Partnering with regions and countries to identify priority endemic pathogens for vaccine research and development

Immunization Agenda 2030 Monitoring and Evaluation – December 2023

I. Introduction

Previous reports in this series (see box) have described how we have identified a global list of 17 priority endemic pathogens for new vaccine research and development (R&D) by combining regional top 10 pathogen lists derived from regional and country stakeholder surveys and regional pathogen burden data. This global list (Table 1) will be the basis for monitoring new vaccine R&D under Immunization Agenda 2030 (IA2030). More importantly, it is intended to inform stakeholder actions, thereby linking new vaccine R&D more closely to regional and country perspectives.

Table 1 Global list of 17 priority endemic pathogens for new vaccine R&D

Cytomegalovirus	*Leishmania* spp
Dengue virus	Non-typhoidal *Salmonella* (NTS)
Extra-intestinal pathogenic *E coli* (ExPEC)	Norovirus
Group A Streptococcus (GAS, *Streptococcus pyogenes*)	*Plasmodium falciparum*
Group B Streptococcus (GBS, *Streptococcus agalactiae*)	Respiratory syncytial virus (RSV)
Hepatitis C virus	*Shigella* spp
HIV-1	*Staphylococcus aureus*
Influenza virus	Tuberculosis (TB, *Mycobacterium tuberculosis*)
Klebsiella pneumoniae	

But this list by itself is not specific enough to achieve these aims. Because pathogens can affect people at various ages and can cause different disease states, multiple vaccines may be needed to address the public health needs related to a particular pathogen. And because R&D is at different levels of maturity for these new vaccines, the stakeholder actions needed will vary widely. To provide the necessary specificity, we have therefore identified vaccine "use cases" relating to each pathogen and assigned each use case to an "action category".

- **Use case.** The intended target population and outcome to be achieved by use of the new vaccine or monoclonal antibody (mAb)
- **Action category.** Three categories ("research", "advance R&D", and "prepare for policy") that broadly describe the activities and actions needed for a particular pathogen and use case

This report gives the method for defining the use cases and assigning them to action categories, the use cases themselves, and baseline data for IA2030 monitoring and evaluation (M&E).

Previous reports:

- *Landscaping and Methods Brief – for PDVAC*, July 2022. Available at: https://www.technet-21.org/en/resources/document/vaccine-r-d-priorities-initial-landscaping-and-proposed-methods
- *MCDA Survey Preparation and Launch – for PDVAC*, December 2022. Available at: https://cdn.who.int/media/docs/default-source/immunization/pdvac/pdvac-2022/combined-slides---day-1_web.pdf?sfvrsn=349ca64b_4, slides 52 – 74.
- *Multi-criteria decision analysis: Survey and preliminary results – for SAGE*, February 2023. Available at: https://terrance.who.int/mediacentre/data/sage/SAGE_eYB_Mar2023.pdf, section 3.3.
- *PDVAC Update – October 23, 2023.* Available by request.
- *SP7.2 Measurement – for IA2030 M&E Working Group*, January 2024. Current draft available by request.

II. Method

A. Defining Use Cases

> ***Use case:***
> *The intended target population and outcome to be achieved by use of the new vaccine or monoclonal antibody*

These use cases are intended for monitoring progress under IA2030 Strategic Priority 7 Research & Innovation (SP7). They reflect existing publicly available sources, and where available, are derived from WHO publications or guidance documents. The use case definitions are dynamic and can be updated as the context evolves.

Use case definitions aim to be ***grounded, comprehensive, streamlined,*** *and* ***responsive:***

- **Grounded**. Use cases were proposed by the project team based on publicly available sources. In order of precedence, these sources informed the use cases:
    - WHO guidance documents, including Preferred Product Characteristics (PPCs), Target Product Profiles (TPPs), Technical Report Series (TRS), and position papers; or equivalent documents from regional or national authorities.
    - Vaccine value profiles (VVPs), modelling studies and expert perspectives from other published literature, or developer strategies. Phase 3 clinical trial descriptions in clinical trial registries also provided information on target populations and intended outcomes.
- **Comprehensive**. Efforts were made to capture all use cases of public health or commercial relevance for the pathogens on the Global List, regardless of region. However, some use cases were excluded:
    - **Use cases met as of November 2023** were not included, in order to focus on unmet needs. For example, a use case for seasonal influenza vaccines was not included.
    - **Therapeutic vaccines and mAbs were considered on a case-by-case basis** and included if called-for by a WHO PPC or TPP or if they have the potential for widespread use. By the same rationale, use cases that are highly personalized, such as cytomegalovirus vaccines for transplant recipients, were not included.
- **Streamlined**. Use cases were grouped in some cases (such as vaccines to treat and/or cure HIV-1 infection) where clinical development is in Phase 1 or Phase 2 and preferred product characteristics have not been defined.
- **Responsive**. These use cases can be revised as TPPs and PPCs are established or revised, and as progress in research and R&D enable greater specificity on use cases and value propositions.

Each use case, including pipeline information, was reviewed by at least one member of WHO's Product Development for Vaccines Advisory Committee (PDVAC). (Reviewer names are given in the Annex.) Then, the full list of use cases was reviewed by all PDVAC members for clarity, consistency, and relevance. The following clarifications emerged from PDVAC review:

- **Focus on endpoints that can be evaluated in pre-licensure trials**. Benefits may be difficult to measure during pre-licensure trials due to low incidence (such as maternal disease due to GBS), extended follow-up

requirements (such as stunting due to *Shigella* or rheumatic heart disease due to Group A streptococcus), or measurement challenges (such as reductions in antimicrobial resistance). Such benefits can be important contributions to vaccine value propositions but may only be measurable in a post-licensure effectiveness study. If included in the use case, they would prolong the interval between product licensure and when we can discern whether the use case is met. In this document, such benefits are mentioned in the notes below each pathogen worksheet (see Annex), but not included in the use cases, or in the assessment of whether the use cases have been met.

- **Focus on use cases valuable to public health.** Use cases should have inherent public health value, and not be merely steps or stage-gates toward more impactful use cases. To accelerate time to market, product developers may choose trial endpoints with less public health value, but that are still considered acceptable for vaccine approval. For example, TB vaccine trials are currently being conducted with prevention of infection (PoI) and prevention of recurrence (PoR) endpoints, however modelling has shown that prevention of active TB disease would be of greater public health value. For this reason, PoI and PoR use cases for TB will be tracked but not counted in SP 7.2 M&E.

At their December 2023 meeting, PDVAC discussed and agreed on the use cases and categorization shown in this report.

B. Pipeline review and SP 7.2 Baseline

The SP 7.2 indicator has been defined as shown in Table 2. For additional background, see *SP7.2 Measurement – for IA2030 M&E Working Group*, January 2024 (draft available by request).

Table 2 Metadata for SP7.2 Indicator

Indicator ID, name	**SP 7.2, Progress in developing new vaccines for pathogens on the Global List of Priority Endemic Pathogens for New Vaccine R&D**
Definitions	SP 7.2.a % of **use cases** that have vaccines or monoclonal antibodies (mAbs) in Phase 3 trials SP 7.2.b % of **use cases** with licensed vaccines or mAbs that have supportive or permissive policy recommendations ***Use case****: the intended target population and outcome to be achieved by use of the new vaccine or mAb* ***Licensed****: by a WHO-listed authority (WLA) of maturity level 3 or above or transitional WLA* [a] ***Policy recommendations****: by SAGE if within SAGE scope, by a national immunization technical advisory group if not in SAGE scope*
Calculation and operational considerations	Denominator: Use cases for vaccines and mAbs targeting the pathogens on the Global List Numerator a: Number of use cases with vaccine or mAb candidates in Phase 3 or other efficacy trials Numerator b: Number of use cases with vaccines or mAbs that are licensed by a WLA or transitional WLA

Baseline values for the indicator were determined based on R&D pipeline reviews for each of the use cases. The following additional definitions were used in this assessment:

- **Vaccine or mAb candidates** include those identified by pipeline trackers, recent reviews, and in searches of the International Clinical Trials Registry Platform (ICTRP) conducted in October and November 2023.
- **Phase 3 or other efficacy trials** include Phase 3 trials, Phase 2/3 trials and controlled human infection studies (if used as the basis for regulatory approval) to establish efficacy. In cases where trial results remained unpublished for more than 3 years after the study concluded, where no follow-on studies have been registered, and where regulatory filings have not been announced, we assumed that the candidates were no longer active.
- **Licensed by a WLA or transitional WLA of maturity level 3 or above.** Such licensure may be by any WLA, regardless of region. See WHO-Listed Authority (WLA)**.**

[a] World Health Organization. A Framework for evaluating and publicly designating regulatory authorities as WHO-listed authorities 2020. https://www.who.int/initiatives/who-listed-authority-reg-authorities

- **In SAGE scope.** Vaccines where the WHO Strategic Advisory Group of Experts on Immunization (SAGE) could potentially consider for global policy recommendations. SAGE scope generally includes vaccines where there is a clear public health need (particularly in lower-resource settings), and where sufficient evidence has been generated to recommend potential use. Vaccines that will potentially be considered by SAGE will also be vaccines that PDVAC engages in as part of its scope.

