INTRODUCTION OF ROTAVIRUS VACCINES

Information for Policy Makers, Programme Managers, and Health Workers

WHO
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Introduction

Why this document?
WHO recommends that rotavirus vaccines be included in all national immunization programmes.

Rotavirus vaccine should be 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.

To maximize the impact of rotavirus vaccine it is important to develop a comprehensive and realistic introduction plan.

What is included in this document?
This document includes:

- information and guidance to assist national managers to consider all the operational preparations that should be included in a rotavirus vaccine introduction plan, once a decision to introduce the vaccine has been made; and

- key technical information and up-to-date references to help programme managers and health workers to successfully incorporate rotavirus vaccine into the national immunization programme.

Each country should develop country-specific plans on how rotavirus vaccine can be introduced in a manner that strengthens the existing national immunization programme and is part of an integrated strategy to preventing pneumonia and diarrhoea child deaths.

KEY MESSAGE
The use of rotavirus vaccines should be part of a comprehensive strategy to prevent diarrhoea and pneumonia

- Globally, pneumonia and diarrhoea are among the leading causes of child mortality.
- Together pneumonia and diarrhoea account for 29% of deaths in children >5 years (an estimated 2 million deaths/year).
- The solutions for tackling pneumonia and diarrhoea do not require major advances in technology. Children are dying because services are provided piecemeal and those most at risk are not being reached.
- Many of the causes and solutions for childhood pneumonia and diarrhoea are inter-related and need to be addressed together.
- The introduction of rotavirus vaccine is an opportunity to integrate and improve the planning, delivery and monitoring of a comprehensive package of health interventions for pneumonia and diarrhoea.
An integrated approach for saving lives: The “Protect, Prevent and Treat” framework for pneumonia and diarrhoea

Among partners, academics, NGOs, governments, communities and health workers themselves, it is well recognized that pneumonia and diarrhoea are most effectively addressed in a coordinated manner. They share the same determinants, and thus also share control strategies, as well as delivery systems. Both pneumonia and diarrhoea are caused by multiple pathogens and no single intervention alone can manage to address either problem. Most of the required actions are common to both diseases.

The goal to end childhood deaths due from pneumonia and diarrhoea by 2025 is the driving force behind the WHO/UNICEF Integrated Global Action Plan for Pneumonia and Diarrhoea (GAPPD)\(^1\). The action plan identifies opportunities to better integrate activities as well as capture synergies and efficiencies. It envisions the various interventions for controlling pneumonia and diarrhoea in children less than five years of age as:

- **protecting** children by establishing and promoting good health practices;
- **preventing** children from becoming ill from pneumonia and diarrhoea by ensuring universal coverage of immunization, HIV prevention and healthy environments;
- **treating** children who are ill from pneumonia and diarrhoea with appropriate treatment.

**Figure 1: Complementarity of pneumonia and diarrhoea interventions**

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Over the past 20 years, research into specific pneumonia and diarrhoea interventions has shown that the following interventions and activities work (see Annex 1 for more details):

- Exclusive breastfeeding for 6 months and continued breastfeeding with appropriate complementary feeding reduces the onset and severity of diarrhoea and pneumonia.
- Preventive vitamin A supplementation reduces all-cause mortality and diarrhoea-specific mortality in children 6-59 months.
- Vaccination against *Streptococcus pneumonia* (Spn) (pneumococcal conjugate vaccine – PCV), *Haemophilus influenza* type b (Hib), rotavirus, measles and pertussis.
- Use of simple, standardized guidelines for the identification and treatment of pneumonia and diarrhoea in the community, at first-level health facilities and at referral hospitals, such as those for integrated management of childhood illness (IMCI), substantially reduces child deaths.
- Oral rehydration solution (ORS), especially the low-osmolarity formula, and use of zinc supplements are proven, life-savers for treatment of children with diarrhoea.
- Innovative demand creation activities are important for achieving behavior change and sustaining long-term preventive practices.
- Water, sanitation and hygiene interventions (WASH), including access to and use of safe drinking-water and sanitation, as well as promotion of key hygiene practices (e.g. handwashing with soap).
- Reduction of household air pollution with improved stoves has been shown to reduce severe pneumonia. Safer and more efficient energy in the home prevents burns, saves time and fuel costs, and contributes to better development opportunities.

Although these interventions form the core of primary health care (PHC) in many places they are not always promoted together to achieve maximum benefit. The proposed interventions outlined in GAPPD are not new, but implementing them to scale will require greater coordination and effort.

This overall approach builds on and is linked to the achievement of the Millennium Development Goal to reduce child mortality (MDG4), as well as to the successful implementation of the *UN Global Strategy for Women’s and Children’s Health*, including *Every Woman, Every Child*, the *UN Commission on Life-Saving Commodities*, the *Global Vaccine Action Plan* (GVAP) and the *A Promise Renewed* commitment to child survival.
**WHO recommendations for rotavirus vaccines**

**Rotavirus vaccines WHO position paper – January 2013**

WHO recommends that rotavirus vaccines be included in all national immunization programmes and considered a priority particularly, in countries with high rotavirus gastroenteritis-associated (RVGE) fatality rates, such as in south and south-eastern Asia and sub-Saharan Africa.

**Recommended vaccination schedule:**

Following a review of new evidence on age-specific burden of rotavirus disease and deaths, timeliness of vaccination, and the safety and effectiveness of different immunization schedules, WHO recommends that the first dose of rotavirus vaccine be administered as soon as possible at or after 6 weeks of age, along with diphtheria-tetanus-pertussis (DTP) or pentavalent vaccination, to ensure induction of protection prior to natural rotavirus infection:

- **Rotarix® (RV1)** should be administered orally in a 2-dose schedule at the time of DTP/penta1 and DTP/penta2 contacts, with an interval of at least 4 weeks between doses.

- **RotaTeq® (RV5)** should be administered orally in a 3-dose schedule at the time of the DTP/penta1, DTP/penta2, and DTP/penta3 contacts, with an interval of at least 4 weeks between doses.

Because of the typical age distribution of RVGE, rotavirus vaccination of children >24 months of age is not recommended. Prematurely born infants should follow the vaccination schedules recommended for their chronological age.

Rotavirus vaccinations can be administered simultaneously with other vaccines in the infant immunization schedule.

**Lifting of previous age restrictions:**

The vaccine manufacturers’ conventional age restrictions on the first and last dose of rotavirus vaccines may prevent vaccination of many vulnerable children in settings where the DTP doses are often given late (i.e. after 15 weeks for DTP/penta1; or after 32 weeks for DTP/penta2 or DTP/penta3)**3.** WHO’s recommendation encourages early vaccination (first dose to be given at, or as soon as possible after, 6 weeks of age) but allows infants to receive rotavirus vaccine together with DTP/penta regardless of the time of vaccination.

This means children who were previously excluded from the benefits of rotavirus vaccines are now eligible to be vaccinated. Nevertheless, since rotavirus is a disease that affects young infants, the introduction of rotavirus vaccine should be accompanied by measures to ensure high vaccination coverage and timely administration of each dose in order to maximize the benefit.

Plans for introduction of rotavirus vaccines should consider the epidemiology of the disease by age, the coverage and actual age at vaccination and an evaluation of the estimated public health impact and potential risks. In addition, cost-effectiveness assessment, issues of affordability of the vaccine, financial and operational impact on the immunization delivery system, and careful examination of current immunization practices should be taken into account.

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2 [http://www.who.int/entity/wer/2013/wer8805.pdf](http://www.who.int/entity/wer/2013/wer8805.pdf)

3 This corresponds to the schedule used in the clinical trials for licensure.
**Need for a comprehensive approach:**

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 for six months, vitamin A supplementation, hand-washing, improved water supply and sanitation) and treatment services.

- WHO/UNICEF recommend that all children receive solutions of low-osmolarity ORS to prevent and treat dehydration due to diarrhoea.
- Breast milk is also an excellent rehydration fluid and should be given to children still breastfeeding, along with ORS.
- In addition to fluid replacement, children with diarrhoea should continue to be fed during the episode. Food intake supports fluid absorption from the gut into the bloodstream to prevent dehydration and helps maintain nutritional status and the ability to fight infection.
- Children should also simultaneously receive zinc treatment which reduces the duration and severity of diarrhoea episodes, stool volume and the need for advanced medical care.

**Vaccine safety:**

Apart from a low risk of intussusception (about 1–2 per 100 000 infants vaccinated), the current rotavirus vaccines are considered safe and well tolerated.

Countries should develop a strategy to inform relevant health staff that although the benefits outweigh the risks, a small potential risk of intussusception after rotavirus vaccination remains.

Countries should also ensure that caregivers are adequately counseled to recognize danger signs of dehydration or intussusception that require immediate medical attention.

Proper planning and training of staff to conduct pharmacovigilance should take place before the vaccine is introduced.

Given the background rate of natural intussusception and the large number of children included in national immunization programmes, intussusception cases are expected to occur by chance alone following rotavirus vaccination. It is important to establish the baseline incidence of intussusception at sentinel sites and to use epidemiological studies, such as the self-controlled case series method\(^4\), to assess the safety of rotavirus vaccines.*

**Contraindications:**

Severe allergic reaction (e.g. anaphylaxis) after a previous dose, and severe immunodeficiency including severe combined immunodeficiency (SCID), are contraindications for rotavirus vaccination.

Precautions are necessary if there is a history of intussusception or intestinal malformations, chronic gastrointestinal disease, and severe acute illness. Vaccination should be postponed in case of ongoing acute gastroenteritis or fever with moderate to severe illness.

**Surveillance:**

The epidemiological impact of rotavirus vaccination should be monitored. High-quality surveillance should be conducted in selected countries and defined populations, including high child mortality settings. However, lack of surveillance should not be an impediment to the introduction of rotavirus vaccine.

* See WER, No. 8, 2011 pp. 61-72.

Overview of the planning process

TEN KEY ELEMENTS OF A SUCCESSFUL NATIONAL PLAN FOR THE INTRODUCTION AND IMPACT EVALUATION OF ROTAVIRUS VACCINES

<table>
<thead>
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<th>Element of the planning process</th>
<th>Why?</th>
<th>What is known?</th>
<th>Further reading</th>
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<tbody>
<tr>
<td><strong>Planning element 1</strong></td>
<td>Analyze the epidemiology of rotavirus disease in your country (e.g. age distribution of rotavirus gastroenteritis)</td>
<td>Need to know the age distribution of RVGE in your country (or in similar or neighbouring countries) to ensure that the infants are protected before they are infected with rotavirus.</td>
<td>Page 10</td>
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<tr>
<td></td>
<td>Rotaviruses (RVs) are globally the leading cause of severe, dehydrating diarrhoea in young children. Most children are infected by the age of 3-5 years regardless of the place where they are born.</td>
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<td>Severe rotavirus gastroenteritis (RVGE) episodes and deaths occur more frequently in low-income countries and mainly affect infants under one year of age. Children in low-income countries acquire their first infection early during the first year of life and the mean age at infection is around 26 weeks of age.</td>
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<td><strong>Planning element 2</strong></td>
<td>Review the age at which children are receiving each dose of DTP/pentavalent vaccine (timeliness) and, the coverage achieved</td>
<td>Rotavirus vaccine doses need to be administered in a timely manner and, it is important to achieve high coverage with each dose of vaccine.</td>
<td>Page 12</td>
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<td></td>
<td>Vaccination should be initiated as early as possible (i.e. at 6 weeks of age or soon thereafter). This is especially important for rotavirus vaccine as many children will be exposed to rotavirus during the first months of life.</td>
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<td>Therefore, the introduction of rotavirus vaccine should be accompanied by measures to ensure high vaccination coverage and timely administration of each dose by the recommended age.</td>
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<td><strong>Planning element 3</strong></td>
<td>Review coverage at subnational level and, identify areas where coverage is lower than national targets</td>
<td>Rotavirus vaccine coverage needs to be high among children at greatest risk of dying from RVGE. These children often live in areas with poor access to health services.</td>
<td>Page 14</td>
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<td></td>
<td>Activities around rotavirus vaccine introduction offer an opportunity to:</td>
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<td>• identify low performing areas;</td>
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<td>• ascertain reasons why children remain unvaccinated and;</td>
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<td>• implement as part of the rotavirus vaccine introduction plan, specific actions to remediate any gaps in routine immunization;</td>
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<td>• support an integrated approach to the prevention of diarrhoea (and pneumonia)</td>
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<tr>
<td>Planning element</td>
<td>Vaccination should be scheduled as early as possible; and this is especially important for rotavirus vaccine as many children will be exposed to rotavirus during the first months of life.</td>
<td>Two safe and effective oral rotavirus vaccines, Rotarix® (RV1) and RotaTeq® (RV5), are prequalified by WHO. The currently available efficacy and safety data support selection of either of these two vaccines for national use. A large number of randomized, controlled trials have shown that both have 80%-90% efficacy against severe RVGE in countries with very low or low child and adult mortality, and have 40% - 60% efficacy in countries with high child mortality and high or very high adult mortality. Administering rotavirus vaccine at the same contacts as DTP/penta can help maintain high coverage and ensure that more children benefit from rotavirus vaccine.</td>
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<td>Planning element 5</td>
<td>To successfully integrate rotavirus vaccine into the national vaccination schedule, existing cold chain and logistic systems will likely need to be adjusted.</td>
<td>Logistics systems should be adjusted to include proper session planning, vaccine forecasting, storage and wastage monitoring of this additional new vaccine. Expanding needs for cold chain and transport capacity at all levels of the supply chain should be anticipated and addressed.</td>
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<td>Planning element 6</td>
<td>To determine other equally important operational considerations that should be well-thought-out during planning for a successful implementation.</td>
<td>Additional issues should be taken into account including: other key activities planned during the year, potential operational impact of the rotavirus vaccine introduction on the immunization delivery system, and careful examination of current immunization practices. Prior to the introduction of any new vaccine it is important to identify the training needs at all levels, ensure that the data recording instruments have been updated to include recording of rotavirus vaccine doses, and strengthen supervisory skills so that adequate support is given to staff during the introduction period and thereafter.</td>
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<td>Planning element 7</td>
<td>Rotavirus vaccine protects against one cause of diarrhoea, but not all causes. Prevention of childhood diarrhoeal disease also needs improved coverage of exclusive 6 months breastfeeding; vitamin A supplementation; safe water, hand washing with soap and sanitation; and use of ORS and zinc treatment.</td>
<td>Diarrhoea and pneumonia remain the major killers of young children. Together, these diseases account for 29% of all deaths of children less than 5 years of age and the loss of an estimated 2 million lives each year. Better coordination and integration between programmes that deliver the different interventions to prevent, protect and treat are fundamental to tackling pneumonia and diarrhoea. The determinants that underlie these two diseases are often the same. The children at risk of diarrhoea are the same ones at risk of pneumonia. If planned properly, the introduction of rotavirus vaccine can help strengthen systems for the delivery of the other diarrhoea (and pneumonia) interventions (integrated logistics, training, etc.).</td>
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### Identify activities to establish/ enhance rotavirus disease surveillance system and to monitor and evaluate progress with implementation of rotavirus vaccine

The epidemiological impact of rotavirus vaccination should be monitored over time, to document the progress made and inform adjustments in policy as appropriate. Monitoring and evaluation are essential to assess how well a public health programme is functioning and what impact it is achieving. High-quality surveillance should be conducted in selected countries and defined populations, including high child mortality settings. However lack of surveillance should not be an impediment to rotavirus vaccine introduction.

