Planning for OPV2 withdrawal: Report from the Polio Working Group

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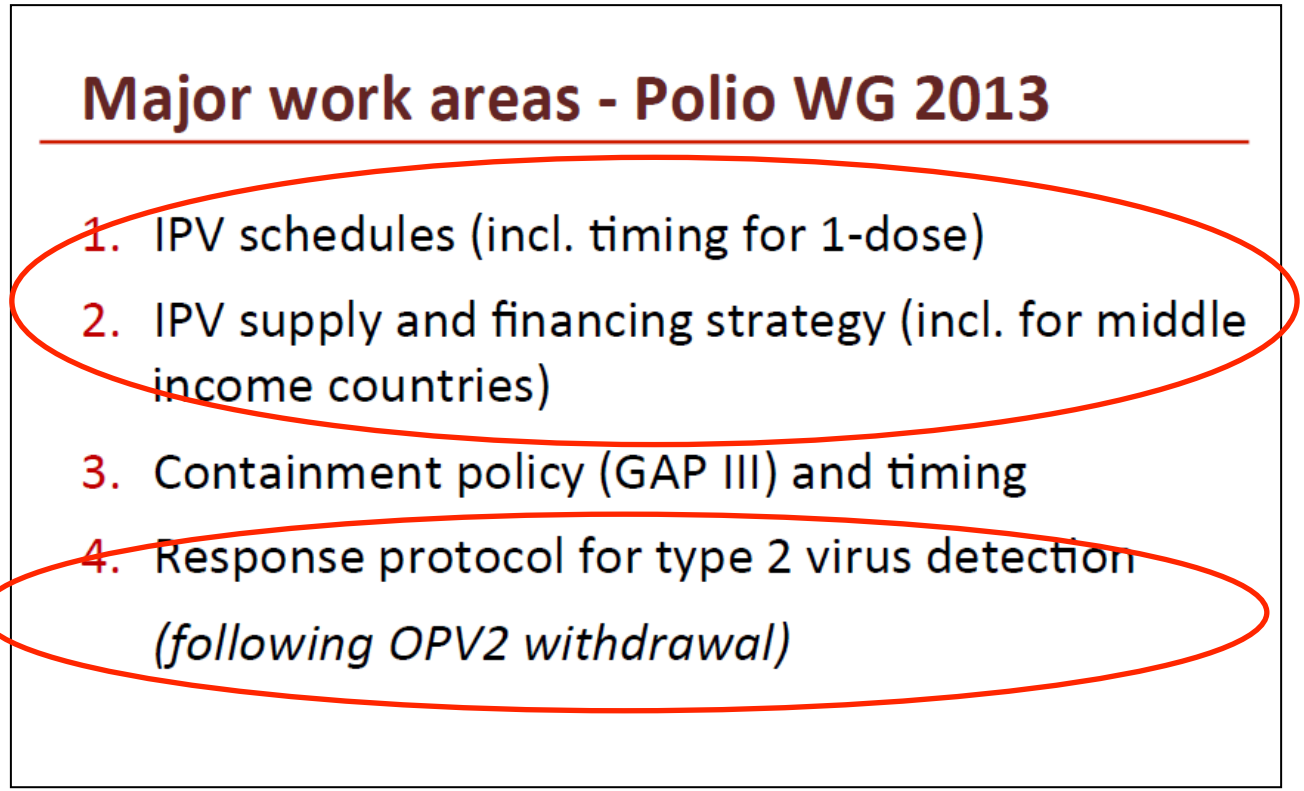
SAGE Recommendation (April 2013)

- SAGE noted that the proposed timeline leading to final OPV2 withdrawal is ambitious but both achievable and urgently needed to ensure the success of the programme

- SAGE requested Polio WG to review the progress in meeting criteria for OPV2 withdrawal and report the updates at the next meeting in November 2013.

