World Health Organization

Highlights from the Meeting of the Strategic Advisory Group of Experts (SAGE) on Immunization 11-13 March 2024

(The full report will be published in the Weekly Epidemiological Record on 31 May 2024, and only the wording of the full report should be considered final)

Session 1

Report from the Department of Immunization, Vaccines, and Biologicals.

- On the 50th anniversary of the establishment of the Expanded Programme on Immunization (EPI) in 1974, the report reflected on the massive achievements of the programme over the past 50 years and aspirations for the next decades.
- Over these 5 decades, immunization has contributed to driving up child survival, controlling, eliminating or eradicating vaccine-preventable diseases, and has served as the backbone of primary healthcare (PHC) and a foundation for improving equity in access.
- The past 50 years have seen innovations in vaccines through platform development like viral vector, bacterial polysaccharide conjugate, and mRNA vaccines; adjuvants; and immunization technologies for facilitating cold chain, improving injection safety, leveraging GIS systems, and temperature monitoring. These innovations have led to a large number of new and improved vaccines and facilitated their distribution and delivery.
- The capacity for manufacturing vaccines of assured quality in emerging economies has substantially increased and African regional vaccine manufacturing will be a crucial additional step to vaccine equity and resilience.
- Despite these achievements, EPI faced a recent setback, and progress towards the Immunization Agenda 2030 (IA2030) goals is off-course for all but one of the 7 impact goals. Preliminary data from the first half of 2023 are a cause for cautious optimism on coverage gains toward pre-pandemic levels.
- Going forward, the four core principles of IA2030, country-owned, people-centred, partnership-based and data-guided will guide actions while accounting for the contextual changes.
- Notwithstanding preventive vaccination programmes, vaccine-preventable disease (VPD) outbreaks will continue to occur, and vaccines will be a key countermeasure for global health security. Preparedness to address future epidemics and pandemics, building on the lessons from the COVID-19 vaccine response will be key.

Update from Gavi, the Vaccine Alliance.

- Gavi is supporting countries in strengthening immunization programmes and reducing the number of zero-dose children. It has also allocated US $290 million to fully fund the

procurement of vaccine doses for catch-up vaccination for those who missed doses during the COVID-19 pandemic.

- There has been significant progress with the introduction of malaria and HPV vaccines in eligible countries through Gavi support.
- The Gavi 6.0 (2025-30) strategy that will be presented to the Gavi Board in June 2024 will remain ambitious despite concerns about financing. An investment strategy will be developed to support replenishment.
- The Gavi Board has approved investments for global health security to use the lessons from the COVID-19 response to address public health emergencies.
- Gavi will sustain support for polio eradication and cholera outbreak prevention and response. In addition, Gavi has simplified its processes to support VPD outbreak prevention.
- Investment cases for new vaccines shortlisted for Gavi support under the Gavi 2024 vaccine investment strategy are under development; among these, the introduction of a new tuberculosis vaccine is expected to be a game-changer.

Regional reports

- All regions experienced setbacks in vaccination during the COVID-19 pandemic though a recovery in vaccination coverage was observed in 2022 in all regions, except for the African region. Despite the progress, there is an accumulation of susceptible individuals that contributed to VPD outbreaks.
- Many, though not all, countries across all regions have revised policies and established catch-up vaccination schedules, developed catch-up vaccination plans to fill immunity gaps using a variety of approaches, and many have started implementing their plans.
- Regions reported major challenges in identifying children who missed vaccination doses and in delivering and monitoring vaccination to children older than 2 years.
- Exemplary initiatives in some countries have resulted in rapid progress. SAGE noted that close monitoring and robust accountability processes were key to success.
- SAGE took note of the challenges with monitoring progress with catch-up vaccination related to weaknesses in health information systems, which will need to be addressed to mainstream catch-up vaccination as part of routine immunization delivery.
- SAGE noted the need for program flexibility especially in fragile, conflict-affected, and vulnerable settings, and to establish linkages with other essential services and engage with local non-state actors to accelerate recovery.

Session 2

Immunization Agenda 2030 (IA2030) deep dive

- SAGE was presented with an overview of the Big Catch-up and progress in its implementation, including the successes and challenges. A country presentation from Cameroon exemplified the efforts taken and challenges faced.
- SAGE underscored the need for political will, community engagement, and health worker capacity strengthening and encouraged National Immunization Technical Advisory Groups (NITAGs) to guide the efforts.
- Monitoring the Big Catch-Up is vital to document progress, learn lessons, inform future actions, and ensure accountability. The IA2030 Data Strengthening and Use Working group has

developed a guidance document laying out indicators and suggested processes and tools to monitor and evaluate catch-up vaccination.

- SAGE acknowledges that generating granular data to fully monitor catch-up efforts will not be feasible in the short term. During this period triangulated data from a combination of data sources using innovative analytic methods should be used to understand the impact of the BCU.
- Long-term investments will be required to strengthen immunization data and VPD surveillance systems and scale up the use of digital and other innovative solutions grounded on the five building blocks stated in the IA2030 Data Action Framework.[1]

Session 3

Poliomyelitis

- SAGE was pleased to note that WPV1 circulation is confined to a small geographic area at the border between Afghanistan and Pakistan and that the genetic diversity of detected WPV1s is very low; however, SAGE expressed concern about the continued circulation of cVDPV2 in Africa and detections of cVDPV1 in several countries.
- SAGE stressed the need for increased efforts to improve routine coverage of all polio vaccinations, especially for IPV1.
- SAGE extended its support to the bOPV Cessation Team in planning for the eventual cessation of the use of Sabin bOPV in routine immunization programmes; SAGE will review the triggers and pre-requisites developed by the bOPV cessation team to ensure a successful cessation, also taking into account the learnings from the tOPV-bOPV vaccine switch.
- SAGE reiterated that only low-polio-risk countries with high coverage with at least two IPV doses in the routine immunization schedule should consider transitioning to IPV-only vaccination schedules ahead of planned synchronised bOPV cessation.
- SAGE recommended that to stop persistent poliovirus circulation, countries opting for off-label fractional dose vaccination of IPV may choose either an intradermal or intramuscular route of administration in outbreak response campaigns.

