Summary

The meeting was jointly hosted by WHO and UNICEF. Its purpose was to provide and consider an update on progress and future plans on the global polio eradication initiative, to consider ideas and plans for post-eradication risk assessment, to strengthen collaboration and partnerships, and to examine projected demands for IPV and OPV for the period 2010-2012, based on policy plans (D. Wood; chair).

1. Four countries currently have endemic polio due to polio types 1 and/or 3 – Northern Nigeria, Afghanistan, Pakistan and India (Bihar and Western Uttar Pradesh). Progress has been reported in Nigeria and in India (in India immunization coverage is very high). In Nigeria the consequence has been that countries closest have become polio-free. In Afghanistan (where the southern region only is affected) a multi-pronged approach is in place and there is a monitoring system that enjoys strong political support. The general challenge is to achieve maximum possible population immunity, world wide. An aggressive research programme is proposed with this objective. Planning includes scale-up of traditional leadership, political involvement and support, working more closely with NGOs, expanding campaigns to the “importation belt” in sub-Saharan Africa, and systematic targeting. Plans are being put into place for the five to seven years after the last wild polio virus case (post-eradication). All plans are flexible and responsive to changes in the field. A best-case set of scenarios for post-eradication activities plus time lines was presented (B. Aylward) over an 8-year period that includes OPV cessation and verification of VAPP/VDPV elimination.

2. mOPV and bOPV licensing and clinical trials were reviewed (R. Sutter). Findings have included: (i) birth dose does not do as well in India as elsewhere although this is rectified and even better by 30 days of age (reason unclear); (ii) no special advantage was found with high titre vaccines compared with normal titre vaccines; (iii) mOPV1 and bOPV are clearly superior to tOPV (results in India of three studies and in Egypt). Wild polio virus is still circulating in communities despite high immunity. The aim is eventually to stop all OPVs. Non-inferiority of bOPV compared with mOPV1 and mOPV3 and superiority of bOPV compared with types 1 and 3 in tOPV has been shown. The Advisory Committee
on Poliomyelitis Eradication has made recommendations for use of bOPV (WER 17 July 2009, 84, 289-300).

3. The meeting was informed of the current status of licensing and prequalification of mOPV and bOPV, with the announcement of the first bOPV licensed in its country of production and prequalified by WHO (J. Fournier-Caruana). Regulatory decisions have been taken on the basis of expert reports, clinical data, stability testing (ongoing), chemistry, and updated post-marketing surveillance data. For mOPV1 and mOPV3 there are strong confirmatory clinical data available; there is less experience in support of bOPV although a clinical trial of bOPV is now completed and a second study is currently in progress. The licensing status of mOPV1, mOPV3 and mOPV2 was reported in detail for prequalification by WHO for procurement by UN agencies and use in India, Afghanistan, Pakistan and Nigeria.

4. Detailed projections have been made of the demand on all OPV types over the coming six years (C. Maher), based on planned activities and epidemiology. These projections will be reviewed every six months. They do not include stockpiling. The following are envisaged: bOPV 2 973 million doses; mOPV1 1 497 million doses; mOPV3 1 037 million doses; tOPV 5 942 million doses; total 11 449 million doses. It is understood that there will be fluctuations on a yearly basis depending upon programmatic and epidemiological changes.

5. UNICEF undertakes all OPV/IPV procurement with the overall objective of Vaccine Security (I. Lewis) – the uninterrupted, sustainable supply of affordable, quality vaccines – and believes the best way to achieve this is by engaging and keeping manufacturers informed of programmatic strategies and changes and vaccine requirements for polio eradication activities. As an important component to Vaccine Security, vaccine costs are closely monitored with awards reflecting any unjustifiable prices increases. Long term arrangements have been established for OPV requirements until end 2010. Currently, UNICEF regularly procures only small quantities of IPV; projected demand is less certain and will depend on programmatic recommendations. Detailed projection of tOPV, mOPV1 and mOPV3 supply and demand were presented during the meeting covering the period 2009-2010. For 2010, 513 million doses of tOPV, 639 million doses of mOPV1 and 94 million doses of mOPV3 are envisaged; however, overall quantities are expected to increase with the introduction of bOPV in late 2009-2010.
6. A SAGE working group of WHO will deliver its final report in April 2010 on OPV and IPV, based on available evidence (R. Tangermann). This should provide a basis for a consolidated WHO position paper on polio immunization for the pre-eradication period, and provide for the development of comprehensive policy guidance in the post-eradication era in low- and low-middle income settings. The cost effectiveness of switching from OPV to IPV (based *inter alia* on the experience reported from the United States, South Africa and Australia) will also be considered. A paradigm for eliminating transmission potential based on coverage, hygiene and socioeconomic status will be presented. Polio-free countries will be evaluated for their risk of importation according to the criteria very high, high and moderate.

7. Oliver Wyman (G. Smith) presented an analysis of the potential supply landscape and manufacturing economics of IPV-containing combination vaccines, looking ahead to the potential for increased use of IPV post-eradication. Current IPV-containing combination vaccines are expected to remain primarily destined for high and middle income markets. Several manufacturers are, however, developing, or are considering developing new IPV-containing combination vaccines for low income markets. If these manufacturers advance these efforts and achieve development targets, a capacity of nearly 300 million doses annually is envisaged by 2014 at a manufacturing cost range of approximately 1-4 US dollars per dose. Several risks to these developments and projections were identified, including technical hurdles, IPV antigen access issues, and potential for supply-demand imbalances.

