
# Cannabis: Chemotyping, Safety, Antibodies, & Clinical Correlates

The Emerald Conference

Jan 23, 2015

# CHEMOTYPING

**The Importance of Compounding**

**WHAT CAN WE LEARN FROM DATA MINING A LARGE DATABASE OF SAMPLES REGARDING CANNABINOIDS & TERPENES ?**

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# Data Mining Strategy

**Sample DB thru 20140806**

- **2280 Entries**
- **Sample Types: “Flower”, “Concentrate” & “Other”**

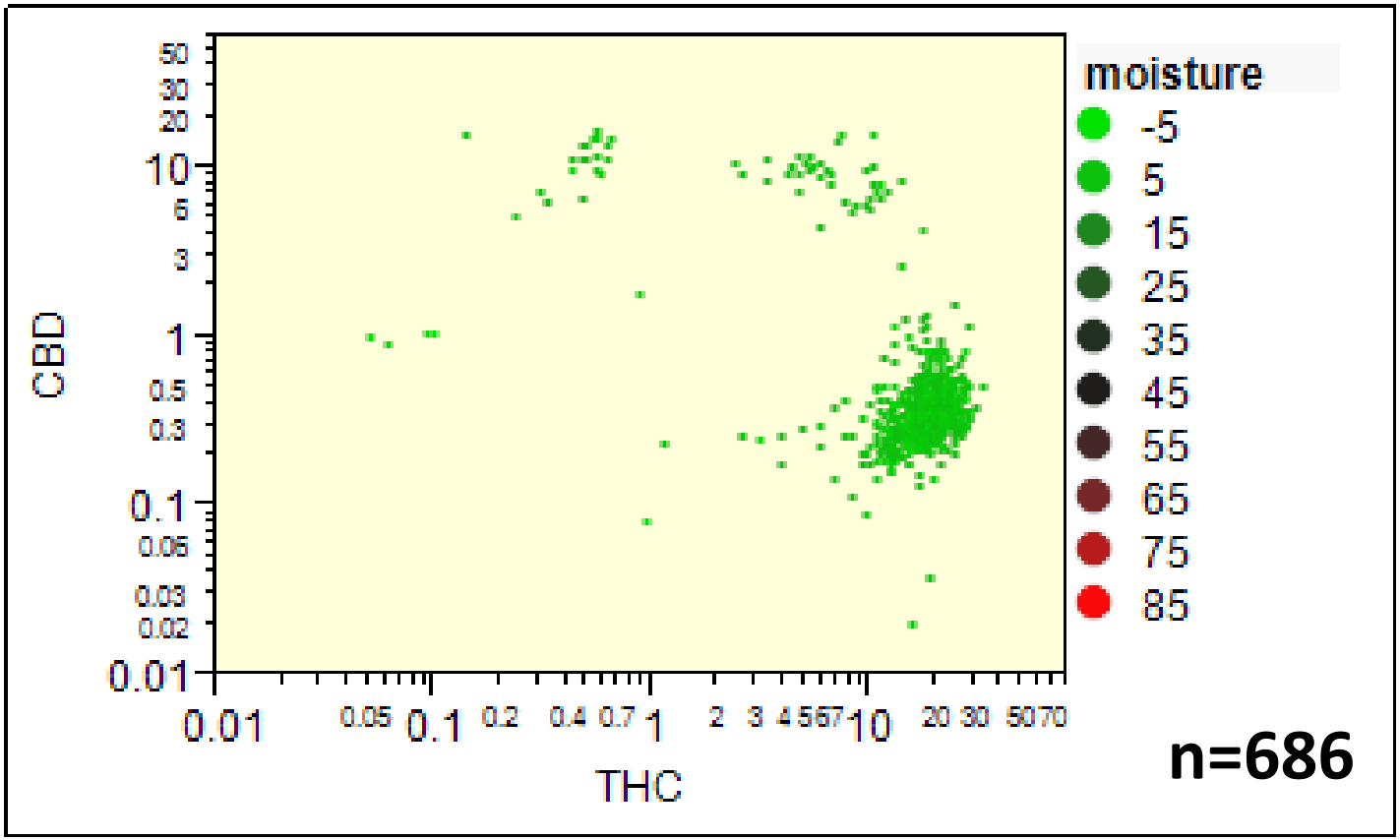
**Subset for Flower**

- **1388 Entries**
- **Analyze CBD content vs THC Content**
- **Stratify by Moisture Content**

