

Highlights from the Meeting of the Strategic Advisory Group of Experts (SAGE) on Immunization

8-10 October 2019

(Full report will be published in the Weekly Epidemiological Record on 29 November 2019.)

Report from the Director and Regional Offices

- The Director of the WHO Department of Immunization, Vaccines and Biologicals reported on how the vaccines and immunization agenda is already pivoting to harness new solutions to address coverage and equity.
- Globally, there are challenges with coverage and equity for immunization. DTP3 coverage globally has stalled at 86%. Africa has the highest proportion of unreached children. Just 10 countries account for 60% of unprotected children. More inequity is seen with measles vaccination coverage than for DTP3 coverage. To achieve solutions for gaps in coverage and equity, vaccine and programme innovations are necessary. An excellent example of programme innovation was the measles-rubella-OPV campaign in Papua New Guinea in June 2019 which leveraged the polio infrastructure to achieve high coverage for MR vaccination and which demonstrated that high coverage for OPV is possible without house-to-house vaccination strategies. Multi-antigen campaigns that integrate bOPV into measles-containing vaccination campaigns have the potential to reach more children, reduce “community fatigue” experienced with polio-only campaigns, and result in cost-savings. Combined bOPV-MCV campaigns in Nigeria, Ethiopia, the Democratic Republic of Congo, Angola and 4 other countries vaccinated an estimated target population of more than 66 million children while saving US \$18 million.
- Innovative work to investigate and track vaccine demand and confidence is underway. WHO engagement with social media platforms, such as Facebook and Instagram, has resulted in changes in platform algorithms so that they support directing users to accurate and authoritative information on vaccines, rather than to misinformation.
- The landmark September 2019 UN declaration on universal health coverage signals Member State commitment to health for all and provides new impetus and synergy for achieving full coverage and equity in vaccination.
- Regional Offices highlighted major achievements and challenges. Measles outbreaks have occurred in all regions and point to the need to strengthen routine immunization to raise coverage levels and to reach pockets of unimmunized populations. A priority for every region is to provide support and guidance to countries to increase confidence and demand for vaccines.

Report from GAVI, the Vaccine Alliance

- SAGE is the main advisory body that provides policy recommendations and technical guidance for the work of GAVI, the Vaccine Alliance.
- Since 2000, the Alliance has expanded its vaccine portfolio and life course approach to vaccination to support more than 430 vaccine introductions and vaccination campaigns.

- To meet the immunization aspirations by 2030 requires major shifts in the Alliance's "Gavi 5.0 strategy" and close alignment with the Immunization Agenda 2030. The strategic shifts include equity as the organizing principle; provision of differentiated support for countries; increased focus on programmatic sustainability before countries transition; support to countries to prioritize vaccine introductions; and catalytic support for middle income countries.

Report on the Vaccine Innovation Prioritization Strategy (VIPS)

- VIPS is an initiative of Gavi and Alliance partners (BMGF, PATH, UNICEF and WHO). Its goal is to prioritise vaccine delivery innovations in vaccine product attributes and to align on innovation priorities to inform investment decisions of manufacturers and partners.
- The scope of VIPS encompasses innovations in vaccine product attributes such as delivery technologies and primary containers, packaging, labelling, and formulation. The VIPS methodology relies on an evaluation process that focuses on country needs.
- In total, 24 vaccine product innovations are being assessed through the process. Selected innovations will be applied to a list of priority vaccines.
- SAGE expressed appreciation for the work of VIPS and welcomed further exchange and update on the proceedings of VIPS.

Measles and Rubella

- Eradication of measles has been discussed and debated since the 1960's, not long after the introduction of measles vaccines. Eradication is complex because it is multi-dimensional, encompassing not only biological, technical, operational and programmatic issues but also political, economic, social and cultural considerations.
- A world without measles and rubella remains the collective vision, and all six WHO Regions have measles elimination goals.
- Global coverage with the first dose of measles-containing vaccine (MCV1) has remained stagnant at 86% and with the second dose of measles-containing vaccine (MCV2) at 69%. Much higher levels of coverage are needed to achieve and sustain elimination. Given the gaps in coverage and population immunity, major outbreaks continue to occur in all six WHO regions.
- Based on a comprehensive assessment of the feasibility of measles and rubella eradication which included mathematical modeling of several coverage scenarios, and with due consideration of the limited progress towards elimination, SAGE concluded that achieving measles eradication is not realistic without significant further effort.
- SAGE therefore recommended that a measles and rubella eradication target date should only be considered when substantial and measurable progress has been made toward achieving country and Regional elimination goals.
- Efforts to achieve and maintain measles and rubella elimination must be based on substantial strengthening of primary health care systems that are effective in delivering routine immunization.

