Developing next generation rotavirus vaccines

Global Vaccine and Immunization Research Forum
March 4-6, 2014
Bethesda, MD

Mary Estes
Gagandeep Khan
Kathleen Neuzil
Umesh Parashar
Duncan Steele
Objectives of Session

- Using rotavirus vaccine as example, discuss approaches to identify public health needs unmet by existing vaccines
- Review improvements desired for next generation vaccines
- Discuss the evaluation of new vaccines vs. currently licensed vaccines to document their added value.

Target Outcome

- Discussion of a framework to guide the development and evaluation of improved vaccines
<table>
<thead>
<tr>
<th>Time</th>
<th>Topic</th>
<th>Speaker(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>16:30-16:35</td>
<td>Introduction</td>
<td>Dr. Kathy Neuzil, PATH</td>
</tr>
<tr>
<td>16:35-16:45</td>
<td>Current rotavirus vaccines: achievements and limitations</td>
<td>Dr. Umesh Parashar, CDC</td>
</tr>
<tr>
<td>16:45-16:55</td>
<td>Prospects from pipeline vaccines to address remaining public health needs</td>
<td>Dr. Mary Estes, Baylor College of Medicine</td>
</tr>
<tr>
<td>16:55-17:05</td>
<td>Evaluation of the next generation of vaccines</td>
<td>Dr. Kathleen Neuzil, PATH</td>
</tr>
<tr>
<td>17:05-17:30</td>
<td>Panel discussion</td>
<td>Dr. Mary Estes, Baylor College of Medicine Dr. Gagandeep Khan, CMC, Vellore Umesh Parashar, CDC Duncan Steele, BMGF</td>
</tr>
</tbody>
</table>
Current Rotavirus Vaccines – Achievements & Challenges

Umesh D. Parashar
Lead, Viral Gastroenteritis Epidemiology Team
Centers for Disease Control Prevention
Atlanta, GA
Human Rotavirus Vaccine (Rotarix, GSK)

Human rotavirus

G1P[8]

2 doses
Human-Bovine Rotavirus Vaccine
(RotaTeq, Merck & Co.)

Bovine rotavirus with single human rotavirus gene substitution

- G1
- G2
- P[8]
- G3
- G4

3 doses
High Efficacy of Both Vaccines in Trials in High/Middle Income Countries

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Region</th>
<th>Efficacy (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rotarix</td>
<td>Europe</td>
<td>96% (90%-99%)</td>
</tr>
<tr>
<td>Rotarix</td>
<td>Latin America</td>
<td>85% (72%-92%)</td>
</tr>
<tr>
<td>RotaTeq</td>
<td>Europe/US</td>
<td>98% (88%-100%)</td>
</tr>
</tbody>
</table>

Vesikari et al and Ruiz-Palacios et al, NEJM 2006
Impact on All-Cause and Rotavirus-Specific Gastroenteritis Hospitalizations in USA

Payne DC, unpublished 2014
Impact on All-Cause and Rotavirus-Specific Gastroenteritis Hospitalizations in El Salvador

70-80% reduction in rotavirus hospitalizations children < 5 years

De Palma, BMJ, 2010
Herd Protection: Reduction in Rotavirus among UNVACCINATED Age Groups in El Salvador

<table>
<thead>
<tr>
<th>Age</th>
<th>Decline in rotavirus hospitalization rate (2008 vs. 2006)</th>
<th>Rotavirus vaccine coverage in 2008 (&gt;=1 dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1 year</td>
<td>84% (80 to 88)</td>
<td>76%</td>
</tr>
<tr>
<td>1 year</td>
<td>86% (82 to 89)</td>
<td>84%</td>
</tr>
<tr>
<td>2 years</td>
<td>65% (50 to 75)</td>
<td>0</td>
</tr>
<tr>
<td>3 years</td>
<td>41% (-7 to 68)</td>
<td>0</td>
</tr>
<tr>
<td>4 years</td>
<td>68% (29 to 85)</td>
<td>0</td>
</tr>
</tbody>
</table>

These age cohorts were ineligible to receive rotavirus vaccine

Yen et al, PIDJ 2011
Effect of Rotavirus Vaccination on Death from Childhood Diarrhea in Mexico

