INTERNATIONAL COUNCIL FOR HARMONISATION OF TECHNICAL REQUIREMENTS FOR PHARMACEUTICALS FOR HUMAN USE

ICH HARMONISED GUIDELINE

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

Q4B(R1)

Final version

Adopted on 5 June 2024

This Guideline has originally 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 ICH regions.

Q4B (R1)
Document History

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

Current *Step 4* version

Q4B(R1)	Revised by the PDG following endorsement of the maintenance procedure to reflect that responsibility for the maintenance of Q4B and its annexes was handed over to the PDG. Process and individual interchangeability statements taken out and transferred to the ICH SOP or specific Q4B annexes.	5 June 2024

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Q4B(R1)

ICH Consensus Guideline

TABLE OF CONTENTS

1. INTRODUCTION

1.1 Objective(s) of the Guideline

This document describes the process for the evaluation and recommendation of selected pharmacopoeial texts to facilitate their recognition by regulatory authorities for use as interchangeable by the ICH regulatory members.

This process was initially under the responsibility of the ICH Q4B Expert Working Group (EWG) until it was disbanded at the end of 2010. The Pharmacopoeial Discussion Group (PDG) took over this responsibility in November 2018.

1.2 Background

When issuing *Q6A: Specifications: Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances*, and *Q6B: Specifications: Test Procedures and Acceptance Criteria for Biotechnological/Biological Products*, ICH had recognised that full use and value of both ICH Guidelines would depend on the successful harmonisation of pharmacopoeial procedures and encouraged the work of the PDG.

1.2.1 The Pharmacopoeial Discussion Group

The PDG, founded in 1989, consists of representatives from the European Directorate for the Quality of Medicines and HealthCare (EDQM) of the Council of Europe; the Ministry of Health, Labour and Welfare (MHLW) of Japan; and the United States Pharmacopoeial Convention (USP). Since 2001, WHO has been an observer to the PDG. The Indian Pharmacopeia Commission (IPC) has participated in an expansion pilot of PDG since October 2022 and has been welcomed as a member of PDG in October 2023.

In November 2018, ICH and the PDG agreed to collaborate on the maintenance of the current ICH Q4B Annexes, following the maintenance procedure described in Annex 5 of the Standard Operating Procedure of the ICH Working Groups. At the June 2023 ICH meeting in Vancouver, the ICH Assembly endorsed the maintenance procedure proposed by PDG.

1.2.2 The Q4B Expert Working Group (EWG)

In November 2003, ICH had established the Q4B EWG to evaluate and recommend pharmacopoeial texts to be proposed for interchangeable use in the three founding ICH regions (USA, European Union, Japan).

The Q4B EWG had evaluated pharmacopoeial text proposals and assessed their regulatory impact. Following its evaluation, the Q4B EWG had made a recommendation on the interchangeable use of the text in the founding ICH regions which had been transmitted to the ICH Steering Committee. For each proposal that had been favourably evaluated, the Q4B EWG had developed a topic-specific annex to the Q4B Guideline. The annex provided information on how the pharmacopoeial texts can be used in the founding ICH regions. Each annex was issued as a stand-alone companion document to the Q4B guideline.

The Annexes were subsequently revised to include the interchangeability statement from Health Canada.

After completion of the evaluation of the regulatory interchangeability of 16 General Test Chapters, resulting in 16 Q4B Annexes, the Q4B EWG was disbanded, in 2010.

1.2.3. Extension of the Q4B maintenance procedure to non-PDG pharmacopoeias

Since 2010, new regulatory members, some of which have a pharmacopoeia, have joined ICH. Therefore, careful consideration of the impact of the maintenance of the Q4B Annexes on those regulatory members (and their pharmacopoeias) as well as of the impact of the General Test Chapters of those pharmacopoeias on the Q4B Annexes is essential.

To take into consideration this increased membership, a new maintenance procedure had been proposed by the PDG to the ICH Assembly and approved by the latter. This procedure is described in Annex 5 of the Standard Operating Procedure of the ICH Working Groups.

2. GUIDELINES

2.1 Scope

The Q4B process focuses on evaluating and maintaining the 16 Q4B Annexes referred to in Attachment I.

2.2 Q4B Maintenance Process

The process is described in Annex 5 of the Standard Operating Procedure of the ICH Working Groups.

2.3 Annex Contents

The Q4B annexes contain the following information at a minimum. Other information might be incorporated on a case-by-case basis.

- Topic title
- Introduction
- Q4B Outcome
- As appropriate, statements that will assist in the use of the referenced pharmacopoeial text by stakeholders
- Implementation timelines indicating regulators' advice on when stakeholders can begin using the pharmacopoeial text as interchangeable
- References to methods and acceptance criteria, as appropriate

2.4 Use of the Pharmacopoeial Text

After a regulatory ICH member has implemented the Q4B annex, the official pharmacopoeial texts referenced in the annex can be used as interchangeable in accordance with the member’s legal framework. The pharmacopoeial references used for the PDG review are specified in the Q4B annexes. However, it is recommended to refer to the current official pharmacopoeial texts when using the annexes. Any general and/or specific implementation recommendations for a regulatory member will be provided in the Q4B topic specific annex as part of Section 4. *Considerations for Implementation.* The basic information will be as provided below:

2.4.1 Considerations for Implementation

General consideration: When sponsors or manufacturers change their existing methods to the implemented Q4B-evaluated pharmacopoeial texts that are referenced in Section 2 of the annex, any change notification, variation, and/or prior approval procedures should be handled in accordance with established national/regional regulatory mechanisms pertaining to compendial changes.

In addition to these general considerations, implementation status for each regulatory member is provided in each annex and specific information for each regulatory member is also provided to assist the implementation in that country/region. Each regulatory member will provide such notification to its stakeholders in conjunction with regional implementation of the annex.

3. GLOSSARY

Interchangeable – Where such status is indicated, any of the official texts from JP, Ph. Eur., USP or from the other pharmacopoeias referenced in the Q4B Annex can be substituted one for the other (appropriately referenced) in the ICH countries/regions for purposes of the pharmaceutical registration/approval process. Using any of the interchangeable methods, an analyst will reach the same accept or reject decisions irrespective of which pharmacopoeia referenced in the Q4B Annex is used.

Q4B Outcome – Produced by the Q4B evaluation; information concerning how the evaluated pharmacopoeial text can be used. The Q4B Outcome is included as part of the topic-specific Q4B annex developed as a result of each favourable evaluation.

ATTACHMENT I: List of General Test Chapters within the scope of the ICH Q4B Guideline

Residue on Ignition/Sulphated Ash
Extractable Volume
Particulate Contamination: Sub-visible particles
Microbiological Examination of Non-Sterile Products: Microbial Enumeration Tests
Microbiological Examination of Non-Sterile Products: Tests for Specified Micro-organisms
Microbiological Examination of Non-Sterile Products: Acceptance Criteria for Pharmaceutical Preparations and Substances for Pharmaceutical Use
Disintegration
Uniformity of Dosage Units
Dissolution
Sterility Test
Tablet Friability
Polyacrylamide Gel Electrophoresis
Capillary Electrophoresis
Analytical Sieving
Bulk Density of Powders
Bacterial Endotoxins