DATA PROVIDED BY PHARMLABS LLC

# Scatterplot: Flower Samples – CBD vs THC

Moisture content < 6%



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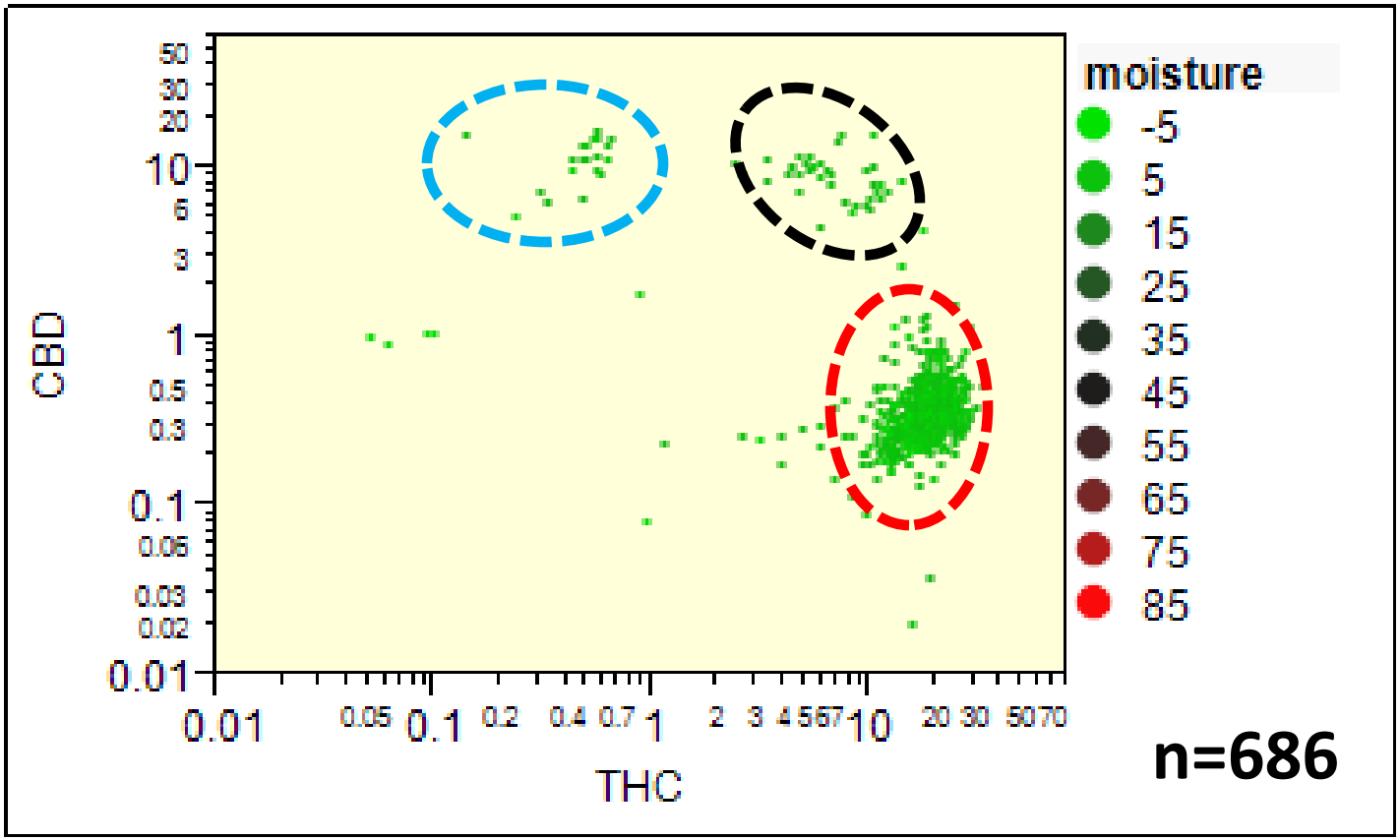

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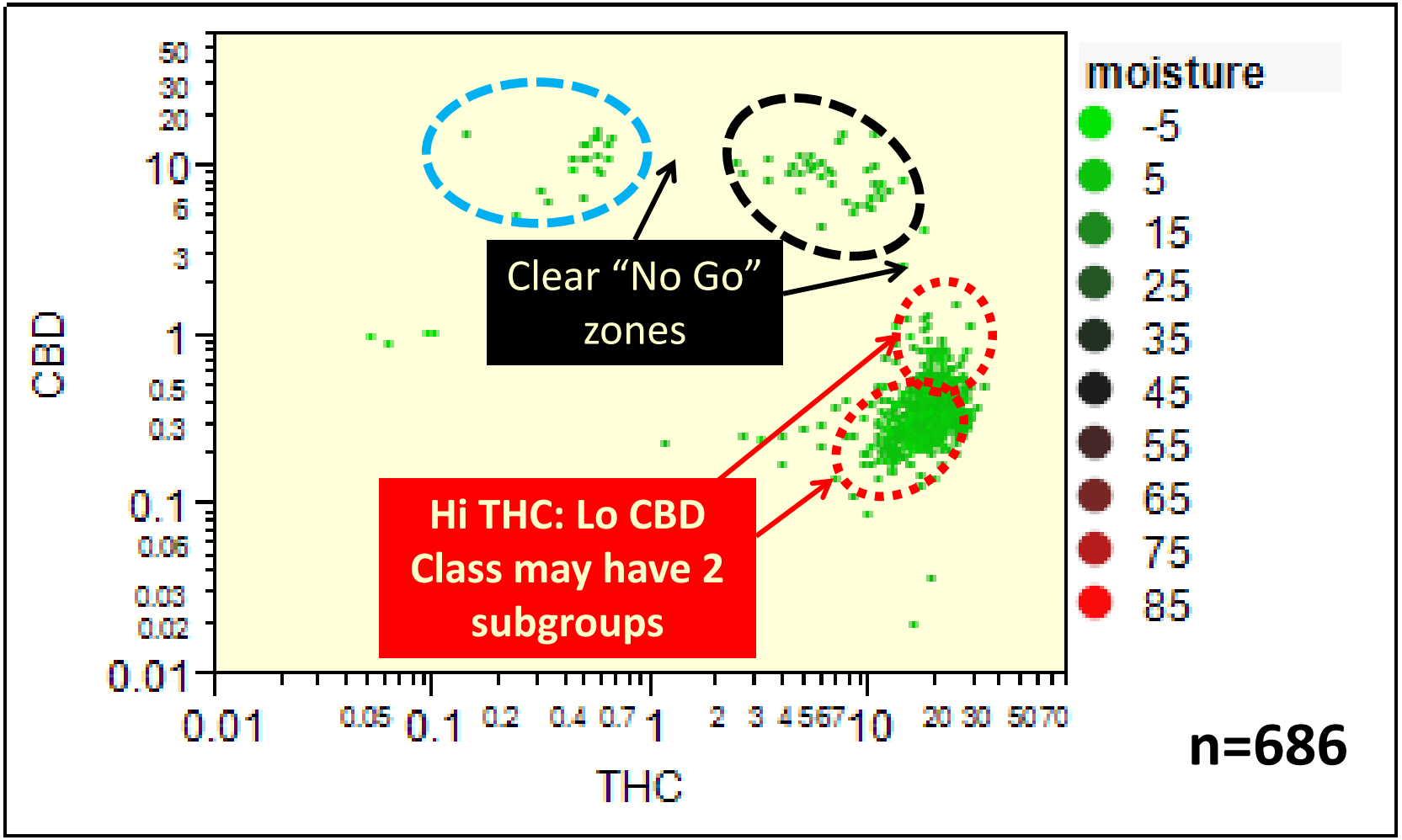
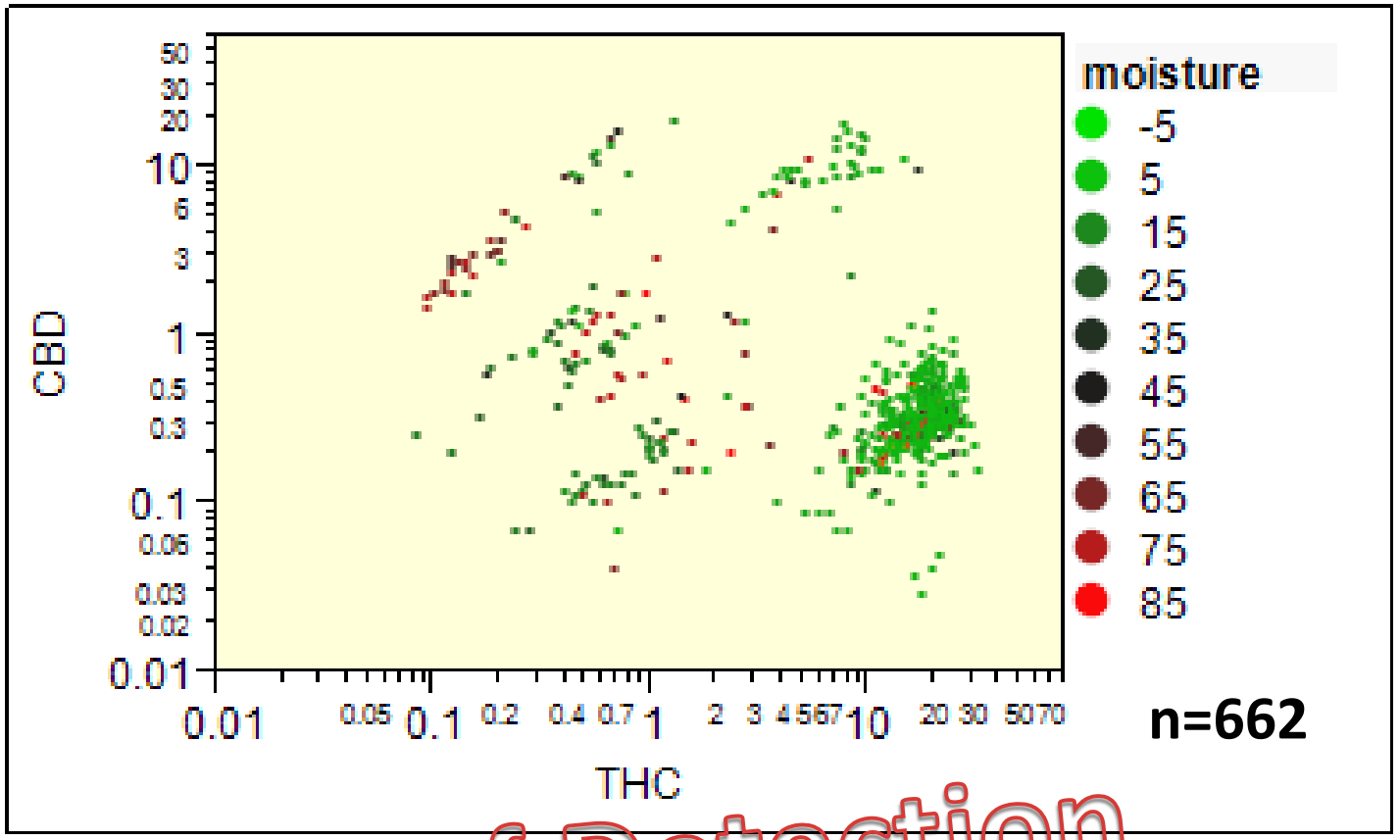


