Highlights from the Meeting of the Strategic Advisory Group of Experts (SAGE) on Immunization
20-22 March 2023

(The full report will be published in the Weekly Epidemiological Record on 2 June 2023, and only the wording of the full report should be considered final)

Session 1

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

- The COVID-19 pandemic vaccination response still requires efforts to reduce inequities, reach high-priority groups, and close coverage gaps.
- Disruptive measles and other disease outbreaks highlight the need for catch-up vaccination and for enhancing preparedness for outbreak response.
- To get back on the trajectory for achieving the Immunization Agenda 2030 (IA2030) goals and targets, a 3-prong approach to provide catch-up vaccination to children who missed scheduled doses, restore coverage, and strengthen immunization programmes is planned.
- Innovations developed for the COVID-19 response and a pipeline of vaccines and innovative technologies and platforms will support actions to strengthen vaccination across the life course.
- The highest priorities for 2023-2025 are the zero-dose child agenda and routine immunization strengthening (which includes catchup, and with special attention on measles, yellow fever, other outbreak prone diseases, and polio), preparedness and response to outbreaks, revitalization of human papillomavirus (HPV) vaccination, integration of COVID-19 vaccination into routine immunization and Primary Health Care (PHC), and malaria vaccine introduction in African countries.

Update from Gavi, the Vaccine Alliance.

- The Gavi 5.1 strategy reaffirms the core priorities in the Gavi 5.0 strategy and additionally includes support for ongoing COVID-19 vaccination in priority use groups and an evolution of its support in pandemic preparedness.
- The Gavi “must-win” priorities for 2023 include the restoration of routine immunization, expansion of malaria vaccination, the relaunch of HPV vaccination, and support for targeted COVID-19 vaccination and its integration with other health services.
- The next update of the vaccine investment strategy to inform Gavi investments in the Gavi 6.0 strategy is expected to be completed in 2024.

- Gavi will continue to support the introduction and use of inactivated poliovirus vaccine (IPV) and preventive and outbreak response vaccination for measles and rubella in eligible countries.

Session 2

Regional reports with a focus on measles.

- SAGE reviewed data on the status of measles elimination in each region, including the impact of the COVID-19 pandemic, and the challenges faced.
- All WHO regions have observed an increase in measles cases in 2022 and the accumulation of immunity gaps has increased the risk of outbreaks. Difficulties with delivering vaccines in conflict-affected settings, weak health systems, competing priorities, and inadequate financing are the challenges faced.
- Delays in securing funding are impeding efforts to conduct preventive vaccination campaigns and mount a timely outbreak response.
- Surveillance quality declined in all regions during the pandemic though there are signs of recovery in several countries.
- SAGE noted the need to review and update policies on age eligibility for measles vaccination to enable catch-up, accelerate the development and use of new technologies and innovations, and review the evidence to support policy recommendations for vaccination of infants below six months and during pregnancy.

Session 3

Partnering with regions and countries to identify priority pathogens for new vaccines.

- WHO in collaboration with all its regional offices has undertaken a process to define targets for new vaccine development for endemic pathogens. Those targets will eventually be included as monitoring indicators for Strategic Priority 7 (on research and development) of Immunization Agenda 2030.
- The process included a multi-criteria decision analysis (MCDA)[1] method with a preference survey to weight the prioritization criteria, followed by regional consultations to review the outcomes and develop a list of priority pathogens for each region.

[1] using the Potentially All Pairwise Rankings of all possible Alternatives (PAPRIKA). https://www.1000minds.com/paprika (accessed 25/03/2023)

- Early results show consensus that tuberculosis, human immunodeficiency virus (HIV), and pathogens that exhibit high levels of antimicrobial resistance such as *Klebsiella pneumoniae* are important across all regions.
- Other pathogens targets including such as *Streptococcus pyogenes* (Group A streptococcus), Shigella, and respiratory syncytial virus (RSV) were identified as important by four or more regions and *Plasmodium falciparum* by the African region.
- Work is ongoing to finalize these priority targets for vaccine development to inform regional, national, and global research and development strategies, and investment.

Session 4

Roadmap for COVID-19 vaccination in the Omicron era.

