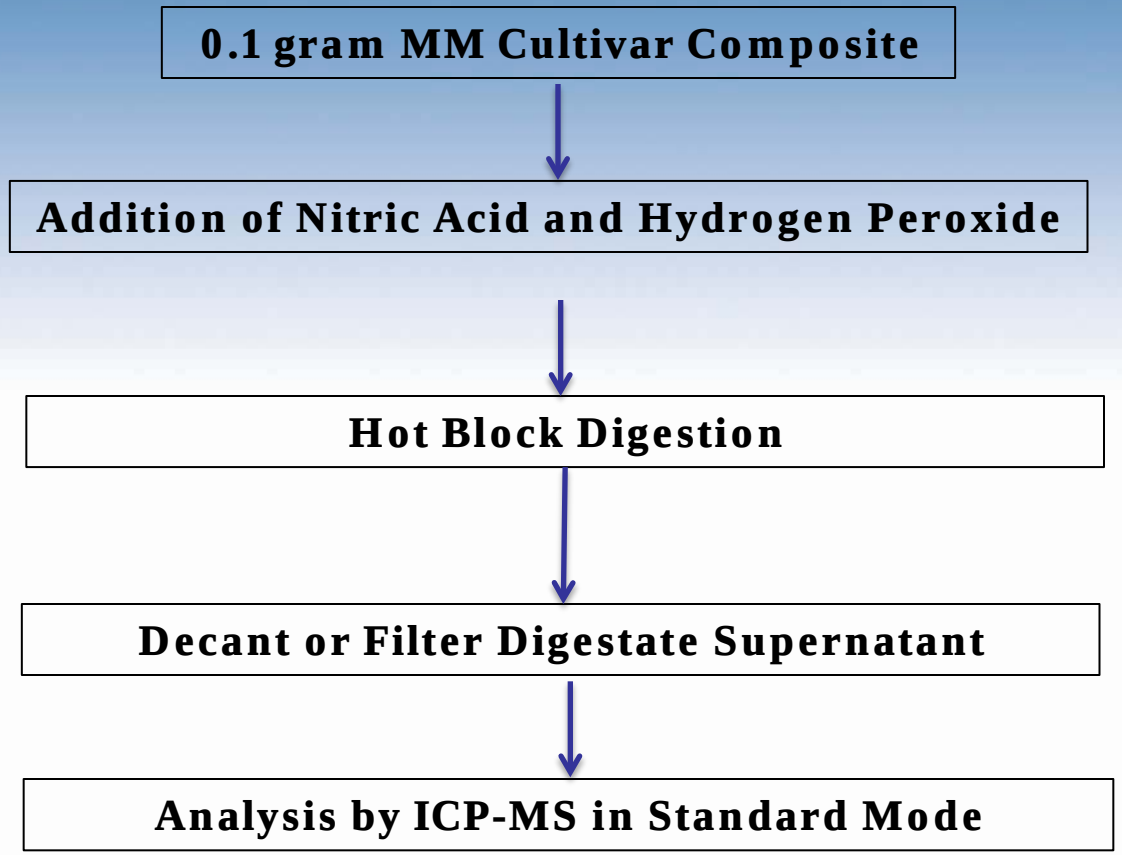
Sample Processing and Analysis of Metals in MM Using ICP-MS



QA/QC

- Internal Standards
- Laboratory Reagent Blank
- Calibration Verification at 3 levels
- Sample Duplicate
- Matrix Spike/Matrix Spike Duplicate

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Summary of Elemental Method Evaluations

- **Method Precision (%RSD)** :
  - 1.2% - 7.2% (< ±30%)

- **Accuracy** (%Recovery on Matrix Spikes):
  85% - 114% (< ±30%)
- **Linearity**
  - Concentration Range: 0.2 - 5 mg/g (± 25%)

