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Report of the interim meeting of the Technical Consultative Group (TCG) on the Global Eradication of Poliomyelitis

Geneva, 13-14 November 2002



Vaccines and Biologicals

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Abbreviations

AFP	acute flaccid paralysis
AFR	African Region
AMR	Region of the Americas
cVDPV	circulating vaccine-derived poliovirus
DR Congo	Democratic Republic of the Congo
GCC	Global Certification Commission
IEC	information, education, communication
IPV	inactivated polio vaccine
iVDPV	vaccine-derived poliovirus associated with immunodeficiency
mOPV	monovalent oral polio vaccine
NID	national immunization day
OPV	oral polio vaccine
SIAs	supplementary immunization activities
SNIDs	subnational immunization days
TAG	technical advisory group
TCG	Technical Consultative Group
UNICEF	United Nations Children's Fund
UP	Uttar Pradesh (India)
VAPP	vaccine-associated paralytic poliomyelitis
VDPV	vaccine-derived poliovirus
WHO	World Health Organization

1. Executive summary

An interim meeting of the Global Technical Consultative Group (TCG) for Poliomyelitis Eradication was held in Geneva from 13 to 14 November 2002 to evaluate the status of eradication at end-2002 and the feasibility of the proposed timeframe for the interruption of transmission, to identify the remaining constraints to eradication and propose potential solutions, and to review progress in the development of appropriate policies for the post-certification era.

Substantial progress continues to be made in the global effort to eradicate polio. Transmission is limited to a small number of countries and, within these countries, to relatively small geographical areas. Nine of the 76 states or provinces in India, Nigeria and Pakistan are responsible for over 90% of cases reported to date in 2002. Surveillance and monitoring data have been used successfully in several countries to identify problem areas, to detect sub-populations at greatest risk, to evaluate programme performance, and to guide the development and modification of strategies.

Surveillance information indicates that the remaining polio burden is caused by a failure to vaccinate children at risk both in routine and supplementary immunization activities (SIAs). Community mobilization efforts have been substantially enhanced, with a detailed evaluation ongoing. Through the identification of new fundraising opportunities and coordinated partner fundraising efforts, there has been some success in narrowing the funding gap, a critical impediment to completing eradication efforts.

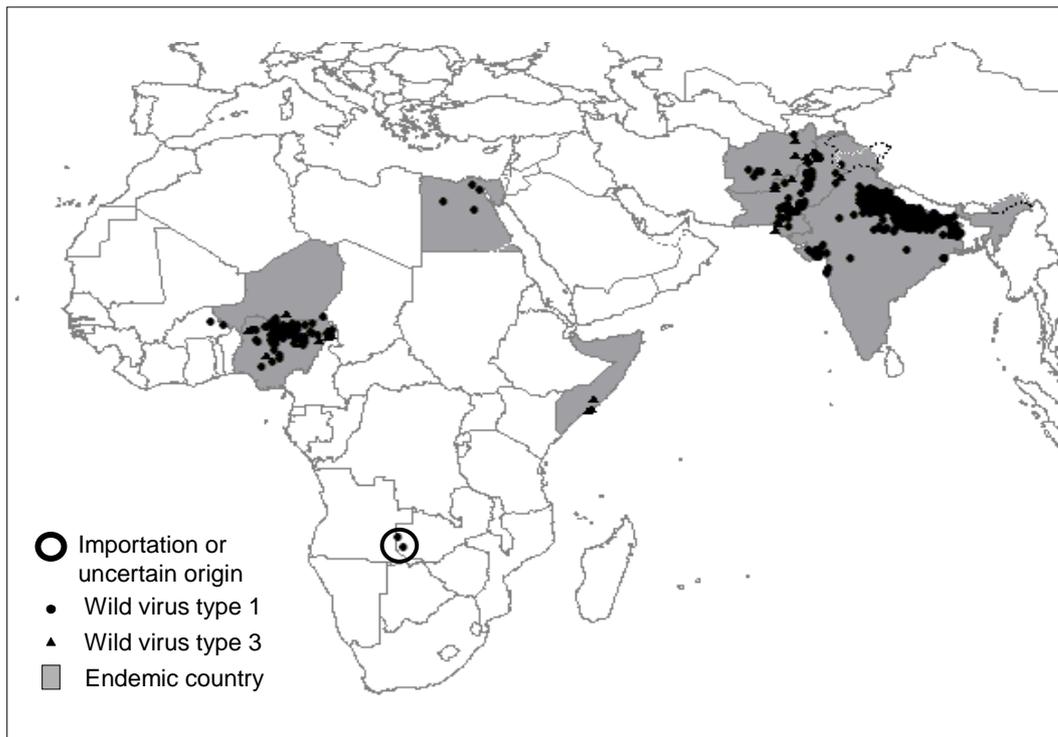
Nevertheless, the TCG has grave concerns about achieving eradication within the next 6-12 months, particularly in India, Nigeria and Egypt. Termination of wild virus transmission is scientifically feasible, and all available data reaffirm the soundness of the polio eradication strategies. However, there are major political, managerial, and operational barriers to be overcome to achieve eradication. Unless such barriers are urgently addressed by an intense effort of the national governments of the affected countries, WHO and the polio eradication partners, polio transmission can be expected to continue throughout 2003 and beyond. The number one priority of the global programme must remain to interrupt transmission of wild poliovirus in the remaining endemic countries. While the resource gap has narrowed, as noted above, substantial financing needs still exist, which must be addressed if critical activities are to be implemented.

2. Stopping polio transmission

2.1 General epidemiological situation and programme progress

The TCG reviewed epidemiological and virological data available to the global programme as of 12 November 2002, and discussed potential messages that the programme could give to the global partnership at end-2002. In 2002 to date, eight countries have reported wild poliovirus, seven of which can be considered endemic (Figure 1), compared to 10 endemic countries at end-2001 and 20 countries at end-2000. Nevertheless, as of 6 November 2002, 1069 cases have been reported, which probably represents more than 200 000 infections, indicating that there still remain areas of intense transmission.

Figure 1: Distribution of indigenous wild poliovirus-confirmed cases in 2002, as of 12 November



Three countries, India, Nigeria and Pakistan, are demonstrating high-intensity transmission, and are responsible for over 95% of cases globally in 2002. However, 90% of these cases occurred in just nine of the 76 states or provinces of these three countries. All of these countries have high population density which facilitates persistence of poliovirus transmission, and all have historically been regional and global reservoirs of wild type poliovirus. In both India and Nigeria a five-fold increase in the number of cases is being reported in 2002 compared to the same period in 2001 (Figure 2).

2.2 Countries and areas with high-intensity transmission

India

In 1999-2000 India implemented 10 national and subnational rounds of supplementary polio immunization, including six rounds within a 12-month period. Cases declined by more than 80%. In contrast, only three large-scale rounds were conducted in 2001 (Table 1), and in 2002 polio transmission surged, reaching nearly 900 cases as of 6 November, accounting for over 80% of the world's polio virus.

