Annex 3

Guidelines for the safe production and quality control of poliomyelitis vaccines

Amendment to Annex 4 of WHO Technical Report Series, No. 1016

Adopted by the World Health Organization (WHO) on the recommendation of the seventy-first meeting of the WHO Expert Committee on Biological Standardization held 24–28 August 2020. A definitive version of this document, which will differ from this version in editorial but not scientific details, will be published in the WHO Technical Report Series.

Introduction 3
Amendments 3
Authors and acknowledgements 4
References 5
Introduction

At its sixty-ninth meeting in 2018, the WHO Expert Committee on Biological Standardization recommended the adoption of the WHO Guidelines for the safe production and quality control of poliomyelitis vaccines (1). These Guidelines outline the biosafety measures required for poliomyelitis vaccine production and quality control during the final poliovirus containment stage (Phase III) as defined in the third edition of the *WHO Global Action Plan to minimize poliovirus facility-associated risk after type-specific eradication of wild polioviruses and sequential cessation of oral polio vaccine use* (GAPIII) (2). The biosafety-related steps outlined in the Guidelines are to be implemented to minimize the risk of accidentally reintroducing poliovirus from a vaccine manufacturing facility into the community after global certification of poliomyelitis eradication. In order to align with GAPIII requirements, the current Guidelines included several requirements related to the physical design of the facility and to quality control testing which were added after the final round of public consultation in 2018. Following the publication of the Guidelines, poliomyelitis vaccine manufacturers requested WHO to reconsider these requirements, taking into consideration the use of facility-specific risk-based approaches. Given the need to balance global vaccine supply (production) and demand, as well as other technical issues associated with the implementation of GAPIII, the Fourth Meeting of the Containment Advisory Group (CAG) was convened on 15–16 July 2019. At this meeting the issues and challenges faced by poliomyelitis vaccine manufacturers were presented for the deliberation of CAG. A consensus was reached that the relevant sections in the Guidelines should be amended to allow for facility-specific risk assessments to be performed in relation to the specific areas highlighted (3). Subsequently, the Committee at its meeting in 2019 recommended amending the Guidelines in accordance with the recommendations made by CAG (4). The amendments provided in the current document comprise:

- a modified requirement for showering when exiting the containment facility;
- permitting the use of non-dedicated quality control laboratories; and
- permitting the testing of certain samples taken from the containment facility outside of containment laboratories.

No attempt was made at this time to review the WHO Guidelines for the safe production and quality control of poliomyelitis vaccines in their entirety and only the above issues have been addressed.

Amendments

Replace section 7.5.6 with the following text:

7.5.6 A full-body shower facility should be available within the personnel exit airlock from the containment facility. The use of a shower upon exit should follow the established procedure supported by the risk assessment and be consistent with the policies established by the latest version of GAPIII¹ and with the most recent CAG recommendations.²

Replace section 11.2 with the following text:

11.2 The use of non-dedicated quality control laboratories may be permissible when all of the following conditions are met:

- The non-dedicated quality control laboratories are located within the containment facility.
- All non-poliovirus-related activities performed within the non-dedicated containment laboratories and all personnel admitted into the non-dedicated containment laboratories adhere to all applicable containment procedures.
- A thorough risk assessment compliant with the requirements set out in the latest version of GAPIII\(^1\) and with the most recent CAG recommendations\(^2\) is performed to identify any additional controls necessary to mitigate the risks introduced by operating non-dedicated laboratories.

Replace section 11.5 with the following text:

11.5 All samples received from the containment production facility should be handled using established procedures to prevent the release of live poliovirus. Procedures used to decontaminate sample containers or packaging materials should be validated and shown to have no impact on sample integrity. The packaging materials should be decontaminated prior to disposal. All samples received from the containment production facilities – with the exceptions described below in sections 11.5.1 and 11.6 – should be tested in containment laboratories. All test procedures using reagents containing live poliovirus should also be performed within the containment laboratories.

11.5.1 On the issue of handling samples outside the containment facility, certain samples (that is, those for water or environment monitoring) taken from within the containment perimeter may be tested outside the containment laboratories if a risk assessment concludes that they are unlikely to contain live poliovirus, based on facility design, equipment used (especially closed systems) and sampling locations \(^3\) provided all sample-handling, transportation and disposal processes adhere to the policies established by the latest version of GAPIII\(^1\) and to the most recent CAG recommendations.\(^2\)

**Authors and acknowledgements**

The first draft of this document was prepared by Ms A. Bonhomme, Public Health Agency of Canada, Canada; Dr K. Chumakov, United States Food and Drug Administration, the USA; Dr J. Martin, National Institute for Biological Standards and Control, the United Kingdom; Dr T. Wu, Health Canada, Canada; and Dr H-N. Kang, World Health Organization, Switzerland.

The document was then posted on the WHO Biologicals website for a first round of public consultation from 25 February to 3 April 2020 and comments were received from: Dr N. Holvast, Bilthoven Biologicals B.V., Netherlands; Dr P. Huntly, Riskren PTE Ltd,

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Taking into consideration the comments received, a second draft document was prepared by Ms A. Bonhomme, Public Health Agency of Canada, Canada; Dr K. Chumakov, United States Food and Drug Administration, the USA; Dr J. Martin, National Institute for Biological Standards and Control, the United Kingdom; Dr T. Wu, Health Canada, Canada; and Dr T.Q. Zhou, World Health Organization, Switzerland, with critical inputs provided by Dr D. Moffett and Dr H. Singh, Department of Polio Operations and Research, World Health Organization, Switzerland.

During the posting of the resulting document on the WHO Biologicals website for a second round of public consultation from 17 June to 3 August 2020, written comments were received from: Dr I. Feavers, Consultant, Nacton, the United Kingdom; Dr M. Janssen, Vaccine PQ Team, World Health Organization, Switzerland; Dr V. Pithon, Agence nationale de sécurité du médicament et des produits de santé, France; and Dr W. Wulandari, Indonesian Food and Drug Authority, Indonesia. The document WHO/BS/2020.2381 was then prepared by Ms A. Bonhomme, Public Health Agency of Canada, Canada; Dr K. Chumakov, United States Food and Drug Administration, the USA; Dr J. Martin, National Institute for Biological Standards and Control, the United Kingdom; Dr T. Wu, Health Canada, Canada; and Dr T.Q. Zhou, World Health Organization, Switzerland.

Further changes were subsequently made to document WHO/BS/2020.2381 by the WHO Expert Committee on Biological Standardization.

References


4. Revision of the WHO Guidelines for the safe production and quality control of poliomyelitis vaccines. In: WHO Expert Committee on Biological Standardization: