GVIRF 2014: title of the session. Plenary 3: Developing Next generation Vaccines: Defining the Improvements Needed and Evaluating Their Potential	
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Session Outline	**Chair:** K. Neuzil **Opening remarks:** K. Neuzil **Presentations:** U. Parashar; M. Estes; K. Neuzil **Discussants:** M. Estes, G. Kang, K. Neuzil, U. Parashar, D. Steele **Closing Remarks**: K. Neuzil
Objectives of the session	To discuss: • Existing vaccines, their deployment and comparison of their benefit in low income, middle income and high income countries. • New vaccines in development, and justifying their need.
Main outcome	• The significant reduction in hospitalizations due to severe diarrhoea in the 3 years following the introduction of the 2 licensed vaccines - Rotarix and RotaTech – in 53 countries was affirmed and the continued expansion of their use in other countries was strongly encouraged • The need for improved vaccines was stated; the attributes desired in such vaccines, the challenges in designing them and the potential regulatory hurdles in testing and licensing were discussed
Summary	Two rotavirus vaccines – Rotarix™and RotaTech™ - have been shown in trials in middle and high income countries to have an efficacy of 85%-98% in preventing serious gastroenteritis. These vaccines have been introduced in 53 countries, in 20 of them with GAVI support, with several more introductions to follow in the near future. Active surveillance in the US has shown a dramatic and rapid decline in all-cause and hospitalization for RV-specific acute gastroenteritis (RVGE) after vaccine introduction while a similar impact was also seen in El Salvador. Significantly, herd protection was observed, with reduction of RVGI in unvaccinated children. All-cause diarrhoeal mortality was seen to decline significantly in Mexico after vaccine introduction. As with other live-attenuated oral vaccines, efficacy of rotavirus vaccines is more modest - 51% to 65% - in lower income countries. Given this, integrated approaches to diarrhoea control as outlined in the Global Action Plan for the Prevention and Control of Pneumonia and Diarrhoea (GAPPD) are to be strengthened. However, studies show that despite the lower efficacy in such settings, because of the higher incidence of disease, rotavirus vaccines prevented more severe rotavirus disease per 100 vaccinated as compared to high resource settings. There was good cross-protection against a range of rotavirus strains. An intussusception risk of 1-5 cases /100 000 vaccinated has been seen, but benefit-risk assessments continue to clearly justify the WHO's recommendation for universal infant vaccination. GAVI Alliance support has made vaccines accessible to low income countries with the present GAVI price ranging from 2.50 to 3.50 USD/dose. New rotavirus vaccines may be needed to improve vaccine efficacy in low

	income settings. Such vaccines should also be safer, continue to provide cross protection against a variety of rotavirus strains, induce longer lasting immunity, have a lower cold chain footprint and improved thermostability and be more cost-effective. These are substantial challenges, particularly since the immunological correlates of protection are not known, and due to difficulties in comparing new products with current vaccines in situations of substantially lowered disease burden. Nevertheless, there is a robust pipeline of new vaccines, including live attenuated vaccines being developed in several countries including India (Bharat) and China (Lanzhou), where domestically produced vaccine are now licensed, Vietnam, Indonesia and Brazil. While live attenuated vaccines induce mucosal IgA and, potentially, herd immunity, and may be cheaper, non-replicating (i.e. killed) vaccines may pose a lower safety risk. The latter may also be useful in older children in low-income settings, where there is substantial RVGE burden. An injectable subunit vaccine, P2-VP8, a fusion protein of the rotavirus VP8 protein and the CD4 epitope of the tetanus toxin P2, is also in development. This vaccine has been shown to rapidly induce neutralizing antibody to rotavirus and is soon to be tested in early phase trials. Parenteral combination products of rotavirus and other enteric vaccines, e.g. against ST-ETEC, EPEC, Shigella and norovirus could be a welcome addition to the existing vaccine portfolio.
Key references or quotes	