Major Work Areas: Polio WG (Requested by SAGE April 2013)



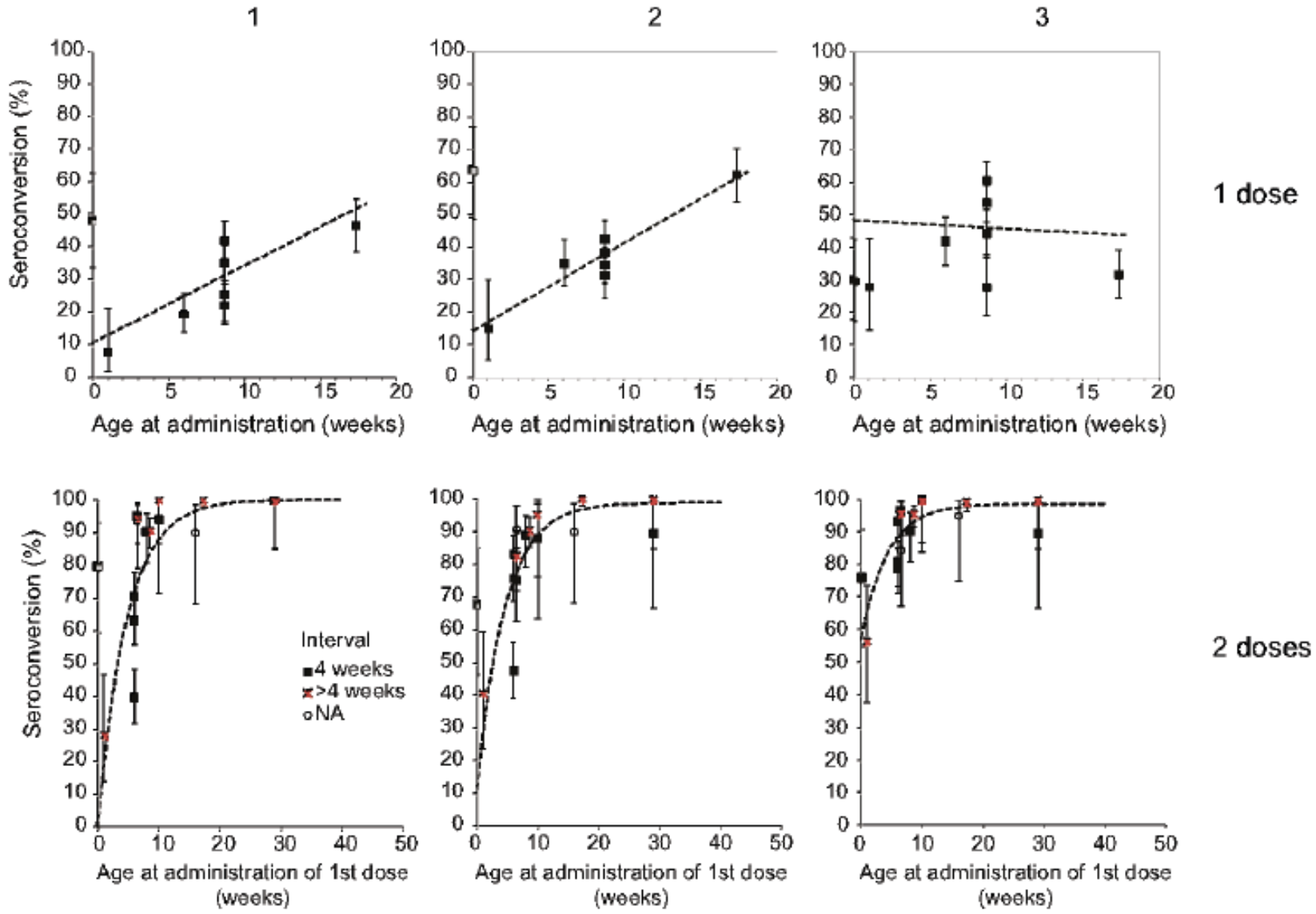
- WG had two meetings (June 4-5, and October 7-8) and reviewed:
  - IPV schedule
  - IPV supply and financing strategy
  - Detection and response strategy for type 2 virus
- It will review containment policy by next SAGE meeting

