

Bacterial vaccines in clinical and preclinical development 2021

An overview and analysis



World Health
Organization

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Abbreviations

Ag	antigen	HICs	high-income countries
AMR	antimicrobial resistance	HKMS	heat-killed multi-serotype <i>Shigella</i> immunogens
BCG	Bacillus Calmette–Guérin	HLA	human leucocyte antigen
BMGF	Bill & Melinda Gates Foundation	HtrA	protease high temperature requirement A
CF	colonization factor	IATS	International Antigenic Typing Schema
CFA	colonization factor antigen	IAVI	International AIDS Vaccine Initiative
CgoX	coproporphyrinogen oxidase	ICMR	Indian Council of Medical Research
CHIM	Controlled Human Infection Model	ICU	intensive care unit
CJCV	capsule conjugate <i>Campylobacter</i> vaccine	IDRI	Infectious Disease Research Institute
CMV	cytomegalovirus	iNTS	invasive non-typhoidal <i>Salmonella</i>
COPS	Group D core + O-polysaccharide	IPD	invasive pneumococcal disease
COVID-19	coronavirus disease	IVI	International Vaccine Institute
CP, CPS	capsular polysaccharide	LMICs	low- and middle-income countries
CS	coli surface	LPS	lipopolysaccharide
dmLT	double-mutant <i>Escherichia coli</i> heat-labile toxin	LT	<i>Escherichia coli</i> heat-labile toxin
dPNAG	deacylated poly-N- β -(1-6)-acetyl-glucosamine	MAPS	multiple antigen presenting system
DT	diphtheria toxoid	MDR	multidrug-resistant
EPA	ExoProtein A; a detoxified form of <i>Pseudomonas aeruginosa</i> Exotoxin A	MEFA	multiepitope fusion antigen
ETEC	enterotoxigenic <i>Escherichia coli</i>	MIP	<i>Mycobacterium indicus pranii</i>
ExPEC	extraintestinal pathogenic <i>Escherichia coli</i>	MSM	men who have sex with men
FTA	fimbrial tip adhesin	Mtb	<i>Mycobacterium tuberculosis</i>
GAPDH	glyceraldehyde 3-phosphate dehydrogenase	MVA	modified Vaccinia virus Ankara
Gates MRI	Bill & Melinda Gates Medical Research Institute	NDA	New Drug Application
Gavi	Gavi, the Vaccine Alliance	NIAID	National Institute of Allergy and Infectious Disease
GGT	gamma-glutamyl transpeptidase	NICED	National Institute of Cholera and Enteric Diseases
GHIT	Global Health Innovative Technology Fund	NICHD	National Institute of Child Health and Human Development
GMMA	generalized modules for membrane antigens	NIH	National Institutes of Health
GVGH	GSK Vaccine Institute for Global Health	NIHCC	NIH Clinical Center
Hib	<i>Haemophilus influenzae</i> type B	NMRC	Naval Medical Research Center
		NOMVs	native outer membrane vesicles
		NRA	national regulatory authority
		NTS	non-typhoidal <i>Salmonella</i>

OMP	outer membrane protein	virG	<i>Shigella</i> outer membrane protein essential for bacterial spreading
OMV	outer membrane vesicle	WHO	World Health Organization
PBPV	protein-based pneumococcal vaccine	WHO SAGE	WHO Strategic Advisory Group of Experts on Immunization
PCV	pneumococcal conjugate vaccine	WHO BPPL	WHO Bacterial Priority Pathogens List
PDVAC	Product Development for Vaccines Advisory Committee	WRAIR	Walter Reed Army Institute of Research
Pephyd	peptidoglycan hydrolase		
PPrV	pneumococcal protein vaccine		
PSSP-1	pan- <i>Shigella</i> surface protein 1		
PPSV	pneumococcal polysaccharide vaccine		
R&D	research and development		
rBCG	recombinant BCG		
rTSST-1v	recombinant toxic shock syndrome toxin-1 variant		
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2		
SEB	staphylococcal enterotoxin B		
ser.	serovar		
spp.	species		
SSI	Staten Serum Institute		
SsIE	secreted and surface-associated lipoprotein from <i>Escherichia coli</i>		
ST	<i>Escherichia coli</i> heat-stable toxin		
TB	tuberculosis		
TBVI	TuBerculosis Vaccine Initiative		
TCV	typhoid conjugate vaccine		
TLR	toll-like receptor		
TPI	triose-phosphate isomerase		
TPP	target product profile		
TPV	typhoid polysaccharide vaccine		
TT	tetanus toxoid		
UPEC	uropathogenic <i>Escherichia coli</i>		
US FDA	US Food and Drug Administration		
UTI	urinary tract infection		
Vi	capsular virulence antigen		
ViPS	Vi polysaccharide		

Executive summary

Vaccines can be highly effective tools in combating antimicrobial resistance (AMR). They reduce the incidence of both resistant and susceptible infections, thereby also decreasing antibiotic consumption. Advances in vaccine technology in recent decades have made developing vaccines against previously challenging targets possible. There is a need to understand what vaccines are currently in development and those which may be available as tools to contribute to controlling AMR in the future. This analysis considers vaccine candidates in preclinical and clinical development against pathogens on the 2017 WHO Bacterial Priority Pathogens List (WHO BPPL), in addition to *Clostridioides difficile* and *Mycobacterium tuberculosis*. Sixty-one vaccine candidates in active clinical development and 94 candidates in confirmed active preclinical development were identified.

The report identified four groups of pathogens with vaccine candidates in various stages of clinical development, and with varying degrees of feasibility for vaccine development.

The first group (Group A) contains pathogens with vaccines already licensed. These exist against four priority pathogens for AMR: *Salmonella enterica* ser. Typhi, *Streptococcus pneumoniae*, *Haemophilus influenzae* type b (Hib), and *Mycobacterium tuberculosis*. The effectiveness of the vaccine against *S. pneumoniae* dramatically reduced mortality in the United States of America (USA) and Europe in comparison to other regions where the vaccine is not widely available and used. The coverage of authorized vaccines should be increased to maximise their impact on AMR. Current Bacillus Calmette-Guérin (BCG) vaccines against tuberculosis (TB) do not adequately protect against TB and the development of more effective vaccines against TB should be accelerated.

The second group (Group B) includes pathogens with vaccines that are in late-stage clinical trials with high development feasibility: extraintestinal pathogenic *Escherichia coli* (ExPEC), *Salmonella enterica* ser. Paratyphi A, *Neisseria gonorrhoeae*, and *Clostridioides difficile*. Hence, for two out of the six leading pathogens for deaths associated with AMR (1), a vaccine either already exists, as for *S. pneumoniae*, or maybe feasible, as for *E. coli*. R&D efforts and development of vaccines in late-stage clinical trials should be continued and where possible accelerated.

The third group (Group C) contains pathogens with vaccine candidates either in early clinical trials or with moderate to high feasibility of vaccine development: enterotoxigenic *E. coli* (ETEC), *Klebsiella pneumoniae*, non-typhoidal *Salmonella* (NTS), *Campylobacter* spp., and *Shigella* spp. Vaccines against these pathogens might be available in the long term, however, short term solutions to prevent resistance should focus on other interventions to reduce AMR.

The fourth group (Group D) contains pathogens with a small number or no vaccine candidates in the pipeline and low vaccine development feasibility: *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Enterobacter* spp., *Enterococcus faecium*, *Staphylococcus aureus*, and *Helicobacter pylori*. Vaccines against these pathogens are unlikely to be available in the short term, and alternative interventions to prevent AMR caused by these pathogens should be considered. It is even more worrying that the drug development pipeline

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