



Achieving the full potential of cannabis-derived medicines

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Grace
Living with Dravet syndrome



GW supports consideration of comprehensive federal framework

Cannabis - Derived

MEDICINES for PATIENTS
FDA-approved | Rx drugs

CONSUMER PRODUCTS
Supplements | Conventional foods



Comprehensive regulatory framework must:

1. **Encourage** development of FDA-approved **cannabis-derived medicines** for serious and life-threatening diseases
2. Ensure that consumer CBD products are **safe** for use in a mass-market setting without physician oversight
3. Establish **clear differentiation** between FDA-approved medicines and consumer-focused foods and supplements

Epidiolex – new treatment for two rare epilepsies



- > First and only plant-derived cannabinoid approved by FDA
- > First FDA-approved treatment in Dravet syndrome
- > First FDA-approved treatment since 2011 in Lennox-Gastaut syndrome



The NEW ENGLAND
JOURNAL of MEDICINE

THE LANCET

Work toward innovative cannabis medicines has just begun

CANNABINOID POTENTIAL

Autism | Rett | MS | TSC | NHIE | Glioblastoma | Schizophrenia | Neuropathic pain

GW studying
cannabinoids for 8
serious illnesses
with unmet need

Research needed
in cancer, glaucoma,
HIV/AIDS,
neurodegenerative
disease, pain, PTSD,
many others



FDA approval answers critical questions important for all, but especially for vulnerable patients

**Vulnerable
populations
and patients with
serious
illnesses**

+

DOES THE DRUG WORK?

- What does it work for?
- What doesn't it work for?
- How well does it work?
- Does something else work better?
- How long does it take to work?
- Will it stop working?
- How much should I take?
- How long should I take it for?
- Should I take it with or without food?

-

IS THE DRUG SAFE?

- What are the side effects?
- How closely should I be monitored?
- Can I take it if I'm pregnant or trying?
- Can my child take it?
- Can the elderly take it?
- Is it free of contaminants?
- Will it conflict with my other drugs?
- How is it manufactured?
- Is it consistently manufactured?

Liver risk



What is it?

- Epidiolex trials demonstrated CBD may cause elevated liver enzymes
- Elevation of liver enzymes means that drug induced liver injury is caused by CBD

How has FDA addressed the risk?

- Epidiolex label instructs physicians to conduct liver tests for 6 months or more after starting therapy
- FDA has mandated additional research on liver risk
- Adverse event monitoring, reporting, and analysis

Interaction with other drugs



What is it?

- Many patients, particularly vulnerable ones, are treated with multiple drugs simultaneously
- CBD may interact with many other common drugs and thus increase the safety concerns
- Interactions could cause these other drugs to have stronger or weaker effects in the patient

How has FDA addressed the risk?

- GW must conduct additional research on drug-drug interactions
- Warnings – physicians and pharmacists informed of DDI risks
- Adverse event monitoring, reporting, and analysis

More safety concerns from non-GW studies

“CBD products” (2015)*
>10% of patients

“Oral cannabis extracts” (2015)*²
>10% of patients

“Oral cannabis extracts” (2017)*³
>19% of patients

ANXIETY Weight gain

drowsiness

Confusion

INSOMNIA

Vomiting

Increased fatigue

Obsessive behavior

Aggressive behavior

Nausea

Increased appetite

Irritability

FATIGUE

somnolence

other less frequent effects

GI symptoms

INCREASED

Seizures

SOMNOLENCE

GI disturbance

1. Hussain et al. (2015) Ep & Beh. 47: 138-141
2. Press & Knupp. (2015) Epi & Beh. 45:49-52.
3. Treat et al. (2017) Epilepsia; 58(1): 123-127.

***Liver transaminases were not monitored in these studies**

Maintain a significant safety margin vs. known risk levels

Large safety margins

- > Lack of data
- > Unknowns in non-epilepsy populations
- > Unknowns in vulnerable sub-populations (e.g., elderly)
- > Potential risks to pregnant women based on pre-clinical data

