FDA & Cannabis Research

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FDLI

FDA’s Perspective

What is the toxicity of CBD use?

- FDA has clinical trial data on CBD showing toxicity effects
- Products have flooded the market with no way of knowing what safe levels of consumptions are

Background

Origins of FDA Safety Concerns

- May 2019 Public Hearing & Public Docket
  - Epidiolex clinical data suggested various safety concerns
- FDA's primary safety concerns
  - Liver injury
  - Drug interactions
  - Male reproductive toxicity
  - Other side effects: drowsiness, gastrointestinal distress, and changes in mood (including irritability and agitation)
- March 2020 Report to Congress – FDA re-emphasized safety concerns, while also highlighting product quality issues and general insufficient scientific research

Background

Other Areas of Research Interest

- Cumulative exposure of CBD from multiple products
  - Proper dosing
  - Methods of exposure (e.g., transdermal penetration)
  - Daily use
- Impact on vulnerable populations (i.e., elderly, pregnant/lactating people, and minors)
- Chemical constituents of smoked and vaped products
- Synthetics and other cannabinoids (e.g., Delta-8 THC, CBG, CBN, etc.)

FDA's Challenge

Inadequate Scientific Evidence

- July 2021 – FDA rejected NDI notices submitted by Charlotte's Web and Irwin Naturals for their full spectrum hemp extract ingredients
- Even if CBD was not excluded from the definition of dietary supplement, the agency still had **"<u>concerns about the adequacy of safety evidence</u>"** because
  - Notifications relied on deficient categories of evidence
  - Evidence of the history of use was insufficient and/or vague
  - Studies were unreliable
  - Studies did not adequately address reported toxicity endpoints of CBD (e.g., hepatotoxicity and reproductive toxicity)

FDA's Challenge

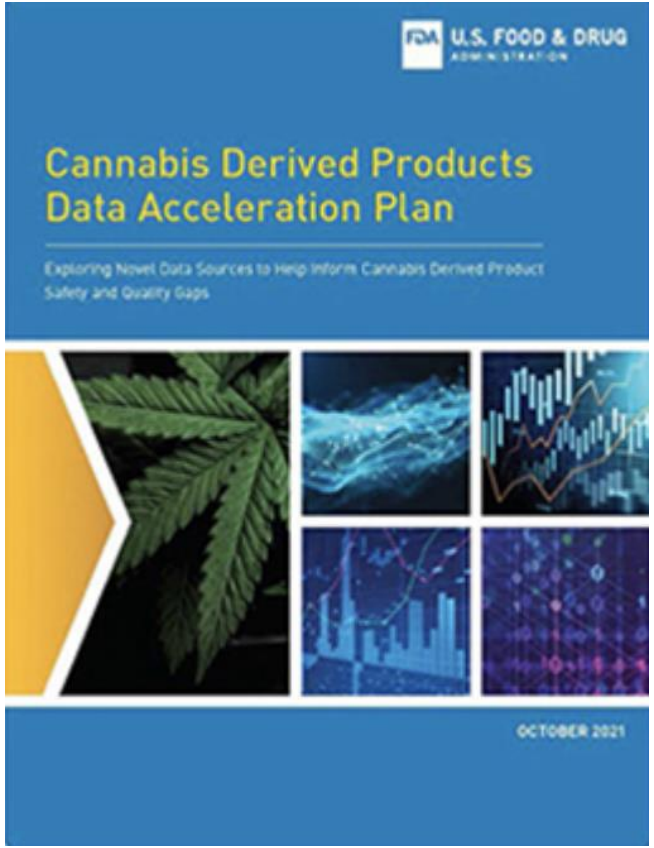
Gathering Data on Everyday Use

- Existing data on CBD use mostly comes from spontaneously reported adverse events (e.g., poison control centers)
- Rates of CBD use are poorly understood
- Data collection systems do not sufficiently identify specific CBD products
- Studies on long-term health effects of CBD use are needed

What's Ahead…

Implementation of the DAP

- Cannabis Derived Products Data Acceleration Plan
  - Initiated toxicological studies
  - Piloting data acceleration initiatives
  - Cultivating partnerships
  - Leveraging existing data sources
- https://www.fda.gov/media/153183/download



What's Ahead…

Areas of Research Interest at NIDA

Develop standards for measuring cannabis/cannabis constituent dose, intoxication, and/or impairment

Enhance existing epidemiology research to study trends for cannabis product use and cannabis use disorder (CUD); including new products (e.g., delta-8 THC products), patterns of use, and reasons for use in different populations

Characterize the composition/potency, pattern of use, and methods of administration of cannabis products

Determine the physical and mental health antecedents of cannabis use, as well as outcomes of use

Explore the impact of polysubstance use on health outcomes, including interactions (substitution/complementation) of cannabis product use with alcohol, tobacco, and prescription and nonprescription opioids

Investigate the effects of different patterns of cannabis use on brain development, educational attainment, and transition to work and adult roles

Identify the effects of maternal cannabis consumption during pregnancy and breastfeeding

https://grants.nih.gov/grants/guide/notice-files/NOT-DA-22-003.html

What's Ahead…

RWD/RWE have a role to play in filling data gaps, but…

- Should be collected in a standardized fashion with intent of developing evidence to support a specific point
- Should accompany other scientific data, generated through clinical studies (e.g., toxicology studies)

Industry's Position

Established Manufacturers Face a Dilemma Too

- Responsible manufacturers waiting for safety studies to be conducted face a dilemma
  - Narrow scope of enforcement
  - Expensive to conduct clinical trial research
- However, product quality will always remain critical to FDA
  - When CBD toxicity limits are established and in place, FDA will enforce through GMP compliance

Questions?

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