# Scatterplot: Flower Samples – CBD vs THC

## Moisture content > 6%




Early Leaf Detection

# Scatterplot: Flower Samples – CBD vs THC

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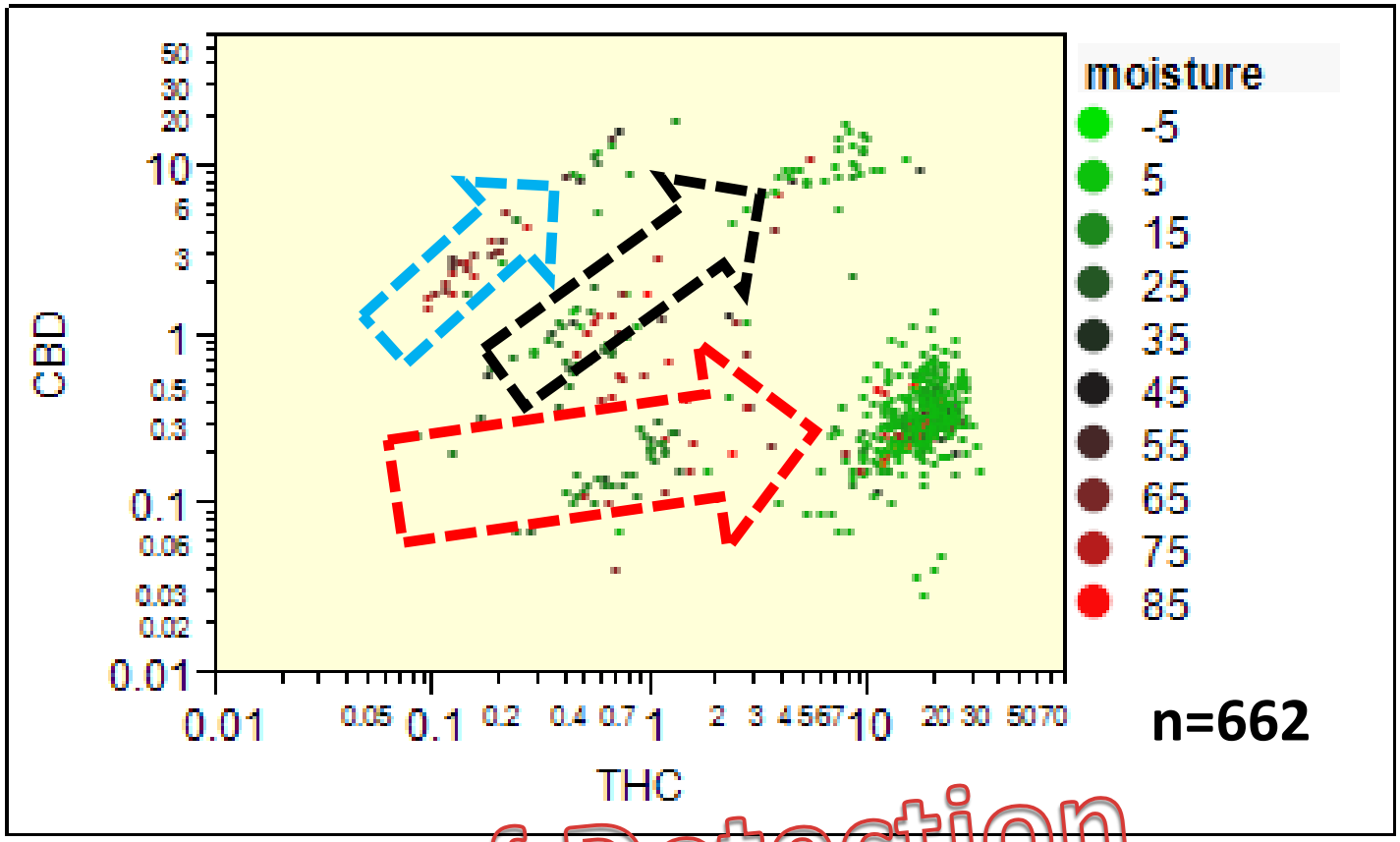


