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**Guidelines for the safe production and quality control of poliomyelitis
vaccines**

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

NOTE:

This draft document has been prepared for the purpose of inviting comments and suggestions on the proposals contained therein which will then be considered by the WHO Expert Committee on Biological Standardization (ECBS). The distribution of this document is intended to provide information on a number of proposed amendments to the WHO Guidelines for the safe production and quality control of poliomyelitis vaccines to a broad audience and to ensure the transparency of the consultation process.

The text in its present form does not necessarily represent the agreed formulation of the ECBS. Written comments proposing modifications to this text MUST be received by 3 August 2020 using the Comment Form available separately and should be addressed to the Department of Health Products Policy and Standards, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland.

Comments may also be submitted electronically to the Responsible Officer: Dr Tiequn Zhou at: zhout@who.int.

The outcome of the deliberations of the ECBS will be published in the WHO Technical Report Series. The final agreed formulation of the document will be edited to be in conformity with the second edition of the *WHO style guide* (KMS/WHP/13.1).

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Introduction

The WHO Expert Committee on Biological Standardization adopted the WHO Guidelines for the safe production and quality control of poliomyelitis vaccines (1) at its sixty-ninth meeting in 2018. 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. 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 GAPIII (2)¹ and with the most recent CAG recommendations².

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 element 2 of GAPIII 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 (i.e. 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 GAPIII.

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 H-N. Kang, World Health Organization, Switzerland; Dr J. Martin, National

¹ See also: Containment Guidance and Tools [website]: <http://polioeradication.org/polio-today/preparing-for-a-polio-free-world/containment/containment-resources/>, accessed 28 May 2020.

² See: Containment Advisory Group [website]: <http://polioeradication.org/tools-and-library/policy-reports/advisory-reports/containment-advisory-group/>, accessed 28 May 2020.

Institute for Biological Standards and Control, the United Kingdom; and Dr T. Wu, Health Canada, Canada.

The document was then posted on the WHO Biologicals website for public consultation during the period 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, Singapore; Dr M. Janssen, WHO Vaccine PQ Team, Switzerland; Dr K. Mahmood, PATH, the USA; Dr A.E. Malkin, Russian Academy of Sciences, Russian Federation; Dr D. Moffett and Dr H. Singh, Department of Polio Operations and Research, World Health Organization, Switzerland; Dr V. Pithon, Agence nationale de sécurité du médicament et des produits de santé, France; Dr J. Rosenstand Jørgensen, Statens Serum Institut, Denmark; Dr J. Southern, Advisor to the South African Health Products Regulatory Authority, South Africa; Dr W. Wulandari, Indonesian Food and Drug Authority, Indonesia; and the International Federation of Pharmaceutical Manufacturers & Associations (sent by Dr C. Bardone, Sanofi Pasteur, and Dr M. Duchene, Johnson & Johnson).

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.

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1. Guidelines for the safe production and quality control of poliomyelitis vaccines. In: WHO Expert Committee on Biological Standardization: sixty-ninth report. Geneva: World Health Organization; 2019: Annex 4 (WHO Technical Report Series, No. 1016; https://www.who.int/biologicals/vaccines/Annex_4_WHO_TRS_1016_web4.pdf?ua=1, accessed 27 May 2020).
2. 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. Geneva: World Health Organization; 2015 (http://polioeradication.org/wp-content/uploads/2016/12/GAPIII_2014.pdf, accessed 27 May 2020).
3. Fourth meeting of the Containment Advisory Group. Geneva, Switzerland, 15–16 July 2019. Meeting report (<http://polioeradication.org/wp-content/uploads/2020/04/Fourth-meeting-of-the-Containment-Advisory-Group-2019071516.pdf>, accessed 12 May 2020).
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