FDA Regulation of Marijuana: Past Actions, Future Plans

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ICSB/ASP Joint Meeting
April 12, 2016

Disclosure Statement

I have no financial relationships with proprietary entities that produce health care goods and services

The opinions and information in this presentation are my own and do not necessarily reflect the views and policies of the FDA

Outline

- State of Marijuana 2016
- FDA Role
  - FDA Scientific Activities
    - Drug Scheduling
    - Marijuana 8-Factor
    - Development of Drugs from Marijuana
  - FDA Enforcement Actions
    - Warning Letters
  - Other Activities:
    - State interactions, Post-marketing Safety Assessment

Central Messages

- FDA has clear role in supporting scientific and rigorous assessment of marijuana, including product development and regulation of marketing
  - The promise of safety, efficacy and reliability is not good enough

<u>However</u>

- FDA needs to do all it can to support the needed scientific research with marijuana to characterize its therapeutic promise

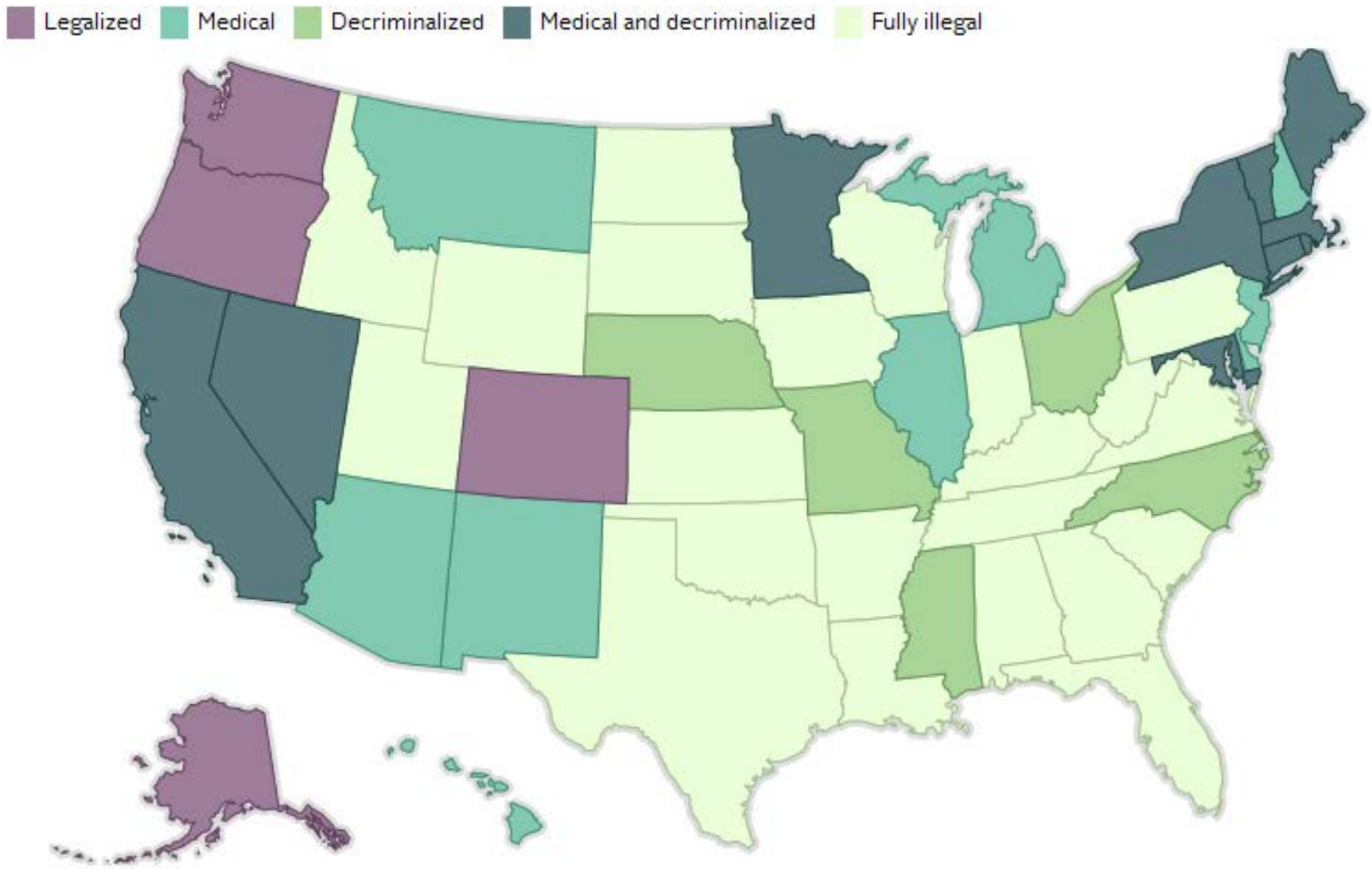
CURRENT STATUS OF MARIJUANA

State and Federal

Status of Marijuana in the States

- As of March 2016
  - 23 States have statutes recognizing “medical marijuana”
  - 4 states (AK, CO, OR, WA) and DC have approved recreational marijuana
  - 13 states have statutes recognizing cannabidiol (CBD) for medical use

Status of Marijuana Laws in the US



Source: NORML, Drug Policy Alliance, and the Marijuana Policy Project

SELECTED FEDERAL ROLES RELATED TO MARIJUANA

NIDA, DEA, and FDA

Status of Marijuana at the Federal Level

- Controlled Substances Act of 1970:
  - Marijuana regulated under **Schedule I**, defined as having:
    - High potential for abuse
    - No currently accepted medical use
    - Lack of accepted safety for use under medical supervision

NIDA/NIH

- **National Institute on Drug Abuse (NIDA):**
  - Conducts and supports scientific research with marijuana and compounds found in marijuana
  - Oversees the cultivation of marijuana at the University of Mississippi (through a contract)
    - Designated by DEA as the **single** source of marijuana for medical research