Major Work Area 1: IPV Schedule

SAGE (November 2012) recommended that all countries should introduce at least one dose of IPV, in order to:

a) Prevent polio if exposed to a VDPV2 or WPV2;
b) Improve response to mOPV2 in an outbreak;
c) Reduce transmission of a reintroduced type 2; and
d) Boost immunity to WPV1 & 3

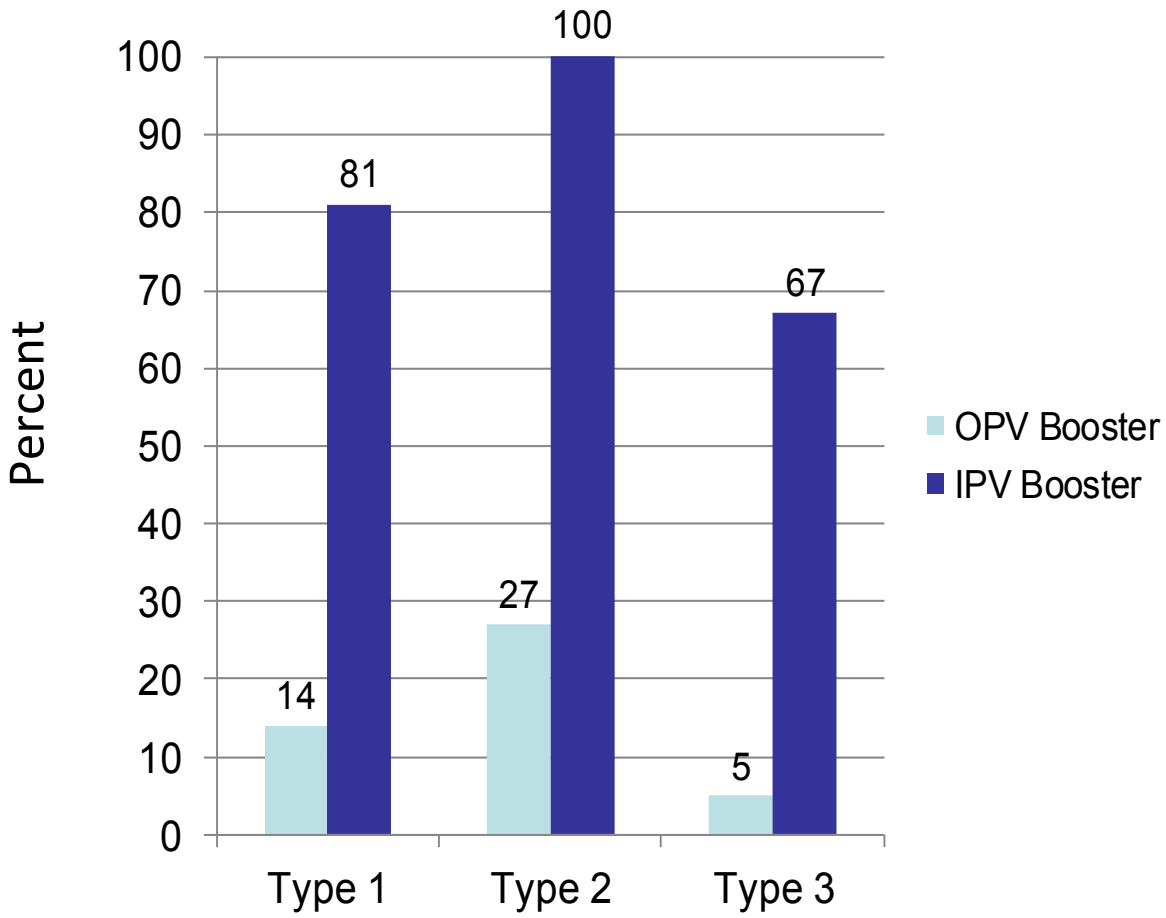
Seroconversion After 1 or 2 Doses of IPV



Source: Grassly et al. Unpublished data

IPV Closes the Immunity Gaps in OPV-vaccinated Infants

Impact of IPV vs. OPV booster after OPV3 in seronegative individuals at 9 months of age, Côte d'Ivoire (Lancet, 1993)



