

Rotavirus Vaccine: Demand Forecast, Impact Analysis & Supply Landscape

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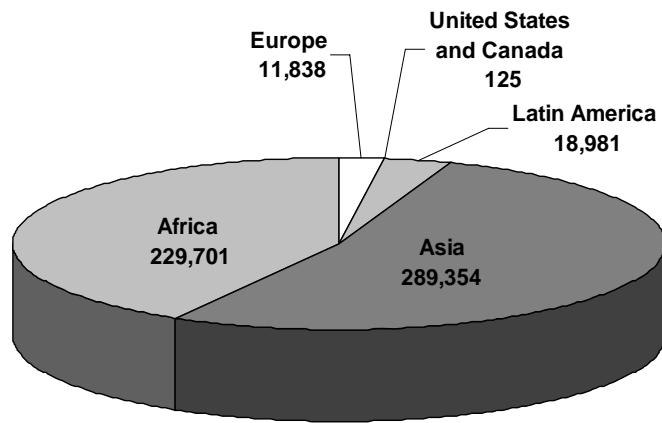


Agenda

- Demand forecast assumptions
- Demand forecast results
- Vaccine impact
- Vaccine supply landscape and scenarios



Estimated Global Distribution of Rotavirus-related Deaths (from Parashar, 2006)



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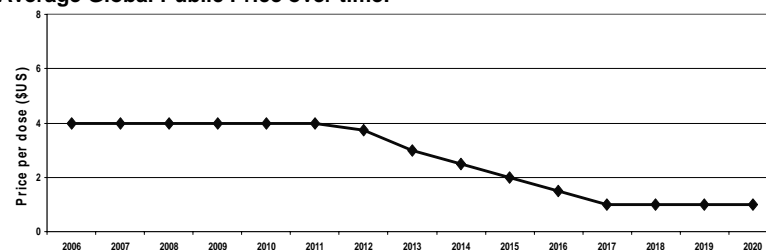
DEMAND FORECAST:
ASSUMPTIONS

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Demand Forecast Assumptions

- Doses/Course: 2.5 (assumes 50/50 market share for 2 and 3-dose vaccine)
- Country Vaccine Coverage Rates: DTP3 used as proxy for rotavirus
- Funding Strategy: to 2015-GAVI subsidy for remaining cost of vaccine after country copayment-copayment based on income status
- Market Equilibrium Price: \$1.00¹
- Base case Price (2007): \$10/course
(If average doses per course = 2.5, price per dose = \$4.00)
- Average Global Public Price over time:



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¹Market equilibrium price based on "Cost of Goods" analysis, conducted by independent consultant



Demand Forecast Assumptions

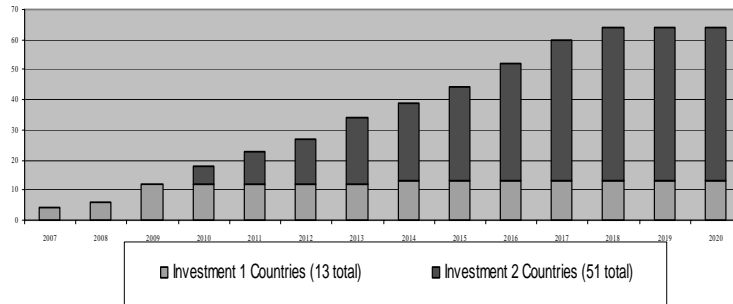
- Order of Adoption, by Country
 - Early, Middle and Late Adopters
 - Quantitative criteria used to model adoption by country, including:
 - DTP3 coverage, Hep B introduction, Hib introduction, burden of disease, presence of rotavirus surveillance network
 - Qualitative, country level indicators of demand
 - Country consultations with ministry officials and WHO regional officers
- Some countries will not introduce vaccine
 - Selected 8 countries-in-conflict that represent approx 8% of the total birth cohort
 - Rate of Vaccine Uptake within country
 - Range: 2-4 years to reach peak coverage¹

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¹Adapted from L. Wolfson "Vaccine Coverage Trajectories" Sept 2004 WHO



Cumulative number of countries adopting rotavirus vaccine, by year: Investment 1 and 2

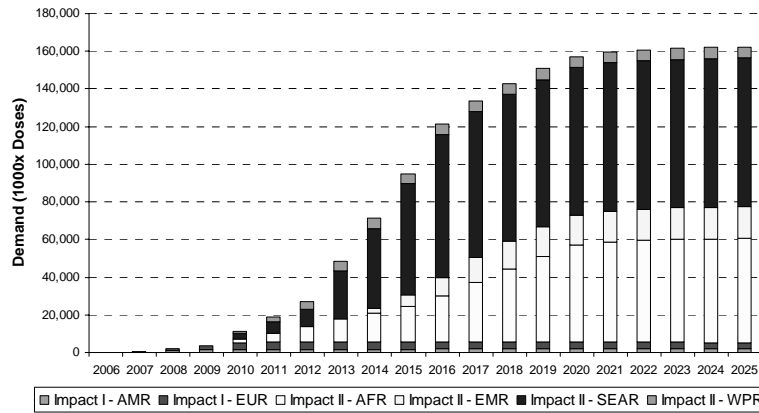


DEMAND FORECAST: RESULTS – GAVI ELIGIBLE



Forecasted Demand-Doses—All Regions

Forecasted Demand, Doses (1000x Doses)



