REVISION OF WHO GMP FOR STERILE PHARMACEUTICAL PRODUCTS – A JOINT EU, PIC/S, WHO PROJECT

(February 2020)

DRAFT FOR COMMENTS

Please send any comments you may have on the attached revision to Dr Sabine Kopp, Team Lead, Norms and Standards for Pharmaceuticals, Technical Standards and Specifications (kopps@who.int) with a copy to Ms Claire Vogel (vogelc@who.int) by 20 April 2020.

Working documents are sent out electronically and they will also be placed on the WHO Medicines website (http://www.who.int/medicines/areas/quality_safety/quality_assurance/guidelines/en/) for comments under the “Current projects” link. If you wish to receive our draft guidelines, please send your email address to jonesi@who.int and your name will be added to our electronic mailing list.

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Please send any request for permission to: Dr Sabine Kopp, Team Lead, Norms and Standards for Pharmaceuticals, Technical Standards and Specifications, Department of Health Products Policy and Standards, World Health Organization, CH-1211 Geneva 27, Switzerland, email: kopps@who.int.

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SCHEDULE FOR DRAFT WORKING DOCUMENT QAS/17.745:

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<table>
<thead>
<tr>
<th>Description</th>
<th>Date</th>
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<tr>
<td>Communications and follow-up between PIC/S, EU and WHO, including official</td>
<td>May 2015–November 2017</td>
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<tr>
<td>exchange of letters with the Chairperson of PIC/S exploring cooperation</td>
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<td>towards convergence on new guidance in data integrity and revision of GMP</td>
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<td>for sterile products. During the drafting process of the GMP text for</td>
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<td>sterile products, input was given by PQT-Inspection.</td>
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<td>Recommendation during “GMP” meeting to work with PIC/S on the update and</td>
<td>29 June–1 July 2015</td>
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<td>new guidance including, e.g. risk classification, data and record</td>
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<td>management practices and sterile products.</td>
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<tr>
<td>Presentation to the WHO Expert Committee on Specifications for Pharmaceutical Preparations for advice regarding convergence of new guidelines in the area of inspection and endorsement of collaboration.</td>
<td>17–21 October 2017</td>
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<tr>
<td>Joint public consultation phase on newly proposed update of the GMP text</td>
<td>20 December 2017–20 March 2018</td>
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<td>for sterile products.</td>
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<td>Compilation of comments and revision of draft based on feedback.</td>
<td>Starting April 2018</td>
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<td>Discussion at Fifty-third meeting of the WHO Expert Committee on</td>
<td>October 2018</td>
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<tr>
<td>Specifications for Pharmaceutical Preparations.</td>
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<td>Continuation of discussions on the update in the Working Group.</td>
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<td>Update and progress report to Fifty-fourth meeting of the WHO Expert</td>
<td>October 2019</td>
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<td>Committee on Specifications for Pharmaceutical Preparations.</td>
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<td>Joint public consultation phase on newly revised version of the update of</td>
<td>20 February - 20 April 2020 /</td>
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<tr>
<td>the GMP text for sterile products following an extensive review of the</td>
<td>20 May 2020</td>
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<td>feedback and comments received during the first consultation.</td>
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<tr>
<td>Activity</td>
<td>Timeframe</td>
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<tr>
<td>Compilation of comments of feedback received by WHO.</td>
<td>Starting April 2020</td>
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<tr>
<td>Review of comments received by WHO in close collaboration with the EU/EMA and PIC/S.</td>
<td>Starting end of April 2020</td>
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<tr>
<td>Review of all comments received in close collaboration with the EU/EMA and PIC/S.</td>
<td>Starting end of May 2020</td>
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<tr>
<td>Discussion at Fifty-third meeting of the WHO Expert Committee on Specifications for Pharmaceutical Preparations.</td>
<td>12-16 October 2020</td>
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<td>Any further action, as necessary.</td>
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As a follow-up to the recommendation of the World Health Organization (WHO) Expert
Committee on Specifications for Pharmaceutical Preparations (ECSPP), the WHO Secretariat
actively pursues its efforts towards an efficient collaboration with the European Union (EU)
and the Pharmaceutical Inspection Co-operation Scheme (PIC/S) in the revision process of
the good manufacturing practices (GMP) for sterile products: WHO Good Manufacturing
Practices for Sterile Pharmaceutical Products:
http://www.who.int/medicines/areas/quality_safety/quality_assurance/GMPSterilePharmaceutical
Series, No. 961, 2011.

