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REGULATORY FRAMEWORKS FOR 3D-PRINTED PHARMACEUTICALS: A COMPARATIVE ANALYSIS OF FDA AND EMA

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ABSTRACT
Three-dimensional (3D) printing has been accepted as an emerging technique in pharmaceutical development with potential for personalized medication, controlled drug release and customizable dose forms. However, its application in pharmaceutical production poses regulatory obstacles to product quality, process validation, and production consistency. This study will try to examine and compare the regulatory systems of the European Medicines Agency (EMA) and the United States Food and Drug Administration (FDA) for 3D-printed pharmaceuticals. The research will concentrate on quality standards, regulatory submissions, approval procedures, and new regulatory aspects. A comparison analysis was undertaken based on official regulatory documents, international legislation, and published scientific research. The findings indicate that both organizations adhere to the established pharmaceutical regulatory standards, encompassing the assessment of final product quality, process validation, quality management, and Good Manufacturing Practice. The FDA's regulatory expertise is demonstrated by the approval of Spritam and the initiation of its Emerging Technology Program. The European Medicines Agency (EMA) established more specific Quality and GMP standards for 3D printing in its 2026 guidelines for solid oral dosage forms. The key issues include the defining of batches, reproducibility, integrity of digital data, variability of materials and processes, and customized and decentralized manufacturing. The study refers to the need for more explicit technology-oriented quality standards, efficient production and digital control, and improved regulatory alignment to promote the development of 3D-printed medications, for the safe, quality and welfare of patients.

Keywords: *Additive manufacturing; Personalised medicine; Pharmaceutical regulation; Regulatory harmonisation; Three-dimensional printing.*

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INTRODUCTION
Three-dimensional (3D) printing, or additive manufacturing, has received great attention in the field of pharmaceutical development due to its abilities to construct complicated dosage forms based on specific drug-release and dosing requirements. The method permits pharmaceutical goods to be developed by sequentially layering components according to digital patterns. Its applications encompass modified release formulations, combination drug dosage forms, and personalized medications, offering novel opportunities for customized drug development and adaptable pharmaceutical development [1-3]. However, the implementation of 3D printing in the pharmaceutical production area faces the difficulty of product quality and process consistency. Critical quality attributes such as drug content uniformity, mechanical strength and dissolving properties may be impacted by material properties, formulation composition, printing parameters, equipment setup and post-processing conditions. In addition, process validation, repeatability and the application of appropriate quality control procedures need to be emphasized [4-6]. The digital component of an additive manufacturing also poses new challenges of software regulation, data dependability, production traceability, and design-file

management. These components are crucial in decentralized and personalized manufacturing procedures, where conventional quality assurance, process oversight, and batch specification techniques could require modification. Hence, there is a need for proper application of the existing pharmaceutical rules in order to handle the distinctive characteristics and potential hazards of the technology ([2,6,7]. The evolution of regulatory frameworks for pharmaceutical 3D printing has been driven by the implementation of current pharmaceutical standards and initiatives that have addressed novel manufacturing technology. The United States Food and Drug Administration (FDA) approved Spritam® (levetiracetam), a medication manufactured using Aprecia's ZipDose® technology, therefore establishing a regulatory milestone. The FDA's Emerging Technology Program additionally promotes regulatory collaboration in the advancement of innovative pharmaceutical production technologies. The European Medicines Agency (EMA) has progressively addressed novel manufacturing technologies in its 2026 Questions and Answers document, which outlines particular Quality and Good Manufacturing Practice (GMP) considerations for the application of 3D printing in solid oral dosage forms [8-12]. Both authorities align themselves to the established guidelines of pharmaceutical quality but the regulatory methodologies, submission procedures and technology specific features differ and require further investigation. Special attention should be given to manufacturing rules and process verification of 3D-printed pharmaceuticals for the use of Common Technical Document (CTD) and electronic Common Technical Document (eCTD) standards. Understanding these aspects is crucial to finding regulatory gaps and inconsistencies that may affect the development and marketing authorization of products.
The study's purpose is to research FDA and EMA guidelines associated with 3D-printed medications with a special focus on pharmaceutical quality standards, GMP variables, CTD/eCTD submissions and approval procedures. It also reviews significant regulatory trends and case studies to identify key difficulties and provide solutions to promote regulatory clarity, harmonization and quality control of pharmaceutical 3D printing .

