April 2017 SAGE meeting

RUNNING ITEMS

• Global WHO Report
• Report from Gavi
• Report from other Advisory Committees on Immunization
  • Global Advisory Committee on Vaccine safety (GACVS)
  • Expert Committee for Biological Standardization (ECBS)
  • Immunization Practices Advisory Committee (IPAC)
  • Implementation Research Advisory Committee (IVIR-AC)

SPECIFIC TOPICS

• Polio eradication
• Oral cholera vaccines
• Ebola vaccines
• National immunization programme management: functions and competencies
• Strengthening of National Immunization Technical Advisory Groups (NITAGs)
• Private providers engagement with immunization programmes
• Diphtheria
GVAP mid-term report: some progress, but too slow to achieve goals

**POLIO:**
Number of new cases of paralytic poliomyelitis due to wild poliovirus
- 2010: 359 cases in 9 countries
- 2015: 79 cases in 2 countries
- 2015 TARGET: 0 cases

**MATERNAL AND NEONATAL TETANUS ELIMINATION:**
Number of countries verified for elimination
- 2015 TARGET: 40 priority countries

**COVERED AND EQUITY:**
Number of countries with national vaccination coverage of 90%, with no district’s coverage less than 80%
- 2015 TARGET: 194 countries
- 2015: 126 Countries achieved 90% national coverage for DTP3
- 2015: 52 Countries achieved 90% national coverage and no districts coverage less than 80% for DTP3

**MEASLES:**
Number of WHO regions to achieve measles elimination
- 2015 TARGET: at least 4 WHO regions
- 2015: 1 region achieved measles elimination

**RUBELLA:**
Number of WHO regions verified for rubella and CRS elimination
- 2015 TARGET: at least 2 WHO regions
- 2015: 1 region achieved rubella elimination
Global WHO Report

- Encouragement to continue work on missed opportunities especially in neglected groups.
- Finalization of tools and guidelines for vaccination in Humanitarian emergencies.
- Plans for action on “polio transition” to reach GVAP goals.
- Deep concern over financing over global funding especially for Gavi/Global Fund transitioning countries.
Wild Poliovirus & cVDPV Cases
Past 6 months

Public Health Emergency of International Concern declared under the International Health Regulations in May 2014 Reiterated on 24 April 2017

Country | Onset of most recent WPV1 case | Number of WPV1 cases | Number of WPV infected districts | cVDPV current 6 months
--- | --- | --- | --- | ---
DRC | 0 | 0 | 0 | 4
AFR | 0 | 0 | 0 | 4
Pakistan | 13-Feb-17 | 3 | 13 | 1
Afghanistan | 16-Apr-17 | 5 | 7 | 0
Syria | NA | 0 | 0 | 2
EMR | 16-Apr-17 | 8 | 20 | 3
Global | 16-Apr-17 | 8 | 20 | 7

2Not shown in table: 1 cVDPV2 healthy child contact of a cVDPV2 case in Maniema, DRC, specimen 02 May 17; 1 cVDPV2 contact of an AFP case in Deir-el-Zour, Syria, specimen 25 Apr 17.
4Current rolling 6 months: 14 December 2016 – 13 June 2017
Same period previous year: 14 December 2015 – 13 June 2016

1Excludes viruses detected from environmental surveillance
3Onset of paralysis 014 December 2016 – 13 June 2017
Post switch* cVDPV2 outbreaks

Total of 6 post-switch cVDPV type2 outbreaks in 4 countries

<table>
<thead>
<tr>
<th>Province</th>
<th>District</th>
<th>Surv. type</th>
<th>Date (collection/onset)</th>
<th>NT change</th>
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<tr>
<td>Pakistan (1)</td>
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<tr>
<td>Balochistan</td>
<td>QUETTA</td>
<td>AFP</td>
<td>17-Dec-2016</td>
<td>14</td>
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<td>ENV</td>
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<td>ENV</td>
<td>28-Dec-2016</td>
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<td>ENV</td>
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<td>Syria (1)</td>
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<tr>
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<td>MAYADEEN</td>
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<td>05-Mar-2017</td>
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<td>Nigeria (2)</td>
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<td>DRC (2)</td>
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<td>AFP</td>
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<td>AFP</td>
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<td>7</td>
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<tr>
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<td>MALEMB-NUKULU</td>
<td>AFP</td>
<td>20-Feb-2017</td>
<td>15</td>
</tr>
</tbody>
</table>

Post-switch SIA containing mOPV2 vaccine was conducted or is planned.

*Switch date: 1st May 2016
Countries with IPV supply disruptions in 2017
Immunogenicity to poliovirus type 2 following two doses of fractional intradermal inactivated poliovirus vaccine: A novel dose sparing immunization schedule

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ABSTRACT
Introduction: The polio eradication endgame strategic plan calls for the sequential removal of Sabin poliovirus serotypes from the trivalent oral poliovirus vaccine (OPV), starting with type 2, and the introduction of >1 dose of inactivated poliovirus vaccine (IPV), to maintain an immunity base against poliovirus type 2. The global removal of oral poliovirus type 2 was successfully implemented in May 2016. However, IPV supply constraints has prevented introduction in 21 countries and led to complete stock-out in >20 countries.

