Coalition for Medical Marijuana Research & Education

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➢ **There is established within the H. Lee Moffitt Cancer Center and Research Institute, Inc., the Coalition for Medical Marijuana Research and Education.**

MOFFITT
CANCER CENTER

Purpose

➢ The purpose of the coalition for Medical Marijuana Research and Education is to:

- conduct rigorous scientific research

- provide education

- disseminate research

- guide policy for the adoption of a statewide policy on ordering and dosing practices for the medical use of marijuana.

Governance

➤ The Medical Marijuana Research and Education Board is established to direct the operations of the coalition.

➤ The board shall be composed of seven members appointed by the chief executive officer of the H. Lee Moffitt Cancer Center and Research Institute, Inc.

➤ Board members must have experience in a variety of scientific and medical fields, including, but not limited to, oncology, neurology, psychology, pediatrics, nutrition, and addiction.

➤ The board shall annually adopt a plan for medical marijuana research, known as the "Medical Marijuana Research and Education Plan," which must be in accordance with state law and coordinate with existing programs in this state.

Marijuana in Medicine

➢ The term **_medical marijuana _** refers to using the whole, unprocessed marijuana plant or its basic extracts to treat symptoms of illness and other conditions.

- Phytocannabinoids – plant leaves, flowers, stems, and seeds collected from the Cannabis sativa plant
- Purified naturally occurring cannabinoids purified from plant sources: examples include cannabidiol (CBD) and delta-9-tetrahydrocannabinol (THC),
- Synthetic cannabinoids synthesized in a laboratory
- Endogenous – cannabinoids made by the body

How might cannabinoids be useful as medicine?

➢ Currently, the two main cannabinoids from the marijuana plant that are of medical interest are <u>THC and CBD.</u>

➢ <u>THC</u> can increase appetite and reduce nausea. THC may also decrease pain, inflammation (swelling and redness), and muscle control problems.

➢ Unlike THC, <u>CBD</u> is a cannabinoid that doesn't make people "high." It may be useful in reducing pain and inflammation, controlling epileptic seizures, and possibly even treating mental illness and addictions

➢ Several other plant components /cannabinoids that may have useful or harmful effects have NOT been evaluated

Synthetic Cannabinoid-based products for medicinal use

➢ Cannabinoid- based **synthetic drugs** have been increasingly available to patients in many countries and approved by the U.S. Food and Drug Administration (FDA)

- Dronabinol (schedule III) used to prevent nausea and vomiting caused by chemotherapy & to stimulate appetite

- Nabilone (schedule II) *used as a*n antiemetic and as an adjunct analgesic for neuropathic pain

Marijuana -Phytocannabis for Medical Use

Phyto (plant) cannabis (Marijuana)- **Still in clinical trials**

The FDA has not recognized or approved the plant-based marijuana plant as medicine.

➢ Nabiximols (Sativex®) (not approved by the U.S. FDA)

- Therapeutic-grade herbal cannabis (marijuana)
- oromucosal spray produced from whole cannabis extracts- reliable delivery system
- Biochemically uniform
- allows dose titration
- Without pulmonary dangers & intoxication
- Effects begin in 15–40 min- allowing a therapeutic window for control of symptoms

➢ Epidiolex, a CBD-based liquid drug to treat certain forms of childhood epilepsy (not approved by the U.S. FDA)

Populations using Medical Marijuana

- (a) Cancer.
- (b) Epilepsy.
- (c) Glaucoma.
- (d) Acquired immune deficiency syndrome.
- (e) Post-traumatic stress disorder.
- (f) Amyotrophic lateral sclerosis.
- (g) Crohn's disease.
- (h) Parkinson's disease.
- (i) Multiple sclerosis.
- (j) Chronic nonmalignant pain
- (k) Inflammation
- (l)substance use disorders

Gaps in the Literature: Cancer

➤ **Safety**
- Concurrent use with other cancer therapies
- Interaction with other drugs
- Increase symptoms or risk of other diseases including cancer

➤ **Effectiveness**
- Lack of clinical trials showing effectiveness in cancer prevention, treatment or to ameliorate symptoms of cancer and cancer treatment
- No standardized doses of marijuana
  (other than smoked or vaporized, which cannot be dose metered)

➤ **Mechanism**
- Other components present other than THC and cannabidiol (CBD) >60-100 different cannabinoids
- How do components of marijuana impact and modulate cancer or symptoms of cancer