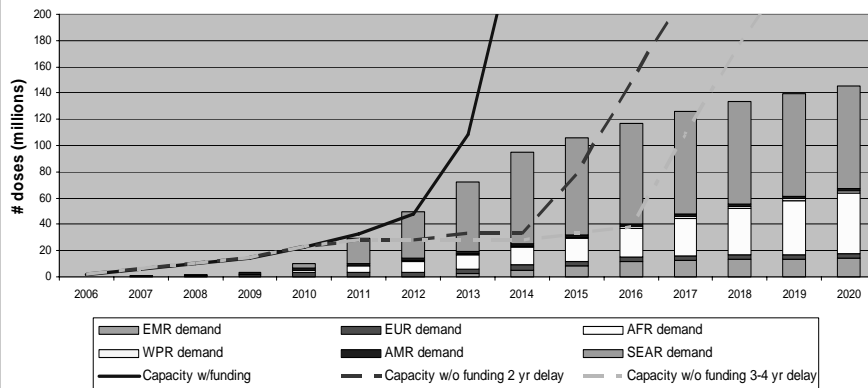
Approximately 160 million doses in peak year 2021—for 64 GAVI-eligible countries

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Matching demand and supply: Importance of strategic planning

Estimated demand for 64 countries with GNI <\$1,000 per capita, and 3 capacity scenarios



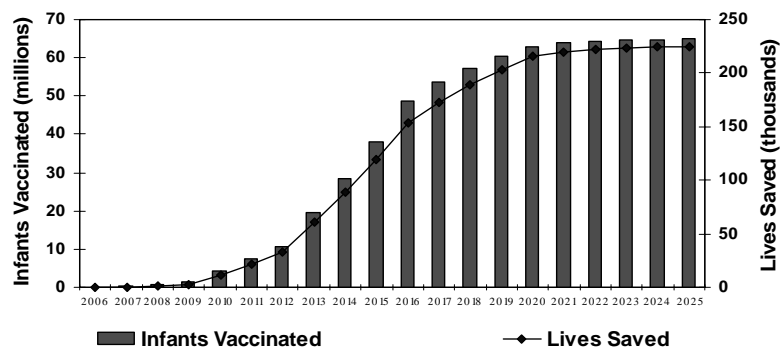
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VACCINE IMPACT



How Many Lives Can Be Saved Over the Next 20 Years?

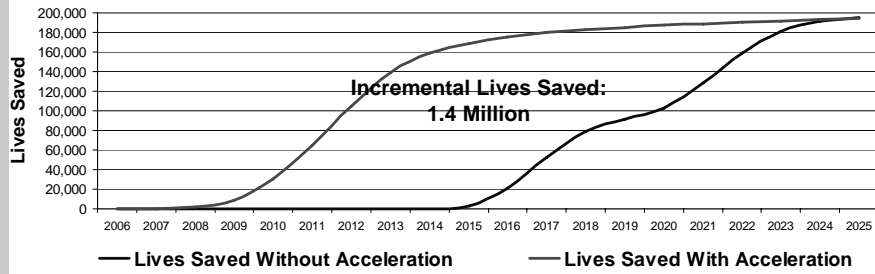


Total Infants Vaccinated: 716 million Lives Saved¹: 2.4 million
Hospital and Outpatient Visits Avoided²: 93M

¹ Adapted from Rheingans et.al 2005 (unpublished) 3.4 lives saved per 1000 infants vaccinated (range: 2.5 to 5 lives saved per 1000; = 1.8 to 3.6 million lives saved)
² Adapted from Rheingans et.al. 2005 (unpublished) and Parachar 2003: 100 hospitalizations avoided per 1000 infants vaccinated



How Many Lives Can Be Saved with Accelerated Introduction?



ROTAVIRUS VACCINE SUPPLY



Supplier Landscape – Multinationals

	Rotarix® (GSK)	RotaTeq® (Merck)
Origin	Human monovalent	Bovine pentavalent
Strain	G1, P(8)	G1, G2, G3, G4, P(8)
Dosage	2 doses	3 doses
Timing	With DTP1, DTP2	With DTP1, DTP2, DTP3
Presentation	Lyophilized; reconstituted	Liquid
Administration	Oral; applicator	Oral; squeeze tube
Storage	2°-8°C	2°-8°C
Co-administration	OPV, IPV, DTaP, DTwP HepB, Hib, PCV-7	IPV, DTaP, DTwP HepB, Hib, PCV-7
Phase 2 & 3 Safety & Efficacy Trials	n=63,225 healthy infants USA, Canada, Latin America (11), Taiwan, Singapore, Hong Kong, Belgium, Germany, Finland, South Africa, Bangladesh, Sweden, Taiwan	n=70,301 healthy infants USA, Mexico, Costa Rica, Jamaica, Guatemala, Puerto Rico, Taiwan, Belgium, Finland, Germany, Italy
Licensure	EMA-2006; > 30 countries, including several GAVI-eligible countries	FDA-2006
Efficacy vs. rotavirus gastroenteritis	85% vs. severe rotavirus gastroenteritis and 100% vs. more severe episodes	98% vs. severe G1-G4 rotavirus gastroenteritis
Efficacy vs. gastroenteritis from any cause	40% vs. severe gastroenteritis of any cause; 42% vs. hospitalization for severe gastroenteritis	59% vs. hospitalization for diarrhea of any cause in first year of life
Intussusception	No association	No association

