Medical Cannabidiol Board

Subcommittee Report on Vaporized or Raw Cannabis

Subcommittee Members

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Purpose

At the August 2025 Board Meeting, this Subcommittee was assigned to review current medical literature evaluating the safety and efficacy of vaporized dried or raw cannabis for the treatment of qualifying medical conditions.

Previous Board or Subcommittee reviews conducted in 2022–2023 concluded that available evidence was limited or insufficient to support safety, efficacy, or reproducibility of effect, leading to the denial of prior petitions to permit vaporized forms. The Subcommittee's current purpose is to update that review and assess whether new or emerging scientific evidence warrants reconsideration of the Board's prior determinations, and for this document to serve as the recommendation to the full Board.

Methods

The medical literature was reviewed through two different approaches: the National Library of Medicine's *PubMed* site and an artificial intelligence large language model (LLM), specifically *ChatGPT5o*.

1. The AI site was asked to "List placebo-controlled, randomized, controlled trials of vaporized, dried, raw cannabis (flower) as treatment for adverse medical conditions published in the medical literature."
2. *PubMed* was searched using terms "vaporized cannabis" and "vaporized marijuana" and then filtered by "Randomized Controlled Trials"; separate searches were filtered by "Reviews".
3. As a previous petitioner of the product form, MedPharm Iowa (Bud & Mary's) was invited to provide literature to support the assertion that dried or raw cannabis is proven beneficial, but declined to participate.

Results

1. *ChatGPT5o* yielded the most succinct list[1] of a half dozen trials that met the search criteria. Although they are all prospective, placebo-controlled and randomized all trials have substantial defects:
    A. small number of study subjects (<50);
    B. short-term, often just one day, a few weeks at most;
    C. dosimetry was poorly-controlled in most, allowing subjects to self-determine the dose;
    D. as a result euphoria was a common feature, although transient.
2. *Pubmed* yielded essentially the same studies with the same features. Of interest, the "Reviews" filter yielded several compositions[2] virtually all addressing, as experience has been gained, the toxic effects of both combusted and vaporized cannabis, whether whole leaf or in extracted forms [example provided].
3. A search of *Chat GPT5o* for a study directly comparing vaporized dried, raw cannabis with vaporized cannabis extracts yielded nothing. It appears such a study has not been done.
4. A search[3] of the *FDA website* for approved "whole plant medications" yielded a short list of topical forms, none administered systemically, along with statements:
    a. "Whole-plant formulations often contain dozens or hundreds of chemical constituents. . . .not clear which constituents are responsible for therapeutic effect or toxicities."
    b. "Ensuring consistent quality, purity, and potency in each batch is more challenging compared to a purified chemical [extract]."

Conclusion

Evidence-based literature supporting dried, raw cannabis in a vaporized form of medical treatment cannot be found. Furthermore, dried, raw cannabis provided for vaporization can readily be diverted for combustion (smoked), a form and use specifically prohibited by Iowa law.

Recommendations.

The Board should make a motion to:

- Affirm its prior opposition to dried raw cannabis in any form as a medical treatment of qualifying conditions, and specifically oppose vaporization as a form in the Iowa's Medical Cannabis Program.

Annotations

Annotation 1

1. **Neuropathic pain (mixed etiologies)** — Wilsey et al., *J Pain* 2013
   Double-blind, placebo-controlled, 3-period **crossover** RCT (n=39). Volcano-vaporized NIDA cannabis flower (THC 1.29% “low” and 3.53% “medium”) vs placebo flower; significant analgesia vs placebo with minimal short-lived cognitive effects. PubMed
2. **Painful diabetic peripheral neuropathy** — Wallace et al., *J Pain* 2015
   Double-blind, placebo-controlled, 4-period **crossover** RCT (n=16). Volcano-vaporized cannabis flower at THC 1%, 4%, 7% vs placebo; dose-dependent reduction in spontaneous and evoked pain, with higher dose producing some cognitive impairment. PubMed
3. **Neuropathic pain from spinal cord injury/disease** — Wilsey et al., *J Pain* 2016
   Double-blind, placebo-controlled **crossover** RCT (n=42). Volcano-vaporized cannabis flower (THC 2.9% and 6.7%) vs placebo; significant analgesic response; lower dose favored for risk-benefit. PubMed
4. **Fibromyalgia** — van de Donk et al., *PAIN* 2019
   Double-blind, placebo-controlled, 4-way **crossover** RCT (n=20). Single inhalation of pharmacy-grade **flower chemovars** via Volcano (Bedrocan: high-THC; Bediol: THC+CBD; Bedrolite: high-CBD) vs placebo flower. Modest, mixed findings: THC-containing varieties increased pressure pain thresholds; spontaneous pain relief not greater than placebo overall (responder signal for THC+CBD). Lippincott Journals
5. **Acute migraine** — Schuster et al., *Neurology* 2024
   Double-blind, placebo-controlled, **crossover** RCT (92 randomized; 247 attacks treated). Patients self-treated up to four attacks with vaporized **cannabis flower**: THC-dominant (6% THC), CBD-dominant (11% CBD), **THC+CBD (6%/11%)**, and **placebo flower**. The **THC+CBD flower** was superior to placebo at 2 h for pain relief, pain freedom, and most-bothersome-symptom freedom, with sustained benefits; no serious AEs. PMC