Figure 2: Wild poliovirus-confirmed cases 2001–2002, comparison at 12 November each year

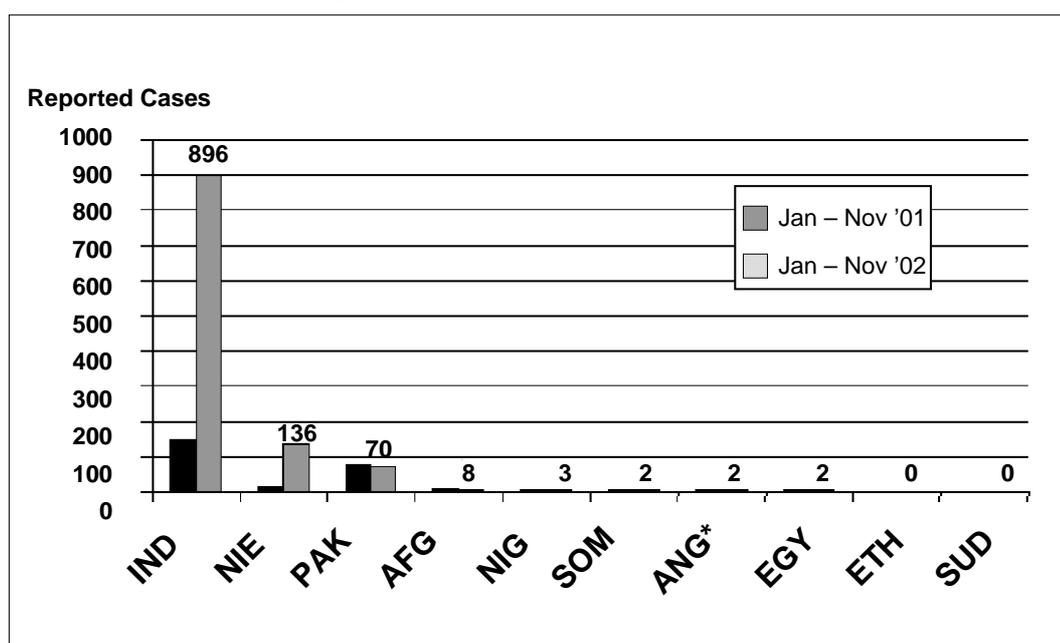


Table 1: Number of national immunization days (NIDs) and subnational immunization days (SNIDs) conducted in high-intensity transmission countries, 2002

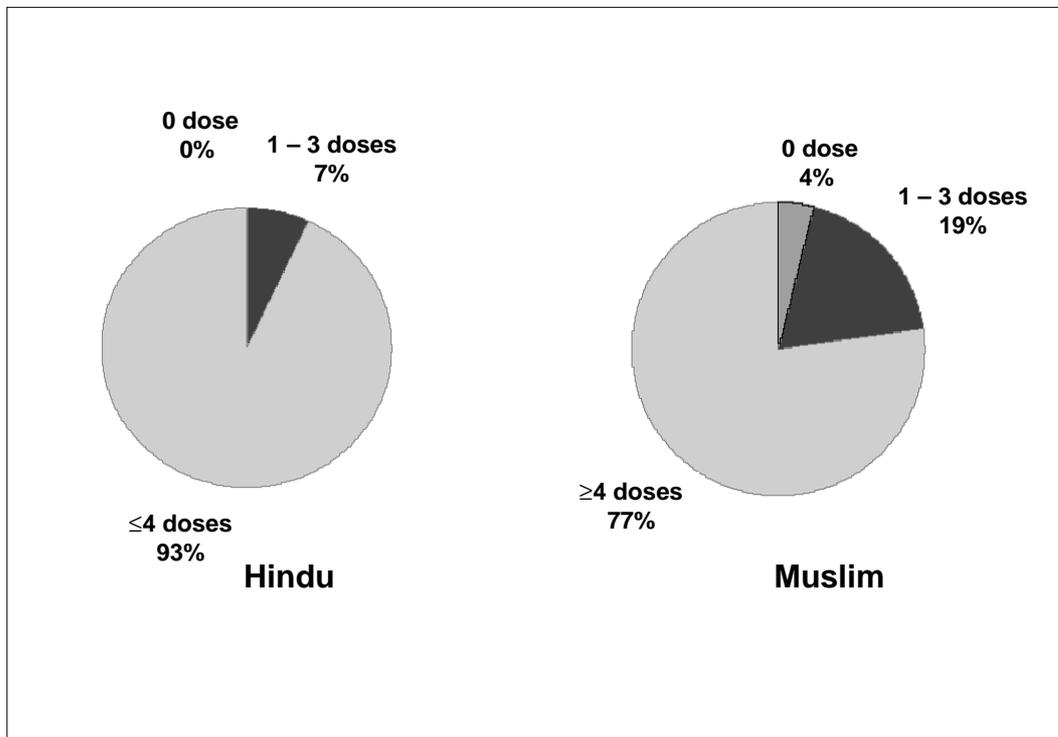
	Pakistan	Nigeria	India
NIDs	4 rounds	2 rounds	2 rounds
SNIDs	4 rounds	4 rounds	1 round

Transmission continues to be most intense in the state of Uttar Pradesh (UP), which contributes over 75% of reported cases nationally in 2002, and is equal to more than 50% of the reported cases globally. Case numbers have increased significantly in 2002 due to a major outbreak of type 1 wild poliovirus in eastern and central UP.

Available programme data show that the cause of the outbreak in east and central UP, and of the ongoing intense endemic transmission in western UP, is the continued existence of gaps in the quality of immunization activities. The data show that, particularly in western UP, the minority Muslim population is much less well immunized than the population as a whole (Figure 3).

Wild poliovirus will continue to circulate until this minority community is effectively covered with oral polio vaccine (OPV). Although there is some evidence that the quality of supplementary immunization activities (SIAs) is improving as a result of the extensive efforts being made both in operations and in social mobilization, these improvements will have to be sustained and greatly expanded over multiple rounds to have a significant impact. Government ownership of polio eradication efforts at national level and state level in UP is essential to ensure that the necessary but difficult strategic and operational decisions to drive improvements in quality are taken, and to mobilize the vast human and material resources available.

Figure 3: Number of doses of OPV received by non-polio acute flaccid paralysis (AFP) cases aged six months to five years by community, Western Uttar Pradesh, India



The TCG considers that India, and the state of Uttar Pradesh in particular, constitutes the greatest challenge to the achievement of global polio eradication. While it is technically feasible to interrupt transmission in 2003, this will require a massive effort by the Government at national, state and district levels, to address quality issues in SIAs, and to reach and engage minority populations in UP. If this effort is not successful, transmission will continue into 2004.