- One dose of IPV can close the immunity gap against type 1 and 3 among OPV-immunized population
- This suggests early IPV introduction may help WPV eradication in endemic countries

IPV Introduction May Help Interrupt WPV Transmission

- The IMB report (Oct 2013) recommended *"the program agrees and makes a clear statement of policy on the use of IPV in stopping polio transmission"*

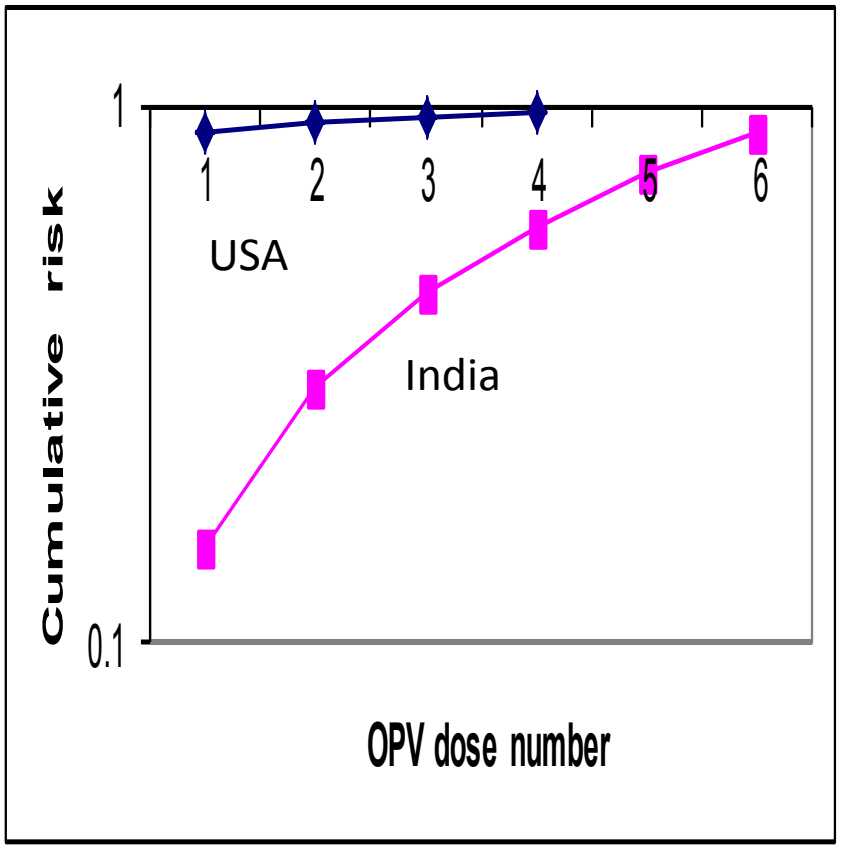
- Based on the evidence, Polio WG recommends early IPV introduction into the routine immunization systems in the remaining polio endemic countries to accelerate interruption of wild poliovirus.

Consideration of VAPP

- VAPP risk data primarily from industrialized countries (total, recipient, contact, community-acquired)
- Epidemiology of VAPP is different in developing countries (e.g., India, Iran)
  - OPV immunogenicity lower
  - Age at VAPP onset higher (mostly associated with subsequent OPV dose, not first dose)
  - Maternally-derived antibodies protect young infants