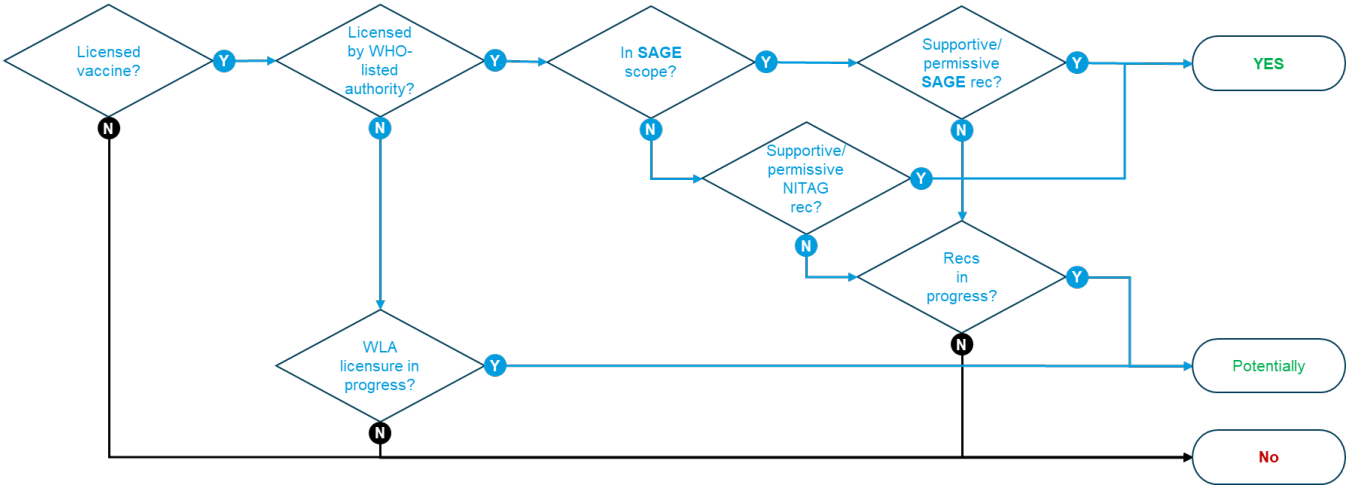
  For vaccines outside of SAGE scope, such as many vaccines for high-income markets, for domestic use, or where the evidence is not anticipated to meet the expectations of SAGE, policy recommendations are likely to be made by national immunization technical advisory groups (NITAGs), independent of SAGE.

Candidates and licensed products were compared to their use cases and scored as shown in Figure 1.

Figure 1 Does the product address the use case?

SP 7.2a Candidates in Phase 3 trials

SP 7.2b Licensed products and policy



NITAG: National immunization technical advisory group; SAGE: WHO Strategic Advisory Group of Experts on Immunization; WLA: WHO-listed authority

C. Categorizing Use Cases by Actions Needed

The use cases for each of the 17 priority pathogens may be at different stages of product development, requiring different types of stakeholder engagement to advance their clinical development and accelerate approval. For this reason, we are proposing to categorise the use cases based on the actions needed to transition into efficacy trials (indicator 7.2a) and to approval by a WLA and supportive or permissive policy recommendations (indicator 7.2b).

Each use case was assigned to one of these 3 action categories based on the current R&D pipeline:

- **Research:** Few candidates in early development (phase 1, 2a) or current candidates are in preclinical phase, substantial technical challenges, other (non-vaccine) interventions may be available.
- **Advance R&D**: Pipeline with several candidates (multiple antigenic targets and vaccine platforms in development) including those in phase 2 studies, with established public health need.
- **Prepare for policy**: Candidates are expected to be licensed by a national regulatory authority that is maturity level 3 or above (as defined by WHO listed authority list) and have a feasible regulatory pathway and high potential for approval before 2030.

III. Results

As shown in Table 3, a total of 34 unmet use cases were identified for the 17 pathogens. Of these, 38% have relevant candidates in Phase 3 trials. While none have licensed products with supportive or permissive policy recommendations, 2 use cases (6%) have licensed products where policy recommendations are in progress.

Table 3 SP 7.2 Baseline Summary

Pathogen	Number of Use cases	SP 7.2a Phase 3 candidates by Use case ☑ relevant candidate(s) in Ph 3 ☒ no relevant candidates in Ph 3	SP 7.2b Licensed & recommended products by Use case ☑ with lic'd & rec'd product(s) ? recommendations pending ☒ none licensed & rec'd
Cytomegalovirus (CMV)	1	☑	☒
Dengue virus	1	☑	☒
Extra-intestinal pathogenic *E coli* (ExPEC)	2	☑ ☒	☒ ☒
Group A streptococcus (GAS, *Streptococcus pyogenes*)	1	☒	☒
Group B streptococcus (GBS, *Streptococcus agalactiae*)	2	☒ ☒	☒ ☒
Hepatitis C virus	2	☒ ☒	☒ ☒
HIV-1	3	☒ ☒ ☒	☒ ☒ ☒
Influenza	2	☑ ☒	☒ ☒
Klebsiella pneumoniae	2	☒ ☑	☒ ☒
Leishmania	1	☑	☒
Non-typhoidal *Salmonella* (NTS)	2	☒ ☒	☒ ☒
Norovirus	2	☑ ☒	☒ ☒
P falciparum	3	☒ ☒ ☒	☒ ☒ ☒
RSV	3	☒ ☒ ☑	? ☒ ?
Shigella	2	☑ ☒	☒ ☒
S aureus	2	☑ ☑	☒ ☒
Tuberculosis	3	☑ ☑ ☒	☒ ☒ ☒
Total	34	With relevant candidates: 13 (38%)	Recs pending: 2 (6%) Licensed and rec'd: 0 (0%)

For each pathogen, Table 4 shows the use cases and action categories. Supporting information is given in the Annex.

Table 4 Unmet vaccine and mAb use cases and their categorization for pathogens on the Global List

Numbering of use cases is for convenience only. Only unmet use cases are listed. Action Category is based on review of candidates potentially relevant to the use case. Potential for SAGE scope not indicated for use cases in the Research category. Click on pathogen names to jump to sources and discussion for each use case.

Pathogen	Target population	Condition to prevent (or indication)	Use case description	Basis for use case	Potential SAGE scope	Action category
Cytomegalovirus (CMV)	Women and girls prior to pregnancy	Congenital CMV	Prevention and/or modification of sequelae associated with congenital CMV, by vaccinating women and girls **prior to pregnancy**	VVP	Unlikely	Advance R&D
Dengue virus	Dengue naïve and seropositive individuals	Dengue fever	Vaccine for dengue naïve and seropositive individuals, to prevent dengue febrile illness induced by any dengue serotype	TRS, SAGE	Yes	Prepare for policy
Extra-intestinal pathogenic *E coli* (ExPEC)	**UC1:** High-risk populations	Invasive *E coli* disease	Prevention of invasive *E coli* disease, including urinary tract infections or bacteraemia, in high-risk populations	Other literature	Unlikely	Prepare for policy
	UC2: Neonates and infants through maternal immunization	Invasive *E coli* disease	Maternal immunization during pregnancy to prevent invasive *E coli* disease, such as neonatal sepsis and meningitis, in neonates and young infants	Other literature	--	Research
Group A streptococcus (GAS, *Streptococcus pyogenes*)	Young children	GAS pharyngitis and/or superficial skin infection (impetigo)	Prevention of GAS disease: pharyngitis, impetigo, and invasive disease in children. Potential for prevention of GAS immune-mediated sequelae: acute rheumatic fever and rheumatic heart disease (RHD)	PPC	Yes, due to WHA resolution on RHD	Research
Group B streptococcus (GBS, *Streptococcus agalactiae*)	**UC1:** Neonates and infants through maternal immunization	GBS-related stillbirth and invasive GBS disease in neonates and young infants	Maternal immunization during pregnancy to prevent GBS-related stillbirth and invasive GBS disease in neonates and young infants	VVP	Yes	Advance R&D
	UC2: Older adults	GBS infections	Prevention of Group B streptococcal infections in older adults	Other literature	--	Research
Hepatitis C virus	**UC1:** Persons at risk for HCV infection	Chronic HCV infection	Prevention of chronic hepatitis C infection for persons at risk	Other literature	--	Research
	UC2: Persons with chronic HCV infection	Treatment of chronic HCV infection	Therapeutic vaccines to improve treatment outcomes for chronic HCV infections	Other literature	--	Research

Pathogen	Target population	Condition to prevent (or indication)	Use case description	Basis for use case	Potential SAGE scope	Action category
HIV-1	**UC1:** Persons at risk of HIV infection	HIV infection	**Prevention** of HIV in high-risk populations	Other literature	Yes	Advance R&D
	UC2: HIV-positive individuals	Treatment and/or cure of HIV infection	**Treatment and/or cure** of HIV infection in HIV-1 positive individuals (includes vaccines, mAbs, and combined approaches)	Other literature	Yes	Advance R&D
	UC3: Persons at risk of HIV infection	HIV infection	**Preventive mAbs** for HIV-1 infection in confirmed HIV-negative individuals at substantial risk of HIV infection and their sexual partners and/or prevention of HIV-1 infection in neonates and infants with HIV exposure	PPC	Yes	Advance R&D
Influenza	**UC1**: Persons aged 6 weeks and older belonging to a group at high risk for severe influenza illness	Influenza A infection	Universal-type influenza A vaccines for prevention of severe influenza illness caused by human influenza A virus infection in persons aged 6 weeks and older belonging to a group at high risk for severe influenza illness (children aged 6 weeks through 59 months, elderly adults, persons with chronic medical conditions, and pregnant women). Duration of efficacy should be a minimum of 5 years	PPC (being revised)	Yes	Advance R&D
	UC2: Children aged 6 weeks through 59 months	Seasonal influenza	Improved seasonal influenza vaccines, with a duration of protection of at least one year	PPC (being revised)	Yes	Advance R&D
Klebsiella pneumoniae	**UC1:** Neonates and infants through maternal immunization	Neonatal sepsis caused by *K pneumoniae*	Vaccine administered during pregnancy to prevent neonatal sepsis caused by the major disease-causing serotypes of *K pneumoniae*	Other literature	--	Research
	UC2: Individuals at high risk for infection with *K pneumoniae*	*K pneumoniae*-attributable disease	Preventing *K pneumoniae*-attributable disease, including pneumonia, blood stream infections, and/or urinary tract infections in high-risk populations such as older adults, the immunocompromised, and those with anticipated prolonged hospital stay or planned surgeries	Other literature	--	Research
Leishmania	All age groups in endemic regions starting from 6 months of age	Visceral leishmaniasis (VL), cutaneous leishmaniasis (CL), and post-kala azar dermal leishmaniasis (PKDL)	Prevention of VL and/or CL in all age groups in endemic regions starting from 6 months of age, and/or prevention or treatment of PKDL	VVP	--	Research