    - NIDA assesses the varieties and quantities needed to meet anticipated US research needs
    - DEA establishes yearly quota of the amount grown
  - NIDA provides marijuana to researchers when:
    - Demonstrated scientific validity and ethical soundness of study
    - Submitted/approved IND to the FDA
    - Have a DEA Schedule 1 controlled substance license

DEA

- Oversees investigator registration and site licensure to conduct studies using marijuana
  - As a Schedule I controlled substance marijuana use in a clinical trial DEA requires special registration for the investigator and the site where the study will be conducted (CFR §1301.18 DEA, Research Protocols)

FDA

- **Scientific role:**
  - Scientific assessment (‘8-factor analysis’) on appropriate controls (‘schedule’) for marijuana to HHS and DEA
- **Regulatory role:**
  - ***Support and regulate scientific research on potential therapeutic uses of marijuana cmpds***
- **Enforcement role:**
  - Take actions as necessary against products containing compounds found in marijuana, particularly those that present human health risks or that make illegal claims in labeling

FDA Work on Marijuana

Office of the
Commissioner

Office of
Regulatory
Affairs

Center for
Food
Safety &
Applied
Nutrition

Center for
Drug
Evaluation
& **R**esearch

Center for
Biologics
Evaluation &
Research

Center for
Devices &
Radiological
Health

Center for
Veterinary
Medicine

National
Center for
Toxicological
Research

Center for
Tobacco

FDA ROLES WITH MARIJUANA

Selected FDA Roles in Regulating Marijuana

- Scientific: providing scientific input ('8-factor analysis') on the appropriate controls for MJ ('**Scheduling**')

Scheduling Basics

- Scheduling: Classification of drugs based on abuse potential; medical use; physical/psychological dependence
- Five Schedules for control (CI- CV) in decreasing abuse potential order
  - Each schedule has different manufacturing, distribution and prescribing controls necessary
  - Aim to ensure medical availability while reducing abuse and diversion
- Different penalties are also associated with the various Schedules