Recommendations:

- A consultation involving national and state Government officials at the highest levels, WHO and UNICEF should be convened in India as soon as possible to ensure Government understanding of the situation at this critical juncture, to obtain firm and ongoing commitment, and to optimize partner support.
- Recognizing the complexity of polio eradication activities in a state as large and diverse as UP, the Government should form substate operational groups to manage operations with the support of partner agencies.
- The Government at national and state level in UP should commit sufficient numbers of high-quality staff to manage polio eradication activities at national, state and substate levels.
- The TCG believes that it is critical to conduct at least six rounds of large-scale supplementary polio immunization in high-risk areas in 2003. This could consist of two rounds of full NIDs and four rounds of SNIDs covering the high-risk states and areas in northern India. Following the NID rounds in January and February 2003, which will be critical to stopping transmission in non-reservoir areas, the first two SNID rounds should be carried out in March and April, to take advantage of the low transmission season.
- Extensive efforts must continue to be made to improve the quality of SIAs, most particularly to engage and immunize minority communities in Uttar Pradesh that are currently under-immunized. Such communities should have appropriate representation in decision-making and implementation of activities at community, district and state level.
- Activities in 2003 must be driven by the analysis of surveillance and SIA monitoring data, which should be used to identify high-risk groups and areas for targeted activities. The programme should allow for flexibility of strategies at district level to reach risk groups based on analysis of data.
- The TCG requested that these recommendations be formally communicated to the Indian Government and also to the India Expert Advisory Group prior to their meeting on 25-26 November 2002 so that the details could be discussed in that forum.

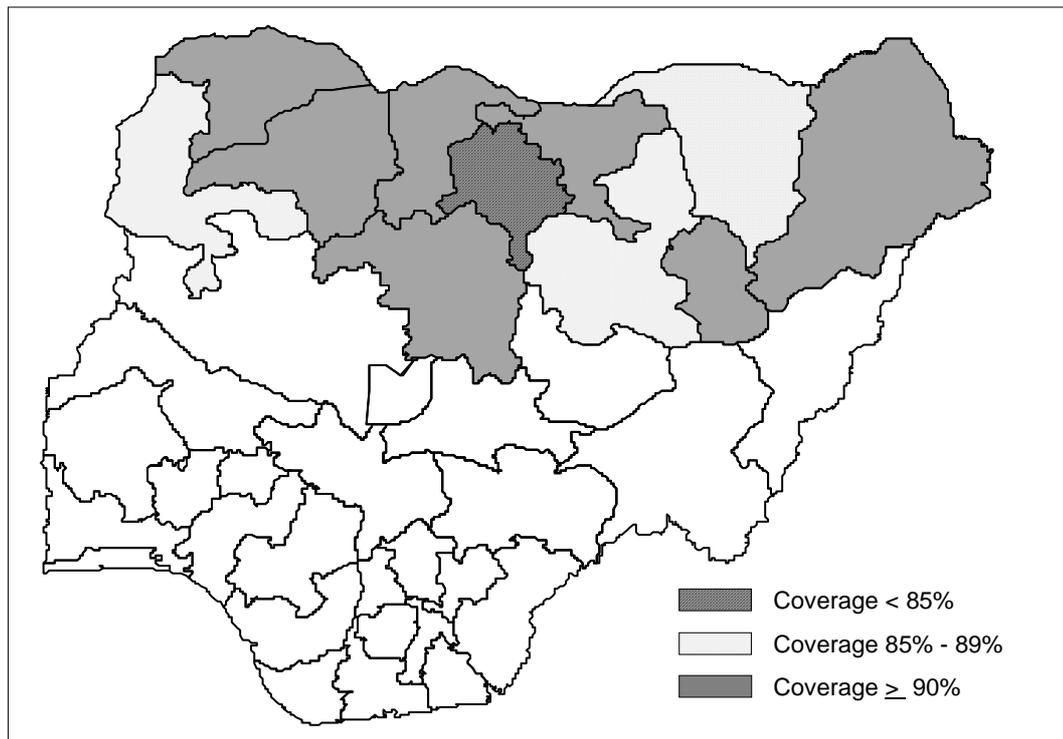
Nigeria

In 2002 there has been a major increase in reported cases compared to 2001. Although this is partly due to a distinct improvement in surveillance quality, particularly in the north, transmission is clearly intense. Cases have been relatively geographically restricted, with seven states in northern Nigeria reporting over 90% of cases. Two states, Kano and Kaduna, have reported nearly half of the total cases to date in 2002, and were the only transmission areas detected during the low transmission season. Surveillance and laboratory indicators began to improve in 2001, and have reached certification standard in 2002. Virological evidence demonstrates that many of the strains causing disease in prior years are no longer circulating, with only a limited number of strains remaining in circulation in 2002.

However, real improvement in the quality of SIAs occurred only in mid-2002. Data from the acute flaccid paralysis (AFP) surveillance system show that in several polio-infected states most non-polio AFP cases aged < 5 years (used as a proxy for this age group overall) have received less than three doses of OPV. Performance indicators used in monitoring SIAs quality in recent rounds have shown marked improvements in both operations and social mobilization, but this needs to be consistently maintained to have an impact on transmission. Of particular concern to the TCG is that despite improvements, SIA quality indicators for Kano and Kaduna remain lower than for other states (i.e. range of 75–85% coverage) (Figure 4). A national technical advisory group (TAG) met in September 2002 and provided specific recommendations on activities in 2002 and early 2003. Government commitment at national level is strong but much higher engagement and advocacy is necessary at state Government level in the high-risk states.

The TCG considers that it is still technically feasible to interrupt transmission of wild poliovirus in Nigeria in 2003, but that major operational issues must be overcome and ownership of the programme must be greatly increased at state Government level and below. If improvements in the qualities of SIAs are not sustained and expanded in 2003, especially in the highest burden states, transmission will continue into 2004.

Figure 4: Coverage of children <5 years in 11 high-risk states in Nigeria, October 2002



Recommendations:

- Government ownership of polio eradication efforts at national level and state level in high-burden states of Nigeria is essential to improving and sustaining quality. A consultation involving national and state Government officials at the highest levels, WHO and UNICEF should be convened as soon as possible to ensure Government understanding of the situation at this critical juncture, to obtain firm commitment of high-quality resources and to optimize partner support.
- As recommended by the national TAG, three rounds of SNIDs should be carried out in high-risk states in the first half of 2003. Ideally these rounds should be carried out as early in the year as possible, taking into account the impact of national elections. Consideration should be given to expanding the January round from four states to seven or eight states in the north. Maximum efforts must be made to ensure the highest quality possible, especially in the highest burden states. Furthermore, extensive independent monitoring should be carried out both to ensure rapid response in problem areas and to provide independent assessment of quality.
- Recognizing the complexity of polio eradication activities in a country as large and diverse as Nigeria, the Government should form subnational operational groups with the support of partners to manage operations. These groups should consist of national and state Government, and partner agency staff.
- Activities in 2003 must be driven by enhanced analysis of surveillance and SIA monitoring data, which should be used to identify high-risk groups and areas for targeted activities. WHO must provide strong technical support for this analysis, given their central role in ensuring surveillance quality in Nigeria.

