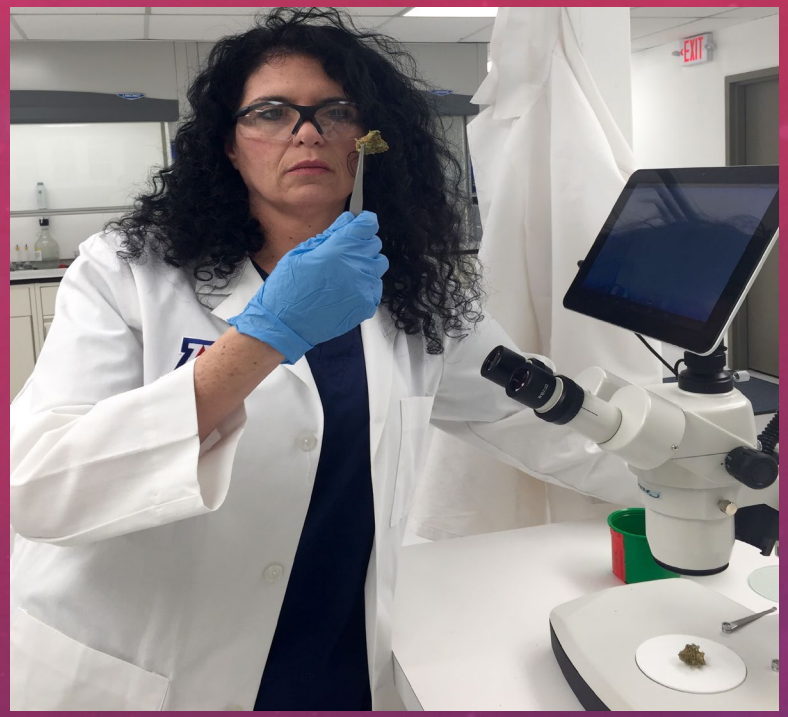
BARRIERS TO CBD/CANNABIS CONTROLLED TRIALS IN US

MONOPOLY

SUE SISLEY, MD



SRI MISSION:

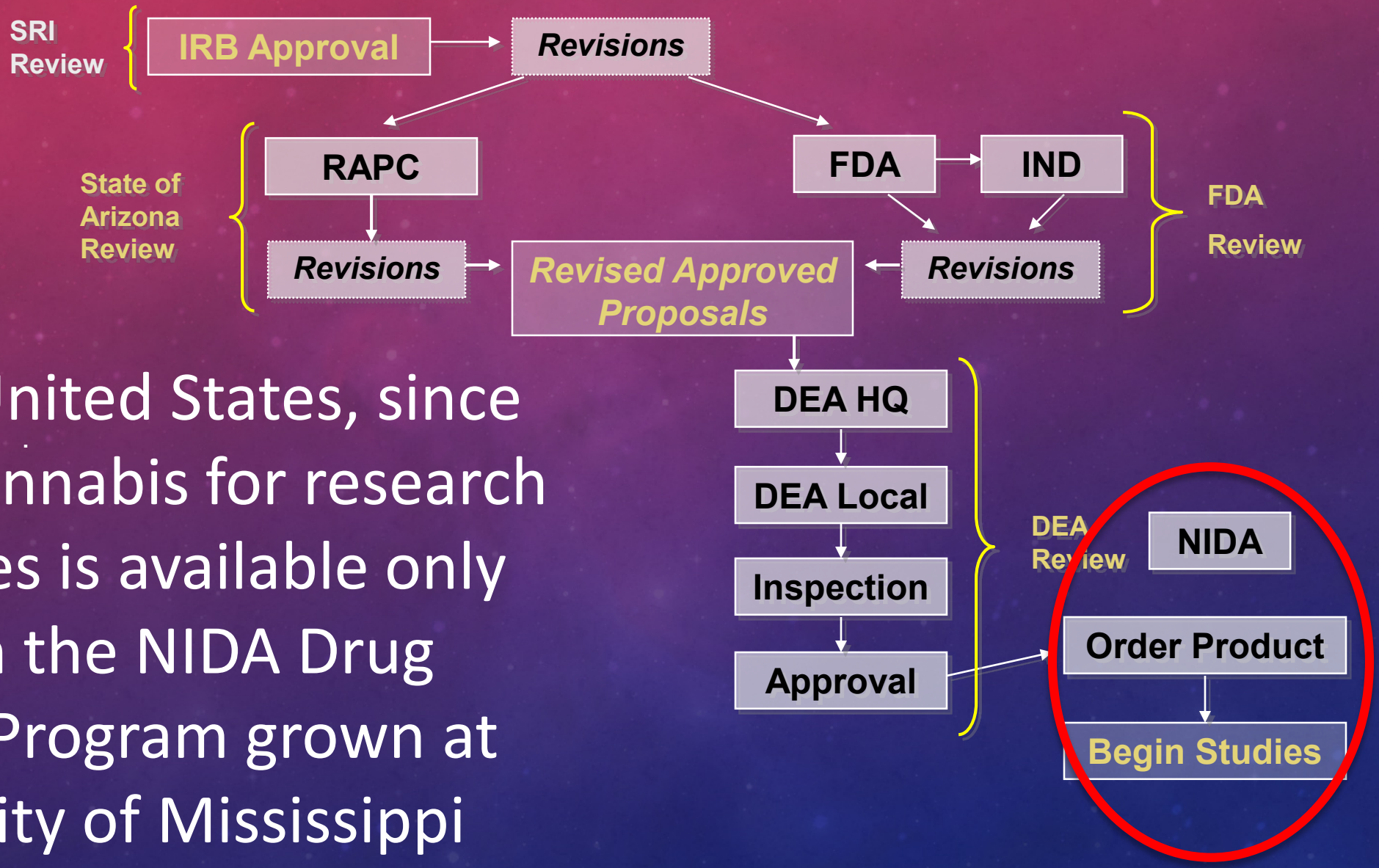
FDA–approved Randomized Controlled Trials evaluating safety/efficacy of smoked & vaporized Cannabis FLOWER