Richardson et al, NEJM 2010
Early Experience with Rotavirus Vaccines

Challenge 1

How well will oral rotavirus vaccines work in the developing world?
Hurdles to Immunization for a Live Oral Rotavirus Vaccine

Factors that lower viral titer

- Breast milk
- Stomach acid
- Maternal antibodies
- OPV

Factors that impair immune response

- Malnutrition - Zn, Vit A
- Interfering microbes - viruses and bacteria
- Other infections - HIV, malaria, TBC
Moderate Efficacy of Rotavirus Vaccines in Africa and Asia

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Region</th>
<th>Countries</th>
<th>Efficacy (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RotaTeq</td>
<td>Africa</td>
<td>Ghana, Kenya, Mali</td>
<td>64% (40%-79%)</td>
</tr>
<tr>
<td>RotaTeq</td>
<td>Asia</td>
<td>Bangladesh, Vietnam</td>
<td>51% (13%-73%)</td>
</tr>
<tr>
<td>Rotarix</td>
<td>Africa</td>
<td>South Africa, Malawi</td>
<td>62% (44%-73%)</td>
</tr>
</tbody>
</table>

Armah et al. Lancet 2010
Zaman et al. Lancet 2010
Madhi et al NEJM 2010
Despite lower efficacy, Rotarix prevented more severe rotavirus disease per 100 vaccinated children in Malawi because of higher baseline incidence.

Efficacy

<table>
<thead>
<tr>
<th>Region</th>
<th>Efficacy</th>
<th>Placebo</th>
<th>Vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Africa</td>
<td>60%</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>South Africa</td>
<td>77%</td>
<td>3.5</td>
<td>1</td>
</tr>
<tr>
<td>Malawi</td>
<td>50%</td>
<td>8</td>
<td>4</td>
</tr>
</tbody>
</table>

Madhi et al. NEJM 2010; 362: 346-357
Challenge 2

How well will vaccines protect against range of strains?
Rotarix (G1P8) efficacy similar against rotavirus GE due to vaccine & non-vaccine types in Africa

Challenge 3

Will new Rotavirus Vaccines cause Intussusception?
An Earlier Vaccine (Rotashield) Withdrawn in US in 1999 Because of Association with Intussusception

1 intussusception per 10,000 vaccinated infants
Current Vaccines Not Associated with Intussusception in Large Pre-Licensure Trials

- Trials of 60-70,000 infants designed to assess intussusception risk
- No risk identified with either vaccine
- Low risk could not be excluded

Vesikari et al and Ruiz-Palacios et al, NEJM 2006
Post-Licensure Intussusception Data

• Mexico, Brazil, Australia, and US have identified a low-level risk of intussusception after both vaccines
  – ~1-5 cases per 100,000 vaccinated

• Key Question – How does this level of risk compare with the observed benefits?
### Mexico: Vaccination Benefit versus Risk

<table>
<thead>
<tr>
<th></th>
<th>Admissions</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rotavirus events averted by vaccination</td>
<td>-12,000</td>
<td>-700</td>
</tr>
<tr>
<td>Intussusception events caused by vaccination</td>
<td>+43</td>
<td>+2</td>
</tr>
<tr>
<td>Rotavirus events averted vs. Intussusception caused</td>
<td>300 to 1</td>
<td>350 to 1</td>
</tr>
</tbody>
</table>
Challenge 4 -- Protecting Children in Early Infancy

Age Distribution of Rotavirus Hospitalizations in First Year of Life

WHO

Blantyre, Malawi

Matlab, Bangladesh
Challenge 5 – Vaccine Supply

Big Pharma
Merck
GSK
Emerging Manufactures
Brazil
Indonesia
China
Germany
India
Challenge 6 -- Financing

Rotarix -- $2.50 per dose
RotaTeq -- $3.50 per dose
Developing Next Generation Rotavirus Vaccines: Prospects from the Pipeline to Address Remaining Public Health Needs

Mary K. Estes, Ph.D.
Cullen Professor of Human & Molecular Virology
Director, TMC Digestive Diseases Center
Rotavirus Vaccine Development

