Final Draft 24/09/04

Conclusions and Recommendations of the Ad Hoc Advisory Committee on Poliomyelitis Eradication (AACPE) Geneva 21-22 September 2004

The Ad Hoc Advisory Committee on Poliomyelitis Eradication was convened in Geneva on 21 and 22 September 2004, to provide the World Health Organization and the global polio eradication initiative, with expert advice on:

- the programme priorities and policies for interrupting wild poliovirus transmission worldwide, and,
- the strategies, policies and products required for the coordinated cessation of OPV immunization following interruption of wild poliovirus transmission.

1. Interrupting wild poliovirus transmission

1.1 Global programme priorities

By end-2003, the number of countries with endemic circulation of indigenous wild polioviruses had been reduced to 6. In January 2004 during an emergency consultation with health ministers of these endemic countries an intensified eradication plan was established, the key elements of which were: high level political oversight, increased frequency of mass campaigns, and emphasis on the quality of SIA activities in all transmission areas.

The AACPE noted that as of 21 September 2004, the intensified effort in Asia was on track. After a marked increase in campaign frequency and quality, polio transmission in India, Pakistan and Afghanistan is generally focal, with just 89 cases reported compared with 196 at the same time in 2003. In Egypt, persistent low level transmission continues in different areas of the country. Sub-Saharan Africa, however, is experiencing epidemic polio (627 cases); cases in Nigeria and Niger have increased to 563 (vs. 155 for the same period in 2003) with virus spread to 12 previously polio-free countries in 2003 and 2004. Finally, surveillance indicators, and the detection of an 'orphan' poliovirus lineage in the Sudan, demonstrate ongoing gaps in surveillance in this key geographic area.

It is clear that the quality of supplementary immunisation and surveillance activities must reach very high levels, particularly in the highest risk areas where transmission is ongoing. It appears that in particular areas of the world, such as western Uttar Pradesh and parts of Egypt, where the population density is extremely high and the transmission of wild poliovirus is very efficient, the quality of work that needs to be achieved to stop transmission is much higher than in some other areas. In these areas of persistent transmission, the youngest children must be reached consistently during immunisation rounds to deliver adequate vaccine for protection and for interrupting transmission.

Recommendations:

1. The AACPE urges the global polio eradication programme to sustain the sense of urgency developed in 2004. Recognising that specific country strategies are established by existing country- or region-specific Technical Advisory Groups, the AACPE endorses the following global programme priorities for the remainder of 2004 and the first half of 2005:

- Stop transmission in Asia, through enhancing the quality of regular national/ subnational immunisation rounds and mop-ups (approximately every six weeks) with a particular focus on remaining areas of transmission, reaching the youngest children, and ensuring district-specific focus & accountability;
- Synchronize NIDs in 23 countries in West, Central, and the Horn of Africa in the last quarter of 2004, followed by an additional 4-6 full rounds in 2005 (potential activities for the second half of 2005 should be reviewed in mid-year);
- Revise the supplementary immunisation strategy in Egypt (informed by planned operational research), including conducting 6-weekly, full NIDs through to mid-2005;
- Enhance surveillance in West and Central Africa, and Horn of Africa countries.

These activities may benefit from selective use of new strategies to enhance the impact of SIAs (see below).

2. To assist the development of programme priorities given the implications of transmission of imported wild polioviruses, the following nomenclature should be used for countries and areas detecting wild poliovirus (infected countries):

- endemic countries/areas: ongoing circulation of indigenous wild polioviruses (currently India, Pakistan, Afghanistan, Egypt, Nigeria, and Niger),
- countries/areas with re-established transmission: circulation of imported virus for > 6 months (currently Chad, Burkina Faso, Cote d'Ivoire, and the Sudan),
- countries/areas with importations: imported virus but circulation for $\leq$ 6 months.

3. Given the importance of the Technical Advisory Groups formed to review individual country polio eradication programmes in endemic countries and provide recommendations on strategies and actions, a TAG for Niger should be formed as soon as possible. Additionally, TAGs should be established for selected countries with re-established transmission, in particular for Chad.

1.2 Enhancing the impact of supplementary immunisation activities

India, Pakistan, Afghanistan, and Egypt have now implemented intensified efforts, relying on high level political oversight, increased frequency of mass campaigns, and a concentration on the quality of the activity to effectively reach target children. As noted above, the impact of these efforts has been noticeable, but as yet there remain quality gaps in some critical endemic areas, resulting in ongoing transmission of wild poliovirus.