SCOTTSDALE RESEARCH INSTITUTE

FDA Phase 2, outpatient TRIPLE BLIND randomized, placebo-controlled, triple-blind, crossover study on safety & efficacy of 4 different THC:CBD ratios of NIDA cannabis flower

1st randomized controlled trial (RCT) to test therapeutic potential of smoked cannabis as TREATMENT for PTSD.

OVERLY COMPLICATED REGULATORY PATHWAY



In the United States, since 1968 cannabis for research purposes is available only through the NIDA Drug Supply Program grown at University of Mississippi

NIDA Cannabis Cigarettes

Three NIDA Cigarettes

TOPICS > NATION

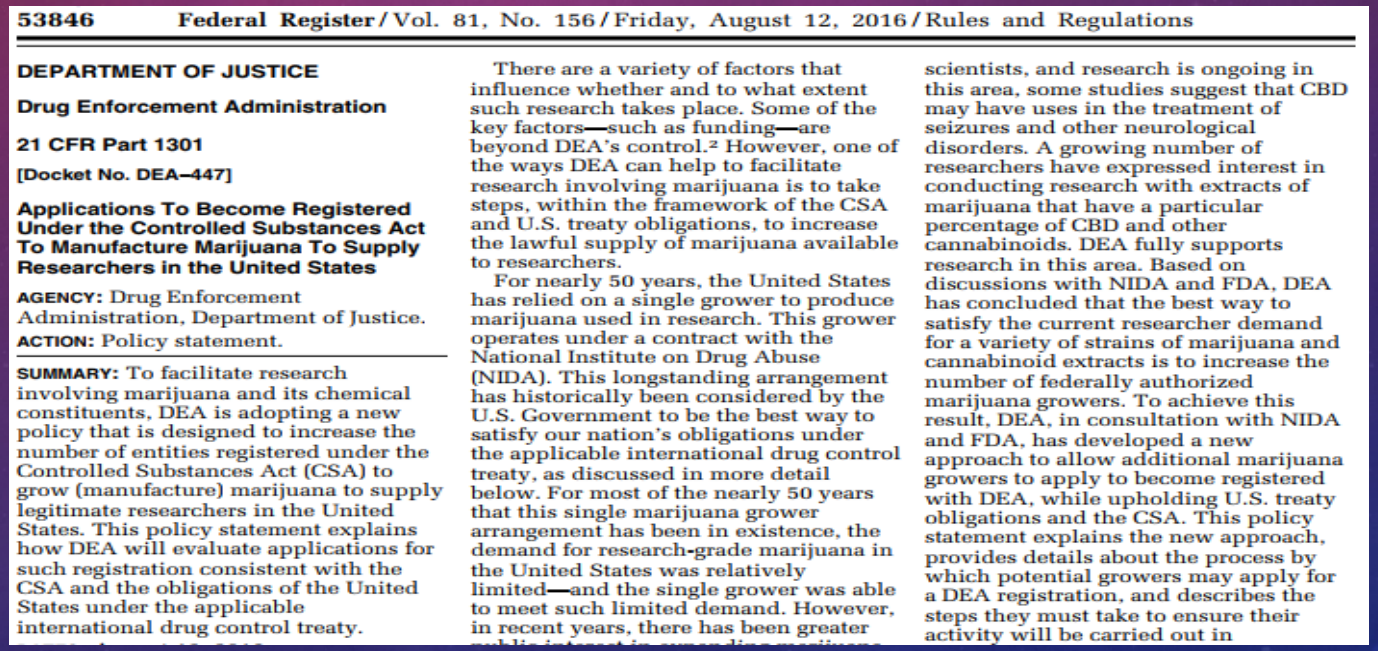
Scientists say the government's only pot farm has moldy samples — and no federal testing standards

