Advancing Development of Botanical Drug Products

Re: Advancing Development of Botanical Drug Products; Request for Information
Docket No. FDA-2026-N-9550 | Federal Register 91 FR 56887 (September 4, 2026)

Comment on Advancing Development of Botanical Drug Products

International Society of Cannabis Pharmacists (ISCPh) | *FDA Docket FDA-2026-N-9550* | *October 27, 2026*

The International Society of Cannabis Pharmacists (ISCPh) appreciates the opportunity to comment on the Food and Drug Administration's (FDA's) request for information on botanical drug development [1]. Pharmacists are medication-use specialists whose expertise is relevant throughout clinical development. They can contribute to product and dose characterization, medication-history collection and reconciliation, and the evaluation of concomitant therapies and drug interactions. Their expertise also supports adverse-effect monitoring and the interpretation of medication-related outcomes. ISCPh encourages FDA to recognize pharmacists as important contributors to interdisciplinary botanical drug research and standards development.

ISCPh supports scientifically rigorous development that preserves appropriate expectations for product quality, safety, and efficacy. Our recommendations focus on practical ways pharmacist expertise can improve characterization of botanical exposure, collection of clinically interpretable data, and medication-safety assessment. These comments address investigational botanical drugs and potential future FDA-approved product pathways. They do not imply that products available through state cannabis programs have received FDA marketing approval.

1. Whole-Plant and Minimally Purified Products

Whole-plant and minimally purified products present challenges that may differ from those of isolated compounds. For cannabis-derived products, relevant variables include phytocannabinoid profiles and concentrations, other constituents, formulation, route of administration, batch variability, and the relationship between labeled content and the amount actually administered. Inhaled or self-titrated products are particularly challenging because product potency does not establish the amount delivered to or absorbed by the patient. Pharmacists can help distinguish these exposure measures, identify administration-related variability, and assess how changes in formulation or regimen may affect medication safety.

ISCPh recommends that FDA provide practical examples of fit-for-purpose product characterization, clinically relevant quality specifications, and comparability assessments for botanical and other complex mixtures. These examples should address phytocannabinoid profiles and concentrations, product strength, administered dose, route of administration, and uncertainty in exposure measurement.

ISCPh recommends distinct, scientifically justified potency specifications for cannabis flower and finished manufactured cannabinoid formulations. For cannabis flower (inflorescence) itself, ISCPh recommends that FDA consider an acceptance range of 80–120% of labeled cannabinoid content, with appropriate sampling, quality controls, and assessment of clinical risk. This reflects an earlier USP Cannabis Expert Panel proposal intended to accommodate botanical variability [2]. ISCPh acknowledges that the final Cannabis Species Inflorescence monograph, published in the United States Pharmacopeial Convention's (USP's) Herbal Medicines Compendium (HMC), specifies 90–110% of

labeled total THC and total CBD content [3]. ISCPh is therefore proposing that FDA evaluate the broader 80–120% range for flower, not representing it as the current USP HMC standard.

For finished manufactured formulations, including tinctures, oils, capsules, and other standardized dosage forms, ISCPh recommends a tighter acceptance range of 90–110% of labeled cannabinoid content, where scientifically appropriate. FDA should clarify how formulation characteristics, manufacturing controls, analytical methods, representative sampling, and clinical risk inform specifications. This distinction would accommodate variability inherent to flower while supporting more consistent dosing from manufactured products.

ISCPh emphasizes that flexibility in botanical potency specifications should not compromise contaminant testing or product safety. FDA should maintain clear expectations for pesticide residues, heavy metals, microbial contamination, mycotoxins, and residual solvents, where applicable. Testing requirements and acceptance criteria should account for formulation, route of administration, and potential risks associated with repeated exposure. ISCPh also recommends practical guidance on documenting pesticide use during cultivation and evaluating existing test results from state-regulated manufacturers to determine whether additional testing is needed for clinical research.

FDA should provide guidance on determining when differences in phytocannabinoid profiles, concentrations, or formulations may be clinically meaningful. These considerations are important for interpreting cannabinoid exposure, therapeutic response, adverse effects, and other medication-related outcomes in clinical research.

ISCPh further recommends incorporating pharmacists and other medication-use experts into multidisciplinary discussions of investigational product administration, dose selection, and the clinical interpretation of product differences. Pharmacists can help evaluate how variations in product composition, strength, formulation, and route of administration may influence cannabinoid exposure, treatment response, and patient safety. Their involvement would help ensure that product characterization and quality expectations remain clinically relevant.

