

Annex 5: Q4B Maintenance Procedure

(Revised version as of May 2024)

1 - Background Information:

The ICH Q4B Guideline Evaluation and Recommendation of Pharmacopoeial Texts for Use in the ICH Regions reached *Step 5* in November 2007. Subsequently, the individual topic-specific Annexes reached *Step 5* in accordance with the dates listed on the ICH website. Because the inputs to the Q4B process were from the Pharmacopoeial Discussion Group (PDG) harmonisation process, it is recognised that the pharmacopoeial texts could be updated as technology and requirements change, or for other reasons. Because changes to the pharmacopoeial texts could have an impact on the interchangeability assessment contained in the Annexes, it is necessary to have a maintenance procedure for updating the Annexes when needed.

In November 2018, ICH and the PDG agreed to collaborate in the maintenance of the current ICH Q4B Annexes, following the maintenance procedure described below.

2 - Maintenance Procedure:

The need to revise an ICH Q4B Annex is triggered by either the PDG's sign-off of a revised text which is the subject of an existing Q4B Annex, or the introduction of new ICH regulatory member(s) who are implementing the Q4B Annex. Potentially non-harmonised and/or local requirements are highlighted in the sign-off coversheet.

The Formal Step Process outlined in section 2.1 of this SOP and highlighted below applies to the maintenance of the Q4B Annexes. However, further to *Step 2a*, based on the level of change made to the revised Q4B Annex, the document should either proceed to *Step 2b* and then be published for comments, or it should directly be submitted to the Regulatory Members of the Assembly for adoption at *Step 4* and published as final. The latter may be deemed appropriate for example in the case of revisions limited to an update on the pharmacopoeial reference texts (i.e. updated versions of the pharmacopoeia).

- **Step 1:**

The PDG compares the corresponding current ICH Q4B Annex, the PDG sign-off text and the corresponding chapters as published in each of the PDG pharmacopoeias, if applicable. All other pharmacopoeias are informed by the PDG of the ongoing review via the contact list of the International meeting of World Pharmacopoeias (IMWP).

The pharmacopoeia of an ICH regulatory member (that is not a PDG pharmacopoeia) intending to have the regulatory interchangeability of its general test chapter considered in the Q4B Annex shall indicate interchangeability by one of the following two options.

Option 1: standard approach. The ICH regulatory member pharmacopoeia indicates that its text is harmonised with the PDG text. The ICH regulatory member pharmacopoeia provides the PDG with the following documents:

- a copy of its current pharmacopoeial text, in English and in the original language (if applicable);
- a self-assessment of its harmonisation status. This self-assessment must include the residual differences, such as local requirements or non-harmonised attributes, compared to the PDG sign-off text.

The PDG will consider all the documents received and may contact the pharmacopoeia in the event of questions. Once complete feedback has been received, the PDG will review the data and information. If the PDG agrees with the harmonisation assessment, it will prepare a revised Q4B Annex. If there are outstanding questions to be addressed before the PDG can agree that the text is harmonised, additional time may be required before this step. Alternatively, the ICH regulatory member pharmacopoeia may wish to employ Option 2 below.

Option 2: Parallel approach. ICH regulatory member pharmacopoeias may publish the PDG harmonised method in parallel with their existing local method. Thus, ICH regulatory member pharmacopoeias still meet the requirements for interchangeability under the following conditions.

- The ICH regulatory member pharmacopoeias must publish the PDG method covered by the Q4B annex in parallel with any local method. The harmonised method needs to be clearly identifiable in the pharmacopoeia. In the spirit of harmonisation, it is expected that the ICH regulatory member pharmacopoeias start a revision cycle of the local method intended to harmonise with the PDG text.
- Both methods are acceptable alternative options for the ICH regulatory member pharmacopoeia.
- Only the method harmonised with the PDG will be referenced in Sections 2.1. and 5 of the ICH Q4B Annex for declaration of interchangeability.
- ICH regulatory members who have implemented the applicable ICH Q4B annex declare that the local pharmacopoeia's method is interchangeable with the corresponding method of the other pharmacopoeias that have implemented the PDG harmonised methods.
- The ICH regulatory member pharmacopoeia provides the PDG with a copy of the current Q4B text as published in their pharmacopoeia, in both English and the original language (if applicable). The PDG confirms that the Q4B text as published is harmonised with the global PDG text. Upon confirmation, the PDG prepares a revised Q4B Annex.

Based on the successful outcomes of either Option 1 or Option 2, the PDG submits the revised Q4B Annex to all ICH regulatory members to seek feedback especially on the respective considerations for implementation of each ICH regulatory member. PDG reviews the feedback and makes any changes to the Annex as appropriate based on this feedback. The revised Q4B Annex is then submitted to the ICH Secretariat.

- ***Steps 2 a/b:***

Further to receiving from the PDG a revised Q4B Annex, the ICH Secretariat initiates *Step 2a* at the level of the ICH Assembly as per section 2.1.2.

ICH will determine whether the revised Q4B Annex should proceed to *Step 2b* and *Step 3* according to the level of change made to the Annex.

- **Step 3:**

Further to the successful completion of *Step 2b*, the revised Q4B Annex becomes the subject of a regulatory consultation, following similar rules described in [section 2.1.5](#).

The regulatory consultation and discussion should focus on the Q4B outcome in the Q4B Annex, i.e. regulatory interchangeability, comments on the harmonised pharmacopoeial text itself are not expected. Comments will be evaluated by the PDG and the Q4B Annex is revised by the PDG where necessary.

- **Step 4:**

Further to successful completion of *Step 3*, the PDG submits the revised Q4B Annex to the ICH Secretariat for adoption by the Regulatory Members of the Assembly, in line with [section 2.1.6](#).

- **Step 5:**

Once *Step 4* is finalised, the revised Q4B Annex moves to the final step of the process. The revised Q4B Annex is published on the ICH website and is implemented by each of the Regulatory Members in their respective regions, as described in [section 2.1.7](#). In case the parallel approach is used ICH regulatory members indicate this in the ICH implementation table.

The corresponding PDG Chapter moves to the PDG stage 5 (inter-regional acceptance). All other pharmacopoeias are informed by the PDG via the contact list of the International meeting of World Pharmacopoeias (IMWP). Each pharmacopoeia of a regulatory ICH member whose general test chapter is mentioned in the Q4B Annex decides on the next steps, in line with its own procedure.