Annex 1

Procedure for the development of World Health Organization medicines quality assurance guidelines

1. Introduction

The process described in this annex is designed to ensure wide consultation and transparency when developing the World Health Organization (WHO) norms and standards for medicines quality assurance for WHO's Member States. These quality assurance (QA) guidelines include good practice quality guidelines and regulations (GXPs) and technical regulatory guidance. The steps outlined in Section 3 are designed to ensure that these texts are made available in a timely manner. These QA guidelines are developed and maintained up to date under the aegis of the WHO Expert Committee on Specifications for Pharmaceutical Preparations (ECSPP), in line with WHO rules and procedures governing expert committees, adopted by WHO Member States. The steps involved in the development of specifications and monographs for inclusion in *The International Pharmacopoeia* (*1*) are addressed separately (*2–4*).

QA guidelines are the recognized WHO technical standards to support the whole life-cycle of medical products, from development through to production (for example, good manufacturing practices, quality control, inspectorate guidelines), marketing authorization (for example, stability and bioequivalence) and distribution (good distribution practices), up to the post-marketing phase (for example, WHO *Guidelines on the conduct of surveys of the quality of medicines* (5) and *WHO guidance on testing of "suspect" falsified medicines* (*6*)).

To reflect the constant technical progress in pharmaceutical development, production, regulatory science and quality control, it is crucial that QA guidelines and guidance texts are kept up to date, that they reflect science, and that the WHO procedures to elaborate or review them are flexible enough to allow rapid interventions by regulators, while maintaining a rigorous public consultation process with all stakeholders.

QA guidelines provide an important element of the quality dimension for the medical products (included on the basis of their efficacy and safety) in the WHO *Model List of Essential Medicines* (*7*) and in WHO treatment guidelines. Major WHO programmes, such as the Prequalification Team-Medicines, and others managed by partner organizations, such as the United Nations Children's Fund and The Global Fund to Fight AIDS, Tuberculosis and Malaria, rely heavily upon the quality specifications set out in *The International Pharmacopoeia* (*1*) and in the QA guidelines.

2. Purpose and scope

The primary objective of this guidance document is to establish a standardized policy when developing new QA guidelines. By increasing transparency and communication, the aim is to involve a wide range and a large number of stakeholders able to bring different perspectives to common issues.

In addition, the transparency and promotion of internationally standardized practices could improve the cooperation between national regulatory authorities and stakeholders, when developing quality standards leading to an optimization of resources on a global scale and reducing duplication of work.

3. Development of guidelines

QA guidelines are developed following recommendations by WHO governing bodies (such as, the Executive Board and the World Health Assembly), the International Conference of Drug Regulatory Authorities, the ECSPP, international organizations and United Nations agencies and other WHO programmes and activities, or in response to major public health needs, and are thereafter adopted by the ECSPP. The procedural steps to follow when developing new QA guidance are outlined in the list that follows.

- *Phase 1*: search for information on the identified QA topic available in the public domain.
- *Phase 2*: identify relevant expert(s) in that field, applying conflict-of-interest screening.
- *Phase 3*: contact the experts who are suitable for the task, sharing the relevant WHO confidentiality rules and policy. Confirm the core team of experts, who can be internal and/or external to WHO. The group of core experts is coordinated by the WHO Secretariat.
- *Phase 4*: make arrangements with the expert(s) for developing the first draft text of the QA guideline.
- *Phase 5*: follow the ECSPP consultative process – circulate widely for public consultation; this will last for a period of between 8 and 12 weeks, depending on the topic.
- *Phase 6*: collect and collate the comments received during the global consultation process.
- *Phase 7*: discuss and review the comments received during the consultation process, in the ECSPP meetings and in an informal consultation with experts and specialists.
- *Phase 8*: incorporate all changes agreed during the discussion in the ECSPP meeting leading to adoption, together with any editorial corrections. Present the final text to the ECSPP for possible formal adoption.
- *Phase 9*: if no consensus is reached by the ECSPP, repeat phases 5–8 until the agreed draft is suitable for adoption.

- *Phase 10*: when consensus is reached, the guidance is adopted by the ECSPP and included as an annex in the meeting report. It is recommended by the WHO Director-General to Member States as new WHO guidelines, GXP guidance, and so on.

The different steps leading to the development of a new WHO QA guideline for medicines are reported in the note "Schedule for the adoption process" outlining the development history of a text from its draft to its adoption, which is included in each working document that is circulated and posted on the Medicine Quality Assurance website for comments.

4. The WHO Technical Report Series

In accordance with the WHO rules and procedures, the Secretariat publishes the QA guidelines adopted by the ECSPP in WHO's Technical Report Series, after every meeting of the ECSPP. The ECSPP report includes all the newly adopted guidelines, including GXPs and regulatory guidance texts. It provides recommendations to the WHO Director-General and to WHO Member States. The report is presented to WHO governing bodies (such as the Executive Board) for final comments, endorsement and implementation by Member States. The report of the ECSPP therefore constitutes WHO technical guidance in medicine quality assurance and regulatory matters.

References

1. The International Pharmacopoeia, 8th ed. Geneva: World Health Organization; 2018 (http://apps.who.int/phint/2018/index.html#d/b.1, accessed 6 February 2019).
2. Procedure for the development of monographs and other texts for *The International Pharmacopoeia*. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations, forty-ninth report. Geneva: World Health Organization; 2015: Annex 1 (WHO Technical Report Series, No. 992; https://www.who.int/medicines/publications/pharmacopoeia/Annex1-TRS992.pdf, accessed 6 February 2019).
3. Updating mechanism for the section on radiopharmaceuticals in *The International Pharmacopoeia*. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations, forty-ninth report. Geneva: World Health Organization; 2015: Annex 2 (WHO Technical Report Series, No. 992; http://apps.who.int/medicinedocs/documents/s21893en/s21893en.pdf, accessed 6 February 2019).
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5. Guidelines on the conduct of surveys of the quality of medicines. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations, fiftieth report. Geneva: World Health Organization; 2016: Annex 7 (WHO Technical Report Series, No. 996; http://apps.who.int/medicinedocs/documents/s22404en/s22404en.pdf, accessed 6 February 2019).

6. WHO guidance on testing of “suspect” falsified medicines. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations, fifty-second report. Geneva: World Health Organization; 2018: Annex 5 (WHO Technical Report Series, No. 1010; http://apps.who.int/medicinedocs/documents/s23452en/s23452en.pdf, accessed 6 February 2019).

7. WHO Model List of Essential Medicines, 20th list. Geneva: World Health Organization; 2017 (https://apps.who.int/iris/bitstream/handle/10665/273826/EML-20-eng.pdf?ua=1, accessed 6 February 2019).