8. The WHO has developed an IPV supply and demand scenario (H. Okayasu). It is a high demand scenario assuming countries adopt IPV universally, and includes a range of schedules, presentations (e.g. standalone and hexavalent products), and formulations. A potential timetable has been developed for IPV introduction, based on information currently available to the WHO team. The supply and demand scenario reflects the fact that, irrespective of the eventual success of the global eradication initiative, some countries (e.g., Japan and China) are interested in producing their own IPV while others are expected to import IPV products. The demand sensitivity analysis indicates that the major driver of IPV demand is the success of wild poliovirus eradication. An IPV adjuvant will affect demand in reducing the necessary dose. Present candidates for the adjuvant are aluminum and MF59. Aluminum may reduce IPV requirements by three quarters (in both standalone or hexavalent products) and MF59 by up to 9/10. A successful intradermal preparation (plus device) would also enable dose- and cost-reduction of a stand-alone vaccine. The WHO will continue supporting research and development
efforts to develop 'safer' (from a production perspective) and more affordable IPVs (e.g. Sabin IPV, adjuvant development) as well as clarifying IPV demand by different countries.

9. The WHO has planned an up-to-date post-eradication policy (B. Aylward), taking into account recent developments and based on the conviction that at that stage live virus will not be suitable. The plan is aligned with the policy to stop OPV. IPV must be affordable if the risk is to be managed. All polio virus world-wide will need to be contained. Four (4) potential strategies for low-income countries have been developed and are currently being considered by SAGE. After OPV cessation, IPV will be the only option for countries wanting to continue immunizing against polio. After OPV cessation IPV would reduce, but not eliminate, cVDPV risks.

10. In preparing the global action plan for polio virus containment there will be wide consultation including with manufacturers and with experts in risk containment. All wild polio viruses will need to be limited to approve laboratories in institutions situated in areas with high general population immunity. Global destruction of the wild polio virus is a distant goal. All Sabin viruses would be destroyed in all but essential facilities in a minimum number of countries. Wide endorsement of the global action plan will need to be sought (C. Wolff).

11. The cost of IPV can be reduced by adjuvants and/or by intradermal administration, each of which would substantially reduce the dose. A SAGE working group on IPV is presently considering a research and product development strategy (R. Sutter). Four potential post-eradication strategies have been identified: reduction in the number of doses; reduction in the size of each dose; reduction in the antigen content per dose; and reduced cost of production.

12. A regulatory pathway has been developed at WHO for inactivated polio virus vaccine (P. Folb). Ideally, a straightforward package insert amendment would be sought for a previously approved and WHO-prequalified effective and safe vaccine for intramuscular administration. The simplest indication would be “as a booster to immunity against all three types of polio virus”. In addition, intradermal administration would require an approved device. The hurdles to be cleared in this approval include the need to prove non-inferiority of the intradermal dose compared with the intramuscular administration of approximately five times the intradermal content, and to show that the vaccine would be effective in tropical countries. Most of the results to date for IPV have been developed in
temperate countries. At least two clinical studies in tropical countries would have to show convincing efficacy and safety compared with the intramuscular vaccine. The device would be robust, reliable, affordable and proven to be suitable for use in the field. A comprehensive surveillance plan and risk management plan would be in place covering three to five years post-registration and following prequalification.

13. With further regard to the proposed device for intradermal administration of IPV (R. Stout and M. Royals) it is necessary that the device should meet WHO specifications (under development) and the ISO 21649 standard for needle free injection devices and be CE marked. In addition, there should be WHO prequalification of the device. Reliability, durability and longevity of the device should be proven by the supplier. The frequency of local adverse events should be acceptable (it will be higher than with intramuscular administration of the vaccine). The syringes should be auto-disabled as they might become contaminated. The device should not become so linked with the vaccine that the vaccine manufacturer is dependent on a single device and source. It should be possible to administer vaccine with aluminum as adjuvant intradermally.

14. UNICEF presented a polio stockpile status report (M. Shirey). The purpose of establishing a polio stockpile is to mitigate the risk of premature and unmanaged termination of OPV and to facilitate the transition to a polio virus-free world. There has been close collaboration with the programme and consultation with industry in developing the stockpile strategy. The stockpile will cover an 8-year period (2010-2017), based on programmatic milestones in achieving eradication and will consist of approximately 750 million doses of each of the Sabin serotypes, making a total of 2.25 billion doses, of OPV, to be stored as bulk, with an option to buy finished, licensed product. The stockpile tender was issued to industry on 30 October 2009 and awards are expected to be made in Q1 2010.

15. Additional technical reports were received on the following: Sabin-IPV development (W. Bakker), its rationale and feasibility, and the necessary skills development and training; the potential of the Takeda Pharmaceutical Company, Japan, to contribute to the global s-IPV initiative (S. Weigand); and the need to establish an International Standard specific for s-IPV given the high inter-laboratory variation observed in the collaborative study (M. Baca-Estrada) – ideally there should be in vivo evaluation too.
In conclusion, the meeting was deemed highly successful in addressing its principle aims of communicating and critically considering proposed technical and policy objectives for the coming years. There are exciting and energetic times ahead. It will reconvene in 2010.