2. Clarifying FDA Guidance

FDA's Botanical Drug Development guidance and Cannabis and Cannabis-Derived Compounds: Quality Considerations for Clinical Research guidance provide important foundations for investigational product development [4, 5]. ISCPh recommends that FDA supplement these documents with practical, cannabis-specific examples showing how existing expectations for product characterization, comparability assessments, dosage documentation, and clinical endpoint selection can be applied to whole-plant and minimally purified botanical products. Such examples would help sponsors interpret regulatory expectations while accounting for the complexity of these products and their clinical use.

ISCPh particularly recommends guidance on documenting variable or incompletely quantifiable cannabinoid exposure. At a minimum, documentation should include product identity, cannabinoid composition or strength when available, formulation, route of administration, estimated amount used, timing and frequency, and the source and certainty of the information. Examples should address as-needed use and distinguish among the intended dose, estimated amount administered, and systemic exposure, recognizing that these measurements are not interchangeable. Guidance on selecting clinically meaningful endpoints, including therapeutic response, tolerability, and functional outcomes when appropriate to the indication, would also support interpretation of clinical findings.

ISCPh further recommends that FDA include pharmacist-informed examples of investigational medication-history collection, reconciliation, and exposure documentation. These examples could

demonstrate how to record product changes, discrepancies between instructed and actual use, concurrent prescription and nonprescription medications, and other cannabinoid products used by study participants. Pharmacist participation in developing these examples would help ensure that documentation expectations are practical and clinically relevant. Clear, standardized guidance could reduce barriers to conducting research and collecting consistent, interpretable data on cannabinoid exposure, therapeutic outcomes, and adverse effects.

3. Standards Developed Outside FDA

Voluntary consensus standards could improve consistency and comparability across sponsors, research settings, and healthcare systems. Opportunities include standardized terminology for botanical product types, routes of administration, cannabinoid concentrations, formulation-specific dosing units, and batch identification. Clinical documentation standards could also establish consistent approaches to recording estimated, patient-reported, unconfirmed, or unknown exposure information.

ISCPh recommends that FDA and relevant standards-setting organizations adopt scientifically precise, consistent, and nonstigmatizing terminology for cannabis and cannabis-derived products. The term “marijuana” should not be used as a general product designation in scientific guidance, clinical documentation, or the naming and labeling of finished pharmaceutical products. Instead, terminology should reflect the botanical source, cannabinoid composition, formulation, and other clinically relevant product characteristics. Where existing statutes or regulations require the term “marijuana,” its use should be limited to those specific legal contexts.

Analytical product standards and clinical medication-data standards are complementary but serve different purposes. Product standards support consistent characterization and quality assessment, while clinical documentation standards help translate product information into interpretable medication-use data.

Where feasible, these standards should align with existing healthcare terminology and data-exchange frameworks to support interoperability between clinical research systems and electronic health records. This could reduce duplicative documentation and facilitate collection and comparison of medication-use data across research and clinical settings.

ISCPh recommends that pharmacists be represented in multidisciplinary standards-development efforts involving pharmacopoeial organizations, researchers, manufacturers, informatics specialists, other healthcare professionals, and patients. Pharmacists can help ensure that product information is translated into medication records that support dose interpretation, medication reconciliation, safety monitoring, and clinical research.

Existing resources, including applicable USP standards, should be evaluated and built upon rather than duplicated. Any proposed clinical documentation dataset should undergo feasibility, reliability, and clinical-utility evaluation before being adopted as an established standard.

4. Study Designs and Medication-Safety Assessment

Clinical study design should reflect the botanical product, therapeutic question, and stage of development. Randomized controlled trials remain important for establishing efficacy, while dose-finding, adaptive, and pragmatic trial designs may offer additional flexibility when scientifically justified. Observational studies may provide complementary evidence regarding real-world use, safety, and longer-term outcomes.

Studies involving complex botanical mixtures should prospectively characterize product composition and account for clinically meaningful variation in batches, formulations, administration, and cannabinoid exposure. Study protocols should include appropriate methods for evaluating therapeutic outcomes, tolerability, and adverse events, with consideration of how product variability and concomitant medication use may influence clinical findings.

Study designs should also account for interpatient and intrapatient variability in cannabinoid dose requirements and treatment response. Where clinically appropriate, protocols should permit individualized dosing and patient-directed titration within predefined parameters, including dose limits, adjustment intervals, and safety monitoring. This flexibility may be necessary to identify doses that provide meaningful therapeutic benefit with acceptable tolerability. When supported by clinical evidence, FDA-approved labeling should reflect individualized dosing needs and provide practical instructions for patient-directed titration and dose adjustments.

