



**GLOBAL
INFECTIOUS
HAZARDS
PREPAREDNESS**

WHO Advisory Committee on Variola Virus Research

Report of the twenty-first meeting,
Geneva, 30 October-1 November 2019



**World Health
Organization**

WHO Advisory Committee on Variola Virus Research

Report of the twenty-first meeting,
Geneva, 30 October-1 November 2019

WHO Advisory Committee on Variola Virus Research: report of the twenty-first meeting, Geneva, 30 October – 1 November 2019
ISBN 978-92-4-001299-8 (electronic version) ISBN 978-92-4-001300-1 (print version)

© World Health Organization 2020

Some rights reserved. This work is available under the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 IGO licence (CC BY-NC-SA 3.0 IGO; <https://creativecommons.org/licenses/by-nc-sa/3.0/igo>).

Under the terms of this licence, you may copy, redistribute and adapt the work for non-commercial purposes, provided the work is appropriately cited, as indicated below. In any use of this work, there should be no suggestion that WHO endorses any specific organization, products or services. The use of the WHO logo is not permitted. If you adapt the work, then you must license your work under the same or equivalent Creative Commons licence. If you create a translation of this work, you should add the following disclaimer along with the suggested citation: “This translation was not created by the World Health Organization (WHO). WHO is not responsible for the content or accuracy of this translation. The original English edition shall be the binding and authentic edition”.

Any mediation relating to disputes arising under the licence shall be conducted in accordance with the mediation rules of the World Intellectual Property Organization (<http://www.wipo.int/amc/en/mediation/rules/>).

Suggested citation. WHO Advisory Committee on Variola Virus Research: report of the twenty-first meeting, Geneva, Switzerland, 30 October-1 November 2019. Geneva: World Health Organization; 2020. Licence: [CC BY-NC-SA 3.0 IGO](#).

Cataloguing-in-Publication (CIP) data. CIP data are available at <http://apps.who.int/iris>.

Sales, rights and licensing. To purchase WHO publications, see <http://apps.who.int/bookorders>. To submit requests for commercial use and queries on rights and licensing, see <http://www.who.int/about/licensing>.

Third-party materials. If you wish to reuse material from this work that is attributed to a third party, such as tables, figures or images, it is your responsibility to determine whether permission is needed for that reuse and to obtain permission from the copyright holder. The risk of claims resulting from infringement of any third-party-owned component in the work rests solely with the user.

General disclaimers. The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of WHO concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

The mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by WHO in preference to others of a similar nature that are not mentioned. Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters.

All reasonable precautions have been taken by WHO to verify the information contained in this publication. However, the published material is being distributed without warranty of any kind, either expressed or implied. The responsibility for the interpretation and use of the material lies with the reader. In no event shall WHO be liable for damages arising from its use.

This publication contains the collective views of the twenty-first meeting of the WHO Advisory Committee on Variola Virus Research and does not necessarily represent the decisions or the policies of WHO.

Contents

<i>EXECUTIVE SUMMARY</i>	<i>iv</i>
<i>MEETING PROCEEDINGS.....</i>	<i>1</i>
Secretariat report.....	1
Variola virus repository reports.....	3
Research reports.....	4
Events, innovations and public health benefit of research	18
Public health benefit of smallpox countermeasures for monkeypox	20
Orthopoxvirus laboratory collaboration	23
<i>PROGRAMME OF RESEARCH</i>	<i>25</i>
<i>RECOMMENDATIONS.....</i>	<i>27</i>
<i>ANNEXES</i>	<i>28</i>
Annex 1 Agenda.....	28
Annex 2 List of participants.....	32
Annex 3 Research proposals for 2020	36
Annex 4 Abstracts of presentations.....	39

EXECUTIVE SUMMARY

The World Health Organization (WHO) Advisory Committee on Variola Virus Research (ACVVR) held its twenty-first meeting from 30 October to 1 November 2019 at WHO headquarters in Geneva, following the conclusion of the May 2019 seventy-second World Health Assembly (WHA) to allow retention of variola virus stocks to advance development of smallpox countermeasures for outbreak preparedness.

Variola virus repositories

The Committee received reports on the variola virus collections held at the authorized repositories at the State Research Centre of Virology and Biotechnology (VECTOR), Koltsovo, Novosibirsk Oblast, Russian Federation and at the Centers for Disease Control and Prevention (CDC), Atlanta, Georgia, the United States of America.

Research update

The Committee received detailed reports on the progress of approved research using live variola virus. Research proposals had been received in 2019 from the two WHO collaborating centres authorized to hold variola virus, the United States Centers for Disease Control and Prevention and VECTOR. Proposals for continuing or new projects were presented for 2020 within the broader context of research goals for a three-year period to 2022.