Human Papillomavirus (HPV) Vaccination

- For the prevention of cervical cancer, SAGE reaffirms the recommendation of vaccinating girls aged 9-14 years with HPV vaccine using a two-dose schedule (0, 6 months). A three-dose schedule is needed in older girls ≥ 15 years of age or in those known to be immunocompromised and/or with human immunodeficiency virus infection.
- SAGE is deeply concerned that the current HPV vaccine shortage could result in failure to introduce or sustain HPV vaccine programmes in some countries, particularly those with a high burden of cervical cancer.
- In this context of limited supply of HPV vaccine, SAGE recommends that all countries should *temporarily* postpone implementation of HPV vaccination strategies that are gender-neutral, for older age groups (≥ 15 years), or for multi-age cohorts.
- Countries may, in consultation with their national immunization technical advisory groups (NITAGs), consider alternative strategies to ensure that girls receive two doses of HPV vaccine before the age of sexual activity, as appropriate to the individual national context.
- The following alternative strategies, which require careful consideration of the programmatic challenges and clear, well-planned communication, are recommended:

- a) To retain the accelerated impact of vaccinating multi-age cohorts (MACs), countries could target an older cohort of girls (e.g., 13 or 14 years old girls or in an equivalent school grade), who are close to initiating sexual activity and thus of high risk of exposure and in whom a high 2-dose coverage can be achieved.

Once the vaccine supply situation has improved, countries could then consider: (i) Continuing with this strategy (i.e., targeting older girls) if high 2-dose coverage is being achieved; or (ii) Shifting to a strategy of targeting younger girls (9 or 10 year old or lower school grade) if vaccinating older girls results in low coverage rates or high drop-out rates between doses 1 and 2 or if vaccination is occurring after the age of sexual activity.

- b) To temporarily reduce vaccine supply needs, countries could adopt a “1+1” schedule with an extended interval of 3-5 years between doses for younger girls (e.g., first dose provided at 9 or 10 years old or lower school grade) and taking measures to ensure that the girls receive two doses each. This strategy constitutes an *off-label use* of the vaccine.
- SAGE calls upon WHO and its partners to urgently convene a dialogue on global access to HPV vaccine, engaging all relevant stakeholders including vaccine manufacturers.

Global Vaccine Action Plan (GVAP) review and Immunization Agenda 2030

(i) GVAP review, lessons learned and recommendations

- SAGE welcomed the GVAP review and lessons learned report, noting that it provided a differentiated and balanced view on the achievements and shortcomings of GVAP and the Decade of

Vaccines. In addition to the lessons learned, the report also provides recommendations for the post-2020 global immunization strategy.

- The 15 high-level recommendations endorsed by SAGE are grouped under 7 headings:
 1. Build on GVAP's lessons learned, ensuring more timely and comprehensive implementation at global, regional and national levels.
 2. Have a key focus on countries for strategy development, decision-making, and innovation for programme performance and research.
 3. Maintain the momentum towards GVAP's goals and add specific focus on humanitarian emergencies, displacement and migration, integration between disease-elimination initiatives and national immunization programmes, and greater collaboration within and outside the health sector.
 4. Establish a governance model better able to turn strategy into action, link to an operational model based on closer collaboration between partners, respond to emerging issues with increased flexibility, and establish a stronger communications and advocacy strategy.
 5. Promote long-term planning for the development and implementation of novel vaccines and other preventive innovations to ensure populations benefit as rapidly as possible.
 6. Promote use of data to stimulate and guide action and to inform decision-making.
 7. Strengthen monitoring and evaluation at the national and sub-national level to promote greater accountability.

(ii) Immunization Agenda 2030

- SAGE endorsed the “Immunization Agenda 2030” (IA2030), which outlines the vaccines and immunization vision and strategy for the next decade. IA2030 has been developed through a co-creation exercise, involving over 750 stakeholders and over 60 organizations from the global, regional and country level. In addition to face-to-face consultations, over 4000 comments were received from a wide range of immunization and non-immunization stakeholders.

