

# **Smallpox eradication: destruction of variola virus stocks**

## **Report by the Secretariat**

1. The Executive Board at its 138th session noted an earlier version of this report.<sup>1</sup> The version of the report that follows has been updated (paragraphs 6, 7 and 13–19).

2. This document reports on work undertaken by the Secretariat in preparation for the Sixty-ninth World Health Assembly. It summarizes the conclusions of the Independent Advisory Group on Public Health Implications of Synthetic Biology Technology Related to Smallpox, which was established at the request of Member States and met in Geneva at the end of June 2015. It reports on the WHO's biosafety inspections of the two variola virus repositories in 2014–2015. It also summarizes the work being carried out on the operational framework for access to WHO's smallpox vaccine stockpile and the conclusions of the WHO Advisory Committee on Variola Virus Research (Geneva, 12 and 13 January 2016).

### **SECRETARIAT ACTIONS**

#### **Independent Advisory Group on Public Health Implications of Synthetic Biology Technology Related to Smallpox**

3. At the Sixty-seventh World Health Assembly, in May 2014, WHO was requested to provide additional information to the Health Assembly on the use and potential impact of technologies for synthetic biology on smallpox preparedness and control, to assist the Health Assembly in its deliberations on the timing of the destruction of existing variola virus stocks.<sup>2</sup>

4. In response to that request, the Secretariat convened a meeting of a group of experts – the Independent Advisory Group on Public Health Implications of Synthetic Biology Technology Related to Smallpox – to provide an up-to-date assessment of technologies for synthetic biology and their potential impact on smallpox preparedness and countermeasure development.

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<sup>1</sup> See document EB138/22 and the summary record of the Executive Board at its 138th session, seventh meeting, section 2 (document EB138/2016/REC/2).

<sup>2</sup> See document WHA67/2014/REC/3, summary record of the twelfth meeting of Committee A, section 8.

5. Prior to that meeting, the Secretariat convened a meeting of a Scientific Working Group, which was held in Geneva on 16 and 17 April 2015, with the aim of providing the Independent Advisory Group with the most current scientific information on synthetic biology technology with regard to the variola virus. The report of the Scientific Working Group served as the background document for the meeting of the Independent Advisory Group.
6. The Independent Advisory Group met in Geneva on 29 and 30 June 2015. It concluded that the risk of the re-emergence of smallpox has increased. The creation of variola virus using information on DNA sequences will be easier and cheaper in the future and may be possible in small laboratories with inadequate biosafety and biosecurity for handling variola virus.
7. The Independent Advisory Group therefore recommended: (1) to increase significantly preparedness efforts to ensure that early detection and rapid response capacities for a potential smallpox re-emergence are widely available; and (2) to revise the WHO regulations for the handling of variola virus (whole virus or fragments) with a special emphasis on biosafety and biosecurity rules to reduce and minimize the risk of a laboratory accident that may occur from the widespread use of synthetic biology technology.
8. The full report of the Independent Advisory Group, including the conclusions of the Scientific Working Group is available on the WHO website.<sup>1</sup>

### **Biosafety inspection of the repository sites**

9. WHO biosafety inspection teams visited and inspected the containment facilities at the two WHO collaborating centres that are the authorized repositories of variola virus: the State Research Centre for Virology and Biotechnology (Koltsovo, Novosibirsk Region, Russian Federation) and the Centers for Disease Control and Prevention (Atlanta, Georgia, United States of America), in December 2014 and May 2015 respectively. The final reports of these two biosafety inspections will soon be available on the WHO website.
10. The protocol that was used followed the European Committee for Standardization's Laboratory Biorisk Management Standard CWA 15793:2011, which covers 16 elements of laboratory biorisk management. The biosafety inspection visits of 2014–2015 confirmed that this approach allows for effective inspections of the repositories, helping to assure the wider community that the research therein is being done safely and securely, in line with the highest standards of biosafety and biosecurity. The WHO inspection team included international experts and WHO staff and involved the other repository's staff as observers. The inspections included discussions with the respective repository's staff and with senior management; a detailed review of the facility; a review of the updates and corrective actions taken since the last inspection; and a review of documents, records, regulatory instruments and other materials of relevance. The next biosafety inspections of the two repositories of variola virus are planned for 2016–2017.

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<sup>1</sup> The Independent Advisory Group on Public Health Implications of Synthetic Biology Technology Related to Smallpox: meeting report. Geneva: World Health Organization; 2015 (document WHO/HSE/PED/2015. 1; <http://www.who.int/csr/resources/publications/smallpox/synthetic-biology-technology-smallpox/en/>, accessed 5 April 2016).

