FDA Public Hearing

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Scientific Research on Cannabis Abuse <u>and</u> its Potential Therapeutic Use

Medical Cannabis:
Marketing vs. scientific evidence?

State Medical Marijuana Laws – Approved Conditions

1. Alzheimer's Disease
2. Anorexia
3. Arnold-Chiari malformation
4. Arthritis
5. Ataxia
6. Cachexia
7. Cancer
8. Cardiopulmonary respiratory syndrome
9. Causalgia
10. Cervical dystonia
11. Crohn's disease
12. Decompensated cirrhosis
13. Dystonia
14. Epilepsy
15. Fibromyalgia
16. Glaucoma
17. Hepatitis C
18. HIV/AIDS
19. Huntington's disease
20. Hydrocephalus
21. Inflammatory autoimmune-mediated arthritis
22. Inflammatory bowel disease (IBS)
23. Inflammatory demyelinating polyneuropathy
24. Interstitial cystitis
25. Lou Gehrig's disease (amyotrophic lateral sclerosis, ALS)
26. Lupus
27. Migraines
28. Multiple Sclerosis
29. Muscle spasms
30. Muscular dystrophy
31. Myasthenia gravis
32. Myoclonus
33. Nail-patella syndrome
34. Nausea or vomiting
35. Neurofibromatosis
36. Neuropathy
37. Pain
38. Pancreatitis
39. Parkinson's disease
40. Peripheral neuropathy
41. Post-traumatic stress disorder (PTSD)
42. Reflex sympathetic dystrophy
43. Residual limb pain from amputation
44. Seizure disorders
45. Sjogren's syndrome
46. Spasticity
47. Spinal cord damage with intractable spasticity
48. Syringomyelia
49. Terminal illness
50. Tourette's syndrome
51. Traumatic brain injury

Science Needed to Inform Public Policy

✓ *Is Cannabis Good or Bad?* **Both. Pharmacologically complex plant with constituents that have the potential for producing <u>both</u> medical benefit and problematic use**

✓ **Societal discussion and public policy polarizing:**
Miracle Cure vs Hazard

✓ **Old Drug/New Science:**

- **Cannabinoid receptors, discovered in 1990s: *ubiquitous* yet function only starting to be understood**

- **Cannabis plant: >100 unique cannabinoids yet research largely limited to only two: Δ^9-THC and cannabidiol (CBD)**

- **Cannabis plant contaminants (pesticides, heavy metals)**
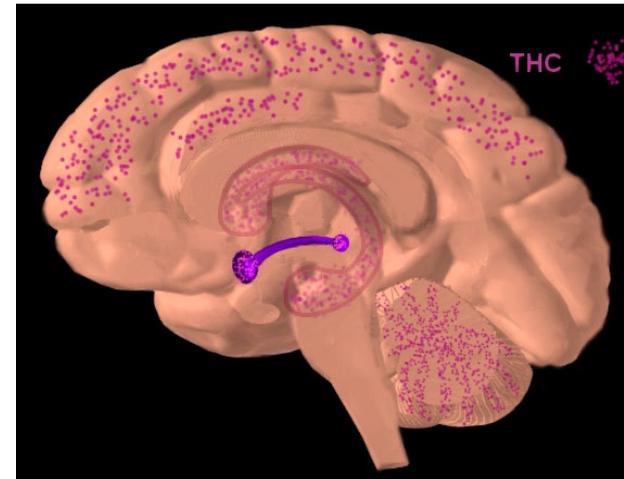
Scientific Vacuum

- ✓ **Cannabis and cannabidiol products are *marketed;* have not been tested for safety and efficacy as other FDA-approved medications**

- ✓ **Randomized, placebo-controlled clinical trials testing a product of known composition is essential**

- ✓ **Public opinion and *marketers* are determining what cannabinoid products are used to treat a range of medical conditions**

- ✓ **_Little regulatory oversight_: <1/3 of edible cannabis and cannabidiol tested from dispensaries and online sources were labelled accurately re. cannabinoid content**
  - *What about Good Manufacturing Practices (GMP) and purity?*
  - *Does the product even contain CBD/THC? What dose is effective?*
  - *What is the bioavailability by different routes of administration?*

Is Cannabis Addictive?

