

Conclusions and recommendations of the Advisory Committee on Poliomyelitis Eradication Geneva, 11-12 October 2006

The 3rd Meeting of the Advisory Committee on Poliomyelitis Eradication (ACPE) was convened in Geneva, Switzerland, on 11-12 October 2006, to provide the World Health Organization (WHO) and the Global Polio Eradication Initiative (GPEI) with expert advice on:

- programme priorities and policies for interrupting wild poliovirus transmission (WPV) worldwide;
- additional measures to limit the international spread of circulating polioviruses;
- the programme of work for eventual cessation of routine immunization with oral poliovirus vaccine (OPV) globally, following interruption of WPV transmission worldwide.

The ACPE provides recommendations on broad strategic issues for the global programme. Individual advisory groups exist in each endemic country and some re-infected countries to provide detailed technical and operational guidance specific to the context of those countries.

The international context

The ACPE met at a time when international concern is very high regarding the pace of polio eradication in the four remaining endemic areas. The ACPE is particularly concerned that the longer it takes to interrupt WPV transmission in the remaining endemic countries the greater the danger of WPV being exported to countries that are currently polio-free. There are significant financial and opportunity costs associated with preventing and responding to polio outbreaks following a WPV importation. The concern of the international community is greatest with respect to Nigeria (where multiple lineages of both WPV1 and WPV3 are circulating) and western Uttar Pradesh (UP) in India, both of which pose a constant risk to polio-free areas within these countries, to neighbouring countries, and to any country receiving travellers from these areas.

The ACPE reaffirms that the global eradication of wild poliovirus is both technically and operationally feasible. This is clearly evidenced in the eradication of endemic poliovirus from all but four countries worldwide. Moreover, the polio-free countries eradicated wild poliovirus using tOPV alone while both mOPV types 1 and 3 are now available, providing a potent additional tool to eradicate wild poliovirus in the remaining endemic countries.

1 Interrupting wild poliovirus transmission

As of 12 October, 1403 paralytic polio cases due to WPV have been reported in 2006 from 14 countries, 4 of which are endemic for WPV and 10 of which were re-infected

by a WPV that originated in an endemic area. These figures compare with 1979 cases from 16 countries for the whole of 2005.

1.1 Strategic priorities

The remaining transmission of WPV globally can be divided into two situations.

a) **Endemic transmission:** endemic transmission of both WPV1 and WPV3 continues in geographically limited areas of only four countries worldwide: Nigeria, India, Pakistan, and Afghanistan. These countries have never completely interrupted WPV transmission and represent the only remaining reservoirs of WPV. These four endemic countries account for 92% of all reported cases globally; Nigeria and India account for 65% and 25% of the global total, respectively. Nigeria, India and Afghanistan have all had a marked increase in the number of polio cases reported in 2006 compared to 2005; in Pakistan case numbers are almost the same.

b) **Importations: wild poliovirus from two endemic areas (Nigeria and India) has in recent years frequently been exported to polio-free areas, often causing multiple case outbreaks.** Between 1 January 2003 and 10 October 2006, 68 separate importation events affected 24 previously polio-free countries, resulting in over 1400 cases of polio globally, and costing more than US \$450 million, in external funding alone, to bring under control. All of the WPV importations that resulted in a multi-case outbreak during this period have been due to WPV1. The risk of an importation is greatest for those countries immediately neighbouring a polio endemic area. However, there is also a substantial risk of importation for countries which neighbour areas that have themselves had an importation associated outbreak. Long distance WPV exportations from endemic areas also occur and in the past 4 years have caused more than 700 of the importation associated polio cases and cost more than US\$ 150 million to control.

Progress in stopping outbreaks due to WPV importations into polio-free areas has been substantial. In 2006 such outbreaks have accounted for only 8% of all cases reported globally to date, down from more than 60% in 2005. In 2006, outbreaks in polio-free areas have declined in terms of the number of importations detected, the number of countries currently dealing with an outbreak, and the number of cases resulting from an importation. Only 8 countries (Angola, Democratic Republic of Congo, Namibia, Niger, Ethiopia, Somalia, Bangladesh, Nepal) currently have ongoing transmission following an importation, the lowest number in 4 years. Appropriate control measures are being taken in response to all of these outbreaks. The ACPE was briefed on outbreak response activities in Angola by the Vice-Minister of Health and noted plans for a further national immunization day (NID) in that country in 2006, with two additional NID rounds in early 2007.

Despite the progress in rapidly controlling outbreaks in polio-free areas following a WPV importation, the ongoing transmission of wild poliovirus in endemic areas poses a constant risk to the achievement of polio eradication globally.