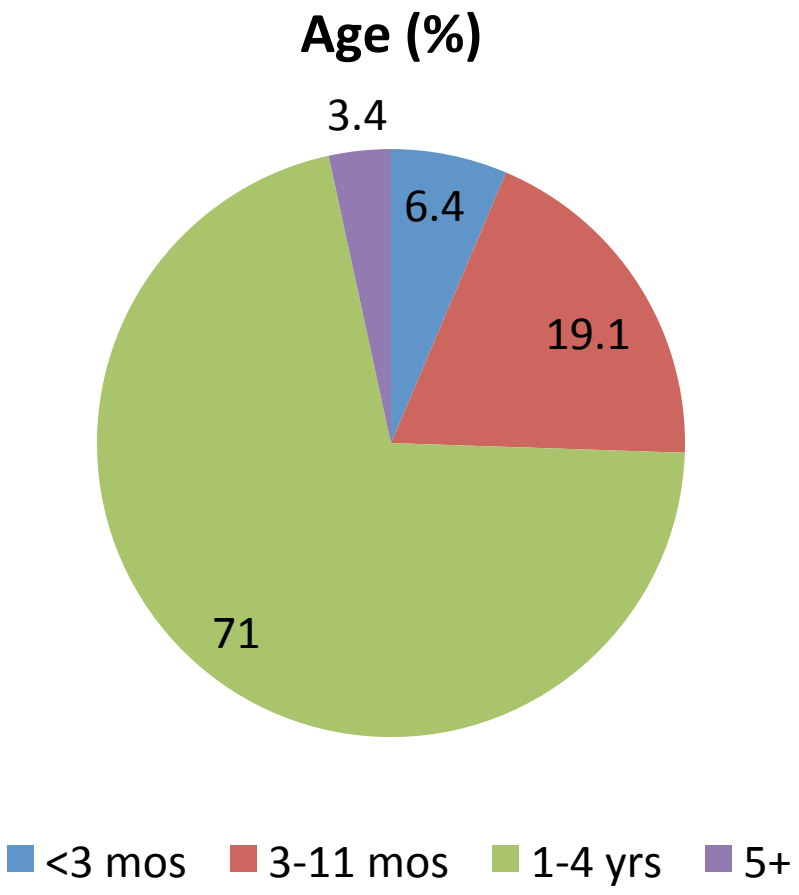
VAPP Risk by Dose, India & United States

- In United States: First dose OPV exposure associated with 85-90% of all VAPP cases
- In India: First dose OPV exposure association much lower in India
- Ratio of recipient to contacts is 1:1 in United States and 1:2 in India



Age distribution of VAPP

(Recipient and Contact VAPP, 2006-2011)



Available data from developing countries suggest:

- IPV administration at DTP3 may potentially prevent majority of VAPP cases
- Incremental risk reduction from administering IPV early (e.g., DTP1) is less than 10%

IPV Schedule: Conclusion

SAGE Working Group recommends:*

- All countries should introduce at least one dose of IPV into their immunization schedules by the third quarter of 2015

- For OPV-only using countries which are introducing one dose of IPV, this should be in addition to the 3-4 doses of OPV in the primary series and given at the immunization contact at or after 14 weeks

- The timing of the IPV dose is as follows:
  - 6, 10, 14 weeks or 2, 3, 4 months schedule: add IPV dose at the DPT3/ OPV3 contact
  - 2, 4, 6 months schedule: add IPV dose at the DPT3-OPV3 contact, though DPT2-OPV2 can be considered

- For children starting the routine immunization schedule late (age > 3 months) the IPV dose should be administered at the first immunization contact