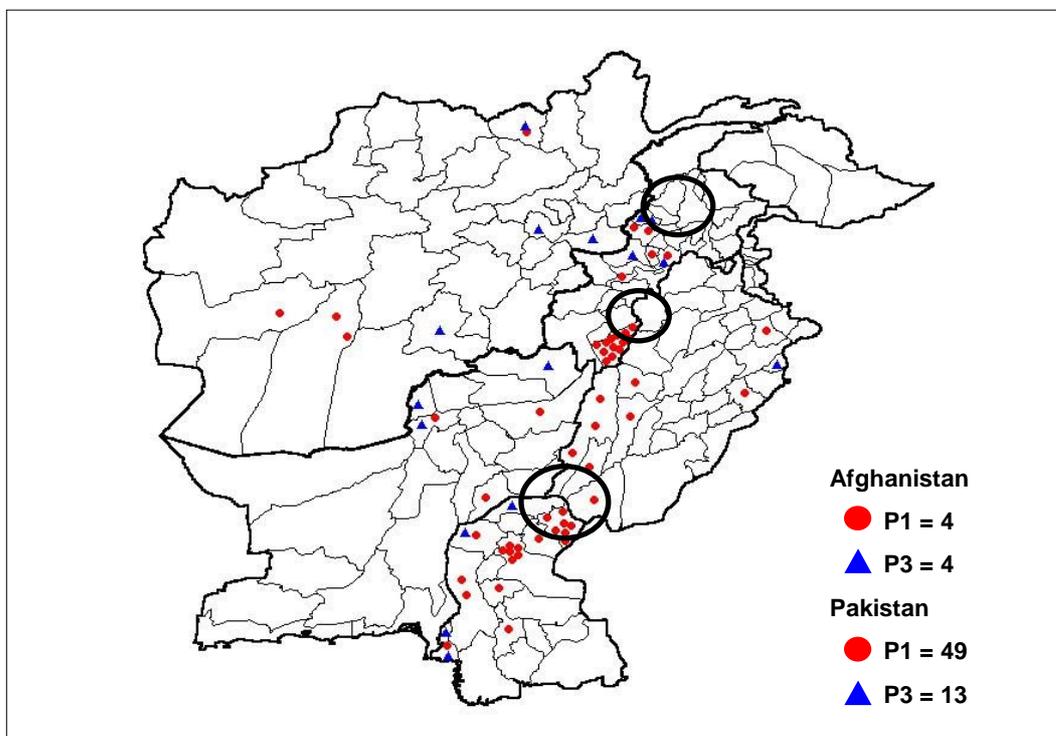
Pakistan

Good quality surveillance data demonstrate that although case numbers in 2002 are similar to 2001, transmission has been reduced significantly in the traditional reservoir areas for wild poliovirus in the country. Nearly half of all cases are due to point outbreaks in non-reservoir areas (Figure 5), and are caused by viruses closely related to the strains circulating in the reservoirs.

Virological evidence also demonstrates that many of the strains causing disease in prior years are no longer circulating in 2002 with only a limited number of strains remaining in circulation. Analysis of surveillance data is thorough and is used to inform programme decisions. Extensive monitoring of the quality of SIAs is carried out prior to, during and after each round. While virus continues to be detected in all four provinces, there is clear evidence of continuing progress and of quality improvement in SIAs. Areas of concern remain, including Baluchistan where AFP surveillance data indicate lower immunization status than in other provinces. Government commitment is high at national, provincial and, increasingly, district levels. A national TAG meets regularly and provides specific recommendations for programme activities.

The TCG considers that if there is continuing progress in improving the quality of SIAs in Pakistan, it is feasible that transmission of wild poliovirus will be interrupted in 2003. However, if efforts are not maintained at high intensity, polio transmission will continue and could even increase.

Figure 5: Distribution of wild virus cases 2002 in Pakistan and Afghanistan as of 12 November



Recommendations:

- The TCG endorses the SIA plan proposed in Pakistan for four rounds of NIDs and four rounds of SNIDs in 2003.
- The TCG endorses the strategy of concentrating on identified reservoir and high-risk areas with the aim of stopping transmission in 2003.
- To continue the progress to date, the TCG urges the new Government of Pakistan to maintain the high level of ownership and commitment that has been demonstrated to date.

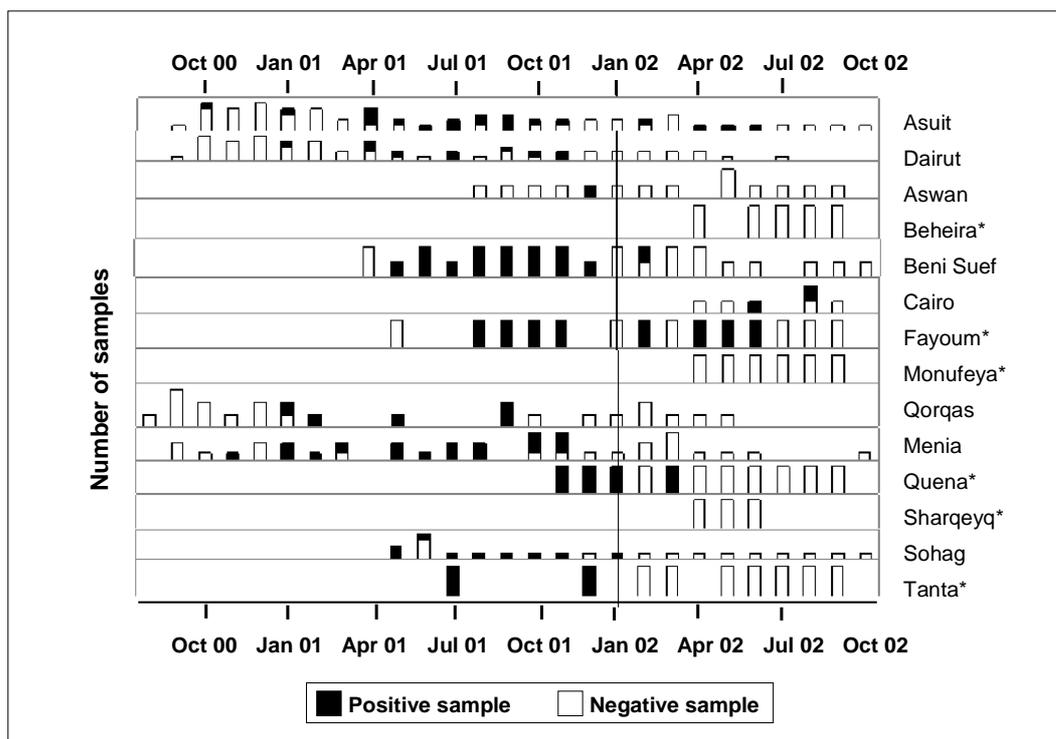
Egypt

Of the remaining countries with wild poliovirus transmission, Egypt is of greatest concern, even greater than those countries affected by conflict. Evidence of persistent transmission of multiple lineages of wild poliovirus from environmental sampling (Figure 6), combined with the failure to identify polio cases despite improving surveillance indicators, raises serious questions about the quality of the programme in Egypt.

