ICH Harmonised Tripartite Guideline

Evaluation and Recommendation of Pharmacopoeial Texts for Use in the ICH Regions on Uniformity of Dosage Units General Chapter Q4B Annex 6

Current Step 4 version
dated 13 November 2013

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 6

**Document History**

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EVALUATION AND RECOMMENDATION OF PHARMACOPOEIAL TEXTS FOR USE IN THE ICH REGIONS ON UNIFORMITY OF DOSAGE UNITS GENERAL CHAPTER Q4B ANNEX 6

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Having reached Step 4 of the ICH Process at the ICH Steering Committee meeting on 13 November 2013, this guideline is recommended for adoption to the three regulatory parties to ICH.

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EVALUATION AND RECOMMENDATION OF PHARMACOPOEIAL TEXTS FOR USE IN THE ICH REGIONS ON
UNIFORMITY OF DOSAGE UNITS GENERAL CHAPTER
Q4B ANNEX 6

1. INTRODUCTION
This annex is the result of the Q4B process for the Uniformity of Dosage Units General Chapter.
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. 2.9.40. Uniformity of Dosage Units, JP 6.02 Uniformity of Dosage Units, and USP General Chapter <905> Uniformity of Dosage Units, can be used as interchangeable in the ICH regions subject to the following conditions:

2.1.1 Unless the 25 milligrams (mg)/25% threshold limit is met, the use of the Mass/Weight Variation test as an alternative test for Content Uniformity is not considered interchangeable in all ICH regions.

2.1.2 For specific dosage forms that appear in local text in the pharmacopoeias by enclosing the text in black diamond symbols, application of the Uniformity of Dosage Units test is not considered interchangeable in all ICH regions.

2.1.3 If a correction factor is called for when different procedures are used for assay of the preparation and for the Content Uniformity Test, the correction factor should be specified and justified in the application dossier.

2.2 Acceptance Criteria
The acceptance criteria are harmonized between the three pharmacopoeias.

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.

FDA finds unsuitable for regulatory purposes the not more than 2% Relative Standard Deviation (RSD) exception to the 25 mg/25% threshold that appears in the JP and the Ph. Eur. Therefore, in accordance with the official text in the USP, for those items below the 25 mg/25% threshold, testing by Content Uniformity should be performed.

### 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 2.9.40, on the basis of the declaration of interchangeability made above.

### 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.

### 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.

### 5. REFERENCES USED FOR THE Q4B EVALUATION

#### 5.1 The PDG Stage 5B sign-off document: *Japanese Pharmacopoeial Forum, Volume 13, number 2 (May 2004).*

#### 5.2 The pharmacopoeial references for Uniformity of Dosage Units for this annex are:

**5.2.1 European Pharmacopoeia (Ph. Eur.):** Supplement 6.1 (official April 2008) Uniformity of Dosage Units (reference 04/2008:20940). Further changes to the official text were made in Supplement 7.4, official April 1, 2012.