Where appropriate, studies should also evaluate medication-related outcomes, including opioid dose reduction or discontinuation and opportunities to reduce or deprescribe other relevant or potentially high-risk medications. These outcomes should be assessed alongside symptom control, functional status, and safety to determine whether medication changes represent meaningful clinical benefit without compromising treatment goals.

ISCPh recommends explicit pharmacist involvement during protocol development and, where feasible, trial conduct. Pharmacists can contribute to medication-history collection, medication reconciliation, and dosing and titration protocols. They can also support investigational product management, drug accountability, and diversion prevention.

Their clinical expertise is particularly valuable for drug-interaction assessment and adverse-event monitoring. This includes evaluating potential pharmacokinetic and pharmacodynamic interactions, additive central nervous system effects, and medication-related risks among older adults and participants with polypharmacy.

Integrating medication-use expertise into clinical study design may improve participant safety, support consistent data collection, and strengthen interpretation of treatment-related outcomes. Pharmacist involvement should complement the expertise of other investigators and clinical research professionals.

5. Regulatory Barriers and Research Feasibility

Recent federal changes placing specified FDA-approved and qualifying state-licensed medical cannabis products in Schedule III present an opportunity to clarify regulatory pathways for clinical research involving whole-plant cannabis and minimally purified botanical preparations. The scheduling action does not, by itself, grant FDA marketing approval to products available through state programs [6].

ISCPh recommends that FDA coordinate with the Drug Enforcement Administration (DEA) to provide practical guidance on investigational product sourcing, researcher registration, handling requirements, and use of products obtained from state-licensed medical cannabis manufacturers that meet applicable federal requirements. Clearer guidance on the interaction between federal and state regulations could reduce administrative barriers, improve access to appropriately characterized investigational products, and facilitate multicenter clinical research.

ISCPh also recommends that FDA explore practical pathways for assessing manufacturing facilities and product quality standards within state-regulated medical cannabis programs. These assessments could consider existing state inspections, manufacturing practices, quality-control procedures,

independent laboratory testing, contaminant and pesticide testing, and batch documentation. FDA should clarify how such information might support the evaluation of commercially available cannabis products for clinical investigation without unnecessarily duplicating existing oversight. Recognition of existing records would not, by itself, establish that a facility or product meets all applicable federal requirements.

ISCPh recommends that FDA clarify how prescription and nonprescription development pathways and labeling requirements may differ among botanical drug products according to their composition, intended use, safety profile, and need for professional oversight. Product-specific labeling should address cannabinoid content, dosing and titration, contraindications, drug interactions, adverse effects, and circumstances requiring medical evaluation. ISCPh also encourages FDA to consider regulatory pathways that could permit selected FDA-approved cannabis-derived medicines to be supplied through pharmacies with meaningful pharmacist involvement.

ISCPh recommends that FDA collaborate with the Drug Enforcement Administration (DEA) to evaluate whether certain cannabis-derived drug products may qualify for Schedule V classification based on product-specific evidence of abuse potential, dependence liability, and accepted medical use. Any such scheduling decision should be evaluated independently of whether a product qualifies for prescription or nonprescription marketing.

ISCPh specifically advocates for consideration of a behind-the-counter, pharmacy-based access model for selected FDA-approved cannabis-derived medicines where nonprescription use is scientifically justified and legally permissible. Under this proposed model, an eligible patient could obtain an approved product without a separate prescriber-issued prescription, but only after a pharmacist consultation. The pharmacist could verify age and other eligibility criteria, assess intended use, review concomitant medications and contraindications, recommend an appropriate approved product when indicated, provide dosing and safety counseling, and refer the patient for further medical evaluation when necessary.

ISCPh recommends that FDA and DEA clarify whether current nonprescription and controlled-substance authorities could accommodate this pharmacist-assisted model or whether additional regulatory or statutory changes would be needed. Schedule V classification does not automatically confer nonprescription status or establish a separate behind-the-counter drug category [7, 8].

ISCPh encourages FDA and DEA to pursue coordinated, scientifically justified approaches that facilitate clinical research and support appropriate access to cannabis-derived medicines. Controlled-substance scheduling should be distinguished from FDA requirements for investigational drug development, product quality, and marketing approval. Efforts to reduce regulatory barriers and explore alternative access pathways should maintain appropriate standards for product quality, safety, effectiveness, and participant and patient protection.

6. Real-World Evidence and Established Use

Established clinical use, generally accepted scientific knowledge, and real-world evidence may provide valuable information to support the development of whole-plant and minimally purified botanical products. These sources can help characterize patterns of use, inform dose selection, and identify potential safety signals. They can also support clinical study design and generate hypotheses for further investigation.