The ACPE reviewed data from the recent mOPV1 clinical trial in Egypt, which demonstrate higher seroconversion rates to type 1 poliovirus, as well as a greater reduction in excretion of a challenge virus, following a single dose of mOPV1 than after a single dose of tOPV. These data confirm that mOPV1 is more effective against WPV1 transmission than tOPV and validate the strategic decisions on mOPV1 use in the GPEI. The ACPE emphasizes that the effective use of this improved tool will enhance current strategies and lead to cessation of WPV1 transmission, provided these strategies are effectively implemented.

Recommendations:

- The ACPE endorses the strategic approach of the Global Polio Eradication Initiative for stopping wild poliovirus transmission globally, specifically:
 - Endemic areas: conduct 7-8 rounds of high quality supplementary immunization activities (SIAs) per year with the appropriate OPV (as per previous ACPE recommendations) until circulation of wild poliovirus has been interrupted. The appropriate mOPV may need on to be interchanged with tOPV depending on the transmission situation in any given area.
 - Re-infected areas: continue SIAs until circulation of wild poliovirus has been interrupted, as per previous ACPE recommendations and WHA Resolution 59.1. The vaccine of choice is the appropriate mOPV.
 - Areas contiguous with endemic areas: conduct SIAs as appropriate until circulation of wild poliovirus is interrupted in the endemic reservoir; maintain highly sensitive AFP surveillance. The vaccine of choice is tOPV if the neighbouring area is endemic for both WPV1 and WPV3.
 - Polio-free areas: achieve and maintain high immunization coverage against polio; maintain certification-standard surveillance.
- Trial data on mOPV3 should be obtained as soon as possible to further guide the more widespread use of this vaccine.
- The GPEI should prepare a new Global Strategic Plan for the period 2007- 2010 to provide a longer term framework for eradication and post-eradication activities.

1.2 Interrupting indigenous transmission

The four countries that still have areas of endemic WPV transmission each reflect a different situation and are facing different challenges.

Nigeria remains the single biggest risk to global polio eradication. It is the only endemic country with widespread, multi-lineage transmission of both WPV1 and WPV3, which is clearly related to extensive gaps in population immunity. In 2006, case numbers are almost double that for the same period in 2005. Despite the recent improvements in reaching children during IPDs, in several northern states more than 20% of children aged less than 5 years have still never had a dose of OPV (based on

AFP case data). This is of grave concern and points to the continued existence of major quality gaps in SIAs that must be rapidly addressed. Consistent high quality rounds of supplementary polio immunization will need to be conducted in the endemic areas to close the immunity gap and restrict transmission.

Despite the increase in cases in Nigeria, the ACPE notes some positive developments. The southern states of Nigeria have remained polio-free. Recent data from the IPDs in a number of northern states suggest that there has been some improvements in accessing children, following the efforts to engage local governments and local communities. Surveillance data indicate that there may also be a reduction in WPV1 case numbers in the northern states following the IPDs. These improvements need to be sustained and expanded.

Afghanistan in 2006 is experiencing a significant outbreak of WPV1 in the Southern Region, with some spill over into Baluchistan in Pakistan. Apart from one case of polio in a bordering province of the Western Region, the outbreak has been confined to Southern region; all other areas of Afghanistan remain polio-free. The main issue in the Southern Region, and increasingly in neighbouring regions, is the deterioration in security which hampers the access of immunization teams to children, and the access of supervisors and monitors to those teams to ensure good quality work.

In Pakistan the bulk of the population lives in polio-free areas; transmission is restricted to security compromised areas (including parts of the Federally Administered Tribal Areas), areas bordering the outbreak in Afghanistan, and mobile populations. The border areas of Pakistan and Afghanistan are areas of common poliovirus transmission. The ACPE appreciates the initiative of the Minister of Health, Pakistan, to arrange meetings with the Ministers of Afghanistan and India to discuss cross border coordination issues.

In India the polio situation is mixed. In Bihar, only 20 cases have so far been reported in 2006, all due to WPV1, and it is certainly possible that local transmission can be stopped in the near future. In Uttar Pradesh, however, an outbreak of type 1 poliovirus is occurring, centred on western UP. This outbreak has resulted in a significant number of cases and has spread outside western UP, although not to the same extent as the outbreak of 2002. In western UP, WPV transmission is aided by very high population density and very poor sanitation. Furthermore, the high prevalence of enteric infections probably interferes with the response to the oral poliovirus vaccine in individual children. This last factor is supported by recent analysis of AFP and polio case data which suggest that the efficacy of OPV is lower in UP than in other parts of India. The same data also suggest, however, that monovalent OPV1 is substantially more protective than tOPV, even in UP. It is clear that in northern India, particularly in western UP, it is necessary to get more doses of OPV into children, including sufficient doses of mOPV1, and to consistently achieve higher coverage than was needed in other parts of India. The current challenge is to consistently reach all children in western UP during every SIA.