Criteria for Scheduling and Schedules under the Controlled Substance Act (CSA)

CRITERIA

Abuse Potential				
High	High	Low relative to CII	Low relative to CIII	Low relative to CIV
No Medical Use	Medical Use			
Lack of accepted safety under medical supervision	Psychological or Physiological Dependence			
	Severe Psych or Physical	High Psych or Moderate to low Physical	Ltd Psych or Physical relative to CIII	Ltd Psych or Physical relative to CIV

SCHEDULES

SCHEDULE I	SCHEDULE II	SCHEDULE III	SCHEDULE IV	SCHEDULE V
Heroin Hallucinogens Marijuana Others	Opioids Barbiturates Cocaine Amphetamine Methylphenidate Methamphetamine PCP	Opioids (Codeine combinations, Buprenorphine) Barbiturates (combinations and products) Ketamine GHB Marinol Anabolic Steroids	Benzodiazepines and other depressants (Zaleplon, Zolpidem, Eszoplicone) Fenfluramine Modafinil Butorphanol Tramadol	Opioids in limited quantities and in combinations (Codeine, Dihydrocodeine, Difenoxin) Pregabalin Lacosamide

Statutory Basis for Scheduling Recommendation

CSA requires HHS to considered 8 Factors :

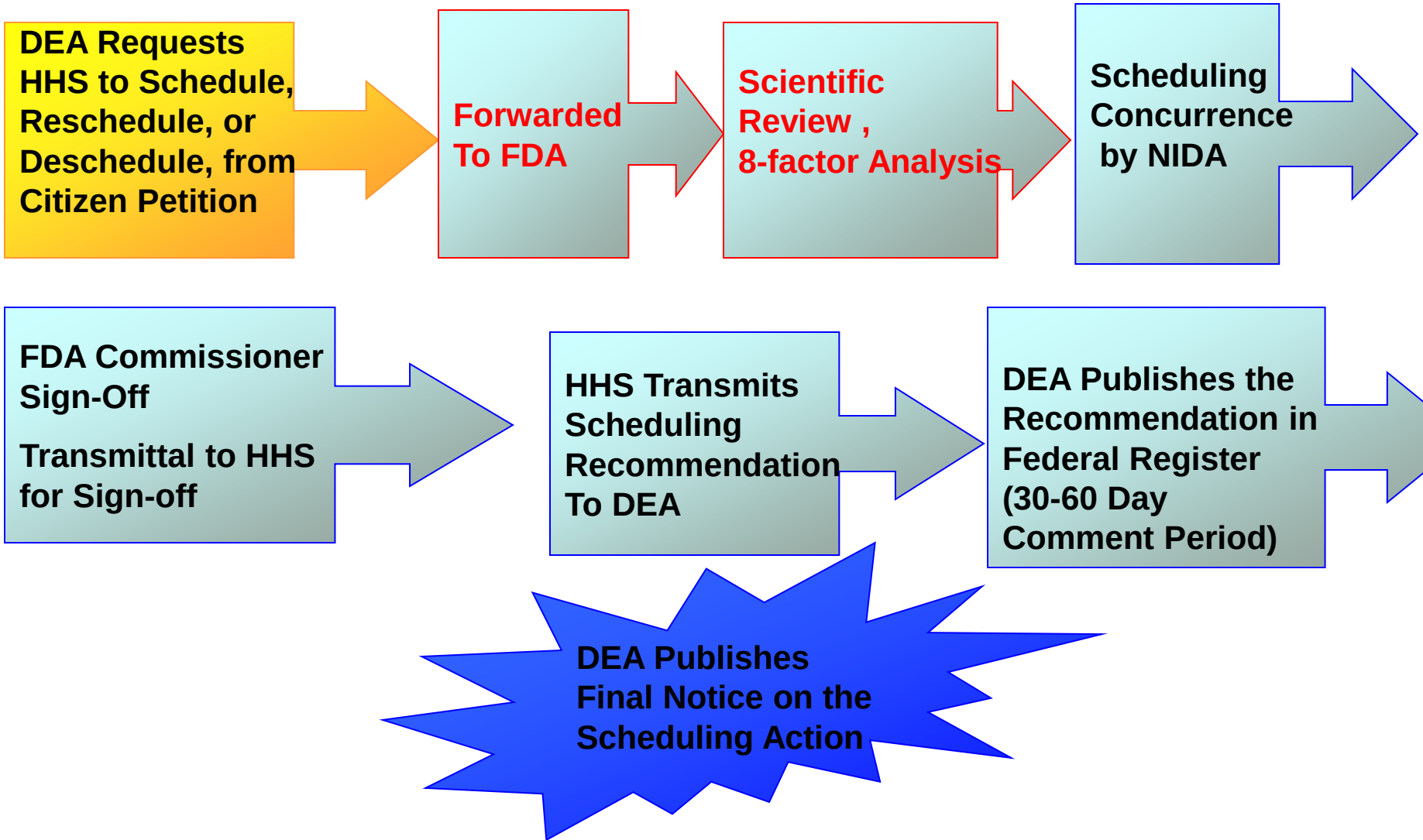
1. Actual or relative potential for abuse
2. Scientific evidence of pharmacological effect
3. Current scientific knowledge regarding the substance
4. History and current pattern of abuse
5. Scope, duration, and significance of abuse
6. Risk to public health
7. Psychic or physiological dependence liability
8. Immediate precursor of a substance already controlled