Early Leaf Detection

# What Can We Learn from Data Mining a Large Database of Samples Regarding Cannabinoids?

- That there are “No Go” zones for certain CBD:THC ratios
- Discrete Hi CBD: Lo THC;  Equal CBD: Equal THC; and Lo CBD: Hi THC groups are discernible
- These groups may actually consist of (largely overlapping) subgroups, i.e. in the case of Hi THC: Lo CBD
- Samples with high moisture content (early leaf detection samples) appear to align with these groups, while demonstrating lower overall cannabinoid production levels as might be expected

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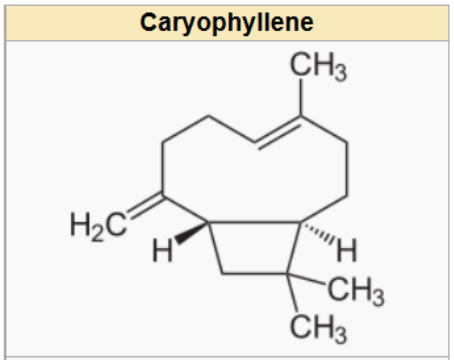
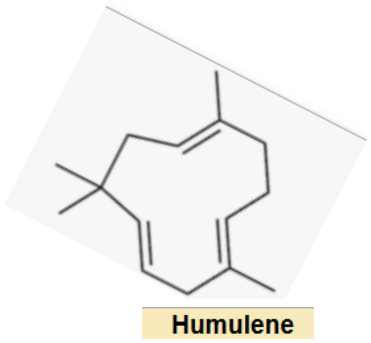
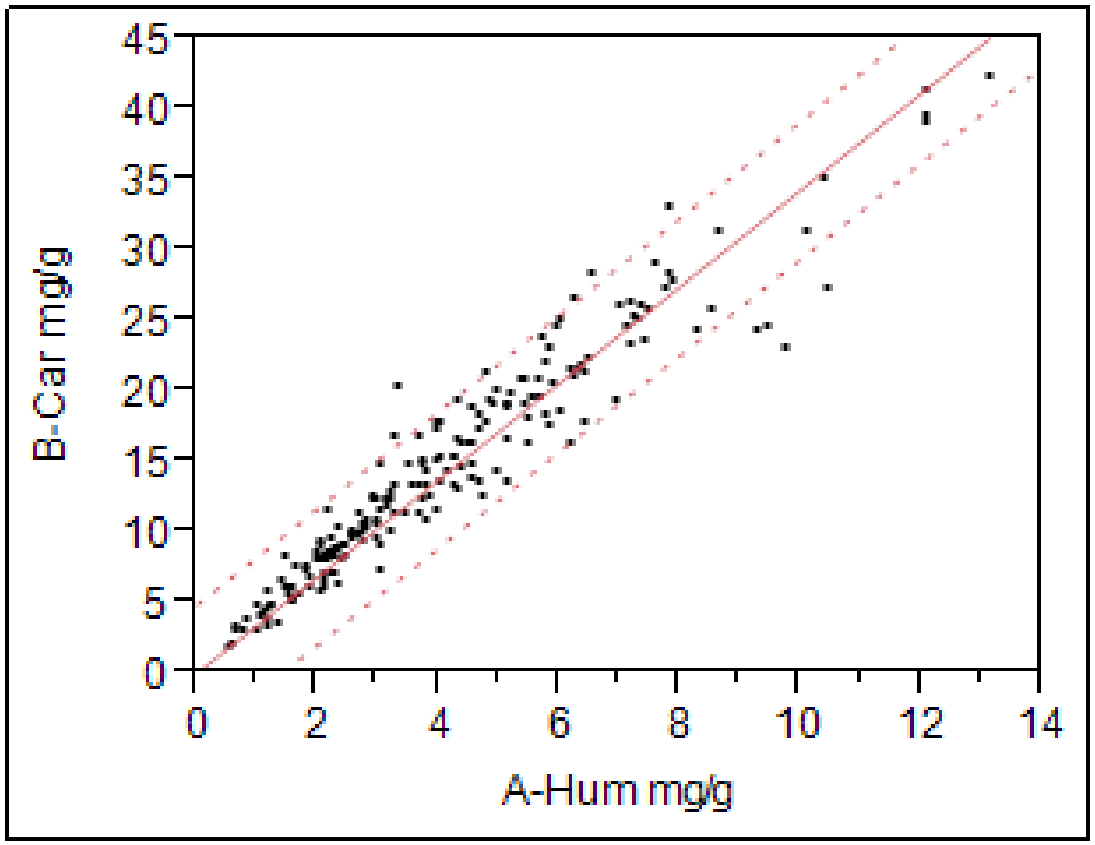
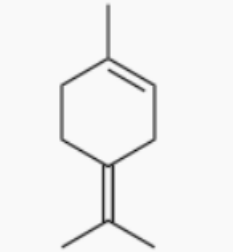
# Scatterplot: β-Caryophylline vs α-Humulene