Both monitoring and evaluation generate data that can be used to improve programme planning and management.

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<th>Planning element</th>
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<tr>
<td>8</td>
<td>Identify activities to establish/ enhance rotavirus disease surveillance system and to monitor and evaluate progress with implementation of rotavirus vaccine</td>
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### Prepare a plan to monitor and investigate any adverse events following immunization (AEFI)

A plan for monitoring of AEFIs and training of staff that will be responsible for AEFI monitoring should be in place before the vaccine is introduced. In large controlled trials, no differences were observed between the vaccine groups and the placebo groups in terms of serious adverse events. However, in some, but not all settings, post-marketing surveillance has detected a small increased risk of intussusception (about 1–2 cases/100 000 infants vaccinated) shortly after the first dose. Still, the benefits that rotavirus vaccination provides, through prevention of severe diarrhoea and death from rotavirus infection, far exceed the risk of intussusception.

Countries should develop a strategy to inform relevant health staff that although the benefits outweigh the risks, a small potential risk of intussusception after rotavirus vaccination remains.

Health staff must be encouraged to strengthen the detection, reporting and investigation of intussusception cases and RVGE cases to further assess risks and benefits of this vaccine\(^6\).

<table>
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<th>Planning element</th>
<th>Description</th>
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<tr>
<td>9</td>
<td>Prepare a plan to monitor and investigate any adverse events following immunization (AEFI)</td>
</tr>
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</table>

### Prepare an introduction plan at national level and facilitate the development of district and local level micro-plans for rotavirus vaccine introduction

When introducing a new vaccine into routine childhood immunization schedules, proper planning to accommodate the various aspects of a new vaccine is crucial for successful introduction. A detailed introduction plan including all required activities and adjustments to the immunization programme is required for an orderly and successful introduction of rotavirus vaccine.

The introduction plan should be accompanied by specific micro-plans at sub-national level that describe the activities, timelines and staff responsibilities at different levels in detail.

The rotavirus introduction plan should be integrated into the national comprehensive multi-year plan for immunization (cMYP) and benefit from the technical inputs of the National Immunization Technical Advisory Group (NITAG) and support from the Inter-Agency Coordinating Committee (ICC) and other relevant stakeholders.

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<td>10</td>
<td>Prepare an introduction plan at national level and facilitate the development of district and local level micro-plans for rotavirus vaccine introduction</td>
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It is estimated that nearly all children will be exposed to rotavirus before 3-5 years of age, regardless of where they are born.

Rotaviruses are the leading cause of severe, dehydrating diarrhoea in children aged <5 years globally. Children in low-income countries acquire the infection early during the first year of life and the median age at the primary rotavirus infection ranges from 6 to 9 months (80% occur among infants <1 year old).

In high income countries, the first episode may be delayed until the age of 2–5 years, though the majority still occur in infancy (65% occur among infants <1 year old)7.

The percentages of all rotavirus gastro-enteritis (RVGE) cases in children ≤3 years old which are estimated to occur by a given age are:

<table>
<thead>
<tr>
<th>Age in weeks</th>
<th>% of RVGE cases in children ≤ 36 months of age</th>
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<tbody>
<tr>
<td>by 6 weeks</td>
<td>1%</td>
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<tr>
<td>by 9 weeks</td>
<td>3%</td>
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<tr>
<td>by 13 weeks</td>
<td>6%</td>
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<tr>
<td>by 15 weeks</td>
<td>8%</td>
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<tr>
<td>by 17 weeks</td>
<td>10%</td>
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<tr>
<td>by 26 weeks</td>
<td>22%</td>
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<tr>
<td>by 32 weeks</td>
<td>32%</td>
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</table>

However, there are substantial differences among countries. In addition, data suggest that children in the poorest, typically rural, households with the highest risk of mortality may have the earliest exposure to rotavirus.

KEY TASKS

Know the age distribution of the RVGE in your country (or in similar or neighbouring countries) to ensure that the infants are protected before they are infected with rotavirus.

1. If available, assemble existing national data on the age distribution of RVGE cases and deaths:
   - Use available data from national surveillance network or sentinel sites;
   - Identify local researchers working in-country through literature review and informal methods and contact them to obtain additional data.

2. Analyze the data using narrow age-groups, particularly for infants (e.g. < 1 month, 1-5 months, 6-11 months, 12-17 months, 18-23 months, > 24 months of age).

3. If available, compare age distributions for RVGE admissions with those for RVGE deaths, RVGE cases in the community, and ‘any diarrhoea’.

4. Compare the age distributions using different potential modifiers (e.g. geographic area, urban and rural settings etc.).

5. If you cannot identify local data, use regional or global reviews or rotavirus epidemiology. The following website can provide you with access to such data (http://immunization_schedules.com/).

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Below is the age distribution of rotavirus gastroenteritis deaths by WHO Mortality Stratum⁶.

In Stratum D (high child and high adult mortality) the peak of the estimated deaths is approximately 26 weeks of age.

Examples of age distribution of rotavirus gastroenteritis cases in some countries are presented⁶.

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⁶ WHO subregions are stratified (A through E) based on levels of child and adult mortality: Stratum A, very low child and very low adult mortality; Stratum B, low child and low adult mortality; Stratum C, low child and high adult mortality; Stratum D, high child and high adult mortality; Stratum E, high child and very high adult mortality. Please consult the List of Member States by WHO region and mortality stratum available at www.who.int/entity/whr/2003/en/member_states_182-184_en.pdf, accessed January 2013.
Eastern Mediterranean Region (EMR)

**Egypt**

**Jordan**

**Morocco**

**Oman**

**Tunisia**

**Yemen**

European Region (EUR)

**England & Wales: laboratory surveillance**

**France: hospital admissions**

**Israel: hospital emergency room visits**

**Kyrgyzstan: hospital admissions**

**Russian Federation: hospital admissions**

**Uzbekistan: hospital admissions**

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South East Asian Region (SEAR)

Bangladesh: hospital admission

Trichy & Vellore, India: hospital admissions

Thailand: hospital admissions

Western Pacific Region (WPR)

Fiji: hospital admissions

Lao: hospital admissions

Mongolia: hospital admissions

New Zealand: hospital admissions

PNG: hospital admissions

Vietnam: hospital admissions
If analysis shows that in your country rotavirus cases occur mostly in young infants you should include actions in your plan to ensure that all doses are given on time in order to have the maximum protective impact of vaccination. This may involve planning training for health workers on the need to vaccinate on time and the use of active defaulter tracking, as well as strong interpersonal skills to explain to caregivers the importance of returning on time for other doses. Effective communication and social mobilization efforts will be very important. Good supervision and on-going monitoring of data will also be necessary.
Review the age at which children are receiving each dose of DTP/pentavalent vaccine (timeliness) and the coverage achieved

The immunization schedule defines the minimum age for receipt of vaccines. It is important to take effective steps to ensure all vaccinations are given at the recommended age and not delayed.

Although the coverage achieved with each dose of DTP/penta by 12 months of age in a country may be >80%, it is important to establish what proportion of those children did not receive their doses of DTP/penta vaccines at the recommended ages (i.e. “on time”).

Rotavirus vaccine can be given to infants at any age, along with the DTP/penta vaccine doses. The first dose should be administered at 6 weeks of age or soon thereafter.

Frequently a significant proportion of children do not receive their doses on time or early enough, thus leaving them unprotected or inadequately protected during the time period where the risk of rotavirus infection and disease is greatest.

Moreover, DTP/pentavalent coverage among infants at the highest risk of death (e.g. lowest socio-economic level) is often lower than the national average.

Implementing strategies to reduce the number of unvaccinated children and/or children vaccinated late is important for rotavirus vaccine and also for strengthening the overall performance of the programme.

Health education and mass mobilization of the community are essential not only to increase the coverage but also for the timely receipt of vaccines. Timely commencement of immunization and completion of the schedule should be emphasized. Health workers need
to be trained to not miss any opportunity to vaccinate children coming to health facilities for any reason and, to implement strategies to reach infants who do not have regular access to immunization services (e.g. outreach, periodic intensification of routine immunization (PIRI), etc).

Strategies to improve the timeliness of vaccination:

1. *Messages to mothers/caregivers:* At time of vaccination, ensure that health workers give clear information to mothers/caregivers about when the child must return for their next scheduled dose.

2. *Health Facility Immunization Reminder Box:* Health workers can keep track of infants due for vaccination by filing a copy of the immunization card in a box with dividers for each month. If an infant received Rota1 in January, then a copy of the card is placed in the February section. Every month, the health worker can review the reminder cards and follow up with those who did not attend when due (e.g. active follow-up of defaulters).

3. *Regular Outreach Planning:* Ensure that outreach sessions are carefully planned and implemented to enable children in these areas to get their vaccines on time.
Below are some examples of analysis of age at vaccination with each dose of DTP using data from coverage surveys.
While childhood immunization coverage levels have increased since the 1980s, inequities in coverage within countries are common.

The introduction of a new vaccine provides the opportunity to strengthen the overall immunization programme and, to increase coverage in low performing areas.

National immunization programmes should estimate and monitor the proportion of unvaccinated children (i.e. those who have received no vaccines at all or with incomplete vaccination).

Factors that have been identified as strongly associated with being unvaccinated include: education of the caregiver, education of caregiver’s partner, caregiver’s tetanus toxoid (TT) status, wealth index and type of family member participation in decision-making when the child is ill.

An analysis of immunization coverage should be performed as part of the rotavirus introduction plan. It should focus on subnational levels or areas where poor performance is suspected. National/subnational representative household surveys can provide evidence on the specific factors that influence access to immunization services.

National immunization programmes should develop specific plans to address the determinants of non-vaccination at national and sub-national levels.

**KEY TASKS**

Rotavirus vaccine coverage needs to be high among children who are at greatest risk of dying from RVGE.

1. Analyze immunization coverage by sub-national levels for the last 3 years.
2. Identify sub-national levels or areas where most unvaccinated or partially unvaccinated children live. For example, using population and coverage data estimate the number of unvaccinated infants and sort the areas, listing first those with greatest number of unvaccinated or partially unvaccinated children.
3. Discuss with relevant immunization staff in those areas, and identify using a similar approach, the areas within the sub-national level where the greatest number of unvaccinated or partially unvaccinated children live.
4. Use available information (or investigate) to identify the factors that may be associated with being unvaccinated in those areas.
5. Identify activities that can address those factors and effectively reduce the number of unvaccinated children.
6. Ensure that the identified activities are reflected in the national plan for introduction and in the sub-national levels micro-plans.
To support country level efforts to improve immunization coverage, the "Reaching Every District" (RED) strategy was developed. RED is a strategy to achieve the goal of 80% immunization coverage in all districts and 90% nationally. RED aims to fully immunize every infant with all vaccines included in the national immunization schedule of countries. In order to achieve this goal, the strategy focuses on building national capacity from district level upward to maximize access to all vaccines, old and new. RED addresses common obstacles to increasing immunization coverage such as poor quality district planning, low quality and unreliable service, inadequate monitoring and supervision of health workers.

Description of the five RED operational components

1. Re-establishing outreach services
   In many countries a large proportion of the population can only be reached regularly though outreach sessions. Outreach is any delivery strategy that requires health facility staff to leave their facility to deliver immunization. Ideally a minimum of four contacts per year are required to fully immunize an infant. For some communities, access can only be provided irregularly, and may require mobile teams to provide outreach, which will involve resources beyond the health facility and district level. Outreach sessions, especially mobile teams present opportunities to provide other interventions with immunization.

2. Supportive supervision
   Supportive supervision implies providing on-site training to health workers at the time of a supervisory visit, or at regular district meetings. To be supportive, supervisors should make regular schedules for visits, help to solve problems locally and follow up regularly with supply and resource issues. Supervisors will themselves need training to adapt their own approaches to supervision.

3. Linking services with communities
   Involving the community with the planning and delivery of the service will encourage community ownership and improve attendance. Identifying community volunteers providing them with a role, such as follow up of defaulters, and holding regular meetings is an important step towards building a link with the community.