In order to interrupt the ongoing transmission, the quality of SIAs in infected countries, particularly in the highest risk areas, must be improved so that every eligible child is reached, using proven strategies as recommended by the Technical Advisory Groups for each of those countries. Additional measures to enhance the impact of SIAs by improving immune response in vaccinated children may add incremental value, and maximise the chance of rapidly interrupting transmission. Options that were reviewed by the AACPE for maximising immunity include 1) the addition of SIA rounds using monovalent OPV; 2) raising the potency of trivalent OPV; and 3) the targeted use of IPV, in addition to routine OPV and SIAs, in focal areas.

Recommendations

- All polio infected countries should continue their efforts to improve the quality of SIAs, particularly in the highest risk areas, so that all eligible children (particularly the youngest children) are reached and immunised during each SIA round;

- In order to potentially enhance the impact of SIAs by improving immune response in vaccinated children, WHO should immediately:
  - work to accelerate the process of regulatory approval of monovalent type 1 OPV (mOPV1), with the aim of having a product available for potential use in critical endemic areas by early 2005 as an adjunct to the existing eradication activities;
  - develop a clear rationale for the use of mOPV1, modelling the potential incremental benefits in terms of immune profile and susceptibility in the target population, and outline how mOPV could be used, in a safe and effective way and in conjunction with other eradication activities, for improving immunity in vaccinated children;
  - ensure consultation between country Technical Advisory Groups and the AACPE to guide the potential use of mOPV in conjunction with other eradication activities;
  - investigate the operational feasibility and potential impact on the immune profile in target groups of using IPV in focal areas to supplement existing SIA strategies.

1.3 Measures to limit the international spread of wild poliovirus

On 16 July 2004, an Ad Hoc Expert Consultative Group on Polio and Public Health convened by the Director-General of WHO recommended measures to prevent or limit the international spread of wild poliovirus. These recommendations were subsequently published in the Weekly Epidemiological Record[1]. The AACPE considers the recommendations of the Ad Hoc Consultative Group on measures to prevent or limit the international spread of wild poliovirus to be a good foundation for use by WHO and

[1] Weekly Epidemiological Record 2004; 79:289-300

countries. However, specific situations in the future will require modification of these measures depending on particular circumstances.

Recommendations:

1. The WHO Executive Board should be informed of the existing recommendations on measures for limiting the international spread of wild poliovirus and the proposed mechanism (i.e. consultation with the AACPE) for their future implementation.

2. The current recommended measures should be considered as generic. These measures may guide future actions in response to episodes of international spread, but will need to be revised and adapted according to specific situations. These recommendations also could form the basis for national decisions on measures to limit internal spread of wild poliovirus from endemic to polio-free areas.

3. Specific consultations should be held with the AACPE on the implementation of measures to limit the international spread of wild poliovirus, if such measures are needed in the future.

2. Plans for globally coordinated cessation of the use of OPV

The implicit promise of any eradication programme is to end the intervention once the causative agent for the disease has been eradicated. In the early years of polio eradication, it was anticipated that following global certification, immunization would simply stop. Since then it has become clear that for immunization to stop, certain conditions need to be met to reduce the risks associated with stopping. In particular, because of what is now known about Vaccine Derived Polioviruses (VDPVs)[2], the process of stopping the use of OPV globally needs to be carefully planned and coordinated.

In September 2003, the WHO Informal Consultation on identification and management of vaccine-derived polioviruses concluded that after eradication of wild poliovirus continued use of OPV would compromise the goal of a polio-free world. The report called for a comprehensive strategy for safely stopping OPV use as soon as possible after global eradication of wild poliovirus, when population immunity and surveillance sensitivity are expected to be high. The earliest possible time for safe cessation of OPV use would be at or around the time that all six WHO Regions are declared free of wild poliovirus transmission, that is, 3 years after detection of the last wild poliovirus worldwide. The process of preparing the world for OPV cessation has therefore been reduced to a very short time period.

[2] Final report of the WHO Informal Consultation on identification and management of vaccine-derived polioviruses, Geneva 3-5 September 2003 (in press).