Pathogen	Target population	Condition to prevent (or indication)	Use case description	Basis for use case	Potential SAGE scope	Action category
Non-typhoidal *Salmonella* (NTS)	**UC1:** Children aged 6 – 36 months	Invasive disease caused by non-typhoidal *Salmonella*	Paediatric vaccines for prevention of invasive disease caused by non-typhoidal *Salmonella* in infants and children aged 6 – 36 months	VVP	Unknown	Advance R&D
	UC2: Individuals at high risk for NTS invasive disease	Invasive disease caused by non-typhoidal *Salmonella*	Prevention of invasive disease caused by non-typhoidal *Salmonella* in other individuals at high risk, including immunocompromised individuals, children over 36 months, the elderly, immunocompromised individuals, and persons living or traveling in settings with poor sanitation and hygiene	VVP	Unlikely	Advance R&D
Norovirus	**UC1**: Children, beginning at 6 weeks of age	Norovirus acute gastroenteritis	Prevention of norovirus acute gastroenteritis for children in all countries from 6 weeks of age	VVP	Unknown	Advance R&D
	UC2: Adolescents, adults, and/or older persons	Norovirus acute gastroenteritis	Prevention of norovirus acute gastroenteritis for adolescents, adults, and/or older persons in all countries (including travellers)	VVP	Unlikely	Advance R&D
P falciparum	**UC1:** Populations or age groups who experience high incidence of infection	Blood-stage infection due to *P falciparum*	Prevention of blood-stage infection due to *P falciparum* malaria at the individual level, for populations or age groups who experience high incidence of infection	PPC	Yes	Advance R&D
	UC2: Children and adults, including women of childbearing age	Malaria transmission at the community level	Prevention of malaria transmission at the community level for children and adults, including women of childbearing age, who represent the infectious reservoir and will need to be targeted to maximize the vaccine's impact on transmission	PPC	Yes	Advance R&D
	UC3: Populations or age groups who experience high incidence of infection	Blood-stage infection due to *P falciparum*	mAbs for prevention of blood-stage infection due to *P falciparum* at the individual level, and/or reduction of clinical malaria, including severe malaria and death due to *P falciparum*	PPC	Yes	Advance R&D

Pathogen	Target population	Condition to prevent (or indication)	Use case description	Basis for use case	Potential SAGE scope	Action category
RSV	**UC1:** Neonates and infants through maternal immunization	RSV lower respiratory tract illness (LRTI)	Active immunization of women during pregnancy, for prevention of severe RSV disease in offspring during the neonatal period and early infancy	PPC	Yes	**Prepare for policy**
	UC2: Infants and young children above the age of 6 months	RSV LRTI	Active immunization of infants, for prevention of RSV disease in infants and young children	PPC	Yes	**Advance R&D**
	UC3: Infants and high-risk toddlers	RSV LRTI	**mAbs** for prevention of severe RSV disease for all infants in the first 6 months of life and for high risk young children entering their second RSV season (e.g with chronic heart or chronic lung disease)	PPC	Yes	**Prepare for policy**
Shigella	**UC1:** Infants from 6 months and children up to 36 months of age	Moderate to severe diarrhoea due to *Shigella*	Prevention of moderate to severe diarrhoea due to *Shigella* in infants from 6 months and children up to 36 months of age	PPC	Unknown	**Advance R&D**
	UC2: High-risk populations	*Shigella*-attributable dysentery and diarrhoea	Prevention of *Shigella*-attributable dysentery and diarrhoea for high-risk populations such as travellers and the military, communities with high incidence, elderly and institutionalized individuals, and/or pregnant women	VVP	Unlikely	**Advance R&D**
S aureus	**UC1:** High-risk populations	*S aureus* infection	Prevention of severe infection in populations at risk, such as children, those over 60 years of age, and/or those in all age groups who are immunocompromised, experiencing recurrent skin and soft tissue infections, suffering from relevant comorbidities, exposed to epidemic strains, or undergoing elective surgery or other invasive procedures with high risk of *S aureus* infection	Other literature	Unlikely	**Advance R&D**
	UC2: Persons at risk for or undergoing treatment for *S aureus* infection	mAbs for prevention or treatment of *S aureus* infection	**mAbs** for prevention or treatment of disease caused by *S aureus*, such as severe pneumonia and/or superinfection in conjunction with viral pneumonia	Other literature	Unlikely	**Prepare for policy**

Pathogen	Target population	Condition to prevent (or indication)	Use case description	Basis for use case	Potential SAGE scope	Action category
Tuberculosis	**UC1:** Adults and adolescents	Prevention of active pulmonary TB disease	Prevention of active pulmonary TB disease (with or without evidence of latent infection), including in those with HIV infection	PPC	Yes	**Prepare for policy**
	UC2: Infants and young children	Prevention of TB disease	Prevention of TB disease in infants and young children, including in infants with HIV infection	PPC	Yes	**Prepare for policy**
	UC3: Persons being treated for TB	Prevent TB recurrence and/or increase the proportion of cure at the end of drug treatment	Adjunctive treatment of TB or to prevent relapse following cure in patients being treated for active TB, both drug sensitive and drug resistant strains.	PPC	Yes	**Advance R&D**
	Additional use cases to be tracked, but not counted in SP7.2 M&E					
	UC4: Adults and adolescents	TB infection	Prevention of TB infection in adults and adolescents, including in those with HIV infection	Other literature	--	--
	UC5: Adults and adolescents	TB recurrence	Prevention of recurrence (defined as either reinfection or relapse, whether pulmonary or extrapulmonary) in patients who are cured from active TB	Other literature	--	--
	UC6: Neonates, infants, and young children	TB infection	Prevention of TB infection in neonates, infants, and young children, including those with HIV infection	Other literature	--	--

IV. ANNEX: Use cases and baseline data

1. Cytomegalovirus (CMV)

Reviewed by: Mark Jit

Table 5 CMV Review

Use Case	Current products and candidates	SP 7.2 Monitoring	Action Category
Target population: **Women and girls prior to pregnancy** Condition to prevent: **Congenital CMV** Description: Prevention and/or modification of sequelae associated with congenital CMV, by vaccinating women and girls prior to pregnancy	Licensed products • None	7.2b • No	**Advance R&D** Studies needed to link seroconversion endpoint in phase III to prevention of congenital CMV Potential SAGE scope: Unlikely
	Candidates in Phase 3 • Moderna **mRNA-1647** trial underway in healthy participants 16 – 40 years of age (NCT05085366) Outcomes include seroconversion against antigens not encoded by mRNA-1647 and antigen-specific neutralizing antibody levels	7.2a • Yes	
	Candidates in Phase 2 • NIAID CMV-MVA Triplex Candidates in Phase 1 • GSK Pentamer/ gB/ Adjuvant	Not applicable	

Notes

1. Source for use case: Suresh B. Boppana, Michiel van Boven, William J. Britt, Soren Gantt, Paul D. Griffiths, Scott D. Grosse, Terri B. Hyde, Tatiana M. Lanzieri, Marisa M. Mussi-Pinhata, Sarah E. Pallas, Swetha G. Pinninti, William D. Rawlinson, Shannon A. Ross, Ann C.T.M. Vossen, Karen B. Fowler, *Vaccine value profile for cytomegalovirus*, Vaccine, 2023, https://doi.org/10.1016/j.vaccine.2023.06.020.
2. Additional potential use cases include CMV vaccination for transplantation-related indications and for immunocompromised individuals. For IA2030 M&E, we propose to focus on congenital CMV.
3. For congenital CMV, maternal immunization use cases are not applicable since vaccination during pregnancy would miss a window of vulnerability in early pregnancy. Rather than targeting pregnant persons, routine delivery strategies would be pre-pregnancy (like HPV for adolescent girls), or routine paediatric immunization (like rubella). Pre-pregnancy vaccination for persons intending to become pregnant could also be conducted.

2. Dengue virus

Reviewed by: Ruth Karron, Raman Rao

Table 6 Dengue Review

Use Case	Current products and candidates	SP 7.2 Monitoring	Action Category
Target population: **Dengue naïve and seropositive individuals** Condition to prevent: **Dengue fever** Description: Vaccine for dengue naïve and seropositive individuals, to prevent dengue febrile illness induced by any dengue serotype	Licensed products • Sanofi **Dengvaxia** licensed in 2015, WHO recommends countries should consider intro of this vaccine only if the minimization of risk among seronegative individuals can be assured. https://www.who.int/publications-detail-redirect/who-wer9335-457-476 • Takeda **Qdenga** licensed by EMA in 2022 but not US FDA. SAGE recommends the vaccine be considered for introduction in settings with high dengue disease burden and high transmission intensity to maximize public health impact and minimize any potential risk in seronegatives. https://cdn.who.int/media/docs/default-source/2021-dha-docs/highlights-3.pdf	7.2b • No, due to risks for dengue-naïve individuals • No, due to risks for dengue-naïve individuals	**Prepare for policy** To inform deployment of Sanofi and Takeda vaccines and in anticipation of Butantan product Potential SAGE scope: Yes
	Candidates in Phase 3 • NIAID/Butantan **Dengue 1, 2, 3, 4 (Attenuated) Vaccine** (NCT02406729) is enrolling an estimated 16,935 subjects 2-59 years of age, additional data expected in 2024	7.2a • Yes	
	Candidates in Phase 2 • Merck V181 • Panacea Tetravalent Candidates in Phase 1 • Additional candidates in Phase 1	Not applicable	