• Based on clear need from global disease burden
• Lack of disease in children > 5 yrs of age indicated immunity develops
• What type of vaccine will best induce protective immunity?
  – Live, attenuated, oral vaccines
    • Less expensive to produce
    • Induce IgA, IgG and herd immunity
  – Non-replicating vaccines
    • May improve efficacy in children
      – in children in some settings
    • Less safety risks
Live Attenuated Rotavirus Vaccine Development

- RotaShield:US
- Rotarix:MX
- RotaTeq:US
- RotaTeq and Rotarix US and globally with different efficacies
- More live, attenuated vaccines
- Intussusception
Rationale for More Live-Attenuated Rotavirus Vaccines

• Currently licensed oral live, attenuated rotavirus vaccines offer great benefit to populations in resource-limited countries but are costly and have reduced efficacy in those populations

• Vaccines must provide protection early, be safe and effective in the presence of maternal antibody

• Production of initial vaccines not sufficient to cover all children
New Rotavirus Vaccines in the Pipeline

• ROTAVAC – Bharat 116E G9P[11]
  – Licensed in India, 2014
• RV3-BB G3P[6] (from Australia) with Biofarma in Indonesia
  – Phase 1 and phase 2 immunogenicity trials completed and phase 2b immuno/safety trial ongoing with evaluation of neonatal dose
• Lanzhou monovalent G10P[12] licensed and in use in China
• Rotavin-IM G1P[8] licensed in Vietnam
• Live, attenuated reassortant rotaviruses
  – BRV-Hu reassortant (pentavalent G1-4 with G9)
  – Multivalent reassortant lamb rotavirus
Rationale: Next Generation Rotavirus Vaccines

• Subunit protein NRRV candidates:
  - May provide superior efficacy in target populations
  - Projected to be less expensive (<$1 per dose)
  - May be added to EPI vaccines, facilitating delivery

• Parenteral vaccines can protect against enteric diseases (e.g., polio, cholera, typhoid, hepatitis A)

• Focus on vaccines capable of eliciting a rotavirus neutralizing antibody response as passive transfer of such antibodies can provide protection
Non-replicating RV Vaccine Candidates

- Protein subunit vaccines
  - two VP8 formulations
- Inactivated virus
- Virus-like particle (VLP) vaccines
Characteristics of P2-VP8 Vaccine

- Developed at US NIH, led by Dr. Yasutaka Hoshino
- Truncated VP8 subunit from human Wa strain (G1P[8]) fused to the tetanus toxin P2 CD4 epitope
  - Expressed in *E. coli*
  - Purified using hydrophobic interaction and anion exchange liquid chromatography
  - Liquid formulation, adsorbed to aluminum hydroxide
- Preclinical toxicity testing in rabbits at doses up to 60 µg
- Non-pyrogenic
- Elicits homotypic and heterotypic antibodies that neutralize P[8] and P[4] rotavirus strains in preclinical studies

Wen 2012 Vaccine
Rotavirus VP8*

VP8*
VP4
VP7
VP6
VP8*
VP7
VP5*
Hsc70 binding site
Trp5
S=S
DGE
HR
IDA
KID
Fusion domain
Rationale for Vaccine Construct and Formulation: Preclinical Studies

- Inclusion of P2 T-cell epitope engendered more rapid rise in neutralizing antibody
- Addition of aluminum adjuvant increased overall titer and promoted earlier neutralizing antibody titer
- P2-VP8 subunit vaccine elicited good heterotypic neutralizing antibody response to P4 strains (but not P6)
- Protection from disease in neonatal piglets (delayed onset and shorter duration; trend to decreased shedding)
“A Phase 1 Double-blinded, Randomized, Placebo-controlled Dose Escalation Study to Examine the Safety, Reactogenicity, Tolerability and Immunogenicity of the P2-VP8 Subunit Rotavirus Vaccine in Healthy Adult Volunteers”