With the current level of surveillance quality, the system should be consistently identifying polio cases and this is not happening. Reporting of two recent polio cases was significantly delayed, and this is not acceptable from a system as well developed as that of Egypt.

While the TCG remains extremely concerned about Egypt, there are several encouraging developments. The country TAG has been active in identifying problem areas and recommending actions to address them. Detection and investigation of AFP cases has improved significantly. Furthermore, data from the latest house-to-house NID rounds indicate substantial improvements in quality. The polio partnership has functioned effectively in support of these improvements in SIA operations, particularly to improve social mobilization and information, education and communication (IEC) activities, with strong UNICEF support.

Figure 6: Frequency of wild poliovirus isolation from environmental samples by site, Egypt 2002



The foundation exists to interrupt transmission of poliovirus in Egypt. However, unless there is further intensification of efforts to improve the quality, timeliness and transparency of all aspects of the programme, wild poliovirus transmission in Egypt is likely to persist throughout 2003 and beyond.

Recommendations:

- The TCG reinforces recommendations of the TAG for polio eradication in Egypt, specifically to improve the promptness and transparency of reporting and investigating AFP cases in Egypt. The detection of wild poliovirus must be seen as helpful for programme implementation, and individuals who report cases should be rewarded.
- A joint international and national surveillance review in Egypt in early 2003 will be critical to restoring faith in the veracity of the surveillance system.
- Independent monitoring of SIAs commenced during autumn 2002. NIDs should be continued to help identify gaps and independently confirm quality.

2.3 Low-intensity transmission countries/areas

Afghanistan and Somalia

Afghanistan and Somalia have maintained strong programmes despite major challenges, including insecurity, conflict and large-scale population movements. In Somalia, continued circulation of wild poliovirus type 3 was reported in the first quarter of 2002, but no case has been found since March of this year. Through an extraordinary cooperative effort by the UN security system, improved access for international staff to Mogadishu has been achieved, allowing monitoring of the quality of the most recent SIA rounds. In Afghanistan, despite the recent war and return of over two million people, only eight virus-confirmed cases of polio have been reported to date in 2002. The only remaining known wild poliovirus reservoir area is the southern region, bordering Baluchistan in Pakistan (see Figure 6). The national TAG for Afghanistan met in early November 2002 and made a number of specific recommendations to address areas of concern. In both Somalia and Afghanistan, the national TAGs are active in identifying constraints to programme implementation and proposing solutions.

Angola

Of the remaining countries that were endemic in 2001, no cases have been detected in Angola to date, but wild type 1 poliovirus was isolated in Zambia as recently as February 2002 from polio cases among the Angolan refugee population. Although access to eastern Angola has improved considerably over the last 6-12 months, and a nationwide AFP surveillance review has been carried out, ongoing transmission in the eastern provinces of Angola cannot be ruled out. This must now be considered the area of greatest concern in southern Africa.

Niger

Niger has demonstrated continued low-intensity virus transmission in 2002. Although the viruses detected are closely related to the Nigerian reservoir viruses, there is evidence of independent wild poliovirus transmission. Recent isolation of a wild poliovirus in Burkina Faso, close to the border with Niger, demonstrates the risk of wild viruses spreading across several West African countries. Poliovirus transmission in Niger and Burkina Faso must be dealt with rapidly through extensive mop-up operations, and high levels of population immunity maintained to guard against importation of wild poliovirus from the reservoir areas in Nigeria.

Ethiopia and the Sudan

In Ethiopia and the Sudan, wild poliovirus-confirmed cases have not been detected for more than 18 months. Although this is very encouraging, surveillance gaps remain, particularly in eastern Ethiopia and southern Sudan. In both countries national TAGs provide specific recommendations for addressing areas of concern.

The TCG noted that the wild poliovirus transmission detected in West Africa in 2001, centred on Mauritania, appears to have been effectively dealt with by an extensive mop-up campaign spanning three countries, with no cases detected in the area to date in 2002. The TCG also noted the recent successful completion of NIDs in Madagascar, in response to the isolation of circulating vaccine-derived poliovirus (cVDPV) in Madagascar in mid-2002.

In summary, the TCG believes that it is feasible to interrupt indigenous transmission of wild poliovirus in all low-intensity transmission countries in 2003, provided that the quality of surveillance and SIAs continues to improve in these areas.

Recommendations:

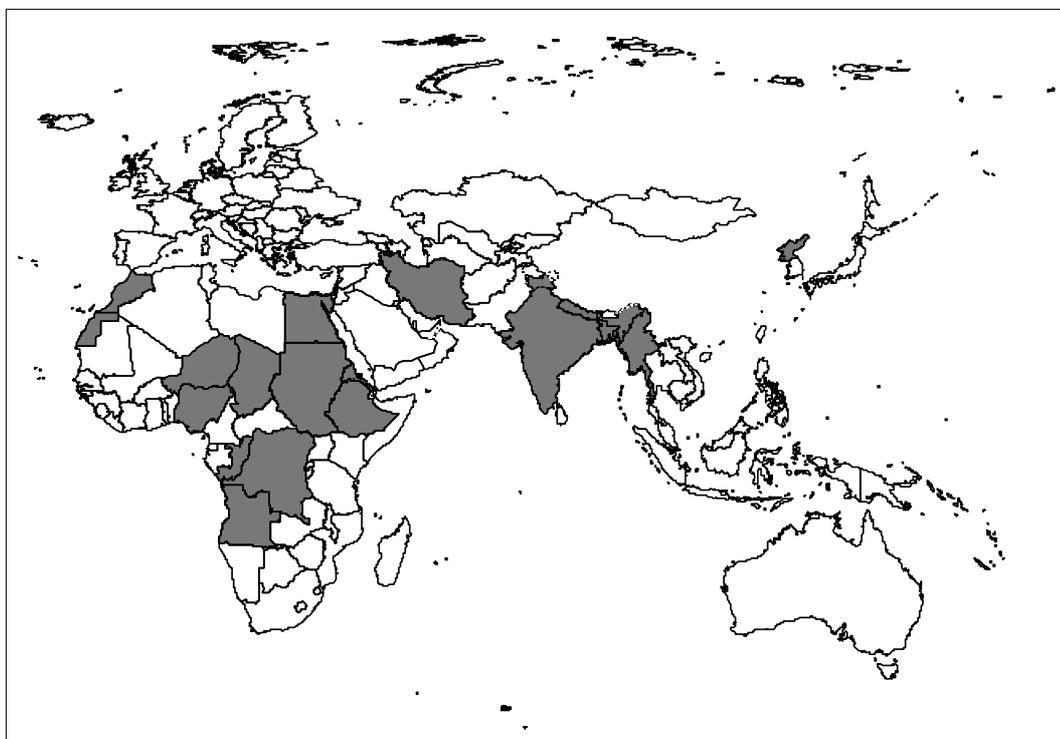
- All countries with low-intensity transmission of wild poliovirus must focus efforts on attaining very high levels of surveillance quality to ensure that any remaining areas of transmission can be rapidly detected and dealt with. SIAs in 2003 must be of the highest possible quality to ensure that transmission is stopped in these areas.
- SIA and surveillance activities in Niger and Burkina Faso must be closely coordinated with those of Nigeria.
- In Angola, in addition to the three NIDs rounds that are planned for 2003, at least two rounds of SNIDs should be carried out in the eastern provinces in early 2003. The planned country TAG should be convened as soon as possible to provide detailed programme recommendations.
- Partnership support to Afghanistan must be maintained at a high level to ensure that planned programme activities can be implemented successfully. In particular, resources should be allocated to the remaining reservoir area in the southern region of that country.
- In low transmission areas where security is an issue, continued efforts should be made to ensure effective access for surveillance and immunization activities, including the placement of security officers where necessary.

3. AFP surveillance: progress and priorities

The TCG reviewed data on the performance of global AFP surveillance. Significant progress was noted in improving surveillance systems in countries in all endemic regions, most particularly the African Region (AFR). The TCG noted specifically the following areas of progress in 2002:

- an increase in the number of countries with certification-standard surveillance;
- a decrease in the proportion of AFP cases classified as polio-compatible, from 6% in 2001 to a more realistic 1% in 2002;
- the successful completion of surveillance reviews in most endemic and high-risk countries, in part in response to recommendations of the seventh TCG (Figure 7);
- the identification of specific areas/countries of concern for follow-up.

Figure 7: Countries in which external AFP surveillance reviews were conducted between April 2001 and November 2002



The TCG noted that despite improvements surveillance quality was still not adequate in all countries of southern Africa and that Mozambique and Madagascar in particular continue to have suboptimal surveillance. The risks of poor surveillance have been amply demonstrated in the African Region in recent years through numerous importations of wild poliovirus from endemic areas into polio-free countries, as well as by the recent vaccine-derived polio virus (VDPV) outbreak in Madagascar. In the Region of the Americas (AMR), the slippage in surveillance quality in some countries is a significant cause for concern. The TCG recognizes the usefulness and importance of surveillance reviews in identifying subnational surveillance gaps and the necessary programmatic actions to close them.

Polio-compatible cases are an indicator of surveillance quality and when occurring in clusters can potentially represent undetected virus circulation. Data from India indicate that clusters of compatible cases were most likely to occur in areas with known wild poliovirus circulation. However, many clusters of compatible cases have been shown not to be the result of wild virus transmission. Thus, the detection of such a cluster should not automatically lead to an SIA but rather trigger a careful investigation as per the existing guidelines on response to a suspected outbreak of poliomyelitis.

Recommendations:

- A number of surveillance gaps have been identified at subnational level by the combination of surveillance reviews and detailed analysis of surveillance data. These gaps should be closed as soon as possible to ensure uniform high-quality in surveillance. Particular attention should be given to geographic areas affected by conflict and/or historical global reservoirs of poliovirus (e.g. Ethiopia, Sudan).
- The TCG endorses the current schedule of surveillance reviews for 2003 but requests the Secretariat to consider repeating reviews in areas where significant problems or challenges have been identified (e.g. DR Congo). The TCG also requests that a revised schedule of reviews be submitted to the next TCG meeting.
- All clusters of polio-compatible cases should be fully investigated to exclude the possibility of missed wild poliovirus transmission, with an assessment as to whether SIAs are indicated.

4. Post-certification polio immunization policy

4.1 Framework for the assessment and management of paralytic polio in the post-certification era

The TCG and other forums have previously noted the need for a relatively simple framework to summarize the risks of paralytic poliomyelitis in the post-certification era and explain how those risks might evolve over time (Table 2). Such a framework will be of particular importance for discussions with OPV-using countries and for developing policy decision models.

Table 2: Probable evolution of the risks of paralytic poliomyelitis through the potential cessation of OPV immunization

Milestone	Risk evolution	1° risks	Timeframe	
Today	WPV > VDPV	Importations		
All 6 Regions certified	VDPV > WPV	VAPP/cVDPV/lab		3–5 years
Global Certification + Containment	VDPV >> WPV	VAPP/cVDPV		1–2 years
OPV cessation	VDPV > WPV	cVDPV		? years
cVDPV Certification	WPV > VDPV	Labs		3 years

WHO has now developed a framework that summarizes these risks into two major categories, including those due to:

- a) vaccine-derived polioviruses:
 - polio cases due to vaccine-associated paralytic poliomyelitis (VAPP);
 - outbreaks due to circulating vaccine-derived polioviruses (cVDPVs);
 - long-term, immunodeficient excretors of vaccine-derived polioviruses (iVDPVs).

-
- b) wild poliovirus cases or outbreaks resulting from:
- inadvertent release from an inactivated polio vaccine (IPV) production site;
 - inadvertent release from a laboratory storing wild poliovirus;
 - intentional release of wild poliovirus from any source.

This framework also summarizes current knowledge on the magnitude of these risks, how these risks are expected to evolve over time, as well as the expected impact of the risk management strategies. The TCG notes that, in line with discussions at the seventh TCG meeting, the risk framework continues to assume that OPV will continue to be used for the foreseeable future.

Recommendations:

- The TCG considers the proposed risk framework to be appropriate; it should, after further revision, form the basis for consultations with OPV-using countries on current and future polio immunization policy, and for developing immunization policy decision models. Feedback on the utility of this framework, following its use during country consultations, should be provided to the TCG at its next meeting.

4.2 Risk assessment: frequency and burden of VAPP, cVDPV and iVDPV

The small but continuing risks of paralytic polio attributable to the vaccine itself is anticipated to be a key factor in the risk assessment for OPV-using countries. WHO has developed preliminary estimates of the frequency and potential burden of disease due to VAPP on the assumption that countries are most likely to be interested in the total burden of VAPP cases, rather than in the traditionally used measures to estimate the risk of VAPP - the rates of VAPP cases by overall (or first) doses of OPV administered. The global VAPP burden, using data from India and the USA and expressed as the number of cases per birth cohort in OPV-using countries, has been calculated as in the range of 250-500 cases per year.

Polio outbreaks caused by cVDPVs have been documented on four occasions, including one outbreak in each of the last three years. A common risk factor contributing to the emergence of cVDPVs has been the low level of routine OPV use in affected populations, resulting in substantial gaps in the immunity to poliovirus. Implementation of the new TCG policy for SIAs in polio-free areas is expected to reduce future occurrences (see Recommendations of the seventh TCG). The cVDPV outbreaks that have been documented have resulted in less than 100 cases, but experience from the pre-eradication era in Egypt shows that cVDPVs may establish endemicity under certain conditions.

