FDA Dissolution Methods and Navigating the Dissolution Database

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Facilitating Generic Product Availability Through Product-Specific Guidances (PSGs)– April 25, 2024

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Outline

- Dissolution Testing for Quality Control
- FDA Dissolution Database
- Summary

Dissolution

- A (kinetic) process of a solid dissolving into a solution
- Is a prerequisite to drug absorption and in vivo performance for almost all solid oral drug products
- Testing is used for quality control (QC) to ensure drug product quality over the shelf life and batch-to-batch consistency

Dissolution Method Development for QC

- Dissolution method is product-specific
- The method should be sensitive to possible changes in drug product quality
- Dissolution medium should be physiologically relevant

Dissolution Method Development for QC

- At least 12 dosage units should be tested
- Samples collected until drug release is complete (at least 85% released or a plateau is reached)
- The %CV should be <20% at early time points and <10% at other time points
- The method should be validated and reproducible

Dissolution Testing for IR Drug Products with High Solubility Drug Substances

A. Basket Method (USP apparatus 1)

- Stirring rate = 100 RPM
- 500 mL of 0.1N HCl in aqueous medium
- No surfactant in medium
- 37±0.5°C

B. Paddle Method (USP apparatus 2)

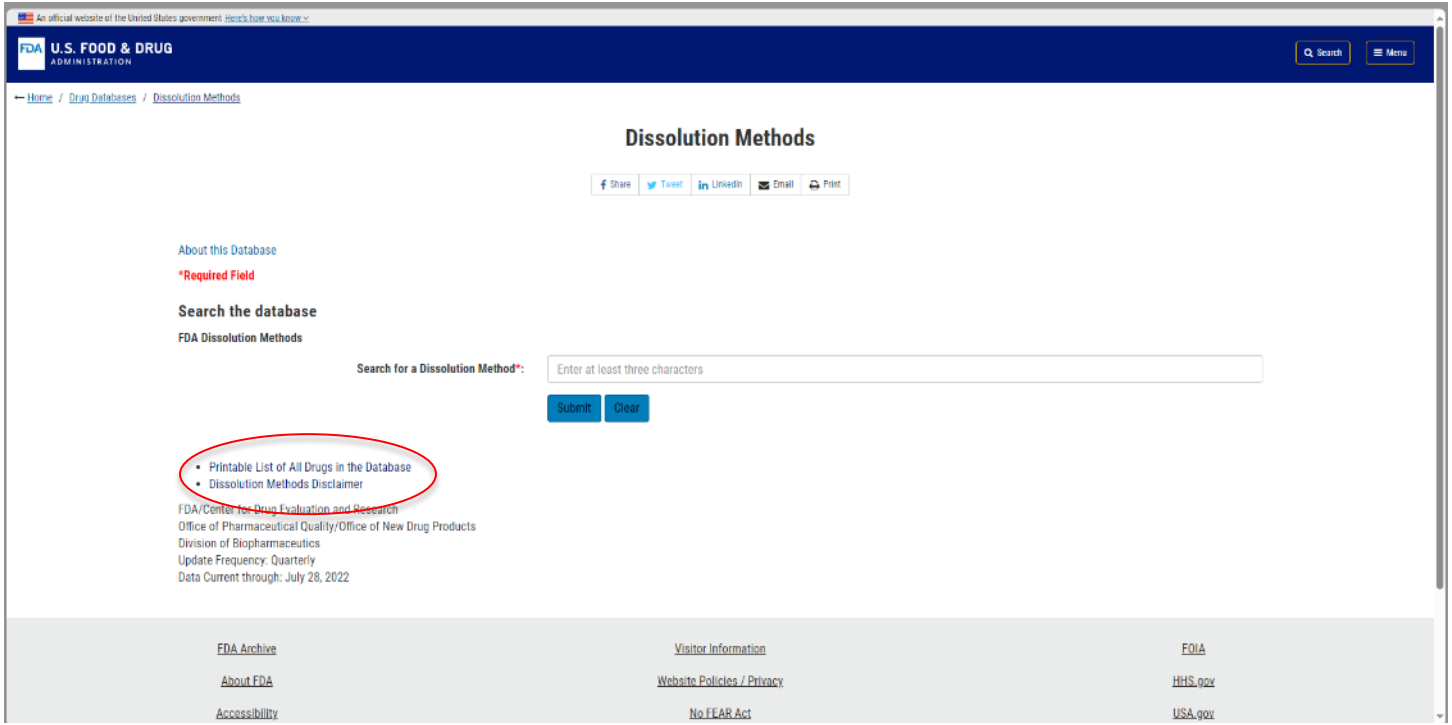
- Stirring rate = 50 RPM
- 500 mL of 0.1N HCl in aqueous medium
- No surfactant in medium
- 37±0.5°C

