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

DRAFT CONSENSUS GUIDELINE

REGULATORY ACCEPTANCE OF ANALYTICAL PROCEDURES AND/OR ACCEPTANCE CRITERIA (RAAPAC)

Q4B

Current *Step 2* version

dated 8 June 2006

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
Document History

Current *Step 2* version

First Codification	History	Date	New Codification **November 2005**
Q4B	Approval by the Steering Committee under *Step 2* and release for public consultation.	8 June 2006	Q4B

REGULATORY ACCEPTANCE OF ANALYTICAL PROCEDURES AND/OR ACCEPTANCE CRITERIA (RAAPAC)

Draft ICH Consensus Guideline

Released for Consultation on 8 June 2006, at *Step 2* of the ICH Process

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REGULATORY ACCEPTANCE OF ANALYTICAL PROCEDURES AND/OR ACCEPTANCE CRITERIA (RAAPAC) [1]

1. INTRODUCTION

1.1 Objective(s) of the Guideline

This document describes a procedure to facilitate acceptance by regulatory authorities of pharmacopoeial analytical procedures and/or acceptance criteria (APAC)[2] for use in the three ICH regions.

1.2 Background

The ICH Q6A Guideline encourages the development of harmonised texts by the Pharmacopoeial Discussion Group (PDG). However, until now, ICH has not addressed the regulatory acceptability of pharmacopoeial-proposed APAC for the three ICH regions. The Q4B EWG has been formed to address this issue.

PDG consists of representatives from the European Directorate for the Quality of Medicines in the Council of Europe; the Ministry of Health, Labour and Welfare, and the United States Pharmacopoeial Convention, Inc. PDG is anticipated to be the principal source of APAC proposals to the Q4B EWG. This Guideline is intended to facilitate regulatory acceptance of these proposed APAC and their interchangeability with those APAC contained in the local regional pharmacopoeias, thus avoiding redundant testing and different acceptance criteria in favour of a common testing strategy in each regulatory region. The Q4B process will initially focus on the 11 General Test Chapters (refer to Attachment I). There are many other pharmacopoeial harmonisation proposals being developed (e.g., excipient monographs and other general test chapters), and these could also be considered for Q4B evaluation.

This guideline provides a general description of the process to facilitate regulatory acceptance of analytical procedures and/or acceptance criteria (RAAPAC). For each APAC evaluated, the EWG intends to develop a topic-specific annexe to the Q4B Guideline following the ICH process.

1.3 Scope of the Guideline

This Guideline addresses RAAPAC for the three ICH regions, especially for APAC provided by PDG. It also provides flexibility so that the Q4B EWG can evaluate, and regulatory authorities can choose to accept, non-PDG text.

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[1] The term *regulatory acceptance of analytical procedures and/or acceptance criteria* (RAAPAC) refers to the acceptance by the ICH member regulatory authorities of analytical procedures and/or acceptance criteria that have been evaluated by Q4B.

[2] The term *analytical procedures and/or acceptance criteria* (APAC) refers to pharmacopoeial monographs, general test chapters, analytical methods, and/or associated acceptance criteria.

1.4 General Principles

The EWG will take scientific evaluations and regulatory impact into consideration when evaluating APAC.

The PDG harmonisation process produces APAC which have been through independent public comment/consultation. The Q4B Outcome in the annexe details an interpretation of how APAC should be used. At the regulatory consultation stage for the Q4B topic-specific annexes, regulators intend to focus on comments received relating to the Q4B Outcome. Interested parties are encouraged to focus their comments on the Q4B Outcome in the annexe.

Implementation details will be described in the topic-specific annexes which will be available on the ICH website.

The EWG will evaluate the proposed APAC and make a recommendation regarding regulatory acceptance. In order to preserve transparency, once the EWG has made a recommendation, any subsequent revisions to the PDG harmonised text should occur only through the PDG process. The EWG should be notified of any revisions to a text that has been submitted to the Q4B process. Any such change will prompt an EWG review in order to assess both the merit of the change and the appropriateness of any subsequent Q4B activity related to that APAC. Unilateral changes/revisions by any of the individual pharmacopoeias will void the ICH final status.

2. GUIDELINES

2.1 Q4B Evaluation Process

The Q4B's goal is to encourage acceptance of APAC by regulatory authorities. The document submission should outline any issues for resolution, and should contain any appropriate supporting data. For PDG submissions, the documentation should be provided after PDG Stage 5B (refer to Attachment II).

The Q4B topic-specific annexe process follows the ICH step process as detailed below (see also Figure I).