The risk of cVDPV emergence is difficult to quantify because of the extreme rarity of these events. However, this risk is not zero. The main determinants which appear to increase the risk of cVDPV emergence are decreasing immunization coverage, leading to increased susceptibility in the population, with continued introduction of OPV. Such a setting potentially seeds susceptible populations with vaccine-derived polioviruses under conditions that could select for increased transmissibility of these viruses.

Following 40 years of OPV use, 19 cases of long-term VDPV excretion associated with immune deficiencies (iVDPV) have been documented, of which four patients are known to excrete iVDPV today. There has been little progress to date to therapeutically clear VDPV excretion in such patients. However, a number of pharmaceutical companies have expressed interest in working with WHO to test existing antiviral compounds for activity against VDPV excreted by immunodeficient individuals.

Recommendations:

- Expressing the VAPP burden in terms of the number of cases per birth cohort in countries using OPV is a useful approach, which will facilitate understanding of the complex issues involved by immunization policy decision-makers. Upon further consultation on the methods, and after the addition of other relevant data, the WHO estimates of VAPP burden should be submitted for peer review and publication. These estimates should then be used in discussions with OPV-using countries on future polio immunization policy.
- Further research is needed to understand the frequency of and burden of disease due to cVDPVs and iVDPVs, as well as the epidemiology of transmission of such viruses. At its next meeting, the TCG requests to be briefed on additional work conducted on the most appropriate way to present risk estimates for cVDPVs and iVDPV to decision-makers.
- WHO should convene an informal consultation of experts on VDPVs in early 2003 to review the current knowledge in this area, to evaluate its implications for polio immunization policy in the post-certification era, and to guide further relevant operational and scientific research.
- WHO should implement its planned programme of work to identify and test antiviral compounds for activity against VDPVs from chronic excretors.

4.3 Risk management

4.3.1 VDPV investigation and response guidelines

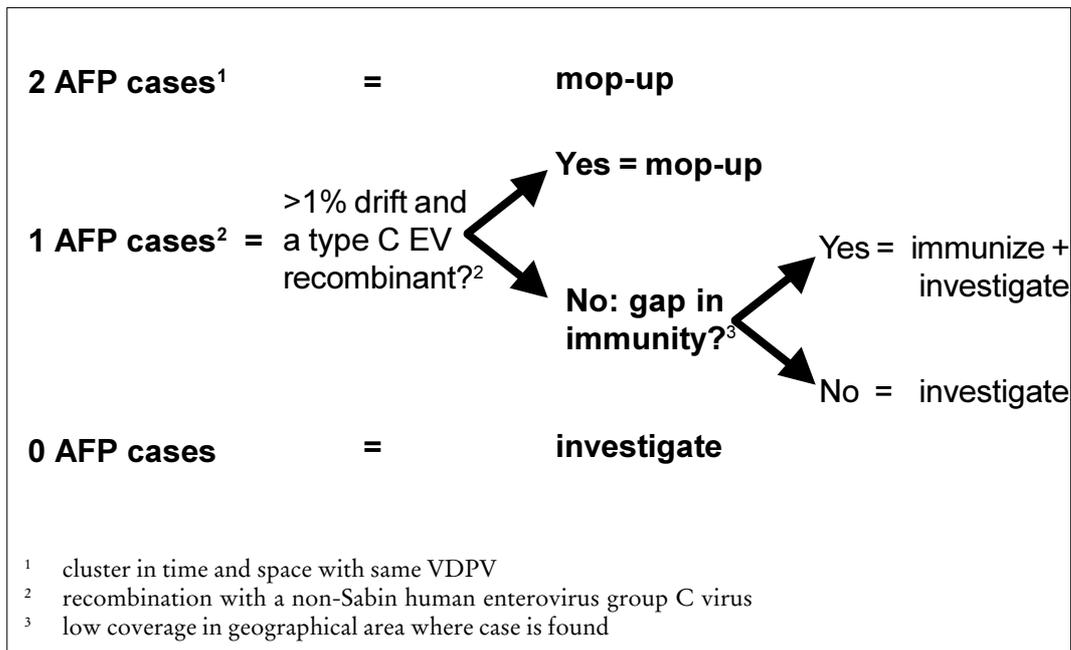
With heightened surveillance, an increasing number and variety of VDPVs are being isolated. Taking into account the existing guidelines for responding to a polio outbreak due to wild poliovirus, interim guidelines have been developed for responding to the isolation of VDPVs, using the limited data and experience available (Figure 8). These guidelines emphasize the need for a mop-up response to (a) any AFP cases from which a VDPV is isolated which has greater than 1% genetic drift and recombination with a group C non-polio enterovirus; and (b) any cluster of AFP cases from which a common VDPV is isolated.

The guidelines state that in all other instances the first response should be an appropriate epidemiological, clinical, immunological and virological investigation. If there is an identified immunization coverage gap, this should be addressed while the investigation is ongoing.

Recommendations:

- The proposed guidelines for VDPV investigation and response should be implemented as soon as possible by all regions. The existing guidelines for responding to a suspected outbreak of polio should be modified to include the response to VDPVs.
- These guidelines should be regarded as “interim” and updated as new information on the significance and programmatic implications of VDPVs becomes available.

Figure 8: Interim decision-tree for responding to the isolation of a vaccine-derived poliovirus (VDPV)



4.3.2 Laboratory containment

The TCG notes that considerable progress is being made in the implementation of the *Global action plan for laboratory containment of wild polioviruses* (WHO/V&B/99.32), and in establishing appropriate containment levels at production sites for IPV worldwide. IPV producers, in particular, have shown excellent cooperation with the global containment efforts.

Increasing attention is now being given to strengthening the oversight of the containment process, and to developing methods for validating the outcomes of the containment process. Guidelines for assessing the quality of the national laboratory survey and inventory activities have been produced and pilot-tested. Similar mechanisms need to be defined and developed for subsequent stages of the containment process. Oversight is needed to ensure appropriate technical inputs in the development of these processes and close alignment of work in the broad areas of “laboratory containment” in general biomedical laboratories and containment at IPV production sites. A number of potential oversight mechanisms are proposed to be discussed by the Global Certification Commission (GCC) in early 2003, with consideration of the formation of a subgroup responsible for all aspects of the containment process, including the validation of containment activities.

Recommendations:

- The TCG endorses the proposal of the Secretariat for the formation of a subgroup with the appropriate expertise in polio eradication and biosafety to advise the GCC on the containment of wild poliovirus. The TCG further recommends that this proposal be submitted to the GCC for consideration at its next meeting.
- Efforts to assess and validate the quality, accuracy and completeness of implementation of each stage of containment activities should continue.
- Further experience should be gathered with the draft guidelines for assessing the quality of the national survey and inventory process so that a systematic plan for its use can be developed. Results on these activities should be reported to the TCG.

4.3.3 The efficacy of IPV in developing countries

The use of IPV for a transitional period is one of the options being considered for post-certification polio immunization policy. The TCG previously recommended that given the complexities (and uncertainties) with routine IPV use in developing countries, a multi-year pilot/demonstration project of IPV routine use (combined with related operational research) should be explored in a tropical island setting. A concept paper on such a project has been developed and two potential study sites identified. The TCG strongly endorsed the concept and suggested that the detailed protocols should include better definition of the outcomes for determining the success of the project and specifics as to how the potential impact of different vaccine formulations would be investigated.

Recommendations:

- Feasibility studies of two or more potential IPV project sites should be undertaken and, if supported by the outcome of these assessments, detailed protocols should be developed for review at the next TCG.
- Further work should be done to ensure there is adequate financing in place to implement the(se) project(s) over a five-year period.
- The TCG also endorses additional IPV immunogenicity studies, particularly to address proposed schedules of administration, in tropical countries with OPV-free environments and large, dense populations.

4.3.4 Vaccine stockpiles

All potential polio immunization policy options for the post-certification era require the preparation of, and equitable access to, a stockpile of vaccine in case of need. Such stockpiles will be needed to cover two distinct periods of risk to populations: the first would be the immediate post-certification period when the risk would most likely come from unrecognized continued chains of transmission or the emergence of a cVDPV; second, the remaining longer-term risk related to the re-introduction of wild polioviruses from a laboratory or IPV production site.

The recommended stockpile vaccine for the first period of risk has been monovalent OPV (mOPV), pending a favourable review of mOPV safety issues, and a more detailed assessment of the implications of the potential persistence of cVDPV. WHO is obtaining expert opinion on mOPV safety issues to be available by the time of the next meeting of the TCG. Whether mOPV, or indeed any live vaccine, would be the stockpile vaccine of choice for dealing with longer-term risks requires further consideration. The TCG notes that current estimates of the necessary size of vaccine stockpiles follow a recommendation from the Polio Research Steering Committee to use estimates of the number of doses that would be needed to cover the at-risk population for an interim period while manufacturing of OPV was re-started.

Recommendations:

- The TCG requests that a comprehensive stockpile plan be developed, including the size, type of vaccine, the form in which the stockpile would be held, locations, and criteria for release, taking into account the needs in the period immediately after stopping OPV use and periods further distant in time.
- The work on vaccine stockpiles for use in the post-certification era should be accompanied by the development of strategies/plans for outbreak control in a post-OPV vaccination era.
- Plans should be developed to ensure that vaccine stockpiles could be developed while there is excess bulk OPV manufacturing capacity.

4.3.5 Economics of potential post-certification policies

In response to a recommendation of the seventh TCG meeting, a meeting on the economics of the proposed polio immunization strategies for the post-certification era was convened in October 2002. This consultation reviewed the five economic analyses relating to polio eradication or post-certification vaccination policy. Among the recommendations was that the three studies, recently conducted on the post-certification era, should be carried through to completion/publication to further the public debate in this area. In addition, as the comparison of these studies found that the existing economic analyses have been based on a variety of assumptions and timeframes, it would be useful to reduce the variability in approach, thus facilitating the comparison of future analyses. Finally, new studies were proposed to evaluate the economic implications of the different strategy options, in addition to the work which had been initiated by WHO and CDC on policy decision models. Two different approaches were proposed; one, already underway, would develop complex decision-making models taking a global perspective; the other, under consideration, would develop a more simplified decision-making model from a country-based perspective.

Recommendations:

- Different analytic approaches are likely to be useful for the many different settings that will arise in discussions of the post-certification policy options with national policy-makers. Simple but robust economic and/or decision-making models, initially based on real data from a limited number of countries in polio-free areas, should be developed for this purpose. The results of these models should be available to the TCG at its next meeting.

Annex 1:

Agenda

Wednesday, 13 November 2002

Day 1 – Stopping polio transmission

08:30–09:00 Registration

09:00–10:30 Opening statements

Introductions and review of agenda

Session 1: Programme objectives and overview

Eradication activities and outcomes
in 2002 to date

Dr B. Aylward

Session 2: Major endemic countries – epidemiology and strategy

Pakistan

Dr R. Hafiz

10:30–11:00 *Coffee break*

Nigeria

WHO/Nigeria

Northern India

Dr J. Wenger

13:00–14:00 *Lunch*

14:00–15:30 Summary of priorities: other endemic areas

- EMR: Afghanistan, Egypt, Somalia
- AFR: Angola, Niger

EMRO
AFRO

Proposed 2003 supplementary immunization
activities and OPV supply

Mr C. Maher
Ms S. Hall

15:30–16:00 *Coffee break*

16:00–17:30 **Closed session of the Global TCG**

Thursday, 14 November 2002

Day 2 – Certification and post-certification priorities

Session 3: Priorities in the pre-certification era

09:00–10:30 AFP surveillance: Dr R. Sutter

- performance and priorities
- role of polio-compatible cases

Laboratory containment: Mr C. Wolff

- tools and timelines for validation
- oversight of the containment process

10:30–11:00 *Coffee break*

Session 4: Post-certification polio immunization policy

“Framework for the assessment and management of paralytic poliomyelitis in the post-certification era” Dr B. Aylward

Risk assessment:

- frequency and burden of VAPP Dr R. Sutter
- outcomes of screening for cVDPVs Dr D. Wood
- frequency and potential clearance of iVDPVs Dr D. Wood

12:30–14:00 *Lunch*

Risk management:

- VDPV investigation and response guidelines Mr C. Maher
- IPV efficacy in developing country settings Dr V. Caceres
- vaccine stockpiles for the post-certification era Dr D. Wood
- economics of post-certification policies Dr U. Griffiths

Risk perceptions: strategies for country consultation Dr D. Tarantola

15:30–16:00 *Coffee break*

16:00–18:00 **Closed session of the Global TCG**

Annex 2:

List of participants

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Ms L. Muller, Polio/V&B
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The Department of Vaccines and Biologicals was established by the World Health Organization in 1998 to operate within the Cluster of Health Technologies and Pharmaceuticals. The Department's major goal is the achievement of a world in which all people at risk are protected against vaccine-preventable diseases.

Five groups implement its strategy, which starts with the establishment and maintenance of norms and standards, focusing on major vaccine and technology issues, and ends with implementation and guidance for immunization services. The work of the groups is outlined below.

The *Quality Assurance and Safety of Biologicals team* ensures the quality and safety of vaccines and other biological medicines through the development and establishment of global norms and standards.

The *Initiative for Vaccine Research* and its three teams involved in viral, bacterial and parasitic

diseases coordinate and facilitate research and development of new vaccines and immunization-related technologies.

The *Vaccine Assessment and Monitoring team* assesses strategies and activities for reducing morbidity and mortality caused by vaccine-preventable diseases.

The *Access to Technologies team* endeavours to reduce financial and technical barriers to the introduction of new and established vaccines and immunization-related technologies.

The *Expanded Programme on Immunization* develops policies and strategies for maximizing the use of vaccines of public health importance and their delivery. It supports the WHO regions and countries in acquiring the skills, competence and infrastructure needed for implementing these policies and strategies and for achieving disease control and/or elimination and eradication objectives.

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