** Recommendation for current OPV-only countries; the WG is not recommending to change existing IPV schedules*

WG Recommendation on the Communication of the IPV Schedule

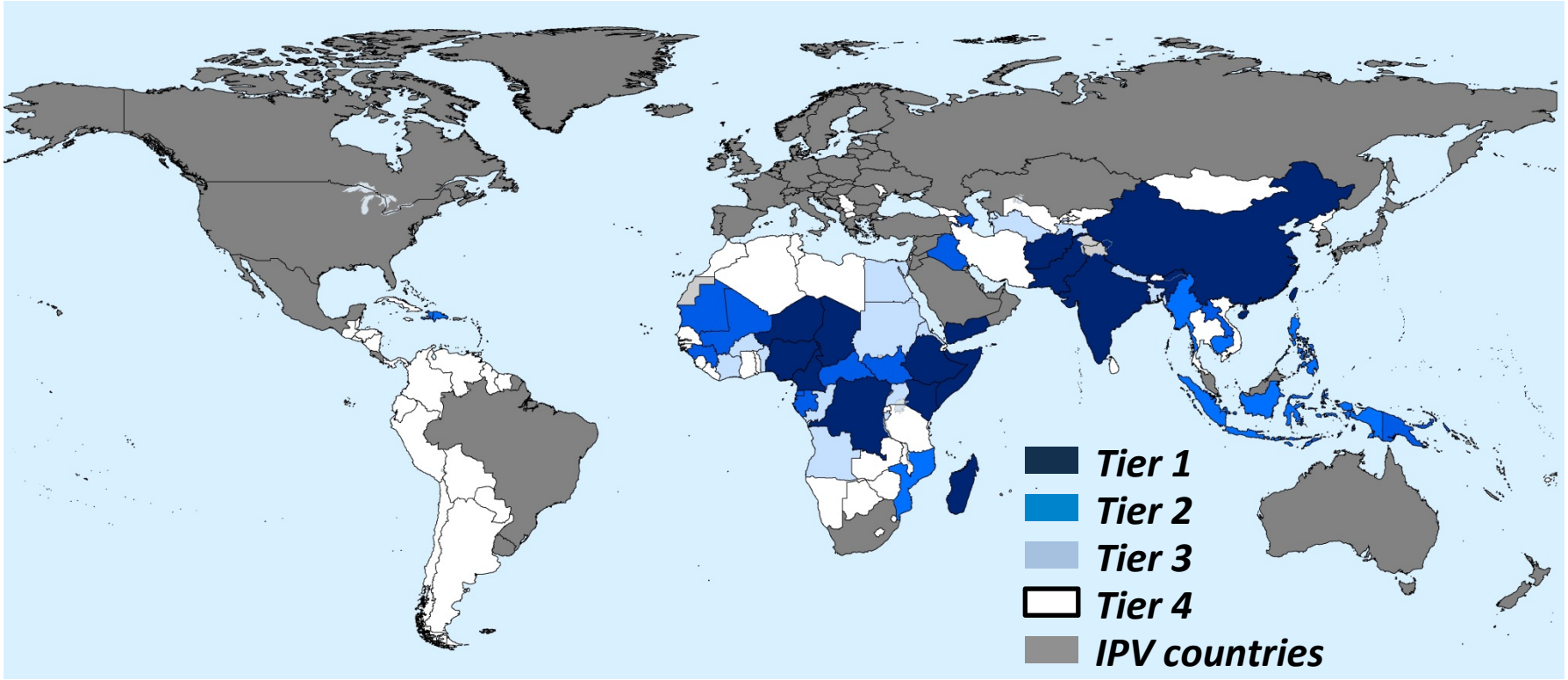
The WG noted that when communicating the recommendation that following should be addressed:

- IPV is an additional dose to OPV and not a replacement (the combined schedule gives the best immunity)
- The *primary* reason for IPV introduction is to mitigate the risks of OPV2 withdrawal (not to reduce VAPP). The potential to accelerate WPV eradication by achieving higher population immunity is also an important benefit
- DTP3 was selected over DTP1 because of the gains in immunogenicity
- The potential risk of an IPV only schedule should be explained to any country considering switching straight to an IPV only schedule (especially those with known high force of transmission)

