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EPIDEMIC ALERT & RESPONSE

Report of the meeting of the Ad Hoc Committee on Orthopoxvirus Infections

Geneva, Switzerland
31 August–1 September 2004

World Health Organization

Department of Communicable Disease Surveillance and Response

Contents

1. Summary

- The Committee was briefed on the WHO Operational Framework for detecting, verifying, characterizing, assessing and responding to epidemic disease threats. A draft paper on mechanisms for the acquisition and release of smallpox vaccine by WHO was discussed in working groups and in plenary session. The Committee supported the concepts described in the document and made a number of recommendations concerning its content. A revised document incorporating these recommendations is to be prepared by the WHO Secretariat.

- The recommendations made in 1994 by the Ad Hoc Committee on orthopoxvirus infections were briefly considered. It was agreed that the Advisory Committee on Variola Virus Research should be empowered to revise the recommendations on research issues in the light of the technological advances that have been made since they were first made. These revisions could be made without seeking approval of the Ad Hoc Committee on Orthopoxvirus infections. The Ad Hoc Committee will be informed of the changes as part of the normal reporting process of the Advisory Committee.

2. Introduction

- Dr Guénaël Rodier, WHO Director Communicable Disease Surveillance and Response (CSR) welcomed participants to the meeting. He indicated that the purpose of the meeting was to help the WHO Secretariat develop a paper that could be submitted to the WHO Executive Board that would define an operational framework for a WHO Smallpox Vaccine Bank for emergency response to an outbreak of smallpox.

- Dr D A Henderson was appointed Chairman and Dr P J Greenaway and Dr N Asgari were appointed Rapporteurs.

3. WHO alert and response operational framework

- Dr Mike Ryan gave a presentation describing the WHO Alert and Response Operational Framework. The aims of this Operational Framework are to ensure that there is early detection, rapid response and effective control of epidemic disease threats. No single institution has the capacity to do this and WHO brings partners together to focus global resources on specific problems. The strategy adopted is based on containing known risks, responding to the unexpected and improving preparedness. A new office within the Communicable Disease Surveillance and Response Directorate has been created to implement this strategy. It ensures that multi-disciplinary technical support teams are available to respond to emergencies.

- Dr Ryan indicated that control of any future smallpox outbreak would heavily depend on access to suitable stocks of vaccine. It was proposed that WHO should create a smallpox vaccine bank in preparation for an emergency response to an outbreak of smallpox. His staff had prepared a draft paper on this topic and advice on the operational requirements of this bank was now needed.
- Dr D Lavanchy then described the proposed mechanisms for acquisition and release of smallpox vaccine and the framework by which the WHO smallpox vaccine bank might operate. He indicated that the bank should have two components. The first would be made of a small vaccine stockpile maintained by WHO in Geneva; this would be immediately available to the Global Alert and Response Network for emergency response to a smallpox outbreak. The second component would be made up of pledges from vaccine stocks held by Member States. The donated stocks would remain under control of the Member States but in the event of a proven outbreak, they may be asked to release some or all of the donated stock for outbreak control.
- The Chairman provided background information on some of the issues concerning smallpox vaccine availability and described some of the basic premises on its deployment. He briefly reviewed the current capacity for smallpox vaccine manufacture and suggested that the bank might usefully have a third component. This would be knowledge of manufacturers with expertise and capacity to manufacture vaccine in response to urgent demands.

4. Recommendations on the proposed operational framework for a WHO smallpox vaccine bank

- Committee Members were divided into two working groups. The first was chaired by Dr Henderson and considered issues surrounding the size and associated issues of the vaccine stockpile. The second was chaired by Dr St John and considered vaccine type, safety, quality and use issues. The full Committee then considered reports from each working group in plenary session.
- The Committee strongly believed that it would be both wasteful and impractical for every country to obtain its own stock of vaccine for protective purposes. It therefore felt that the establishment of an effective global vaccine reserve would minimize this possibility. The Committee supported the concepts described in the draft document and made the following recommendations concerning its content and asked for these to be taken into consideration during the preparation of the final proposals.

4.1 General recommendations

1. WHO should give specific consideration to the creation of a small advisory group of experts with knowledge of smallpox disease management, epidemiology, vaccine control and regulations, involving where possible the major vaccine manufacturers, to provide advice to the Director General on an ongoing basis and in an emergency. This group should assist the Global alert and Response Network (GOARN) and complement the work of the proposed International Health Regulation Emergency Panel.

2. WHO should continue to support a strategic group within the GOARN secretariat that focuses exclusively on smallpox issues. This support should be in the form of providing at least one whole time equivalent staff and associated operating costs.

3. WHO should review the global manufacturing capacity for smallpox vaccine and it should work with the Member States to ensure that there are at least two manufacturing sites capable of producing 20 million doses per month for a prolonged period of at least 10 years. This would act as the third component of the WHO smallpox vaccine bank.

4. WHO should develop a smallpox emergency plan for circulation to, and agreement by, all Member States in advance of any emergency, that addresses specifically priorities linked to the shipment of vaccines in case of an emergency. This emergency plan will contain standard operating procedures for the contributions that both Member States and WHO will make to control the outbreak as well as legal disclaimers and vaccine release conditions. This plan should also include the necessary instruments to facilitate an urgent mass vaccination programme under high pressure.

5. WHO should review the current surveillance and containment Standard Operating Procedures so that these reflect the existence and proposed developments of smallpox vaccine stockpiles. Attention should also focus on expiry dates issues for vaccines, and solvents.

