WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
Coden USA: WJPRAP Impact Factor 8.63
Volume 15, Issue 22, 182-193. Review Article ISSN 2277–7105

REGULATORY REQUIREMENTS AND GENERIC DRUG DOSSIER COMPILATION FOR ORAL DISINTEGRATING TABLETS IN THE USA

Y. Manjula[1], Sravani[2], B. Chandra Shekhar Reddy*[3]

[1,2]Students, Department of Regulatory Affairs, Sarojini Naidu Vanita Pharmacy Maha Vidyalaya, Affiliated to Osmania University.

[3]Professor and Head, Department of Pharmaceutics, Sarojini Naidu Vanita Pharmacy Maha Vidyalaya, Affiliated to Osmania University.

Article Received on 14 Oct. 2026,
Article Revised on 04 Nov. 2026,
Article Published on 16 Nov. 2026

https://doi.org/10.5281/zenodo.24271899

***Corresponding Author**

Dr. B. Chandra Shekhar Reddy

Professor and Head, Department of Pharmaceutics, Sarojini Naidu Vanita Pharmacy Maha Vidyalaya, Affiliated to Osmania University.

How to cite this Article: Y. Manjula1, Sravani2, B. Chandra Shekhar Reddy*3. (2026). Regulatory Requirements and Generic Drug Dossier Compilation For Oral Disintegrating Tablets In The Usa. World Journal of Pharmaceutical Research, 15(22), 182–193.
This work is licensed under Creative Commons Attribution 4.0 International license.

ABSTRACT

Orally disintegrating tablets (ODTs) are solid oral dosage forms that disintegrate rapidly in the mouth and offer an alternative to conventional tablets that require water for administration. They are especially useful for patients who have difficulty swallowing, including children and older adults. Developing generic ODTs requires thorough evaluation of formulation, manufacturing, quality control, dissolution, stability, taste masking, and bioequivalence. In the United States, eligible generic ODTs are generally submitted through the Abbreviated New Drug Application (ANDA) pathway. The regulatory dossier contains administrative, quality, nonclinical, and clinical or bioequivalence information organized within the Common Technical Document (CTD) framework. This review discusses the regulatory pathway, dossier compilation, quality and chemistry, manufacturing and controls (CMC), ODT-specific formulation considerations, bioequivalence, BCS-based biowaivers, and recent developments in US regulatory requirements. Particular emphasis is placed on the assimilation of pharmaceutical development data into a complete generic ODT dossier for submission to the US Food and Drug Administration (FDA).

KEYWORDS: Orally disintegrating tablets; generic drugs; ANDA; US FDA; regulatory

dossier; CTD; CMC; bioequivalence; BCS biowaiver.

INTRODUCTION

Generic medicines improve access to pharmaceutical treatment by providing alternatives to innovator products at possibly lower cost. Generic drug development focuses on demonstrating pharmaceutical equivalence and bioequivalence to the appropriate reference product while complying with regulatory requirements for quality, manufacturing, and labeling. In the United States, the ANDA pathway is the principal regulatory pathway for eligible generic medicines. The information supporting an application must be organized into an appropriate regulatory dossier containing the necessary administrative, quality, and bioequivalence information.[2-5]

Orally disintegrating tablets have gained considerable interest as patient-centric oral dosage forms because they disintegrate rapidly in the oral cavity and can generally be administered without water. Their characteristics make them particularly useful for individuals who have difficulty swallowing conventional tablets. However, developing ODTs requires balancing rapid disintegration with adequate mechanical strength, while additionally addressing taste, dissolution, stability, and manufacturing considerations.[6,7]

For a generic ODT, pharmaceutical development and regulatory dossier preparation are closely interconnected. Formulation development generates the scientific information needed to establish product quality, while analytical, stability, and bioequivalence studies provide evidence supporting equivalence of the reference product.[1,3,5]

ORALLY DISINTEGRATING TABLETS

Definition and characteristics

ODTs are designed to disintegrate rapidly after placement in the oral cavity. Unlike conventional tablets, which are generally swallowed with water, ODTs are intended to provide convenient administration with little or no water. Rapid disintegration is therefore a fundamental characteristic of this dosage form.[6,11]

An ODT's performance depends on several formulation and physical properties, including porosity, tablet hardness, particle features, excipient selection, and compression conditions. The formulation must provide sufficient mechanical strength for manufacturing and handling without adversely affecting disintegration and dissolution.[6,8]