Session 4

Hepatitis E

- SAGE recommended that in fragile, conflict-affected and vulnerable (FCV) settings with documented hepatitis E virus circulation, the benefits of vaccinating women of childbearing age (≥16 years and over) outweigh the potential harms, including during pregnancy where the risk of severe disease in particularly high during the second and third trimester.
- When implementing vaccination campaigns, SAGE stressed the importance of accompanying hepatitis E vaccine (HEV) use with public health research, whenever possible.
- SAGE recommended the use of an off-label 2-dose schedule (0 and 1 month) instead of the 3-dose schedule during campaigns in FCV settings.
- SAGE encouraged additional research on hepatitis E vaccination during pregnancy, in people living with HIV and in individuals under 16 years of age. In addition, SAGE asked to be informed of the outcomes of further analysis of the Bangladesh trial.

[1] https://www.immunizationagenda2030.org/resources/34-ia2030-data-action-framework

Session 5

COVID-19

- The number of cases, hospitalizations and deaths from COVID-19 continues to show a declining trend.
- While inequity in access to COVID-19 vaccines, in particular updated vaccine formulations, persists, demand has also declined, especially in low- and middle-income countries (LMICs).
- Booster doses of the Omicron-adapted bivalent vaccines (BA.1/2 and BA.4/5) continue to protect against symptomatic disease and severe disease during the XBB dominant period; there is a moderate benefit of the monovalent XBB vaccines over the bivalent or index virus vaccines.
- SAGE reiterated that monovalent XBB vaccines should be used when available. However, countries should not delay the administration of ancestral or bivalent vaccines to high-priority-use groups if monovalent XBB vaccines are not available.
- SAGE reaffirmed the priority-use groups and frequency of re-vaccination as outlined in the WHO SAGE Roadmap for prioritizing the use of COVID-19 vaccines.

Session 6

Mpox

- SAGE reviewed the most recent data on the epidemiology of mpox and noted that while reported cases and deaths had declined in all other WHO regions, reported cases and deaths persisted in the African region which has a distinct epidemiology and case distribution, including a reported high morbidity and mortality in children under 15 years old.
- SAGE was presented with data from systematic reviews of available smallpox/ mpox vaccines that demonstrated MVA-BN vaccine effectiveness in pre-exposure vaccination but more limited effectiveness in post-exposure vaccination, noting that all data were generated during the multi-country outbreak.
- Based on the data presented, SAGE updated its recommendations on the use of vaccines to prevent mpox in outbreak settings and preventive vaccination for high-risk groups in non-outbreak settings.
- In the context of an outbreak, to allow the greatest flexibility for local risk assessment, varied modes of transmission and response options, populations to consider for vaccination may include: (i) adults and children in a geographically defined area or community (e.g. villages) with a documented risk of exposure; (ii) persons with multiple sexual contacts; (iii) health workers at risk of repeated exposure; and (iv) known contacts of persons with mpox.
- Noting the endemicity of disease in the African continent, the distinct epidemiology of mpox in this region and the inequitable access to vaccination, SAGE issued a strong call to action to promote epidemiological and vaccine research on mpox in the region and urgent steps to facilitate equitable access to vaccination. Research should also be embedded in the outbreak response.

Session 7

Immune correlates

- For some vaccines, the Phase 3 trials with clinical outcomes are challenging either because they require very large sample sizes (e.g., group B streptococcus [GBS]) or because of the unpredictability of outbreaks (e.g., chikungunya). In such instances, regulatory approval may be

issued based on immunological correlates of protection against disease, followed by post-authorization requirements to demonstrate effectiveness.

- SAGE was briefed on the proposed regulatory pathways using this approach for GBS and chikungunya vaccines and the evidence in support of the proposed immunological correlates of protection.
- Since a chikungunya vaccine had received regulatory approval and there was interest in introducing this vaccine in several countries, SAGE requested WHO to initiate a process to conduct a detailed review of the evidence and assess use case scenarios for the optimal use of this vaccine.
- SAGE also noted that requiring evidence of clinical efficacy for GBS vaccines before issuing policy recommendations could delay the use of the vaccine in LMICs.

Session 8

Respiratory syncytial virus (RSV)

- SAGE was provided with data on products that recently received regulatory approval for the prevention of RSV disease in infants and adults. These included RSV pre-F protein vaccines for use in pregnant women to provide protection to young infants and to protect older adults, and long-acting monoclonal antibodies to protect young infants.
- All products demonstrated high efficacy in protecting the target groups against medically attended and severe RSV lower respiratory tract illness. The products have been rolled out in a few countries.
- A SAGE Working Group has been established to review the evidence on the use of these products and the findings of their review will be presented to SAGE in September 2024.
- SAGE recommended that products for the prevention of RSV disease in infants be prioritised for presentation in September 2024, followed by vaccines for the protection of older adults and articulated several issues that should be considered by the Working Group in their review of the evidence.
- Since a numerical imbalance was seen towards preterm births in the RSV vaccinated pregnant women compared to the control vaccine pregnant women, particular attention will be given to that signal.