➤ **Knowledge**
- Health professionals
- Patients/Patient families
- General population
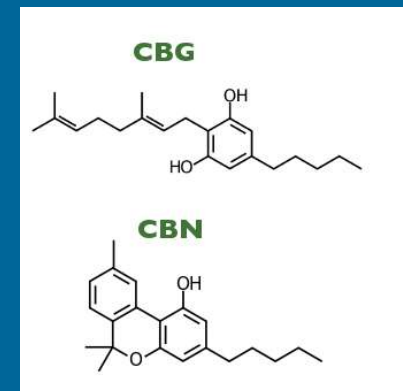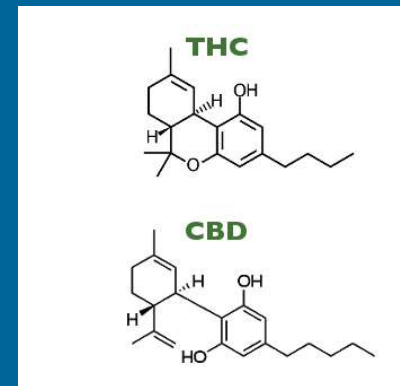
Challenges & Risks

➢ Federal law

- Marijuana is classified as a Schedule I agent (drug with a high potential for abuse and no accepted medical use)
- FDA has not approved use as a treatment for any medical condition

➢ To conduct clinical research with Marijuana, researchers must

- File an Investigational New Drug (IND) application with the FDA
- Obtain a Schedule I license from the DEA
- Have an infrastructure for housing this agent/supply chain
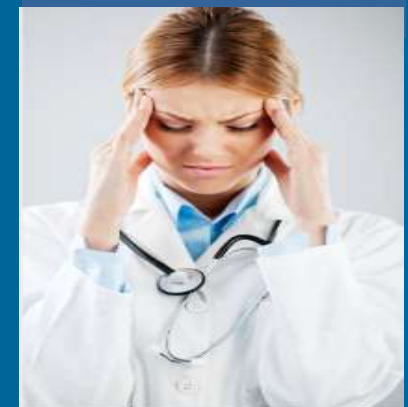- Obtain approval from the National Institute on Drug Abuse

➢ Burden to the Doctors:

- Requirements/risks/Fear of breaking the law (DEA Lic)
- Stigma
- Divided practitioners
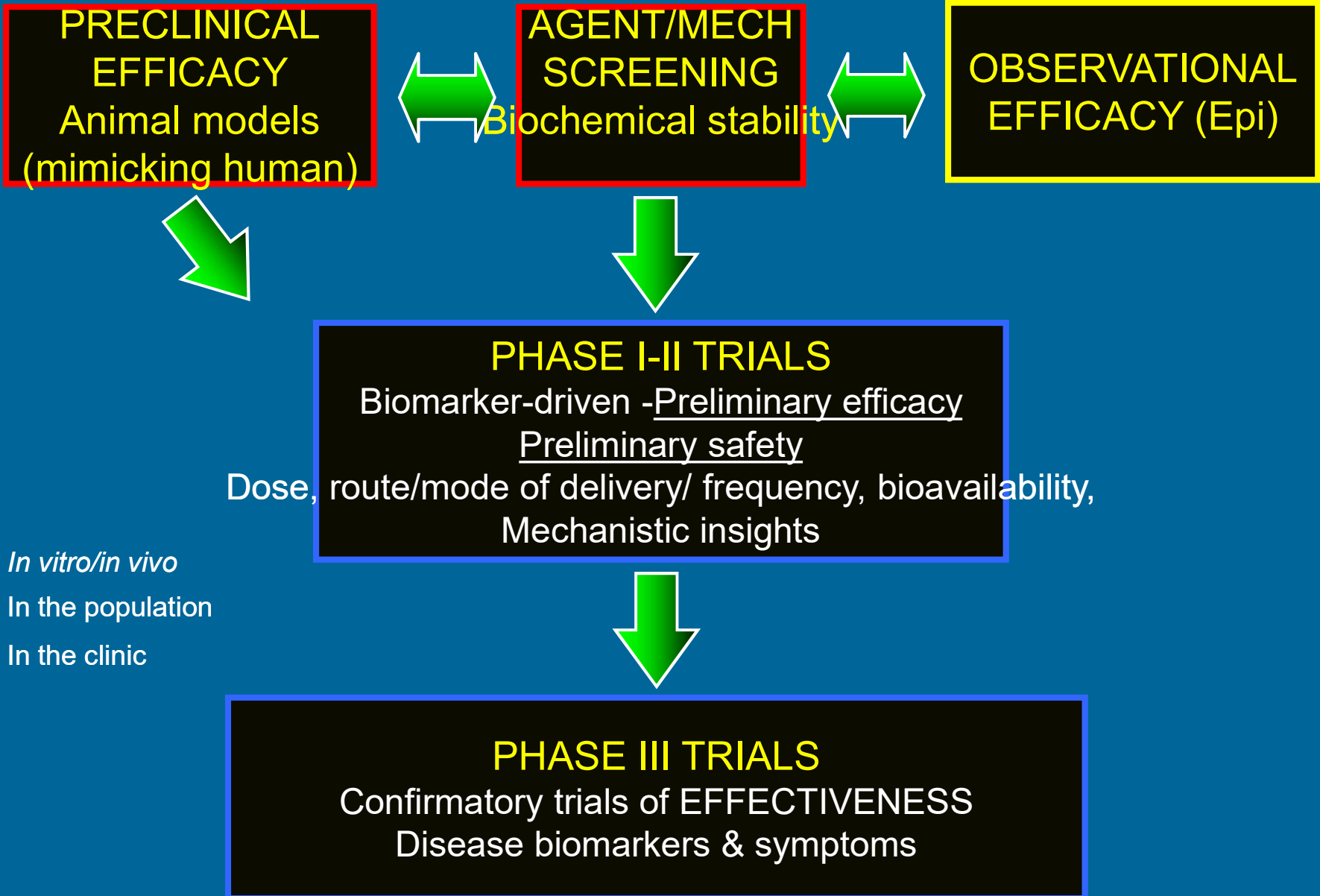
Pathway for Medical Marijuana to mainstream medicine

