WORLD HEALTH ORGANIZATION

ORGANISATION MONDIALE DE LA SANTÉ

SME/77.2

REPORT OF A WORKSHOP MEETING ON SAFETY MEASURES IN LABORATORIES RETAINING VARIOLA VIRUS

Geneva, 1-4 August 1977

1.0 Introduction

With the interruption of smallpox transmission expected to occur in the near future, the only known source of variola virus and potential for smallpox epidemics will be in laboratories maintaining the virus. Following the recommendation of the 30th World Health Assembly (1977) that variola virus be retained only by World Health Organization (WHO) Collaborating Centres under conditions ensuring maximum safety, WHO convened a group of experts (Annex 1) to consider safety standards for the maintenance and use of variola virus in laboratories. The group recognized the need to retain a minimum number of such laboratories for archival, diagnostic and research purposes.

1.1 Objectives

The objectives of the meeting were to define physical containment standards for maintaining the virus, establish requirements to ensure the safety of personnel and propose administrative control measures. The group formulated recommendations addressed to these objectives and, with WHO, strongly urges that national safety measures for containing variola virus in laboratories embody these recommendations.

1.2 Laboratories with variola virus

Since 1975 WHO queried 181 countries and territories in the world regarding maintenance of stocks of variola virus in laboratories within these countries and territories. One hundred and seventy six of these countries and territories have responded as of 31 July 1977 and it is expected that the remaining countries (Cape Verde, China, Comoros, Democratic Kampuchea and Seychelles)* will respond shortly. Of 823 laboratories contacted, 74 reported that they retained variola virus. Fifty-seven of these transferred or destroyed their strains of variola leaving 17 known laboratories currently maintaining this virus (Annex 2).

2.0 Agents subject to safety recommendations

2.1 Variola and whitepox viruses

Among the orthopoxviruses only variola virus is recognized as a highly dangerous pathogen but because whitepox virus is currently indistinguishable from variola it too must be subject to these safety measures.

*The Comoros and Seychelles report that variola virus is not retained in laboratories (26 September 1977)

2.2 Other orthopoxviruses

Monkeypox and vaccinia viruses pose no major public health danger. Although suitable precautions, including vaccination, should be taken by personnel working with these and other orthopoxviruses, they need not be subject to the same safety measures as variola and whitepox viruses.

3.0 Numbers and functions of laboratories

Risk is directly related to the number of laboratories maintaining variola virus stocks. It was recommended that only the WHO Collaborating Centres for Poxvirus Research and the WHO Collaborating Centre for Smallpox Vaccine (hereinafter called WHO Centres) be repositories of variola virus and this number should be subject to periodic review. Further recommendations were:

3.1 Archival

Only WHO Collaborating Centres should maintain variola virus for archival purposes and there should be assurance that a representative group of strains will be retained for the future.

3.2 Diagnostic

The laboratories at the Viral Exanthems Branch, CDC, Atlanta, and the Laboratory of Smallpox Prophylaxis, Research Institute of Virus Preparations, Moscow, should continue as the principal WHO Centres for diagnosis of suspect human smallpox cases.

3.3 Research

3.3.1 The use of variola for research purposes should be restricted to only the two institutions cited above and in three other WHO Centres (Rijks Instituut voor de Volksgezondheid, Bilthoven, Netherlands; Virology Department, the Wright-Fleming Institute of Microbiology, St Mary's Hospital Medical School, London; Poxvirus Laboratory, Department of Enteroviruses, National Institute of Health, Tokyo).

However, should national authorities deem smallpox research necessary in their institutions, the WHO should be notified and be assured that the physical containment system of the laboratory and the personnel safety measures meet the standard safety requirements. However, it is urged that national authorities and their institutions follow the procedures presented in section 3.3.2.

3.3.2 It is strongly recommended that all other institutions maintaining variola virus destroy these stocks or transfer them to one of the above-mentioned WHO Centres; they should be informed that the WHO Centres would accept visiting investigators who wish to work with variola if the research protocol involves the differentiation of variola and whitepox viruses, differentiation of antibodies to variola virus from antibodies to other poxviruses, and comparison of variola viruses and monkey pox viruses. Other research projects for which there is no possible substitute for variola virus should not be excluded.