Antiviral agents

The Committee received progress reports on approved antiviral agent research on antiviral agents. Additional studies on the only approved smallpox antiviral tecovirimat are approaching completion. The United States Centers for Disease Control and Prevention proposes study of a new antiviral agent, ST-357. VECTOR expects to achieve licensure of NIOCH-14 in the Russian Federation by 2022 and proposes to continue preclinical evaluation of other compounds. Both centres propose continuing to explore individual, or mixtures of, monoclonal antibodies as alternative avenues to treatment of smallpox, and several studies look promising. The United States Centers for Disease Control and Prevention continues to characterize mouse models susceptible to systemic variola virus infection for evaluating antiviral agents.

Vaccines

Development of vaccinia-based vaccines against smallpox continues, with the primary objective being to enhance vaccine safety and a main challenge being to ascertain correlates of effectiveness. A modified vaccinia Ankara (MVA) vaccine licensed in the EU and Canada against smallpox was approved in the US in September 2019 for prevention of smallpox and monkeypox, the first vaccine approved for monkeypox. VECTOR continues to develop an attenuated 4th generation vaccine, VacDelta6, with Phase 1, 2 and 3 trials planned and licensing expected by 2022. Japan continues to study the 3rd generation vaccine LC16m8, licensed for prevention of smallpox, to ensure protectiveness in an outbreak.

Diagnostics

With respect to diagnostics, polymerase chain reaction (PCR)-based detection systems approved by the US FDA or licensed in the Russian Federation have the capacity to detect and distinguish variola virus from other orthopoxviruses. It was recommended that work continue to transition the technology to new platforms to keep it up to date. Work for protein-based point of care assays was presented and discussed.

Paleogenomics

The Committee discussed the emerging issue of paleogenomic research in human remains, where variola virus DNA may be the subject of investigation or an incidental finding. The Committee observed that the WHO Recommendations on the distribution, handling, and synthesis of variola virus DNA prohibit retention of more than 20% of the variola virus genome in any single place except for the two approved WHO collaborating centers. It also noted that the highly fragmented DNA found in ancient samples did not represent a risk to human health. It was recognized that further guidance was needed for laboratories undertaking this type of work and that WHO Recommendations concerning variola virus DNA will need revision.

Monkeypox

The Committee reviewed updates on monkeypox emergence in affected countries and discussed the application of smallpox medical countermeasures to monkeypox prevention and control, including a vaccine study underway in the Democratic Republic of the Congo, and a proposed a field study of the antiviral tecovirimat in the Central African Republic. The Committee expressed interest in continuing discussions to develop orthopoxvirus laboratory collaboration in a form which would cover both smallpox and monkeypox diagnostic capacity.

Smallpox archives

The Committee was informed that the WHO Smallpox Archives had been inscribed in the United Nations Educational, Scientific and Cultural Organization Memory of the World Register in 2017. WHO had announced plans to commemorate the fortieth anniversary of the declaration of smallpox eradication. All participants of the twenty-first Committee meeting were invited to visit the WHO Smallpox Archives on the third meeting day.

Conclusion

The Committee expressed support for the continued development of antiviral agents against smallpox to supplement the single approved agent to date. The Committee noted progress on monoclonal antibodies as well as their limited applicability for outbreak response currently. The Committee agreed to recommend that work continue for those vaccines already in development. The Committee noted that point-of-care tests are desirable but was split as to whether the use of live variola virus for this work is essential.

Research not already approved during the meeting would be reviewed in detail by the Committee following written submission of proposals.

Other recommendations offered by the Committee are summarized in this report.

MEETING PROCEEDINGS

Secretariat report

1. Opening of the meeting

The twenty-first meeting of the WHO Advisory Committee on Variola Virus Research (hereinafter referred to as “Committee”) was held at WHO headquarters, Geneva, Switzerland from 30 October to 1 November 2019. The meeting was chaired by Professor Geoffrey L. Smith and Dr Supamit Chunsuttiwat served as session chair on the third day. The rapporteur was Dr Nina Mattock. The agenda is appended as Annex 1 and the list of participants as Annex 2.

The objectives of the meeting were to:

- Review progress of approved research with live variola virus
- Discuss the public health benefit of approved smallpox research and identify emerging issues
- Agree on a research programme and recommendations for 2019–2022

Dr Mike Ryan, Executive Director, WHO Health Emergencies Programme opened the meeting. He recalled that the Committee had performed important functions since 1999, and that we are now 40 years on from the eradication of smallpox. Nonetheless, there was genuine concern that we were in an era of increasing biologic risk, in part due to advances in technology. Therefore, it was important now to reflect on how the global community scrutinized all research projects, including those involving variola virus. Citing the reemergence of monkeypox, he mentioned that opportunities were presenting themselves, such as how the countermeasures developed over the last 20 years could be useful for other orthopoxviruses, as well as the need to continue to encourage better networking between laboratories. Dr Ryan appreciated the coordination and communication in two recent incidents (mentioned below) and said that although biologic risk remained, we were now in a better position to manage it. Due to rapidly changing technology and new areas of research, WHO would seek

预览已结束，完整报告链接和二维码如下：

https://www.yunbaogao.cn/report/index/report?reportId=5_24977