Notes

1. The 2018 WHO position paper for dengue vaccines notes that, "The development of safe, effective, and affordable dengue vaccines for use irrespective of serostatus remains a high priority."
2. Sources for use cases:
    - *Dengue vaccines: WHO position paper* – September 2018. https://www.who.int/publications-detail-redirect/who-wer9335-457-476
    - *Guidelines on the quality, safety and efficacy of dengue tetravalent vaccines (live, attenuated),* Annex 2, TRS No 979 https://www.who.int/publications/m/item/TRS_979_annex-2-dengue

3. Extra-intestinal pathogenic *E coli* (ExPEC)

Reviewed by: Isabelle Bekeredjian-Ding, Marco Cavaleri, Alejandro Cravioto

Table 7 ExPEC Review

Use Case	Current products and candidates	SP 7.2 Monitoring	Action Category
UC1 Target population: **High-risk populations** Condition to prevent: **Invasive *E coli* disease** Description: Prevention of invasive *E coli* disease, including urinary tract infections or bacteraemia, in high-risk populations	Licensed products • None	7.2b • No	**Prepare for policy** To inform decision making for approved vaccines Potential SAGE scope: Unlikely
	Candidates in Phase 3 • Janssen Phase 3 of **ExPEC9V** for prevention of Invasive ExPEC in older adults, NCT04899336, launched 2021, estimated enrollment 18,556, estimated primary completion 2025 • Glycovaxn trial of MV140 (**Uromune**) for prevention of urinary tract infections in older adults (ACTRN12623000258651) planned launch 2023. (See Note 3)	7.2a • Yes • Yes	
	Candidates in Phase 1 or Phase 2 • None found	Not applicable	
UC2 Target population: **Neonates and infants through maternal immunization** Condition to prevent: **Invasive *E coli* disease** Description: Maternal immunization during pregnancy to prevent invasive *E coli* disease, such as neonatal sepsis and meningitis, in neonates and young infants	Licensed products • None	7.2b • No	**Research**
	Candidates in Phase 3 • None	7.2a • No	
	Candidates in Phase 1 or Phase 2 • None found	Not applicable	

Notes

1. Sources for use cases:
    - Wellcome Trust, Boston Consulting Group. *Vaccines for AMR*. 2018. Available at https://vaccinesforamr.org/wp-content/uploads/2018/09/Vaccines_for_AMR.pdf

- Penders, J., Huylenbroeck, A., Everaert, K. et al. *Urinary infections in patients with spinal cord injury*. Spinal Cord 41, 549–552 (2003). https://www.nature.com/articles/3101499
- Janssen NCT04899336
- Stoll BJ, Puopolo KM, Hansen NI, et al. *Early-Onset Neonatal Sepsis 2015 to 2017, the Rise of Escherichia coli, and the Need for Novel Prevention Strategies* [published correction appears in JAMA Pediatr. 2021 Feb 1;175(2):212]. JAMA Pediatr. 2020;174(7):e200593. Doi:10.1001/jamapediatrics.2020.0593).
- Miselli F, Cuoghi Costantini R, Creti R, Sforza F, Fanaro S, Ciccia M, Piccinini G, Rizzo V, Pasini L, Biasucci G, et al. *Escherichia coli Is Overtaking Group B Streptococcus in Early-Onset Neonatal Sepsis*. Microorganisms. 2022; 10(10):1878. https://doi.org/10.3390/microorganisms10101878

2. **Uromune**, a commercial preparation of heat-killed bacteria licensed in Spain, is has been evaluated in a Phase 2 trial in Canada for the prevention of recurrent urinary tract infections. (NCT04096820) See: Nickel JC, Saz-Leal P, Doiron RC. Could sublingual vaccination be a viable option for the prevention of recurrent urinary tract infection in Canada? A systematic review of the current literature and plans for the future. Can Urol Assoc J. 2020;14(8):281-287. Doi:10.5489/cuaj.6690.

4. Group A Streptococcus (GAS, *S pyogenes*)

Reviewed by: Marco Cavaleri, Pierre Gsell, Mark Jit, Ruth Karron

Table 8 GAS Review

Use Case	Current products and candidates	SP 7.2 Monitoring	Action Category
Target population: **Young children** Condition to prevent: **GAS pharyngitis and/or superficial skin infection (impetigo)** Description: Prevention of GAS disease: pharyngitis, impetigo, and invasive disease in children. Potential for prevention of GAS immune-mediated sequelae: acute rheumatic fever and rheumatic heart disease (RHD)	Licensed products • None found	7.2b • No	**Research** Potential SAGE scope: Yes, due to World Health Assembly resolution on RHD
	Candidates in Phase 3 • None found	7.2a • No	
	Candidates in Phase 2 • U. of Alberta J8-K4S2 and p*17-K4S2 Candidates in Phase 1 • U. Tennessee/Vaxent StretpAnova • Griffith U./ U. Alberta J8/S2 combivax, P*17/S2 combivax • Butantan StreptInCor	Not applicable	

Notes

1. Sources for use cases:
    - *WHO Preferred Product Characteristics for Group A Streptococcus Vaccines*. Geneva: World Health Organization; 2018. Licence: CC BY-NC-SA 3.0 IGO. Available at https://www.who.int/publications/i/item/who-preferred-product-characteristics-for-group-a-streptococcus-vaccines
    - *WHO expert review of Group A Streptococcus vaccines 1st joint expert consultation of Product Development for Vaccines Advisory Committee (PDVAC) and Immunization and Vaccines Related Implementation Research Advisory Committee (IVIR-AC)*: https://cdn.who.int/media/docs/default-source/immunization/pdvac/pdvac-2022/who-expert-review-of-gas-vx-exec-summary-pdvac-and-ivirac-final.pdf?sfvrsn=d558c2da_3
2. GAS pharyngitis is considered a relatively more feasible indication. Licensure of vaccines to prevent GAS pharyngitis could facilitate development of vaccines to prevent more severe disease outcomes such as rheumatic fever and rheumatic heart disease.
3. For additional information, see: Walkinshaw DR, Wright MEE, Williams M, Scarapicchia TMF, Excler JL, Wiley RE, Mullin AE. *A Strep A vaccine global demand and return on investment forecast to inform industry research and development prioritization*. NPJ Vaccines. 2023 Aug 9;8(1):113. Doi: 10.1038/s41541-023-00690-2. PMID: 37558685; PMCID: PMC10412591.

5. Group B Streptococcus (GBS, *S agalactiae*)

Reviewed by: Mark Jit, Ruth Karron, Sonali Kochhar

Table 9 GBS Review

Use Case	Current products and candidates	SP 7.2 Monitoring	Action Category
UC1 Target population: **Neonates and infants through maternal immunization** Condition to prevent: **GBS-related stillbirth and invasive GBS disease in neonates and young infants** Description: Maternal immunization during pregnancy to prevent GBS-related stillbirth and invasive GBS disease in neonates and young infants	Licensed products • None	7.2b • No	**Advance R&D** Potential SAGE scope: Yes
	Candidates in Phase 3 • None	7.2a • No	
	Candidates in Phase 2 • Minervax GBS NN/NN2, NCT05154578, NCT04596878 • Pfizer multivalent Phase 1/2, NCT03765073	Not applicable	
UC2 Target population: **Older adults** Condition to prevent: **GBS infections** Description: Prevention of Group B streptococcal infections in older adults	Licensed products • None	7.2b • No	**Research**
	Candidates in Phase 3 • None	7.2a • No	
	Candidates in Phase 1 • Minervax Phase 1, NCT05782179	Not applicable	

Notes

1. Sources for use cases:
   - Caroline L. Trotter, Mark Alderson, Ziyaad Dangor, Margaret Ip, Kirsty Le Doare, Eve Nakabembe, Simon R. Procter, Musa Sekikubo, Philipp Lambach, *Vaccine value profile for Group B streptococcus*, Vaccine, 2023, https://doi.org/10.1016/j.vaccine.2023.04.024.
   - Minervax, NCT05782179
   - Nuccitelli A, Rinaudo CD, Maione D. *Group B Streptococcus vaccine: state of the art*. Ther Adv Vaccines. 2015;3(3):76-90. Doi:10.1177/2051013615579869
2. Maternal vaccination could also provide protection against preterm births and maternal GBS disease, depending on the characteristics of the vaccine.
3. Other high-risk groups, such as immunocompromised persons are another potential use case (see Nuccitelli et al). Because indications for such groups are likely to be evaluated in post-licensure studies of vaccines licensed for other populations (such as older adults), they were not listed as a separate use case.

6. Hepatitis C virus

Reviewed by: Alejandro Cravioto, Ghassan Dbaibo

Table 10 Hepatitis C Review

Use Case	Current products and candidates	SP 7.2 Monitoring	Action Category
UC1 Target population: **Persons at risk for HCV infection** Condition to prevent: **Chronic HCV infection** Description: Prevention of chronic hepatitis C infection for persons at risk	Licensed products • None	7.2b • No	**Research**
	Candidates in Phase 3 • None	7.2a • No	
	Candidates in Phase 2 • None found Candidates in Phase 1 • GeneOne Life Science GLS-6150 (NCT03674125)	Not applicable	
UC2 Target population: **Persons with chronic HCV infection** Indication: **Treatment of chronic HCV infection** Description: Therapeutic vaccines to improve treatment outcomes for chronic HCV infections	Licensed products • None	7.2b • No	**Research**
	Candidates in Phase 3 • None	7.2a • No	
	Candidates in Phase 2 • None found Candidates in Phase 1 • GeneCure HCVax (NCT04318379)	Not applicable	

Notes

1. Sources for Use cases:
   - Phelps, Christopher C., Christopher M. Walker, and Jonathan R. Honegger. 2021. *"Where to Next? Research Directions after the First Hepatitis C Vaccine Efficacy Trial"* Viruses 13, no. 7: 1351. https://doi.org/10.3390/v13071351
   - GeneCure Biotechnologies, https://genecure.com/pipeline.html

2. Greater clarity is needed on the value propositions for HCV vaccines in the context of existing interventions such as direct-acting antivirals.
3. Therapeutic monoclonal antibodies for hepatitis C have been explored clinically but no active candidates were found in ICTRP search.

