Strategic Advisory Group of Experts (SAGE) on Immunization Evidence to recommendations framework[i]

Question: Can Sabin Inactivated Poliovirus Vaccine (sIPV) be used interchangeably with Salk-based IPV (wIPV), in other words, is it equally effective?
Population: Immunocompetent individuals, Children
Intervention: sIPV
Comparison(s): wIPV
Outcome: Serological levels of type 1, 2 and 3 poliovirus antibodies / cases of polio / VAPP

Background:
SAGE recommended that vigorous efforts be made to improve IPV coverage in locations at risk of cVDPV2 outbreaks to reduce the number of susceptible children before transmission or outbreaks can occur, especially in the context of reduced coverage caused by the COVID-19 pandemic. An IPV based on the attenuates Sabin virus strains (sIPV) was developed and licensed in Japan 2012 and is already in use in national immunization programs there and in China. In December 2020, LGChem (Eupolio) sIPV was the first WHO prequalified sIPV product.

	CRITERIA	JUDGEMENTS				RESEARCH EVIDENCE	ADDITIONAL INFORMATION
PROBLEM	Is the problem a public health priority?	*No* ☐	*Un-certain* ☐	*Yes* ☒	*Varies by setting* ☐	The international spread of poliovirus was first declares as a Public Health Emergency of International Concern (PHEIC) in May 2014. Most recently, this status was extended in November 2021[1] because of the risk of cVDPV2 outbreak and WPV1 transmission (in Pakistan and Afghanistan).	

[1] World Health Organization. Statement of the Thirtieth Polio IHR Emergency Committee. 23 November 2021. Available at https://www.who.int/news/item/23-11-2021-statement-of-the-thirtieth-polio-ihr-emergency-committee, Accessed Jan 25, 2022.

BENEFITS & HARMS OF THE OPTIONS	Benefits of the intervention Are the desirable anticipated effects large?	*No* ☐ *Un-certain* ☐ *Yes* ☒ *Varies* ☐	The primary objective of Sabin-IPV development is to increase the availability and affordability of IPV production for low- and middle-income countries. Using Sabin poliovirus strains instead of using the wild strains for conventional Salk-IPV reduces the biosafety risks associated with the production of this vaccine. LGChem sIPV was demonstrated to be non inferior for seroconversion, seroprevalence and safety signals are comparable to wIPV.	
	Harms of the intervention Are the undesirable anticipated effects small?	*No* ☐ *Un-certain* ☐ *Yes* ☒ *Varies* ☐	Numerous studies suggest that IPV is safe to administer. The risks are associated to procedural harms of injection. Safety is reported to be comparable between sIPV and wIPV.	
	Balance between benefits and harms	***Favours inter-vention*** ☒ ***Favours com-parison*** ☐ ***Favours both*** ☐ ***Favours neither*** ☐ **Unclear** ☐	There are no apparent harms in administering sIPV compared to wIPV. The benefits favoring the intervention are the reduction in biohazard risk and increasing availability/affordability of IPV into lower/middle-income countries.	
	What is the overall quality of this evidence for the critical outcomes?	Effectiveness of the intervention ***No included studies*** ☐ ***Very low*** ☐ ***Low*** ☐ ***Mod-erate*** ☐ ***High*** ☒ Safety of the intervention ***No included studies*** ☐ ***Very low*** ☐ ***Low*** ☐ ***Mod-erate*** ☐ ***High*** ☒	See GRADE table for detailed assessment.	There are key publications of and data on the immunogenicity and safety of Sabin IPV (both from clinical trials and experience from national immunisation

			programmes in China and Japan).	
VALUES & PREFERENCES	How certain is the relative importance of the desirable and undesirable outcomes?	*Important uncertainty or variability* ☐ *Possibly important uncertainty or variability* ☐ *Probably no important uncertainty or variability* ☐ *No important uncertainty or variability* ☒ *No known undesirable outcomes* ☐	It is of great importance that sIPV can safely be manufactured in low/middle-income countries. This will aid in cost reduction and increase availability. There are no remarkable undesirable outcomes.	
	Values and preferences of the target population: Are the desirable effects large relative to undesirable effects?	*No* ☐ *Probably No* ☐ *Uncertain* ☐ *Probably Yes* ☐ *Yes* ☒ *Varies* ☐	On the individual level, avoidance of poliomyelitis related disease would likely outweigh any adverse effect of vaccination (pain during immunization, AEFIs). There is no difference between sIPV and wIPV in safety and efficacy profile.	
RESOURCE USE	Are the resources required small?	*No* ☒ *Uncertain* ☐ *Yes* ☐ *Varies* ☐	The WHO entered a collaboration with Intravacc (formerly the Netherlands Vaccine Institute (NVI)) to develop and optimise sIPV technology and transfer this	sIPV adjuvanted with aluminum hydroxide has been demonstrated to allow a 50% (or higher) dose reduction and still exhibit an equitative immunogenic response to stand-alone sIPV or wIPV[2,3].

[2] Resik et al. Reactogenicity and immunogenicity of inactivated poliovirus vaccine produced from Sabin strains: A phase I trial in healthy adults in Cuba. Vaccine. 2014; 32: 5399-5404.