2.1.1 Step 1

Each Q4B member party independently evaluates the documents for regulatory impact. Additional discussion within the Q4B EWG, and/or communication with the submitting party, might be warranted in order to resolve any issues prior to sign-off.

2.1.2 Step 2

The Q4B EWG signs off on a draft annexe to this Guideline which is presented to the Steering Committee as an ICH Step 2 document.

2.1.3 Step 3

Regulatory consultation (generally within 3 months) focuses on the Q4B Outcome in the annexe. The annexe can be revised based on comments received.

2.1.4 Step 4

The ICH Steering Committee adopts the annexe and adds it to this guideline.

2.1.5 Step 5

The annexe moves to the regional regulatory implementation step.

2.2 Annexe Contents

The topic-specific annexes will contain the following information. Other information might be incorporated on a case-by-case basis.

- Topic title
- Introduction
- Q4B Outcome
- As appropriate, statements, decisions and other information that will assist in the use of the accepted APAC by stakeholders
- Statement or implementation timelines indicating regulators' advice on when stakeholders can begin using the APAC (at Step 4)
- References to methods and acceptance criteria, as appropriate.

2.3 Use of the Accepted APAC

APAC that have reached Step 5 can be used by stakeholders. When changing to the Step 5 APAC, any change notification and/or prior approval should be handled in accordance with established regional regulatory mechanisms. These regional mechanisms will be described in the topic-specific annexes.

3. GLOSSARY

Analytical Procedures and/or Acceptance Criteria (APAC):
Pharmacopoeial monographs, general test chapters, analytical methods, and/or associated acceptance criteria.

Document Submission:
The working documents received from PDG or Non-PDG sources that contain the proposed APAC and any other support documents provided for Q4B evaluation.

Non-PDG:
One or two of the regional pharmacopoeias, but not all 3 pharmacopoeias acting together as the PDG.

PDG:
The three-party Pharmacopoeial Discussion Group, comprised of representatives from the European Directorate for the Quality of Medicines in the Council of Europe; the Ministry of Health, Labour and Welfare, and the United States Pharmacopoeial Convention, Inc.

Q4B Outcome:

The Q4B process produces an interpretation of how APAC should be used. The Q4B Outcome is included as part of the topic-specific annexe developed for each APAC.

Regulatory Acceptance of Analytical Procedures and/or Acceptance Criteria (RAAPAC):

Acceptance by the ICH member regulatory authorities of APAC that have been evaluated by Q4B.

ATTACHMENT I: ICH Q6A General Chapters

Dissolution	
Disintegration	
Uniformity of Content →	Harmonised to Uniformity of Dosage Units
Uniformity of Mass →	
Extractable Volume	
Particulate Matter	
Sterility	
Microbiological Quality	
Bacterial Endotoxins	
Sulphated Ash/ROI	
Colour and Clarity (per ICH SC, work will just be on "Colour")	

ATTACHMENT II: PDG Document Submission Provided for ICH Q4B EWG Evaluation

For the purposes of the process, the Coordinating or Lead Pharmacopoeia, on behalf of PDG, is asked to provide, as soon as possible after PDG Stage 5B sign-off and usually within six months, the following texts and information (termed the "document submission" as defined in the *Guideline*) to the Q4B EWG, via the ICH secretariat, with a copy to the Q4B EWG Rapporteur (for awareness):

1) The PDG sign-off document containing the PDG-harmonised text (PDG Stage 5B).

2) A Briefing Note dealing in particular with:

    a. Residual differences between one or more of the pharmacopoeias, to include a commentary on any difference from the point of view of harmonisation;

    b. Any specific issues relating to publication;

    c. If any equivalency study was conducted, a summary of the outcome;

    d. The projected publication schedule in each pharmacopoeia, with clear indication as to the anticipated final PDG Stage 7 implementation date; and

    e. Any additional clarifying or awareness information not covered above.

3) The texts as intended for adoption and publication in each pharmacopoeia together with a statement of any local differences with respect to the sign-off text.

4) Additional clarifying information may be separately incorporated by one or more of the PDG pharmacopoeias in their respective information chapters on pharmacopoeial harmonisation. Therefore, the revised information chapter on harmonisation from each pharmacopoeia incorporating such information (in draft form where this is available) should accompany the provided documents.

If any changes occur or additional differences are discovered after submission to Q4B, the Q4B EWG should be informed promptly by the pharmacopoeia concerned.

Figure I – Topic-Specific Annexe Process