6. WHO should undertake an inventory of laboratories worldwide that are capable of diagnosing smallpox and establish list of responsible decision-making personnel. The data from this undertaking should be used to create a network of smallpox diagnosis laboratories and public health units. Where possible, these should be incorporated into the global network involved in the diagnosis and management of special pathogens. Additional resources should be made available to facilitate the provision of standardized reagents, standard operating procedures and external quality assessment panels. These resources should also provide support for the training laboratory personnel and for meetings of those engaged in smallpox diagnosis.

7. Additional resources should be made available to mobilize trained personnel that can cascade and facilitate appropriate training for local staff who might respond to a smallpox outbreak. Instruction materials for vaccination and precautions should be made available.

4.2 Recommendations for the WHO Geneva stockpile

1. Member States should be requested to assist WHO through donations of cash or kind to create, monitor and maintain a strategic stock of smallpox vaccines to be held in Geneva. This strategic stockpile should be made available for emergency use only, where emergency is defined as the confirmed presence of at least one case of smallpox in the human population. The volume of the Geneva stockpile should be at least 5 million doses of either lymph-derived or cell culture derived vaccines. The appropriate number of bifurcated needles and volume of diluent should be included in this stockpile.

2. It is preferred that any donated or purchased vaccine should be manufactured under current good manufacturing practice (GMP). However this may not be possible for the lymph-derived vaccine, therefore these vaccines are required to be evaluated and authorized for use in an emergency by the competent authorities.

3. Any donated or purchased vaccine should be freeze-dried and should have been evaluated and authorized for use in an emergency by the competent national authority. The stock should be in such a form that once reconstituted, it should contain a minimum of 5×10^7 pock forming units per ml, or the equivalent.

4. The preferred use of WHO Geneva stockpile should be in an undiluted form. If in an exceptional situation, there is a requirement to deliver the reconstituted vaccine at a 1:5 dilution, there should be contingency plans available to do this as long as appropriate supporting data on vaccine take rate and stability is available. The decision to use diluted vaccine should be made in consultation with the Ad Hoc Committee on Orthopoxvirus Infections or the small emergency advisory group referred to previously.

5. WHO is requested to provide sufficient and earmarked funds to maintain the strategic smallpox vaccine stockpile in Geneva.

6. The WHO Geneva stockpile should not include anti-viral drugs, as currently there are no experimentally, well-controlled data to support their efficacy. Likewise, the stockpile would not be expected to have specific vaccinia virus immunoglobulins (VIG) as this product is only used in therapy for rare severe cutaneous complications. If requested, WHO could assist in making VIG available in a timely manner.

4.3 Recommendations for the WHO-pledged stockpile kept by donating countries

1. A stockpile of smallpox vaccine should be created through pledges made by Member States. The size of the pledged stockpile should be at least that available to WHO at the end of the eradication programme (200 million undiluted doses). Pledged stocks will remain under the control of the donor Member State and held as part of its national stock. Any donated vaccine must be evaluated and be authorized for use in an emergency by the competent authorities.

2. WHO should ask Member States what amount of vaccine they are willing to pledge for WHO use, suggesting that this might be 10% or more of the national stockpile. In making this pledge, Member States will provide WHO with relevant information relating to the donated vaccine both at the time of making the commitment and on a continuing basis. This should describe the manufacturing process and include all relevant quality assurance data.

3. Member States committing vaccine to the WHO pledged stockpile should be asked to also provide adequate diluent for reconstitution and appropriate numbers of bifurcated needles to deliver vaccine at the standard concentration. Member States will retain responsibility for maintenance and quality assurance of pledged materials.

4. Once released, vaccine in the pledged stockpile from donating countries will become the property of WHO under transfer of ownership agreements. The vaccine will reach recipient countries as WHO vaccine.

5. The Committee then made a page-by-page review of the draft framework document and made additional amendments in the light of the recommendations already made. During this review it was noted that legal advice would be obtained on the liability issues associated with, and any disclaimers that might be needed for, the distribution of vaccine from the WHO Smallpox Vaccine Bank. This advice, once obtained, will be discussed with the relevant manufacturers.

5. Revisions to the 1994 Ad Hoc Committee recommendations

- Dr R Wittek introduced this topic by reminding the Committee that it had made a number of recommendations in 1994 concerning the manipulation of live variola virus and the distribution and use of variola virus DNA. These recommendations had been made largely to address biosafety concerns and their relevance is now questionable due to the technological advances that had been made since the recommendations were first issued.
- The Advisory Committee on Variola Virus Research, convened by WHO to provide independent oversight of essential research on live variola virus, needs advice on the best way to seek revisions to the 1994 Ad Hoc Committee recommendations so that this research can be conducted in a timely manner. In so doing it has sought advice from an expert technical sub-committee and WHO's Biosafety Advisory Group.
- Following discussion, it was agreed that the Advisory Committee on Variola Virus Research should be empowered to revise the 1994 recommendations on research issues made by the Ad Hoc Committee on Orthopoxvirus Infections in the light of the technological advances that have been made. It was also agreed that these revisions could be made without seeking further approvals from the Ad Hoc Committee that will, in turn, be informed of the changes as part of the normal reporting process of the Advisory Committee.

6. Conclusions

- The Ad Hoc Committee on Orthopoxvirus Infections supported the concept of creating a WHO Smallpox Vaccine Bank for emergency response to an outbreak of smallpox. It made a number of recommendations for the WHO Secretariat to incorporate in a paper describing the operational framework for this bank that is to be submitted to the WHO Executive Board for approval. The Ad Hoc Committee also agreed that the Advisory Committee on Variola Virus Research should be empowered to make appropriate revisions to the recommendations it had previously made on research issues in the light of technological advances that have been made since 1994.

Annex – List of participants

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