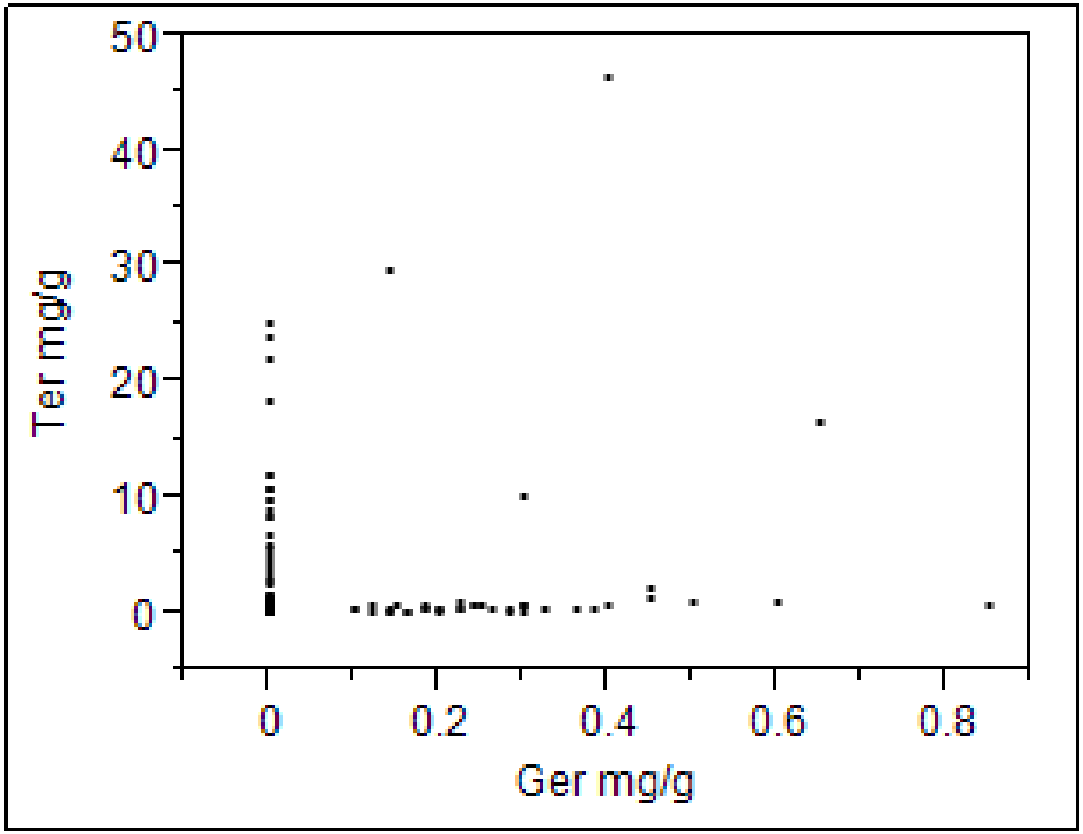



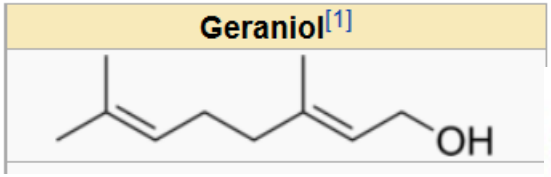



# Scatterplot: Terpinolene vs Geraniol



δ-Terpinene
(terpinolene)



# What Can We Learn from Data Mining a Large Database of Samples Regarding Terpenes ?

- One pair of terpenes is extremely tightly correlated with a fixed ratio of one to the other
- Another terpene pair shows extreme selectivity:  if one is present in a sample, the other will be absent in almost all cases

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# What Can We Learn from Data Mining a Large Database of Samples Regarding Cannabinoids & Terpenes ?

**OVERALL CONCLUSION:**

**That compounding (ie “making a salad”) with post-harvest stocks may offer the best option to derive cannabis products with a defined content of various actives.**

# SAFETY

**Setting draft guidance for mold & yeast content in Cannabis**

## ESTABLISHING REGULATORY BEST PRACTICES THAT ARE SCIENTIFICALLY SOUND AND EVIDENCE-BASED

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# Rationale & Background

- The elaboration of regulations and guidance informing Best Practices for Cannabis production is a necessary corollary of this rapidly evolving industry.
- Such guidance should be established in a manner that is both scientifically sound and evidence-based.
- To that end, we have quantified the anti-microbial activity of burning mold-infected Cannabis inflorescence.
- Our goal is to evaluate these results in the context of current draft guidance for mold & yeast content.