7. HIV-1

Reviewed by: Sophie Biernaux, Sinead Delaney-Moretlwe

Table 11 HIV-1 Review

Use Case	Current products and candidates	SP 7.2 Monitoring	Action Category
UC1 Target population: **Persons at risk of HIV infection** Condition to prevent: **HIV infection** Description: Prevention of HIV in high-risk populations	Licensed products • None	7.2b • No	**Advance R&D** Potential SAGE scope: Yes
	Candidates in Phase 3 • None	7.2a • No	
	Candidates in Phase 2 • MRC/UVRI and LSHTM Uganda Research Unit (NCT04066881) Group A DNA-HIV-PT123 and AIDSVAX® B/E; Group B DNA-HIV-PT123 and CN54gp140+MPLA-L, then MVA-CMDR and CN54gp140+MPLA-L Candidates in Phase 1 • ANRS, Fundacion Clinic per a la Recerca Biomaedica,HVTN, IAVI, NIAID, U.S. Army Medical Research and Development Command, U. of Oxford, Vir Biotechnology, and Worcester HIV Vaccine have conducted recent Phase 1 trials for HIV vaccines	Not applicable	

Use Case	Current products and candidates	SP 7.2 Monitoring	Action Category
UC2 Target population: **HIV-positive individuals** Indication: **Treatment and/or cure of HIV infection** <u>Description:</u> Treatment and/or cure of HIV infection in HIV-1 positive individuals (includes vaccines, mAbs, and combined approaches)	Licensed products • None • HIV mAb Ibalizumab, Trogarzo	7.2b • No, existing mAb not widely used due to limited indication	**Advance R&D** Potential SAGE scope: Yes
	Candidates in Phase 3 • None	7.2a • No	
	Candidates in Phase 2 or Phase 1/2 • ANRS/Inserm bnAbs (3BNC117LS & 10-1074LS) (NCT05300035) • European HIV Vaccine Alliance MVA HIV-B (NCT04120415) • GSK/NIAID/ViiV monoclonal antibody GSK3810109A (NCT04871113) • Janssen (NCT04983030) Experimental Ad26.Mos4.HIV, MVA-BN-HIV Vaccine Plus PGT121, PGDM1400, and VRC07-523LS bNAbs; Active comparator Ad26.Mos4.HIV, MVA-BN-HIV Vaccine Plus Placebo; Active comparator Placebo Plus PGT121, PGDM1400, and VRC07-523LS bNAbs • NIAID (NCT06071767) ChAdOx1.tHIVconsv1, ChAdOx1.HIVconsv62, MVA.tHIVconsv3, MVA.tHIVconsv4 • U. of California (NCT04357821) IL-12 adjuvanted p24CE DNA prime (p24CE/IL-12) at Weeks 0 and 4; IL-12 adjuvanted DNA boost (p24CE plus p55gag) at Week 12; MVA/HIV62B (MVA62B) boost at Week 20; single dose of two bNAbs (VRC07-523LS and 10-1074), at week 24 with a TLR9 agonist (lefitolimod) administered weekly between Weeks 24 and 33; ATI with single dose of VRC07 and 10-1074 at Week 34 • U. of Zurich BCG (NCT05004038) Candidates in Phase 1 • ANRS, Henry M. Jackson Foundation, IrsiCaixa, Madhu Chhanda Choudhary, and UNC Chapel Hill have conducted recent Phase 1 trials of vaccine candidates and/or monoclonal antibodies in HIV-infected individuals or for treatment purposes	Not applicable	

Use Case	Current products and candidates	SP 7.2 Monitoring	Action Category
UC3 Target population: **Persons at risk of HIV infection** Condition to prevent: **HIV infection** Description: **Preventive mAbs** for HIV-1 infection in confirmed HIV-negative individuals at substantial risk of HIV infection and their sexual partners and/or prevention of HIV-1 infection in neonates and infants with HIV exposure	Licensed products • None	7.2b • No	**Advance R&D** Potential SAGE scope: Yes
	Candidates in Phase 3 • None	7.2a • No	
	Candidates in Phase 2 • None found, however monoclonal antibodies currently being evaluated for therapeutic use case may also have utility in prevention Candidates in Phase 1 • CAPRISA trial CAP256V2LS PGT121 VRC07-523.LS (PACTR202003767867253) • HVTN VRC01.23LS, PGT121.414.LS, PGDM1400LS (NCT05959707) • NIAID VRC-HIVMAB0115-00-AB, VRC-HIVMAB0102-00-AB, PGT121.414.LS, VRC07-523LS (NCT05627258, NCT04408963, NCT04212091)	Not applicable	

Notes

1. WHO has not yet defined PPCs for HIV vaccines.
2. Use case for preventive mAbs is from: *WHO preferred product characteristics for monoclonal antibodies for HIV prevention*. Geneva: World Health Organization; 2022. Licence: CC BY-NC-SA 3.0 IGO. https://www.who.int/publications/i/item/9789240045729
3. PPCs for mAbs for HIV prophylaxis notes that, “While mAbs could be used in HIV-negative women during pregnancy and the post-partum period, they should not be used in HIV-infected pregnant women to avoid selection for and transfer of resistant viruses to the infant.”

8. Influenza virus

Reviewed by: Gerd Zettlmeisl

Table 12 Influenza Review

Use Case	Current products and candidates	SP 7.2 Monitoring	Action Category
UC1 Target population: **Persons aged 6 weeks and older belonging to a group at high risk for severe influenza illness** Condition to prevent: **Influenza A infection** Description: Universal-type influenza A vaccines for prevention of severe influenza illness caused by human influenza A virus infection in persons aged 6 weeks and older belonging to a group at high risk for severe influenza illness (children aged 6 weeks through 59 months, elderly adults, persons with chronic medical conditions, and pregnant women). Duration of efficacy should be a minimum of 5 years	Licensed products • None	7.2b • No	**Advance R&D** Potential SAGE scope: Yes
	Candidates in Phase 3 • Moderna mRNA-1010, mRNA-1083 • Pfizer/BioNTech Modified mRNA vaccine • Novavax/Emergent BioSolutions NanoFlu (qNIV) Current Phase 3 candidates are being tested only in adults, age de-escalation would be required to satisfy the PPC.	7.2a • Yes • Yes • Yes	
	Candidates in Phase 1 or Phase 2 • 11 Phase 2 candidates listed by CIDRAP (See Note 3) • 15 Phase 1 candidates listed by CIDRAP	Not applicable	
UC2 Target population: **Children aged 6 weeks through 59 months** Condition to prevent: **Seasonal influenza** Description: Improved seasonal influenza vaccines, with a duration of protection of at least one year	Licensed products • Multiple influenza vaccines licensed for children aged 6 months and older	7.2b • No, current vaccines do not address the full age range	**Advance R&D** Potential SAGE scope: Yes
	Candidates in Phase 3 • None	7.2a • No	
	Candidates in Phase 1 or Phase 2 • Telethon Kids trial: A Phase 2 study of quadrivalent influenza vaccines in Australia is enrolling infants aged 6-12 weeks (ACTRN12620000644965) • No other recent trials found enrolling infants younger than 6 months	Not applicable	

Notes

1. Source for use cases: WHO Preferred Product Characteristics for Next-Generation Influenza Vaccines, 2017 https://www.who.int/publications-detail-redirect/9789241512466. PPCs for influenza vaccines are being updated in 2024: use cases will be updated to reflect the revised PPCs.
2. Pipeline data from https://ivr.cidrap.umn.edu/universal-influenza-vaccine-technology-landscape, which tracks "novel vaccine candidates designed to provide broader and more durable protection against circulating and pandemic influenza viruses, compared with current strain-specific seasonal influenza vaccines."

9. *Klebsiella pneumoniae*

Reviewed by: William Hausdorff, Mariagrazia Pizza, Senjuti Saha

Table 13 *K pneumoniae* Review

Use case	Current products and candidates	SP 7.2 Monitoring	Action Category
UC1 Target population: **Neonates and infants through maternal immunization** Condition to prevent: **Neonatal sepsis caused by *K pneumoniae*** Description: Vaccine administered during pregnancy to prevent neonatal sepsis caused by the major disease-causing serotypes of *K pneumoniae*	Licensed products • None	7.2b • No	**Research**
	Candidates in Phase 3 • None	7.2a • No	
	Candidates in Phases 1 or 2 • None found	Not applicable	
UC2 Target population: **Individuals at high risk for infection with *K pneumoniae*** Condition to prevent: ***K pneumoniae*-attributable disease** Description: Preventing *K pneumoniae*-attributable disease, including pneumonia, invasive disease, and/or urinary tract infections in high-risk populations such as older adults, the immunocompromised, and those with anticipated prolonged hospital stay or planned surgeries	Licensed products • None	7.2b • No	**Research**
	Candidates in Phase 3 • Uromune (see note)	7.2a • Yes	
	Candidates in Phase 2 • LimmaTech Kleb4V. A Ph1/2 trial in 18-40 year olds and older adults (55-70 years) was completed in Germany in September 2022. (NCT04959344) Candidates in Phase 1 • None found	Not applicable	

Notes

1. Sources for use cases:
    - Wantuch PL, Rosen DA. *Klebsiella pneumoniae: adaptive immune landscapes and vaccine horizons*. Trends Immunol. 2023 Oct;44(10):826-844. Doi: 10.1016/j.it.2023.08.005. Epub 2023 Sep 11. PMID: 37704549.

