WHO PREFERRED PRODUCT CHARACTERISTICS FOR **vaccines against *Shigella***

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Abbreviations and glossary

AMR	antimicrobial resistance
CoP	correlates of protection
CHIM	controlled human infection models
CF	colonization factor
DALY	disability-adjusted life-year
EPI	expanded programme on immunization
ETEC	enterotoxigenic *Escherichia coli*
EIEC	enteroinvasive *Escherichia coli*
EED	environmental enteric dysfunction
ELISA	enzyme-linked immunosorbant assay
FVVA	full value of vaccine assessment
GBD	global burden of disease
GEMS	Global Enteric Multicenter Study
HIC	high-income country
IVB	Department of Immunization, Vaccines and Biologicals, WHO
IHME	Institute for Health Metrics and Evaluation
LMIC	low- and middle-income country
LSD	less severe diarrhoea
MAL-ED	The Aetiology, Risk Factors and Interactions of Enteric Infections and Malnutrition and the Consequences for Child Health and Development Project
MCEE	Maternal Child Epidemiology Estimation
MSD	moderate-to-severe diarrhoea
MSM	men who have sex with men
qPCR	quantitative polymerase chain reaction
PDVAC	Product Development for Vaccines Advisory Committee
PPCs	preferred product characteristics
PQ	pre-qualification
R&D	research and development
SAGE	Strategic Advisory Group of Experts (on Immunization)
TPP	target product profile
US	United States
WHO	World Health Organization

Executive summary

Diarrhoeal diseases are among the leading causes of morbidity and mortality worldwide. Among children younger than 5 years of age, diarrhoea is responsible for an estimated 441 100 (WHO and the Maternal Child Epidemiology Estimation (MCEE) 2000-2017) - 446 000 deaths (Institute for Health Metrics and Evaluation (IHME) 1990-2016) annually, which are geographically concentrated in the WHO African Region and South-East Asia Region. Significant reductions in diarrhoeal disease mortality have been achieved over the last 20 years; however, these reductions have not been paralleled by similar declines in diarrhoea-associated morbidity, which continues to impact negatively infant and child health, costing households and health systems millions of dollars each year in many low- and middle-income countries (LMICs). Consequently, the need to develop better and more equitable diarrhoeal prevention and control measures, such as vaccines, remains a public health priority for the World Health Organization (WHO).

Shigella was the second leading cause of diarrhoeal mortality in 2016 among all ages, and the leading bacterial cause of diarrhoea, accounting for approximately 212 000 deaths and about 13% of all diarrhoea deaths. Although *Shigella* infections occur worldwide, with broad geographical distribution and across all age groups, the greatest burden is among children in low- and middle-income countries (LMICs). Here, annually, it is responsible for an estimated 28 000 (MCEE) to 64 000 (IHME) deaths among children under 5 years of age. It is also an important cause of diarrhoea with or without dysentery in people older than 5 years of age, with an estimated 270 million episodes occurring annually among all ages, according to IHME's 2016 Global Burden of Disease study.

> "According to IHME, *Shigella* was the second leading cause of diarrhoeal

Shigella infections spread easily in areas with poor sanitation and hygiene, where there is limited access to clean water. For young children, symptomatic or asymptomatic infections due to this pathogen can result in malnutrition and induce or exacerbate stunting. Both malnutrition and growth stunting have long-term adverse consequences on physical and cognitive development. In addition, *Shigella* can cause severe illness among travellers, deployed military personnel and expatriates in LMICs, and is associated with reactive arthritis and irritable bowel disease. *Shigella* infections also have the potential to cause large outbreaks in both younger and older age groups, especially with *S. dysenteriae* type 1.

Treatment options for shigellosis include oral rehydration salts, therapeutic zinc and, when dysentery is present, antimicrobials are recommended. The rise of antibiotic-resistant enteric bacteria, particularly *Shigella* spp, means that, in addition to the potential direct effects on morbidity and mortality, a *Shigella* vaccine might also have indirect effects on reducing the use of antibiotics and consequent emergence of antimicrobial resistance (AMR). Accordingly, WHO and