4. Monitoring and use of data for action
   Monitoring and use of data for action implies not only the timely collection of data at district level, but the use of the data to solve problems. Some simple tools, including wall charts that display access and utilization, need little training, but are very useful to take action according to monthly progress. Not only do districts collect coverage data, but also a large amount of other information, including logistics, supply, surveillance, all of which should be used to improve the immunization system. Some qualitative data may not be available in regular reports and may need to collected though supervisory visits.

5. Planning and management of resources
   The district micro plan is the key to the RED strategy. The micro plan should be based upon a local situation analysis which involves every health facility and through them the community that they serve. At the national level, there is a responsibility to ensure the needed financial and human resources are available to the district, while the district must ensure the resources are efficiently used, through regular monitoring and adjusting the micro plan. Continuing to fund the RED strategy for more than the first year of implementation is vital for sustainability of coverage increase.

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http://www.who.int/immunization_delivery/systems_policy/red/en/
Select the vaccine and vaccination schedule that is most suitable for your country

Two WHO prequalified oral rotavirus vaccines are marketed internationally:\n- the monovalent (RV1) Rotarix® (GlaxoSmithKline Biologicals, Rixensart, Belgium) and
- the pentavalent (RV5) RotaTeq® (Merck & Co. Inc., West Point, PA, USA).

Currently available efficacy and safety data support selection of either of the two vaccines for national use.

Although both rotavirus vaccines are efficacious, data show that their efficacy is higher in settings with low mortality in children under five years of age (vaccine efficacy ~ 90%) than in settings with high mortality in children under five years of age (vaccine efficacy~ 60%).

Because the incidence of rotavirus disease is significantly higher in high child mortality settings, the number of severe disease and deaths averted by rotavirus vaccines in these settings is likely to be greater than in low mortality settings, despite the lower vaccine efficacy.

Observational studies in countries that have already introduced rotavirus vaccine have reported a substantial reduction in disease burden within a few years after introduction and also some evidence of herd protection expressed as disease reduction in unvaccinated older children and adults. Data also suggest that rotavirus vaccination has delayed the onset and decreased the size of the annual seasonal peaks of rotavirus disease.

KEY TASKS
Vaccination should be scheduled as early as possible; and this is especially important for rotavirus vaccine as many children will be exposed to rotavirus during the first months of life.

1. Review the operational characteristics of the two commercially available rotavirus vaccines.

2. Consider given the current national immunization schedule which vaccine could be more suitable for your country (e.g. opportunities to deliver during already established immunization contacts, cold chain capacity, etc.).

3. Seek inputs from the country National technical Advisory Group (NITAG) on your proposed vaccine and schedule choices.
Table 1. WHO Recommended Vaccination Schedules for Rotarix® and RotaTeq®

<table>
<thead>
<tr>
<th>Antigen</th>
<th>Age of 1st dose</th>
<th>Doses in primary series</th>
<th>Interval between doses</th>
<th>Booster dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rotavirus</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rotarix® (RV1)</td>
<td>6 weeks (min) given with DTP1/penta1</td>
<td>2</td>
<td>4 weeks (min) given with DTP2/penta2</td>
<td>none</td>
</tr>
<tr>
<td>Rotateq® (RV5)</td>
<td>6 weeks (min) given with DTP1/penta1</td>
<td>3</td>
<td>4 weeks (min) given with DTP2/penta2</td>
<td>4 weeks (min) given with DTP3/penta3</td>
</tr>
</tbody>
</table>

- Rotavirus vaccinations can be administered simultaneously with other vaccines in the infant immunization programme.
- The interchangeability of Rotarix® and RotaTeq® has not been studied.
- Severe allergic reaction (e.g. anaphylaxis) after a previous dose, and severe immunodeficiency including severe combined immunodeficiency (SCID), are contraindications for rotavirus vaccination.
- Precautions are necessary if there is a history of intussusception or intestinal malformations, chronic gastrointestinal disease, and severe acute illness. Vaccination should be postponed in case of on-going acute gastroenteritis or fever with moderate to severe illness until the child recovers. The presence of minor infections, however, is not a contraindication for vaccination.
- Current rotavirus vaccines are generally well tolerated. They do not appear to cause any serious adverse events. A small proportion of infants receiving the vaccine may suffer short episodes of mild diarrhoea, vomiting or fever in the week following vaccination.
- Intussusception was found to be a rare but significant side effect of the first generation rotavirus vaccine (RotaShield®) that was available in the United States in 1998-1999 but is no longer available. The new vaccines Rotarix® and RotaTeq® were both tested in large studies designed to exclude a risk of intussusception similar to RotaShield®. In these studies no increased risk of intussusception was observed. As even large pre-registration safety studies cannot detect rare events, post-marketing studies have been undertaken in a number of countries. Apart from a low risk of intussusception (about 1–2 per 100 000 infants vaccinated) the current rotavirus vaccines are considered safe and well tolerated (for more information see Annex 4).

Assess the logistic implications of your vaccine and schedule selection

The national immunization manager should assess the available vaccine formulation options (lyophilized/liquid) and presentation (type of prefilled oral applicator/tube) with respect to immunization programme’s requirements.

Factors that need to be considered during the selection include:

- number of other vaccines administered per visit
- cold storage space available and additional needs
- VVM on the label
- vaccine wastage (e.g. for Rotateq which has no VVM)
- staff training and supervision
- recording and reporting mechanisms
- programme costs, not just for the price of the vaccine but for the programmatic/operational costs of the different options and, the sustainability over time.

The assessment should lead to a decision on one or more preferred options. The results should include a summary of a ranking of options, criteria considered during the selection process, as well as planning of the steps to tackle any issues/constraints.

The two available rotavirus vaccines differ in operational characteristics which are summarized in Table 2 below.

These different vaccine characteristics should be carefully considered within the context of the current national immunization programme, infant immunization schedule, infrastructure, and budget in order to select the most appropriate vaccine for the country. All four presentations of rotavirus vaccine require additional space for transport and storage in the cold chain (see Annex 2).

KEY TASKS

To successfully integrate rotavirus vaccine into the national vaccination schedule, existing logistic systems may need to be adjusted.

1. Review the operational characteristics of the commercially available prequalified rotavirus vaccines.
2. Evaluate any vaccine supply considerations in the short and long term.
3. Assess any budget implications of your choice of vaccines (e.g. vaccine price, operational and logistics costs associated).
4. Seek inputs from the country National technical Advisory Group (NITAG) on your proposed adjustments to logistics and other key issues.
Table 2. Important attributes of commercially available Rotavirus vaccines

| **GSK Rotarix® - monovalent, human strain, live, attenuated, oral rotavirus vaccine** |
|-----------------|---------------------------------------------------------------|
| **Vaccine type** | RV1 is a live vaccine |
| **Route of administration** | Oral |
| **Immunization schedule** | 2-dose schedule, given with first and second doses of DTP/penta. |
| **Dose** | Each dose contains a suspension of at least 10⁶.0 — the median cell culture infective dose (CCID₅₀) — of live, attenuated human G1P[8] rotavirus particles. |
| **Shelf life** | The vaccine shelf-life is 36 months. |
| **Storage requirements** | Should be kept at 2–8 °C, protected from light, and should not be frozen. |
| **Presentation** | Liquid Rotarix™ in oral applicator (single dose) |
| | Liquid Rotarix™ in squeezable polyethylene tube (single dose) |
| | Lyophilized Rotarix™ vaccine reconstituted with CaCO₃ buffer (single dose) |
| **Volumes** | 1.5 ml |
| | 1.5 ml |
| | 1 ml |
| **Packaging** | 1 and 10 single-dose oral applicators per pack. |
| | 1,10, or 50 single dose tubes per pack |
| | 1 and 10 single-doses per pack. |
| | The vaccine is packed together with diluent and should be stored as such. Significant cold chain volume implications (156 cm³/dose) |
| **Storage volume** | See Annex 3 |
| | See Annex 3 |
| | See Annex 3 |
| **Vaccine vial monitor** | It has a VVM 14 |
| | It has a VVM 14 |
| | It has a VVM 14 |
| **Source** | Source: GSK Biologicals |

12 Further information may be found on the following website:
**Merck RotaTeq® - pentavalent, human-bovine reassortant strain, live, attenuated, oral, rotavirus vaccine**

<table>
<thead>
<tr>
<th><strong>Vaccine type</strong></th>
<th>RV5 is a live vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Route of administration</strong></td>
<td>Oral</td>
</tr>
<tr>
<td><strong>Immunization schedule</strong></td>
<td>3-dose schedule, given with three doses of DTP/penta.</td>
</tr>
<tr>
<td><strong>Dose</strong></td>
<td>Each dose (2 ml) of the vaccine contains a minimum titre of approximately $2.0 - 2.8 \times 10^6$ infectious units per reassortant, and not greater than $116 \times 10^6$ infectious units per aggregate dose.</td>
</tr>
<tr>
<td><strong>Shelf life</strong></td>
<td>The vaccine shelf life is 24 months.</td>
</tr>
<tr>
<td><strong>Storage requirements</strong></td>
<td>Should be stored at 2–8 °C, protected from light and should not be frozen. Following removal from refrigeration, the vaccine should be used as soon as possible.</td>
</tr>
<tr>
<td><strong>Presentation</strong></td>
<td>One presentation: oral squeezable tube (single dose)</td>
</tr>
<tr>
<td><strong>Administration</strong></td>
<td>Administered orally using the squeeze tube.</td>
</tr>
<tr>
<td><strong>Volume per dose</strong></td>
<td>2 ml/dose</td>
</tr>
<tr>
<td><strong>Packaging</strong></td>
<td>Available in cartons of 1,10, 25 single-dose tubes per pack</td>
</tr>
<tr>
<td><strong>Storage volume</strong></td>
<td>See Annex 3</td>
</tr>
<tr>
<td><strong>Vaccine vial monitor</strong></td>
<td>The vaccine tubes do not have VVMs.</td>
</tr>
<tr>
<td><strong>Source</strong></td>
<td>Source: Merck &amp; Co.</td>
</tr>
</tbody>
</table>
To successfully integrate rotavirus vaccine into the national vaccination schedule, existing systems may need to be modified.\(^{13}\)

It will be useful to consider the additional points below when updating a country multi-year plan (cMYP) to include rotavirus vaccine introduction:

- supply needs
- cold-chain readiness
- vaccine wastage (e.g. for Rotateq which does not have a VVM)
- revision of records and reporting tools
- staff training and supervision
- information, education and communication

**Supply needs**

Estimate the number of doses of rotavirus vaccine needed per year. The process for estimating the number of vaccine doses needed is similar to other vaccines. In the forecasting of vaccine needs, safety stock (also referred to as buffer stock) should be adequate to cover unexpected delays in shipments and fluctuations in demand.

Since rotavirus vaccines are orally administered, syringes and equipment for safe needle disposal are not required and therefore do not need to be calculated.

**Cold storage and transport readiness**

Review current storage and transport capacity in the cold chain and assess if additional capacity is required and at which level.

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As mentioned above, as with any new vaccine introduction, the introduction of rotavirus vaccine requires additional cold chain and transport capacity (see Annex 1 and 2 for a detailed summary of volume per dose for all available products).

It is important that a comprehensive assessment and gap analysis of the storage space at all levels is carried out once the decision has been made to introduce rotavirus vaccine. Such an analysis should be done as early as possible in order to have sufficient time to fund, procure, receive and install new equipment before vaccine introduction.

The use of digital temperature monitoring devices, such as fridge tags and log tags, is strongly recommended at national and sub-national levels to accurately record any excursions outside the recommended temperature range of 2° to 8°C and develop and implement measures to prevent their recurrence.

**Monitoring of the cold chain**

Rotavirus vaccine should be stored and transported at 2° to 8°C from receipt at national level to its final point of administration to infants. Maintaining temperatures within this range is critical to protect the potency of the vaccine.

These vaccines should not be exposed to sub-zero temperatures, and all frozen water packs should be properly conditioned prior to packing in cold boxes or vaccine carriers. If the vaccines are stored at WHO recommended temperatures, the vaccines have a shelf-life of two or three years (depending on the product) from the point of manufacture.

At storage points, temperatures should be recorded twice daily on a monitoring chart and corrective action taken immediately if there is a cold chain failure. Establishing an effective temperature monitoring and recording system of cold chain performance is particularly critical in cases where the chosen vaccine does not have a VVM.

Exposure to high temperatures does not result in any visual difference to the product. In the absence of a VVM, there is no means to determine the extent of heat damage which can occur at multiple points in the distribution chain.

It is, therefore, extremely important that cold chain conditions are rigorously maintained and closely monitored both during storage and transport from vaccine receipt to vaccine administration.

For rotavirus vaccine furnished without VVMs (Rotateq®), it is highly recommended to use continuous temperature monitoring devices to store and transport vaccines under cold chain conditions as specified by the manufacturer. Any break in the cold chain should be recorded and immediately reported through the supervisory channels. VVMs attached to other vaccines cannot be used as a proxy to determine the cumulative level of heat exposure experienced by RotaTeq®.

In situations where continuous temperature monitoring devices are not available, the following is recommended:
- Discard unopened tubes immediately if there is a complete and sustained rupture in the cold chain and the ambient temperature exceeds 25°C;
- Discard unopened tubes if there is a temporary rupture in the cold chain and the vaccine is exposed to temperatures between 9° to 25°C for more than 36 consecutive hours;
- Discard unopened vaccine tubes at the end of outreach or mobile sessions if there is no assurance that the cold chain was maintained.
**Vaccine wastage**

Wastage rates should be routinely monitored for all vaccines. It is important to minimize wastage. In addition to saving funds, monitoring and preventing wastage can be an indicator of good programme management, especially relevant if the vaccine being used does not have a VVM.

In countries with a dispersed population and extensive outreach, a higher wastage rate may be acceptable in order to achieve and maintain high coverage levels. Therefore, the appropriate goal is wastage optimization, which means to minimize preventable wastage without compromising coverage or safety.