Acceptance Criterion is Q=80% in 30 minutes

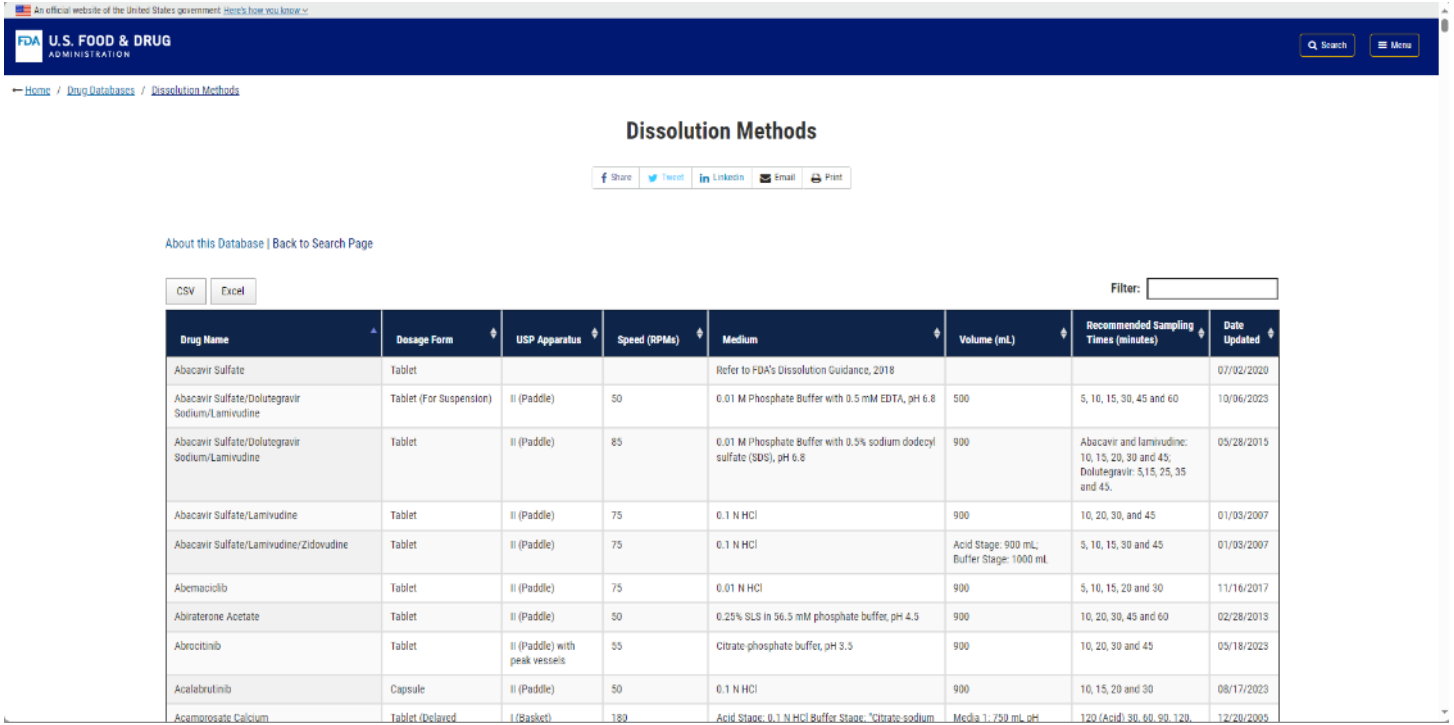
FDA Dissolution Database

- To date, 1,518 dissolution methods are published
- These methods should be used as a starting point for method development
- Final method should be optimized and justified