Annotation 2

Respir Med 2024 Jan:221:107494.
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Effects of cannabis smoking on the respiratory system: A state-of-the-art review

Lugain Khoj [1], Vincenzo Zagà [2], Daniel L Amram [3], Karishma Hosein [4], Giovanni Pistone [5], Mario Bisconti [6], Antonella Serafini [7], Liborio M Cammarata [5], Maria Sofia Cattaruzza [8], Marco Mura [4]

Abstract

The diminished perception of the health risks associated with the consumption of cannabis (marijuana) lead to a progressive increase in its inhalational use in many countries. Cannabis can be smoked through the use of joints, spliffs and blunts, and it can be vaporised with the use of hookah or e-cigarettes. Delta-9 tetrahydrocannabinol (THC) is the main psychoactive component of cannabis smoke but contains numerous other substances. While the recreational use of cannabis smoking has been legalised in several countries, its health consequences have been underestimated and undervalued. The purpose of this review is to critically review the impact of cannabis smoke on the respiratory system. Cannabis smoke irritates the bronchial tree and is strongly associated with symptoms of chronic bronchitis, with histological signs of airway inflammation and remodelling. Altered fungicidal and antibacterial activity of alveolar macrophages, with greater susceptibility to respiratory infections, is also reported. The association with invasive pulmonary aspergillosis in immunocompromised subjects is particularly concerning. Although cannabis has been shown to produce a rapid bronchodilator effect, its chronic use is associated with poor control of asthma by numerous studies. Cannabis smoking also represents a risk factor for the development of bullous lung disease, spontaneous pneumothorax and hypersensitivity pneumonitis. On the other hand, no association with the development of chronic obstructive pulmonary disease was found. Finally, a growing number of studies report an independent association of cannabis smoking with the development of lung cancer. In conclusion, unequivocal evidence established that cannabis smoking is harmful to the respiratory system. Cannabis smoking has a wide range of negative effects on respiratory symptoms in both healthy subjects and patients with chronic lung disease. Given that the most common and cheapest way of assumption of cannabis is by smoking, healthcare providers should be prepared to provide counselling on cannabis smoking cessation and inform the public and decision-makers.

Keywords: Asthma; Bullous lung disease; Cannabis; Chronic bronchitis; Lung cancer; Marijuana; Pulmonary aspergillosis; Smoking.

Annotation 3

Here's a summary of how and why the FDA (via its Center for Drug Evaluation and Research, CDER) is typically reluctant or declines to approve "whole-plant" or complex botanical medicinal products. The key reasons relate to challenges in ensuring identity, quality control, reproducibility, safety, and evidence of efficacy.

Regulatory Framework & Context

- The FDA has a **Botanical Drug Development Guidance for Industry** that sets forth the agency's "current thinking" on how to handle botanical products being developed as drugs. U.S. Food and Drug Administration+2U.S. Food and Drug Administration+2
- Under this framework, a "botanical drug" is a product comprising plant materials (e.g. roots, leaves, extracts, etc.), and not one that is highly purified or chemically modified to a single molecular entity. U.S. Food and Drug Administration+2U.S. Food and Drug Administration+2
- The guidance emphasizes that botanical drugs must meet essentially the same standards of safety, efficacy, and manufacturing controls as conventional small-molecule drugs (though with certain accommodations or flexibilities). U.S. Food and Drug Administration+3U.S. Food and Drug Administration+3U.S. Food and Drug Administration+3
- A key concept is that sponsors must show the "identity, strength (potency), purity, and quality" (i.e. reproducible manufacturing) of the botanical drug. U.S. Food and Drug Administration+3U.S. Food and Drug Administration+3U.S. Food and Drug Administration+3

Because many "whole-plant" formulations present special difficulties in meeting those standards, the FDA often declines or refuses approval unless those challenges can be satisfactorily addressed.

Below are the major rationales (barriers) FDA cites or implicitly uses in rejecting or not approving whole-plant medicines.

