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

# Annex 4B(R1) Microbiological Examination of Nonsterile Products: Tests for Specified Microorganisms General Chapter

# Guidance for Industry

**U.S. Department of Health and Human Services**
**Food and Drug Administration**
**Center for Drug Evaluation and Research (CDER)**
**Center for Biologics Evaluation and Research (CBER)**

**September 2017**
**ICH**

**Revision 1**

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

# Annex 4B(R1) Microbiological Examination of Nonsterile Products: Tests for Specified Microorganisms General Chapter Guidance for Industry[1]



## I. INTRODUCTION (1)[2]

This annex is one in a series of guidance documents that describe the evaluations and recommendations by the Q4B Expert Working Group (EWG) of selected pharmacopoeial texts to facilitate their recognition by regulatory authorities for use as interchangeable in the ICH regions. Implementation of the Q4B annexes is intended to avoid redundant testing by industry. For general information on the Q4B process, the reader is referred to the core guidance *Q4B Evaluation and Recommendation of Pharmacopoeial Texts for Use in the ICH Regions.*[3]

[1] This guidance was developed within the Expert Working Group (Quality) of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), formerly the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use, and has been subject to consultation by the regulatory parties, in accordance with the ICH process. This document has been endorsed by the ICH Steering Committee at *Step 4* of the ICH process, September 2010. At *Step 4* of the process, the final draft is recommended for adoption to the regulatory agencies.

[2] Arabic numbers reflect the organizational breakdown of the document endorsed by the ICH Steering Committee at Step 4 of the ICH process, September 2010.

[3] We update guidances periodically. To make sure you have the most recent version of a guidance, check the FDA Drugs guidance page at https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm or the FDA Biologics guidance page athttps://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/default.htm .

This annex is the result of the Q4B process for Microbiological Examination of Nonsterile Products: Tests for Specified Microorganisms. The proposed texts were submitted by the Pharmacopoeial Discussion Group (PDG). This revision, Q4B Annex 4B(R1), adds the Health Canada interchangeability statement in section IV.E (4.5).

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

## II. Q4B OUTCOME (2)

### A. Analytical Procedures (2.1)

The ICH Steering Committee, based on the evaluation by the Q4B Expert Working Group (EWG), recommends that the official pharmacopoeial texts, Ph. Eur. 2.6.13. Microbiological Examination of Non-Sterile Products: Tests for Specified Micro-organisms, JP 4.05 Microbiological Examination of Non-Sterile Products: II. Microbiological Examination of Non-Sterile Products: Tests for Specified Micro-organisms, and USP <62> Microbiological Examination of Nonsterile Products: Tests for Specified Microorganisms, can be used as interchangeable in the ICH regions.

### B. Acceptance Criteria (2.2)

The proposed texts evaluated did not contain acceptance criteria.

## III. TIMING OF ANNEX IMPLEMENTATION (3)

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.

## IV. CONSIDERATIONS FOR IMPLEMENTATION (4)

### A. General Consideration (4.1)

When sponsors or manufacturers change their existing methods to the implemented Q4B-evaluated pharmacopoeial texts that are referenced in section II.A (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.

### B. FDA Consideration (4.2)

Based on the recommendation above, and with reference to the conditions set forth in this annex, the pharmacopoeial texts referenced in section II.A (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.

### C. EU Consideration (4.3)

For the European Union (EU), the monographs of the Ph. Eur. have mandatory applicability. Regulatory authorities can accept the reference in a marketing authorization application, renewal or variation application citing the use of the corresponding text from another pharmacopoeia as referenced in section II.A (2.1), in accordance with the conditions set out in this annex, as fulfilling the requirements for compliance with the Ph. Eur. Chapter 2.6.13. on the basis of the declaration of interchangeability made above.

### D. MHLW Consideration (4.4)

The pharmacopoeial texts referenced in section II.A (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.

### E. Canada Consideration (4.5)

In Canada, any of the pharmacopoeial texts cited in section II.A (2.1) of this annex and used in accordance with the conditions set out in this annex can be considered interchangeable.

## V. REFERENCES USED FOR THE Q4B EVALUATION (5)

**A. (5.1)** The PDG Stage 5B sign-off document: *Japanese Pharmacopoeial Forum,* Volume 14, Number 4 (December 2005).

**B. (5.2)** The pharmacopoeial references for Microbiological Examination of Nonsterile Products: Tests for Specified Microorganisms for this annex are:

*1. (5.2.1) European Pharmacopoeia* (Ph. Eur.): 6.3 Edition (official on January 2009) Microbiological Examination of Non-Sterile Products: Tests for Specified Micro-organisms (reference 01/2009:20613).

*2. (5.2.2) Japanese Pharmacopoeia* (JP): 4.05 Microbiological Examination of Non-Sterile Products: II. Microbiological Examination of Non-Sterile Products: Tests for Specified Micro-organisms as it appears in Supplement I to the Japanese Pharmacopoeia Fifteenth Edition (September 28, 2007, The Ministry of Health, Labour and Welfare Ministerial Notification No. 316). The English version was published on January 9, 2008.

*3. (5.2.3) United States Pharmacopeia* (USP): <62> Microbiological Examination of Nonsterile Products: Tests for Specified Microorganisms official in USP 30, January 2007.