• First-in-human testing of the P2-VP8 subunit rotavirus vaccine

• Enrollment: Dec 2012 – Feb 2013
# VAC 009 Study Schema

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Dosing Groups</th>
<th>N</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>10 µg vaccine with Al(OH)\textsubscript{3}</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>4</td>
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<tr>
<td>2</td>
<td>30 µg vaccine with Al(OH)\textsubscript{3}</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>4</td>
</tr>
<tr>
<td>3</td>
<td>60 µg vaccine with Al(OH)\textsubscript{3}</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td><strong>Total</strong></td>
<td><strong>36 vaccine</strong></td>
</tr>
</tbody>
</table>

Vaccine Schedule: Days 0, 28 and 56
Good Safety Profile

- No SAEs during the active vaccination phase
- One SAE identified in long-term follow-up
  - Pneumonia 4 months after final vaccination
Anti-P2-VP8 IgA EIA Titers (IgG also)

Vertical lines represent GMT & corresponding 95% CI

Proportion of responses >4-fold

<table>
<thead>
<tr>
<th>Vaccination</th>
<th>Week 0</th>
<th>Week 28</th>
<th>Week 56</th>
<th>Week 84</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>0.0%</td>
<td>0.0%</td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
<tr>
<td>10 µg</td>
<td>0.0%</td>
<td>66.7%</td>
<td>90.9%</td>
<td>100.0%</td>
</tr>
<tr>
<td>30 µg</td>
<td>0.0%</td>
<td>75.0%</td>
<td>91.7%</td>
<td>100.0%</td>
</tr>
<tr>
<td>60 µg</td>
<td>0.0%</td>
<td>66.7%</td>
<td>91.7%</td>
<td>100.0%</td>
</tr>
</tbody>
</table>
Neutralization Antibody Responses to Human Rotavirus VP4 (P) Types at 60 µg (> 4-fold increase 28 days after 3d dose)

Santos and Hoshino, 2004
Conclusions from Phase 1 Trial

- Vaccine safe and well tolerated
- Vaccine elicits a robust antibody response to several homologous P[8] strains of rotavirus
  - Modest response to a P[4] strain
  - Meager response to a P[6] strain
- Response rates lower in those with high levels of pre-existing antibody
- Performance of the vaccine in immunologically naïve subjects remains to be determined
Next Steps

• Descending-age, dose-escalation trial in toddlers and infants in South Africa
  – Safety/tolerability
  – Immunogenicity
  – “Efficacy” against shedding with Rotarix challenge

• Preclinical assessment of additional P genotypes to broaden neutralizing responses
Live Attenuated Rotavirus Vaccine Development

RotaShield:US  Rotarix:MX  RotaTeq:US

RotaTeq and Rotarix US and globally with different efficacies

More live, attenuated vaccines

Intussusception

!? ?

NRRV
NRRV Vaccine Development: Discussion

• What level of efficacy will be expected/needed in developing country populations?

• Safety – will NRRVs reduce the small risk of intussusception observed?

• Pricing – will NRRVs be much less expensive?

• Programatic issues: will another injectable vaccine be acceptable in the EPI system?
  – Will the potential for combination vaccines with other enteric pathogens (ST-ETEC, EPEC, Shigella, Norovirus) help address this question?

• Manufacturers: in developing countries?
Acknowledgements

PATH
Jorge Flores
Alan Fix
Stan Cryz

NIAID
Fred Cassels

GATES Foundation
Duncan Steele

WHO
Thomas Cherian
Rotavirus Vaccines

Questions?
Neutralizing Antibody to Other Rotavirus Strains
(>4-fold increase 28 days after 3rd dose)