The two currently available rotavirus vaccines are packaged as single-dose presentations for oral administration. For single-dose presentations, the wastage rate when administering the vaccine is negligible. However, for planning purposes a wastage rate of up to a maximum of 1%\(^\text{14}\) per storage point can be used for the estimation of needs. This 1% wastage rate is set by EVM\(^\text{15}\) to account for unexpected unopened wastage during handling operations in the supply chain. For any part of the supply chain, the anticipated wastage rate for planning purposes should not exceed the number storage levels times(x) 1%. In most countries, for the national level the wastage rate will not exceed 5%.

If the wastage rate for rotavirus vaccine begins to increase nationally or in specific sub-national locations, an investigation should be undertaken to ascertain the reason for the increase.

**Waste Disposal**

Used rotavirus vaccine oral applicators or squeeze tubes should be disposed of in the same manner as other vaccine vials are discarded and in accordance with national waste management guidelines.

**Revision of records and reporting tools\(^\text{16}\)**

The main recording tools that are used for immunization-related activities should be adapted/revised to include rotavirus vaccine. At the service delivery level these include:

- Immunization or child health card
- Tally sheet
- Register
- Defaulter tracking system
- Stock record
- Integrated monthly report.

**Immunization or child health card**

The card may be the only record of immunization history and status available for health workers if the facility registers do not exist or if clients move from one health facility to another. Each child should have a card with the rotavirus vaccine doses marked clearly with dates of administration (not tick marks).

**Tally Sheet**

Tally sheets are the forms that health workers use to document an immunization session, by making a record for every dose of vaccine given. Tally sheets should be used for all sessions whether fixed, outreach or conducted by mobile teams. It is always worthwhile for

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\(^{14}\) Wastage could be higher if vaccine does not have a VVM.


a supervisor to spend time reviewing tally sheets with staff to improve the quality of reporting. Tally sheets need to be adapted to include rotavirus vaccines.

**Immunization Register**
While tally sheets record the doses given for each session, the immunization register records doses given to each individual and helps health workers keep track of the immunization services that they have given each child (and pregnant woman).

The register should be adapted so that the same can be done for each dose of rotavirus vaccines. Each dose of rotavirus vaccine given to every child in the catchment area should be recorded against their names in the register.

In this way, the immunization register is the basis for tracking individual immunization status (if, for example, the child health or vaccination card is lost), and for tracking defaulters.

**Staff training and supervision**
The introduction of a new vaccine provides an opportunity for training health care workers on administering the new vaccine, while also providing the opportunity for refresher training on other vaccine-related issues, such as the cold chain, waste management, communication with the population, etc.

Appropriate training and temperature monitoring practices should be enforced to promote proper vaccine handling at all stages of the cold chain. As with any new vaccine introduction plan, for the introduction of rotavirus vaccine, immunization programme managers at national and sub-national levels must determine whose work will be affected and how.

### Training of health workers
The following key issues should also be considered in preparing for health-worker training:

- It is important to familiarize health workers with relevant issues concerning rotavirus infection and the new vaccine since they will need to communicate effectively with community leaders, parents and other members of the public concerning these topics. Frequently Asked Questions are provided in Annex 7.
- Health workers should be trained on the correct way to store the vaccine, which is sensitive to freezing.
- They should also be trained on how to properly administer the full volume of the vaccine through the oral route, taking time to assist the infant to swallow. Package inserts from each manufacturer contain helpful details on administering the vaccines. Further information on vaccine administration is shown in Annex 8: *Rotavirus Vaccines: A Pocket Guide for Health Workers*.
- In countries that introduce monovalent lyophilized rotavirus vaccine, it is important to ensure that health workers receive clear instructions on the correct practice for reconstituting the lyophilized formulation, and/or administering rotavirus vaccine, and subsequent supervision in the field, until they become familiar with using the new vaccine.
- Health workers will need to make adjustments in order to include rotavirus vaccinations in routine recording and reporting practice.

After training and once the new vaccine has been introduced, supervisors should routinely ensure that staff are following the recommended practices that they have been taught. If standards are not met, supervisors should address and help staff resolve any obstacles.
Advocacy, Communication and Social Mobilization

In order to assure good uptake and acceptability, effective advocacy, communication and social mobilization activities need to be planned and implemented as part of rotavirus vaccine introduction (Annex 6).

It is best practice to develop an advocacy and communications plan. The communications plan and subsequent activities, materials, and messages will be most effective if they are informed by a study of the public’s knowledge, attitudes, beliefs and practices (KABP) about rotavirus disease, rotavirus vaccine, and immunization in general.

KABP studies can range from a series of focus group discussions to more involved community and household surveys. They should target a range of different groups, including community and opinion leaders, teachers, health workers, and parents. The study can identify gaps in the public’s knowledge and attitudes about diarrhoea, misperceptions and concerns about receiving rotavirus vaccine, and other factors that may affect the public’s acceptance and thus uptake of the vaccine, such as the influence of anti-vaccination publicity.

It is important to develop materials tailored for different target audiences and to use a range of different channels and media to deliver the messages. Obtaining the support from and involving respected political, religious and community leaders and a broad range of influential groups and members of society is vital to communicate information to the community, to renew awareness of immunization, and to allay possible safety concerns about rotavirus vaccine and to correct misinformation.

Health workers are encouraged to build regular linkages with community leaders, local authorities and community mobilisers to raise awareness on the value of rotavirus vaccination and the importance of children receiving doses on time.

The health worker should advise community leaders of the time, date and location of the next outreach/mobile visit, or the next scheduled immunization session at the fixed-site, and invite leaders to influence the attendance of families.

Key messages for health workers

Many caretakers are familiar with the signs of diarrhoeal disease and will welcome the opportunity to vaccinate their children to prevent one of the important causes of infant diarrhoea and mortality.

Health workers should be equipped with appropriate communication tools to be able to explain key messages to the community.

**KEY MESSAGES FOR HEALTH WORKERS**

- The infant must receive all doses of the vaccine to be fully protected and he/she must complete the schedule as early as possible (e.g. receive doses on time).

- Health workers should clearly communicate the time, date and location of the next outreach/mobile visit, or the next scheduled immunization session at the fixed-site, and encourage the caretakers’ return.
- The rotavirus vaccine protects the infant against one important cause of diarrhea, but not all causes. Therefore, a child vaccinated with Rotavirus vaccine may still get diarrhoea from other agents.

- Prevention of childhood diarrhoeal diseases also requires improvements in exclusive breastfeeding for 6 months, vitamin A supplementation, safe water, hygiene (such as handwashing with soap), and vitamin A supplementation.

- If the infant suffers from severe diarrhoea, take him or her to the health center or community health worker immediately to get treatment – e.g. oral rehydration solution (ORS), zinc tablets, and continued feeding.

- Know how to recognize the signs and symptoms of intussusception in an infant (see Annex 5) and refer immediately to a health care facility for treatment.
Rotavirus vaccine protects against one cause of diarrhoea, but not all causes. Therefore, the use of rotavirus vaccine needs to be part of a comprehensive strategy to control diarrhoeal diseases with the scaling up of both prevention and treatment packages.

The Integrated Global Action Plan for the Prevention and Control of Pneumonia and Diarrhoea (GAPPD) from WHO and UNICEF (April 2013)\(^7\) goes to the heart of this challenge: recognizing that prevention and control of pneumonia and diarrhoea cannot be adequately dealt with separately but only through integrated programmes.

WHO/UNICEF recommend that all children receive solutions of low-osmolarity oral rehydration solution (ORS) to treat diarrhoea.

Breast milk is also an excellent rehydration fluid and should be given to infants still breastfeeding, along with ORS. In addition to fluid replacement, children with diarrhoea should continue to be fed during the episode. Food intake supports fluid absorption from the gut into the bloodstream to prevent dehydration and helps maintain nutritional status and ability to fight infection. Children should also simultaneously receive zinc treatment which reduces the duration and severity of diarrhoea episodes, stool volume and the need for advanced medical care.

Therefore the rotavirus introduction plan should include clear strategies and activities to facilitate the coordination of strategies at national level, the convergence of activities in the micro-plans at sub-national level, and the integration of tasks at the service delivery level.

Monitoring and evaluation are essential to assess how well a public health programme is functioning and achieving its objectives.

Both monitoring and evaluation generate data that can be used to improve programme planning and management.

WHO recommends that all countries that have introduced rotavirus vaccine conduct a post-introduction evaluation (PIE) six to 12 months following introduction.

The purpose of the assessment is to evaluate the impact of introduction on the country’s immunization programme and to rapidly identify problems needing correction that are the result of the introduction of rotavirus vaccine or that pre-existed it.

The evaluation can not only lead to improvements in the implementation of the new vaccine and overall immunization programme, but can also provide valuable lessons for future vaccine introductions.

WHO has prepared a user-friendly tool for assessing new vaccine implementation, which includes questionnaires and checklists that countries can adapt18.

### KEY TASKS

The impact of rotavirus vaccination should be monitored over time, to document the progress made and inform adjustments in policy as appropriate.

1. Review progress of your introduction plan with your NITAG (6-12 months after vaccine introduction) and assess whether or not the plan is being implemented as proposed. Conduct a post-introduction evaluation (PIE) to:
   - Identify areas of weak performance or specific areas where further input may be needed and take action to address them.
   - Collect information demonstrating success that can be used in future advocacy efforts that will support the long-term sustainability of the programme.
   - Identify the major bottlenecks for successful implementation and propose solutions as appropriate.

2. Select a surveillance strategy and identify activities to establish/strengthen rotavirus surveillance.

3. Incorporate into the vaccine-preventable diseases surveillance system the necessary activities to set in place surveillance of rotavirus disease.

4. Continue to review progress regularly (e.g. each year).

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18 The generic protocol can be found at: [http://www.who.int/nui/PIE_tool/en/index.html](http://www.who.int/nui/PIE_tool/en/index.html)
Epidemiological surveillance data are important to guide decisions around vaccine introduction and use. However, if countries have not yet established rotavirus surveillance, this should not be an impediment to the introduction of rotavirus vaccine.

**Objectives of the surveillance system of diarrhoea caused by rotavirus**

The main objectives are to define the epidemiology of rotavirus gastroenteritis, to estimate the burden of disease prior to introduction of rotavirus vaccine, to guide the implementation of adequate control measures (including but not limited to rotavirus vaccine) and, to evaluate the impact of the rotavirus vaccine after introduction.

Two general approaches would meet the objectives of monitoring disease trends in the context of assessing vaccine impact:

- Analyzing primary data sources, such as an active, gastroenteritis surveillance system;
- or
- Analyzing secondary data sources, for example national data on gastroenteritis hospitalizations.

Countries should consider the following:

- Sentinel hospital-based surveillance sites at a few selected hospitals can provide data to document disease burden, baseline trends in epidemiology, seasonality, age distribution and strain distribution. Although sentinel surveillance has certain limitations in terms of population representativeness, valuable data can be obtained far more cost-effectively than establishing rotavirus surveillance nationwide.
- Using surveillance data to assess vaccine impact on disease burden requires consistent and reliable surveillance data from before vaccine introduction and for at least 3 years after vaccine introduction to provide an accurate estimate of disease incidence.

WHO recommends that rotavirus surveillance target all children aged 0-59 months admitted for the treatment of acute (i.e. ≤14 days) watery gastroenteritis/diarrhoea to a sentinel hospital conducting surveillance.

Excluded are children with bloody diarrhoea and children transferred from another hospital. Rotavirus surveillance must use laboratory analysis to confirm whether an acute diarrhoea case is caused by rotavirus, as there are many other causes of diarrhoea that are not prevented by rotavirus vaccine.

As rotavirus vaccination becomes more widely established in immunization programmes, new birth cohorts will be immunized and protected. Thus, a greater proportion of severe diarrhoea cases will be caused by pathogens other than rotavirus, however, overall a reduction in diarrhoea hospitalizations should be observed in the longterm.

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Prepare a plan to monitor and investigate any adverse events following immunization (AEFI)

WHO recommends that all immunization programmes have routine AEFI monitoring in place, regardless of what vaccines are included in the national immunization schedule. All countries should at least have a system for spontaneous reporting of AEFI and for investigating those that are serious.

It is increasingly important that any country introducing a new vaccine be able to adequately monitor its safety, including detecting and investigating possible reactions or AEFI. Not being able to promptly deal with suspected severe vaccine-related adverse events can cause concern amongst the public, especially in countries with active anti-vaccine groups.

This can lead to low utilization of rotavirus vaccines and potentially of other vaccines as well, and may reduce public confidence in the immunization programme as a whole.

Core variables for AEFI

For optimal vaccine safety monitoring and meaningful analysis of AEFI data, systematic and standard collection of critical parameters is essential. A limited number of variables are required to properly manage AEFI information. This includes a unique identification of the report, the primary source of information, patient characteristics, details of the event(s) and vaccine(s) of interest and the possibility of collecting additional information if needed (see example Annex 4).

Apart from a low risk of intussusception (about 1–2 per 100 000 infants vaccinated) the current rotavirus vaccines are considered safe and well tolerated (see 21 http://www.who.int/vaccine_safety/en/#story-02

KEY TASKS

A plan for AEFI monitoring and, training of staff that will be responsible for AEFI monitoring should be in place before the vaccine is introduced

1. Develop a strategy to inform relevant health staff that although the benefits outweigh the risks, a small potential risk of intussusception after rotavirus vaccination remains.
2. Identify in-country staff who are well-informed about all aspects of the vaccine and are able to discuss the vaccine benefits, risks and how risk is being monitored.
3. Establish channels of reporting and communication in case of reporting of serious adverse events.
4. Develop/adapt forms and standards for the systematic collection and investigation of AEFI and train staff on their use.
5. Ensure that caregivers are adequately trained to recognize danger signs of dehydration or intussusception that need immediate medical consultation.
6. Conduct regular analysis of the rates of reported AEFIs with support of the NITAG and assess the quality of the investigations and response.