BY CALEB HELLERMAN *March 8, 2017 at 3:55 PM EDT*

A researcher in Dr. Sue Sisley's lab pours out a sample of marijuana produced by the federal facility responsible for growing cannabis for clinical research. When she received marijuana for a PTSD trial last year, Sisley says the packages contained mold and weren't as potent as she requested. Photo courtesy of MAPS.

Sue Sisley, a primary care physician in

- In 2016, DEA adopted new policy that increases number of entities that may be registered under Controlled Substances Act (CSA) to grow/manufacture marijuana to supply legitimate researchers in US



53846 Federal Register / Vol. 81, No. 156 / Friday, August 12, 2016 / Rules and Regulations

DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1301

[Docket No. DEA–447]

Applications To Become Registered Under the Controlled Substances Act To Manufacture Marijuana To Supply Researchers in the United States

AGENCY: Drug Enforcement Administration, Department of Justice.

ACTION: Policy statement.

SUMMARY: To facilitate research involving marijuana and its chemical constituents, DEA is adopting a new policy that is designed to increase the number of entities registered under the Controlled Substances Act (CSA) to grow (manufacture) marijuana to supply legitimate researchers in the United States. This policy statement explains how DEA will evaluate applications for such registration consistent with the CSA and the obligations of the United States under the applicable international drug control treaty.

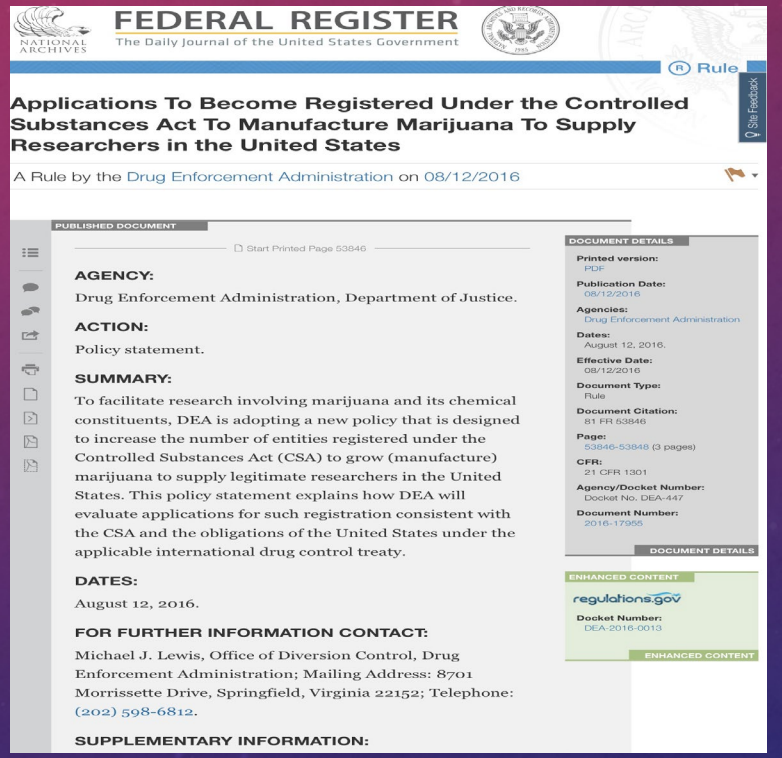
There are a variety of factors that influence whether and to what extent such research takes place. Some of the key factors—such as funding—are beyond DEA's control.[2] However, one of the ways DEA can help to facilitate research involving marijuana is to take steps, within the framework of the CSA and U.S. treaty obligations, to increase the lawful supply of marijuana available to researchers.