➢ Time honored process that any <u>pharmaceutical</u> that is used as medicine must attain to receive regulatory approval:

- comprehensively screen to understand the components and biological targets
- proof of biochemical uniformity and stability
- safety
- Effectiveness for specific indications as proven by randomized clinical trials

The Most Promising Drugs
Emerge from a Converging Premise

PRECLINICAL EFFICACY
Animal models (mimicking human)

AGENT/MECH SCREENING
Biochemical stability

OBSERVATIONAL EFFICACY (Epi)

PHASE I-II TRIALS
Biomarker-driven -Preliminary efficacy
Preliminary safety
Dose, route/mode of delivery/ frequency, bioavailability,
Mechanistic insights

■ *In vitro/in vivo*
■ In the population
■ In the clinic

PHASE III TRIALS
Confirmatory trials of EFFECTIVENESS
Disease biomarkers & symptoms

Research using botanicals and biologics for Cancer Prevention & Treatment (Kumar Lab)

> ## For Cancer Prevention

- Soy Isoflavones (Breast, Prostate, Lung)*
- Carotenoids (lycopene, ß-Carotene)(Prostate)*
- Green tea catechins (Prostate)
- Curcumin(Colon,Lung, Oral)
- Tannic acid derivative (Prostate)
- Sulforaphane (Bladder)
- Quercetin (Melanoma)
- Omega-3 fatty acids

> ## For Cancer Treatment

- Omega-3 fatty acids
- Marinol (Appetite stimulants)

> ## For Cancer Survivors

- Anthocyanins
- Omega-3 fatty acids
- Green tea polyphenols
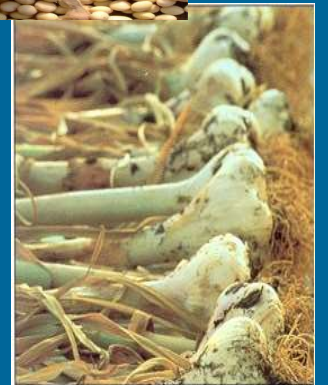
Benchmark – What has to change?

➢ **Composition**

➢ Significant **biochemical variability**

➢ Harbor pesticide residues, molds, bacteria, or heavy metals that endanger public health

➢ The most common **delivery system**, smoking, imposes risks: chronic cough, phlegm production, bronchitis, and inhalation of pyrolytic by-products

➢ Alternate modes/routes of administration, e.g., transdermal patches and rectal suppositories: N**ot evaluated in clinical trials**.