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21 http://www.who.int/vaccine_safety/en/#story-02
Because in the countries where Rotarix® and RotaTeq® have been first introduced, the doses are generally being administered in accordance with the recommended age, data on the risk of intussusception for administration of either vaccine at older ages are not available.

However, an analysis of intussusception risk in infants receiving the doses at the recommended ages suggest that both vaccines continue to exhibit a good safety profile, but may be associated with an increased risk of intussusception after the first dose of vaccine in some populations but not in others. The levels of risk observed are substantially less than those observed with the previous vaccine, Rotashield®.

Based on available evidence, both the WHO Global Advisory Committee on Vaccine Safety (GACVS) and the WHO Strategic Advisory Group of Experts (SAGE) on Immunization concluded that the risk benefit analysis continues to favour early immunization but the previous age restrictions for the first dose (<15 weeks) and last dose (<32 weeks) were preventing vaccination of many vulnerable children. By removing the age restrictions, programmes are now being able to immunize children who are currently excluded from the benefits of rotavirus vaccines and this is likely to include some of the children most vulnerable to severe rotavirus disease. Many thousands more deaths would be averted, but may be associated with a small additional increase in intussusception cases22. Therefore, for rotavirus vaccine (as for any other vaccine) it is necessary to establish or strengthen post-marketing surveillance, which should focus on documenting any intussusception cases.

WHO has developed an E-learning course on vaccine safety basics23. The course is designed to serve a broad range of individuals involved in vaccine safety: vaccinating health professionals, national regulatory staff, immunization staff, etc. Health staff must be aware of the small risk of intussusception after rotavirus vaccination and be encouraged to strengthen the detection, reporting and investigation of intussusception cases and RVGE cases to further assess risks and benefits of this vaccine. In addition, caregivers should be adequately counseled to recognize danger signs of an ill infant that requires immediate medical attention (see Annex 5).

**Vaccine safety communication**24

Immunization managers should develop vaccine safety communication plans at country level to promote awareness of vaccine risks and benefits, understand perceptions of risk, and prepare for managing any adverse events and concerns about vaccine safety promptly.

**Communicating about vaccine safety is always important**

It is essential in at least three situations, namely:

1. explaining properly the benefits and risks of a recommended vaccine;
2. addressing public concerns and upcoming or persistent rumours about vaccine safety;
3. preparing to address vaccine safety crises if and when they occur.

Effective communication is an ongoing process that involves all stakeholders. Vaccine safety crises are rare and most are not related to problems with vaccine products. However, unfounded or not, such crises have the potential to disrupt immunization activities, and thereby affect public health.

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Once a decision has been taken to introduce a new vaccine, the strategies and activities needed for the vaccine introduction have to be identified and integrated into the national comprehensive multi-year plan for immunization (cMYP).

Guidelines have been developed to assist country programme managers to prepare or update cMYPs.25

A cMYP Costing and Financing Tool has been developed to estimate the past costs and financing of immunization, and to make projections of future costs, future resource requirements, future financing needs to achieve programme objectives, and to analyze the corresponding financing gaps.

This tool is accompanied by a User Guide which provides an overview of important immunization costing and financing concepts, methodologies and definitions, as well as a step-by-step instruction on how to use the tool, including how to analyze the data and findings26.

It is equally important to encourage and support the development of detailed micro-plans in all the subnational levels. National introduction plans are needed but are not sufficient to ensure the successful introduction of rotavirus vaccines.

The introduction plan should be accompanied by specific micro-plans at sub-national level that describe all the activities, timelines and

KEY TASKS

When introducing a new vaccine into the routine childhood immunization schedule, proper planning to accommodate the various aspects of a new vaccine is crucial to for a successful introduction.

1. Seek guidance from the National Technical Advisory Group (NITAG) on the key elements and strategic considerations for the introduction of rotavirus vaccines.
2. Convene meetings of all key immunization actors, including those working at sub-national level, to identify linkages and coordinate and integrate all aspects of the rotavirus vaccine introduction plan.
3. Prepare a detailed list of all activities required for the successful vaccine introduction and identify the resource needs and potential sources of funding for implementation.
4. Use all the inputs to prepare an introduction plan.
5. Convene the Inter-Agency Coordinating Committee (ICC) or health sector steering committee or other relevant stakeholders meeting to discuss the plan and to take steps to incorporate the rotavirus introduction activities into the cMYP.
6. Support/encourage the development of micro-plans for rotavirus vaccine introduction at sub-national level
7. Work with sub-national level staff to monitor implementation of activities.

25 WHO-UNICEF. 2005. Guidelines for developing a comprehensive multi-year plan (cMYP)

staff responsibilities at different levels in detail.

In countries where there is a large proportion of immunization sessions conducted through outreach or mobile teams, implementation plans require careful consideration.

In the case of outreach or mobile activities, careful micro-planning is encouraged so that the appropriate numbers of rotavirus vaccines are placed in the vaccine carrier; this will minimize unnecessary wastage at the end of the session.

Proper session planning by health centers to reach their catchment populations in a timely manner and the commitment to hold those sessions as planned cannot be over emphasized.

**Seven Planning Steps for the development of comprehensive multi-year plan (cMYP) for immunization**

**STEP 1 Situation Analysis**: Develop a situation analysis based on a review of health system barriers, successes and promising practices as well as identifying the strengths and weaknesses of the immunization system and disease control initiatives. Remember to revisit the recommendations from recent EPI Reviews or other assessments (Cold Chain, Surveillance, Data Quality, etc) to inform the analysis.

**STEP 2 Objectives, Milestones and Priority Setting**: Provide national goals, objectives and strategies for three to five years based on this situational analysis and on priority setting.

**STEP 3 Planning Strategies**: Outline the means (the how) by which national immunization objectives will be achieved.

**STEP 4: Link to National Health Plans and International Goals and Targets**: Link the immunization strategy to National Health Sector strategies, goals and targets, and to Regional targets and the Global Vaccine Action Plan (GVAP) (see: [http://www.who.int/immunization/global_vaccine_action_plan/en/](http://www.who.int/immunization/global_vaccine_action_plan/en/)).

**STEP 5 Set an Activity Timeline and Monitoring and Evaluation Framework**: Establish a timeline for main activities and milestone achievement and develop a national monitoring and evaluation framework for all immunization components.

**STEP 6 Costs, Financing and Financing Gaps**: In the context of the relevant planning cycle and the planning and budgeting cycles of the Ministry of Health, calculate costs and assess financing. Identify financing gaps, resource mobilization strategies and cost benefit analysis, to re-evaluate the plan against available resources.

**STEP 7 Put the cMYP into Action**: Prepare a detailed annual work plan and link the plan to national planning and budgeting cycles at national and sub-national levels of the health system.
### Annex 1: Documented reductions in pneumonia and diarrhoea morbidity and mortality with selected interventions

#### Interventions to Protect

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Reductions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Exclusive breastfeeding for 6 months</strong></td>
<td>23% reduction in pneumonia incidence (1); 10.5 times greater risk of death from diarrhoea and 15.1 times greater risk of death from pneumonia if not breastfed in first 6 months (2); not breastfeeding associated with 165% increase in diarrhoea incidence in 0-5 month-old infants (3); not exclusively breastfeeding resulted in excessive risk of diarrhoea incidence (RR 1.26 – 2.65), prevalence (RR 2.15 – 4.90), mortality (RR 2.28 – 10.52) and all-cause mortality (RR 1.48 – 14.40) in infants 0-5 months (4)</td>
</tr>
<tr>
<td><strong>Continued breastfeeding from 6 – 23 months</strong></td>
<td>2.8 times greater risk of death from diarrhoea if not breastfed (2); not breastfeeding associated with 32% increased diarrhoea incidence in infants 6-23 months (3); not breastfeeding resulted in excessive risk of diarrhoea incidence (RR 1.32) in infants 6-11 months and prevalence (RR 2.07), mortality (RR 2.18) and all-cause mortality (RR 3.69) in infants 6-23 months (4)</td>
</tr>
<tr>
<td><strong>Adequate complementary feeding among children 6 – 23 months, including adequate micronutrient intake</strong></td>
<td>6% reduction in all child deaths, including from pneumonia and diarrhoea (5)</td>
</tr>
<tr>
<td><strong>Vitamin A supplementation (preventive)</strong></td>
<td>23% reduction in all-cause mortality (6a) and 30% reduction in diarrhoea-specific mortality (6b) in children 6-59 months</td>
</tr>
</tbody>
</table>

#### Interventions to Prevent

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Reductions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vaccination against measles, pertussis, PCV, Hib and rotavirus</strong></td>
<td>Hib vaccine reduces radiologically confirmed pneumonia by 18% (7); 23 – 35% reduction in incidence of radiological pneumonia for PCV (1); reduction in very severe rotavirus infection by 74% (8); potential effectiveness of 30% for PCV in reduction of overall childhood pneumonia mortality (9)</td>
</tr>
<tr>
<td><strong>Prevention of HIV in children</strong></td>
<td>2% reduction in all child deaths (5)</td>
</tr>
<tr>
<td><strong>Cotrimoxazole prophylaxis for HIV-infected children</strong></td>
<td>33% reduction in AIDS deaths (10)</td>
</tr>
<tr>
<td><strong>Handwashing with soap</strong></td>
<td>31% diarrhoea risk reduction (11); 48% diarrhoea risk reduction (2)</td>
</tr>
<tr>
<td><strong>Improved sanitation</strong></td>
<td>36% diarrhoea risk reduction (2)</td>
</tr>
<tr>
<td><strong>Increase quantity of water</strong></td>
<td>17% diarrhoea risk reduction (recognizing a minimum quantity of at least 25 litres per person per day is recommended) (11)</td>
</tr>
<tr>
<td><strong>Household water treatment and safe storage (to ensure safe drinking-water)</strong></td>
<td>31 – 52% diarrhoea risk reduction (greater reductions realized when used correctly and exclusively by vulnerable populations) (3, 12)</td>
</tr>
<tr>
<td><strong>Reduction in household air pollution (HAP) through lower emission stoves and/or clean fuels</strong></td>
<td>Halving of HAP exposure with a chimney stove reduced severe pneumonia by 33% (13); other evidence indicates large exposure reductions may further reduce risk (14)</td>
</tr>
</tbody>
</table>

#### Interventions to Treat

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Reductions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Health facility case management for very severe pneumonia cases and vulnerable groups such as newborns, HIV-infected and malnourished children</strong></td>
<td>29 – 45% reduction in case fatality (1); 6% reduction in all child deaths (5); 90% reduction in neonatal deaths due to pneumonia with hospital-based case management (15)</td>
</tr>
<tr>
<td><strong>Increasing access to appropriate care through community-based case management of pneumonia/diarrhoea (CCM)</strong></td>
<td>CCM results in 70% reduction in pneumonia mortality (16); 35% reduction in child pneumonia mortality (16); CCM of diarrhoea with ORS and zinc reduced diarrhoeal deaths among under-fives by 93% (17); 42-75% reduction in neonatal deaths due to pneumonia (15)</td>
</tr>
<tr>
<td><strong>ORS</strong></td>
<td>ORS reduces diarrhoea mortality by 69% with current coverage, or 93% if 100% coverage (17)</td>
</tr>
<tr>
<td><strong>Zinc</strong></td>
<td>Zinc for the treatment of diarrhoea reduces diarrhoea mortality by 23% (18); 14–15% reduction in incidence of pneumonia or diarrhoea (1)</td>
</tr>
</tbody>
</table>
References:


### Annex 2: Overview of storage volumes for “traditional” versus “rotavirus” vaccines

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Vaccine Presentation</th>
<th>Doses Required (for fully immunized child)</th>
<th>Per dose volume (cm³)</th>
<th>Total volume for fully immunized child (cm³)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>“Traditional Vaccines”</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BCG</td>
<td>10-dose vial, diluent inside cold chain</td>
<td>1</td>
<td>1.9</td>
<td>1.9</td>
</tr>
<tr>
<td>OPV</td>
<td>10-dose vial</td>
<td>3</td>
<td>2.0</td>
<td>6.0</td>
</tr>
<tr>
<td>Pentavalent (DTP-HepB-Hib)</td>
<td>Single-dose vial liquid vaccine</td>
<td>3</td>
<td>12.9</td>
<td>38.7</td>
</tr>
<tr>
<td>Measles</td>
<td>10-dose vial, diluent inside cold chain</td>
<td>2</td>
<td>7.5</td>
<td>15.0</td>
</tr>
<tr>
<td><strong>Rotavirus Vaccines</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rotarix®</td>
<td>Pack of 1 single-dose liquid vaccine</td>
<td>2</td>
<td>115.3</td>
<td>230.6</td>
</tr>
<tr>
<td>Rotarix®</td>
<td>Pack of 10 single-dose liquid vaccine</td>
<td>2</td>
<td>43.3</td>
<td>86.6</td>
</tr>
<tr>
<td>Rotarix®</td>
<td>Pack of 50 single-dose liquid vaccine</td>
<td>2</td>
<td>17.1</td>
<td>34.2</td>
</tr>
<tr>
<td>Rotarix®</td>
<td>Pack of 1 single-dose lyophilized vaccine, packed together with diluent</td>
<td>2</td>
<td>256</td>
<td>512.0</td>
</tr>
<tr>
<td>Rotarix®</td>
<td>Pack of 10 single-dose lyophilized vaccine, packed together with diluent</td>
<td>2</td>
<td>156.0</td>
<td>312.0</td>
</tr>
<tr>
<td>RotaTeq®</td>
<td>Pack of 1 single-dose liquid vaccine</td>
<td>3</td>
<td>146.0</td>
<td>438.0</td>
</tr>
<tr>
<td>RotaTeq®</td>
<td>Pack of 10 single-dose liquid vaccine</td>
<td>3</td>
<td>76.2</td>
<td>228.6</td>
</tr>
<tr>
<td>RotaTeq®</td>
<td>Pack of 25 single-dose liquid vaccine</td>
<td>3</td>
<td>45.9</td>
<td>137.7</td>
</tr>
</tbody>
</table>
Annex 3: Storage volumes for rotavirus vaccine products