For nearly 50 years, the United States has relied on a single grower to produce marijuana used in research. This grower operates under a contract with the National Institute on Drug Abuse (NIDA). This longstanding arrangement has historically been considered by the U.S. Government to be the best way to satisfy our nation's obligations under the applicable international drug control treaty, as discussed in more detail below. For most of the nearly 50 years that this single marijuana grower arrangement has been in existence, the demand for research-grade marijuana in the United States was relatively limited—and the single grower was able to meet such limited demand. However, in recent years, there has been greater

scientists, and research is ongoing in this area, some studies suggest that CBD may have uses in the treatment of seizures and other neurological disorders. A growing number of researchers have expressed interest in conducting research with extracts of marijuana that have a particular percentage of CBD and other cannabinoids. DEA fully supports research in this area. Based on discussions with NIDA and FDA, DEA has concluded that the best way to satisfy the current researcher demand for a variety of strains of marijuana and cannabinoid extracts is to increase the number of federally authorized marijuana growers. To achieve this result, DEA, in consultation with NIDA and FDA, has developed a new approach to allow additional marijuana growers to apply to become registered with DEA, while upholding U.S. treaty obligations and the CSA. This policy statement explains the new approach, provides details about the process by which potential growers may apply for a DEA registration, and describes the steps they must take to ensure their activity will be carried out in

https://www.gpo.gov/fdsys/pkg/FR-2016-08-12/pdf/2016-17955.pdf

Although DEA reportedly received nearly 30 applications from potential cultivators wanting to grow for US clinical trials,
the agency has not processed any of these applications



FEDERAL REGISTER
The Daily Journal of the United States Government

Rule

Applications To Become Registered Under the Controlled Substances Act To Manufacture Marijuana To Supply Researchers in the United States

A Rule by the Drug Enforcement Administration on 08/12/2016

PUBLISHED DOCUMENT

Start Printed Page 53846

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DATES:
August 12, 2016.

FOR FURTHER INFORMATION CONTACT:
Michael J. Lewis, Office of Diversion Control, Drug Enforcement Administration; Mailing Address: 8701 Morrissette Drive, Springfield, Virginia 22152; Telephone: (202) 598-6812.

SUPPLEMENTARY INFORMATION:

DOCUMENT DETAILS
Printed version: PDF
Publication Date: 08/12/2016
Agencies: Drug Enforcement Administration
Dates: August 12, 2016.
Effective Date: 08/12/2016
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CFR: 21 CFR 1301
Agency/Docket Number: Docket No. DEA-447
Document Number: 2016-17955

ENHANCED CONTENT
regulations.gov
Docket Number: DEA-2016-0013

- Members of Congress have *repeatedly* urged DEA to process applications or explain the delay, with no response to multiple letters

https://www.forbes.com/sites/tomangell/2017/11/07/dea-wants-feds-to-grow-almost-1000-pounds-of-marijuana-next-year/2/#34ecc21a44ae

United States Senate
WASHINGTON, DC 20510

July 25, 2018

The Honorable Jeff Sessions
Attorney General
U.S. Department of Justice
950 Pennsylvania Avenue, NW
Washington, DC 20530-0001

Dear Attorney General Sessions:

We write to encourage you to finalize your review of applications submitted to the Drug Enforcement Administration (DEA) for licenses to manufacture marijuana for scientific research. Our nation's need for meaningful federally sanctioned research is critical. Research and medical communities should have access to research-grade materials to answer questions around marijuana's efficacy and potential impacts, both positive and adverse. Finalizing the review of applications for marijuana manufacturing will assist in doing just that.