In Afghanistan, Pakistan, and India, WPV1 outbreaks are occurring. Analysis of genetic data from each outbreak shows a close relationship between viruses. This is not a pattern of wide endemic transmission, which is characterized by genetic diversity; it is more similar to outbreaks in polio free areas where WPV is re-

introduced. The implication is that these outbreaks can be brought under control in the same way as outbreaks in polio-free areas, with consistent application of proven strategies. In order to reach the level of quality and consistency of work necessary to interrupt transmission in the remaining endemic areas, an even higher level of political commitment must be achieved and sustained in these countries to ensure effective government ownership and oversight.

Recommendations

- Recognizing the international health risks posed by continuing wild poliovirus transmission in the remaining endemic areas and the need for extraordinary cross-ministry cooperation to reach all children, and following the example of Afghanistan where the President has formed a polio working group that reports directly to him, mechanisms should be established to regularly brief the Head of State in each of the endemic countries on progress and programme requirements.
- All endemic countries should plan for 7-8 SIA rounds per year in endemic areas until transmission is interrupted.
- All endemic countries need enhanced plans for systematically engaging and reaching those populations which are continuing to harbour wild poliovirus. These plans should be shared with the ACPE by end-January 2007.
- Recognizing that improvement in SIA quality in endemic areas has been incremental, endemic countries should establish realistic targets and planning timeframes that extend beyond 18 months. This is essential to facilitate international risk management and domestic allocation of resources.
- The following actions should be taken to address specific issues in each of the remaining endemic countries:
 - Nigeria should carefully plan SIA activities for the remainder of 2006 and early 2007, taking into account upcoming elections, to ensure that endemic areas are adequately covered by sufficient numbers of high quality SIA rounds. Plans recommended by the ERC should be made available to the ACPE members in December 2006.
 - State and local governments in Nigeria need to take strong ownership of the programme, particularly in the coming months leading up to Presidential elections.
 - The Director General of WHO should continue to interact with the UN Secretary General's office to facilitate the negotiation of cease fires in security compromised areas of Afghanistan, particularly in Southern Region, to allow supplementary immunization activities to take place.
 - Pakistan and Afghanistan should ensure close coordination of activities, so that populations at risk of WPV transmission are effectively and consistently covered by surveillance and immunization.

- In India, interrupting transmission in Bihar and controlling the outbreak that originated in UP there should be pursued simultaneously as a prelude to interrupting any remaining endemic transmission in western UP. Eradication efforts in UP should focus on engaging local governments and local communities to ensure sustained high quality SIAs and improved routine immunization. The recommendations of the India Expert Advisory Group (IEAG) should be made available to the ACPE following the next IEAG meeting in December.
- The Governments of Nigeria and Pakistan should commit additional national resources for polio eradication in order to finish the job.

1.3 Limiting the International Spread of Circulating Polioviruses

Although WPV transmission persists in endemic areas, all outbreaks following importations into polio-free countries between 2003 and 2005 have been stopped or are under control. Outbreaks following WPV importations in 2006 are being responded to appropriately and in accordance with ACPE recommendations and WHA Resolution 59.1 (May 2006). No importation during this period has resulted in long term re-establishment of wild poliovirus transmission, and experience has shown that an appropriate response, as per the ACPE recommendations, will stop such outbreaks. However, the ACPE emphasizes that the four remaining polio endemic areas constitute a risk for all polio-free areas and that the risk of international spread of WPV remains high until WPV transmission is stopped globally.

The ACPE noted the recent decision of the Kingdom of Saudi Arabia to enhance its polio immunization requirements for persons intending to travel to the Kingdom from polio-infected areas. The Kingdom now requires that all travellers aged less than 15 years from polio infected areas provide evidence of immunization against polio, in advance of travel, to be granted an entry visa. Because of the intensity of WPV transmission in Nigeria, the Kingdom requires that *all* Nigerians, regardless of age, meet these requirements prior to travel. To further reduce the risk of polio infection of visiting pilgrims, the Kingdom also requires that travellers from polio-infected areas be immunized with a dose of OPV on arrival.