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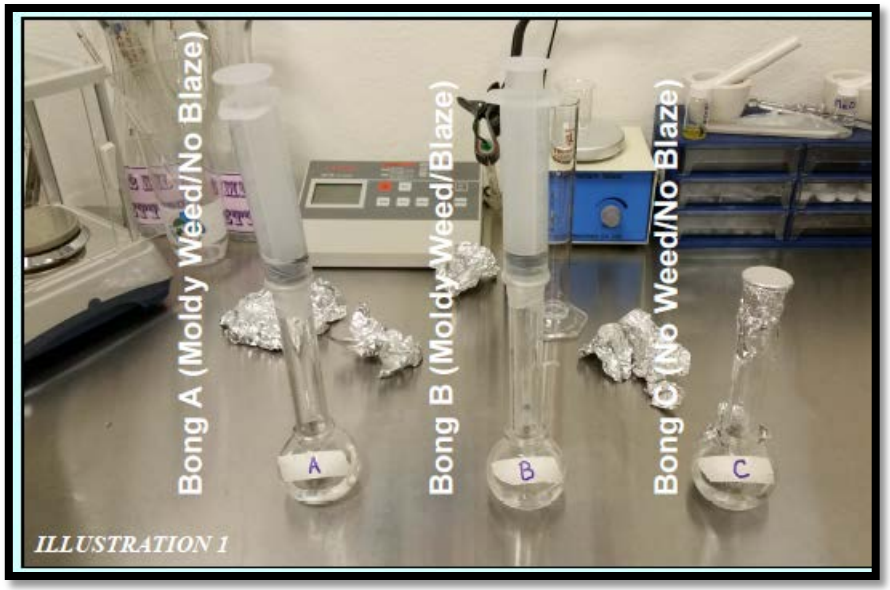
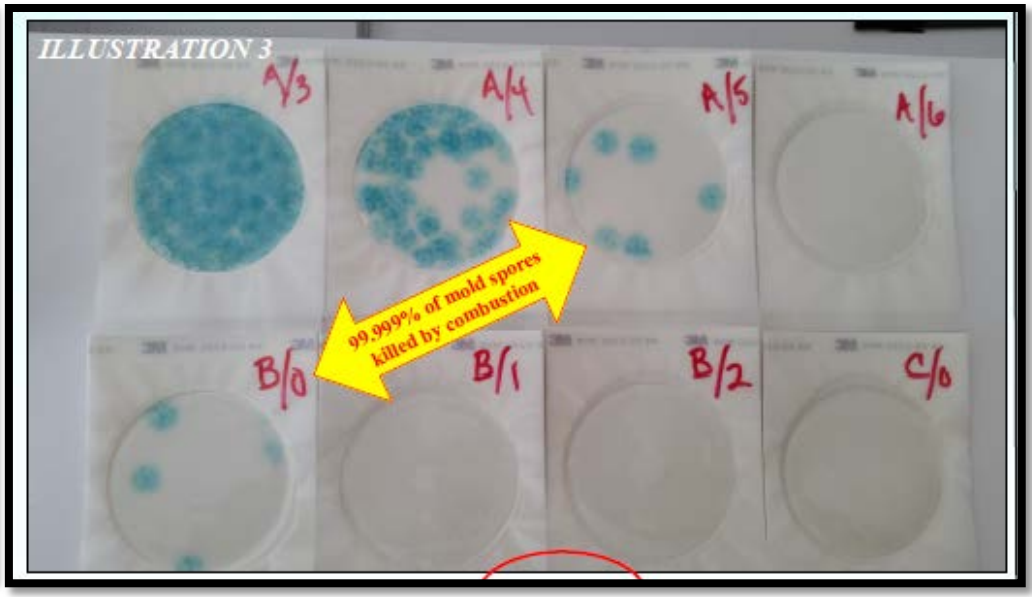
# Experimental Design & Results




$$\frac{Before}{After} = \frac{6 \times 10^5}{5 \times 10^0} = 1.2 \times 10^5$$

Or > 5 Logs of Mold Killed or > 99.999% Spores Killed!!!

PharmLabs

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**Table 9** Microbial and fungal limits recommended for orally consumed botanical products in the US (CFU/g)

| | Total viable aerobic bacteriat | Total yeast and mold | Total coliforms | Bile-tolerant gram-negative bacteria | *E. coli* (pathogenic strains) and *Salmonella* spp. |
|---|---|---|---|---|---|
| Unprocessed materials* | $10^5$ | $10^4$ | $10^3$ | $10^3$ | Not detected in 1 g |
| Processed materials* | $10^5$ | $10^4$ | $10^3$ | $10^3$ | Not detected in 1 g |
| $CO_2$ and solvent-based extracts | $10^4$ | $10^3$ | $10^2$ | $10^2$ | Not detected in 1 g |

* Unprocessed materials include minimally processed crude cannabis preparations such as inflorescences, accumulated resin glands (kief), and compressed resin glands (hashish). Processed materials include various solid or liquid infused edible preparations, oils topical preparations, and water-processed resin glands ("bubble hash"). Significant microbial contamination can occur during post-harvesting handling.

# Summary & Conclusions

- Results from this experiment show that the number of mold and yeast colonies that survive when cannabis is burned would be well below the American Herbal Pharmacopeia (AHP) and European Herbal Pharmacopeia (EHP) recommended limits.
  - These recommended limits, which are for orally consumed botanical products = $10^4$ CFU/g
- To our knowledge, no such guidance has yet been established for botanical products destined for smoking
- PharmLabs results would therefore support an absolute upper threshold for ***non-mycotoxin producing*** mold strains of $10^5$ CFU/g for cannabis intended for smoking.
  - We are currently carrying out studies to establish appropriate mold and yeast contaminant levels for cannabis intended for vaporizing.

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# ANTIBODIES

**Research Reagents & Immunoassay for Clinical Studies - Pharnacokinetics**

# DEVELOPMENT OF ANTI-CBD ANTIBODIES

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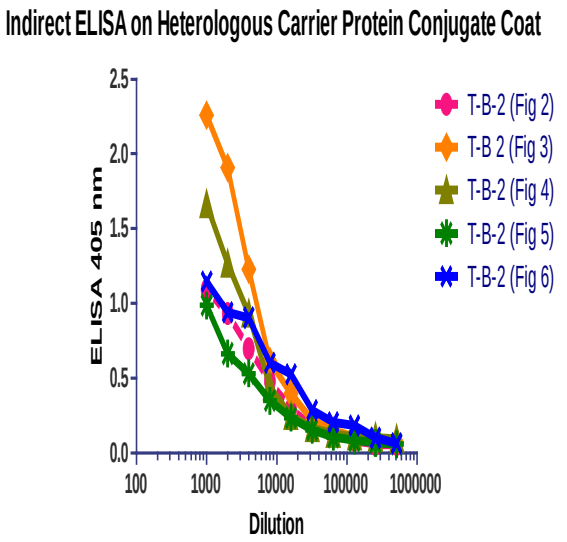
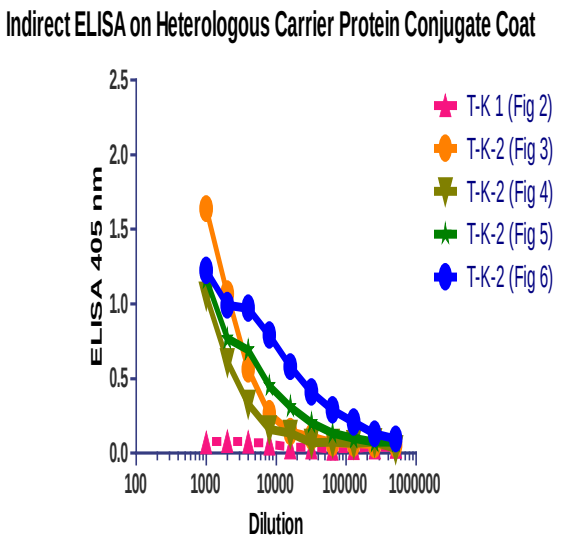
# Anti-CBD Antisera Development in Rabbits