METHODOLOGY

Comparative Regulatory Assessment and Source Selection

A comparative analysis of regulations was conducted in order to examine the frameworks governing three-dimensional (3D)-printed medicinal products in the United States and the European Union. The analysis evaluated the established pharmaceutical regulatory guidelines alongside the features of additive manufacturing, including material properties, formulation and feedstock preparation, digital dosage form design, manufacturing process variables, and the possibility of their impact upon the quality of the end product [1,2,6]. The United States and the European Union were selected due to the implementation of robust pharmaceutical regulatory systems, characterized by various organizational frameworks and approaches to the regulation of pharmaceutical products. The assessment was based on authoritative documents from the United States Food and Drug Administration (FDA), European Medicines Agency (EMA), European Commission, and International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH), alongside peer-reviewed research.
The assessment for the United States included current Good Manufacturing Practice (cGMP) regulations specified in 21 CFR Parts 210 and 211, in addition to the FDA's guidance on the Advancement of Emerging Technology Applications for Pharmaceutical Innovation and Modernization. EudraLex Volume 4 was analyzed alongside the relevant EMA regulatory documents for the European Union. The ICH quality guidelines Q8(R2), Q9(R1), and Q10 were assessed in relation to pharmaceutical development, quality risk management, and pharmaceutical quality systems, respectively. A considerable emphasis was placed on the FDA Emerging Technology Program and the EMA's 2026 Questions and Answers document regarding Quality and GMP considerations associated with the implementation of 3D-printing technology in solid oral dosage forms. The scholarly articles regarding the pharmaceutical applications of additive manufacturing, modified-release dosage forms, multi-drug formulations, personalized medicine, feedstock characteristics, and manufacturing process parameters were also examined [1-4,6,13,14].

Manufacturing Operations and Quality Considerations

The major manufacturing techniques related to pharmaceutical 3D printing were assessed, encompassing material selection through to the packaging and storage of the finished dosage form. These included the selection and characterisation of materials, preparation of feedstock or formulations, computer-aided design (CAD), slicing and printer setup, layer-by-layer printing, post-processing, quality control, and packaging and storage. The assessment investigated the influence of material characteristics, formulation properties, digital design, and printing parameters on printability, manufacturing consistency, dosage-form structure, drug distribution, and drug-release kinetics [1-3, 13, 14]. A significant importance was laid on fundamental material properties, critical process variables, and their relationship with the key quality attributes of the end product. Quality attributes included the pharmaceutical

formulation, uniformity of content, mechanical properties, dissolving performance, stability, and procedural consistency. The assessment also considered the effects of post-processing tasks, equipment and software oversight, digital file integrity, data dependability, and manufacturing traceability. The anticipated impacts of personalized and decentralized production were examined for variations in dosage strength, form, and combinations of active ingredients [6,12,15,16]. These metrics were evaluated in relation to pertinent GMP standards and ICH quality principles to discern manufacturing and quality-control factors pertinent to 3D-printed pharmaceutical items.

Assessment of CTD/eCTD Requirements

The frameworks of the Common Technical Document (CTD) and electronic Common Technical Document (eCTD) were evaluated to assess the arrangement and submission of regulatory data for 3D-printed pharmaceutical products in the United States and European Union. The CTD consists of five components, with Module 1 containing region-specific administrative information, while Modules 2 to 5 include the common scientific and technological aspects. The eCTD provides an electronic structure for submitting regulatory documents and managing their entire life cycle [17]. The standards were evaluated separately for the United States and the European Union to identify regional differences in administrative data, submission procedures, and technical requirements. The evaluation for the United States took into account FDA eCTD conditions for corresponding pharmaceutical submissions, encompassing Investigational New Drug (IND) applications, New Drug Applications (NDAs), and Abbreviated New Drug Applications (ANDAs). Module 1 was investigated for U.S.-specific administrative data, application particulars, labeling, and regional technical specifications. Modules 2–5 were assessed for the provision of quality summaries, pharmaceutical development, nonclinical data, and clinical trial data. A significant focus was placed on Module 3, which includes information on drug substances and drug products, formulation and feedstock characteristics, manufacturing processes, process controls, finished product specifications, analytical methods, process validation, packaging, and stability [6, 9, 17-19].

The evaluation for the European Union analyzed the CTD framework inside the EU regulatory framework, comprising EU-specific administrative and product information in Module 1, as well as related scientific and technical data in Modules 2–5. The evaluation included data from the marketing authorization application, specifics regarding the production site, product information, Summary of Product Characteristics, Package Leaflet, labeling, and pertinent regional eCTD requirements. Module 3 gained major emphasis owing to the EMA's 2026 Q&A paper, which deals to Quality and GMP elements of 3D printing for solid oral dosage forms. The analysis of the two regions emphasized shared CTD prerequisites, variations in regional administration, and how well current quality documentation addresses the material, manufacturing, digital, and product-quality attributes of 3D-printed pharmaceuticals [6,12,17].