- Kumar CK, Sands K, Walsh TR, O'Brien S, Sharland M, Lewnard JA, Hu H, Srikantiah P, Laxminarayan R. *Global, regional, and national estimates of the impact of a maternal Klebsiella pneumoniae vaccine: A Bayesian modeling analysis*. PloS Med. 2023 May 22;20(5):e1004239. Doi: 10.1371/journal.pmed.1004239. PMID: 37216371; PMCID: PMC10270628.
- *Marr CM, Russo TA. Hypervirulent Klebsiella pneumoniae: a new public health threa*t. Expert Rev Anti Infect Ther. 2019;17(2):71-73. doi:10.1080/14787210.2019.1555470

2. "Populations at high risk" could be split into multiple use cases. For example, endemic, hypervirulent strains could be considered separately from nosocomial infections. Also, urinary tract infections could be considered separately from invasive disease. Given the technical challenges associated with all of these use cases, we propose grouping them together for the purposes of IA2030 M&E.
3. **Uromune**, a commercial preparation of heat-killed bacteria licensed in Spain, has been evaluated in a Phase 2 trial in Canada for the prevention of recurrent urinary tract infections. (NCT04096820) A Phase 3 trial has been registered in Australia (ACTRN12623000258651) but no further information on that study was found. See: Nickel JC, Saz-Leal P, Doiron RC. *Could sublingual vaccination be a viable option for the prevention of recurrent urinary tract infection in Canada? A systematic review of the current literature and plans for the future*. Can Urol Assoc J. 2020;14(8):281-287. doi:10.5489/cuaj.6690.

10. *Leishmania* spp

Reviewed by: Ghassan Dbaibo, Kamel Senouci

Table 14 *Leishmania* Review

Use Case	Current products and candidates	SP 7.2 Monitoring	Action Category
Target population: **All age groups in endemic regions starting from 6 months of age** Conditions to prevent: **Visceral leishmaniasis (VL), cutaneous leishmaniasis (CL), and post-kala azar dermal leishmaniasis (PKDL)** Description: Prevention of VL and/or CL in all age groups in endemic regions starting from 6 months of age, and/or prevention or treatment of PKDL	Licensed products • None	7.2b • No	**Research** Category may be updated based on the status of the Kerman U. candidate
	Candidates in Phase 3 • Kerman U. of Medical Sciences **gentamicin-attenuated line of Leishmania major H-line** *Candidate may be inactive*: the Phase 3 Safety, immunogenicity and efficacy study in Iran (IRCT20151019024604N3), completed enrolment in 2020 with an actual enrolment of 298 (but an original target of 5000 subjects). No further information found.	7.2a • Yes	
	Candidates in Phase 2 • U. of York ChAd63-KH (NCT04107961, NCT03969134). According to the VVP, "Licensure for at least one indication is planned for 2026/27 assuming trials are successful." (Kaye et al 2023) Also "has attributes for a pan-leishmaniasis vaccine", according to Younis BM, Osman M, Khalil EAG, et al. Safety and immunogenicity of ChAd63-KH vaccine in post-kala-azar dermal leishmaniasis patients in Sudan. Mol Ther. 2021;29(7):2366-2377. doi:10.1016/j.ymthe.2021.03.020 Candidates in Phase 1 • None found	Not applicable	

Notes

1. Source for use case: Paul M. Kaye, Greg Matlashewski, Sakshi Mohan, Epke Le Rutte, Dinesh Mondal, Ali Khamesipour, Stefano Malvolti, *Vaccine value profile for leishmaniasis*, Vaccine, 2023, https://doi.org/10.1016/j.vaccine.2023.01.057
2. PKDL: VL cases could be vaccinated after treatment to prevent PKDL development. Therapeutic use of a vaccine for PKDL could replace arduous treatment regimens for persistent cases in East Africa or all cases in South-east Asia
3. Leishmaniasis is among the African targets for mRNA vaccine development, with Institut Pasteur Tunis establishing collaborations to advance candidates into clinical development.

11. Non-typhoidal *Salmonella* (NTS)

Reviewed by: Adwoa Bentsi-Enchill, Alejandro Cravioto, Senjuti Saha

Table 15 Non-typhoidal *Salmonella* Review

Use case	Current products and candidates	SP 7.2 Monitoring	Action Category
UC1 Target population: **Children aged 6 – 36 months** Condition to prevent: **Invasive disease caused by non-typhoidal *Salmonella*** Description: Paediatric vaccines for prevention of invasive disease caused by non-typhoidal *Salmonella* in children aged 6 – 36 months	Licensed products • None	7.2b • No	**Advance R&D** Potential SAGE scope: Unknown
	Candidates in Phase 3 • None	7.2a • No	
	Candidates in Phase 2 • UMB TSCV (NCT05784701, Phase 2, age de-escalation), combination with WHO-prequalified typhoid conjugate vaccine (TCV) Candidates in Phase 1 or Phase 1/2a • GVGH-STm+SEn GMMA-TCV (NCT05480800, Phase 1/2a), combination with WHO-prequalified TCV, estimated completion in 2024 • GVGH STm+SEn GMMA (EudraCT Number: 2020-000510-14)	Not applicable	
UC2 Target population: **Individuals at high risk for NTS invasive disease** Condition to prevent: **Invasive disease caused by non-typhoidal *Salmonella*** Description: Prevention of invasive disease caused by non-typhoidal *Salmonella* in individuals at high risk, including immunocompromised individuals, children over 36 months, the elderly, and persons living or traveling in settings with poor sanitation and hygiene	Licensed products • None	7.2b • No	**Advance R&D** Potential SAGE scope: Unlikely
	Candidates in Phase 3 • None	7.2a • No	
	Candidates in Phase 1 or Phase 2 • UMB TSCV combination with WHO-prequalified typhoid conjugate vaccine (TCV) Phase 1 in persons aged 18-49 years (NCT05525546) completed in 2023 • GVGH-STm+SEn GMMA-TCV (NCT05480800, Phase 1/2a), combination with WHO-prequalified TCV, estimated completion in 2024 • GVGH STm+SEn GMMA (EudraCT Number: 2020-000510-14)	Not applicable	

Notes

1. Sources for use cases:
    - *PDVAC (virtual) meeting on invasive non-typhoidal Salmonella (iNTS) vaccines: Summary and outcomes from PDVAC closed discussion*. Available at https://cdn.who.int/media/docs/default-source/immunization/pdvac/pdvac-2022/final-summary-outcomes-pdvac-closed-discussion-feb-2022.pdf
    - Draft *Vaccine Value Profile for Invasive non-typhoidal Salmonella (iNTS)*
    - *Salmonellosis, Nontyphoidal*. CDC Yellow Book 2024 https://wwwnc.cdc.gov/travel/yellowbook/2024/infections-diseases/salmonellosis-nontyphoidal
2. Categorized as "Advance R&D" due to high technical feasibility.
3. Pipeline view available at: https://www.who.int/teams/immunization-vaccines-and-biologicals/diseases/nontyphoidal-salmonella-disease

12. Norovirus

Reviewed by: Shaowei Li, Gerd Zettlmeisl

Table 16 Norovirus Review

Use Case	Current products and candidates	SP 7.2 Monitoring	Action Category
UC1 Target population: **Children, including infants beginning at 6 weeks of age** Condition to prevent: **Norovirus acute gastroenteritis** Description: Prevention of norovirus acute gastroenteritis for children in all countries from 6 weeks of age	Licensed products • None	7.2b • No	**Advance R&D** Potential SAGE scope: Unknown
	Candidates in Phase 3 • Sinopharm Human Norovirus Bivalent (GⅠ.1/GⅡ.4) Vaccine, NCT05916326, trial in healthy people aged 6 months to 13 years.	7.2a • Yes	
	Candidates in Phase 1 or Phase 2 • Phase 2: Anhui Zhifei Quadrivalent • HilleVax HIL-214, NCT05281094, infants 5 months at time of first dose	Not applicable	
UC2 Target population: **Adolescents, adults, and/or older persons** Condition to prevent: **Norovirus acute gastroenteritis** Description: Prevention of norovirus acute gastroenteritis for adolescents, adults, and/or older persons in all countries (including travellers)	Licensed products • None	7.2b • No	**Advance R&D** Potential SAGE scope: Unlikely
	Candidates in Phase 3 • None	7.2a • No	
	Candidates in Phase 2 • Anhui Zhifei Quadrivalent • HilleVax HIL-214 • Vaxart VXA-G1.1-NN and VXA-G2.4-NS Candidates in Phase 1 • Icon Bivalent VLP • Moderna Mrna-1403 and Mrna-1405 • Syneos hexavalent	Not applicable	

Notes

1. Source for use cases: George Armah, Ben A. Lopman, Jan Vinjé, Miguel O'Ryan, Claudio F. Lanata, Michelle Groome, Jared Ovitt, Caroline Marshall, Elizabeth Sajewski, Mark S. Riddle, *Vaccine value profile for norovirus*, Vaccine, 2023, https://doi.org/10.1016/j.vaccine.2023.03.034.
2. Adult vaccines include vaccines for travellers and the military. Although long-term protection is not required for such vaccines, these markets can incentivize R&D for vaccines for routine use.
3. Vaccines for the elderly are included in the adult vaccines use case, but could be considered separately.

13. *P falciparum*

Reviewed by: Sophie Biernaux, Faith Osier

Table 17 *Plasmodium falciparum* Review

Use case	Current products and candidates	SP 7.2 Monitoring	Action Category
UC1 Target population: **Populations or age groups who experience high incidence of infection** Condition to prevent: **Blood-stage infection due to *P falciparum*** Description: Prevention of blood-stage infection due to *P falciparum* malaria at the individual level, for populations or age groups who experience high incidence of infection	Licensed products • GSK RTS,S/AS01 • Serum Institute of India R21/Matrix M	7.2b • No, not a blood-stage vaccine • No, not a blood stage vaccine	**Advance R&D** Potential SAGE scope: Yes
	Candidates in Phase 3 • None	7.2a • No	
	Candidates in Phase 2 • Sanaria PfSPZ, PfSPZ-Cvac • U Oxford MVA ME-TRAP, ChAd63 ME-TRAP, RH5.1, RH5.2 • Vac4All MSP3-CRM-Vac4All blood stage Candidates in Phase 1 • BioNTech BNT165e • BioNTech BNT165b1 • STPHI SumayaVac-1 • U Oxford R78C	Not applicable	

Use case	Current products and candidates	SP 7.2 Monitoring	Action Category
UC2 Target population: **Children and adults, including women of childbearing age** Condition to prevent: **Malaria transmission at the community level** Description: Prevention of malaria transmission at the community level for children and adults, including women of childbearing age, who represent the infectious reservoir and will need to be targeted to maximize the vaccine's impact on transmission	Licensed products • None	7.2b • No	**Advance R&D** Potential SAGE scope: Yes
	Candidates in Phase 3 • None	7.2a • No	
	Candidates in Phase 2 • NIAID Pfs230D1-EPA • Pfs48/45 TBV phase 2 Candidates in Phase 1 • EDCTP R0.6C and ProC6C • CRM Lambaréné AnAPN1 (PamTBVac) • Radboud TB31F (transmission-blocking monoclonal antibody)	Not applicable	
UC3 Target population: **Populations or age groups who experience high incidence of infection** Condition to prevent: **Blood-stage infection due to *P falciparum*** Description: **mAbs** for prevention of blood-stage infection due to *P falciparum* at the individual level, and/or reduction of clinical malaria, including severe malaria and death due to *P falciparum*	Licensed products • None	7.2b • No	**Advance R&D** Potential SAGE scope: Yes
	Candidates in Phase 3 • None	7.2a • No	
	Candidates in Phase 2 • NIAID L9LS, CIS43LS Candidates in Phase 1 • Gates MRI MAM01	Not applicable	

Notes

1. Sources for use cases:
   - *Malaria vaccines: preferred product characteristics and clinical development considerations*. Geneva: World Health Organization; 2022. Licence: CC BY-NC-SA 3.0 IGO. https://iris.who.int/bitstream/handle/10665/362694/9789240057463-eng.pdf?sequence=1
   - Wu RL, Idris AH, Berkowitz NM, et al. *Low-Dose Subcutaneous or Intravenous Monoclonal Antibody to Prevent Malaria*. N Engl J Med. 2022;387(5):397-407. doi:10.1056/NEJMoa2203067

2. Preferred product characteristics for malaria vaccines correspond to the three strategic goals for malaria vaccines and are not mutually exclusive. For example, at high levels of coverage, a vaccine that prevents infection could also reduce transmission.
3. The malaria vaccine PPCs also include a "**Disease reduction**" use case. This use case was not included because two licensed products, GSK RTS,S/AS01 and Serum Institute of India R21/Matrix M, already meet this use case.
4. Infection prevention is being evaluated post-licensure. For RTS,S, data are insufficient to evaluate infection prevention.

14. Respiratory syncytial virus (RSV)

Reviewed by: Ghassan Dbaibo, Ruth Karron

Table 18 RSV Review

Use Case	Current products and candidates	SP 7.2 Monitoring	Action Category
UC1 Target population: **Neonates and infants through maternal immunization** Condition to prevent: **RSV lower respiratory tract illness (LRTI)** Description: Active immunization of women during pregnancy, for prevention of severe RSV disease in offspring during the neonatal period and early infancy	Licensed products • Pfizer RSV preF Protein (Abrysvo)	7.2b • Potentially, SAGE recommendation not yet issued	**Prepare for policy** Potential SAGE scope: Yes SAGE Working Group is being launched and impact studies are being planned
	Candidates in Phase 3 • None	7.2a • No	
	Candidates in Phase 1 • Moderna • NIH/NIAID/VRC	Not applicable	
UC2 Target population: **Infants and young children above the age of 6 months** Condition to prevent: **RSV LRTI** Description: Active immunization of infants, for prevention of RSV disease in infants and young children	Licensed products • None	7.2b • No	**Advance R&D** Potential SAGE scope: Yes R&D strategies will need to factor in new products
	Candidates in Phase 3 • None	7.2a • No	
	Candidates in Phase 2 • Advaccine BARS13 • Meissa MV-012-968 • Sanofi Live attenuated Candidates in Phase 1 • Codagenix, CodaVax-RSV Additional Phase 1 candidates, use case not known • Blue Lake BLB-201 • Smorodintsev RSV/Flu-01E • Virometix V-306	Not applicable	

Use Case	Current products and candidates	SP 7.2 Monitoring	Action Category
UC3 Target population: **Infants and high-risk toddlers** Condition to prevent: **RSV LRTI** Description: **Monoclonal antibodies (mAbs)** for prevention of severe RSV disease for all infants in the first 6 months of life and for high risk young children entering their second RSV season (e.g with chronic heart or chronic lung disease)	Licensed products • Astra Zeneca Palivizumab • Astra Zeneca/Sanofi Nirsevimab	7.2b • No, indicated for high-risk infants • Potentially, SAGE recommendation not yet issued	**Prepare for policy** Potential SAGE scope: Yes Market shaping is also needed for access and affordability
	Candidates in Phase 3 • Merck Anti-F mAb	7.2a • Yes	
	Candidates in Phase 2 • Trinomab Candidates in Phase 1 • Gates MRI RSM01	Not applicable	

Notes

1. Sources for use cases:
    - *WHO Preferred Product Characteristics for Respiratory Syncytial Virus (RSV) Vaccines*. 2017. https://www.who.int/publications/i/item/WHO-IVB-17.11
    - *WHO preferred product characteristics of monoclonal antibodies for passive immunization against respiratory syncytial virus (RSV) disease*. 2021 https://iris.who.int/bitstream/handle/10665/341635/9789240021853-eng.pdf?sequence=1
2. Use case for older adult vaccines not included because it has been met by an existing, licensed vaccine.
3. Pipeline data are as of September 2023, from the PATH RSV Vaccine and mAb Snapshot: https://www.path.org/resources/rsv-vaccine-and-mab-snapshot/
4. Maternal vaccines and mAbs for infants and high-risk toddlers: licensed products have been recommended for these target populations in some countries. WHO position paper is anticipated in 2024.

15. *Shigella*

Reviewed by: William Hausdorff, Senjuti Saha

Table 19 *Shigella* Review

Use case	Current products and candidates	SP 7.2 Monitoring	Action Category
UC1 Target population: **Infants from 6 months and children up to 36 months of age** Condition to prevent: **Moderate to severe diarrhoea due to *Shigella*** Description: Prevention of moderate to severe diarrhoea due to Shigella in infants from 6 months and children up to 36 months of age	Licensed products • None	7.2b • No	**Advance R&D** Potential SAGE scope: Unknown
	Candidates in Phase 3 • Beijing Zhifei Lvzhu Biopharmaceutical S. *Flexneriza-S. Sonnei* Bivalent Conjugate Vaccine (NCT05156528)	7.2a • Yes	
	Candidates in Phase 2 • GSK GVGH altSonflex1-2-3 • Institut Pasteur/UMB SF2a-TT15 Candidates in Phase 1 • Eviliqure ShigETEC live	Not applicable	
UC2 Target population: **High-risk populations** Condition to prevent: ***Shigella*-attributable dysentery and diarrhoea** Description: Prevention of *Shigella*-attributable dysentery and diarrhoea for high-risk populations such as travellers and the military, communities with high incidence, elderly and institutionalized individuals, and/or pregnant women	Licensed products • None	7.2b • No	**Advance R&D** Potential SAGE scope: Unlikely
	Candidates in Phase 3 • None	7.2a • No	
	Candidates in Phase 2 • GSK GVGH altSonflex1-2-3 • Institut Pasteur/UMB SF2a-TT15 • NIAID WRSs2 Candidates in Phase 1 • Eviliqure ShigETEC live • Leiden U. InvaplexAR-Detox • LimmaTech Shigella4V • UMB CVD 1208S-122	Not applicable	

Notes

1. Sources for use cases:
    - World Health Organization. *WHO preferred product characteristics for vaccines against Shigella*. 2021. https://www.who.int/publications/i/item/9789240036741.
    - Hausdorff WP, Anderson JD 4th, Bagamian KH, Bourgeois AL, Mills M, Sawe F, Scheele S, Talaat K, Giersing BK. *Vaccine value profile for Shigella.* Vaccine. 2023 Nov 3;41 Suppl 2:S76-S94. doi: 10.1016/j.vaccine.2022.12.037. Epub 2023 Oct 10. PMID: 37827969.

2. Reduction in long-term sequelae associated with *Shigella* infection, including undernutrition, stunting, altered immune function, enteric environmental dysfunction, arthritic sequelae, long-term bowel disorders, and other chronic conditions (Hausdorff et al 2023) could contribute to the value of vaccine to prevent *Shigella*-attributable disease, thereby contributing to vaccine uptake.

16. *Staphylococcus aureus*

To be reviewed by: Isabelle Bekeredjian-Ding, Mariagrazia Pizza

Table 20 *S aureus* Review

Use Case	Current products and candidates	SP 7.2 Monitoring	Action Category
UC1 Target population: **High-risk populations** Condition to prevent: ***S aureus* infection** Description: Prevention of severe infection in populations at risk, such as children, those over 60 years of age, and/or those in all age groups who are immunocompromised, experiencing recurrent skin and soft tissue infections, suffering from relevant comorbidities, exposed to epidemic strains, or undergoing elective surgery or other invasive procedures with high risk of *S aureus* infection	Licensed products • None	7.2b • No	**Advance R&D** Potential SAGE scope: Unlikely
	Candidates in Phase 3 • Chengdu Olymvax Biopharmaceuticals Phase 3 trial evaluating efficacy of **recombinant *S aureus* vaccine** against *S aureus* infection in persons aged 18-70 years undergoing orthopaedic surgery. ChiCTR2200062998 (see note 5).	7.2a • Yes	
	Candidates in Phase 2 • Biomedizinische Forschungsgmbh ORG28077 • GSK GSK3878858A Candidates in Phase 1 • None found	Not applicable	
UC2 Target population: **Persons at risk for or undergoing treatment for *S aureus* infection** Indication: **Prevention or treatment of *S aureus* infection** Description: **mAbs** for prevention or treatment of disease caused by *S aureus,* such as severe pneumonia and/or superinfection in conjunction with viral pneumonia	Licensed products • None	7.2b • No	**Prepare for policy** Potential SAGE scope: Unlikely
	Candidates in Phase 3 • Aridis Pharmaceuticals **AR-320** (suvratoxumab), efficacy of a single IV dose of suvratoxumab in mechanically ventilated subjects in the ICU who are at high risk for *S aureus,* NCT05331885 • Aridis Pharmaceuticals **AR-301** (KBSA301, tosatoxumab). Trial evaluating efficacy and safety as adjunct therapy to antibiotics in the treatment of Ventilator associated Pneumonia (VAP) caused by *S aureus*. (CTRI/2020/05/025104) Top-line data from Phase 2 trial at: https://www.aridispharma.com/ar-301/	7.2a • Yes • Yes	
	Candidates in Phase 1 or Phase 2 • None found	Not applicable	

Notes

1. Use cases based on:
   - *Bacterial vaccines in clinical and preclinical development: an overview and analysis*. Geneva: World Health Organization; 2022. Licence: CC BY-NC-SA 3.0 IGO. https://www.who.int/publications/i/item/9789240052451
   - Aridis https://www.aridispharma.com/ar-301/

2. "Vaccines" could be split into multiple use cases, reflecting distinct target populations. Given the technical challenges associated with these use cases, we propose grouping them together for the purposes of IA2030 M&E.
3. Relevant comorbidities include diabetes, renal insufficiency (in particular with peritoneal dialysis), chronic obstructive pulmonary disease, and other lung disorders.
4. Phase 1a/1b trial results published: Zhu FC et al., *Evaluation of a recombinant five-antigen Staphylococcus aureus vaccine: The randomized, single-centre phase 1a/1b clinical trials*. Vaccine. 2022 May 20;40(23):3216-3227. doi: 10.1016/j.vaccine.2022.04.034. Epub 2022 Apr 23. PMID: 35473663.
5. Chengdu Olymvax Biopharmaceuticals Candidate listed as "discontinued" in *Bacterial vaccines in clinical and preclinical development: an overview and analysis*. Geneva: World Health Organization; 2022. Licence: CC BY-NC-SA 3.0 IGO. Therefore categorizing this use case as "Advance R&D".

17. Tuberculosis (TB)

Reviewed by: Willem Hanekom, Sonali Kochhar

Table 21 Tuberculosis Review

Use Case	Current products and candidates	SP 7.2 Monitoring	Action Category
UC1 Target population: **Adults and Adolescents** Condition to prevent: **Active pulmonary TB disease** Description: Prevention of active pulmonary TB disease (with or without evidence of latent infection), including in those with HIV infection	Licensed products • None	SP 7.2b • No	**Prepare for policy** In anticipation of product licensures from Serum Institute (India) and Gamaleya (Russia) M72 (global use) Potential SAGE scope: Yes Note: Full vaccine value assessment identified this use case as most impactful. https://www.who.int/publications-detail-redirect/9789240064690.
	Candidates in Phase 3 • Serum Institute of India **VPM1002** (CTRI/2019/01/017026), data expected in 2024 • Gamaleya **02-GamTBvac-2020** (NCT04975737) estimated study completion in 2025 • Gates/MRI **M72** phase 3 trial to start in 2024, and interim data expected by 2027	SP 7.2a • Yes • Yes • Yes	
	Candidates in Phase 2 • Biofabri **MTBVAC** Phase 2b expected to start in 2025 • Anhui Zhifei Longcom AEC/BC02 • Quratis, NIH (ACTG/HVTN), AAHI - ID93/GLA-SE (QTP101) Candidates in Phase 1 • Cansino AdHu5Ag86A • BioNTech BNT164a1, BNT164a2	Not applicable	
UC2 Target population: **Infants and young children** Condition to prevent: **TB disease** Description: Prevention of TB disease in infants and young children, including in infants with HIV infection	Licensed products • None	SP 7.2b • No	**Prepare for policy** See below – in additional to MTBVAC, VPM1002 will have Phase III data on a PoI endpoint. Need to evaluate the perspective of policy makers. Potential SAGE scope: Yes
	Candidates in Phase 3 • Biofabri **MTBVAC** (NCT04975178), data expected 2024. Endpoint is prevention of disease.	SP 7.2a • Yes	
	Candidates in Phase 1 or 2 • None found	Not applicable	

Use Case	Current products and candidates	SP 7.2 Monitoring	Action Category
UC3 Target population: **Persons being treated for TB** Indication: **Prevent TB recurrence and/or increase the proportion of cure at the end of drug treatment** Description: Adjunctive treatment of TB, or to prevent relapse following cure in patients being treated for active TB, both drug sensitive and drug resistant strains	Licensed products • Mycobacterium Vaccae for Injection (Vaccae®), Anhui Zhifei Longcom Biopharmaceutical Co. http://en.zflongkema.com/skin/default/file/%E5%BE%AE%E5%8D%A1%E8%AF%B4%E6%98%8E%E4%B9%A6.pdf. Phase 4 effectiveness trial underway (NCT05680415), estimated study completion 2027	SP 7.2b • No	**Advance R&D** While there is a licensed vaccine for prevention of recurrence, the regimen is 6 doses, 2 weeks apart, and administered at the end of TB treatment, i.e. part of TB control programme Potential SAGE scope: Yes
	Candidates in Phase 3 • None	SP 7.2a • No	
	Candidates in Phase 2 • Archivel RUTI	Not applicable	
Additional use cases to be tracked, but not counted in SP7.2 M&E (see Note 2)			
UC4 Target population: **Adults and Adolescents** Condition to prevent: **TB infection** Description: Prevention of TB infection in adults and adolescents, including in those with HIV infection	Licensed products • None	Not applicable	Not applicable
	Candidates in Phase 3 • HJF is evaluating BCG as a travel vaccine. NCT04453293	Not applicable	
	Candidates in Phase 2 • Gates MRI BCG revaccination • U Oxford ChAdOx1.85A+MVA85A • Dartmouth College, St. Louis University (DAR-901) Candidates in Phase 1 • Smorodintsev TB/FLU-05E	Not applicable	

Use Case	Current products and candidates	SP 7.2 Monitoring	Action Category
UC5 Target population: **Adults and Adolescents** Condition to prevent: **TB recurrence** Description: Prevention of recurrence (defined as either reinfection or relapse, whether pulmonary or extrapulmonary) in patients who are cured from active TB	Licensed products • None	Not applicable	Not applicable
	Candidates in Phase 3 • Serum Institute of India **VPM1002** (CTRI/2019/01/017026), data expected in 2024 • Immuvac (MIP) ICMR (https://newtbvaccines.org/vaccine/immuvac/)	Not applicable	
	Candidates in Phase 2 • SSI, IAVI, EDCTP, Valneva H56 • MTBVAC is going into Phase 2b in 2024, data expected 2027/8	Not applicable	
UC6 Target population: **Neonates, infants, and young children** Condition to prevent: **TB infection** Description: Prevention of TB infection in neonates, infants, and young children, including those with HIV infection	Licensed products • Bacillus Calmette-Guérin (BCG), multiple products	Not applicable	Not applicable
	Candidates in Phase 3 • Serum Institute of India **VPM1002** (NCT04351685), data expected 2024.	Not applicable	
	Candidates in Phase 2 • U Oxford ChAdOx1.85A+MVA85A	Not applicable	

Notes

1. Sources for use cases:
    - *WHO Preferred Product Characteristics for New Tuberculosis Vaccines*. Geneva: World Health Organization; 2018. Licence: CC BY-NC-SA 3.0 IGO. https://iris.who.int/bitstream/handle/10665/273089/WHO-IVB-18.06-eng.pdf?ua=1
    - *Preferred Product Characteristics for Therapeutic Vaccines to Improve Tuberculosis Treatment Outcomes*. Geneva: World Health Organization; 2019. Licence: CC BY-NC-SA 3.0 IGO. https://iris.who.int/bitstream/handle/10665/330448/WHO-IVB-19.05-eng.pdf?ua=1
    - Stop TB Partnership, https://newtbvaccines.org/pipeline-sortable/
    - Treatment Action Group 2023_pipeline_TB_vaccines_final.pdf (treatmentactiongroup.org)

2. TB vaccine trials are currently being conducted with prevention of infection (PoI) and prevention of recurrence (PoR) endpoints, however modelling has shown that prevention of active TB disease would be of greater public health value. For this reason, PoI and PoR use cases for TB will be tracked but not counted in SP 7.2 M&E.
3. Pipeline information from the Stop TB Partnership, https://newtbvaccines.org/pipeline-sortable/
4. DRAFT *WHO Evidence Considerations for Vaccine Policy Development for Tuberculosis Vaccines Intended for Adults and Adolescents* https://cdn.who.int/media/docs/default-source/immunization/product-and-delivery-research/who_evidence_considerations_vaccine_policy_development_tuberculosis_vaccines_intended_adults_adolescents.pdf?sfvrsn=4997b3f5_3