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 STERILITY TEST GENERAL CHAPTER Q4B ANNEX 8

Current *Step 4* version
dated 11 June 2009

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 8
Document History

Code	History	Date
Q4B Annex 8	Approval by the Steering Committee under *Step 2* and release for public consultation.	13 November 2008

Current *Step 4* version

Q4B Annex 2	Approval by the Steering Committee under *Step 4* and recommendation for adoption to the three ICH regulatory bodies.	11 June 2009

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

ON

STERILITY TEST GENERAL CHAPTER
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ICH Harmonised Tripartite Guideline

Having reached *Step 4* of the ICH Process at the ICH Steering Committee meeting on 11 June 2009, this guideline is recommended for adoption to the three regulatory parties to ICH

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STERILITY TEST GENERAL CHAPTER
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1. INTRODUCTION

This annex is the result of the Q4B process for the Sterility Test 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. 2.6.1. Sterility, JP 4.06 Sterility Test, and USP <71> Sterility Tests, can be used as interchangeable in the ICH regions subject to the conditions detailed below. Testing conditions for medical devices, such as sutures, are outside the scope of the ICH recommendation.

2.1.1 Diluting and rinsing fluids should not have antibacterial or antifungal properties if they are to be considered suitable for dissolving, diluting, or rinsing an article under test for sterility.

2.1.2 When testing liquid parenteral preparations with a nominal volume of 100 milliliters in batches of more than 500 containers, the test is considered interchangeable if the minimum number of containers selected is either 20 or is 2 percent of the total number of containers, whichever is lower.

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.

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, Sterility: 2.6.1., 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 16, number 4 (December 2007).

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

5.2.1 *European Pharmacopoeia* (Ph. Eur.): Supplement 6.3 (official in January 2009), Sterility (reference 01/2009:20601);

5.2.2 *Japanese Pharmacopoeia* (JP): The 4.06 Sterility Test as it appeared 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;

5.2.3 *United States Pharmacopeia* (USP):<71> Sterility Tests as presented in *Pharmacopeial Forum*, Volume 34(6), Interim Revision Announcement No. 6, December 1, 2008, official on May 1, 2009.