➢ **Adverse events:** Cannabis inhalation (smoking or vaporizer) produces a rapid peak in serum and brain concentrations that maximizes intoxication and possible reinforcement that are risk factors for drug abuse liability

Benchmark -Requirement for a prescription medical marijuana product

A prescription medical marijuana product must be:

➢ Standardized

➢ Consistent

➢ Display a quality equal to any New Chemical Entity that has passed muster as a pharmaceutical

➢ Possess a practical and <u>suitable delivery system</u> that minimizes patient risk

- Intoxication

- Drug abuse liability (DAL)

- Serious adverse events, such as pulmonary sequelae.

- Supply chain that ensures security that it is being distributed to its intended target patients.

Benchmark -Requirement for a prescription medical marijuana product

➤ Proof that it a safe and effective evidence-based pharmaceutical

➤ Physicians prescribe with confidence

➤ Pharmacists endorse and supply

➤ Government health services and third party payers will cover.

Coalition for Medical Marijuana Research & Education: Research Goals

➢ ***Identify and prioritize the research to be conducted by the Coalition to develop a comprehensive evidence base on the short- and long-term health effects of marijuana for medical use (both beneficial and harmful effects), addressing the key gaps in the evidence base.***

➢ Using **_observational research_** techniques, evaluate bioavailability, potential beneficial and harmful health effects of using different forms of marijuana, such as inhaled smoked or vaporized, tincture, sprays, suppositories, oils etc), targeting specific patient populations. (Examples: childhood and adult cancers, symptoms of posttraumatic stress disorder; ophthalmology: glaucoma, diabetic neuropathy, multiple sclerosis/neurological disorders, refractory pediatric epilepsy)

➢ Using a systematic approach, utilize state-of-the art techniques to **screen components of marijuana** and validate the potential targets *in vitro* and *in vivo to inform* for potential use in specific indications.

Coalition for Medical Marijuana Research & Education: Research Goals

➢ Investigate the pharmacokinetic and pharmacodynamics properties of marijuana, modes of delivery, different concentrations, in various populations, including the dose–response relationships of marijuana to other cannabinoids as well as standard treatment modalities.

➢ Conduct well-controlled, phase I-III trials on the potential beneficial and harmful health effects of using different forms of marijuana, such as inhaled (smoked or vaporized, tincture, sprays, suppositories, oils etc) targeting specific unstudied and understudied health endpoints (Examples: childhood and adult cancers, symptoms of posttraumatic stress disorder; ophthalmology: glaucoma, diabetic neuropathy, multiple sclerosis/neurological disorders, refractory pediatric epilepsy)

Coalition for Medical Marijuana Research & Education: Research Goal

➤ *Public Health and Public Safety Research*

➤ Document statewide incidence and reported indication for use of medicinal marijuana as a function of age, gender, race, county, indications, adverse events, other risk exposures, census-track based socio economic status and provider.

➤ Perform ecological evaluation contrasting statewide cause-specific death rates in the calendar year preceding and year following passage of the law.

➤ Utilizing the State of Florida Medical Marijuana Registry, characterize the health effects of marijuana on marijuana-related overdoses and poisonings; traffic accidents, work productivity, depression, fatigue and other health endpoints.

Coalition for Medical Marijuana Research & Education: Research & Education Goal

➤ ***Education to improve knowledge of Health Professionals***:

➤ Identify gaps in the medical marijuana -related knowledge and skills of health care and public health professionals, and assess the need for education programs that address these gaps.

➤ Provide the most up-to-date research and clinical guidelines to guide clinical practice, from National sources (NIH-NIDA,NCI,NIA; ASCO, APA, etc), including research evidence from the coalition, and to ultimately provide the highest level of healthcare to residents in the State of Florida

Coalition for Medical Marijuana Research & Education: Education Goal

➢ ***Education to Improve Research Quality***

➢ To conduct workshops of multi-disciplinary research scientists and relevant stakeholders:

- to develop research standards and benchmarks

- to guide and ensure the production of high-quality medical marijuana research in the State of Florida.

Coalition for Medical Marijuana Research & Education: Education Goal

➢ ***Education to Improve Public Knowledge***

➢ Evaluate public knowledge regarding medical marijuana, in terms of current and potential medical applications and risks.

➢ Utilize the current knowledge to guide the development of educational efforts and to evaluate the success of these efforts over time.

Patients are not seeking altered states from their medicine, in this case medical marijuana- but rather relief of pain or other medical complaints.

➤ Special thanks to our patients and their families - for their courage, resiliency and inspiration to continue our work.