

Summary of the WHO position paper on Rotavirus vaccines WHO position paper- 16 July 2021

Background

Before rotavirus vaccines first became available in 2006, rotaviruses infected nearly every child by the age of 3–5 years. Globally, rotavirus was the leading cause of severe, dehydrating diarrhoea in children aged <5 years, resulting in an estimated >500 000 childhood deaths and >2 million hospitalizations worldwide in 2000. Between 2013 and 2017, an estimated 122 000–215 000 child deaths due to rotavirus occurred annually, representing a decline of 59%–77% since 2000. In most low-income countries in Asia and Africa, the rotavirus epidemiology is characterized by episodes of relatively intense viral circulation against a background of year-round transmission. However, in high income countries in temperate climates, a distinct winter seasonality is typically observed.

Rotaviruses belong to the *Reoviridae* family. The outermost layer of these viruses contains the proteins VP7 and VP4 which stimulate the production of neutralizing antibodies. In human rotaviruses, at least 12 different VP7 antigens (G-types) and 15 different VP4 antigens (P-types) have been identified. Currently, 5 G-P combinations (G1P[8], G2P[4], G3P[8], G4P[8]) and G9P[8]) account for approximately 90% of all human rotavirus infections.

Rotaviruses damage the enterocyte lining of the small intestinal villi, leading to reduced absorptive capacity and diarrhoea. The wide clinical spectrum of rotavirus disease ranges from transient loose stools to severe diarrhoea and vomiting causing dehydration, electrolyte disturbances, shock and, in untreated cases, death. The cornerstones of treatment of severe RVGE are fluid replacement and zinc supplementation.

Currently available rotavirus vaccines are live, oral, attenuated rotavirus strains of human and/or animal origin that replicate in the human intestine to elicit an immune response. The first 2 rotavirus vaccines prequalified by WHO were: RotaTeq (Merck & Co. Inc., Whitehouse Station, NJ, USA) in 2008, and Rotarix (GlaxoSmithKline Biologicals, Rixensart, Belgium) in 2009. In 2018, 2 additional vaccines were prequalified by WHO: Rotavac (Bharat Biotech International Ltd, India) and ROTASIIL (Serum Institute of India, India).

A recent Cochrane review of the 4 WHO prequalified rotavirus vaccines showed that vaccine efficacy against severe RVGE was higher for low-mortality strata countries than for high-mortality strata countries. Based on 11 randomized controlled trials (RCTs) of RotaTeq, 15

RCTs of Rotarix, 1 RCT of Rotavac, and 2 RCTs of ROTASIIL, this review showed protection against severe RVGE after 1 and/or 2 years of follow-up with modest waning over the period of observation, ranging from approximately 90%–95% in low-mortality strata countries as compared to approximately 44%–70% efficacy in high-mortality strata countries. A sub-analysis of high-mortality countries in Africa and Asia showed that the 4 vaccines had comparable vaccine efficacy against severe RVGE at 1 year of follow-up, ranging from 48% to 57%.

Each of the WHO prequalified rotavirus vaccines has demonstrated a good safety profile. Intussusception has been associated with rotavirus vaccines; no other serious adverse event has been identified.

WHO position

Rotavirus vaccines should be included in all national immunization programmes and considered a priority, particularly in countries with high rotavirus gastroenteritis (RVGE)-associated fatality rates, such as in South and South-eastern Asia and sub-Saharan Africa. Introduction of rotavirus vaccine should be accompanied by measures to ensure high vaccination coverage and timely administration of each dose.

The use of rotavirus vaccines should be part of a comprehensive strategy to control diarrhoeal diseases with the scaling up of both prevention (promotion of early and exclusive breastfeeding, handwashing, improved water supply, and sanitation) and treatment packages (low osmolarity ORS and zinc).

WHO emphasizes the importance of integration of immunization services with other health interventions throughout the life course to help maximize each interaction with a family.

Based on review of evidence on age-specific burden of rotavirus disease and deaths, timeliness of vaccination, risk of intussusception, and efficacy, and effectiveness of different immunization schedules, WHO recommends that the first dose of rotavirus vaccine be administered as soon as possible after 6 weeks of age, to ensure induction of protection prior to exposure to rotavirus.

A minimum interval of 4 weeks should be maintained between doses. RotaTeq, Rotavac, and ROTASIIL should be administered in a 3-dose schedule, while a 2-dose schedule should be used for Rotarix. WHO prequalified rotavirus vaccines are safe and effective. The choice of product to be used in a country should be based on programmatic characteristics, vaccine supply, and vaccine price.

Current evidence indicates that local data on circulating rotavirus strains should not drive product choice, as the WHO prequalified rotavirus vaccines provide protection against heterologous strains. The rotavirus vaccination series for each child should be completed with the same product whenever feasible.

However, if the product used for a prior dose is unavailable or unknown, the series should be completed with any available licensed product. Restarting the vaccine series is not recommended.

If a child <24 months of age misses a rotavirus dose or series for any reason, WHO recommends rotavirus vaccination for that child. The need for rotavirus vaccination for children with missed, delayed or interrupted routine immunization is particularly important after significant disruptions to immunization programmes and in high-mortality or crisis contexts.

Interrupted schedules should be resumed without repeating the previous dose. Because of the typical age distribution of RVGE, rotavirus vaccination of children >24 months of age is not recommended. This WHO-recommended upper age limit for rotavirus vaccination is higher than the age restrictions indicated in the product information for Rotarix, RotaTeq, and Rotavac and thus constitutes an off-label recommendation for these products.¹

Rotavirus vaccinations may be administered simultaneously with other vaccines of the childhood immunization programme. As oral rotavirus vaccines have been shown to have a pain mitigating effect due to their sucrose content, it is useful to administer rotavirus vaccines prior to co-administered injectable vaccines.

Rotavirus vaccine should not be given to children with prior history of intussusception, severe allergic reaction (e.g. anaphylaxis) after a previous dose, or severe immunodeficiency, including severe combined immunodeficiency.

Malnourished children or HIV-positive children may be vaccinated with rotavirus vaccine using a standard schedule. With all prequalified rotavirus vaccines, prematurely born infants, including those who remain hospitalized, should follow the vaccination schedules recommended for their chronological age.

¹ The recommendations contained in this publication are based on the advice of independent experts, who have considered the best available evidence, a risk–benefit analysis, and other factors, as appropriate. This publication may include recommendations on the use of vaccine products for an indication, in a dosage form, dose regimen, population or other use parameters that are not included in the approved labelling. Relevant stakeholders should familiarize themselves with applicable national legal and ethical requirements. WHO does not accept any liability for the procurement, distribution and/or administration of any product for any use.