### GSK Rotarix® (Liquid presentation in oral applicator - 2 dose schedule)

<table>
<thead>
<tr>
<th>Presentation</th>
<th>10 oral applicators of single-dose per pack</th>
<th>1 oral applicator of single-dose per pack</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical dimensions of pack (cm)</td>
<td>Length 16.0</td>
<td>13.3</td>
</tr>
<tr>
<td></td>
<td>Breadth 13.0</td>
<td>4.2</td>
</tr>
<tr>
<td></td>
<td>Height 4.1</td>
<td>2.4</td>
</tr>
<tr>
<td>Total volume (cm³)</td>
<td>Length x Breadth x Height 852.8</td>
<td>134.1</td>
</tr>
<tr>
<td></td>
<td>Total volume / dose 85.3</td>
<td>134.1</td>
</tr>
<tr>
<td>Storage volume (cm³) for standard vaccination schedule (1)</td>
<td>National/provincial level (2) 61</td>
<td>61</td>
</tr>
<tr>
<td></td>
<td>Peripheral level 86.5</td>
<td>86.5</td>
</tr>
<tr>
<td>Storage volume (cm³) for vaccination schedule including rotavirus vaccine(3)</td>
<td>National/provincial level (2) 240.5</td>
<td>343.2</td>
</tr>
<tr>
<td></td>
<td>Peripheral level 264.0</td>
<td>368.7</td>
</tr>
</tbody>
</table>

Notes:
1. 1xBCG, 3xOPV, 3xDTP/HepB/Hib, 2xmeasles, 2xTT for women
2. +4°C to +8°C storage only
3. same as (1), with addition of 2 doses of Rotarix® plus 5% wastage

### GSK Rotarix® (Liquid presentation in squeeze tube - 2 dose schedule)

<table>
<thead>
<tr>
<th>Presentation</th>
<th>50 tubes of single-dose per pack</th>
<th>10 tubes of single-dose per pack</th>
<th>1 tube of single-dose per pack</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical dimensions of pack (cm)</td>
<td>Length 14.6</td>
<td>12.8</td>
<td>5.3</td>
</tr>
<tr>
<td></td>
<td>Breadth 8.5</td>
<td>16.1</td>
<td>8.7</td>
</tr>
<tr>
<td></td>
<td>Height 6.9</td>
<td>2.1</td>
<td>2.5</td>
</tr>
<tr>
<td>Total volume (cm³)</td>
<td>Length x Breadth x Height 856.3</td>
<td>432.8</td>
<td>115.3</td>
</tr>
<tr>
<td></td>
<td>Total volume / dose 17.1</td>
<td>43.3</td>
<td>115.3</td>
</tr>
<tr>
<td>Storage volume (cm³) for standard vaccination schedule (1)</td>
<td>National/provincial level (2) 61</td>
<td>61</td>
<td>61</td>
</tr>
<tr>
<td></td>
<td>Peripheral level 86.5</td>
<td>86.5</td>
<td>86.5</td>
</tr>
<tr>
<td>Storage volume (cm³) for vaccination schedule including rotavirus vaccine(3)</td>
<td>National/provincial level (2) 97</td>
<td>151.1</td>
<td>303.7</td>
</tr>
<tr>
<td></td>
<td>Peripheral level 122.5</td>
<td>177.6</td>
<td>329.2</td>
</tr>
</tbody>
</table>

Notes:
1. 1xBCG, 3xOPV, 3xDTP/HepB/Hib, 2xmeasles, 2xTT for women
2. +4°C to +8°C storage only
3. same as (1), with addition of 2 doses of Rotarix® plus 5% wastage
### GSK Rotarix® (Lyophilized presentation with diluents carried INSIDE cold chain - 2 dose schedule)

<table>
<thead>
<tr>
<th>Presentation</th>
<th>Lyophilized 10 single-dose pack</th>
<th>Lyophilized 1 single-dose pack</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical dimensions of pack (cm)</td>
<td>Length</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>Breadth</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td>Height</td>
<td>6</td>
</tr>
<tr>
<td>Total volume (cm³)</td>
<td>1560.0</td>
<td>256.0</td>
</tr>
<tr>
<td>Volume per dose (cm³)</td>
<td>156.0</td>
<td>256.0</td>
</tr>
<tr>
<td>Storage volume (cm³) for standard vaccination schedule (1)</td>
<td>National/provincial level (2)</td>
<td>61</td>
</tr>
<tr>
<td></td>
<td>Peripheral level</td>
<td>86.5</td>
</tr>
<tr>
<td>Storage volume (cm³) for vaccination schedule including rotavirus vaccine (3)</td>
<td>National/provincial level</td>
<td>224.8</td>
</tr>
<tr>
<td></td>
<td>Peripheral level</td>
<td>250.3</td>
</tr>
</tbody>
</table>

Freeze-dried vaccine packed with diluents carried INSIDE the cold chain. The 10 dose carton contains: 2 blisters of 5 applicators of diluents, 1 plastic bag with ten transfer adapter + 1 box with ten vials of vaccine.

Notes:
1. 1xBCG, 3xOPV, 3xDTP/HepB/Hib, 2xmeasles, 2xTT for women
2. +4°C to +8°C storage only
3. same as (1), with addition of 2 doses of Rotarix® plus 5% wastage

### Merck Rotateq® - (Liquid presentation in Squeeze Tube - 3 dose schedule)

<table>
<thead>
<tr>
<th>Presentation</th>
<th>25 tubes of single-dose per pack</th>
<th>10 tubes of single-dose per pack</th>
<th>1 tube of single-dose per pack</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical dimensions of pack (cm)</td>
<td>Length</td>
<td>12.86</td>
<td>13.97</td>
</tr>
<tr>
<td></td>
<td>Breadth</td>
<td>8.26</td>
<td>9.53</td>
</tr>
<tr>
<td></td>
<td>Height</td>
<td>10.80</td>
<td>5.72</td>
</tr>
<tr>
<td>Total volume (cm³)</td>
<td>length x breadth x height</td>
<td>1147.21</td>
<td>761.53</td>
</tr>
<tr>
<td>Volume per dose (cm³)</td>
<td>46.3</td>
<td>75.3</td>
<td>146.0</td>
</tr>
<tr>
<td>Storage volume (cm³) for standard vaccination schedule (1)</td>
<td>National/provincial level (2)</td>
<td>61</td>
<td>61</td>
</tr>
<tr>
<td></td>
<td>Peripheral level</td>
<td>86.5</td>
<td>86.5</td>
</tr>
<tr>
<td>Storage volume (cm³) for vaccination schedule including rotavirus vaccine (3)</td>
<td>National/provincial level (2)</td>
<td>205.9</td>
<td>301.6</td>
</tr>
<tr>
<td></td>
<td>Peripheral level</td>
<td>231.4</td>
<td>327.1</td>
</tr>
</tbody>
</table>

Notes:
1. 1xBCG, 3xOPV, 3xDTP/HepB/Hib, 2xmeasles, 2xTT for women
2. +4°C to +8°C storage only
3. same as (1), with addition of 3 doses of RotaTeq® plus 5% wastage
Annex 4: Sample AEFI reporting form using core variables

REPORTING FORM FOR ADVERSE EVENTS FOLLOWING IMMUNIZATION (AEFI)

<table>
<thead>
<tr>
<th>*Patient name:</th>
<th>*Date of birth (DD/MM/YYYY):</th>
<th></th>
<th>*Reporter’s Name:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Institution / Designation, Department &amp; address:</td>
</tr>
<tr>
<td>*Patient’s full Address:</td>
<td>OR Age at onset:</td>
<td>☐ ☐Years ☐ ☐ Months ☐ ☐ Days</td>
<td>Telephone &amp; e-mail:</td>
</tr>
<tr>
<td>Telephone:</td>
<td>OR Age Group:</td>
<td>☐ &lt; 1 Year ☐ 1 to 5 Years ☐ &gt; 5 Years</td>
<td></td>
</tr>
<tr>
<td>Sex: ☐ M ☐ F</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Health facility (or vaccination centre) name:**

<p>| | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>*Name of Vaccines Received</td>
<td>*Date of vaccination</td>
<td>*Time of vaccination</td>
<td>Dose (e.g. 1st, 2nd, etc.)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>*Adverse event(s):</td>
<td>*Batch/ Lot number</td>
<td>Expiry date</td>
</tr>
<tr>
<td>☐ Severe local reaction ☐ &gt;3 days ☐ beyond nearest joint</td>
<td></td>
<td></td>
</tr>
<tr>
<td>☐ Seizures ☐ febrile ☐ afebrile</td>
<td></td>
<td></td>
</tr>
<tr>
<td>☐ Abscess ☐ Sepons ☐ Encephalopathy ☐ Toxic shock syndrome ☐ Thrombocytopenia ☐ Anaphylaxis ☐ Fever&gt;38°C ☐ Other (specify).</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Date &amp; Time AEFI started (DD/MM/YYYY):</td>
<td></td>
<td></td>
</tr>
<tr>
<td>/   /   /</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Was the patient hospitalized? ☐ Yes ☐ No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Date patient notified event to health system (DD/MM/YYYY):</td>
<td></td>
<td></td>
</tr>
<tr>
<td>/   /   /</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Describe AEFI (Signs and symptoms):**

*Outcome:*

<p>| | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
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Past medical history (including history of similar reaction or other allergies), concomitant medication and other relevant information (e.g. other cases). Use additional sheet if needed:

**First Decision making level to complete:**

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**Comments:**

*Compulsory field

27 Form can be downloaded from [http://www.who.int/vaccine_safety/initiative/detection/en/](http://www.who.int/vaccine_safety/initiative/detection/en/)
Annex 5: Intussusception

What is intussusception?
Intussusception is a telescoping of one segment of the bowel into itself, causing obstruction. It is a rare condition. The peak incidence is between 5 and 10 months of age, with 80% of cases before 24 months of age. It is more common in males than females. Most cases in infants are idiopathic, with no recognized triggering event or underlying structural abnormality. There may be some familial predisposition. Recurrence is seen in 5-10% of non-surgically-treated cases, usually within 6 months.

What are the common presenting symptoms of intussusception?
Intussusception initially causes pain, manifested as crying but often associated with pallor. The crying may be intermittent initially. Vomiting is the single most common symptom and signs of intestinal obstruction (distension and absent or reduced bowel sounds) are usually present. If there is vascular compromise due to the obstruction, there may be intestinal bleeding (the classic red currant jelly stool) but this is often late and/or absent.

The first sign of intussusception in an otherwise healthy infant may be sudden, loud crying caused by abdominal pain. Infants who have abdominal pain may pull their knees to their chests when they cry. The pain of intussusception comes and goes, usually every 15 to 20 minutes at first. These painful episodes last longer and happen more often as time passes.

Other frequent signs and symptoms of intussusception include:
- Stool mixed with blood and mucus (sometimes referred to as "currant jelly" stool because of its appearance)
- Vomiting
- A lump in the abdomen
- Lethargy

Less common signs and symptoms include:
- Diarrhoea
- Fever
- Constipation

Some infants have no obvious pain, don't pass blood or have a lump in the abdomen. Some older children have pain but no other symptoms.

Intussusception and the current rotavirus vaccines

The pathogenic mechanisms involved in intussusception following rotavirus vaccination remain poorly defined.

Post-licensure surveillance showed that the previously marketed rotavirus vaccine, RotaShield® (Wyeth- Lederle), carried an attributable risk of intussusception estimated at 1:10 000 recipients. This serious and potentially fatal condition was associated primarily with the first of the 3 oral vaccine doses and the highest attributable risk.

29 WHO Rotavirus Vaccine Position Paper (January 2013) http://www.who.int/entity/wer/2013/wer8805.pdf
was found in infants >3 months of age receiving the vaccine.

Randomized control trials (RCTs) conducted so far have lacked power to rule out very small relative risks of association between Rotarix® or RotaTeq® and intussusception in narrow risk windows, for example the 1–7 day period after dose 1. However, no increased risk of intussusception was detected with either vaccine in two RCTs, each of which included approximately 60 000–70 000 infants (30 000–35 000 received rotavirus vaccine) and designed to detect a risk similar to that seen with Rotashield®.

Using self-controlled case-series and case-control methods the potential association between Rotarix® and intussusception was investigated after routine immunization of infants in Mexico and Brazil. The study included 615 intussusception case patients (285 in Mexico and 330 in Brazil) and 2,050 controls. An increased risk of intussusception 1–7 days after the first dose of Rotarix® was identified among infants in Mexico using both the self-controlled case-series method (incidence ratio, 5.3; 95% CI: 3.0–9.3) and the case-control method (odds ratio, 5.8; 95% CI: 2.6–13.0). Among infants in Brazil no significant risk was found after the first dose, but an increased risk by a factor of 1.9 to 2.6 was seen 1–7 days after the second dose. A combined annual excess of 96 cases of intussusception in Mexico (approximately 1 per 51 000 infants) and in Brazil (approximately 1 per 68 000 infants) and of 5 deaths due to intussusception was attributable to Rotarix® in this analysis.

