INTERNATIONAL CONFERENCE ON HARMONISATION OF TECHNICAL REQUIREMENTS FOR REGISTRATION OF PHARMACEUTICALS FOR HUMAN USE

ICH HARMONISED TRIPARTITE GUIDELINE

EVALUATION AND RECOMMENDATION OF PHARMACOPOEIAL TEXTS FOR USE IN THE ICH REGIONS ON DISSOLUTION TEST GENERAL CHAPTER

Q4B ANNEX 7(R2)

Current *Step 4* version
dated 11 November 2010

This Guideline has been developed by the appropriate ICH Expert Working Group and has been subject to consultation by the regulatory parties, in accordance with the ICH Process. At Step 4 of the Process the final draft is recommended for adoption to the regulatory bodies of the European Union, Japan and USA.

Q4B Annex 7(R2)
Document History

Code	History	Date
Q4B Annex 7	Approval by the Steering Committee under *Step 2* and release for public consultation.	13 November 2008
Q4B Annex 7	Approval by the Steering Committee under *Step* 4 and recommendation for adoption to the three ICH regulatory bodies.	29 October 2009
Q4B Annex 7(R1)	Integration of the Health Canada Interchangeability Statement under Section 4.5 after approval by the Steering Committee.	27 September 2010

Current *Step 4* version

Q4B Annex 7(R2)	Approval by the Steering Committee of the second revision directly under *Step 4* without further public consultation.	11 November 2010

EVALUATION AND RECOMMENDATION OF PHARMACOPOEIAL TEXTS FOR USE IN THE ICH REGIONS

ON

DISSOLUTION TEST GENERAL CHAPTER

Q4B Annex 7(R2)

ICH Harmonised Tripartite Annex

Having reached *Step 4* of the ICH Process at the ICH Steering Committee meeting on 11 November 2010, this annex is recommended for adoption to the three regulatory parties to ICH

(This annex includes the Interchangeability Statement from Health Canada added on September 27, 2010)

TABLE OF CONTENTS

EVALUATION AND RECOMMENDATION OF PHARMACOPOEIAL TEXTS FOR USE IN THE ICH REGIONS

ON

DISSOLUTION TEST GENERAL CHAPTER
Q4B ANNEX 7(R2)

1. INTRODUCTION

This annex is the result of the Q4B process for Dissolution Test.

The proposed texts were submitted by the Pharmacopoeial Discussion Group (PDG).

2. Q4B OUTCOME

2.1. Analytical Procedures

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:

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.

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

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.

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*.

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 (GMP).

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

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).

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.

2.2. Acceptance Criteria

Acceptance criteria should be specified in the application dossier.

3. TIMING OF ANNEX IMPLEMENTATION

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.

4. CONSIDERATIONS FOR IMPLEMENTATION

4.1. General Consideration

When sponsors or manufacturers change their existing methods to the implemented Q4B-evaluated pharmacopoeial texts that are referenced in Section 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.

4.2. FDA Consideration

Based on the recommendation above, and with reference to the conditions set forth in this annex, the pharmacopoeial texts referenced in Section 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, [1] when properly executed, should satisfy the current good manufacturing practice (CGMP) requirement for dissolution apparatus calibration under § 211.160(b)(4) of Title 21 of the Code of Federal Regulations.

4.3. EU Consideration

For the European Union, regulatory authorities can accept the reference in a marketing authorisation application, renewal or variation application citing the use of the corresponding text from another pharmacopoeia as referenced in Section 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 2.1.5 of this annex would normally be submitted in the marketing authorisation dossier.

[1] 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.

4.4. MHLW Consideration

The pharmacopoeial texts referenced in Section 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.

4.5. Health Canada Consideration

In Canada any of the pharmacopoeial texts cited in Section 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.

5. REFERENCES USED FOR THE Q4B EVALUATION

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

5.2 The pharmacopoeial references for Dissolution Test for this annex are:

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

5.2.2 J*apanese 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), in the partial revision of the JP Fifteenth 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 Fifteenth edition made official July 30, 2010, by the Ministry of Health, Labour and Welfare Ministerial Notification No. 322.

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.