<table>
<thead>
<tr>
<th>Strain</th>
<th>P type</th>
<th>10 µg % (CI)</th>
<th>30 µg % (CI)</th>
<th>60 µg % (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wa</td>
<td>8</td>
<td>67 (35, 90)</td>
<td>42 (15, 72)</td>
<td>58 (28, 85)</td>
</tr>
<tr>
<td>89-12</td>
<td>8</td>
<td>83 (52, 98)</td>
<td>67 (35, 90)</td>
<td>83 (52, 98)</td>
</tr>
<tr>
<td>P</td>
<td>8</td>
<td>58 (28, 85)</td>
<td>67 (35, 90)</td>
<td>83 (52, 98)</td>
</tr>
<tr>
<td>WI61</td>
<td>8</td>
<td>42 (15, 72)</td>
<td>67 (35, 90)</td>
<td>83 (52, 98)</td>
</tr>
<tr>
<td>DS1</td>
<td>4</td>
<td>0 (0, 26)</td>
<td>50 (21, 79)</td>
<td>58 (28, 85)</td>
</tr>
<tr>
<td>SC2</td>
<td>4</td>
<td>8 (0, 38)</td>
<td>17 (2, 48)</td>
<td>25 (6, 57)</td>
</tr>
<tr>
<td>ST3</td>
<td>6</td>
<td>0 (0, 26)</td>
<td>8 (0, 38)</td>
<td>17 (2, 48)</td>
</tr>
<tr>
<td>BRD</td>
<td>6</td>
<td>0 (0, 26)</td>
<td>25 (6, 57)</td>
<td>25 (6, 57)</td>
</tr>
</tbody>
</table>
Evaluation of the Next Generation of Rotavirus Vaccines

Global Vaccine and Immunization Research Forum
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Kathleen M. Neuzil, MD, MPH
Director, Vaccine Access and Delivery Global Program
WHO recommends the inclusion of rotavirus vaccination of infants into all national immunization programs

Rotavirus vaccination
Data from trials in Latin America, Europe and the United States of 2 oral, live, attenuated rotavirus vaccines, Rotarix (GlaxoSmithKline) and RotaTeq (Merck & Co., Inc.) were reviewed by SAGE in 2005. Noting the variable efficacy of live, oral vaccines in different populations, SAGE considered that the introduction of vaccines would be appropriate only in regions where successful phase III efficacy trials had been conducted. SAGE therefore recommended that rotavirus vaccines be included in national immunization programmes in countries where data on vaccine efficacy suggest a significant public health impact; SAGE also noted the need to urgently generate such data in Africa and Asia.

Vaccination antirotavirus
En 2005, le SAGE a examiné les données d’essais cliniques menés en Amérique latine, en Europe et aux États-Unis concernant 2 vaccins antirotavirus vivants atténués pour voie orale, le Rotarix (GlaxoSmithKline) et le RotaTeq (Merck & Co. Inc.). Notant que l’efficacité des vaccins vivants pour voie orale variait selon les populations, le SAGE a estimé judicieux de les adopter seulement dans les Régions où des essais d’efficacité de phase III avaient été effectués avec succès. Il a par conséquent recommandé que les vaccins antirotavirus soient inclus dans les programmes de vaccination nationaux des pays où les données sur l’efficacité des vaccins semblent indiquer qu’ils ont des répercussions importantes en santé publique; il a par ailleurs noté qu’il était urgent d’obtenir des données de ce type en Afrique et en Asie.
National RV introductions by WHO region: 53 countries*

AMRO
- Bolivia
- Brazil
- Cayman Islands**
- Colombia
- Dominican Republic
- Ecuador
- El Salvador
- Guatemala
- Guyana
- Haiti
- Honduras
- Mexico
- Nicaragua
- Panama
- Paraguay
- Peru
- United States
- Venezuela

AFRO
- Botswana
- Burkina Faso
- Burundi
- Ethiopia
- The Gambia
- Ghana
- Malawi
- Mali
- Rwanda
- South Africa
- Tanzania
- Zambia

EURO
- Armenia
- Austria
- Belgium
- Finland
- Georgia
- Israel
- Luxembourg
- Moldova
- United Kingdom

EMRO
- Bahrain
- Iraq
- Libya
- Morocco
- Qatar
- Saudi Arabia
- Republic of Sudan
- Yemen

SEARO
- Philippines

WPRO
- Australia
- Fiji
- Marshall Islands
- Micronesia
- Palau

Not GAVI-eligible [33]
GAVI-eligible [20]

*National introductions by WHO region as of 14 January 2014
**Not a WHO member state
RV= rotavirus vaccine
GAVI-supported RV introductions by WHO region: 20 countries*