ISCPh encourages FDA to expand consideration of established clinical experience and scientifically credible real-world evidence in botanical drug development. Whole-plant cannabis and minimally purified preparations have extensive histories of human use, including within state-regulated medical cannabis programs. ISCPh recommends that FDA clarify when high-quality real-world evidence and established clinical experience may contribute to evidence supporting safety and effectiveness, including as confirmatory evidence or, where applicable regulatory standards can be met, through alternative study designs. Greater clarity could help sponsors avoid duplicative clinical investigations while preserving the evidentiary requirements for regulatory approval [9].

ISCPh also recommends that FDA facilitate research involving cannabis products already available through state-regulated medical cannabis markets. Patients independently choosing to use these products offer an opportunity to prospectively evaluate therapeutic outcomes, medication changes, and safety in real-world settings. FDA should clarify the regulatory distinctions between observational studies of independently initiated cannabis use and studies in which investigators direct product selection or administration. Clearer guidance on applicable investigational drug requirements could help investigators and institutional review boards (IRBs) review appropriate studies without unnecessary administrative barriers, while maintaining informed consent, participant protections, and scientific oversight.

To support these efforts, FDA should encourage feasible minimum standards for documenting cannabinoid exposure and medication-related outcomes. These should include product identity and composition when available, dose or amount used, route of administration, and timing and frequency of use. Additional elements should capture therapeutic indications, concurrent medications, treatment changes, patient-reported benefit, and adverse effects. Documentation should preserve the source and degree of certainty of the information rather than imply unsupported precision.

Pharmacists can contribute to developing and evaluating practical data-collection workflows across clinical and research settings. Their expertise in medication-history collection, medication reconciliation, drug-interaction assessment, and adverse-effect monitoring can improve the consistency and clinical interpretation of real-world data.

Existing pharmacist-led medical cannabis programs also provide opportunities to evaluate models of pharmacist-assisted access and medication management. Real-world evidence from these settings could help assess the impact of pharmacist involvement on product selection, individualized dosing, medication safety, and clinical outcomes. Such findings may inform future regulatory approaches to pharmacist-assisted access for selected cannabis-based medicines.

FDA should establish clear expectations for evaluating real-world evidence, including product comparability, exposure characterization, missing data, selection bias, and confounding. Established use alone should not be considered sufficient evidence of safety or efficacy for a proposed indication. However, high-quality real-world evidence should be considered within scientifically justified regulatory pathways that may reduce unnecessary research duplication, development costs, and barriers to investigating botanical products with extensive histories of human use.

Closing Recommendation

ISCPh recommends that FDA ensure meaningful pharmacist representation in future stakeholder meetings, guidance-development discussions, standards initiatives, and clinical research collaborations involving botanical drug products. Pharmacists bring expertise in medication management, individualized dosing, drug-interaction assessment, safety monitoring, and interpretation of real-world medication-use data. Their involvement can strengthen clinical research, improve the interpretation of

medication-related outcomes, and support evidence-informed regulatory decision-making. ISCPh welcomes opportunities to contribute this expertise through collaboration with FDA and other interdisciplinary stakeholders.

Selected References and Regulatory Resources

[1] Food and Drug Administration. Advancing Development of Botanical Drug Products; Request for Information. 91 FR 56887 (Sept. 4, 2026). Docket FDA-2026-N-9550. Source

[2] Sarma ND, et al. Cannabis Inflorescence for Medical Purposes: USP Considerations for Quality Attributes. Journal of Natural Products. 2020. DOI: 10.1021/acs.jnatprod.9b01200. Source

[3] United States Pharmacopeial Convention. Cannabis Species Inflorescence. Herbal Medicines Compendium, Version 1.0, Final Authorized. Source

[4] Food and Drug Administration. Botanical Drug Development: Guidance for Industry. December 2016. Source

[5] Food and Drug Administration. Cannabis and Cannabis-Derived Compounds: Quality Considerations for Clinical Research: Guidance for Industry. January 2023. Source

[6] Drug Enforcement Administration. Schedules of Controlled Substances: Rescheduling of Food and Drug Administration Approved Products Containing Marijuana From Schedule I to Schedule III; Corresponding Change to Permit Requirements. 91 FR 22714 (Apr. 28, 2026). Source

[7] Food and Drug Administration. Nonprescription Drug Product With an Additional Condition for Nonprescription Use: regulatory information. Source

[8] Drug Enforcement Administration. 21 CFR § 1306.26, Dispensing Without Prescription (conditional retail dispensing by pharmacists of certain nonprescription controlled substances). Source

[9] Food and Drug Administration. Real-World Evidence: Considerations Regarding Non-Interventional Studies for Drug and Biological Products. Draft Guidance. March 2024. Source