

Highlights from the Meeting of the Strategic Advisory Group of Experts (SAGE) on Immunization – 3-6 October 2022

*(Full report will be published in the Weekly Epidemiological Record on 16 December 2022,
and only the wording of the full report should be considered as final)*

Report from the department of Immunization, Vaccines, and Biologicals

- Immunization programmes globally face many challenges in an increasingly complex world that faces unprecedented pressures, including state-based conflict, massive population displacement, economic crisis, and the existential threat of climate change.
- Two years into the pandemic, disruptions to service delivery persist in countries across income levels with backsliding in coverage and an increase in the number of zero-dose children.
- The decline in vaccination coverage has led to large disruptive outbreaks of measles and circulating vaccine derived polio viruses mainly affecting low- and low-middle-income countries, while outbreaks of Monkeypox has newly affected high-income countries in the Americas and Europe. These competing priorities divert attention from other essential health services.
- While COVID-19 vaccination targets were not achieved, including among priority-use groups, lessons learned from the pandemic response can be leveraged to strengthen immunization programmes and deliver vaccine across the life-course.

Report from Gavi, the Vaccine Alliance

- The zero-dose agenda and supporting countries in recovering will remain a priority for the Alliance.
- The refresh of the Gavi strategy (Gavi 5.1) will reiterate the focus on the zero-dose agenda and the relaunch of human papilloma virus (HPV) vaccination, while also adding the objective for the potential of long-term support for COVID-19 vaccination and regional vaccine manufacturing.
- The Alliance will continue its support for polio eradication while leveraging lessons learned to support the zero-dose agenda.
- The Alliance is preparing to launch malaria vaccination in the Malaria Vaccine Implementation Plan (MVIP) countries initially, and plans to expand the use of Zaire ebolavirus vaccines held in a stockpile to prevent vaccines passing their expiry dates.

- The Alliance is closely monitoring the Monkeypox, and Sudan ebolavirus outbreaks and stands ready to engage with partners if required.

Progress with implementation of IA2030

- SAGE was presented with the 2022 technical progress report on the Immunization Agenda 2030 (IA2030), providing an overview of global immunization data for 2021, an update on the operationalisation of the strategy and proposed recommendations to address the short- and long-term challenges to achieving the IA2030 goals and targets.
- SAGE was also presented with updates from each of the WHO regional offices on the status of implementation of IA2030, the challenges and lessons learned, and actions being taken to operationalize IA2030 in each region.
- Several factors that impede the achievement of the IA2030 goals and targets cut across the regions and country income levels and include: inadequate and overstretched health workforce, exacerbated through the COVID-19 response; insecurity and population displacement; competing priorities and diversion of resources from routine service delivery; and inadequate financing.
- Most regions have developed regional strategies in alignment with IA2030 and have developed or are in the process of finalizing operationalization frameworks and M&E processes and are taking urgent actions to mitigate the risk of further VPD outbreaks.
- The Measles & Rubella Initiative (M&RI) will join the IA2030 partnership structure to promote alignment in efforts to use measles as a tracer to identify service delivery gaps and take coordinated measures to strengthen immunization systems.

Monkeypox

- SAGE was presented with the monkeypox vaccination strategy developed under the umbrella of the Strategic Preparedness, Readiness and Response Plan (SPRP) and with the results of a rapid review on the performance and safety of smallpox vaccines for the prevention of monkeypox in the current multi-country monkeypox outbreak.
- Based on the available, limited data, SAGE recommended primary preventive (pre-exposure) vaccination (PPV) for groups at high risk for exposure to monkeypox. The group at highest risk of exposure in the current outbreak is gay, bisexual, or other men who have sex with men (MSM) with multiple sexual partners. Others at risk include individuals with multiple casual sexual partners; sex workers; health workers at repeated risk of exposure; laboratory personnel working with *orthopoxviruses*; clinical laboratory and health care personnel performing diagnostic testing for monkeypox; and

outbreak response staff. The level of risk of infection may be used for prioritization in case of limited vaccine supply.

- Post-exposure vaccination (PEPV) is recommended for close contacts of cases, ideally within 4 days of first exposure and up to 14 days in the absence of symptoms.
- For healthy adults, any of the three currently available vaccines is appropriate. For individuals for whom replicating or minimally replicating vaccines are contraindicated, non-replicating vaccines should be used. Specific recommendations apply on vaccine choice for special populations.
- SAGE emphasized that research on monkeypox in previously affected countries has been neglected, and strongly recommended that evidence on the epidemiology and zoonotic situation of monkeypox disease in previously affected countries and the relationship with animal vectors be generated. In addition, vaccine use need to be accompanied with research to assess safety and effectiveness of interventions.
- Updated interim recommendations on monkeypox vaccination will be published.

