

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  
RESIDUE ON IGNITION/SULPHATED ASH GENERAL CHAPTER  
Q4B ANNEX 1(R1)**

Current *Step 4* version  
dated 27 September 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 1(R1)** **Document History**

Code *	History	Date
Q4B Annex 1	Approval by the Steering Committee under <i>Step 2</i> and release for public consultation.	8 June 2006
Q4B Annex 1	Approval by the Steering Committee under <i>Step 4</i> and recommendation for adoption to the three ICH regulatory bodies.	1 November 2007

### **Current Step 4 version**

Q4B Annex 1(R1)	Integration of the Health Canada Interchangeability Statement under Section 4.5 after approval by the Steering Committee.	27 September 2010
-----------------	---------------------------------------------------------------------------------------------------------------------------	-------------------

\* *Code as per the new codification system adopted by the ICH Steering Committee in November 2007*

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

**ON**

**RESIDUE ON IGNITION/SULPHATED ASH GENERAL CHAPTER**

**ICH Harmonised Tripartite Guideline**

Having reached *Step 4* of the ICH Process at the ICH Steering Committee meeting on 1 November 2007, this guideline is recommended for adoption to the three regulatory parties to ICH

*(This annex was revised -R1- to include the Interchangeability Statement from Health Canada on September 27, 2010)*

**TABLE OF CONTENTS**

<b>1.</b>	<b>INTRODUCTION .....</b>	<b>1</b>
<b>2.</b>	<b>Q4B OUTCOME .....</b>	<b>1</b>
2.1	Analytical Procedures .....	1
2.2	Acceptance Criteria.....	1
<b>3.</b>	<b>TIMING OF ANNEX IMPLEMENTATION .....</b>	<b>1</b>
<b>4.</b>	<b>CONSIDERATIONS FOR IMPLEMENTATION .....</b>	<b>1</b>
<b>5.</b>	<b>REFERENCES USED FOR THE Q4B EVALUATION .....</b>	<b>2</b>



**EVALUATION AND RECOMMENDATION OF  
PHARMACOPOEIAL TEXTS FOR USE IN THE ICH REGIONS  
ON  
RESIDUE ON IGNITION/SULPHATED ASH GENERAL CHAPTER**

**1. INTRODUCTION**

This annex is the result of the Q4B process for Residue on Ignition/Sulphated Ash. 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. 20414 Sulphated Ash, JP 2.44 Residue on Ignition Test, and USP <281> Residue on Ignition can be used as interchangeable in the ICH regions given the following:

- 2.1.1** Unless otherwise specified in a monograph, an appropriate sample weight is chosen, typically 1-2 g, to result in a level of residue sufficient to be accurately measurable by weight (typically 1 mg). If not specified in the monograph, the appropriate sample weight should be justified, and the sample weight and the acceptance criteria should be specified in the application dossier.
- 2.1.2** The muffle furnace should be appropriately calibrated to ensure compliance with regional GMP requirements.

**2.2 Acceptance Criteria**

The proposed texts evaluated did not contain acceptance criteria.

**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 may 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 in accordance with 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, Sulphated Ash: 20414, 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 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 14, Number 4 (December 2005). (Note: the PDG cover letter published in this volume was subsequently changed based on Q4B comments.)
- 5.2 The pharmacopoeial references for Residue on Ignition/Sulphated Ash for this annex are:
  - 5.2.1 European Pharmacopoeia (Ph. Eur.): Supplement 5.6 (official on January 2007) (reference Sulphated Ash 01/2007:20414);
  - 5.2.2 Japanese Pharmacopoeia (JP): 2.44 Residue on Ignition Test 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): <281> Residue on Ignition official in USP 29, 2<sup>nd</sup> Supplement, August 2006.