FDA Dissolution Database

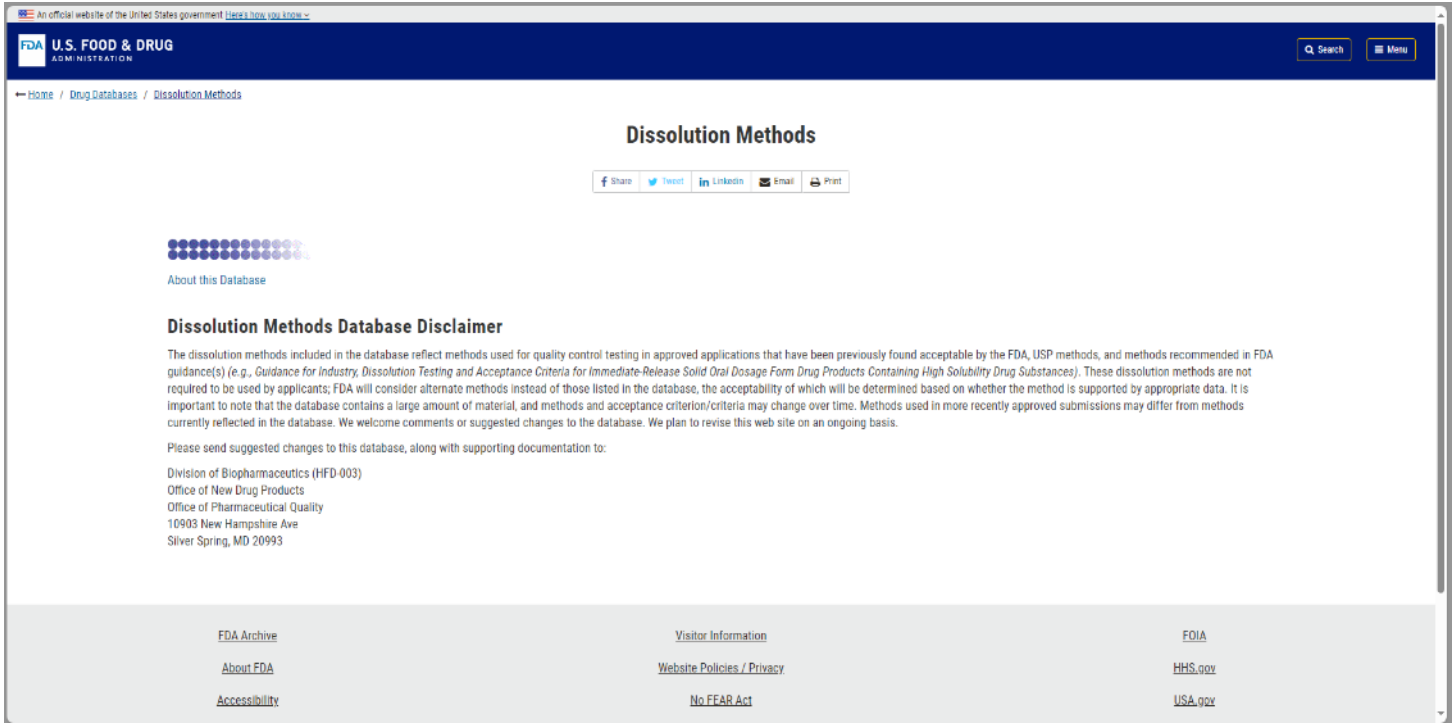


FDA Dissolution Database

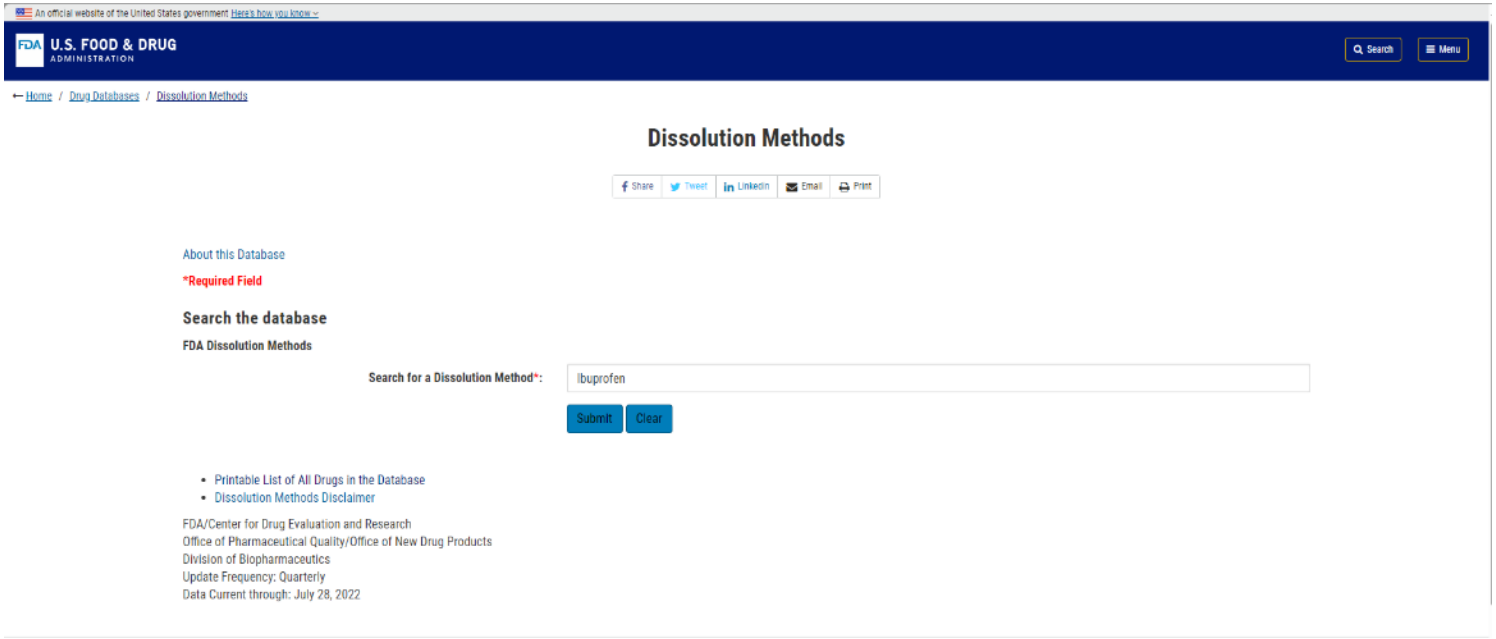


Drug Name	Dosage Form	USP Apparatus	Speed (RPMs)	Medium	Volume (mL)	Recommended Sampling Times (minutes)	Date Updated
Abacavir Sulfate	Tablet			Refer to FDA's Dissolution Guidance, 2018			07/02/2020
Abacavir Sulfate/Dolutegravir Sodium/Lamivudine	Tablet (For Suspension)	II (Paddle)	50	0.01 M Phosphate Buffer with 0.5 mM EDTA, pH 6.8	500	5, 10, 15, 30, 45 and 60	10/06/2023
Abacavir Sulfate/Dolutegravir Sodium/Lamivudine	Tablet	II (Paddle)	85	0.01 M Phosphate Buffer with 0.5% sodium dodecyl sulfate (SDS), pH 6.8	900	Abacavir and lamivudine: 10, 15, 20, 30 and 45; Dolutegravir: 5,15, 25, 35 and 45.	05/28/2015