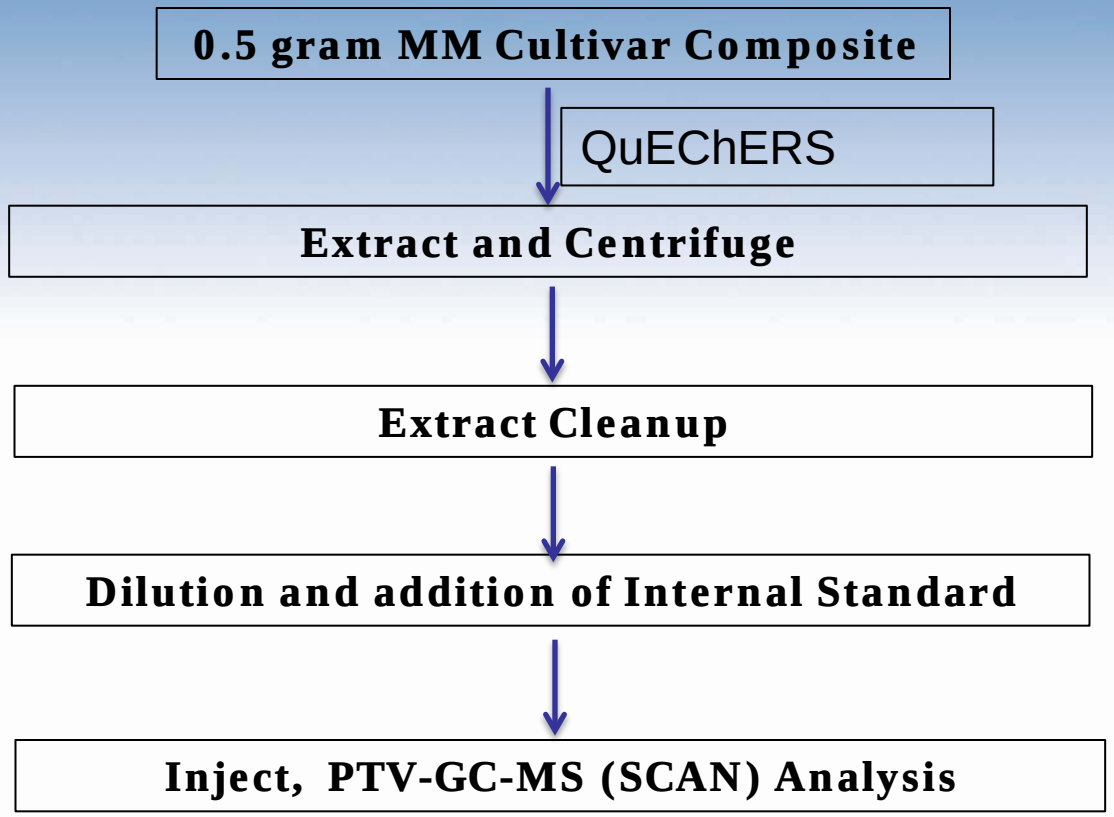
- **Detection Limits:** 0.2 – 5.0 mg/g

Analysis of Pesticides in MM by GC-MS

Chemical Class	Example Pesticides	Use
Organophosphates	Diazinon,	Insecticide
	Phosmet	Insecticide
	Dichlorovos	Insecticide
Pyrethroids	Resmethrin	Insecticide, Repellent
	Pyrethrin	Insecticide, Repellent
	Allethrin	Insecticide, Repellent
Carbamates	Terbucarb	Insecticide
	Fenunucarb	Insecticide
Avermectins	Abamectin (Avid)	Insecticide , Anthelmintic
Thiabendazoles	Thiabendazole	Parasiticide
Miscellaneous	Atrazine	Herbicide
	Bifenazate	Acaricide
	Bromocil	Herbicide
	Chlorpropham	Growth Regulator
	Fenarimol	Fungicide
	Pyrimethanil	Fungicide
	Metribuzin	Fungicide

**Note: A total of 83 commonly used pesticides were tested but currently 56 are incorporated into method.*

Sample Processing and Analysis of Pesticides in MM Using GC-MS



QA/QC Parameters

- Precision
- Accuracy
- Sensitivity

Summary of Method Evaluation Results for Pesticides*

- **Method Precision (%RSD)**: < 25%
- **Accuracy (%Recovery)**: 80-115%
- **Linearity (Concentration Range 50-2000 ppb)**: Coefficient of Determination (R^2) > 0.995
- **Method Detection Limit**: 2.5 µg/g

**Number of Pesticides (n = 56)*

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Mycotoxin Analysis in MM by HPLC-Fluorescence Detection