For nearly fifty years, the University of Mississippi has had the sole contract with the National Institute on Drug Abuse (NIDA) to grow cannabis for research purposes. To expand the number of manufacturers, the DEA submitted a notice in the Federal Register on August 11, 2016, soliciting applications for licenses to manufacture marijuana for research purposes. Under this notice, DEA explained its legal authority to "increase the number of entities registered under the Controlled Substances Act (CSA) to grow (manufacture) marijuana to supply legitimate researchers in the United States."[1] However, almost two years have passed since the DEA's notice without any new schedule I marijuana manufacturer registrations.

On April 25, 2018, during testimony before the Senate Appropriations Subcommittee on Commerce, Justice, Science, and Related Agencies, in response to questioning you stated: "We are moving forward and we will add, fairly soon . . . additional suppliers of marijuana under the Controlled [Substances Act]."[2] In a prior hearing, you testified: "It would be healthy to have some more competition in the [marijuana] supply."[3]

Additional registered marijuana manufacturers in the United States will assist not only in expanding legitimate research opportunities, but also will act in a way that allows for the United States' continued compliance with the United Nations' Single Convention on Narcotics Drugs. Specifically, in DEA's August 2016 notice, the agency explained, "DEA believes it would be consistent with the purposes of articles 23 and 28 of the Single Convention for DEA to register marijuana growers outside of the [National Institute on Drug Abuse]-contract system to supply researchers, provided the growers agree that they may only distribute marijuana with prior, written approval from DEA."

To prevent further delays in approving the at least twenty-six pending DEA applications for licenses to manufacture marijuana for research purposes, we ask you to respond to the following questions and requests by August 10, 2018:

1) What is the currents status of the twenty-six marijuana manufacturer applications?

2) What steps have both DEA and DOJ taken to review the twenty-six marijuana manufacturer applications currently pending?

3) By what date do you estimate the DEA will have completed its review of the twenty-six marijuana applications and commence registration of new marijuana manufacturers?

4) Please share DOJ's analysis of the Single Convention and if the opinion of the Justice Department is the same or similar to that of DEA's.

5) If there are legal barriers to licensing multiple schedule I marijuana manufacturers under the Single Convention, please identify and explain them.

Thank you for your attention to this matter.