Abacavir Sulfate/Lamivudine	Tablet	II (Paddle)	75	0.1 N HCl	900	10, 20, 30, and 45	01/03/2007
Abacavir Sulfate/Lamivudine/Zidovudine	Tablet	II (Paddle)	75	0.1 N HCl	Acid Stage: 900 mL; Buffer Stage: 1000 mL	5, 10, 15, 30 and 45	01/03/2007
Abemaciclib	Tablet	II (Paddle)	75	0.01 N HCl	900	5, 10, 15, 20 and 30	11/16/2017
Abiraterone Acetate	Tablet	II (Paddle)	50	0.25% SLS in 56.5 mM phosphate buffer, pH 4.5	900	10, 20, 30, 45 and 60	02/28/2013
Abrocitinib	Tablet	II (Paddle) with peak vessels	55	Citrate-phosphate buffer, pH 3.5	900	10, 20, 30 and 45	05/18/2023
Acalabrutinib	Capsule	II (Paddle)	50	0.1 N HCl	900	10, 15, 20 and 30	08/17/2023
Acamprosate Calcium	Tablet (Delayed	I (Basket)	100	Acid Stage: 0.1 N HCl Buffer Stage: *Citrate-sodium	Media 1: 750 mL pH	120 (Acid) 30, 60, 90, 120,	12/20/2005