The ACPE reviewed the scientific basis for polio immunization requirements for travellers from polio-infected areas. The ACPE found the scientific basis for these requirements to be sound, noting that such measures would reduce the risk of poliovirus infection and excretion by travellers from polio-infected areas. The ACPE evaluated the options for enhancing national and international advice to both individual travellers and governments, including the WHO publication International Travel and Health and the International Health Regulations 2005 (IHR 2005).

Recommendations:

A multi-pronged strategy is needed to address the risk of international spread of circulating polioviruses. In addition to the technical recommendations previously made by the ACPE, the following steps should be taken to reduce the risk of international spread of wild poliovirus:

- Countries bordering the endemic areas of Nigeria and India should continue to conduct SIA rounds of an appropriate scale annually until transmission in the neighbouring endemic reservoir is interrupted.
- The WHO publication "International Travel and Health" should be updated to recommend that all travellers to polio infected areas should be fully immunized against poliomyelitis in accordance with national policy. Individuals without a prior history of polio immunization should complete a full primary series by one month prior to the date of intended travel. Previously immunized individuals should receive a booster dose between one and twenty-four months prior to travel.
- A Standing Recommendation on polio immunization for travellers from polio-infected areas¹ should be established under the International Health Regulations 2005. Among other provisions, this should recommend that:
 - a) individuals who have not completed a full series of polio immunization should complete a full primary series by at least one month prior to the date of intended travel,
 - b) previously immunized individuals should receive a booster dose of OPV between one month and twenty-four months prior to travel, and
 - c) individuals undertaking travel on short notice (i.e. less than one month before departure) should receive a dose of polio vaccine prior to departure.
- The immunization of travellers arriving from polio-infected areas with a single dose of polio vaccine at the point of entry may reduce the risk of spread of an imported virus.
- The vaccine of choice for immunizing travellers from polio infected areas is trivalent OPV.
- These recommendations should remain in effect for a minimum of 6 months after detection of the last wild poliovirus in the polio-infected area. If certification standard surveillance is not in place in the infected country, the recommendations should remain in effect for a minimum of 12 months.
- WHO should take immediate steps to ensure appropriate polio expertise is available to the expert roster for the IHR (2005).

2 Eventual OPV Cessation

¹ For the purposes of these recommendations, polio-infected areas are considered (a) areas with endemic transmission of indigenous polioviruses, and (b) areas with a multiple case outbreak of polio due to an imported wild poliovirus, the most recent of which was detected within the last 6 months. The list of polio infected areas is published quarterly in the WHO Weekly Epidemiological Record and available online at www.polioeradication.org .

2.1 Risk Assessment

To further inform decision-making on longterm policies to minimize and manage the risks of polio re-emergence and/or reintroduction into a polio-free world, the GPEI has taken a multi-pronged approach utilizing a combination of programmatic observations (e.g. impact of OPV campaigns on cVPDVs), studies (e.g. prevalence of iVDPVs) and mathematical modelling.

The ACPE was presented with a comprehensive analytic, decision-making model that has been developed over the past 5 years to quantify the risks associated with different policy options in a post-eradication world, test the robustness of the predicted outcome of each option, and identify areas of particular uncertainty in terms of model inputs (assumptions). This modelling reaffirms that with ongoing use of OPV after interruption of WPV transmission globally, outbreaks of cVDPVs will occur unless very high universal coverage is achieved and then maintained. Cost-effectiveness analyses found that the policy option of 'no routine immunization post-eradication' may be both cost and life saving in the setting of low and middle income countries. However, ACPE members noted the need to incorporate ethical considerations in the programme of work to inform post-eradication policy development.

Of the risks associated with eventual OPV cessation, the ACPE recognizes that in particular further work needs to be done with respect to the risk posed by iVDPVs. The ACPE reviewed a protocol that WHO has developed for assessing the prevalence of iVDPVs in middle and low income settings.

Recommendations:

- Decision-analytic modelling reaffirms the ACPE recommendation that the GPEI work towards the eventual cessation of routine use of OPV in a post-eradication era. The ACPE recommends continuation of this work and the allocation of further time in upcoming meetings to review in greater detail the outcomes and implications of this work, particularly the newer work on the cost-effectiveness of the various post-eradication options.
- The ACPE endorses the proposed protocol for assessing the prevalence and consequences of iVDPVs, recommends its immediate application, and requests an update on findings at its next meeting. The ACPE further recommends that the geographic area targeted for such studies be expanded to include sub-Saharan Africa and other low income sites.