Limitations

Despite their advantages, ODTs have several formulation challenges. The API may have an unpleasant taste because it comes into direct contact with taste receptors. ODTs may also have lower mechanical strength and increased sensitivity to moisture compared with conventional tablets. Consequently, formulation development must consider taste masking, tablet strength, disintegration, dissolution, and packaging simultaneously.[6,9,10]

Generic Drug Development in the United States

US FDA regulatory pathway

In the United States, generic drugs that meet the applicable requirements are generally submitted through an ANDA. Unlike an NDA, the ANDA relies on the reference product's established safety and efficacy and focuses on demonstrating that the proposed generic meets the applicable requirements for equivalence, quality, and manufacturing.[2-5]

For generic ODTs, establish the regulatory strategy early in development. The applicant should identify the appropriate reference listed drug and evaluate the applicable FDA guidance. Recent research shows that FDA-approved ODT products can have product-specific regulatory considerations, making early regulatory assessment especially important.[1]

Reference Listed Drug

The reference listed drug provides the basis for comparison of the proposed generic product. Carefully evaluate its dosage form, strength, route of administration, labeling, and other relevant product characteristics before developing the generic ODT. The reference product is particularly important for establishing comparative dissolution and bioequivalence requirements.[1,4]

Product-Specific Guidance

FDA Product-Specific Guidance provides recommendations for the development of individual generic products. For ODTs, these recommendations may address formulation, dissolution, administration conditions, and bioequivalence study design. Therefore, review the relevant PSG during product development and before finalizing the ANDA strategy.[1]

GENERIC DRUG DOSSIER COMPILATION

A regulatory dossier is a structured collection of administrative, pharmaceutical, nonclinical,

and clinical information submitted to a regulatory authority. The CTD provides a standardized structure for organizing regulatory information into five major modules. For generic drug applications, dossier preparation requires compilation and integration of data generated throughout product development.[3,5]

The five CTD modules include

1. Module 1 – Administrative and regional information
2. Module 2 – CTD summaries
3. Module 3 – Quality
4. Module 4 – Nonclinical information
5. Module 5 – Clinical information

For a US generic ODT, the dossier should be prepared in accordance with applicable FDA requirements and should demonstrate that the proposed product meets relevant quality and equivalence requirements.[2,3]

MODULE 1: ADMINISTRATIVE AND REGIONAL INFORMATION

Module 1 contains region-specific administrative and regulatory information. In a US ANDA, this includes the applicable administrative forms, labeling information, and other FDA-specific documentation.

All administrative information should be consistent throughout the submission. Product name, strength, dosage form, manufacturer information, packaging, and labeling should correspond with the information presented in the quality and other sections of the application.[3,5]

MODULE 2: CTD SUMMARIES

Module 2 provides summaries of the detailed information presented in the other CTD modules. The Quality Overall Summary should clearly overview the drug substance, drug product, formulation, manufacturing process, analytical procedures, specifications, and stability program.

MODULE 3: QUALITY AND CMC

Module 3 is a major component of the generic ODT dossier because it contains detailed information on chemistry, manufacturing, and controls. It should establish that the proposed product can be consistently manufactured and controlled according to appropriate quality

standards.[3,5]

Drug substance

The drug-substance section includes information on identity, structure, physicochemical properties, the manufacturing process, impurities, specifications, analytical procedures, and stability.

API characteristics such as particle size, solubility, permeability, flowability, compressibility, and taste may influence ODT development. These characteristics should therefore be evaluated during formulation development.[6,8]

Excipients

Excipients play a key role in determining ODT performance. Common excipients include diluents, binders, lubricants, superdisintegrants, sweeteners, flavors, and taste-masking agents. Superdisintegrants are particularly important because they facilitate rapid breakup of the tablet after administration.[6,8]

Formulation development

Formulation development should evaluate how material and process variables affect the ODT's critical quality attributes. Important variables include superdisintegrant concentration, compression force, tablet hardness, drug loading, lubricant concentration, granule properties, and taste-masking strategy.[6-9]

CRITICAL QUALITY ATTRIBUTES OF GENERIC ODTS

Several important quality attributes determine ODT quality. These include disintegration, dissolution, assay, content uniformity, hardness, friability, moisture content, and stability.