Case Law on Meaning of "Currently Accepted Medical Use"

1. The drug's chemistry is known and reproducible
2. There are adequate safety studies
3. **There are adequate and well-controlled studies proving efficacy**
4. The drug is accepted by qualified experts
5. The scientific evidence is widely available

57 FR 10499, 10504-06 (March 26, 1992).

Inter-Agency Drug Scheduling Process



Recent Scheduling History of MJ

- Controlled Substances Act of 1970 – MJ in Schedule 1
- 2001, 2006, FDA/HHS recommends that marijuana remain in Schedule I
- 2009 – Bryan Krumm submits a petition to DEA requesting that marijuana be removed from Schedule I
- 2011 – Governors of Rhode Island and Washington petition DEA “for the reclassification of medical cannabis from Schedule I to Schedule II of the CSA”

Status of Current 8-Factor Analysis and HHS Recommendation

- Scientific review of publically-available data on clinical uses of MJ by FDA and NIDA ongoing
  - Risk of abuse
  - Accepted medical use
- Results and recommendation follow process described earlier

Selected FDA Roles in Regulating Marijuana

- Scientific: providing scientific input ('8-factor analysis') on appropriate controls on MJ
- **Regulatory: supporting drug development from MJ**

FDA & Marijuana Drug Development

- Two products approved:
  - Marinol (dronabinol) (1985): nausea from cancer chemotherapy
  - Cesamet (nabilone) (1985 (2006)): nausea & neuropathic pain

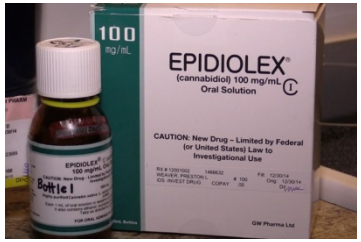
FDA & Drug Development from Marijuana*

- FDA actively supports development of drugs from marijuana:
  - Guidance on the use of botanicals (e.g., marijuana) as sources for drugs – August 2015
    - Focus on measures to take to help assure quality manufacturing
  - Expediting drug development using available tools:
    - Orphan Disease designation, Priority Review, Fast Track Designation

* http://www.fda.gov/newsevents/publichealthfocus/ucm421168.htm

FDA & Marijuana Drug Development

- Current research focused on two compounds:
  - Cannabidiol (CBD)
  - Tetrahydrocannabinol (THC)
- Drugs in clinical testing (3 therapeutic areas):
  - Sativex (CBD & THC) for cancer pain & spasticity
    - Approved in Europe and Asia
  - Epidiolex (CBD) for childhood seizures
    - **March 14: GW Pharmaceuticals announced positive phase 3 pivotal study results in Dravet's Syndrome**
    - INSYS also investigating CBD for infantile spasms