4.0 Recommended safety procedures pertaining to physical construction and administration of laboratories with variola virus

4.1 Physical containment

A place authorized to hold, or work with, variola virus stocks (hereinafter called the laboratory) must be constructed and operated in such manner to prevent dissemination of variola virus. Experiments involving smallpox virus shall be confined to work areas in a laboratory of the type designed to contain microorganisms that are extremely hazardous to man or may cause serious epidemic disease. The laboratory is either a separate building or it is a controlled area, within a building, which is isolated from all other areas of the building. Access to the laboratory is under strict control, excluding entry of unauthorized persons. Requirements for laboratories holding and working with variola are:

4.1.1 Imperviously sealed walls, floors and ceilings in which all penetrations (such as for air ducts, electrical conduits, and utility pipes) are sealed to assure the physical isolation of the work area and to facilitate housekeeping and space decontamination.

4.1.2 Air locks through which supplies and material can be brought into the laboratory without breach of containment.

4.1.3 Contiguous clothing change and shower rooms through which personnel enter into and exit from the laboratory.

4.1.4 Double-door autoclaves to sterilize and safely remove wastes and other materials from the laboratory.

4.1.5 A biowaste treatment system to decontaminate liquid effluents if laboratory drains are installed.

4.1.6 A separate ventilation system which maintains negative air pressures and directional air flow within the laboratory.

4.1.7 Passage of supply air through a prefilter and high efficiency particulate air (HEPA) filter before entering the laboratory. Exhaust air should be decontaminated by passage through two HEPA filters before discharge to the atmosphere.

4.1.8 All primary doors leading into the laboratory are always locked except when in use, making entry of unauthorized persons impossible. The laboratory director controls the keys.

4.1.9 Rooms for animals infected with variola virus and diagnostic cultures kept locked.

4.1.10 A biohazard warning sign on all exterior doors of the laboratory and a list of authorized personnel posted on the entries.

4.1.11 Laboratory windows not accessible from the outside of the building.

4.1.12 Biological safety cabinets to prevent release of virus into the air of the room.

4.1.13 Windows from which all parts of the laboratory can be seen.

4.1.14 Special biocontainment procedures for personnel and environmental protection used for animals.

4.1.15 Appropriate design and operational measures employed to prevent and eliminate introduction of insects, rodents and other pests.

4.2 Storage

For security and biocontainment reasons, storage of variola and whitepox viruses, as well as their handling, must be subject to the physical containment requirements described in section 4.1. Secure storage is considered part of standard laboratory procedure and should be described in the laboratory operations manual. Containers of variola virus must be locked when not in use.

4.3 Administrative control

4.3.1 Responsibility, authority and compliance

An effective safety system defines clear lines of responsibility and authority. It is appreciated that different countries have different methods for ensuring safety. The day-to-day safety in the laboratory is the responsibility of the laboratory director, who is responsible to national health authorities. National authorities should delegate a local safety committee to ensure compliance with established standards. The local safety committee should be independent of the management structure of the laboratory itself. The local committee should submit yearly reports to national authorities. WHO should be informed of the safety measures in each country and will be available to consult on such matters. WHO will devise a safety report form which the laboratories will be requested to submit yearly.

4.3.2 The authorization to receive, maintain and use variola virus shall be issued by national authorities and only to WHO Centres. This authorization should be obtained in writing and WHO should be kept informed of all such authorizations issued.

4.3.3 Personnel

Only personnel authorized by the director shall enter the laboratory and these persons shall be indicated on a list posted on entries to the laboratory. This list shall be updated as necessary. All such persons must have been satisfactorily trained, briefed and immunized as judged by the director. Persons can be added to the list only on authorization of the director.

4.3.3.1 Prerequisites for authorization to enter the laboratory:

i) Vaccination within the previous 3 years with potent WHO approved vaccine and proper technique and measurement of detectable antibodies at least every 3 years. This information must be recorded.

ii) All such persons must have been given a written copy of the safety instructions and must have signed a statement that they have been read and understood.

4.3.3.2 All untoward incidents and accidents, even minor ones, must be reported to the director immediately and recorded.

4.3.3.3 All entries into the laboratory should be documented in a permanent record.

4.3.3.4 Any absence must be reported to the director who should verify cause of absence.

4.3.3.5 Workers in the laboratory must inform their personal physician that they work with variola virus in case of illness. The physician should be provided with the telephone number of the director.

4.3.4 Special situations

Action in case of major accidents and other emergencies will be detailed in the laboratory operations manual.

5.0 Packaging and shipping

Diagnostic specimens and cultures should be packaged and shipped in accordance with national regulations and those of the International Air Transportation Association (IATA) and International Postal Union (IPU). Shipments should be sent by airfreight to prevent loss. The shipment and arrival details should be cabled to the receiving laboratory before arrival.