Disintegration

Rapid disintegration defines an ODT. However, rapid disintegration should not compromise the tablet's physical integrity during manufacturing, packaging, and transportation.[1,6,8]

DISSOLUTION

Dissolution is an important quality attribute for generic oral dosage forms. For ODTs, dissolution should be evaluated together with disintegration because rapid tablet disintegration does not necessarily ensure appropriate drug dissolution or equivalent drug-release behavior.[1,13,18]

Stability

Stability studies should demonstrate that the product continues to meet established specifications throughout its proposed shelf life. Moisture may be especially important for ODTs because it may affect tablet hardness, disintegration and dissolution.[6,7]

MANUFACTURING TECHNOLOGIES

ODTs can be manufactured using several techniques, including direct compression, wet and dry granulation, freeze drying, molding, spray drying and sublimation. The choice of manufacturing technology depends on API characteristics, formulation composition, desired disintegration behavior, and manufacturing feasibility.[6,8,11]

Direct compression is attractive because it is relatively simple to manufacture, whereas technologies such as lyophilization can produce highly porous tablets that facilitate rapid disintegration. Compressed ODTs call for careful optimization of excipient properties and processing conditions to achieve an appropriate balance between disintegration and mechanical strength.[8,9]

TASTE-MASKING STRATEGIES

Taste masking is an important consideration in ODT development because the formulation is exposed to the oral cavity before swallowing. An unpleasant taste can negatively affect patient acceptability and adherence.[7,10]

Various approaches include sweeteners, flavors, polymer coatings, microencapsulation, complexation, and ion-exchange systems.[6,10]

ANALYTICAL AND QUALITY CONTROL REQUIREMENTS

The finished ODT should undergo appropriate quality control testing to demonstrate conformity with established specifications. Depending on the product, testing may include identification, assay, content uniformity, disintegration, dissolution, hardness, friability, moisture, and degradation products.[5,6]

Analytical procedures used for release and stability testing should be appropriately developed, validated, and documented.[3,5]

COMPARATIVE DISSOLUTION TESTING

Comparative dissolution testing is an important component of generic oral pharmaceutical

development. It can evaluate similarities in drug-release behavior between the proposed generic product and the reference product and can support certain regulatory strategies.[13-17]

For generic ODTs, dissolution should be evaluated under appropriate conditions and interpreted together with the product's disintegration characteristics. The relevant FDA Product-Specific Guidance should be considered when establishing the dissolution strategy.[1,19]

BIOAVAILABILITY AND BIOEQUIVALENCE

Importance of bioequivalence

Bioequivalence is an essential element of generic drug development. It provides evidence that the proposed generic product produces comparable systemic exposure to the reference product when evaluated using the appropriate study design and statistical criteria.[13,14]

For pharmacokinetic studies, parameters such as the area under the concentration-time curve (AUC) and maximum plasma concentration (Cmax) are commonly used to characterize the rate and extent of drug exposure.[14,21]

Bioequivalence considerations for ODTs

ODTs may present additional bioequivalence considerations because they can be administered without water and may disintegrate in the oral cavity before being swallowed. Consequently, administration conditions may affect product performance and should be considered when designing BE studies.[1]

Recent regulatory literature has emphasized harmonization of BE approaches for immediate-release solid oral dosage forms, including consideration of ODT administration conditions.[1,18,23]

BCS-BASED BIOWAIVERS

The Biopharmaceutics Classification System classifies drug substances by aqueous solubility and intestinal permeability. Under appropriate conditions, BCS-based biowaivers may allow certain immediate-release oral products to avoid an in vivo bioequivalence study.[15-17]

Regulatory requirements for BCS-based biowaivers have historically differed among the FDA, EMA, and WHO. International efforts have increased harmonization, particularly through ICH M9, which provides recommendations concerning eligibility, dissolution, and

excipient considerations for BCS-based biowaivers.[15,16,22]

GLOBAL HARMONIZATION OF BIOEQUIVALENCE REQUIREMENTS

Differences in bioequivalence requirements among regulatory authorities can complicate global generic-drug development. Comparative assessments have identified differences in study design, statistical evaluation, dissolution requirements, and biowaiver criteria between regulatory agencies.[13,15,16]

ICH aims to develop harmonized recommendations to reduce unnecessary differences in bioequivalence assessment. ICH M13A provides recommendations for bioequivalence assessment of immediate-release solid oral dosage forms and is particularly relevant to generic oral medication development.[18,23]

MODULE 4: NONCLINICAL INFORMATION

Module 4 contains applicable nonclinical study reports within the CTD framework. For conventional generic products submitted through the ANDA pathway, extensive new nonclinical studies are generally not required because the reference product has already established the relevant safety and efficacy profile.[3-5]

MODULE 5: CLINICAL AND BIOEQUIVALENCE INFORMATION

Module 5 contains clinical information and is particularly relevant to the bioequivalence documentation of generic products. For a generic ODT, this section may contain BE study protocols, clinical study reports, pharmacokinetic analyses and statistical evaluations, together with supporting information for applicable biowaivers.[3,13,14,21]