It is viewed that a common language would be beneficial to the authorities and the
manufacturers, save resources and, thus, would ultimately benefit patients in having better
access to quality medicines.

The manufacture of sterile medical products covers a wide range of product types (sterile
active substance through to finished dosage form), batch sizes (single unit to multiple units),
processes (from highly automated systems to manual processes), primary packaging materials
and technologies (e.g. biotechnology, classical small molecule manufacturing and closed
systems). This Annex provides general guidance that should be used for all sterile medical
products and sterile active substances, via adaption, using the principles of quality risk
management (QRM) to ensure that microbial, particulate and pyrogen contamination
associated with microbes is prevented in the final product.

In order to maintain the global alignment of standards, achieving at the same time assurance
for the highest quality, the document will be, in parallel, subject to a second joint targeted
consultation by the European Commission (EC)/European Medicines Agency (EMA), WHO
and PIC/S.
Objective of the consultation

This revision is intended (i) to add clarity, (ii) introduce the principles of QRM to allow for the inclusion of new technologies and innovative processes and (iii) to change the structure to a more logical flow. Key changes are as follows:

- Introduction of new sections;
- Introduction of QRM principles;
- Restructured to give more logical flow; and
- Added detail to a number of the previous sections to provide further clarity.

A first consultation, conducted from 20 December 2017 to 20 March 2018, allowed approximately 140 companies and/or organizations to comment. The joint PIC/S-EMA drafting group (with WHO participation) processed more than 6200 lines of comments.

Due to widespread interest from industry following the first consultation, and because of substantial modifications introduced in several sections, the EC, EMA, WHO and PIC/S have agreed to engage a second consultation with stakeholders on the updated draft guidance (version 12) focusing on the sections and/or significantly modified paragraphs that raised the most concerns from stakeholders.

The second consultation aims to gather experience from the sectors on certain manufacturing steps. It is expected to receive contribution from the associations representing the sectors.

There are two options in sending feedback to this new draft document:

1. VIA THE TARGETED STAKEHOLDERS’ CONSULTATION PROCESS COORDINATED BY THE EU

Period of consultation

From 20 February to 20 May 2020.
How to submit a contribution

Comments will be collected by the EC directly, as well as a number of organisations representing relevant stakeholders who have agreed to receive all the comments from their members, to compile and send the comments to the EC. For the list of stakeholders, please refer to the EC’s website (link provided below), in particular to the section on “Targeted Stakeholders”.

To download the consultation document and the template required to submit comments, as well as the process on how submit comments, please refer to the EC’s website using this link: https://ec.europa.eu/health/medicinal_products/consultations/2020_sterile_medicinal_products_en and “How to submit a contribution”.

Contact details

Responsible service:

Health and Food Safety Directorate General
Unit B4 - Medicinal products: quality, safety, innovation

Any queries about the public consultation should be sent to: SANTE-REVISION-OF-ANNEX-1@ec.europa.eu.

2. DIRECTLY TO THE WHO SECRETARIAT

Period of consultation

From 20 February to 20 April 2020.

Objective of the consultation

As an opportunity for convergence in the area of GMP, WHO is once again widely circulating the new proposal, developed by EU and PIC/S with input from WHO, in order to
obtain feedback and comments on the revision following the first joint consultation in December 2017 and a review of the more than 6,200 comments by the drafting group. The proposal is to replace the text *WHO Good Manufacturing Practices for Sterile Pharmaceutical Products* published as Annex 6, WHO Technical Report Series, No. 961, 2011, with the text of the newly revised “EU-PIC/S GMP Annex 1 on the Manufacture of Sterile Medicinal Products”.

*How to submit a contribution*

Please send any comments you may have on the attached revision to Dr. Sabine Kopp, Team Lead, Norms and Standards for Pharmaceuticals (kopps@who.int) with a copy to Ms Claire Vogel (vogelc@who.int) by 20 April 2020.

The draft guideline under consultation can be downloaded:


It has been formatted with prescribed line and page numbers in order to support a joint international consultation with the EC, PIC/S and WHO.

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