FDA & Drug Development from MJ

- FDA supports access to investigational drugs from MJ:
  - Expanded Access (EA) programs allow access to investigational drugs during development under IND
    - Set up by developer and investigator
      - Requires safety data collection and human subjects protection
    - Example: EA program for Epidiolex
      - Over 400 children have received Epidiolex through EA
    - FDA and NIDA are reviewing the scientific data on CBD to identify gaps in the database on CBD abuse potential

http://www.fda.gov/newsevents/publichealthfocus/ucm421168.htm

Selected FDA Roles in Regulating Marijuana

- Scientific: providing scientific input ('8-factor analysis') on appropriate controls on MJ
- Regulatory: supporting drug development from MJ
- **Enforcement: taking enforcement actions against products containing MJ when necessary**

Cannabidiol Edibles

CBD Warning Letters

- FDA has enforcement role to target nationally marketed products making egregious health claims
  - Includes products that allege to contain CBD
- FDA has issued two sets (Feb 2015 & Feb 2016) of warning letters (14 total) to those marketing unapproved drugs for the diagnosis, cure, mitigation, treatment, or prevention of diseases
- Some of these firms claim that their products contain cannabidiol (CBD)

--http://www.fda.gov/NewsEvents/PublicHealthFocus/ucm421163.htm

Examples of Claims

- "[S]tudies have found CBD to possess the following medical properties: … Antipsychotic – combats psychosis disorders…combats neurodegenerative disorders … Anti-tumoral – combats tumor and cancer cells …combats…depression disorders"
- Treats rheumatoid arthritis
- CBD helps with cancer, multiple sclerosis …diabetes, arthritis, dystonia, Crohn's disease…

http://www.fda.gov/NewsEvents/PublicHealthFocus/ucm435591.htm

Results of Analytic Testing

- FDA has tested these products, and many were found to not contain the levels of CBD they claimed to contain. **Consumers should beware purchasing and using any such products.**
  - http://www.fda.gov/newsevents/publichealthfocus/ucm484109.htm

Other FDA Marijuana Activities

- Work with outside groups on issues related to marijuana:
  - States that have legalized use of MJ, either recreational or medical
    - Discuss state experiences and data related to safety
  - States interested in supporting research and in expanded access for patients
  - Press, state officials, legislators, advocacy groups, patients, researchers

Other FDA Marijuana Activities: Safety Surveillance on MJ

- Databases and data on MJ safety are limited:
  - FDA Adverse Event Reporting System (FAERS) focused on collecting reports for drugs, MJ collected incompletely
- Need new data sources to help:
  - Describe relationship between levels of CBD or THC and adverse outcomes
  - Characterize at-risk populations (e.g., children)
- FDA supporting CDC requested (Mar 2016) report from National Academies of Science, Engineering and Medicine to assess health risks and consequences of MJ use

Summary

- FDA has multiple activities ongoing around marijuana
- Ongoing FDA work includes:
  - Providing scientific advice on the risks of marijuana and its constituents
  - Supporting rigorous scientific research into therapeutic value of marijuana and its constituents
  - Taking appropriate actions related to the marketing of products containing marijuana or its constituents

Conclusions

- FDA will continue to support development of specific new drugs that are safe, effective, and manufactured to a high quality
- Drug development, grounded in rigorous scientific research is essential to determining the appropriate uses of marijuana and its constituents in the treatment of human disease
- FDA is committed to making this process as efficient as possible and looking for ways to speed the availability of new drugs from marijuana for the American public

Thank You

- **CDER Human Drug Information**
  Division of Drug Information
  - (855) 543-3784, or
  - (301) 796-3400
  - http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm082585

- douglas.throckmorton@fda.hhs.gov

“It was impossible to get a conversation going, everybody was talking too much.”

Yogi Berra