Respiratory Syncytial Virus (RSV)

- SAGE was presented with data on the burden of RSV disease, the product pipeline for long-acting monoclonal antibody (mAb) and on maternal vaccines for protection of young infants.
- The burden of acute lower respiratory tract infections (ALRTI) remains high with an estimated more than 100 000 deaths attributed to RSV in children under 5 years; 97% of deaths occur in low-income (LICs) and lower middle-income countries (LMICs) and 45% occur in infants < 6 months.
- Market authorization of a long-acting monoclonal antibody by a stringent regulatory authority (SRA) is imminent (Q4 2022); also, a maternal vaccine in phase 3 development is expected to have an interim efficacy readout by end of 2022 with possible licensure in 2023 by a SRA.
- The WHO RSV vaccine technical advisory group reviewed available evidence on the performance and mechanism of action of the long-acting monoclonal antibodies and maternal immunization and concluded that these products would likely work equally well in countries across income levels, despite the fact that high-income countries (HICs) accounted for the majority of subjects enrolled in the clinical trials.

- A pre-fusion F protein vaccine when administered to pregnant women showed 85% efficacy against medically attended RSV ALRTI and 91% against severe RSV ALRTI in infants in a phase 2b clinical trial; a phase 3 trial is underway with results from an interim analysis expected in mid-2023.
- SAGE noted the potential availability of effective preventive interventions to prevent severe RSV disease in a relatively short time frame and recommended to conduct a thorough review of the existing and emerging data, especially as relevant to LIC and LMIC populations where most deaths occur.
- The need for more data in LIC and LMIC to understand the full public health potential of these vaccines will require studies that should be initiated now, in collaboration with WHO.

Poliomyelitis

- SAGE expressed concern about renewed wild poliovirus 1 (WPV1) circulation in Pakistan; and about continuing detections of WPV1 in South-eastern Africa. Further, SAGE noted ongoing the transmission of vaccine-derived poliovirus type 2 (VDPV2), particularly in the African region and in Yemen, as well as detections in New York, London, and Jerusalem. SAGE stressed the need for increased efforts to improve routine coverage of polio vaccination.
- SAGE endorsed the option for the timely initial use of the inactivated poliovirus vaccine (IPV) to respond to outbreaks, in countries that use only IPV for routine childhood immunization. This option is recommended if the poliovirus transmission is confined to a well-defined population group or geographical area and with high levels of sanitation; preparation for a response with oral polio vaccines (OPVs) should begin in parallel should transmission continue following the response with IPV.
- SAGE provided guiding principles on selection of target age group in outbreak response campaigns. SAGE reiterated that the outbreak response campaigns should primarily target children less than 5 years, though wider age range response may be considered when there is evidence of immunity gaps in older age groups or low historical vaccination coverage rates.
- SAGE stressed the importance of improving routine immunization coverage and called on the polio eradication programme to take actions to ensure that zero dose children identified by the programme are included in routine immunization micro plans for all

recommended pediatric vaccines. SAGE also recognized the importance of accelerated efforts to develop and authorize novel OPVs against type 1 and 3 virus.

- SAGE also recommended that all countries have outbreak response plans to be prepared for timely response against VDPV or WPV1 outbreak.

COVID-19 vaccines

- SAGE reviewed the safety and immunogenicity of the bivalent vaccines containing the mRNA of the original strain and of the Omicron sub lineages when given as a booster dose in adults, and the clinical trial results from a protein subunit vaccine manufactured by Biological E, BECOV-2 (Corbevax™).

Variant-containing COVID-19 vaccines

- Achieving high and equitable rates of primary series vaccination with ancestral strain vaccines remain the highest public health priority.
- Four variant-containing bivalent mRNA vaccines which either include BA.1 or BA. 4-5 in combination with the ancestral virus have been authorized for use as booster doses.
- SAGE reviewed and endorsed a good practice statement stating that currently available data are not sufficient to support the issuance of any preferential recommendation for bivalent variant-containing vaccine boosters over ancestral-virus-only boosters.
- Booster vaccination 4-6 months after the last dose provides improved protection against currently circulating SARS-CoV-2. Either the monovalent ancestral virus vaccines or bivalent variant-containing vaccines can be used as boosters. The bulk of the benefit is from the provision of a booster dose, irrespective of whether it is a monovalent or bivalent vaccine.

Vaccine product specific recommendations: Biological E BECOV-2 vaccine (Corbevax™)

- SAGE reviewed data on the Biological E BECOV-2 COVID-19 vaccine (Corbevax™) and will issue recommendations once the product is listed by WHO for emergency use (EUL).

Briefing on the Sudan ebolavirus outbreak

- SAGE was provided with an update of the ongoing outbreak of the Sudan ebolavirus vaccine in Uganda. The outbreak was declared on the 20th of September 2022 with the

index case detected on the 11th of September 2022. As of October 6, there are 44 confirmed cases, 20 suspected cases and 10 deaths reported from 5 districts in Uganda.

- Vaccines against the Zaire ebolavirus do not offer cross-protection against the Sudan ebolavirus. There are 6 candidate vaccines under development against the Sudan ebolavirus, 3 of which have undergone phase 1 or 2 clinical trials.
- The opportunity of a vaccination response will be used to evaluate the efficacy of one of the candidate vaccines using a ring vaccination approach similar to that used for the Guinea trial with the Zaire ebolavirus vaccine, with the difference that only contacts will be offered vaccination to optimize the use of the limited doses of vaccine. The protocols are undergoing regulatory and ethics review.