Major Work Area 2: Draft IPV Supply, Financing, and Introduction Strategy

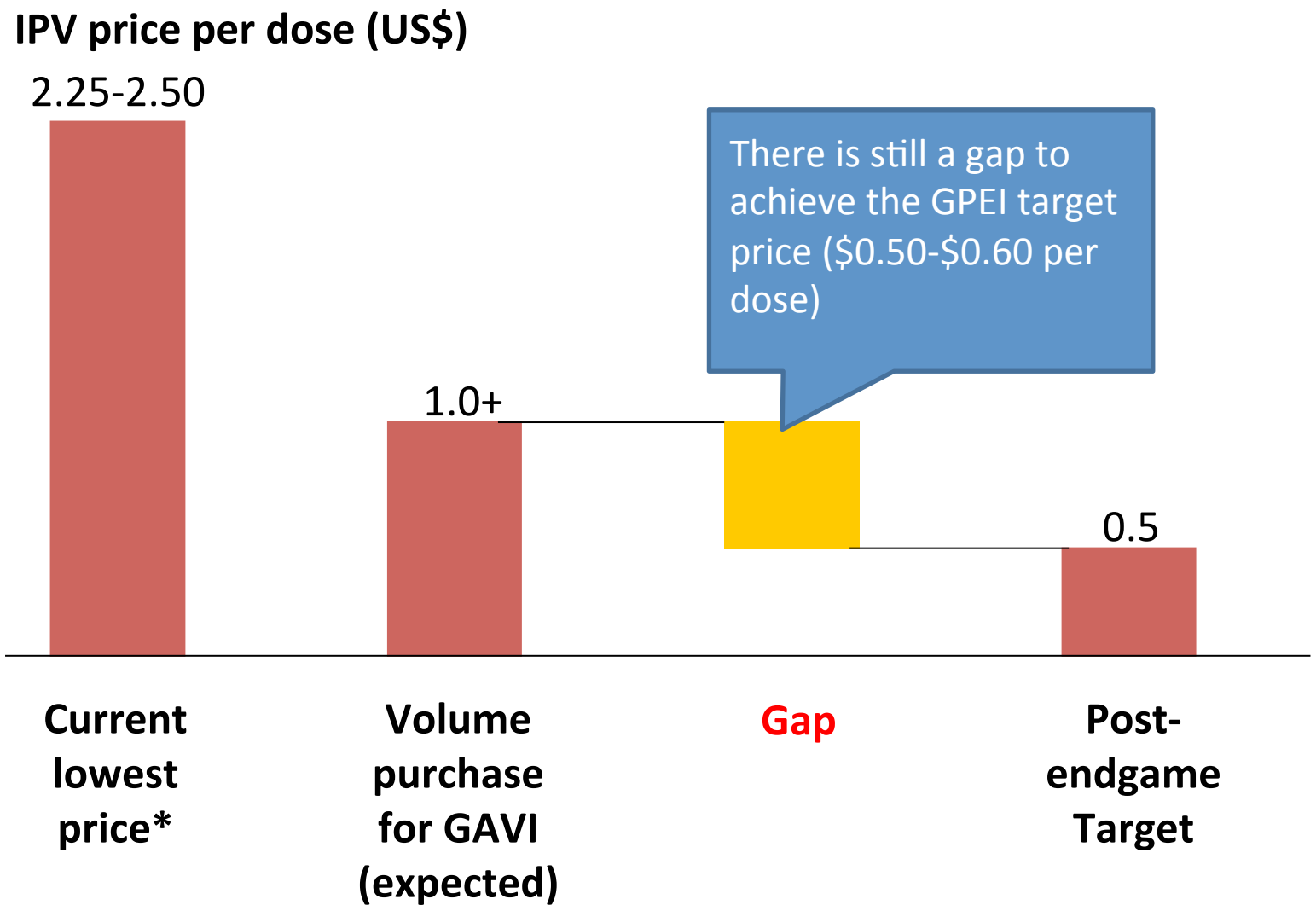
- WG acknowledges the extensive work done by WHO, GAVI, and partners for IPV introduction, including
  - The commitment from GAVI to support rapid IPV introduction by adapting their policies to align with the timeline of the Polio Endgame
  - The commitment from donors to allocate funds specifically for IPV
  - The extensive work done on country prioritization, demand forecast, financing, readiness for introduction, and planning
  - The extensive negotiations to achieve the lowest possible IPV price for low- and low- middle income countries
- Recognizing the tight timelines and the significant progress in preparation, the WG encourages a WHA resolution in 2014 on accelerated IPV introduction
- Early introduction in routine immunization system in the remaining endemic countries is encouraged to accelerate interruption of wild polio virus

Proposed Country "Tiering" for IPV Introduction



- The WG endorses the methodology of tiering (based on the risk) for focusing technical support while reinforcing the importance of accelerated introduction in all four tiers
- All Tier 1 and 2 countries should have a plan for IPV introduction by mid-2014; Other countries should have a plan by end-2014

Current and Anticipated IPV Prices



* Current IPV Supply, Recent tender Results & Outlook for the Future (UNICEF, November 2012)

Status of Intradermal IPV Development

- In April 2012, SAGE recommended to fast-track the development of intradermally delivered (ID) IPV

