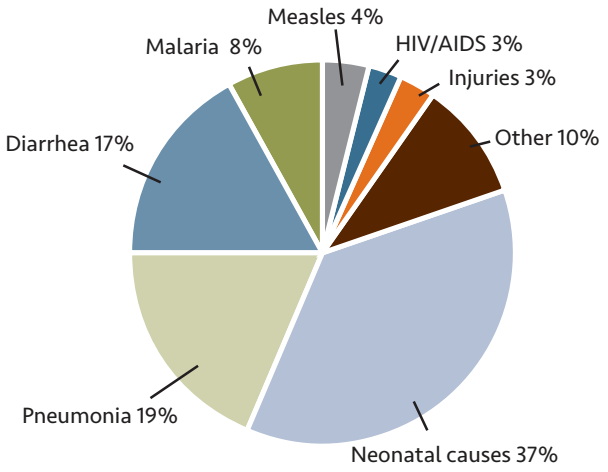
The Case for Investment in **Enterotoxigenic *Escherichia coli* Vaccines**

No public health tool has been as successful and cost-effective as vaccines at saving lives, particularly among the world's children. The World Health Organization estimates that vaccines save more than 2.5 million lives every year and protect millions more from disease and disability. Despite the number of vaccines already available, many children are still dying from diseases for which no vaccine exists. New vaccines would not only save these young lives but could also lessen disease and suffering among a variety of populations, and investment in their development represents a potential area of opportunity for vaccine manufacturers and donors worldwide. PATH and BIO Ventures for Global Health (BVGH) have teamed together to evaluate the business case for investment in vaccines against enterotoxigenic *Escherichia coli* (ETEC), a leading global cause of bacterial diarrhea.

Diarrhea is a leading cause of death in children under age five[1]



ETEC is responsible for an estimated 300,000 to 500,000 deaths each year, mostly among children in the developing world.[2] Bacterial pathogens are spread more easily in areas with poor sanitation and limited access to clean water, a frequent occurrence in the developing world. ETEC is also the leading cause of diarrhea among international travelers, as well as one of the top infectious disease threats to military personnel deployed in ETEC-endemic countries. Recent studies suggest that ETEC incidence among all of these populations—children in the developing world, travelers, and the military—may be even higher than current estimates.[3] In addition, growing evidence points to the long-term health implications of diarrheal disease. This can include malnutrition and delays in physical and cognitive development among children in the developing world, as well as long-term health conditions like irritable bowel syndrome and reactive arthritis among individuals who experience travelers' diarrhea.[4]

An effective ETEC vaccine could have a significant impact on global health, saving the lives of hundreds of thousands of children each year and preventing considerable physical suffering and malnutrition due to repeated bouts of illness. These recurring episodes of diarrhea have a significant detrimental effect on poverty in ETEC-endemic countries. Beyond this, an ETEC vaccine could benefit visitors to endemic countries, saving millions of dollars in lost productivity and acute and chronic medical costs. In addition, a vaccine may benefit local economies in these endemic areas by providing an effective safeguard against the risk of travelers' diarrhea, which could encourage tourism. Many prevention and treatment options to address diarrheal illness from ETEC exist and are important parts of the solution. Global access to improved sanitation and clean water is a key long-term goal for addressing all diarrheal diseases. However, interventions like new ETEC vaccines could play a critical and complementary role in many parts of the world where appropriate medical treatment for severe diarrhea and dehydration is limited and access to sanitation and safe water is currently inadequate.

In the last few years, momentum has been building in both the public and private sectors around research and development efforts to develop new diarrheal disease interventions, including an ETEC vaccine. Public funding for diarrheal diseases from high-income country governments and multilaterals has increased substantially, and several pharmaceutical/biotechnology companies have recently shown an interest in ETEC vaccine development. Major philanthropic players have also announced new investments in ETEC vaccines over the last several years. In addition, global agencies have made greater commitments to understanding diarrheal disease burden and the impact of specific pathogens. Finally, there have been increased opportunities to leverage private markets for the public good through

implementation of tiered pricing schemes, which allow companies to achieve a return on investment in profitable markets such as the travel and military segments, while providing those products at substantially lower cost in the developing world.

The purpose of this ETEC vaccine market assessment is to provide relevant information for product developers interested in the development of these vaccines. Specifically, we aim to increase the awareness of biotechnology and pharmaceutical companies in Europe and the United States, as well as companies in emerging markets like China and India, about the opportunities and potential markets that exist for low-cost and effective ETEC vaccines. In addition, we hope to provide donors and commercial investors with a better understanding of the potential risks, rewards, and gaps in knowledge relative to these opportunities as they consider their own investment strategies. Given the myriad investment scenarios that can arise in this market, this report focuses on the primary inputs to financial return scenarios. This allows companies and their investors to run their own investment scenarios to estimate net present value and internal rate of return, based on their individual circumstances.

Through this assessment, we found that the recent increase in investments in ETEC vaccine research and development, as well as encouraging technological developments and promising field data on the protective efficacy of ETEC vaccine candidates in travelers, may help to reduce the perceived risk associated with investment in this technology. Our analysis demonstrates that ETEC vaccines may represent a moderate opportunity for industry investment with an estimated annual revenue potential of more than US$600 million, 10 years after global launch. This opportunity is driven primarily by travel and middle-income markets (both public and private), but military and low-income markets are also represented. The growing body of evidence about longer term, post-infection health conditions from travelers' diarrhea also bolsters the potential market. However, it should be noted that it may be challenging to meet the target product profile used in this assessment within the next decade, and there are some key uncertainties that affect the results of this estimate. These uncertainties are typical for a market assessment conducted years in advance of an actual product and for products that rely on the limited epidemiological data available from developing countries.

Financial return scenario planning depends on a number of key assumptions which can vary widely. The investment return calculation based on these assumptions also varies significantly and needs to be conducted by each investor to reflect individual conditions. Initial estimates based on our model suggest that in order to attract private investment, public sector funding may well be essential to facilitate development of ETEC vaccines in order to offset the high front-end costs and technical risks of development.

The full market-assessment report provides detailed background information, including an overview of ETEC illness, disease burden, current treatment and prevention methods, and the scientific feasibility and current status of ETEC vaccine development. In addition, we share the market assessment itself, detailing the key inputs used in the analysis and resulting estimates for potential pricing, market penetration, and revenue for each of the markets we analyzed. Finally, we outline challenges and opportunities in developing ETEC vaccines and recommend next steps for moving the development process forward and making affordable, safe, effective, and accessible ETEC vaccines a reality for each of these markets.

To download a free copy of the full report, *The Case for Investment in Enterotoxigenic* Escherichia coli *Vaccines*, please visit: **www.path.org** or **www.bvgh.org**.

Endnotes

[1]Bryce J, Boschi-Pinto C, Shibuya K, Black RD, WHO Child Health Epidemiology Reference Group. WHO estimates of the causes of death in children. *The Lancet*. 2005;365(9465):1147–1152.

[2]World Health Organization (WHO). *Weekly Epidemiological Record*. Geneva, Switzerland: WHO; 2006; 81:97–104. Available at: www.who.int/wer/2006/wer8111.pdf.

[3]Gupta SK, Keck J, Ram PK, Crump JA, Miller MA, Mintz ED. Analysis of data gaps pertaining to enterotoxigenic *Escherichia coli* infections in low and medium human development index countries, 1984–2005. *Epidemiology and Infection*. 2008;136(6): 721–738.

[4]Connor BA. Sequelae of traveler's diarrhea: focus on postinfectious irritable bowel syndrome. *Clinical Infectious Diseases*. 2005;41(Suppl.8):S577–S586.

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