

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

## **Annex 7: Dissolution Test General Chapter**

This draft guidance, when finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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.

For questions regarding this draft document contact (CDER) Robert King 301-796-1242, or (CBER) Christopher Joneckis 301-827-0373.

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

**DRAFT CONSENSUS GUIDELINE**

**EVALUATION AND RECOMMENDATION OF  
PHARMACOPOEIAL TEXTS FOR USE IN THE ICH REGIONS  
ON  
DISSOLUTION TEST GENERAL CHAPTER  
Q4B ANNEX 7**

Current *Step 2* Version  
dated 13 November 2008

*At Step 2 of the ICH Process, a consensus draft text or guideline, agreed by the appropriate ICH Expert Working Group, is transmitted by the ICH Steering Committee to the regulatory authorities of the three ICH regions (the European Union, Japan and the USA) for internal and external consultation, according to national or regional procedures.*

39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54

**Q4B Annex 7  
Document History**

**Current *Step 2* version**

Code	History	Date
Q4B Annex 7	Approval by the Steering Committee under <i>Step 2</i> and release for public consultation.	13 November 2008

55  
56

57  
58  
59  
60  
61  
62  
63  
64  
65  
66  
67  
68  
69  
70  
71  
72  
73  
74  
75  
76  
77  
78  
79  
80  
81  
82  
83  
84  
85  
86  
87  
88  
89  
90  
91  
92  
93  
94

**EVALUATION AND RECOMMENDATION OF  
PHARMACOPOEIAL TEXTS FOR USE IN THE ICH REGIONS  
ON  
DISSOLUTION TEST GENERAL CHAPTER  
Q4B Annex 7**

**Draft ICH Consensus Guideline**  
Released for Consultation on 13 November 2008, at *Step 2* of the ICH Process

**TABLE OF CONTENTS**

<b>1. INTRODUCTION.....</b>	<b>1</b>
<b>2. Q4B OUTCOME.....</b>	<b>1</b>
2.1 Analytical Procedures.....	1
2.2 Acceptance Criteria.....	1
<b>3. TIMING OF ANNEX IMPLEMENTATION.....</b>	<b>1</b>
<b>4. CONSIDERATIONS FOR IMPLEMENTATION.....</b>	<b>2</b>
4.1 General Consideration.....	2
4.2 FDA Consideration.....	2
4.3 EU Consideration.....	2
4.4 MHLW Consideration.....	3
<b>5. REFERENCES USED FOR THE Q4B EVALUATION.....</b>	<b>3</b>

95  
96 **EVALUATION AND RECOMMENDATION OF**  
97 **PHARMACOPOEIAL TEXTS FOR USE IN THE ICH REGIONS**  
98 **ON**  
99 **DISSOLUTION TEST GENERAL CHAPTER**  
100 **Q4B Annex 7**

101  
102  
103  
104 **1. INTRODUCTION**  
105

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

107  
108 The proposed texts were submitted by the Pharmacopoeial Discussion Group (PDG).

109  
110 **2. Q4B OUTCOME**  
111

112 **2.1 Analytical Procedures**  
113

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

118  
119 **2.1.1** The Dissolution Test is not considered to be interchangeable in the ICH regions  
120 when enzymes are used in the media.

121  
122 **2.1.2** The dissolution apparatus should be appropriately calibrated to ensure  
123 compliance with regional good manufacturing practice (GMP) requirements.

124  
125 **2.1.3** Except for Apparatus 1 and 2, apparatus numbers are not consistent in the three  
126 pharmacopoeias. Accordingly, other apparatus should be referred to in the  
127 dossier by an unambiguous descriptive title or compendial reference.

128  
129 **2.1.4** The Dissolution Test is not considered to be interchangeable in the ICH regions  
130 for dosage forms referred to in the regional compendia as *delayed-release*,  
131 *gastro-resistant*, or *enteric-coated*.

132  
133 **2.1.5** Validation studies should be conducted to demonstrate that the test results are  
134 not adversely affected if the thermometer is to remain in the dissolution vessel  
135 per regional good manufacturing practice (GMP).

136  
137 **2.1.6** The Dissolution Test is not considered to be interchangeable in the ICH regions  
138 for JP Interpretation 2.

139  
140 **2.1.7** The Dissolution Test is not considered to be interchangeable in the ICH regions  
141 for use of *large* vessels (greater than 1 liter).

142  
143 **2.1.8** Product-specific parameters such as media, stirring rate, sampling time, and the  
144 use and type of sinkers should be specified and justified in the application  
145 dossier.

146  
147  
148  
149  
150  
151  
152  
153  
154  
155  
156  
157  
158  
159  
160  
161  
162  
163  
164  
165  
166  
167  
168  
169  
170  
171  
172  
173  
174  
175  
176  
177  
178  
179  
180  
181  
182  
183  
184  
185  
186  
187  
188  
189  
190  
191  
192  
193  
194  
195  
196  
197  
198  
199  
200  
201  
202

**2.1.9** When using the small cell tablet holder with the flow-through cell apparatus, only the dimensions described in the PDG harmonised text Figure 5 are considered interchangeable.

**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 (such as ASTM International's ASTM E2503-07, Standard Practice for Qualification of Basket and Paddle Dissolution Apparatus, or the procedures for Mechanical Qualification of Dissolution Apparatus 1 and 2, DPA-LOP.002, on the FDA Web site), when properly executed, will 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, the monographs of the Ph. Eur. have mandatory applicability. 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

203  
204  
205  
206  
207  
208  
209  
210  
211  
212  
213  
214  
215  
216  
217  
218  
219  
220  
221  
222  
223  
224  
225  
226  
227  
228  
229  
230  
231  
232  
233  
234  
235  
236  
237  
238

validation studies referred to in Section 2.1.5 of this annex would normally be submitted in the marketing authorisation dossier.

#### **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.

#### **5. REFERENCES USED FOR THE Q4B EVALUATION**

**5.1** The PDG Stage 5B sign-off document (Rev. 1): *Japanese Pharmacopoeial Forum*, Volume 14, number 4 (December 2005).

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

**5.2.1** *European Pharmacopoeia* (Ph. Eur.):  
6th Edition (official on January 2008) Dissolution Test (reference 01/2008: 20903).

**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).

**5.2.3** *United States Pharmacopoeia* (USP):  
<711> Dissolution Test USP 28, 2<sup>nd</sup> Supplement, official August 1, 2005.