



**World Health Organization
Organisation mondiale de la Santé**

EXECUTIVE BOARD
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**Smallpox eradication: report of the
Ad Hoc Committee on Orthopoxvirus
Infections**

Report by the Director-General

This report contains a brief outline of one of the major issues remaining after the declaration of the global eradication of smallpox in 1980 - the retention or destruction of the last known stocks of variola virus kept in two WHO collaborating centres. The attention of the Board is drawn to the recommendation of the *Ad Hoc* Committee on Orthopoxvirus Infections to destroy these stocks of variola virus. The Board is invited to consider suggestions for a draft resolution for submission to the Health Assembly.

BACKGROUND

1. Since the global eradication of smallpox was declared on 8 May 1980, the stock of variola viruses has been gradually reduced and is now restricted to two WHO collaborating centres on smallpox and other poxvirus infections designated at the Centers for Disease Control and Prevention, Atlanta, Georgia, USA, and at the Institute for Viral Preparations, Moscow, Russian Federation.
2. The members of the Committee on Orthopoxvirus Infections which met in March 1986 unanimously recommended the destruction of the virus stocks kept in the two laboratories. The Committee noted that the variola gene pool could be cloned into non-expressing sites of bacterial plasmids for future studies of variola virus and that archival records of variola virus would be satisfied by such cloned DNA. The Committee also considered that the cloned DNA would provide sufficient reference material to resolve any future diagnostic problem involving suspected smallpox.
3. The meeting of the *Ad Hoc* Committee on Orthopoxvirus Infections in December 1990 confirmed the recommendation and proposed a deadline of 31 December 1993 for the destruction. The Committee recommended that, in the meantime, the complete nucleotide sequence of the genome of at least one variola virus strain should be determined. It considered that the sequence information might represent a useful and potentially safer record than the cloned material for archival purposes.

STOCKS OF VARIOLA VIRUS: RECENT DEVELOPMENTS

4. The WHO Technical Committee on the Analysis of Nucleotide Sequences of Variola Virus Genomes reviewed the data obtained in the sequencing project at a meeting in January 1994. It acknowledged that the information obtained in the project exceeded the minimum requested by WHO.

5. The publication of the *Ad Hoc* Committee's recommendation to destroy the variola viruses had, however, given rise to mixed reactions among the public and in the scientific community. Diverging views attracted the attention of the media and were the subject of letters to WHO showing people's concern. The question was therefore given a frank and open airing at a round-table discussion organized in conjunction with the IX International Congress of Virology in Glasgow in August 1993, where scientists with opposing views were invited to make them public.

6. The arguments as they appeared in the media, in the scientific literature, during the Glasgow conference or otherwise communicated to WHO can be summarized as follows:

Against destruction:

- all possibility of future studies on the variola virus will be lost (properties of viral genes and proteins, biological functions of the virus, pathogenesis, etc.);
- destruction of the viruses in the two known repositories does not guarantee the complete removal of the virus from the earth (preserved corpses of smallpox cases, forgotten or hidden stocks elsewhere);

For destruction:

- the escape of the virus from the laboratories would be a serious risk as an increasing proportion of the population lacks immunity to the disease since cessation of vaccination and revaccination against smallpox more than 10 years ago;
- the sequence information and the cloned DNA fragments of the full genome of several strains of variola virus allow most scientific questions about the properties of the viral genes and proteins to be solved. The cloned DNA fragments of the virus genome are non-infectious and can be handled in safety;
- the decision to eradicate smallpox was a collective decision of the world community, based on public health considerations.

7. In view of the controversy over this crucial subject and the fact that the destruction of the virus is irrevocable, WHO once more asked the advice of the *Ad Hoc* Committee on Orthopoxvirus Infections, bearing in mind the arguments raised since the meeting in December 1990.

8. The *Ad Hoc* Committee discussed the issues related to the destruction of the last stocks of variola virus thoroughly during a meeting on 9 September 1994. It unanimously agreed that at some date all remaining stocks of variola and whitepox viruses, viral genomic DNA and clinical specimens and other material containing infectious material should be destroyed.¹

9. There was debate over the date on which destruction should occur. The majority of members of the *Ad hoc* Committee favoured early destruction and considered that the genomic sequence information from several strains of variola virus, with the availability of other sequences cloned in bacterial plasmids, satisfied the need for an archival record of the virus. They noted that these cloned DNA fragments would provide sufficient reference material to resolve any future diagnostic problem involving suspected smallpox and allowed for future studies of properties of variola virus genes and proteins. They also stressed that escape of variola virus from the laboratory would be a serious risk to the increasing proportion of the population that

¹ The report of the meeting (document CDS/BVI/94.3) is available in English.

lacks immunity to smallpox. Destruction of the stocks of variola virus kept in the two WHO collaborating centres was seen as the last step in the complete and final global eradication of smallpox.