ANNEX 1

PARTICIPANTS

Temporary Advisers:

1.	Professor K. R. Dumbell	Dept. of Virology, The Wright-Fleming Institute of Microbiology, St Mary's Hospital Medical School, London (Discussion coordinator).
2.	Dr T. Kitamura	Division of Poxviruses, National Institute of Health, Tokyo.
3.	Dr N. N. Maltseva	Research Institute of Virus Preparations, Moscow.
4.	Dr J. H. Nakano	Viral Exanthems Branch, Center for Disease Control, Atlanta (Secretary).
5.	Dr J. H. Richardson	Office of Biosafety, Center for Disease Control, Atlanta.

WHO staff:

1.	Dr I. Arita	Chief, Smallpox Eradication Unit (SME)
2.	Dr J. G. Breman	Medical Officer, (SME), (Secretary)
3.	Dr A. Gromyko	Medical Officer, (SME)
4.	Dr E. Shafa	Medical Officer, (SME)

DOCUMENTS

1.	Working Paper 1	Registration and safety measures of laboratories retaining variola virus (Dr J. H. Richardson and Dr J. H. Nakano)
2.	Working Paper 2	Safety regulations for laboratory work using variola virus in the present facilities of the smallpox laboratory (Division of Poxviruses, National Institute of Health, Tokyo, Japan)
3.	Working Paper 3	Control of laboratory use of pathogens very dangerous to humans (Dangerous Pathogens Advisory Group, Department of Health and Social Security, Ministry of Agriculture, Fisheries and Food, United Kingdom)
4.	Working Paper 4	Progress Report on Register of Laboratories retaining Variola Virus, WHO, 28 July 1977
5.	Working Paper 5	Resolution of the Thirtieth World Health Assembly. Smallpox Eradication (WHA 30.52), 19 May 1977
6.	Working Paper 6	Resolution of the Executive Board of the WHO. Smallpox Eradication (EB 59.R28), 25 January 1977

7.	Working Paper 7	Nineteenth Report of the Committee on International Surveillance of Communicable Diseases: Control of Variola Virus in Laboratories (WHO/IQ/76.155 Rev. 1, page 56), 22-26 November 1976
8.	Working Paper 8	"Collection, packaging and despatch of specimens, Reference 2" in Protocol for Investigation and Reporting of Smallpox-like Disease in African Regions where human monkeypox has occurred, (SME, WHO, 1976)
9.	Working Paper 9	"Specimen Collection Kits", SME, WHO, 8 February 1977
10.	Working Paper 10	Facilitation and Safety in the International Transfer of Research Materials (CDS/SMM/76.1 Rev.1)

ANNEX 2

LABORATORIES RETAINING VARIOLA VIRUS[1] (28 July 1977)

Number	Region/Country	Laboratory	Reason for retaining			
			Archival	Diagnosis	Current research	Unknown
1	AFRO/South Africa	National Institute for Virology, Sandringham	X			
2	AMRO/Brazil	Instituto Adolfo Lutz, Serv.de Virol., Sao Paulo	X			
3	AMRO/Peru	Virus Instituto Salud Publica, Lima	X			
4*	AMRO/USA	Viral Exanthems Branch, CDC, Atlanta		X	X	
5	AMRO/USA	American Type Culture Collection, New York	X			
6	AMRO/USA	Walter Reed Army Institute of Research, Washington	X			
7*	EURO/France	Laboratoire National de la Santé publique, Paris			X	
8	EURO/FR Germany	Landesimpfanstalt Dusseldorf, Dusseldorf	X			
9	EURO/FR Germany	Bayerische Landesimpfanstalt, Munich				X
10	EURO/FR Germany	Institut für Schiffs und Tropenkrankheiten, Virus abteilg., Hamburg				X
11*	EURO/Netherlands	Rijks Instituut voor de Volksgezondheid, Bilthoven		X		
12*	EURO/USSR	Laboratory of Smallpox Prophylaxis, Research Institute of Virus Preparations, Moscow		X	X	
13*	EURO/United Kingdom	Virology Department, St Mary's Hospital Medical School, London			X	
14	EURO/United Kingdom	University of Birmingham, Dept. of Bacteriology, Medical School, Birmingham			X	
15	EURO/United Kingdom	University of Liverpool, Dept. of Medical Microbiology, Liverpool	X			
16	EURO/United Kingdom	Microbiological Research Establishment, Virus Section, Porton Down, Salisbury	X			
17*	WPRO/Japan	Poxvirus Laboratory, Dept. of Enteroviruses, National Institute of Health, Tokyo		X	X	

* WHO Collaborating Centre

[1] Countries not yet responding to query: Cape Verde, China, Comoros, Democratic Kampuchea, Seychelles
(The Comoros and Seychelles report that variola virus is not retained in laboratories, 26 September 1977)