The risks of paralytic poliomyelitis occurring in the post-eradication era fall into two major categories:

- Risks related to the use of OPV; and
- Risks associated with the unsafe handling of polioviruses.

These risks, and their potential consequences, will change substantially over time. This variability is the result of several factors, including future immunization, surveillance, and laboratory containment policy decisions at the international level; the degree to which such policies are implemented at national and sub-national levels; and the development of additional tools for addressing each risk. These progressive changes fall into a series of three periods:

- Before OPV cessation: the three years after detection of the last wild poliovirus and before cessation of OPV use.
- During OPV cessation: the three or more years immediately after global cessation of OPV use.
- After OPV cessation: the period starting 3 or more years after cessation of OPV use and detection of the last VDPV (when the risk of undetected cVDPV and iVDPV is considered to be minimal).

Each period presents different risks and requires a range of different activities at national and international level.

Reducing the risks of poliomyelitis during and after OPV cessation must be achieved through the immediate and simultaneous development and phased implementation of strategies covering five major areas of activity:

- Containment and control of poliovirus infectious materials, including wild, vaccine and VDPVs, in laboratories and vaccine production facilities;
- Continued high quality surveillance for poliomyelitis and poliovirus, and maintenance of systems for outbreak detection and investigation;
- Coordinated cessation of OPV use, including recall and destruction, or centralised safe storage, of distributed OPV stocks;
- Continued capacity for outbreak response, including establishment and maintenance of polio vaccine stockpiles;
- Finalization and implementation of national decisions on long term polio immunization policy.

Recommendations:

1. A comprehensive package of information covering the synchronized and coordinated cessation of OPV use, the storage/containment of polioviruses, and establishment/use of a stockpile of vaccine should be submitted to the 58th World Health Assembly as background to proposed resolutions, and for broader communication purposes to achieve a global consensus on cessation of OPV. As a

first step the WHO Executive Board meeting in January 2005 should be informed of the recommendations of the AACPE.

2. In order to prepare for OPV cessation, WHO should ensure that all countries, particularly those in Regions currently certified as polio-free, complete Phase I containment activities (national laboratory survey and inventory), conduct a quality assessment of the work, and provide complete documentation to Regional Certification Commissions. The strategy for poliovirus containment after OPV cessation should be outlined in a 3rd edition of the Global Action Plan for Laboratory Containment of Polioviruses. As recommended by the WHO Biosafety Advisory Group, this strategy should use the containment requirements for wild polioviruses as a basis for developing requirements and strategies for containment of *all* polioviruses, including Sabin strains. WHO should conduct a wide consulatative process, similar to the approach used to develop previous containment policies, in order to finalize GAP 3 by end 2005.

3. The use of OPV following cessation, including the establishment of a vaccine stockpile that is accessible and acceptable to countries, should be guided by the International Health Regulations and an international oversight body which advises the DG of WHO on releasing live poliovirus vaccines. The AACPE would appreciate a full briefing on the IHR at their next meeting.

4. Further work is required to define the composition, size, and operation of the vaccine stockpile for the OPV-cessation period, and to ensure that the stockpile and operating mechanisms are in place in advance of OPV cessation. A final draft of the proposed stockpile framework should be available by mid-2005. Full, front-loaded financing for the stockpile should urgently be sought to allow WHO to engage manufacturers in development of the necessary vaccines while sufficient production capacity is still available.

5. The draft National Guidelines for OPV Cessation should be finalized and tested through interaction with national immunization policy makers in selected countries. The revised version should be shared with the AACPE in November 2004. These broad guidelines should be finalized by mid 2005.

6. The AACPE encourages WHO to continue to identify and address remaining gaps in knowledge (iVDPV prevalence, risks associated with each type of monovalent OPV, relevance of "other" VDPVs, review of historic data on use of IPV in outbreak response) that may contribute to more informed decision making on the process of stopping OPV use, reducing risks in the post-cessation period, and developing capacity to respond to any events during that period.

7. The AACPE is encouraged by the prospect of a potentially effective IPV using Sabin poliovirus strains, and urges acceleration of studies to demonstrate safety and protective efficacy. An update on the status of Sabin-IPV, including the current situation, (protective efficacy in monkeys and transgenic mice, production

and licensing issues, documentation of attenuation), remaining questions to be answered, and the prospects for its development and use, should be prepared by WHO by end 2004.