Guidance for Industry

Q4B Evaluation and Recommendation of Pharmacopoeial Texts for Use in the ICH Regions

Annex 7(R2)
Dissolution Test General Chapter

U. S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

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Revision 2

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Contains Nonbinding Recommendations

Guidance for Industry[1]
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Annex 7(R2)
Dissolution Test General Chapter

This guidance represents the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

1. INTRODUCTION (1)[2]

This annex is one in a series of guidance documents that describe the evaluations and recommendations by the Q4B Expert Working Group (EWG) of selected pharmacopoeial texts to facilitate their recognition by regulatory authorities for use as interchangeable in the ICH regions. Implementation of the Q4B annexes is intended to avoid redundant testing by industry. For general information on the Q4B process, the reader is referred to the core guidance *Q4B Evaluation and Recommendation of Pharmacopoeial Texts for Use in the ICH Regions*.[3]

This guidance is a revision of the ICH guidance entitled *Q4B Evaluation and Recommendation of Pharmacopoeial Texts for Use in the ICH Regions; Annex 7: Dissolution Test General Chapter* (April 2010). In September 2010, the April 2010 guidance was revised to add guidance on Health Canada consideration. This second revision, Q4B Annex 7(R2), specifies additional dissolution apparatuses to which interchangeability applies in the ICH regions: the Basket

[1] This guidance was developed within the Expert Working Group (Quality) of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) and has been subject to consultation by the regulatory parties, in accordance with the ICH process. This document has been endorsed by the ICH Steering Committee at *Step 4* of the ICH process, November 2010. At *Step 4* of the process, the final draft is recommended for adoption to the regulatory bodies of the European Union, Japan, and the United States.

[2] Arabic numbers reflect the organizational breakdown of the document endorsed by the ICH Steering Committee at Step 4 of the ICH process, November 2010.

[3] We update guidance documents periodically. To make sure you have the most recent version of a guidance, check the FDA Drugs guidance page at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm or the FDA Biologics guidance page at http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/default.htm.

Apparatus (Apparatus 1), the Paddle Apparatus (Apparatus 2), and the Flow-Through Cell. Q4B Annex 7(R2) also updates the considerations for implementation for the FDA; the European Union (EU); and the Ministry of Health, Labour and Welfare (MHLW) of Japan. In addition, it updates the references used for the Q4B evaluation.

This annex is the result of the Q4B process for the Dissolution Test General Chapter. The proposed texts were submitted by the Pharmacopoeial Discussion Group (PDG).

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. Q4B OUTCOME (2)

A. Analytical Procedures (2.1)

The ICH Steering Committee, based on the evaluation by the Q4B Expert Working Group (EWG), recommends that the official pharmacopoeial texts, Ph. Eur. 2.9.3. Dissolution Test for Solid Dosage Forms, JP 6.10 Dissolution Test, and USP <711> Dissolution, can be used as interchangeable in the ICH regions subject to the following conditions:

1. (2.1.1) The declaration of interchangeability applies to the Basket Apparatus (Apparatus 1), the Paddle Apparatus (Apparatus 2), and the Flow-Through Cell. The Flow-Through Cell should be referred to in the dossier by an unambiguous descriptive title or compendial reference because it is referred to by different numbers in the three pharmacopoeias.

2. (2.1.2) The Dissolution Test is not considered to be interchangeable in the ICH regions when enzymes are used in the media.

3. (2.1.3) The dissolution apparatus should be appropriately calibrated to ensure compliance with regional good manufacturing practice (GMP) requirements. For example, an appropriately designed and executed mechanical calibration strategy should be in compliance with good manufacturing practice requirements.

4. (2.1.4) The Dissolution Test is not considered to be interchangeable in the three ICH regions for dosage forms referred to in the regional compendia as *delayed-release*, *gastro-resistant*, or *enteric-coated*.

5. (2.1.5) Validation studies should be conducted to demonstrate that the test results are not adversely affected if the thermometer is to remain in the dissolution vessel per regional good manufacturing practice.

6. (2.1.6) The Dissolution Test is not considered to be interchangeable in the ICH regions for JP Interpretation 2.

7. (2.1.7) The Dissolution Test is not considered to be interchangeable in the ICH regions for use of *large* vessels (greater than 1 liter).

