ROTAVAC® - does it need a buffer?

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Background
Currently licensed oral rotavirus (RV) vaccines contain a buffering agent (either as part of a ready-to-use liquid formulation or added during reconstitution) to reduce possible degradation of the vaccine virus in the infant's gut. The presence of a buffer in RV vaccines, poses several programmatic challenges, such as a larger volume of vaccine, increasing the cold chain footprint and spit ups during administration, and introducing the need for reconstitution steps during administration.

The acidic environment of the stomach affects the viability of RV. In addition, in humans, homologous RVs (human origin RV in a human) are much more (>1000 fold) infectious than heterologous RV (non-human origin RV in a human) and only minimal quantities of homologous RV (10 infectious doses or less) are generally able to cause infection, immune response, and illness. Given its human origin and the age at immunization, it is plausible that the ORV 116E strain may replicate and confer immunity without a buffer administration. We evaluated the immunogenicity and safety of ROTAVAC® without buffer and ROTAVAC® with buffer in a phase 4, multicentre, single-blind, randomized clinical trial in healthy infants in India.

Methods
900 infants, approximately 6, 10 and 14 weeks of age, were assigned to 3 groups to receive ROTAVAC® (0.5mL dose) orally: (i) 2.5 mL of citrate-bicarbonate buffer (Group I), (ii) ROTAVAC® (alone, without any buffer (Group II), or (iii) ROTAVAC® mixed with buffer immediately before administration (Group III)). Non–inferiority was compared among the groups for differences in serological responses (detected by serum anti-RV IgA) and safety.

Results
The proportion of infants who seroconverted were 30.7% (95%CI: 25.6, 36.2), 35.2% (95%CI: 29.9, 40.8), and 33.6% (95%CI: 28.3, 39.2) in group I, II and III respectively.

Conclusions
Administration of ROTAVAC® without buffering agent was shown to be well tolerated and immunogenic. If this buffer is not required by health workers, important programmatic issues, such as incorrect reconstitution of, temporary unavailability of the buffer, reduction of the cold chain footprint and waste management may be eliminated. ROTAVAC® is the first rotavirus vaccine to be commercially adopted without a buffer at a 0.5mL dose volume.

Citation Reference: *Ella R, Bobba R, Muralidhar S, Babji S, Vadrevu KM, Bhan MK. A Phase 4, multicentre, randomized, single-blind clinical trial to evaluate the immunogenicity of the live, attenuated, oral rotavirus vaccine (116E), ROTAVAC®, administered simultaneously with or without the buffering agent in healthy infants in India. Human vaccines & immunotherapeutics. 2018:01-32.*

Clinical Trials Registry of India (www.ctri.nic.in) as CTRI/2014/04/004548