*National introductions by WHO region as of 14 January 2014

RV = rotavirus vaccine
Currently licensed & prequalified rotavirus vaccines

**Name: Rotarix®**
- **Manufacturer:** GlaxoSmithKline
- **Date prequalified:** Mar 12, 2009
- **Presentation:** 1-dose plastic tube, liquid
- **VVM:** Type 14
- **GAVI price:** $2.50 per dose
- **Shelf life:** 36 months @ 2-8 °C
- **Cold chain volume per dose:**
  - 1-dose carton: 115.3 cm$^3$
  - 10-dose carton: 43.3 cm$^3$
  - 50-dose carton: 17.1 cm$^3$

**Name: RotaTeq®**
- **Manufacturer:** Merck & Co. Inc.
- **Date prequalified:** Oct 7, 2008
- **Presentation:** 1-dose plastic tube, liquid
- **VVM:** none
- **GAVI price:** $3.50 per dose
- **Shelf life:** 24 months @ 2-8 °C
- **Cold chain volume per dose:**
  - 10-dose carton: 75.3 cm$^3$
  - 25-dose carton: 46.3 cm$^3$
Rotavirus vaccine product choice in GAVI-eligible countries*

*National introductions as of 14 January 2014

AFRO
- Burkina Faso (2013)
- Burundi (2013)
- Ethiopia (2013)
- Gambia (2013)
- Ghana (2012)

EURO
- Armenia (2012)
- Georgia (2013)
- Moldova (2012)

AMRO
- Bolivia (2008)
- Guyana (2010)
- Haiti (2013)
- Honduras (2009)
- Nicaragua (2006)

EMRO
- Yemen (2012)
- Sudan (2011)

Rotarix® (Year) [15]   RotaTeq® (Year) [5]
Significant declines in diarrhea hospitalizations

Rotavirus hospitalizations: reductions of 50% or more in children 0-2 years old following rotavirus vaccination

- Belgium 50-77% RotaTeq® & Rotarix®
- Bolivia 70% Rotarix®
- Australia 87% RotaTeq® & Rotarix®
- US 66-86% RotaTeq®

All-cause diarrhea hospitalizations: reductions of nearly 20% or more in children 0-2 years old following rotavirus vaccination

- Brazil 17-48% Rotarix®
- El Salvador 28-37% Rotarix®
- USA 29-52% RotaTeq®
- Belgium 33% RotaTeq® & Rotarix®
- Austria 74-79% RotaTeq & Rotarix®
- Mexico 40% Rotarix®

Note: Data derived from Table 2 from Patel MM, Glass R, Desai R, Tate JE, Parashar UD. Fulfilling the Promise of Rotavirus Vaccines: How Far Have We Come Since Licensure? The Lancet Infectious Diseases. 2012;12(7):561-570.
Percentage of hospitalized diarrhea due to rotavirus in African countries in WHO-coordinated Global Rotavirus Surveillance Network (GRSN), 2006-2012

**Hospital-based gastroenteritis cases positive for rotavirus**

- Kenya (rural west): 20%
- Ethiopia: 21%
- Uganda (Kampala): 33%
- Sudan: 36%
- Mauritius: 42%
- Togo: 48%
- Zimbabwe: 49%
- Ghana (south): 49%
- Nigeria (southeast): 56%

African total: 40.7%
March 2014: Where are we now with rotavirus vaccines?

- Global recommendation for rotavirus vaccine introduction
- 53 countries have introduced rotavirus vaccines into their national immunization programs
- 13 additional GAVI-eligible countries approved to introduce in 2014/2015
- Impact has been demonstrated – while substantial, efforts to further reduce severe disease in low resource countries warranted
- Two pre-qualified rotavirus vaccines
- No correlate of protection
What are the potential advantages or challenges of “new” rotavirus vaccines?

• More effective at preventing severe rotavirus gastroenteritis?
• Cross-protection?
• Longer lasting immunity (second year of life)?
• Safety?
• Mode of administration?
• Logistics/cold chain?
• Lower cost and more stable supply?
What are the potential advantages or challenges of “new” rotavirus vaccines?

- More effective at preventing severe rotavirus gastroenteritis?
- Cross-protection?
- Longer lasting immunity (second year of life)?
- Safety?
- Mode of administration?
- Logistics/cold chain/vaccine delivery?
- Lower cost and more stable supply?

What are the relative trade-offs of the above characteristics?

How will/should products be compared?

How will/should safety be assessed?