- ✓ **Yes:** **30% regular users meet DSM criteria for Cannabis Use Disorder (CUD) and there are ~300,000 treatment admissions/year**

- ✓ **Cannabis produces intoxication and impairment**

- ✓ **Why seek treatment?** **Dissatisfaction with functioning, smoke more than they intend to, memory effects, withdrawal, health concerns, neglect responsibilities, <u>unable to stop use</u>*** **qualitatively similar to other substance use disorders*

- ✓ **Few patients achieve continued abstinence, ca. 20%**

- ✓ **Treatment options are needed, including medications to reduce withdrawal and facilitate abstinence (as used for opioids, tobacco, alcohol)**

Cannabis Abstinence Withdrawal
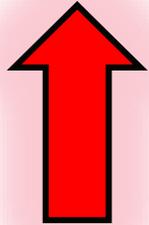
⬆ **Anxiety**

Irritability

Cannabis craving

Restlessness
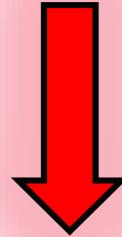
⬇ **Food intake**
Sleep quality

✓ **Withdrawal symptoms emerge >24 hrs after not using cannabis and with continued abstinence lasts 1-2 weeks**

✓ **Women have an accelerated trajectory from first use to the development of problems and seeking treatment for CUD**

✓ **Women experience more severe withdrawal and have worse treatment outcomes**
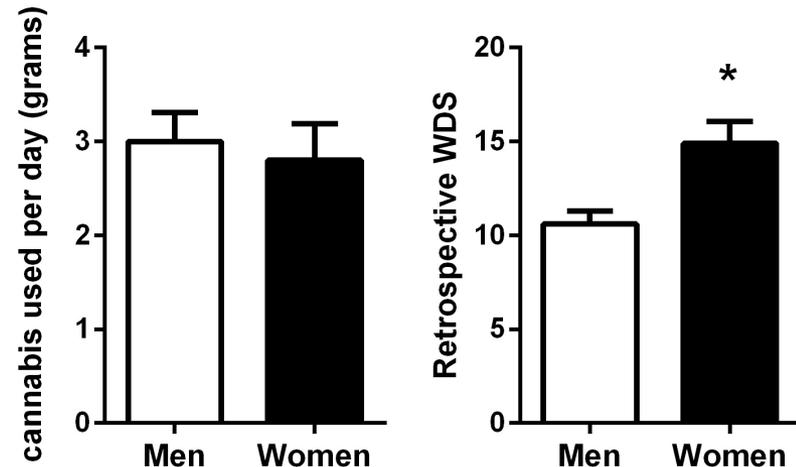
Human Laboratory
(PI, M. Haney)

HIV: Relative to placebo, smoked cannabis and oral THC dose-dependently increased caloric intake and reduced GI distress in HIV+ patients

Laboratory Pain Model:

✓ Smoked cannabis and oral THC dose-dependently reduced pain sensitivity relative to placebo

✓ Low opioid dose produced no analgesia alone but significant analgesia when combined with smoked cannabis

✓ Women appear less sensitive to analgesic effects of cannabis than men

National Academy of Sciences

Conclusive or substantial evidence that cannabis or cannabinoids are effective for the treatment of:

✓ **Chronic pain**

✓ **Chemotherapy-induced nausea and vomiting**

✓ **Patient-reported multiple sclerosis spasticity symptoms**
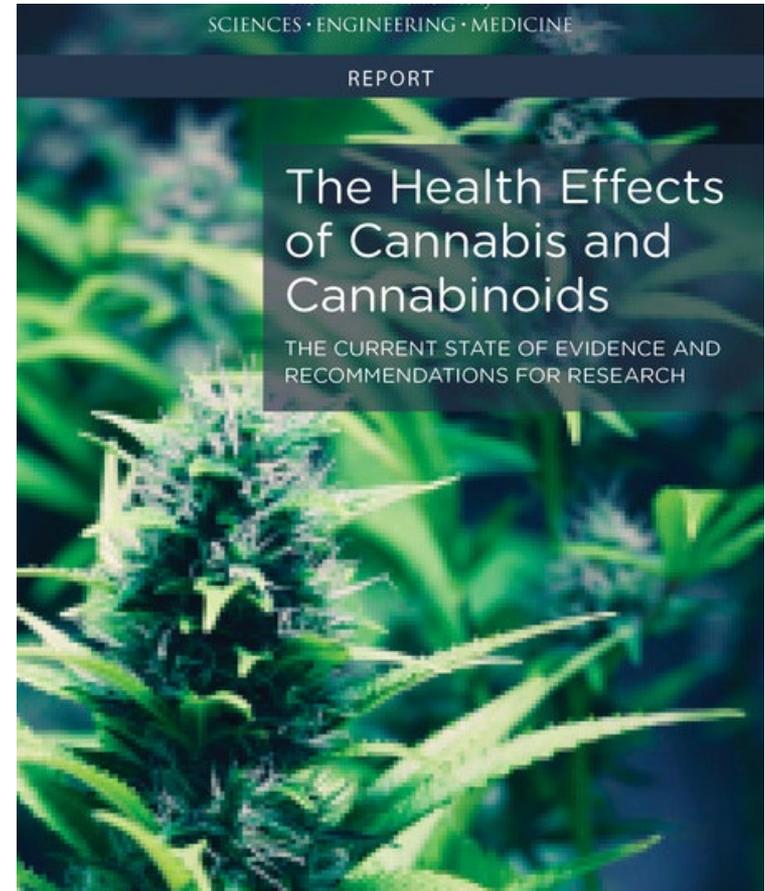
Effects of Cannabis Use
More Research is Needed

- ✓ **With increased 'legalization' and acceptance, daily use of cannabis/cannabinoid products by adolescents and adults (including pregnant women) is <u>rising</u>**

- ✓ **Research is needed to address the consequences of these *marked* societal changes, but is hampered by regulatory barriers**

- ✓ **No regulatory pathway for researchers to obtain, store, or test cannabinoid products sold in retail stores or online; need source for GMP full range of cannabinoids (THCv, CBC, CBN, CBG etc.)**

- ✓ **How can researchers evaluate health claims and product constituents (e.g. THC, CBD 'dose') without access?**

Medical Cannabis: *More Research Needed*

Cannabis legalization has resulted in a proliferation of novel products for which we lack a basic scientific understanding of risk/benefit

- ✓ **Impact of cannabis legalization on public health**
- ✓ **Pharmacology, safety, and abuse liability of novel products**
- ✓ **Impact of cannabinoid exposure on fetal and child development and health**
- ✓ **Valid methods of detecting cannabis use and impairment (driving)**
- ✓ **Impact of legalization on use of other drugs e.g., opioids, tobacco**
- ✓ **Mechanisms and interactive effects of cannabis constituents**
- ✓ **Regulatory policies needed for product packaging, labeling, advertising and retail sales?**
- ✓ **Can we develop cannabinoid medications with low abuse liability and better safety/efficacy?**
- ✓ **Need new medications to treat Cannabis Use Disorder**

Cannabis Regulatory *Recommendations*

- ✓ **Create a regulatory pathway that allows researchers with a DEA Schedule I license to obtain, store and conduct research on retail cannabis products**

- ✓ **Streamline the regulatory process to allow GMP manufacturing of cannabinoids from cannabis and hemp**

- ✓ **Allow for concurrent submission of new/amended INDs and protocols to FDA, DEA and IRB to accelerate research**

- ✓ **Set time limits for FDA review of new and amended applications**

- ✓ **Streamline processes for DEA and FDA review/approval of new drug codes**

Thank you!

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The College on Problems of Drug Dependence