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

Annex 6: Uniformity of Dosage Units General Chapter

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

DRAFT CONSENUS 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 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.

Q4B Annex 6
Document History

Current *Step 2* version

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Q4B Annex 6	Approval by the Steering Committee under *Step 2* and release for public consultation.	13 November 2008

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Draft ICH Consensus Guideline

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

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UNIFORMITY OF DOSAGE UNITS GENERAL CHAPTER

Q4B Annex 6

1. INTRODUCTION

This annex is the result of the Q4B process for Uniformity of Dosage Units.

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 The Uniformity of Dosage Unit test is not considered to be interchangeable in the three regions unless the target test sample amount at time of manufacture (T) is 100% (i.e., T=100%).

2.1.2 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.

2.1.3 For specific dosage forms which have been indicated in local text in the pharmacopoeias by enclosing the text within the black diamond symbols, application of the Uniformity of Dosage Units test is not considered interchangeable in all ICH regions.

2.1.4 For Mass/Weight Variation, the PDG-harmonised definition for ‘W Bar’ should be used.

2.1.5 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 (NMT) 2% relative standard deviation (RSD)* exception to the 25 mg/25% threshold. Accordingly, 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.

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 01/2008: 20940)

5.2.2 *Japanese Pharmacopoeia* (JP):
6.02 Uniformity of Dosage Units, as it appears in the JP Fifteenth Edition (March 31, 2006, The Ministry of Health, Labour and Welfare Ministerial Notification No. 285).

5.2.3 *United States Pharmacopeia* (USP):
<905> Uniformity of Dosage Units, *Pharmacopeial Forum*, Volume 34, Number 5, to be official December 2009.