- To date, WHO has defined the regulatory requirements needed to change the label of IPV to include ID delivery and developed a protocol for the regulatory trial (label change expected in 2014)

- Additionally, the current ID methodology (needles and syringes) presents significant operational issues. For this reason, WHO is accelerating the development ID delivery devices (e.g., ID needle adapters, needle-free jet injectors, and microneedle patches)

- The WG recommends that GPEI accelerate the research on intradermal IPV to ensure access to affordable IPV
  - Only option to achieve the target price (0.5-0.6 USD/dose) in the near term
  - ID devices will be critical in the post-OPV era as a tool for VDPV outbreak response

Major Work Area 3: Strategic Framework for Type 2 Detection and Response

- The WG reviewed the draft strategy and recommended that it should be comprised of the following 5 major components and include the following provisions:
  - **Notification:** all type 2 viruses –wild, vaccine-related or Sabin – should require immediate notification under IHR (2005) after OPV2 withdrawal;
  - **Surveillance:** AFP surveillance must be complimented by expanded environmental surveillance;
  - **Stockpile:** the planned mOPV2 stockpile should be complemented with IPV to facilitate population immunity;
  - **Response:** the principles for response should reflect the nature of the virus (e.g. wild vs. Sabin virus), the time since OPV2 withdrawal; and
  - **Travellers:** travel in and out of infected areas should be restricted to the degree possible; people undertaking essential travel in or out of an infected area should receive a booster dose of IPV.

Other Issue: Global bOPV Access Strategy

- The WG endorses the global access strategy, including:
  - Supporting label-change of bOPV products to allow for use in routine immunization (currently bOPV is for campaign use only)
  - Assuring that international suppliers are able to produce sufficient bOPV for the global demand
  - Supporting countries that rely on domestic producers to rapidly develop, license and produce sufficient bOPV
  - Registering bOPV in all OPV-using countries (for routine immunization use)

- The WG notes the importance of tOPV campaigns to increase type-2 population immunity prior to the OPV2 withdrawal

Other Issue: Assessment and the Trigger for OPV cessation

- The WG recommends that the programme differentiates between the criteria to determine global readiness for OPV2 withdrawal and the 'trigger' for initiating globally synchronized OPV2 withdrawal.
  - Criteria for judging OPV2 withdrawal readiness include:
    - Status of IPV introduction into all OPV-using countries;
    - Access by all OPV-using countries to a registered bOPV for routine immunization;
    - Implementation of surveillance and response protocols for type 2 poliovirus;
    - Completion of global Phase 1 containment activities for all wild poliovirus and provisions for the appropriate handling of type 2 residual materials and production sites under GAP3; and
    - GCC affirmation of wild poliovirus type 2 global eradication.
  - The trigger for OPV2 withdrawal would be the evidence for absence of all 'persistent' cVDPV2s* for at least 6 months globally.

* Persistent cVDPVs refer to cVDPVs known to circulate more than six months

SAGE Polio WG: Areas of Further Work

- Comprehensive review of cVDPV risk management
- Review of plans for environmental surveillance expansion in the coming years, and the research to improve the efficiency and sensitivity of environmental surveillance
- A further, more complete review of the WPV-1 circulation in Israel
- Update on the alignment of GAP III containment and the polio endgame
- Review of the draft type 2 virus detection and response protocols

Conclusion

- The Polio WG acknowledges the significant progress towards meeting criteria for ensuring global readiness for OPV2 withdrawal, which was made possible by the collaboration between GPEI, GAVI, and other partners

- To facilitate the preparation at global, region and country-level, the WG recommends that the SAGE should:
  - Endorse the proposed timing of one dose of IPV (i.e., given at the immunization contact at or after 14 weeks)
  - Endorse IPV supply, financing and introduction strategy
  - Endorse the principles of type 2 poliovirus detection and response strategy
  - Support a WHA resolution in 2014 on accelerated IPV introduction (especially in high risk countries)

- It also encourages the early introduction of IPV into the routine immunization systems in the remaining polio-endemic countries to accelerate interruption of wild polio virus