Common Rationales or Barriers

1. **Complex mixture and lack of a single active ingredient / indistinct "active" constituents**
    - Whole-plant formulations often contain dozens or hundreds of chemical constituents. It may not be clear which constituent(s) are responsible for the therapeutic effect (or toxicities). U.S. Food and Drug

Administration+4European Pharmaceutical Review+4U.S. Food and Drug Administration+4
    - Because of that, it becomes difficult to define and standardize "potency" or "strength" in a way acceptable to FDA. U.S. Food and Drug Administration+2PubMed+2
    - The guidance notes the need for "multiple, sometimes overlapping" chemical or biological assays to characterize the botanical material. U.S. Food and Drug Administration
2. **Batch-to-batch (lot-to-lot) consistency / reproducibility issues**
    - The natural variability of plant sources (geography, harvest time, growing conditions, weather, soil, genetic variation) can lead to variable chemical composition. U.S. Food and Drug Administration+3PubMed+3U.S. Food and Drug Administration+3
    - Ensuring consistent quality, purity, and potency in each batch is more challenging compared to a purified chemical. U.S. Food and Drug Administration+3U.S. Food and Drug Administration+3PubMed+3
    - Without that consistency, FDA reviewers may question whether the clinical studies reflect what would be produced commercially.
3. **Insufficient chemistry, manufacturing, and controls (CMC) data**
    - The sponsor must fully describe raw botanical materials, the processing steps, standardization criteria, assays, controls for degradation, contaminants, etc. U.S. Food and Drug Administration+2U.S. Food and Drug Administration+2
    - In past botanical drug reviews, the FDA has declined approval or recommended against it because the identity, strength, purity, or quality assurance data were inadequate. European Pharmaceutical Review+2Fieldfisher+2
    - Because botanical drugs may contain many compounds, establishing a robust CMC package is more complex.
4. **Poor or insufficient evidence of clinical efficacy (and/or safety) via "adequate and well-controlled trials"**
    - Even if a botanical has long history of human use, FDA generally expects *well-controlled, statistically rigorous clinical trials* to support claims. U.S. Food and Drug Administration+5U.S. Food and Drug Administration+5U.S. Food and Drug Administration+5
    - FDA will scrutinize the design of those trials (e.g. endpoints, controls, blinding, patient population) as it does for conventional drugs. European Pharmaceutical Review+1
    - Insufficient efficacy evidence is one of the most commonly cited reasons why many botanical drug candidates fail. European Pharmaceutical Review+2Fieldfisher+2
    - Safety data must be robust, especially for chronic use. Unknown interactions among the multiple constituents may complicate safety assessment.
5. **Regulatory classification and labeling / intended use issues**

- Some botanicals may already be marketed as dietary supplements or foods, complicating their transition to drug status. The intended use (e.g. claim of treating disease) is a key discriminator. U.S. Food and Drug Administration+2U.S. Food and Drug Administration+2
- If prior marketing as a supplement exists, claims made must not mislead or conflict with FDA's expectations for drugs.
- The sponsor must demonstrate that the botanical drug is appropriate for prescription or OTC use, and that the indications justify the level of regulatory scrutiny.

6. **Safety, toxicology, and drug–constituent interactions**
   - With multiple constituents, there is greater risk of unknown or unpredicted toxicities or interactions among constituents.
   - The FDA expects nonclinical (animal) toxicology studies, pharmacokinetics, ADME, and possibly interaction studies. Botanical complexity can complicate interpretation of these studies. ScienceDirect+3U.S. Food and Drug Administration+3U.S. Food and Drug Administration+3
   - Impurities, contaminants (heavy metals, pesticides, microbial, mycotoxins), adulterants must be controlled.
7. **"Totality of evidence" burden & higher uncertainty risk**
   - The guidance talks about a "totality of evidence" approach, meaning that FDA will weigh all available pharmacologic, toxicologic, clinical, and prior human use data. But the more gaps or uncertainties there are, the more risk that FDA will deem the evidence insufficient. Exploration Publishing+2PubMed+2
   - For botanicals, gaps or variability in data are more common; sponsors have to "connect the dots" more rigorously.
8. **Resource, cost, and strategic factors (less direct but practical)**
   - Because of the complexities above, the cost, time, and scientific risk of developing a botanical drug can be high, which leads some sponsors to abandon or not push through to full approval. European Pharmaceutical Review+1
   - With fewer patent protections or exclusivity, the financial return may not justify the regulatory burden. European Pharmaceutical Review+1

Examples & Lessons

- The FDA has approved very few botanical drugs (e.g. **Veregen®**, a green tea extract for genital warts; **Mytesi™** / crofelemer for HIV-associated diarrhea). European Pharmaceutical Review+3U.S. Food and Drug Administration+3U.S. Food and Drug Administration+3

- In some cases, initial review by FDA has flagged that the CMC package was inadequate, or that the sponsor did not sufficiently show consistency or identity of the botanical material. European Pharmaceutical Review+2Fieldfisher+2
- In reviews of cannabis / cannabis-derived botanicals, FDA has repeatedly noted difficulty in controlling heterogeneity, ensuring quality, demonstrating standard dosing, and dealing with controlled substance issues. Exploration Publishing