WHO/CDS/CSR/GAR/2003.5

WHO Advisory Committee *on* Variola Virus Research

Report of the Fourth Meeting

GENEVA, SWITZERLAND
20–21 NOVEMBER 2002

WORLD HEALTH ORGANIZATION
DEPARTMENT OF COMMUNICABLE DISEASE
SURVEILLANCE AND RESPONSE

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Summary

The WHO Advisory Committee on Variola Virus Research reviewed progress of research involving live *Variola virus*. Considerable progress has been made during the past year but it is clear that further high priority research is still necessary. Significant advances have been made in the characterization of the *Variola virus* strains held in each repository and in the methodologies associated with virus detection and smallpox diagnosis. Work on the further refinement of the non-human primate model of smallpox is proceeding. This model is being used to assess existing antiviral compounds and there is a drug discovery programme underway. The Committee made the following recommendations:

- Inventory systems across both repositories should be standardized and improved. These inventories should be shared between the two repositories and the information reported in both hard copy and electronic formats to WHO at least once each year (paragraph 2.3).

- Records on material used for work in progress should be available for inspection and audit. The volumes of live virus suspensions generated as a result of this work should be kept to the minimum needed to successfully complete the agreed studies (paragraph 2.3).

- Where possible, information on the origin, biological properties, passage history and other characteristics of the material held in each repository should be included as part of the inventory. WHO agreed to seek information from archival records about the derivation of some of the isolates held in each collection (paragraph 2.4).

- Isolates for which there is no scientific justification for retention (particularly the chimeric and non-variola viruses held in the Centers for Disease Control and Prevention (CDC) repository) should be destroyed after informing the original donating countries of this intention (paragraph 2.4).

- Further consideration should be given to sequence analyses on additional material derived from authenticated clinical material without prior cloning (paragraph 3.3).

- Further work should be done to refine the primate model of human smallpox to facilitate its better use in assessments of candidate vaccines and antiviral agents (paragraph 7.3).

- A technical panel, containing relevant safety experts, should be convened to consider and revise the existing guidelines on the simultaneous handling of different orthopoxvirus strains with *Variola virus* (paragraph 2.5).

- This technical panel should also be charged with developing appropriate guidance on the supply of cloned DNA fragments, taking into account advances that have been made in oligonucleotide synthesis, and the possibility to modify DNA fragments of other orthopoxviruses by site-directed mutagenesis to produce the corresponding *Variola virus* gene sequence (paragraphs 5.4 and 9.4).

- Laboratories conducting approved research should produce written annual progress reports that can be disseminated to the wider scientific community in due course. Wherever possible, this research should be published in the open peer-reviewed literature (paragraph 9.5).

1. Introduction

1.1 Dr David Heymann, Executive Director, WHO Programme on Communicable Diseases welcomed participants to the meeting and asked the Committee to review progress on research using live *Variola virus* that has been conducted since its last meeting. He reminded Committee members that they had been charged with determining what research, if any, must be carried out in order to reach global consensus on the timing for the destruction of existing *Variola virus* stocks and advise WHO accordingly.

1.2 Dr Peter Greenaway was appointed Chairman and Dr Robert Drillien was appointed Rapporteur. The meeting agenda is given in Annex 1 and the meeting participants are listed in Annex 2. The meeting heard presentations from scientists from the United States of America, the United Kingdom of Great Britain and Northern Ireland and the Russian Federation who were directly involved in WHO approved research that required access to stocks of live variola viruses.

2. Update on *Variola virus* strains held in the two repositories

2.1 The VECTOR laboratory in Koltsovo, Russian Federation, reminded the Committee that their collection contains 120 samples of *Variola virus* either as passaged virus or as primary clinical specimens from various geographic areas. Some 55 isolates have been selected for further analysis. This has involved viability studies in tissue cultures or chick embryos, biological characterization and genome analysis. Of the 39 isolates studied so far only 29 were shown to be viable. DNA has been isolated from the two non-viable isolates.

2.2 The CDC laboratory in Atlanta reported progress on their analysis of a collection containing 451 isolates. It was noted that a number of these isolates are not *Variola virus* but rather *Monkeypox virus, Camelpox virus* or recombinants between *Variola virus* and other orthopoxviruses. The geographic origin and year of isolation are known for some 229 isolates. Forty-six out of the 50 isolates selected for further study on the basis of year of isolation, region of isolation, passage history and clinical information available were subsequently shown to be viable.

2.3 During these talks it became clear that systems were needed for the better audit of isolates contained within both repositories. It was therefore recommended that inventory systems across both repositories should be standardized and improved, that these inventories