FACT SHEET

PATH
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Developing New Vaccines Against Diarrheal Disease

Each year, approximately 1.3 million children worldwide die from severe, dehydrating diarrhea, mostly in low-resource countries. The leading bacterial causes of diarrhea are enterotoxigenic *Escherichia coli* (ETEC) and *Shigella*, and, together, they account for about one billion cases of diarrhea annually. Insufficient data exist, but conservative estimates suggest that ETEC and *Shigella* are responsible for the deaths of approximately 500,000 children under the age of five each year. Access to appropriate medical care for diarrhea and dehydration is limited in low-resource countries, and *Shigella* is becoming increasingly more resistant to the antibiotics most commonly used for treatment. Therefore, vaccination is a critical part of the strategy to reduce the incidence and severity of diarrheal disease.

PATH is collaborating with public- and private-sector partners to accelerate the development of safe, effective, and affordable vaccines against ETEC and *Shigella* for children in endemic areas. By pursuing a wide range of promising vaccine approaches and related research, PATH aims to identify at least one vaccine candidate for each pathogen to prioritize for late-stage development. PATH is also assessing manufacturing partners, mostly in emerging countries, to participate in the late development and eventual manufacture and distribution of these vaccines.

PATH has supported early clinical research on ACE527, a live attenuated ETEC vaccine candidate developed by TD Vaccines, a Danish biotechnology company. Results from these studies were promising, and PATH is planning to conduct further testing of ACE527 in a descending-age study in an ETEC-endemic country, expected to launch in 2012. In addition, PATH is currently supporting early-stage clinical trials of an inactivated whole-cell ETEC vaccine candidate in development by the University of Gothenburg in Sweden, as well as preclinical research on two separate subunit ETEC vaccine candidates with the International Enteric Vaccine Consortium and the US Naval Medical Research Center.

For *Shigella*, PATH is working with the Walter Reed Army Institute of Research to conduct early clinical research on an inactivated whole-cell vaccine candidate, while also supporting the University of Maryland, Baltimore, to optimize and conduct early-stage trials of a live attenuated vaccine candidate. In addition, PATH is collaborating with the International Vaccine Institute in South Korea and Oklahoma State University to conduct preclinical research on two separate subunit *Shigella* vaccine candidates.

Adjuvants, ingredients that may enhance the effectiveness of some vaccines, are another important area of research. PATH in-licensed a highly promising new vaccine/adjuvant from Tulane University which could offer additional protection against both diarrhea and intestinal infection, and it may be tested in conjunction with a number of candidates in PATH's vaccine portfolio. PATH is currently working with the US National Institutes of Allergy and Infectious Diseases on early clinical studies of the vaccine/adjuvant and plans to begin testing it in combination with other candidates soon.

In recognition that new vaccines must be practical for use with infants and children in low-resource countries, PATH is also optimizing vaccine stabilization and investigating new formulations that may make the vaccines more effective and easier to administer in these populations. In addition, PATH is supporting the development of improved testing methods for these candidates and conducting assessments of the market opportunities for ETEC and *Shigella* vaccines. PATH also aims to increase awareness of diarrheal disease and the need for new vaccines by pursuing an advocacy and policy strategy that integrates information about diarrheal diseases within broader public-health priorities.

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