SAGE provided feedback on the objectives, key focus areas and goals of the seven strategic priorities of IA2030, concluding that the strategic framework outlined in IA2030 is well formulated to address the challenges of the next decade. The seven strategic priorities cover: Immunization for Primary Health Care/Universal Health Coverage; Commitment and Demand; Coverage and Equity; Life course and Integration; Outbreaks and Emergencies; Supply and Sustainability; Research and Innovation.

- SAGE agreed that these seven strategic priorities will be informed by four core principles of being people-focused, country-owned, partnership-based and data-enabled.
- SAGE also provided feedback on the elements related to the operationalization of IA2030, notably the Monitoring & Evaluation Framework and the governance structure, underlining that operationalization of IA2030 should take into consideration lessons-learned from GVAP.

Ebola vaccination

- An update on the current epidemiological situation of Ebola in the Democratic Republic of Congo was provided, which suggested a more positive outlook on the outbreak, however, challenges remain.
- Over the course of recent years, SAGE has provided multiple recommendations on Ebola vaccination strategies. All but one of the SAGE recommendations have been implemented and have been shown to be effective. The only recommendation not implemented is the dose reduction to half of the Guinea dose (1×10^7 pfu), as the vaccine supply situation did not require that step.
- A comprehensive review of the safety of the rVSV-ZEBOV-GP Ebola vaccine (manufactured by Merck) will be discussed at the next meeting of the WHO Global Advisory Committee on Vaccine Safety (GACVS).
- Positive news was shared in relation to vaccine development, including the likely start of a vaccine study of a second investigational Ebola vaccine (manufactured by Johnson & Johnson) using a two-dose schedule, and progress towards licensure of the rVSV-ZEBOV-GP Ebola vaccine.
- Under the guidance of the WHO Director-General and in close collaboration with Gavi, UNICEF and other partners, WHO is building a framework to ensure global vaccine security.
- The SAGE Ebola Working Group will develop *a priori* defined criteria for implementation of a further dose reduction in the event that future vaccine supply is constrained. Additionally, the Working Group will develop policies for the preventive use of Ebola vaccine.

Quality and Use of Immunization and Surveillance Data

- The session summarized major findings and knowledge gaps around immunization data quality and use, including vaccine-preventable disease (VPD) surveillance data. The SAGE Working Group on Quality and Use of Immunization and Surveillance Data presented its proposed recommendations around strengthening governance, tools, workforce capacities for data management and use and assessment for continued quality improvement.
- WHO's Western Pacific Regional Office presented its regional priorities in the strategic area of "Managing Health Intelligence on VPDs & Immunization" to highlight how the recommendations proposed by the SAGE Working Group are fully aligned with them, particularly around VPD surveillance, Monitoring & Evaluation and data for action.
- India then illustrated how the purposeful and intensified use of immunization, VPD surveillance and other process data, supported by strong leadership and innovation has helped the country improve its universal immunization program performance and efficiency.
- SAGE endorsed the following recommendations:
 - Integration of data activities under the broader umbrella of Universal Health Coverage and Primary Health Care.
 - Incorporation of the proposed recommendations into the Immunization Agenda 2030.
 - Incorporation of multi-component interventions for improving data quality and use into the 2021–2030 strategies of regions and countries.

Polio

- SAGE expressed serious concerns about the overall state of eradication efforts, particularly about the upsurge in wild poliovirus cases detected in Afghanistan and Pakistan and by the inability of the program to effectively control outbreaks of circulating vaccine-derived polioviruses (cVDPV) in Africa and Asia.
- Having sufficient mOPV2 remains essential for cVDPV2 outbreak response. SAGE therefore endorsed securing an uninterrupted mOPV2 supply.
- SAGE recognized the problem of countering cVDPV2 outbreaks with mOPV2, which may seed further cVDPV2 circulation in the absence of robust mucosal immunity. SAGE therefore endorsed accelerated clinical development of novel OPV2 vaccine (nOPV2), which is expected to have a reduced rate of reversion to wildtype and urged that the nOPV2 assessment under Emergency Use and Listing be prioritized.
- In the event of critically low levels of mOPV2 supply that is insufficient for cVDPV2 outbreak control, SAGE endorsed using one-drop of mOPV2 instead of the two-drop strategy.