The bioequivalence strategy should preferably be established during early product development because it can influence formulation selection, dissolution testing and manufacturing decisions.[1,13]

STABILITY AND PACKAGING CONSIDERATIONS

ODTs may be particularly sensitive to environmental moisture because moisture changes can affect tablet mechanical strength, disintegration, and dissolution. Therefore, appropriate packaging and storage conditions are important components of product development.[6,7]

QUALITY BY DESIGN CONSIDERATIONS

Quality by Design provides a systematic approach to understanding how formulation

variables, process parameters, and product quality relate. In ODT development, important critical quality attributes may include disintegration, dissolution, hardness, friability, assay, content uniformity, and stability.[6,8,9]

A systematic development approach may help identify critical material attributes and process parameters and provide a scientific basis for formulation and process enhancement. The resulting knowledge can strengthen the CMC information presented in the regulatory dossier.[3,6]

CHALLENGES IN GENERIC ODT DOSSIER COMPILATION

Developing and submitting generic ODTs involves multiple challenges. These include achieving rapid disintegration while maintaining sufficient mechanical strength, masking unpleasant taste, maintaining dissolution performance, and demonstrating bioequivalence to the reference product.[1,6,8-10]

Regulatory differences in bioequivalence study design, administration conditions, and biowaiver criteria can complicate development, particularly for products intended for multiple international markets.[13,15-18]

Another important consideration is consistency within the dossier. Information regarding formulation composition, manufacturing processes, specifications, analytical procedures, manufacturing sites, and product characteristics should be consistent across the relevant CTD sections.[3-5]

RECENT REGULATORY DEVELOPMENTS

Recent regulatory developments have increased emphasis on science-based generic-drug development, product-specific guidance, and harmonized bioequivalence approaches. The FDA's ODT guidance remains an important reference for development of orally disintegrating products, while more recent international recommendations such as ICH M13A provide a harmonized framework for bioequivalence of immediate-release solid oral dosage forms.[1,18,19,23]

ICH M9 also introduced a harmonized framework for BCS-based biowaivers, replacing reliance on earlier standalone regional approaches.[22]

Recent analyses of FDA-approved ODTs further show that regulatory considerations vary by

product, underscoring the importance of reviewing applicable FDA guidance and Product-Specific Guidance during development.[1]

FUTURE PERSPECTIVES

Future generic ODT development is expected to focus on patient-centric formulations, advanced taste-masking technologies, improved manufacturing processes, and more efficient regulatory strategies. Advances in formulation technology may enable ODT development for poorly soluble and challenging APIs whilst maintaining acceptable mechanical properties and rapid disintegration.[6,7]

Emerging model-informed approaches may also provide opportunities to reduce the burden of conventional BE studies in selected circumstances, although their applicability will depend on regulatory acceptance and scientific justification.[18,23]

CONCLUSION

Generic orally disintegrating tablets are an important patient-centric dosage form that requires integrating pharmaceutical development and regulatory science. In the United States, eligible generic ODTs are generally submitted through the ANDA pathway, with the regulatory dossier providing evidence concerning product quality, manufacturing, and bioequivalence. The CMC section is particularly important because ODT performance depends on formulation composition, excipient selection, manufacturing process, mechanical strength, disintegration, dissolution, taste masking, and stability. Bioequivalence is an additional critical component, and ODT administration conditions require particular consideration.

A successful generic ODT dossier therefore requires a scientifically justified connection between reference-product selection, formulation development, manufacturing controls, analytical testing, dissolution, stability, and bioequivalence. Continued regulatory harmonization and advances in ODT technology are expected to facilitate the development of high-quality generic ODTs for the US market.

REFERENCES

1. Bagde S, Xi X, Boyce H, Kim MJ. Evaluation of orally disintegrating tablets: regulatory pathways, administration practices and harmonization of bioequivalence study design. AAPS Open, 2026; 12: 2. doi:10.1186/s41120-025-00138-y.

