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Short communication

Challenges in preparation and adaptation of CTD dossiers for medical cannabis products

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Introduction

Cannabis-derived medicinal products are increasingly used in pharmaceutical practice due to expanding therapeutic applications and evolving regulatory acceptance. . Unlike conventional synthetic pharmaceuticals, cannabis-based products present specific pharmaceutical and regulatory challenges because of their botanical origin, multicomponent composition, and variability in cannabinoid and terpene content. Current European regulatory requirements increasingly demand Common Technical Document (CTD)-compliant dossiers equivalent to those required for finished medicinal products (EMA, 2022). This review summarizes the major scientific and regulatory challenges associated with preparation and adaptation of CTD dossiers for cannabis-derived medicinal products.

Regulatory and pharmaceutical challenges in Cannabis CTD dossier preparation

Classification and CTD adaptation challenges

One of the main challenges relates to classification of cannabis-derived materials within the manufacturing chain. Cannabis-derived substances may exist as crude extracts, cannabinoid concentrates, bulk oil preparations, or finished medicinal products. The distinction between active pharmaceutical ingredients (API), intermediate, bulk product, and finished product is often unclear and varies between jurisdictions, directly influencing GMP requirements, stability expectations, release procedures, and dossier structure (Arjun et al., 2025). Additional variability arises because cannabis products may be classified as phytopharmaceuticals, herbal medicinal products, magistral preparations, narcotic medicines, or conventional pharmaceutical products.

CTD Module 3 challenges

Preparation of CTD Module 3 documentation is particularly demanding because cannabis-derived medicinal products contain multiple cannabinoids and other secondary metabolites with naturally variable compositions. Variability may result from cultivar differences, cultivation conditions, harvesting parameters, extraction methods, and purification processes. Key challenges include establishment of scientifically justified specifications, impurity characterization, and control of pesticides, heavy metals, residual solvents, and microbiological quality (EMA, 2022). Adaptation of the finished product section additionally requires pharmaceutical development data regarding excipient compatibility, cannabinoid solubility, dose uniformity, container closure compatibility, and physical stability of lipid-based cannabis oil formulations.

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CTD Module 4 and Module 5 limitations

Preparation of non-clinical and clinical documentation presents additional complexity because available scientific evidence is often heterogeneous and based on non-standardized formulations. Differences in cannabinoid ratios, terpene composition, dosage forms, and routes of administration complicate extrapolation of published data to newly developed products. Consequently, manufacturers frequently rely on bibliographic data , bridging approaches, and risk-based scientific justifications during dossier preparation (ICH, 2025).

Stability and specification challenges

Stability assessment represents one of the most critical aspects of cannabis product development. Cannabinoids, particularly THC, are susceptible to degradation induced by heat, oxygen, and light exposure, leading to the formation of degradation products such as cannabinol (CBN) (Trofin et al., 2012). Stability studies must therefore evaluate potency retention, formation of degradation products, microbiological quality, physical appearance, and packaging performance. Specification setting also remains challenging because narrow specifications may be difficult to maintain due to natural botanical variability, while broad specifications may compromise consistency and therapeutic reproducibility.

Risk-based quality approaches and regulatory observations

Implementation of risk-based quality systems according to ICH Q9 and EU GMP principles is essential for cannabis-derived medicinal products (EC, 2022; ICH, 2025). Regulatory assessment frequently reveals challenges associated with classification strategies, adequacy of stability data, suitability of specifications, and relevance of supporting clinical documentation. Authorities commonly request additional justification regarding cannabinoid assay ranges, degradation limits, microbiological controls, and differentiation between botanical extracts and purified cannabinoid-containing pharmaceutical products. Regulatory authorities frequently request additional scientific justification regarding classification strategies, and applicability of published clinical literature to specific cannabis formulations.

Conclusion

The transition from API-oriented cannabis documentation toward CTD-compliant dossiers for finished cannabis-derived medicinal products represents a substantial pharmaceutical and regulatory challenge. Cannabis-derived medicinal products differ fundamentally from conventional synthetic pharmaceuticals because of their botanical origin, multicomponent composition, and inherent variability. Successful preparation of CTD dossiers therefore requires integration of pharmaceutical development, stability science, GMP compliance, and risk-based regulatory strategies.

Further harmonization of international regulatory expectations and development of cannabis-specific pharmaceutical guidance may facilitate future preparation and assessment of high-quality medicinal cannabis dossiers within the European regulatory framework.

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