A prospective, active surveillance study for intussusception in infants following Rotarix® vaccination was conducted in Mexico during the period 2008–2010. The relative incidence of intussusception within 31 days of vaccination was 1.8 (95% CI: 1.2–2.5; p=0.001) post dose 1 and 1.1 (95% CI: 0.8–1.5; p=0.8) post-dose 2. The relative incidence of intussusception within 7 days of vaccination was 6.5 post-dose 1 (95% CI: 4.2–10.1; p<0.001) and 1.3 post-dose 2 (95% CI: 0.8–2.1; p=0.3).

The attributable risk of intussusception within 7 days of vaccine dose 1 was estimated at 3 to 4 additional cases of intussusception per 100 000 vaccinated infants. In Australia, an excess of observed compared to expected cases of intussusception was reported for both Rotarix® and RotaTeq® among children 1–3 months of age. With Rotarix®, the relative risk was 3.5 (95% CI: 0.7–10.1) 1–7 days after the first dose and 1.5 (95% CI: 0.4–3.9) 1–21 days after the first dose. The corresponding figures for RotaTeq® were 5.3 (95% CI: 1.1–15.4) and 3.5 (95% CI: 1.3–7.6).

Two large cohort studies with active follow-up assessed the risk of intussusception following receipt of RotaTeq® in the USA. In one covering the period 2006–2010, a total of 786 725 RotaTeq® doses, including 309 844 first doses, were administered to infants 4–34 weeks of age. Comparing the incidence of intussusception between rotavirus vaccine recipients and similarly aged recipients of other infant vaccines, no statistically significant increased risk of intussusception with RotaTeq® was observed for either comparison group following any dose in either the 1–7 day or 1–30 day risk window. The other US study, which compared the risk of intussusception between 85 397 RotaTeq® recipients and 62 820 DTaP recipients found 6 and 5 confirmed cases of intussusception, respectively, within 30 days following either dose. The relative risk of intussusception was 0.8 (95% CI: 0.2–3.5).

Thus, in some but not all settings, post-marketing surveillance of both currently available rotavirus vaccines has detected a small increased risk of intussusception (about 1–2/100 000 infants vaccinated) shortly after the first dose. Where present, this risk is 5–10 times lower than that observed with the previously licensed RotaShield®, and the benefits of rotavirus vaccination against severe diarrhoea and death from rotavirus infection far exceeds the risk of intussusception.
Annex 6: Key Advocacy & Communications Messages Related to Rotavirus Vaccines

1. WHO recommends including rotavirus vaccine in all national immunization programmes.

2. More than 85% of rotavirus deaths occur in high mortality settings. Studies demonstrate that approximately 30-60% of rotavirus gastroenteritis (RVGE) deaths can be prevented by use of rotavirus vaccine.31

3. Because there are many microbiological causes of diarrhoeal disease, a comprehensive approach to diarrhoeal disease control should be implemented together with rotavirus vaccine introduction. This comprehensive approach strategy, should include exclusive breastfeeding for 6 months, vitamin A supplementation, safe drinking water, hygiene (including hand washing with soap), and sanitation; treatment with low-osmolarity oral rehydration solution (ORS), zinc supplements, and continued feeding.

4. WHO, UNICEF, and other partners are working together in a new accelerated and integrated approach to combat rotavirus diarrhoea and pneumonia, the two leading child-killers, which together account for more than 29% of all under five child deaths every year, the majority of which are in the developing world.

5. Key messages about rotavirus vaccine use (all messages apply to both Rotarix® and RotaTeq®)

**KEY MESSAGES**

- Diarrhoeal disease remains a serious public health issue for children across the globe.
- In developing countries, diarrhea is a major cause of under-5 year old mortality, accounting for up to 11% of all childhood deaths.
- These deaths are preventable.
- Worldwide, it is estimated that around 40% of all pediatric hospitalizations for diarrhoea are attributable to rotavirus infections.
- Vaccination against rotavirus is an effective way to prevent this deadly disease.
- Rotavirus infects nearly every child by the age of 3-5 years.
- In developing countries, first rotavirus infections usually occur between by 26 weeks of age, and nearly 80% occur among infants <1 year old, although there are some differences among countries.
- In 2008, rotavirus was estimated to have caused 453,000 deaths worldwide among infants and very young children, with 90% of these deaths occurring in Africa and Asia alone.
- Given that there are many causes of diarrhoeal disease, the rotavirus vaccine must be part of a comprehensive control strategy, including exclusive breastfeeding for 6 months, vitamin A supplementation, safe drinking water, hygiene (especially hand-washing with soap) and sanitation, and treatment with ORS, zinc supplementation, and continued feeding.
- Rotavirus is resilient and traditional hygiene measures that might prevent other sanitation-related illnesses are not sufficient to limit its impact, hence the comparable rate of infection globally.

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Annex 7: Frequently Asked Questions for Health Workers

What is rotavirus disease?
Rotavirus is the most common cause of severe diarrhoea in infants and young children worldwide. It can lead to severe dehydration and death. WHO estimates (2008) that approximately 453,000 children died from rotavirus infection and many more were hospitalized.

Who can get rotavirus infection?
Nearly all children in the world, regardless of where they live, will suffer at least one rotavirus infection in the first five years of life. However, the vast majority of rotavirus deaths occur in developing countries, where prompt medical care may be out of reach.

How is rotavirus spread?
Rotaviruses are easily spread primarily by the faecal-oral route, directly from person-to-person, or indirectly via contaminated fomites.

What are the symptoms of rotavirus disease?
Clinical illness from rotavirus infection ranges from mild watery diarrhoea of limited duration, to severe diarrhoea with vomiting that may result in dehydration and death if appropriate treatment is not available. Following an incubation period of 1–2 days, the illness can begin abruptly, and vomiting often precedes the onset of diarrhoea. Up to one-third of patients may have a temperature greater than 39°C. Gastrointestinal symptoms generally resolve within 3–7 days. Children with rotaviruses often suffer frequent vomiting that may sometimes make it difficult to administer oral rehydration solution (ORS) at home, and medical care is required. It is not possible to distinguish rotavirus from other causes of gastroenteritis on clinical grounds alone, and a laboratory test is required to confirm the diagnosis. The first infection is usually the most severe; later infections may be milder or asymptomatic due to previous acquired immunity.

How can rotavirus infection be prevented?
Improvements in sanitation, safe water supply, promotion of exclusive breastfeeding for 6 months and improvement in children's nutrition, including vitamin A supplementation are important to prevent diarrhoeal disease. However, such interventions have limited benefits in preventing rotavirus infection. Childhood rotavirus vaccination is the best method to prevent severe disease and rotavirus deaths.

Is there a vaccine against rotavirus disease?
Two orally-administered, live, attenuated vaccines against rotavirus infection have been demonstrated to be safe and highly efficacious in large-scale clinical trials; Rotarix® manufactured by GlaxoSmithKline Biologicals, and RotaTeq®, manufactured by Merck and Co. They provide good protection against severe rotavirus-related diarrhoea in young children, but they do not provide 100% protection against the infection. Both vaccines are prequalified by WHO, and have already been introduced into the routine childhood immunization in many countries. The current rotavirus vaccines differ in antigen composition and immunization schedule, but they are considered equally safe and efficacious by WHO.

Do the locally prevalent strains of rotavirus influence the choice of vaccine?
Available evidence shows that both vaccines provide cross-protection against strains not contained in the vaccine. The efficacy and effectiveness of either vaccine does not seem to be affected by the strains of rotavirus prevalent in the population.
Who should get the rotavirus vaccine?

Generally, all children should receive rotavirus vaccine in infancy with their other childhood vaccines.

How many doses are needed? When should they be given?

Rotavirus vaccines can be administered from the age of 6 weeks of age and given simultaneously with DTP/penta vaccines.

Rotarix® should be administered orally in a 2-dose schedule at the time of DPT1/penta1 and DPT2/penta2 with an interval of at least 4 weeks between doses.

RotaTeq® should be administered orally in a 3-dose schedule at the time of the DTP1/penta1, DTP2/penta2, and DTP3/penta3 contacts, with an interval of at least 4 weeks between doses.

Rotavirus vaccines must never be injected.

Can the rotavirus vaccines be co-administered with other vaccines?

Rotavirus vaccinations can be administered simultaneously with other vaccines in the infant immunization programme.

Is there any reason why a child should not be given rotavirus vaccine?

Severe allergic reaction (e.g. anaphylaxis) after a previous dose, and severe immunodeficiency including severe combined immuno-deficiency (SCID), are contraindications for rotavirus vaccination.

What are the precautions to rotavirus vaccine administration?

Precautions are necessary if there is a history of intussusception or intestinal malformations, chronic gastrointestinal disease, and severe acute illness. Vaccination should be postponed in case of ongoing acute gastroenteritis or fever with moderate to severe illness until the child recovers. The presence of minor infections, however, is not a contraindication for vaccination.

What are the possible adverse events following rotavirus vaccine?

Apart from a low risk of intussusception (about 1–2 per 100 000 infants vaccinated) the current rotavirus vaccines are considered safe and well tolerated.

Countries should develop a strategy to inform relevant health staff that although the benefits outweigh the risks, a small potential risk of intussusception after rotavirus vaccination remains. Countries should also ensure that caregivers are adequately counseled to recognize danger signs of dehydration or intussusception that need immediate medical attention. Proper planning and training of staff to conduct pharmacovigilance should take place before the vaccine is introduced.

Given the background rate of natural intussusception and the large number of children included in national immunization programmes, intussusception cases are expected to occur by chance alone following rotavirus vaccination. It is important to establish the baseline incidence of intussusception at sentinel sites and to use epidemiological studies, such as the self-controlled case series method, to assess the safety of rotavirus vaccines.

How should the rotavirus vaccines be stored?

Rotavirus vaccines should be stored between 2°C and 8°C. This vaccine should not be frozen.
Annex 8: Rotavirus vaccines: A Pocket Guide for Health Workers

Annex 8

Rotavirus Vaccines: A Pocket Guide for Health Workers

UPDATE 2013
Foreword

Countries are introducing the rotavirus vaccine. This Pocket Guide is a hands-on practical document that is part of the learning material for rotavirus vaccine introduction training. The Pocket Guide is structured by topic. Each topic is addressed with short descriptions, illustrations, and key messages. This Pocket Guide provides an illustrative framework for users and is to be adapted to local conditions.
Introduction to rotavirus disease

Rotavirus disease is a diarrhoeal disease caused by a virus called rotavirus. The name rotavirus comes from the wheel-like appearance of the virus under the microscope. Rotavirus is the most common cause of severe diarrhoeal disease in infants and young children worldwide.
Who is at most risk?
- Infants after the age of 3 months
- Low to no immunity
- Vulnerable to dehydration
- Older children if they are immunocompromised

What are the signs and symptoms of rotavirus disease?
- Fever
- Vomiting
- Watery diarrhoea
Abdominal pain may also occur. Diarrhoea usually stops after 3 to 7 days.

The virus damages the cells of the small intestine so that the body cannot absorb water and nutrients. Children may lose interest in eating and drinking and become dehydrated from loss of fluids. Vomiting is especially dangerous because it is difficult to replace fluids in young children who are vomiting frequently. Young children can become dehydrated, requiring urgent treatment.

How does rotavirus spread?
Rotavirus is very contagious, and spreads easily from children who are already infected to other children and sometimes adults. Large amounts of rotavirus are excreted in the stool of infected persons and the virus can be easily spread via contaminated hands and objects, such as toys. This is known as a fecal-oral route of transmission.

Rotavirus is not the only cause of diarrhoea, several other agents may also cause diarrhoea.

Confirmation of rotavirus diarrhoeal illness requires laboratory testing. Strains of rotavirus may be further characterized by special testing with enzyme immunoassay or polymerase chain reaction. Such testing is not commonly available or necessary.
High level of rotavirus morbidity continues to occur in the world
Rotavirus vaccine protects against one cause of diarrhoea, but not all causes. Therefore, the use of rotavirus vaccine needs to be part of a comprehensive strategy to control diarrhoeal diseases with the scaling up of both prevention (promotion of early and exclusive breastfeeding for six months, vitamin A supplementation, safe drinking water, hygiene, especially hand-washing with soap, and sanitation) and treatment packages (ORS, zinc, and continued feeding).
Two oral rotavirus vaccines are marketed internationally:
- the monovalent (RV1) Rotarix® (GlaxoSmithKline Biologicals, Rixensart, Belgium)
- the pentavalent (RV5) RotaTeq® (Merck & Co. Inc., West Point, PA, USA).

Currently available efficacy and safety data support selection of either of the two vaccines for national use. Although both rotavirus vaccines are efficacious, data show that their efficacy is higher in settings with low mortality in children under five years of age (vaccine efficacy ~ 90%) than in settings with high mortality in children under five years of age (vaccine efficacy ~ 60%). Because the incidence of rotavirus disease is significantly higher in high child mortality settings, the number of severe disease and deaths averted by rotavirus vaccines in these settings is likely to be greater than in low mortality settings, despite the lower vaccine efficacy.

It is important to bear in mind that rotavirus vaccine will not prevent or protect diarrhoea or vomiting caused by other germs, but it is very effective at preventing diarrhoea and vomiting caused by rotavirus. This means that even when children are fully immunized against rotavirus, they may still get diarrhoea caused by other agents.
### GSK Rotarix® - monovalent, human strain, live, attenuated, oral rotavirus vaccine

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### Merck RotaTeq® - pentavalent, human-bovine reassortant strain, live, attenuated, oral, rotavirus vaccine

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Rotavirus vaccine storage

The rotavirus vaccine should be stored in a refrigerator. **Do not put rotavirus vaccine in the freezer.** If the vaccines are frozen, they lose their potency and no longer provide protection against the disease. Vaccines with **early expiration dates** (and/or VVM in stage 2 (or nearing stage 2) if it has a VVM) should be kept in the front of the refrigerator for first use.

Good temperature control during the storage and transport of vaccines is critical to ensure the potency and safety of vaccines. Rotavirus vaccines must be stored between **+2°C and +8°C**.