2. Vallabhaneni MKP, Meka VS. FDA recent expectations on generic product development: a comprehensive review. Ther Innov Regul Sci., 2026. doi:10.1177/17411343261449684.
3. Naseeb M, Goyal A. Formation of a new regulatory dossier for marketing authorization of a generic drug: a review. Int J Med Pharm Sci., 2026; 2(5): 107-112.
4. Patel BD, Suthar SP, Mansuri AM, Joshi VD. A comparative analysis of generic drug assessment and regulatory approval in the USA, Europe and India. Zhongguo Ying Yong Sheng Li Xue Za Zhi., 2024; 40: e20240029. doi:10.62958/j.cjap.2024.029.
5. Thambavita D, Galappatthy P, Jayakody RL. Regulatory requirements for the registration of generic medicines and format of drug dossiers: procedures in Sri Lanka in comparison with selected regulatory authorities. J Pharm Policy Pract., 2018; 11: 14. doi:10.1186/s40545-018-0141-2.
6. Ghourichay MP, Kiaie SH, Nokhodchi A, Javadzadeh Y. Formulation and quality control of orally disintegrating tablets (ODTs): recent advances and perspectives. Biomed Res Int., 2021; 2021: 6618934. doi:10.1155/2021/6618934.
7. Chinwala M. Recent formulation advances and therapeutic usefulness of orally disintegrating tablets (ODTs). Pharmacy (Basel), 2020; 8(4): 186. doi:10.3390/pharmacy8040186.
8. Al-Khattawi A, Mohammed AR. Compressed orally disintegrating tablets: excipients evolution and formulation strategies. Expert Opin Drug Deliv, 2013; 10(5): 651-663. doi:10.1517/17425247.2013.769955.
9. Al-Khattawi A, Mohammed AR. Challenges and emerging solutions in the development of compressed orally disintegrating tablets. Expert Opin Drug Discov, 2014; 9(10): 1109-1120. doi:10.1517/17460441.2014.941802.
10. Douroumis D. Orally disintegrating dosage forms and taste-masking technologies. Expert Opin Drug Deliv, 2011; 8(5): 665-675. doi:10.1517/17425247.2011.566553.
11. Parkash V, Maan S, Deepika, Yadav SK, Hemlata, Jogpal V. Fast disintegrating tablets: opportunity in drug delivery system. J Adv Pharm Technol Res., 2011; 2(4): 223-235. doi:10.4103/2231-4040.90877.
12. Chimombe T, Mukhopadhyay S, Veroniaina H, Han L, Xu X, Juan T, et al. Orally disintegrating tablets: formulation, preparation, evaluation and recent advances: a review. World J Pharm Pharm Sci., 2020; 9(1): 304-328.
13. Davit BM, Braddy AC, Conner DP, Yu LX. International guidelines for bioequivalence of systemically available orally administered generic drug products: a survey of

similarities and differences. AAPS J., 2013; 15(4): 974-990. doi:10.1208/s12248-013-9499-x.

14. Chow SC. Bioavailability and bioequivalence in drug development. Wiley Interdiscip Rev Comput Stat., 2014; 6(4): 304-312. doi:10.1002/wics.1310.
15. Davit BM, Kanfer I, Tsang YC, Cardot JM. BCS biowaivers: similarities and differences among EMA, FDA, and WHO requirements. AAPS J., 2016; 18(3): 612-618. doi:10.1208/s12248-016-9877-2.
16. Van Oudtshoorn JE, García-Arieta A, Santos GML, Crane C, Rodrigues C, Simon C, et al. A survey of the regulatory requirements for BCS-based biowaivers for solid oral dosage forms by participating regulators and organizations of the International Generic Drug Regulators Program. J Pharm Pharm Sci., 2018; 21(1): 27-37. doi:10.18433/J3X93K.
17. Saluja V, Singh A, Algradi AM. The gradually expanding scope for biowaivers of oral products: an overview. Curr Pharm Des., 2016; 22(42): 6434-6443. doi:10.2174/1381612822666160707234936.
18. Kotsybar J, Hakeem S, Zhang L, Jiang W. Global harmonization of immediate-release solid oral drug product bioequivalence recommendations and the impact on generic drug development. Clin Transl Sci., 2023; 16(12): 2756-2764. doi:10.1111/cts.13670.
19. US Food and Drug Administration. Orally disintegrating tablets: guidance for industry. Silver Spring (MD): US Food and Drug Administration, 2008.
20. US Food and Drug Administration. Size, shape, and other physical attributes of generic tablets and capsules: guidance for industry. Silver Spring (MD): US Food and Drug Administration, 2022.
21. US Food and Drug Administration. Bioequivalence studies with pharmacokinetic endpoints for drugs submitted under an abbreviated new drug application: guidance for industry. Silver Spring (MD): US Food and Drug Administration, 2026.
22. US Food and Drug Administration. M9 Biopharmaceutics classification system-based biowaivers: guidance for industry. Silver Spring (MD): US Food and Drug Administration, 2021.
23. US Food and Drug Administration. M13A bioequivalence for immediate-release solid oral dosage forms: guidance for industry. Silver Spring (MD): US Food and Drug Administration, 2024.