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Supplier Landscape: Developing Country Manufacturers

Supplier	Potential Year of Market Entry	Comments
Butantan Institute (Brazil)	<2010	Supply primarily to Brazil; WHO pre-qual. unlikely
Bharat Biotech International Ltd.(India)	2011	Initial supply only to India; limited international procurement
Serum Institute (India)	2012	Multivalent reassortant licensed from NIH
Shantha Biotech (India)	2013	Multivalent reassortant licensed from NIH
Wuhan Institute of Biological Products (China)	2013	Multivalent reassortant licensed from NIH
Chengdu Institute of Biological Products (China)	2014	Multivalent reassortant licensed from NIH

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*Manufacturers considered most likely to enter the marketplace



Potential Supply Landscape: 2007 - 2010

- Both GSK and Merck eager to supply vaccine
 - Estimated Demand is Modest – < 20 million doses total, over 4 year period
- GSK
 - Submitted price-volume offer to UNICEF in 2004
 - Establishing global manufacturing capacity (formulation-fill-finish) through acquisition and contract manufacturing
 - Current formulation is lyophilized; regulatory submission of liquid formulation dossier expected in 1-2Q2008
- Merck
 - Indication by Merck of 8-10M doses per year available for GAVI-eligible countries without increased investment in production capacity
 - Concerned about meeting projected demand in GAVI-eligible countries beyond 2010

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Potential Supply Landscape: 2011 and beyond

- Estimated demand increases significantly, reaching 160 million doses per year by 2021
- Emerging suppliers may begin entering market as early as 2011
- Uncertainty in development and production timelines with emerging suppliers
- Role of multinationals vs. emerging suppliers
 - Multinationals may be needed for a limited time, or potentially long-term based on outcomes of emerging supplier development efforts

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Advancing Rotavirus Vaccine Development (ARVAC)

- Goal: Accelerate the development and introduction of affordable, safe and efficacious rotavirus vaccines into the developing world by providing technical and financial support to developing country manufacturers.
- Stimulate market development
 - Increasing total supply of rotavirus vaccines for low-income countries
 - Introducing price competition in the market
- Support
 - Bharat
 - NIH technology licensees

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Manufacturer commitments-impact on GAVI supply

- Multinationals likely to dedicate proportion of doses to GAVI
- Merck to cover first 3 years of vaccine costs for Nicaragua
- Chinese manufacturers will undoubtedly dedicate a fraction of their supply to national populations. Current potential vaccine market in China is approx. 48 million doses per year (3 doses per course).
- Chinese and Indian suppliers will likely reach out to middle-income markets as well;

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Preliminary estimates of potential supply available to GAVI: 2007-2015*

Year	Multinationals Potential Supply: # of doses available for GAVI (millions)	Emerging Suppliers Potential Supply: # doses available for GAVI (millions)	Total Supply: Multinationals + Emerging suppliers	Estimated Demand-Doses in GAVI-eligible countries (millions)
2007	6	0	6	0.5
2008	10	0	10	2
2009	14	0	14	4
2010	18	0	18	11
2011	18	15	33	19
2012	18	20	38	27
2013	18	60	78	50
2014	18	150	168	70
2015	18	240	258	95

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*Based on preliminary analysis conducted by RVP, assumes external support for emerging suppliers



Major Issues to Consider

- Cost of Goods
 - Estimated that multinational COGs approximately 3-4 times higher than emerging suppliers
- Supply uncertainty
 - Manufacturers typically require 3-5 year lead time if new investment in production capacity is needed
 - Emerging country supplier timelines and probability of successful development and production
- Demand uncertainty
 - Early adopter demand fairly predictable, but modest
 - African and Asian countries will await results of clinical trials & subsequent GAVI decision in early 2010
 - GAVI will play a key role in stimulating demand

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Conclusions

- Rotavirus acute gastroenteritis is ubiquitous, with developing world infants bearing an overwhelming proportion of severe disease and death.
- Very unlikely that multinational firms will manufacture sufficient quantities of vaccine at an affordable price to satisfy demand in developing countries.
- Efforts underway to accelerate development of new Rotavirus vaccines by emerging-country manufacturers to meet expected global demand.
- Supply-demand strategy will need close monitoring and course corrections over time.