For rotavirus vaccine furnished without VVMs (RotaTeq®), it is highly recommended to use continuous temperature monitoring devices to store and transport vaccines under cold chain conditions as specified by the manufacturer. Any break in the cold chain should be recorded and immediately reported through the supervisory channels. VVMs attached to other vaccines cannot be used as a proxy to determine the cumulative level of heat exposure experienced by RotaTeq®.

In situations where continuous temperature monitoring devices are not available, the following is recommended:

- Discard unopened tubes immediately if there is a complete and sustained rupture in the cold chain and the ambient temperature exceeds 25°C;
- Discard unopened tubes if there is a temporary rupture in the cold chain and the vaccine is exposed to temperatures between 9°C to 25°C for more than 36 consecutive hours;
- Discard unopened vaccine tubes at the end of outreach or mobile sessions if there is no assurance that the cold chain was maintained.
### Vaccine eligibility

#### Immunization schedule for Rotarix® (RV1) vaccine

Rotarix® should be administered orally in a 2-dose schedule at the time of DTP/penta1 and DTP/penta2 with an interval of at least 4 weeks between doses. The first dose of rotavirus vaccine should be given at 6 weeks of age or soon thereafter.

#### Immunization schedule for RotaTeq® (RV5) vaccine

RotaTeq® should be administered orally in a 3-dose schedule at the time of the DTP/penta1, DTP/penta2, and DTP/penta3 contacts, with an interval of at least 4 weeks between doses. The first dose of rotavirus vaccine should be given at 6 weeks of age or soon thereafter.

On-time vaccination is very important for rotavirus vaccine.

However, if a child is late for vaccination:

- He/she **can** get rotavirus vaccine
- He/she **can** get all other vaccines in the schedule

Because of the typical age distribution of rotavirus gastro-enteritis, rotavirus vaccination of children >24 months of age is not recommended.

Prematurely born infants should follow the vaccination schedules recommended for their chronological age.

Rotavirus vaccinations can be administered simultaneously with other vaccines in the infant immunization programme.

Early vaccination (first dose to be given as soon as possible after 6 weeks of age) is encouraged but infants can receive rotavirus vaccine together with DTP/penta regardless of the time of vaccination.

Nevertheless, as rotavirus is a disease that affects young infants, the introduction of rotavirus vaccine should be accompanied by measures to ensure high vaccination coverage and timely administration of each dose in order to maximize the benefits of the vaccine.
Vaccine contraindications

Contraindications

- Hypersensitivity after previous administration of rotavirus vaccines
- Severe immunodeficiency
- Precautions are necessary if there is a history of intussusception or intestinal malformations, chronic gastrointestinal disease and severe acute illness.
- Administration of rotavirus vaccine should be postponed in subjects suffering from on-going acute diarrhea or vomiting and in need of rehydration therapy, or fever with moderate to severe illness.

Note that mild illness such as an upper respiratory tract infection is not a contraindication.
1. ROTARIX®

**Before preparing rotavirus vaccine**
Before administering the vaccine, you need to verify and interpret the Vaccine Vial Monitor (VVM) and always check the *expiration date* marked on the tube cap.

**Prepare for vaccination**

**Step 1:** Pull off the cap from the tube. Clear the fluid from the upper part of the tube by tapping the tube.

**Step 2:** Turn the cap upside-down and place the cap vertically onto the tip seal. Insert the tip seal into the small hole in the top of the cap.
Administer the vaccine

The child should be seated in a semi reclining position (i.e. normal feeding position) to take the vaccine orally. Before administration of the vaccine, make a final visual inspection to ensure that the tip has not fallen inside the tube.

Step 1: Open the mouth of the child by gently pressing the cheeks.

Step 2: Put the tube towards the inner cheek. Make every effort to aim the tube containing the vaccine down one side and toward the back of the child's mouth. **Do not** put the tube too far back in the mouth. **Never** place the tube into the center of the mouth to prevent the risk of choking.

Step 3: Administer the vaccine slowly by pressing the tube. Prevent spitting by administering the vaccine in small portions slowly.

Step 4: Make sure the child is swallowing the vaccine. Hold the cheeks together and stroke him/her under the chin to help with swallowing. A replacement dose maybe given if the child spits part of the vaccine.

2. ROTATEQ®

Before preparing rotavirus vaccine

Before administering the vaccine, you need to always check the **expiration date** marked on the tube cap.
Administer the vaccine
The child should be seated in a semi reclining position (i.e. normal feeding position) to take the vaccine orally. Before administration of the vaccine, make a final visual inspection to ensure that the tip has not fallen inside the tube.

**Step 1:** Open the mouth of the child by gently pressing the cheeks.

**Step 2:** Put the tube towards the inner cheek. Make every effort to aim the tube containing the vaccine down one side and toward the back of the child's mouth. Do not put the tube too far back in the mouth. Never place the tube into the center of the mouth.

**Step 3:** Administer the vaccine slowly by pressing the tube. Prevent spitting by administering the vaccine in small portions slowly.

**Step 4:** Make sure the child is swallowing the vaccine. Hold the cheeks together and stroke him/her under the chin to help with swallowing. A replacement dose is not necessary if the child spits part of the vaccine.

**Vaccine recording**
**Immunization card**

Each time a vaccine is administered, complete the vaccination card outlining which vaccines have been given.

You should also note the date of the next appointment on the immunization card and remind the caretaker to return on that date with the card.

Parents should be reminded to bring the immunization card at each visit.

Note that the immunization card has been updated to include the rotavirus vaccine doses, and the generic abbreviation for rotavirus vaccine is "Rota." Use this abbreviation when recording the vaccine being administered.

**Tally sheet**

Tally sheets have been updated to reflect the inclusion of rotavirus vaccine in the national immunization program. Keep a tally of each vaccine dose given. At the end of an immunization session, count the tally sheets to identify the total number of vaccinations given (for each dose). If you have old tally sheets, include a line for Rota1 and Rota2 and Rota3, as appropriate (depending on which rotavirus vaccine was introduced in your country).

**Monthly report**

Reporting forms have been updated to reflect the inclusion of rotavirus vaccine in the national immunization program. Report rotavirus vaccine doses administered each month, along with other vaccine doses.

If you have old reporting forms, add lines to report Rota1 and Rota2 and Rota3 as appropriate.

Use tally sheets to prepare monthly reports to send to supervisors.

**Arranging for a return visit**

Make an appointment for the **next dose of rotavirus vaccine** and other vaccines according to the immunization schedule.

Ensure that a minimum gap of **4 weeks** is maintained. Ensure that there is a session on the given date (no public holiday, weekend, etc.).
Write the date of the next visit on the **immunization card** and remind the caretaker to come on the specified date and to **bring the card**.
The first dose of rotavirus vaccine can be given to infants from 6 weeks of age. In order to protect infants from catching the disease, rotavirus vaccine needs to be given as soon as possible.

Use volunteers to inform and motivate parents of newborns to bring their children for vaccination on time. Parents of infants who are due for vaccination, but have not yet come to the health center, should be reminded and followed up with.

A copy of the immunization card may be filed under the month the infant should return for the next dose of rotavirus vaccine. For example, if an infant receives pentavalent vaccine and rotavirus vaccine in January, place a copy of the card in the February section. Every month, review the reminder cards and follow up with those who did not attend when due.

Involve community volunteers to bring children who are eligible for the second dose. Also explain to the volunteers why it is important to bring children back for the subsequent doses at the recommended ages.

**Monitor uptake of rotavirus vaccine**

Use a wall monitoring chart to track the number of infants who received each of the recommended doses of rotavirus vaccine.

If the gap between each dose of rotavirus vaccine is large, this means that several children received the first dose but not the second or the third dose, as appropriate. Thus, follow-up systems need to be strengthened.

A big gap between monthly targets and infants getting Rota1 means newborns need to be followed up with regularly.
KEY MESSAGES

- The infant must receive all doses of the vaccine to be fully protected and he/she must receive the doses as soon as possible from 6 weeks of age. Because rotavirus disease affects young infants the most, it is important that they get vaccinated on time.

- The caretaker must bring the infant back to the health center as advised or make efforts to attend the next scheduled outreach/mobile session visit.

- Health workers should clearly communicate the time, date and location of the next outreach/mobile visit, or the next scheduled immunization session at the fixed-site, and encourage the caretakers’ return.

- The rotavirus vaccine protects the infant against one cause of diarrhoea, but not all causes.

- Prevention of childhood diarrhoeal diseases also requires early and exclusive breastfeeding for six months, vitamin A supplementation, safe drinking water, hygiene (especially handwashing with soap) and sanitation.

- If the infant suffers from severe diarrhoea, take him or her to the health center or community health worker immediately to get treatment (e.g., low-osmolarity oral rehydration solution (ORS), zinc tablets, and continued feeding).

Intussusception

Intussusception (IS) is a rare type of bowel obstruction that occurs when one portion of the bowel slides into an immediately adjacent segment (also known as telescoping or prolapse). Symptoms of IS include stomach pain with severe crying (which may be brief); several episodes of vomiting; blood in the stool; weakness, or irritability.
Intussusception was found to be a rare but significant side effect of the first generation rotavirus vaccine (RotaShield®) that was available in the United States in 1998-1999. Both Rotarix® and RotaTeq® vaccines were tested in large studies designed to exclude a risk of intussusception similar to RotaShield®. In these studies no increased risk of intussusception observed.

As even large pre-registration safety studies cannot detect rare events, post-marketing studies have been undertaken in a number of countries. Apart from a low risk of intussusception (about 1–2 per 100 000 infants vaccinated) the current rotavirus vaccines are considered safe and well tolerated.

**Monitoring AEFIs**

An adverse event following immunization (AEFI) is a medical incident that takes place after an immunization, causes concern, and is believed to be caused by the immunization. The safety profile of the rotavirus vaccines currently available is good. Most infants who get the rotavirus vaccine do not experience any side effects.

**Report adverse events**

Health workers, who administer the vaccine, should ask the parents to immediately report any reaction that may be related to the vaccine. Report the identified AEFI through the existing AEFI reporting systems established by national immunization programmes. Other problems related to the vaccines, such as administering the vaccines to infants who should not be vaccinated, or errors in vaccine administration, should also be reported.

**Core variables for AEFI**

For optimal vaccine safety monitoring and meaningful analysis of Adverse Event Following Immunization (AEFI) data, systematic and standard collection of critical parameters is essential. This includes:

- a unique identification of the report,
- the primary source of information,
- patient characteristics,
- details of the event(s) and vaccine(s) of interest and
- the possibility of collecting additional information if needed.

Important: Reassure the caretaker – Admit uncertainty, investigate fully, and keep the community informed
Communicating with caretakers

Triple A communication
There are three ways of communicating with parents:

- **Advice**: Provide advice to parents on what is given: the name of the vaccine, the disease to prevent, etc.
- **Alert**: Alert parents of side effects after immunization and how to respond to them.
- **Arrange**: Arrange with parents the next appointment for administering the next dose of the vaccine.

To effectively communicate with caretakers, you must first understand the concerns of parents regarding immunization and understand factors that can lead to misinformation about the safety and effectiveness of vaccines. You should establish an open, friendly dialogue with vaccine-hesitant parents at an early stage and provide clear answers to their questions and accurate information about vaccination.

In sum, you should:

- Be respectful: Smile often, be friendly.
- **Use simple words** to make sure the caretaker understands your key messages: Look directly at caretakers and try to judge by their body language if they have understood your messages. Reword and simplify if needed.
- Listen to caretaker's concerns: Do not get angry or irritated when caretakers ask questions or raise concerns.

Ongoing dialogue may successfully reassure vaccine-hesitant parents that immunization is the best and safest option for their child.
Inform about rotavirus disease
- Rotavirus is a virus that causes diarrhoea, sometimes severe, mostly in babies and young children. It is often accompanied by vomiting and fever and can lead to dehydration.
- Rotavirus is not the only cause of diarrhoea, but it is one of the most serious. Almost every child in the world will suffer from at least one infection by the time he or she is 3-5 years old.
- The primary mode of transmission of rotavirus is the passage of the virus in stool to the mouth of another child.

Communicate about diarrhoea prevention methods
Prevention methods against rotavirus disease include: early and exclusive breastfeeding for six months, vitamin A supplementation, safe drinking water, hygiene (especially hand-washing with soap), sanitation and ORS/zinc/continued feeding (treatment). These interventions can reduce diarrhoeal disease and child mortality where diarrheal disease is a serious burden.

But enhancing sanitation and hygiene alone is not enough to prevent rotavirus disease and stop the spread. Currently, vaccination is the only way to prevent severe episodes of rotavirus infection.

Communicate about the new rotavirus vaccine
Millions of children have received rotavirus vaccine in the last 8 years and the vaccine is considered safe and effective.

The rotavirus vaccine must be given to babies orally, which means swallowed and not injected. This vaccine is given at the same time as pentavalent vaccine, therefore no extra visit is required for this vaccine. Your child can still get diarrhoea due to other agents.

Explain to the caretakers that it is important to get vaccinated on time, so that young infants are protected when they are most at risk.

Rotavirus vaccine is given orally. The first dose should be given at 6 weeks of age or soon thereafter along with the DTP/pentavalent vaccine doses. There should be an interval of at least 4 weeks between each dose doses.
Communicating about side effects and how to respond

Current rotavirus vaccines are generally **well tolerated**. Following vaccination, children may be more irritable and have loss of appetite. Some children may also experience fever, fatigue, diarrhoea, and vomiting.

- If the child has a fever (>39°C), caretakers can give him/her **paracetamol**
- If the child shows any **unusual symptoms**, caretakers should take him/her directly to the **hospital**

Parents have to understand that the risk of the side effects after rotavirus vaccination are **much lower** than the risk of severe rotavirus disease in unvaccinated children.