2.2 Risk Reduction & Risk Management

Recognizing that there are inherent, residual risks associated with all policy options for polio immunization in a post-eradication era, the ACPE has recommended a comprehensive strategy for minimizing and managing the risks of polio re-emergence and/or re-introduction in such a period. The six-pronged strategy in place as of September 2006, to minimize and manage the long term risks of polio, consists of:

- a. Confirmation of the interruption and containment of wild poliovirus globally,
- b. Highly-sensitive surveillance for, and immediate notification of, polioviruses,
- c. Establishment of an mOPV stockpile for responding to emergent or re-introduced circulating poliovirus,
- d. In all countries with poliovirus (essential) facilities, as defined and provided for in GAP III, maintenance of high (>90%) nationwide IPV coverage,
- e. Synchronous global cessation of OPV for routine immunisation, and
- f. Containment of Sabin poliovirus strains

The ACPE reviewed the current working draft of the *Third Edition of the WHO Global Action Plan to Minimize Poliovirus Facility-associated Risk in the Post-eradication/post-OPV era* (GAP III) which had been updated to reflect revisions proposed by the Committee. The central component of this strategy is to reduce the number of facilities retaining virus to < 20 worldwide, conducting essential international vaccine, reference and research functions. These facilities would undergo a rigorous, annual review and biennial accreditation process to ensure ongoing compliance with the primary safeguards of facility containment and secondary safeguards of location in areas of low population risks.

The conceptual framework for the *Standard Operating Procedures for The Stockpile of Monovalent Oral Poliovirus Vaccines (mOPV) in the Post-eradication/Post-OPV era* was presented to the ACPE. These SOPs outline the rationale for an mOPV stockpile, indicate the composition (i.e type and quantities of vaccine), and provide a proposal for the governance, release criteria, decision-making process, physical management and post-response monitoring of its use. The draft SOPs build on current processes for the management and use of international stockpiles of other vaccines (e.g. yellow fever, meningococcal meningitis), existing WHO procedures for assessing and verifying potential international health threats, and the impending provisions of IHR 2005. The ACPE welcomed the development of these SOPs, providing comments to clarify specific technical aspects and proposing amendments to the introduction.

WHO and the GPEI has established an extensive programme of work on IPV in the context of both eradication and the post-eradication era. This programme of work includes studies on the impact of IPV on poliovirus transmission, alternative IPV schedules (e.g. 2 dose studies), dose reduction approaches (e.g. intradermal delivery of fractional doses), and cost-effectiveness. In addition, WHO is coordinating demonstration projects to evaluate operational issues related to the introduction of stand alone IPV, as well as the protection conferred by IPV against VDPV emergence (in a setting of high routine immunization coverage). WHO has also developed a 'proof-of-principle' collaboration to evaluate the technical and economic feasibility of producing a new IPV vaccine using Sabin poliovirus strains ('Sabin-IPV').

This WHO and GPEI programme of work on IPV continues to inform and update the WHO policy on IPV, which has been recently summarized in a WHO position paper and supplement (April 2006). The outcomes of a recent meeting on polio eradication that was sponsored by the National Institutes of Health (NIH) was presented to the ACPE and reaffirmed in particular the importance of this expanded programme of work on IPV.

The ACPE also reviewed the deliberations and outcomes of a meeting that was convened by the U.S. National Research Council to explore the programmatic utility and options for the development of an antiviral compound to facilitate risk management in the post-OPV era. The meeting generated specific recommendations proposing the development of at least 2 polio antiviral drugs, the primary use of which would be to assist in the control of VDPVs in the post OPV era. The ACPE was presented with a proposal for the establishment of a Poliovirus Antiviral Initiative (PAI) to take forward the key recommendations arising from that meeting.

Recommendations:

- The ACPE endorses the goal, strategy and proposed implementation steps of GAP III, concurs with the plan for finalizing the technical biosafety details of GAP III by end-2006, and recommends the dissemination of GAP III for review and comment by a broader group of stakeholders in early 2007.
- The ACPE endorses the concepts outlined in the draft stockpile SOPs contingent on the inclusion of the comments provided. The SOPs should now be reviewed with a broader group of stakeholders, particularly manufacturers and NRAs, to facilitate longterm international planning. The next draft of the SOPs should be shared with the ACPE in Q1 2007.
- The ACPE endorses the extensive WHO/GPEI programme of work on IPV and suggests that WHO should communicate this extensive programme of work to the broader scientific community.
- An open consultative forum should be held in 2007 (if the data are available), to better explore the implications of the use of IPV in the interruption of wild poliovirus transmission as well as in a post-eradication era.
- The ACPE concurs with the proposal to establish a Poliovirus Antiviral Initiative (PAI) with an NGO-based secretariat. The ACPE encourages the proposed primary partners of the PAI to develop and initiate a plan of action, including for resource mobilization, with a report back to the ACPE at its next annual meeting.