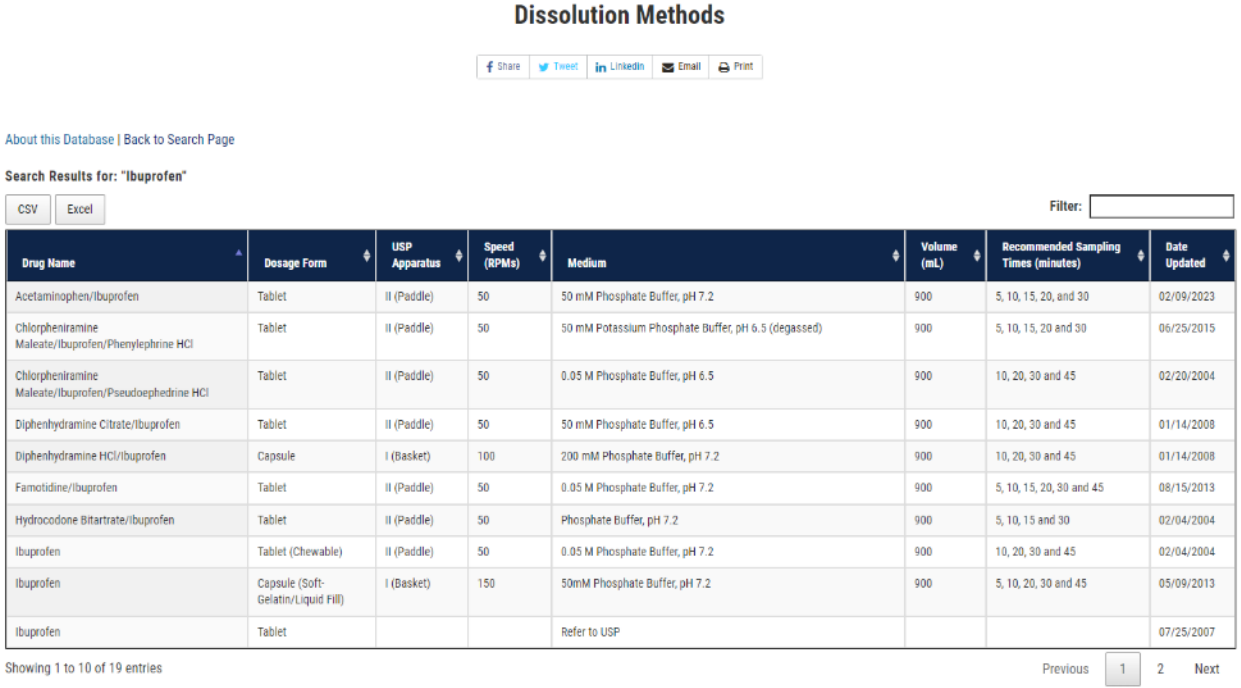
FDA Dissolution Database



FDA Dissolution Database



FDA Dissolution Database



Dissolution Methods

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Search Results for: "Ibuprofen"

CSV | Excel

Filter:

Drug Name	Dosage Form	USP Apparatus	Speed (RPMs)	Medium	Volume (mL)	Recommended Sampling Times (minutes)	Date Updated
Acetaminophen/Ibuprofen	Tablet	II (Paddle)	50	50 mM Phosphate Buffer, pH 7.2	900	5, 10, 15, 20, and 30	02/09/2023
Chlorpheniramine Maleate/Ibuprofen/Phenylephrine HCl	Tablet	II (Paddle)	50	50 mM Potassium Phosphate Buffer, pH 6.5 (degassed)	900	5, 10, 15, 20 and 30	06/25/2015
Chlorpheniramine Maleate/Ibuprofen/Pseudoephedrine HCl	Tablet	II (Paddle)	50	0.05 M Phosphate Buffer, pH 6.5	900	10, 20, 30 and 45	02/20/2004
Diphenhydramine Citrate/Ibuprofen	Tablet	II (Paddle)	50	50 mM Phosphate Buffer, pH 6.5	900	10, 20, 30 and 45	01/14/2008
Diphenhydramine HCl/Ibuprofen	Capsule	I (Basket)	100	200 mM Phosphate Buffer, pH 7.2	900	10, 20, 30 and 45	01/14/2008
Famotidine/Ibuprofen	Tablet	II (Paddle)	50	0.05 M Phosphate Buffer, pH 7.2	900	5, 10, 15, 20, 30 and 45	08/15/2013
Hydrocodone Bitartrate/Ibuprofen	Tablet	II (Paddle)	50	Phosphate Buffer, pH 7.2	900	5, 10, 15 and 30	02/04/2004
Ibuprofen	Tablet (Chewable)	II (Paddle)	50	0.05 M Phosphate Buffer, pH 7.2	900	10, 20, 30 and 45	02/04/2004
Ibuprofen	Capsule (Soft-Gelatin/Liquid Fill)	I (Basket)	150	50mM Phosphate Buffer, pH 7.2	900	5, 10, 20, 30 and 45	05/09/2013
Ibuprofen	Tablet			Refer to USP			07/25/2007

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Database Updates

- PSG Batch Postings
- Requests from Applicants via External Correspondence Operation (ECO) System
- Prior Approval Supplements (PAS) for NDA

Water as a Dissolution Medium

- Methods using water as a medium were revised September 2023
- Water is not physiologically relevant
- Water lacks buffering capacity
- Applicants should develop a dissolution method for their proposed product

Summary

- Published dissolution methods should be used as a starting point for method development
- Dissolution method is product-specific
- Water is not a recommended dissolution medium
- Adequacy of the method and acceptance criterion/criteria will be determined during the assessment of the ANDA

Resources

- Dissolution Methods (fda.gov)
- Dissolution Testing and Acceptance Criteria for Immediate-Release Solid Oral Dosage Form Drug Products Containing High Solubility Drug Substances Guidance for Industry | FDA
- Tablet Scoring:Nomenclature, Labeling, and Data for Evaluation | FDA

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- Dissolution Database Working Group Members


QUESTIONS