Table 01a: Comparison of CTD/eCTD Requirements for 3D-Printed Pharmaceuticals in the United States and European Union

CTD Module / Aspect	United States – FDA	European Union – EMA	References
Module 1 – Administrative information	Contains FDA-specific data on regions and FDA administration.	Contains regional and administrative information specific to EU.	[18-20]
Module 2 – CTD summaries	Summarizes clinical, nonclinical, and overall quality.	Includes clinical, nonclinical and Quality Overall summaries.	[17]
Module 3 – Quality	Covers quality data for drug substance, drug product, manufacturing process and controls.	Relates to the quality data of the active ingredient, pharmaceutical product, method of manufacture and controls.	[17]
3D-printing focus in Module 3	3D printing is already on the radar in the existing framework for pharmaceutical quality and manufacturing.	EMA talks about quality issues related to GMP and 3D printing in particular for solid oral forms of medication.	[6,9,12]
Module 4 –	Includes	Includes the	[17]

Nonclinical studies	the required non-clinical study reports.	required non-clinical study reports.	
Module 5 – Clinical studies	Includes the required clinical study reports.	Includes the required clinical study reports.	[17]
eCTD implementation	FDA accepts eCTD v4.0 for new regulatory submissions to CDER and CBER .	EU filings comply with the EU Module 1 requirements and EU eCTD implementation.	[18-20]
Regional differences	The FDA has its own technical specification and its own regional implementation of Module 1.	EMA has a Module 1 specification for the EU specific to the European regulatory system.	
3D-printing-specific regulatory guidance	There is no particular FDA CTD module for 3D printed drugs.	EMA has published detailed Q&A guidance on GMP regulations and quality for 3D printing in 2026. considerations for solid oral dosage forms.	[6,9,12].

Marketing Authorisation Pathways

The pathways for regulatory approval of 3D-printed pharmaceutical products were examined within the current drug licensing systems of the United States and European Union. The assessment concentrated on conventional development and approval procedures rather than assuming a separate clearance pathway specifically for 3D-printed pharmaceuticals [20-22]. In the United States, the assessment included the progression from preclinical development to clinical trials and marketing authorization, necessitating the submission of an IND application, clinical development, NDA filing, and FDA evaluation and decision. The essential quality and production specifications to ensure supervision of the formulation, manufacturing process, and finished pharmaceutical product were also considered. Spritam® (levetiracetam) was examined as a prototype of an FDA-approved drug manufactured using 3D-printing technology [8,21,23]. The assessment for the European Union considered the relevant marketing authorization methods, including centralized, decentralized, and mutual recognition processes, depending on the pharmaceutical product and its legal basis. The centralized process included the evaluation of eligibility and pre-submission activities, the submission of the Marketing Authorization Application (MAA), scientific review by the Committee for Medicinal Products for Human Use (CHMP), approval of the CHMP recommendation, and the subsequent ruling by the European Commission [20,22].The importance of manufacturing and quality data under the current authorization framework was assessed alongside the FDA Emerging Technology Program and the EMA's 2026 Q&A document.

Case Studies and Regulatory Initiatives

Selected cases of pharmaceutical 3D-printing applications and regulatory activities were analyzed in order to demonstrate the evolution and regulatory acceptability of additive manufacturing in the pharmaceutical sector. The assessment included an FDA-approved 3D-printed medication, ongoing new manufacturing technologies, collaborative regulatory initiatives, customized dosage form development, and the EMA's regulatory progress. These examples offered a platform for examining the practical applications, development status, and regulatory considerations related with pharmaceutical 3D printing.

Case study 1: Spritam® (Levetiracetam)

The FDA approval of Spritam® was investigated as an example of a commercialized pharmaceutical product made employing 3D-printing technology. The evaluation examined Aprecia Pharmaceuticals' ZipDose® technology, its porous tablet composition, swift disintegration properties, and the regulatory implications of integrating an unusually formulated manufacturing method into the current pharmaceutical approval system [8,23].

Case study 2: Triastek and MED® Technology

The Melt Extrusion Deposition (MED®) technology developed by Triastek and its T21 initiative was studied to understand the application of extrusion-based 3D printing in manufacturing oral dosage forms. The

assessment focused on dosage-form formulation, drug-release objectives, material properties, printing criteria, and regulatory considerations relevant to clinical development [2,24].

Case study 3: FDA Emerging Technology Program

The FDA Emerging Technology Program (ETP) was studied as an instance of initial regulatory engagement for innovative pharmaceutical manufacturing techniques. The assessment included its purpose, potential for collaboration between developers and regulators, and its importance in addressing technical and regulatory challenges before official regulatory submission. The program was considered as a mechanism for regulatory engagement rather than a standalone marketing approval pathway [9].