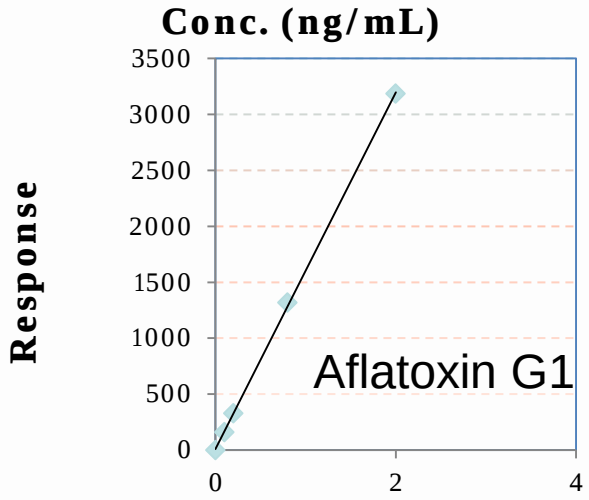
- NJDA cooperates with NJ Department of Health to perform Mycotoxins analyses for medical marijuana plant materials
- The tests are aflatoxins (B1, B2, G1, and G2) and Ochratoxin A
- High Performance Liquid Chromatograph with fluorescence detection

Mycotoxins Determination Method for Medical Marijuana

- Weigh 0.25 g
- Add extraction solution
- Vortex for 3 minutes
- Centrifuge for 10 minutes
- Transfer supernant into sample reservoir
- Drive out at the end
- Vortex the elution
- Diluted with MQ H_20
- Vortex the diluted elution
- Inject on HPLC - fluorescence detection for analysis

Summary of Method Evaluation Results for Mycotoxin

- Coefficient of Determination (R^2) ≥ 0.995
- %Recovery (spiked on matrix): 82-95%
- Precision (RSD %) ≤ 5%
- Detection Limit : 0.143 – 0.357 ng/g



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Summary Results of Cannabinoids Analysis (%wt) (October 2012 – April 2015)

Analyte	N	Median	Min	Max	%Detected	DL
CBD	283	ND	ND	2.130	27.9	0.012
CBDA	283	0.025	ND	17.59	79.5	0.012
CBG	283	0.050	ND	0.303	77.7	0.012
CBGA	283	0.299	ND	1.856	98.2	0.012
CBN	283	ND	ND	0.125	24.4	0.012
Δ-8-THC	283	ND	ND	0.282	12.7	0.012
Δ-9-THC	**283**	**0.446**	**ND**	**3.789**	**99.6**	**0.012**
THCA	283	14.7	0.396	34.2	100	0.012

Summary Results of Metals Analysis (µg/g) (October 2012 – April 2015)

Analytes	N	Median	Min	Max	%Detected	DL
Arsenic	49	ND	ND	1.00	0	1.0
Cadmium	49	ND	ND	0.89	26.5	0.2
Chromium	49	2.0	ND	2.1	0	4.0
Iron	49	211	94.9	493	100	5.0
Lead	49	0.10	ND	0.29	14.3	0.2
Manganese	49	228	70.3	443	100	0.2
Mercury	49	ND	ND	0.43	6.1	0.5
Nickel	49	ND	ND	1.3	26.5	0.5
Selenium	49	ND	ND	2.0	10.2	1.0
Zinc	49	113	52.6	239	100	5.0

Summary Results of Mycotoxins Analysis (ng/g) (October 2012 – April 2015)

Analyte	N	Median	Min	Max	% Detected	DL
Aflatoxin	47	ND	ND	2.3	2	1.0
Ochratoxin	47	ND	ND	0.21	2	0.18

Major Challenges

Administrative and Regulatory Perspective

- Staff
- Funding
- Time line
- Supply - DEA license, standards availability, sample collection, submission and receipt procedures
- No official reference values for pesticides, heavy metals or mycotoxins acceptance levels for the MM products in US.

Major Challenges-cont'

Technical Perspective

- Complex marijuana matrix
  - Interference in pesticide and metal analyses
  - Contamination of the analytical system
- Limited testing materials
- No SRM or PT samples
- Lack of partnership on MM analysis
- Difficulty in comparison among the results obtained from different analytical methods

Future Plan

- Development of a test method for pesticides analysis using Mass Quadrupole Time of Flight (TOF) Liquid Chromatography Mass Spectrometry (Q-TOF LC/MS).
  - increase sensitivity; increase capacity & capability
- Develop a test method for the measurement of microbial contaminants in MM.
- Develop a test method for MM edible forms.
- Establishment of national standardized testing procedures for the analysis of MM.
- Establishment of national acceptable limits for target analytes
- Transition from a routine testing laboratory to a regulatory laboratory

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