[3] Verdijk P et al. Safety and immunogenicity of inactivated poliovirus vaccine based on Sabin strains with and without aluminum hydroxide: a phase I trial in healthy adults. Vaccine. 2013; 31(47): 5531-5536

					technology to manufacturers in low and middle income country settings. Between 2010 and 2016, WHO called four Expressions of Interest (EoI) from private or public sector vaccine manufacturers in developing countries to select recipients of sIPV production technology transfer, appropriate for public sector use in developing countries. LG Chem in Korea have been the first prequalified sIPV product.	
	Cost-effectiveness	*No* ☐	*Un-certain* ☐	*Yes* ☐	*Varies* ☒	The production cost per dose is significantly higher for wIPV or sIPV than for OPV. WHO prequalified sIPV is USD 1.75 per dose (UNICEF SD, Jan 2021). The current range of IPV price for UNICEF market is about 1-3 USD per dose. Since sIPV has lower biosafety risks in for manufacture (see below), sIPV can be safely manufactured in developing countries so this can increase supply and reduce costs.	
EQUITY	What would be the impact on health inequities?	*Increa-sed* ☐	*Un-certain* ☐	*Re-duced* ☒	*Varies* ☐	Introduction of sIPV manufacture would provide an alternative and additional source of polio vaccination. Wild-type IPV production poses an unacceptable biosafety risk for developing countries, where population immunity is seldom sufficiently high to prevent the spread of these strains, should these be released from an IPV production site. Thus, development of IPV from safer (ie, less	

			transmissible) poliovirus strains and noninfectious methods of production have become a priority. The WHO has established a collaboration with the Netherlands Vaccine Institute (Bilthoven, the Netherlands) (now the Institute for Translational Vaccinology; Intravacc) to develop Sabin-IPV for potential technology transfer to manufacturers in developing countries.	
ACCEPTABILITY	Which option is acceptable to key stakeholders (Ministries of Health, Immunization Managers)?	*Inter-vention* ☒ *Comparison* ☐ *Both* ☐ *Neither* ☐ *Unclear* ☐	The previous SAGE recommendation to introduce one IPV dose into the routine immunization was adopted by all countries, so the recommendation of an sIPV should be acceptable as a policy, given the sufficient funding and tech transfer is available.	The SAGE WG also emphasised the long-term importance of sIPV as a strategic option for the GPEI, to ensure adequate global IPV supply, and GPEI communication around the product.
	Which option is acceptable to target group?	*Inter-vention* ☐ *Comparison* ☐ *Both* ☒ *Neither* ☐ *Unclear* ☐	IPV coverage of one dose has increased from 47% in 2016 to 82% in 2019. With sIPV there are no additional visits to healthcare facilities than those already existing with routine vaccination since it would be replacing IPV administration.	

FEASIBILITY	Is the intervention feasible to implement?	*No* ☐	*Probably No* ☐	*Uncertain* ☐	*Probably Yes* ☐	*Yes* ☐	*Varies* ☒	The sIPV produced by LGChem (Eupolio) was WHO prequalified in December 2020 and is the only WHO prequalified sIPV product to date. The Netherlands Vaccine Institute (NVI) developed the micro-carrier technology for large-scale production of IPV (late 1960s). With the new WHO policy encouring sIPV over wIPV manufacture, NVI has responded positively by technology transfer to different countries (predominantly developing countries) for large-scale sIPV development.[4]	There are several licensed sIPV products that are used in national immunization programmes in China and Japan.
Balance of consequences		Undesirable consequences *clearly outweigh* desirable consequences in most settings ☐	Undesirable consequences *probably outweigh* desirable consequences in most settings ☐	The balance between desirable and undesirable consequences *is closely balanced or uncertain* ☐	Desirable consequences *probably outweigh* undesirable consequences in most settings ☐	Desirable consequences *clearly outweigh* undesirable consequences in most settings ☒		

[4] Kreeftenberg H et al. Technology transfer of Sabin-IPV to new developing country markets. Biologicals. 2006; 34(2): 155-158.

Type of recommendation	We recommend the intervention ☒	We suggest considering recommendation of the intervention ☐ Only in the context of rigorous research ☐ Only with targeted monitoring and evaluation ☐ Only in specific contexts or specific (sub)populations	We recommend the comparison ☐	We recommend against the intervention and the comparison ☐
Recommendation (text)	Please see Polio vaccines: WHO position paper – June 2022 (www.who.int/publications/i/item/WHO-WER9725-277-300)			
Implementation considerations	Please see Polio vaccines: WHO position paper – June 2022 (www.who.int/publications/i/item/WHO-WER9725-277-300)			
Monitoring and evaluation	Please see Polio vaccines: WHO position paper – June 2022 (www.who.int/publications/i/item/WHO-WER9725-277-300)			
Research priorities	Please see Polio vaccines: WHO position paper – June 2022 (www.who.int/publications/i/item/WHO-WER9725-277-300)			

[i]This Evidence to Recommendation table is based on the DECIDE Work Package 5: Strategies for communicating evidence to inform decisions about health system and public health interventions. Evidence to a recommendation (for use by a guideline panel). http://www.decide-collaboration.eu/WP5/Strategies/Framework