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WHO Advisory Committee on Variola Virus Research

Report of the Twentieth Meeting

Geneva, Switzerland

26 – 27 September 2018

INFECTIOUS HAZARDS MANAGEMENT

World Health Organization

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EXECUTIVE SUMMARY

The Advisory Committee on Variola Virus Research held its twentieth meeting on 26 and 27 September 2018 at WHO headquarters in Geneva. The Committee acknowledged its role in preparing for the discussion on smallpox at the Seventy-Second World Health Assembly in May 2019 by reviewing progress on the live variola virus research agenda.

Achievements and considerations for variola virus research

The Committee unanimously recognized the extraordinary achievements of the research using live variola virus it had authorized, and considered that it continues to meet its commitments to ensure the delivery of medical countermeasures against smallpox.

As a result of the scientific work done under its auspices, Member States now have a range of public health tools to respond to a re-emergence of smallpox, which may also benefit the diagnosis, prevention and treatment of other orthopoxvirus infections. Most attending members of the Committee considered that live variola virus is needed for further development of antiviral agents.

Variola virus repositories

The Committee received reports on the status of the variola virus collections held at the two WHO Collaborating Centres that are authorized as repositories of variola virus, the Centers for Disease Control and Prevention (CDC), Atlanta, Georgia, United States of America, and the State Research Centre of Virology and Biotechnology (VECTOR), Koltsovo, Novosibirsk Oblast, Russian Federation. The number of stocks remained unchanged from last year in both repositories.

The reports of the respective repository inspections in the 2016-2017 cycle have been published. For the next cycle, inspections are planned for VECTOR in January 2019 and for CDC in May 2019.

Global health security

The Committee was informed that the WHO Smallpox Vaccine Emergency Stockpile remained unchanged in size and composition from the previous year and that the Secretariat was planning simulation exercises to test the procedures for the emergency use of smallpox vaccines.

The Committee acknowledged the establishment of the WHO Strategic and Technical Advisory Group for Infectious Hazards, whose remit included diseases that could threaten global health security, such as smallpox. The Committee appreciated receiving information on a monkeypox outbreak in Nigeria, as smallpox medical countermeasures could be relevant for monkeypox control.

Research update

The Committee received detailed updates on the progress of previously approved research using live variola virus. Ten research proposals had been received in 2018 from the two WHO Collaborating Centres authorized to hold variola virus. The Committee suggested that the work for one of the projects be undertaken collaboratively by the two Collaborating Centres.

Diagnostics

Researchers at VECTOR reported on development and use of a new multiplex real-time PCR technique and reagent kit for species-specific identification of human pathogenic orthopoxviruses and described investigation of variola virus strains from geographical regions not previously studied.

CDC researchers reported the development of multiplexed assays specific for variola virus for application in automated diagnostic platforms for use in remote areas and protein-based tests for variola virus. CDC was collaborating with partners in the Democratic Republic of the Congo on the field application of a commercial assay to detect monkeypoxvirus.

Antiviral agents

The Committee received updates on research on antiviral agents. An oral formulation of tecovirimat was approved for treatment of smallpox by the US Food and Drug Administration (FDA) in July 2018. The manufacturer was also developing an intravenous formulation.

Researchers at VECTOR continue to develop NIOCH-14, a compound that is structurally similar to tecovirimat, as well as a range chemical compounds and monoclonal antibodies.

Researchers at CDC are investigating monoclonal antibodies and mixtures thereof to neutralize variola virus in vitro and undertaking post-exposure prophylaxis efficacy studies in animals. CDC researchers are assessing the usefulness of humanized mice for evaluating anti-variola virus agents.

The manufacturer of brincidofovir reported progress on development of this an agent that acts against variola virus by a different mechanism to that of tecovirimat. It is available in liquid and tablet form, with an intravenous formulation in development. The activity profile of this antiviral includes inhibition of orthopoxvirus replication.

Vaccines

With regard to vaccines, researchers at VECTOR had engineered a strain of vaccinia virus that was more immunogenic than the parent strain and led to reduced reactogenicity.

Researchers at both CDC and VECTOR have been investigating the neutralizing activity of sera of vaccinated subjects and animals, with CDC optimizing an assay to support vaccine studies.

A non-inferiority trial of two smallpox vaccines suggested that the MVA vaccine may be used in some subjects for whom ACAM2000 may pose some residual risk.

Following a transfer of business in Japan, the new manufacturer of the third-generation smallpox vaccine LC16m8 assured the Committee that it would continue producing vaccine for national and WHO stockpiles.

Approval of smallpox countermeasures

An overview was given of FDA's role in the development of smallpox medical countermeasures for approval, licensure or clearance, highlighting recent landmarks including approval of a real-time PCR