8. (2.1.8) Product-specific parameters such as media, stirring rate, sampling time, and the use and type of sinkers should be specified and justified in the application dossier.

B. Acceptance Criteria (2.2)

Acceptance criteria should be specified in the application dossier.

III. TIMING OF ANNEX IMPLEMENTATION (3)

When this annex is implemented (incorporated into the regulatory process at ICH Step 5) in a region, it can be used in that region. Timing might differ for each region.

IV. CONSIDERATIONS FOR IMPLEMENTATION (4)

A. General Consideration (4.1)

When sponsors or manufacturers change their existing methods to the implemented Q4B-evaluated pharmacopoeial texts that are referenced in section II.A (2.1) of this annex, any change notification, variation, and/or prior approval procedures should be handled in accordance with established regional regulatory mechanisms pertaining to compendial changes.

B. FDA Consideration (4.2)

Based on the recommendation above, and with reference to the conditions set forth in this annex, the pharmacopoeial texts referenced in section II.A (2.1) of this annex can be considered interchangeable. However, FDA might request that a company demonstrate that the chosen method is acceptable and suitable for a specific material or product, irrespective of the origin of the method.

An appropriately rigorous mechanical calibration method,[4] when properly executed, should satisfy the current good manufacturing practice (CGMP) requirement for dissolution apparatus calibration under 21 CFR 211.160(b)(4).

C. EU Consideration (4.3)

For the European Union, regulatory authorities can accept the reference in a marketing authorization application, renewal or variation application citing the use of the corresponding

[4] See the guidance for industry, *The Use of Mechanical Calibration of Dissolution Apparatus 1 and 2 – Current Good Manufacturing Practice (CGMP)*, available on the Internet at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm.

text from another pharmacopoeia as referenced in section II.A (2.1), in accordance with the conditions set out in this annex, as fulfilling the requirements for compliance with the Ph. Eur. Chapter 2.9.3. on the basis of the declaration of interchangeability made above.

EU considers that it could accept the approach to the dissolution test for delayed-release products, as published in the USP, as meeting the criteria of the Ph. Eur. The validation studies referred to in section II.A.5 (2.1.5) of this annex would normally be submitted in the marketing authorization dossier.

D. MHLW Consideration (4.4)

The pharmacopoeial texts referenced in section II.A (2.1) of this annex can be used as interchangeable in accordance with the conditions set out in this annex. Details of implementation requirements will be provided in the notification by MHLW when this annex is implemented.

MHLW considers that it could accept the approach to the dissolution test for reciprocating cylinder apparatus as published in Ph. Eur. and USP, if the validation studies have been submitted in the marketing authorization dossier.

E. Health Canada Consideration (4.5)

In Canada any of the pharmacopoeial texts cited in section II.A (2.1) of this annex and used in accordance with the conditions set out in this annex can be considered interchangeable.

The dissolution tests for delayed-release/enteric coated products as published in the USP and in the Ph. Eur. can be considered interchangeable in Canada.

V. REFERENCES USED FOR THE Q4B EVALUATION (5)

A. (5.1) The PDG Stage 5B sign-off document (Rev. 2): *Japanese Pharmacopoeial Forum*, Volume 18, number 1 (April 2009).

B. (5.2) The pharmacopoeial references for Dissolution Test for this annex are:

1. (5.2.1) European Pharmacopoeia (Ph. Eur.): Supplement 6.6 (official January 2010), Dissolution Test for Solid Dosage Forms (reference 01/2010: 20903).

2. (5.2.2) Japanese Pharmacopoeia (JP): 6.10 Dissolution Test as it appears in Supplement I to the JP Fifteenth edition (September 28, 2007, The Ministerial Notification No. 316) and in the partial revision of the JP 15th edition made official March 31, 2009, by the Ministry of Health, Labour and Welfare Ministerial Notification No. 190, and in the partial revision of the JP 15th edition made official July 30, 2010, by the Ministry of Health, Labour and Welfare Ministerial Notification No. 322.

3. (5.2.3) United States Pharmacopeia (USP): <711> Dissolution as presented in *Pharmacopeial Forum*, Volume 35(3), May/June 2009, published in USP 33-Reissue, official October 1, 2010.