



**Recent FDA  
Guidance For Industry;  
BCS Class 1 and 3  
August 2015**

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# FDA Guidance for Industry: Dissolution Testing and Specification Setting for IR BCS 1 & 3 Drugs

**August, 2015:**

FDA issues Draft Guidance on “Dissolution Testing and Specification Criteria for Immediate-Release Solid Oral Dosage Forms Containing Biopharmaceutics Classification System Class 1 and 3 Drugs”

- Comments and suggestions regarding this draft document should be submitted to FDA within 60 days of publication
- Check for updates while in Draft form until official...

<http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>

FDA Guidance for Industry; Dissolution Testing and Specification Criteria for Immediate-Release Solid Oral Dosage Forms Containing Biopharmaceutics Classification System Class 1 and 3 Drugs; August, 2015

# FDA Guidance for Industry: Dissolution Testing and Specification Setting for IR BCS 1 & 3 Drugs

## Key Points:

The guidance is intended to describe when a standard release test and criteria may be used in lieu of extensive method development and specification-setting exercises.

When final, this guidance will supersede the guidance for industry on *Dissolution Testing of Immediate Release Solid Oral Dosage Forms (August 1997)* for biopharmaceutics classification system (BCS) class 1 and 3 drug substances in immediate-release drug products that meet the criteria in this guidance

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## The Biopharmaceutical Classification System (BCS):

This classification can be used as a basis for determining when in vivo BA and BE studies are needed and can be used to determine when a successful in vitro-in vivo correlation (IVIVC) is likely.

Class 1: High Solubility – High Permeability

Class 2: Low Solubility – High Permeability

Class 3: High Solubility – Low Permeability

Class 4: Low Solubility – Low Permeability

Owing to their high solubility, BCS class 1 and 3 drugs are considered to be relatively low risk regarding the impact of dissolution on performance

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## Solubility:

To be considered BCS class 1 or 3, the drug substance should be considered highly soluble with the highest dose strength soluble in 250 mL or less of aqueous media over the pH range of 1 to 6.8.

This guidance does not apply to narrow therapeutic index (NTI) drugs because of the critical relationship between the bioavailable dose (and therefore dissolution) on clinical performance.

If the time to maximum plasma concentration is critical to the intended use, this guidance does not apply.

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For BCS Class 1 and 3 products:

- These recommendations will supersede those in the Dissolution Methods Database, and upon finalization of this guidance FDA will update the Dissolution Methods Database or remove entries from the Database that are covered by this guidance.
- For products where the method described in a United States Pharmacopeia (USP) drug product monograph differs from the recommendations of this guidance, ANDA applicants may propose to use the approaches in this guidance as an alternative method and seek revision of the relevant monograph.

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## Standard Dissolution Test Conditions:

Manufacturing and testing history, including stability testing, should demonstrate that the product will meet the specifications in this guidance when using the standard dissolution test conditions.

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## Standard Dissolution Test Conditions:

### **Basket Method (USP apparatus 1)**

- Stirring rate = 100 RPM
- 500 mL of 0.01M HCl aqueous media
- No surfactant in media
- $37 \pm 0.5^\circ\text{C}$

*Note: 100 RPM has been found to be discriminatory for the basket method*

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## Standard Dissolution Test Conditions:

### **Paddle Method (USP apparatus 2)**

- Stirring rate = 75 RPM
- 500 mL of 0.01M HCl aqueous media
- No surfactant in media
- $37 \pm 0.5^\circ\text{C}$

*Note: 75 RPM can be discriminatory while minimizing coning effects seen with lower rates.*

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## Rationale:

The acid conditions of the media reflect the conditions of the stomach whose volume is estimated at 250 mL when a glass of water is co-ingested with the oral dosage form.

This volume is too low to use with the current basket and paddle apparatus; however, 500 mL of media is commonly used and should be a sufficient volume of media for a highly soluble, rapidly dissolving drug.

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## Specification Setting:

- For BCS class 1 products, a single point dissolution specification of  $Q=80\%$  in 30 minutes.
- For BCS class 3 products, a single point dissolution specification of  $Q=80\%$  in 15 minutes.

BCS class 3 products that meet the more stringent specifications will better ensure that the bioavailability of the drug is not limited by dissolution, and the rate-limiting step for drug absorption becomes gastric emptying.

FDA Guidance for Industry; [Dissolution Testing and Specification Criteria for Immediate-Release Solid Oral Dosage Forms Containing Biopharmaceutics Classification System Class 1 and 3 Drugs](#); August, 2015

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## Substitution of Disintegration for Dissolution:

For drug products in both BCS classes 1 and 3, USP disintegration testing can be used in lieu of the dissolution test if the product is shown to meet a dissolution specification of Q=80% in 15 minutes.

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## Substitution of Disintegration for Dissolution (Rationale):

- For drug products that meet this criterion, the USP disintegration test, which requires the product to completely disintegrate within 5 minutes (via USP apparatus in 0.01M HCl), may serve as a surrogate for routine release and stability dissolution testing.
- However, the approved dissolution method should be retained as the primary method and the approved disintegration method as an alternate method.
- Note that to support post-approval changes for which dissolution testing would be typically be needed, you should use the approved dissolution method.

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Drug products which do not meet the eligibility requirements of this draft guidance will continue to require conformance with the existing FDA Guidance for Industry from 1997: Dissolution Testing of Immediate Release Solid Oral Dosage Forms

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# QUESTIONS?