No safe level

Data does not yet support a “safe” level with reasonable assurance

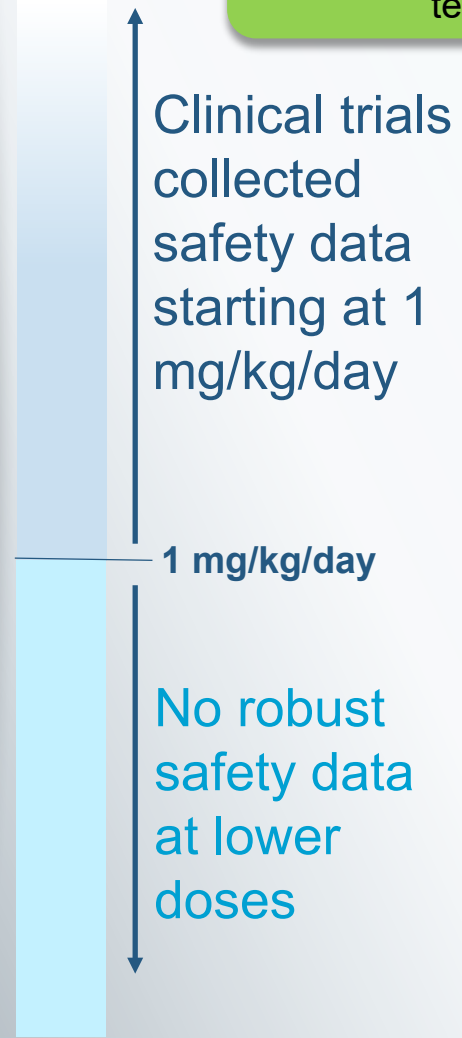
Cumulative exposure

Anticipated widespread use creates risk of cumulative daily exposure at unsafe levels

Other substances

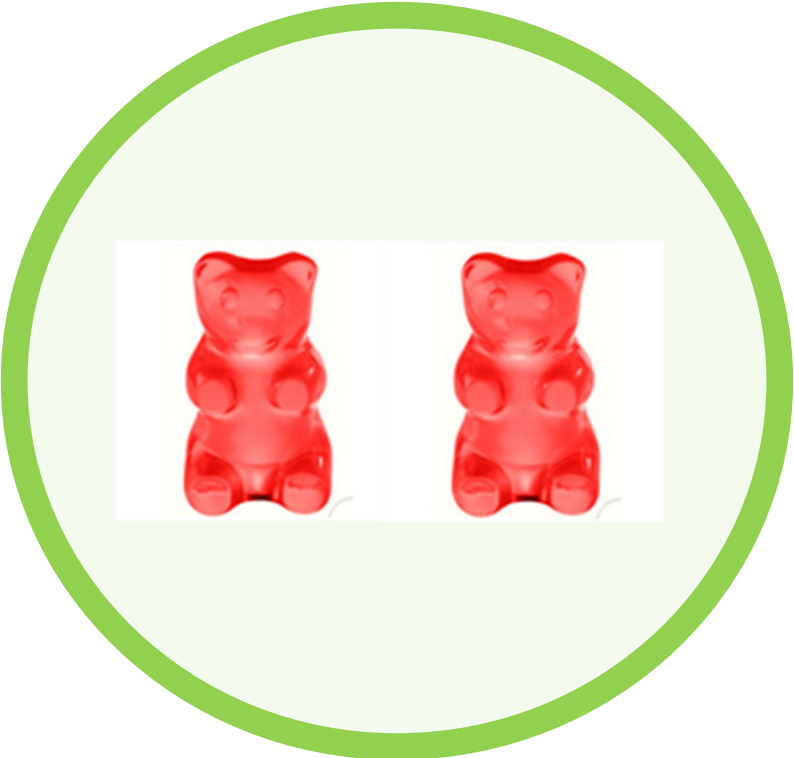
Must account for presence of other substances in a plant-based product, like THC

1mg
kg/day
side effects and drug interactions at lowest tested dose



CBD consumer products can contain significant amounts of THC

Up to 24mg THC delivered



Up to 17 mg THC delivered total



A path forward – proven medicines for patients in need & safe consumer goods

MEDICINES for PATIENTS

FDA-approved | Rx drugs

- Research into medicinal potential just getting started
- FDA's decision could make or break the future of cannabis Rx medicine
- Strengthen incentives
- Clear and wide differentiation between consumer products and medicines

CONSUMER PRODUCTS

Supplements | Conventional foods

- Safety concerns with CBD
- FDA should identify safe concentration and daily intake levels
- Safety margin to account for:
 - (1) Known and unknown safety issues
 - (2) Vulnerable populations
 - (3) High consumer demand and the likelihood of cumulative exposure