Methods: We conducted a literature review and contacted corresponding authors of recent studies with fractional-dose IPV (FIPV), one-fifth of intramuscular dose administered intradermally, to conduct additional type 2 immunogenicity analyses of FIPV doses compared with one full-dose IPV.

Results: Four studies were identified that assessed immunogenicity of two FIPV doses compared to one full-dose IPV. Two fractional doses are more immunogenic than 1 full-dose, with type 2 seroconversion rates improving between absolute 19–42% (median: 37%; p < 0.001) and relative increase of 51–129% (median: 82%), and antibody titer to type 2 increasing by 2–32-fold (median: 10-fold). Early age of administration and shorter intervals between doses were associated with lower immunogenicity.

Discussion: Overall, two FIPV doses are more immunogenic than a single full-dose, associated with significantly increased seroconversion rates and antibody titers. Two FIPV doses together use two-fifth of the vaccine compared to one full-dose IPV. In response to the current IPV shortage, a schedule of two FIPV doses at ages 6 and 14 weeks has been endorsed by technical oversight committees and has been introduced in some affected countries.

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1. Introduction

Indigenous wild poliovirus type 2 was last detected in Northern India in 1999, and declared as eradicated by the Global Certification Commission in September 2015 [1]. The Global Polio Eradication Initiative (GPEI) prepared a strategic action plan which called for the sequential removal of Sabin serotypes from the trivalent oral poliovirus vaccine (OPV), and the introduction of inactivated poliovirus vaccine (IPV) (2). By May 2016, Sabin type 2 was successfully withdrawn globally when IPV at age ≥14 weeks, with IPV at ages 6,10 and 14 for the sequential removal of Sabin serotypes from the trivalent oral poliovirus vaccine (OPV), and the introduction of inactivated poliovirus vaccine (IPV) (2). By May 2016, Sabin type 2 was successfully withdrawn globally when IPV at age ≥14 weeks, with IPV at ages 6,10 and 14 weeks, to provide an immunity base to type 2 poliovirus after cessation of Sabin type 2 [3]. The immunity base against type 2 should decrease the paralytic consequences of poliovirus type 2 exposure and improve immunological response to type 2 containing poliovirus vaccine administered in the event of a type 2 poliovirus outbreak. IPV introduction (in previously OPV-only using countries) has increased global IPV demand, stand-alone as well as that used in combination vaccines, from about 80 million doses in 2013 to about 200 million doses in 2016. The supply commitments by IPV manufacturers were expected to meet the increased demand.

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Given ongoing global IPV shortage, SAGE recommends that:

- Available IPV supply prioritized for use in routine immunization (high risk countries)
- Regional and National immunization TAGs should recommend 2 fractional IPV doses in routine immunization schedules, provided
  - access to appropriate IPV presentations (e.g. single-dose or 5-dose vials),
  - capacity to administer intradermal injections,
  - good advocacy and communication plan for parents and providers;
- WHO reviews risk classification of countries to take into account:
  - the size of the population with no IPV protection and
  - the recent VDPV2 events.
April 2017 SAGE meeting - Recommendations on polio vaccine use after OPV withdrawal

• Countries should include at least 2 doses of IPV in their routine immunization schedule, the first at or after 14 weeks (e.g. with the 2nd or 3rd dose of DTP-containing vaccine) and the second dose ≥4 months after the first dose, administered either as full or fractional doses.

• Countries without Poliovirus Essential Facilities (PEFs) should maintain IPV in their routine immunization schedule for at least 10 years after global OPV withdrawal, to address: immediate (VDPVs), intermediate (iVDPVs) and longer term (e.g. containment failure) risks of polio virus reintroduction;
Three killed whole-cell OCVs are currently pre-qualified by WHO – Dukoral®, Shanchol™ and Euvichol®. All vaccines have good safety profiles and >60% effectiveness against disease for at least 3 years after 2 doses. A single dose gives protection of 63% against severe disease over a 6-month period. Protection is lower among children aged <5 years.

Alternative delivery strategies covering self-administration, outside-the-cold-chain (CTC / ECTC), linking OCV with other health interventions should be further evaluated in a large variety of settings.
New packaging for OCV
April 2017 SAGE meeting – Cholera vaccination
SAGE general recommendations

- Given the current availability of pre-qualified killed whole-cell OCVs and data on their safety, efficacy, field effectiveness, feasibility, impact and acceptability in cholera-affected populations, these vaccines should be used:
  - in areas with endemic cholera;
  - in humanitarian crises with high risk of cholera;
  - during cholera outbreaks, in conjunction with other cholera prevention and control strategies.

* In countries meeting the WHO criteria for the introduction of rubella containing vaccines into national immunization programmes as outlined in the rubella vaccine position paper. See No. 29, 2011, pp. 301–16.
April 2017 SAGE meeting – Cholera vaccination
SAGE general recommendations

- Countries that have access to OCV should implement systematic monitoring and evaluation (GTFCC).

