WORLD HEALTH ORGANIZATION

FIFTY-EIGHTH WORLD HEALTH ASSEMBLY A58/10
Provisional agenda item 13.6 14 April 2005

Smallpox

Destruction of variola virus stocks

Report by the Secretariat

1. Resolution WHA55.15 authorized the further temporary retention of the existing stocks of live variola virus, held at two locations,[1] on the understanding that all approved research would remain outcome-oriented and time-limited. The resolution requested the Director-General to continue the work of the WHO Advisory Committee on Variola Virus Research, and to report annually to the Health Assembly, through the Executive Board, on what research, if any, must be carried out in order to reach consensus on the timing of destruction of virus stocks.

2. At its sixth meeting (Geneva, 4-5 November 2004) the Advisory Committee reviewed data on the inventory of variola viruses held at the two locations and was satisfied that stocks were maintained with appropriate safeguards in place.

3. The Committee concluded that the need for sequence analysis of variola virus DNA and for rapid, sensitive and reliable diagnostic tests had been met; no further research requiring access to live variola virus was considered essential for these purposes.

4. The Committee reaffirmed the need to develop better vaccines and antiviral drugs. Access to live variola virus remains necessary in order to assess the efficacy of new vaccines and antiviral drugs and, ultimately, to obtain regulatory approval. Progress in both areas was considered satisfactory, notably in developing a safer vaccine, based on a modified Ankara strain of vaccinia virus, and in moving towards licensing of the antiviral drug, cidofovir.

5. Work to develop an animal model for smallpox continued to encounter problems. The high doses of virus needed to induce disease in the most promising model (intravenous injection in cynomolgus monkeys) resulted in direct onset of the viraemic stage, bypassing the normal incubation and prodromal phases seen in humans.

6. The Committee considered the safety and scientific value of proposed experiments and procedural changes that might expedite the development of new antiviral drugs, yet were precluded by guidelines issued by the Ad Hoc Committee on Orthopoxvirus Infections in 1994.[2] The Committee

[1] Centers for Disease Control and Prevention, Atlanta, Georgia, United States of America, and the Russian State Centre for Research on Virology and Biotechnology, Koltsovo, Novosibirsk Region, Russian Federation.

[2] Document WHO/CDS/BVI/94.3, (accessible at: http://whqlibdoc.who.int/hq/1994/WHO_CDS_BVI_94.3.pdf).

acknowledged that technological advances since the guidelines were issued may have altered their relevance.

7. The Committee issued advice and recommendations for permissible research in five areas: (a) distribution of variola virus DNA between laboratories; (b) simultaneous handling of variola virus and other orthopoxviruses; (c) in vitro synthesis of variola virus DNA and mutagenesis of orthopoxvirus DNA; (d) expression of individual variola virus genes in other orthopoxviruses; and (e) generation of a variola virus expressing a green fluorescent marker protein.

8. The Committee recommended extending permissible distribution of variola virus DNA to include chips containing minute amounts of multiple short fragments of variola virus DNA, irreversibly bound to a solid support. To facilitate drug screening, the Committee recommended that the two repositories be allowed to handle variola virus simultaneously with other orthopoxviruses, provided that certain strict conditions are met. Attempts to synthesize full-length variola virus genomes or infectious variola viruses from smaller DNA fragments remain strictly prohibited. In vitro synthesis of variola virus DNA exceeding a designated length requires explicit authorization by WHO, as does mutagenesis of orthopoxvirus DNA, larger than a designated length, with the aim of producing the corresponding variola virus sequence.

9. The Committee recommended that the expression of individual variola virus genes in other orthopoxviruses might be permitted, in order to obviate the use of live variola virus and facilitate the development of antiviral drugs, provided that several conditions are met. The Committee further recommended permission to generate a variola virus expressing the green fluorescent marker protein, in designated conditions in the two repositories, to accelerate screening for antiviral drugs. Such work could only be performed following approval by WHO.

10. The implications of these recommendations, which are explained in greater detail in the Committee's full report,[1] have been reviewed by the Director-General. Concerning the recommended permission, under certain conditions, to allow the expression of individual variola virus genes in other orthopoxviruses, the Director-General appreciated the need to expedite the development of antiviral drugs and vaccines in ways that do not require use of live variola virus. Nevertheless, as such research could have broader implications, including certain biosafety and biosecurity concerns, the Director-General recommended that this issue should be reconsidered by the Committee at its next meeting.

ACTION BY THE HEALTH ASSEMBLY

11. The Health Assembly is invited to note the above report.

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[1] Reports of the Committee's meetings and abstracts summarizing recent research are accessible at: http://who.int/csr/disease/smallpox/research/en/.