## **Operational framework for access to WHO's smallpox vaccine stockpile**

11. Work continues on an operational framework for access to WHO's emergency stockpile of smallpox vaccine in response to a smallpox event. The framework includes legal considerations for donating smallpox vaccines, standard operating procedures for both donor countries and recipient countries, logistical requirements and a vaccine request form, with terms and conditions for the donation and reception of smallpox vaccines. The Secretariat has begun discussions with the national regulatory agencies of donating countries on the creation of a regulatory framework for the donation of smallpox vaccines.

## **WHO Advisory Committee on Variola Virus Research**

12. The Seventeenth meeting of the WHO Advisory Committee on Variola Virus Research was held in Geneva on 12 and 13 January 2016.

13. The Advisory Committee received reports on the virus collections held at the two authorized repositories of variola virus, in the Russian Federation and the United States of America. It was also provided with updates on the continuation of research projects using live variola virus for the development of diagnostic tests, animal models, smallpox vaccines, and antiviral and therapeutic agents. As concluded in the Fifteenth meeting of the Advisory Committee (24 and 25 September 2013),<sup>1</sup> the only new projects that have been approved are for antiviral agents against smallpox. The Advisory Committee discussed the estimated timelines for the ongoing research projects and expects that the completion and final review of these projects will take a minimum of three years.

14. The full report of the Advisory Committee is accessible on the WHO website.<sup>2</sup> The major conclusions are presented below.

15. The Advisory Committee noted the conclusion of the Independent Advisory Group on Public Health Implications of Synthetic Biology Technology Related to Smallpox that the nature of the risk of re-emergence of smallpox has changed significantly and is evolving.

16. The Advisory Committee concluded that there was no need to increase the number of sites where research using live variola virus could be undertaken beyond the two existing authorized global repositories. However, it recommended that more laboratories around the world should develop capacity for smallpox diagnostics which did not need live variola virus.

17. The Advisory Committee recognized the need for increased preparedness to deal with the potential consequences of the synthesis and possible re-emergence of variola virus and encouraged the expansion of expertise in the area of laboratory biosafety and biosecurity and diagnostics for this purpose.

18. Given the change in the risk of re-emergence of smallpox due to advances in synthetic biology technology, the Advisory Committee reviewed its terms of reference and concluded that they were broad enough to include the area of synthetic biology technology, if necessary. However, the Advisory

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<sup>1</sup> See document A67/37 and Report of the Fifteenth Meeting WHO Advisory Committee on Variola Virus Research ([http://www.who.int/csr/resources/publications/smallpox/WHO\\_HSE\\_PED\\_CED\\_2013\\_2/en/](http://www.who.int/csr/resources/publications/smallpox/WHO_HSE_PED_CED_2013_2/en/), accessed 5 April 2016).

<sup>2</sup> <http://www.who.int/csr/resources/publications/smallpox/variola-research-2016/en/> (accessed 21 April 2016).

Committee agreed that additional members, with appropriate expertise related to new technologies, such as synthetic biology, would be welcome. The Advisory Committee gave special attention in its review of the current research agenda to assessing whether there are or will be additional needs for smallpox control measures in case of re-emergence of a synthesized and/or modified variola virus.

19. Finally, as recommended by the Independent Advisory Group on on Public Health Implications of Synthetic Biology Technology Related to Smallpox, the Advisory Committee revised the *WHO recommendations concerning the distribution, handling and synthesis of variola virus DNA*, the text of which can be found on the WHO website.<sup>1</sup> The Advisory Committee specified that permission to express one or more variola virus genes must be sought from the Secretariat. The Advisory Committee further strongly recommended that the revised recommendations be widely distributed and adopted by Member States as part of their national biosafety regulations.

#### **ACTION BY THE HEALTH ASSEMBLY**

20. The Health Assembly is requested to note the report.

21. Given the minimum estimated timeline for the completion of ongoing, approved research, and the need for the Advisory Committee on Variola Virus Research to give further consideration to the implications of synthetic biology for the research agenda, the Secretariat proposes that the Health Assembly decide to include a substantive item entitled “Smallpox eradication: destruction of variola virus stocks” on the provisional agenda of the Seventy-second World Health Assembly.

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<sup>1</sup> [www.who.int/csr/disease/smallpox](http://www.who.int/csr/disease/smallpox).