

Using innovation to combat diarrheal disease in Vietnam



Evaluating a new rotavirus vaccine formulation to ensure that it is safe, effective, and practical for use in low-resource settings

Rotavirus disease burden

Each year, approximately half a million children die from diarrheal disease. The most common and deadly cause of severe diarrhea and dehydration in infants and young children is rotavirus.¹ More than 90 percent of rotavirus-related deaths occur among children in poor countries. Estimates from 2013 (the most recent data available) determined that Vietnam had a total of 2,083 diarrhea-related deaths, of which 49.9 percent were due to rotavirus.² Vietnam also has one of the highest rotavirus hospitalization figures in South East Asia.³

Rotavirus is highly contagious and resilient and spreads easily via contaminated hands and objects. Regardless of water quality and available sanitation, nearly every child in the world is at risk of infection. Mild rotavirus diarrhea can be treated effectively in the same manner as other forms of diarrhea, by providing fluids and oral rehydration therapy. However, children with severe rotavirus diarrhea can become rapidly dehydrated and often need intravenous fluid replacement. In low- and middle-income countries, particularly in rural areas, this type of urgent health care is often inaccessible or unavailable. Children with serious rotavirus diarrhea can then become at risk of death. In Vietnam, the number of children that die each day of preventable causes is 3.5 times higher among ethnic minorities in the northern mountainous areas.⁴

Using vaccines to strengthen health

Vaccination offers the best protection for infants against severe diarrhea and death from rotavirus infection, and the World Health Organization (WHO) recommends the routine use of rotavirus vaccine in infants in all countries worldwide. To date, 96 countries have introduced rotavirus vaccine, however, 57 percent of all children—over 70 million infants—still lack access to rotavirus vaccines.⁵

Four rotavirus vaccines are currently available on the global market, but most are very expensive—around US\$45 per dose in the private market. This cost is prohibitive for most low- and middle-income countries. A key strategy for creating and maintaining a long-term, financially sustainable supply of rotavirus vaccines is for additional manufacturers—especially those based in emerging countries—to develop rotavirus vaccines and enter the marketplace.



Vietnam has a population of about 96 million people, including approximately 26 million children. With limited access to quality health care, every day 100 children under five years of age die of preventable illnesses. Rural clinics like this one are critical to providing health care and vaccines to children in Vietnam. PATH

In Vietnam, locally state-owned vaccine manufacturer POLYVAC (Center for Research and Production of Vaccines and Biologicals) produces a licensed rotavirus vaccine—ROTAVIN-M1—that is available in the domestic private market and more than one million doses have been administered to infants across Vietnam since 2012. The price of this Vietnamese-made vaccine is one-third the cost of an imported vaccine, at just \$15 per dose.

However, ROTAVIN-M1 requires frozen storage at -20°C. This presents significant challenges for the vaccine cold chain in Vietnam, which was designed to keep vaccines at 2-8°C. PATH is currently collaborating with POLYVAC on evaluating a second-generation formulation of their rotavirus vaccine (simply called ROTAVIN), which does not need to be kept frozen, in a clinical trial in Vietnam. ROTAVIN contains the same rotavirus strain as ROTAVIN-M1 and is produced in the same way, but only needs to be stored at 2-8°C. This is more compatible with the cold chain currently in place in Vietnam, allowing for easier storage and transport. This will also make the vaccine more attractive for use in many low- to middle-income settings, including in Vietnam.

¹Diarrhoeal disease fact sheet. World Health Organization. <https://www.who.int/news-room/fact-sheets/detail/diarrhoeal-disease>. Published May 2, 2017. Accessed January 23, 2019.

²Tate JE, Burton AH, Boschi-Pinto C, Parashar UD. Global, Regional, and National Estimates of Rotavirus Mortality in Children <5 Years of Age, 2000–2013. *Clinical Infectious Diseases*. 2016;62(Suppl 2):S96-S105.

³O'Brien MA, Rojas-Farreras S, Lee H et al. Family impact of rotavirus gastroenteritis in Taiwan and Vietnam: An ethnographic study. *BMC Infectious Diseases*. 2015;15(240). doi: 10.1186/s12879-015-0968-y

⁴Children in Viet Nam. UNICEF. <https://www.unicef.org/vietnam/children-viet-nam>. Accessed January 23, 2019.

⁵Global Introduction Status. ROTA Council. <http://rotacouncil.org/vaccine-introduction/global-introduction-status/>. Accessed January 23, 2019.

Harnessing vaccine innovation to increase equitable access

From November 2015 to December 2017, PATH provided technical assistance to POLYVAC in developing a second-generation rotavirus vaccine that is prepared as a more heat-stable formulation in an oral delivery device. This new product (ROTAVIN) has been manufactured under full compliance with the Vietnamese Ministry of Health regulations, as was the case for the frozen formulation of the vaccine (ROTAVIN-M1).



PATH has worked with Vietnamese vaccine manufacturers for over 10 years. Now we are partnering with POLYVAC to test a new formulation of their rotavirus vaccine. POLYVAC

PATH, POLYVAC, and the National Institute of Hygiene and Epidemiology (NIHE) are evaluating ROTAVIN in a Phase 3 bridging study designed to compare the new vaccine formulation with ROTAVIN-M1. The purpose of the study is to determine whether the new liquid formulation of the vaccine is as safe and immunogenic (meaning that it induces an immune response against rotavirus infection) as the currently licensed frozen formulation of the vaccine. This project builds upon the previous support that PATH has provided, along with WHO, to assist Vietnam and other middle-income countries in preparing for the eventual licensure and commercial-scale manufacture of affordable and accessible vaccines.

Starting in March 2019, the study team is enrolling approximately 825 healthy infants aged between 60 to 91 days at NIHE clinical trial sites in two provinces in northern Vietnam, Quang Ninh and Nam Dinh.

The infants enrolled in the study will be randomly assigned to receive either ROTAVIN or ROTAVIN-M1 and will receive two doses of vaccine administered eight weeks apart. Multiple safeguards are in place to protect the health and safety of the children involved in the study.

The study protocol was approved by the NIHE Institutional Review Board, the Western Institutional Review Board in the United States, and the National Independent Ethics Committee of Vietnam's Ministry of Health. In addition, the trial is being strictly monitored for adherence to the highest international clinical trial standards.

The future of rotavirus vaccination in Vietnam

The study will take about 12 months to complete, with an additional 6 months for data analysis. Final results should be available by mid-2020.

If the trial successfully confirms that ROTAVIN is as safe and immunogenic as the currently licensed frozen formulation, POLYVAC will apply for licensure of the new vaccine in Vietnam and the government of Vietnam will consider its inclusion in the national immunization program. In addition, it may be possible in the future for POLYVAC to export ROTAVIN for use in other countries in the Mekong region.

Improving access to rotavirus vaccines in Vietnam will not only save children's lives, but also pave the way for a more sustainable and affordable rotavirus vaccination program in the country to lessen the heavy economic and health burden of rotavirus disease.



Improving access to rotavirus vaccines will save the lives of Vietnamese children for years to come, developing healthier and stronger communities. PATH/Nguyen Phu Cuong



PATH is a global organization that works to accelerate health equity by bringing together public institutions, businesses, social enterprises, and investors to solve the world's most pressing health challenges. With expertise in science, health, economics, technology, advocacy, and dozens of other specialties, PATH develops and scales solutions—including vaccines, drugs, devices, diagnostics, and innovative approaches to strengthening health systems worldwide.

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