10. Members of the *Ad Hoc* Committee (2/10) in favour of postponing destruction of the virus recommended that the archival storage of variola virus be continued in the two collaborating centres. They considered that the rapid advances in science and technology now occurring would enable new questions to be addressed in the future and that it was therefore too early to take this irrevocable step. They urged that serious consideration be given to storing the virus for a further five years.

11. In conclusion, the majority (8/10) of the members of the *Ad Hoc* Committee on Orthopoxvirus Infections recommended that the remaining stocks of variola virus, including whitepox virus, viral genomic DNA and clinical specimens and other materials containing infectious variola virus held in the WHO collaborating centres for smallpox and other poxvirus infections in the Centers for Disease Control and Prevention, Atlanta, Georgia, USA, and in the Institute for Viral Preparations, Moscow, Russian Federation, should be destroyed in both centres on Friday 30 June 1995. Recommendations on the procedure for destroying the variola virus, the establishment of a commission for the certification of the destruction and the text of the certificate can be found in the report of the Committee.

KEEPING OF CLONED MATERIAL

12. Cloned DNA fragments of the variola virus genome are themselves not infectious but safe and provide a useful resource and tool for analysing variola virus genes and protein structure and function. The majority (9/10) of the members of the *Ad Hoc* Committee recommended that such cloned material be kept. The Committee also recommended the establishment of two international repositories for the storage, maintenance, distribution and monitoring of the cloned DNA fragments of the variola virus genome - one at the WHO Collaborating Centre for Smallpox and other Poxvirus Infections, Centers for Disease Control and Prevention, Atlanta, Georgia, USA and the second at the Russian State Research Centre of Virology and Biotechnology, Koltsovo, Novosibirsk Region, Russian Federation.

13. The *Ad Hoc* Committee formulated the terms of reference of these repositories and made recommendations on the handling of cloned DNA fragments of variola virus genome.

FURTHER CHARACTERIZATION OF ORTHOPOXVIRUS NUCLEOTIDE SEQUENCES

14. Following these deliberations the *Ad Hoc* Committee reviewed the programme of work currently in progress and recommended that further characterization of additional orthopoxvirus nucleotide sequences and the preparation of archival material should be given priority.

RESERVE OF SMALLPOX VACCINE

15. The *Ad Hoc* Committee also recommended that 500 000 doses of smallpox vaccine should be kept by WHO in case of an emergency and that the smallpox vaccine seed virus (vaccinia virus strain Lister Elstree) be maintained in the WHO Collaborating Centre on Smallpox Vaccine at the National Institute of Public Health and Environmental Protection, Bilthoven, Netherlands.

ACTION BY THE EXECUTIVE BOARD

16. The Executive Board is invited to consider the following draft resolution on destruction of variola virus stocks recommending a resolution for submission to, and adoption by, the Forty-eighth World Health Assembly:

The Executive Board

RECOMMENDS the following resolution for adoption by the Forty-eighth World Health Assembly:

The Forty-eighth World Health Assembly,

Noting that on 8 May 1980 the Thirty-third World Health Assembly in resolution WHA33.3 declared the global eradication of smallpox and that the stock of variola virus has since been reduced and restricted to two WHO collaborating centres on smallpox and other poxvirus infections designated at the Centers for Disease Control and Prevention, Atlanta, Georgia, USA, and the Institute for Viral Preparations, Moscow, Russian Federation;

Recognizing that sequence information of the genome of several variola virus strains and the cloned DNA fragments of genome of variola virus allow most scientific questions about the properties of the viral genes and proteins to be solved as well as any problem with diagnosis of suspected smallpox and that the escape of variola virus from laboratories would be a serious risk as an increasing proportion of the population lack immunity to smallpox,

RECOMMENDS that the remaining stocks of variola virus, including all whitepox viruses, viral genomic DNA sequences, clinical specimens and other material containing infectious variola virus held in the WHO collaborating centres on smallpox and other poxvirus infections designated at the Centers for Disease Control and Prevention, Atlanta, Georgia, USA, and the Institute for Viral Preparations, Moscow, Russian Federation, be destroyed in both collaborating centres on 30 June 1995.

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