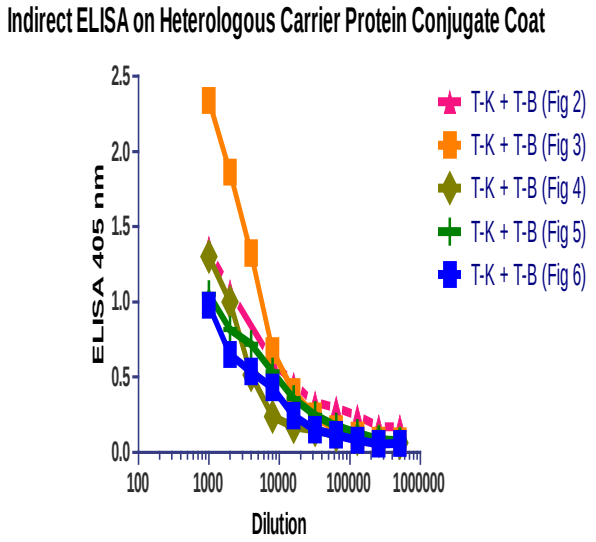
**B-conjugate immunized; Tested on K-conjugate coat**

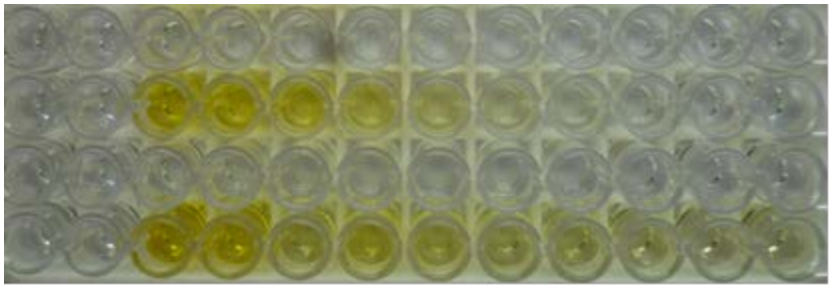



**K-conjugate immunized; Tested on B-conjugate coat**




**B + K-conjugate immunized; Tested on B-conjugate coat**



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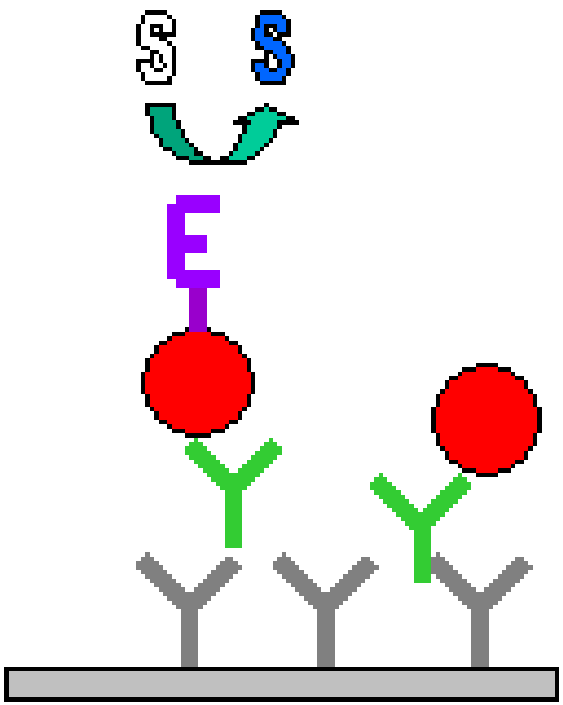


Substrate reaction

Tracer (Cannabinoid peroxidase)

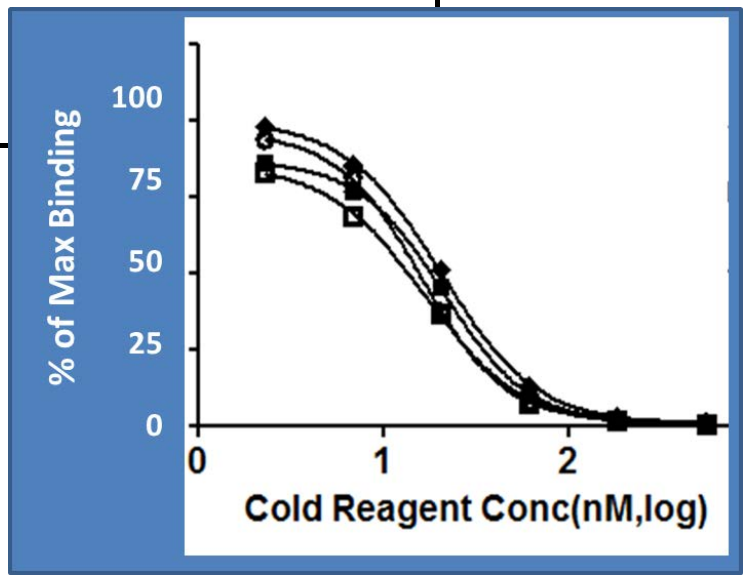
Cannabinoid (sample)

Anti-Cannabinoid Antibody

Coating antibody
(2nd antibody, IgG-specific)

Mikrotiter plate

# Assay Schematic for CBD Competitive EIA

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# CLINICAL CORRELATES

**A web-based, crowd-sourced observational study designed to establish baseline dosing standards**

## PROVIDING ACCURATE DOSING GUIDELINES FOR CANNABIS USE

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# Clinical Cannabis Consortium:

## Why Project Dose?

**To Provide Accurate Dosing Guidelines for Cannabis Use**

**Current State: Mayo Clinic aggregated research data, mostly from cannabis-based pharmaceuticals**

Use Initial Results to:

- Establish initial Dose & Mode of Administration (MOA) recommendations
- ID commercially viable indications at today's COGs
- Provide sourcing opportunities for patients

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# Clinical Cannabis Consortium (CCC)

**Mission: To advance the state of the art in cannabis research through industry-wide collaboration**

Founders & Roles:

- Abrams BioConsulting  Scientific Direction / Ad Hoc Beer Consultant
- Medicann:  Patients, clinical expertise
- CalStateCareGivers : Distributes batch tested products to patients.
- PharmLabs LLC: cannabis laboratory testing and analysis.
- Your Name Here

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# CCC : Project Dose

**POC Phase:**

- A web-based, crowd-sourced observational study designed to establish baseline dosing standards
- Indications limited to Sleep & Pain
- Record responses on simple 3-level improvement questionnaire
- **Cannabinoid & terpene content analytical testing of all samples included in study**

**Phase One:**

- Expand to full range of NP, Pain, and MS indications seen @ MediCann
- Record responses on either NPQ or Pain / Range of Motion Questionnaires as appropriate for indication

**Phase Two:**

- Expand to additional indications

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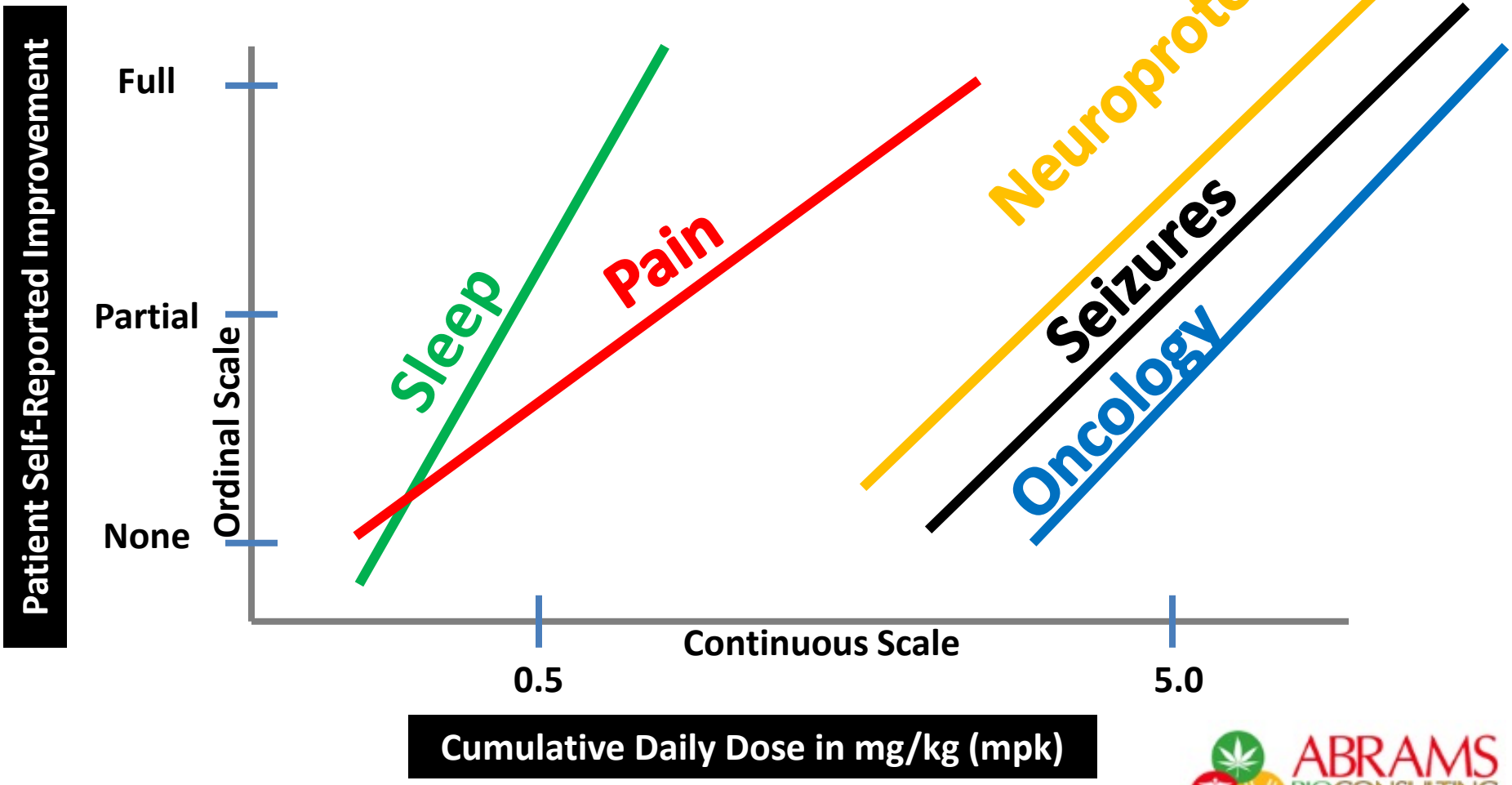
# Logistic Regression: Whole Model Test Mining for a significant $\chi^2$

**Stratified by Indication; Grouped by: Agent, MOA**

**Additional Regressors: Gender, Age, & Ethnicity (?)**

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# Cannabinoid & Terpene Content Analytical Testing Of All Samples Included In Project Dose Study

How best to do this?

- Participation of multiple analytical labs
  - Set criteria to eliminate discrepant data
- Adequate sample replicate analysis to permit estimation of mean, standard deviation, and statistical significance
- Incorporation of appropriate sampling techniques

# Project Dose: Overall Roadmap

| Project Phase | Questionnaire | Indication Class * | Sum(% of TOTAL) |
|---|---|---|---|
| POC | Simple 3-level Improvement | Sleep, Pain | 52% |
| I | NPQ | NP | 40% |
| | Pain & Range of Motion | P | 31% |
| | | MS | 13% |
| II | TBD | CV | 2% |
| | TBD | I | 2% |
| | TBD | ON | 2% |
| | TBD | GYN | 1% |
| | TBD | AI | 1% |
| | | | 90% |

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