- Pregnant women should be included in OCV campaigns after evidence indicated high potential benefits and minimal risks.

- Vaccination not recommended for travellers unless their activities involve high exposure to cholera, especially during humanitarian emergencies or when visiting areas with poor health facilities and high exposure to contaminated water and food.
As was recently shown in the DRC, Ebola outbreaks can be controlled through well-defined interventions:

- early isolation of patients to prevent transmission at home and in the community;
- early detection of new Ebola cases through close monitoring of contacts and isolation of contacts when they show symptoms and;
- safe burial of the deceased to reduce transmission through contact with cadavers.

In the 2013–2016 outbreak in West Africa, these measures were not fully implemented initially, resulting in unprecedented geographical spread, a large number of cases, urban spread of disease, and high mortality.
The Phase 3 trial for an rVSV-vectored candidate vaccine (rVSVΔG-ZEBOV-GP), undertaken in Guinea, is the only study that has reported clinical efficacy and effectiveness for any candidate Ebola vaccine.

The rVSVΔG-ZEBOV-GP candidate vaccine was granted access to the Priority Medicine (PRIME) scheme by the European Medicine Agency, and Breakthrough Therapy designation by the US Food and Drug Administration.

Should an Ebola disease outbreak occur before the candidate vaccine is licensed, SAGE recommended that the rVSVΔG-ZEBOV-GP vaccine be promptly deployed under the Expanded Access framework, with informed consent and in compliance with Good Clinical Practice.
April 2017 SAGE recommendations – Ebola vaccines

- Refine mathematical modeling to indicate potential immunization strategies and future vaccine supply and needs.

- Support for regulatory convergence through national regulatory activities for registration and licensing of Ebola vaccines.

- Encourage producers to engage with national or regional regulatory authorities regarding licensure requirements.

- Encourage GamEvac-Combi vaccine producers to submit dossier for pre-qualification and licensing the vaccine in Russia.

- Support for development and/or testing of new Ebola vaccines submission of data to WHO to inform policies.
National Immunization Technical Advisory Groups (NITAGs) in 2015

- 79 Countries meeting the 6 Process Indicators
- 116 Countries having a NITAG with administrative or legislative basis
- 118 Countries Reporting the Existence of a NITAG with ToRs
- 124 Countries Reporting the Existence of a NITAG
- Not available/ No NITAG established
- Not applicable

Data Source: Joint Reporting Form, 2015, as at 18 November 2016
Map production: Immunization Vaccines and Biologicals, (IVB), World Health Organization
Date of slide: 30 March 2017

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

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April 2017 SAGE meeting - Diphteria

- Decreasing diphtheria incidence has stalled in the last 5 years, with approximately 5000 cases reported per year in all 6 Regions.

- Most cases were unvaccinated, or incompletely vaccinated, underlining the need for the full primary immunization series plus booster doses.

- SAGE highlighted the need for strengthening surveillance systems to enhance the capacity to detect and investigate diphtheria cases, and to prevent outbreaks and respond promptly when outbreaks occur.
SAGE concluded that coverage with diphtheria-containing vaccines in paediatric immunization programmes needs to increase, and that vaccination schedules for diphtheria, tetanus and pertussis, should be harmonized as these antigens are often provided in combination vaccines.

SAGE reiterated its previous recommendation that combination vaccines containing tetanus and diphtheria toxoids should also be administered for catch-up vaccination of older children and adults, maternal and neonatal tetanus prevention, and prevention of tetanus among those with an injury if indicated.
SAGE advised that WHO collaborate closely with partners to establish and manage a global procurement mechanism and a physical or virtual DAT stockpile that would be available to all countries.

SAGE urged that regulatory pathways be established to ensure the rapid deployment of DAT.

In the long term, SAGE advised WHO to identify mechanisms to support the development of a monoclonal antibody as an alternative to DAT of equine origin.

SAGE expressed concern with the shortage of Td vaccine (tetanus toxoid+reduced diphtheria toxoid content) reported from some countries for routine immunization of children and adolescents, and recommended that the demand and supply scenarios for Td vaccines should be assessed.
SAGE: Selected topics on the horizon
(*tentatively planned for October 2017)

CROSS-CUTTING

- GVAP monitoring of progress*
- Plans for post GVAP*
- Report from immunization partners*
- Data quality
- Use of vaccines in immunocompromised populations
- Vaccine health economics
- Strategies to reach older age groups
- Maternal vaccination
- Emergency vaccine development
- Middle income countries strategies
- Implementation science
- ....

VACCINE SPECIFIC

- Polio eradication*
- Measles and rubella elimination*
- BCG*
- Typhoid*
- Rabies*
- Pneumococcal conjugate
- Meningitis B
- Rotavirus
- RSV
- Influenza vaccines
- ....
Thanks!

- Phil Duclos
- Melanie Martin
- Malin Finkernagel
- Michel Zaffran