Case study 4: FabRx Printlets and Personalised Medicines

The advancement of FabRx was examined to determine the application of pharmaceutical 3D printing in the production of personalized dosage forms. The assessment analyzed printing technologies and their ability to modify dosage strength, form, and drug-release characteristics. Quality and manufacturing parameters were examined for customized pharmaceutical production [13,15].

Case study 5: EMA Regulatory Development for 3D-Printed Medicines

The examination focused on EMA's efforts on innovative manufacturing technologies and customized medications, as well as the regulatory considerations of 3D printing and the development of the 2026 Questions and Answers document. A considerable focus was directed into the Quality and GMP aspects related to 3D-printed solid oral dosage forms and their importance within the current European pharmaceutical quality framework [10,12,25].

Comparative Evaluation and Identification of Regulatory Challenges

The FDA and European regulatory systems were evaluated based on shared regulatory and technical criteria, encompassing regulatory architecture, marketing authorization routes, GMP standards, pharmaceutical development, quality risk management, pharmaceutical quality systems, process validation, manufacturing process oversight, material and feedstock attributes, finished product quality, CTD/eCTD stipulations, digital manufacturing, personalized production, and technology-specific regulatory advancements.
Factors related to materials and processes were evaluated about the potential influence of feedstock variability and production conditions on product quality and uniformity. Digital design, file transmission, software management, data fidelity, and manufacturing traceability were also taken into account, especially regarding personalized and decentralized production (International Council for Harmonization, 2008, 2009, 2023; Alzhrani et al., 2025; European Medicines Agency, 2026).
The comparative analysis was employed to identify underlying regulatory obstacles associated with material and feedstock inconsistency, essential process-parameter regulation, process validation, manufacturing consistency, digital-file administration, finished-product quality evaluation, batch characterization, customized manufacturing, decentralized and point-of-care production, and regulatory alignment. These results served as the framework for establishing concepts associated with technology-specific quality standards, production regulations, digital oversight, and regulatory conformity.

RESULTS

The comparative analysis revealed that the FDA and EMA assess 3D-printed drugs under existing pharmaceutical regulatory systems, focusing on Good Manufacturing Practice (GMP), drug development, manufacturing controls, and quality assurance. The endorsement of Spritam® and the commencement of the Emerging Technology Program in the United States indicate regulatory proficiency in cutting-edge pharmaceutical production procedures. In the European Union, the EMA's 2026 Questions and Answers document specifies several Quality and GMP considerations relevant to the implementation of 3D printing in solid oral dosage forms. The review also found substantial regulatory hurdles, such as inconsistencies in raw materials and printing settings, manufacturing consistency, process verification, digital data governance, batch characterisation, and quality control in customized and decentralized manufacturing. The comparison of CTD and eCTD found that both areas conform to the standardized five-module CTD framework while respecting region-specific administrative and electronic submission constraints.

CONCLUSION

The study shows that both the FDA and EMA modify existing pharmaceutical regulatory criteria for 3D-printed medications while progressively adjusting to the requirements of innovative manufacturing technologies. The FDA's engagement with Spritam® and its Emerging Technology Program shows the integration of innovative manufacturing within the existing regulatory framework, whereas the EMA has developed more comprehensive Quality and GMP standards for 3D printing of solid oral dosage forms. Despite these developments, challenges related to material uniformity, manufacturing dependability, process validation, digital data integrity, batch characterisation, and personalized decentralized production remain critical concerns. Improved transparency in technology-related regulatory mandates, more robust control of manufacturing and digital

processes, and greater collaboration among regulatory agencies and researchers are important for the consistent regulatory assessment of 3D-printed pharmaceuticals. Initially anticipated regulatory improvements should support technological innovation while maintaining the quality, safety, and reliability of pharmaceutical products.

ABBREVIATIONS

3D: Three-Dimensional; **ANDA:** Abbreviated New Drug Application; **CAD:** Computer-Aided Design; **CFR:** Code of Federal Regulations; **CHMP:** Committee for Medicinal Products for Human Use; **cGMP:** Current Good Manufacturing Practice; **CTD:** Common Technical Document; **eCTD:** Electronic Common Technical Document; **EMA:** European Medicines Agency; **EU:** European Union; **FDA:** Food and Drug Administration; **GMP:** Good Manufacturing Practice; **ICH:** International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use; **IND:** Investigational New Drug; **MAA:** Marketing Authorisation Application; **MED:** Melt Extrusion Deposition; **NDA:** New Drug Application; **Q&A:** Questions and Answers; **U.S.:** United States.

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AUTHOR CONTRIBUTION

Both are contributed equally.

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