Sincerely,

BRIAN SCHATZ
United States Senator

CHUCK GRASSLEY
United States Senator

CORY GARDNER
United States Senator

KIRSTEN GILLIBRAND
United States Senator

AMY KLOBUCHAR
United States Senator

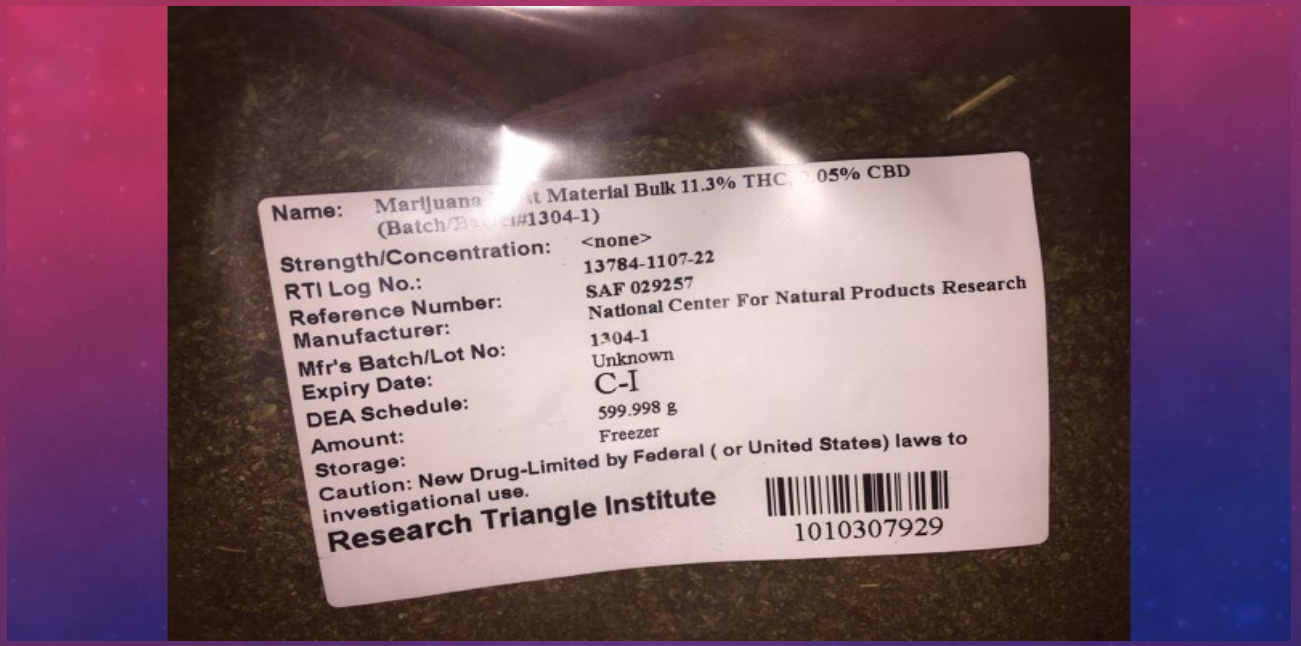
CHRISTOPHER A. COONS
United States Senator

ORRIN HATCH
United States Senator

TIM KAINE
United States Senator

[1] https://www.federalregister.gov/documents/2016/08/12/2016-17955/applications-to-become-registered-under-the-controlled-substances-act-to-manufacture-marijuana-to.
[2] "Attorney General Sessions on Justice Department Budget Request," C-SPAN, 25 April 2018, https://www.c-span.org/video/?444368-1/attorney-general-declines-resign-mueller-rosenstein-fired.
[3] "Justice Department Oversight Hearing," C-SPAN, 18 Oct. 2017, https://www.c-span.org/video/?434413-1/attorney-general-interviewed-special-counsel.

FDA REQUIRES PHASE 3 STUDIES BE DONE WITH EXACT SAME DRUG THAT SPONSOR IS SEEKING TO MARKET LATER



NIDA authorized to provide marijuana for research but not for sale by prescription as FDA-approved medicine

FDA PARADIGMS NEED TO EVOLVE WHEN EVALUATING BOTANICAL MEDICINE

- Allow for rapid patient self-titration instead of only traditional FIXED DOSING model (which allows for small variations in the potency of natural flower)
- Enables patients to discover therapeutic dose at lower amount and avoid AE's that arise from forcing patients to take more than they really need.

FDA PARADIGMS NEED TO EVOLVE WHEN EVALUATING BOTANICAL MEDICINE

Adjust definition of GMP to ensure flower is

- ONLY FLOWERING TOPS OF PLANT
- FREE from pesticides, heavy metals, microbials/mycotoxins but NOT so overprocessed that it no longer resembles flower from “real world” (in excessive effort to standardize for controlled trials)

ADDITIONAL MANUFACTURERS ARE ESSENTIAL FOR CBD/OTHER CANNABIS RESEARCH TO ADVANCE INTO PHASE 3 TRIALS

- Cannot put CBD rich Flower/DRY BUD thru entire FDA drug development process since there is NO federally legal supply of CBD rich flower in US **that can be SOLD AS PRESCRIPTION MEDICINE**

NEXT CLINICAL TRIAL @ SRI:

INHALED CANNABIS FLOWER VERSUS FENTANYL BUCCAL TABLETS FOR MANAGEMENT OF BREAKTHROUGH PAIN IN CANCER PATIENTS:

AN OPEN-LABEL, CROSSOVER, COMPARISON STUDY FOLLOWED BY A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED PILOT TRIAL

- **FDA Approval pending to import GMP-grade Flower from Canada**

Scottsdale Research Institute
Research for Humanity

Suzanne Sisley, M.D.
President/ Principal Investigator

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THANK YOU!