- SAGE discussed an updated roadmap on uses of COVID-19 vaccines considering the evolving public health needs in the era of the Omicron variant and high population-level immunity.
- The update is based on the scenario that assumes that the virus will continue to evolve but cause less severe disease with possible surges in infections that will require periodic booster doses of the vaccine to protect the highest priority group, and the recommendations apply only in the context of this epidemiological scenario.
- The update considers the steep increase in the seroprevalence of SARS CoV2 antibodies globally in all age groups, indicating high levels of immunity due to infection-induced, vaccine-induced, or hybrid immunity.
- The update also considers the overall decline in disease severity, including post-COVID conditions, and acknowledges the programmatic and financial opportunity cost of COVID-19 vaccination .
- A simplified risk classification now includes three risk groups (high, medium, and low) and proposes a differentiated approach for the provision of the primary series and additional booster doses for each risk group.
- Very briefly, the key recommendations in the updated roadmap comprise: (i) administration of additional boosters doses (beyond the first booster dose) for high-priority groups, including frontline health workers 12 months after the previous booster dose; (ii) additional booster doses are no longer routinely recommended for the medium risk group; (iii) administration of a booster dose during pregnancy if the last dose was given more than 6 months earlier; and (iv) considering the primary series and booster dose for healthy children

and adolescents only within country context, including disease burden in this age group, cost-effectiveness, other health or programmatic priorities, and opportunity costs. The updated roadmap with more details on the recommendations is to be published shortly.

Session 5

Status of new tuberculosis vaccine candidates intended for adults and adolescents: preparing the pathway for use.

- Tuberculosis (TB) is a leading infectious killer and is estimated to cause over 10 million cases and 1.6 million deaths in 2021. The COVID-19 pandemic has reversed years of progress made in the fight against TB.
- A vaccine that prevents TB in adolescents and adults is needed to reduce the disease burden among them and transmission to other target age groups. Several candidates are in late-stage clinical trials and a few vaccines could receive regulatory authorization within 3 years.
- SAGE was provided with preliminary clinical trial data on a promising TB vaccine candidate for adults and adolescents – M72/AS01$_E$.
- SAGE encouraged investigators and funders to explore research design approaches to demonstrate the prevention of Mtb infection in infection-naive individuals in the context of the upcoming efficacy trials.
- SAGE proposed that a cluster randomized trial to assess the potential indirect effect of M72/AS01$_E$ be considered in parallel to the phase 3 trial, and studies to accelerate recommendations for use in adolescents below 15 years of age, ease implementation and improve cost-effectiveness.

Session 6

Polio eradication.

- SAGE was presented with an epidemiological update on poliomyelitis, data to inform vaccination strategies for areas with persistent poliovirus transmission and the use of the novel type 2 oral poliovirus vaccine (nOPV2) at shorter intervals for outbreak response, and the report from the Polio SAGE Working Group on restricting the use of Sabin oral poliovirus vaccines (OPV).

- SAGE was pleased to note the reduction in type 1 wild poliovirus (WPV1) cases in the endemic countries. However, SAGE expressed concern about the persistence of circulating vaccine-derived poliovirus (cVDPV) type 2 in Africa and a sharp increase in cVDPV type 1 cases in several countries which highlighted the urgent need to improve routine immunization coverage to mitigate this risk in the short and longer term.
- SAGE recommended the preferential use of nOPV2 for a cVDPV type 2 outbreak response with oral vaccines, and that type 2 Sabin OPV should only be used in exceptional circumstances.
- SAGE recommended that in areas of persistent poliovirus circulation, an additional IPV (full or fractional dose) campaign should be conducted to supplement nOPV2 and Sabin OPV campaigns as a means to enhance mucosal immunity and reduce the likelihood of ongoing poliovirus circulation.
- SAGE recommended a flexible approach using nOPV2 for outbreak response in shorter than 4-week intervals but maintaining a minimum 1-week interval if dictated by programme needs.

Session 7

Malaria vaccination.

- SAGE was presented with an update on the malaria vaccine implementation programme (MVIP), and the plans for future roll-out and the Framework for allocation of currently limited supply. SAGE noted that MVIP will end in 2023, having answered the key questions for which the programme was established, i.e., showing vaccine delivery in routine immunization programmes is feasible, the vaccine is safe, and the impact is high. Vaccine introduction resulted in substantial reduction in severe malaria and all-cause mortality among children eligible to receive the vaccine.
- There is a high demand for the vaccine with at least 28 countries expressing interest in introducing the vaccine. Of these, 15 countries already submitted an application to Gavi for support, and more than 15 additional applications are expected later this year. Vaccine supply remains highly constrained and will be made available based on the Framework for allocation of limited supply.
- Evidence and options for the minimal interval between doses 3 and 4 for vaccination in areas of highly seasonal malaria transmission or perennial transmission with seasonal peaks were presented. SAGE concurred with the SAGE and Malaria Policy Advisory Group

(MPAG) Working Group (WG) on malaria vaccines proposal to allow for flexibility in the immunization schedule and to reduce the minimum interval between the doses 3 and 4 to 6 months to optimize impact.

- The SAGE MPAG WG is in the process of reviewing the R21 Matrix M malaria vaccine, which is in the late stages of clinical development. Initial results presented appear promising. The safety of the vaccine will be reviewed by the WHO Global Advisory Committee on Vaccine Safety (GACVS). The next SAGE/MPAG malaria vaccine WG review will occur later this year when 18-month follow-up for seasonal delivery and 12-month follow-up for age-based delivery are completed.