



Reply to Letter to the Editor

Response to: Letter from P. Gillard and B. Benninghoff



To the Editor,

We thank P. Gillard and B. Benninghoff for their letter and present a point by point reply. Their comments do not allude to the primary objectives of the study – lot to lot consistency of Rotasiil and immunological non-interference with UIP vaccines by Rotasiil. For the latter objective, we needed to include a control arm of a WHO prequalified rotavirus vaccine. The choice was to use RotaTeq which has a three-dose schedule as also the same IgA assay as Rotasiil. Its lack of availability at that time precluded its use leaving us with Rotarix, the only one available vaccine in the market at that time (We started the study in December 2015). Rotarix thus merely served as a control and comparison was not an intent or primary objective. The Rotarix results were in fact added in the abstract in response to a reviewer's comment.

The use of the IgA assay and timing of sample collection have already been alluded to in the discussion and have been placed in perspective. Timing of blood sampled also appears in Section 3.1 [A placebo dose was used in the Rotarix group at 14 weeks of age] and not merely in the last paragraph of the discussion. Perhaps, this could have been little more explicitly presented within the methods.

An immunogenicity study of Rotasiil can only be done using a validated assay which we did. This assay was also used in an earlier phase of testing. The study by Libster et al. quoted where Rotarix immunogenicity was tested both by WC3 (heterologous) and 89–12 (homologous) antigens, actually shows that the seropositivity rates of Rotarix using both antigens were not statistically different though the absolute difference was 9% [1]. Similarly, another study cited by the authors for the timing issue [2], too tested antibody levels at least 2 months after the last dose of Rotarix; just like in our study, with no significant difference seen in the Rotarix seroresponse rates and GMC with testing done two or three months after the last dose. As regards the 20 U/mL cut-off defined for the immune responses induced by Rotasiil, it was chosen because it is traditionally used as evidence of a natural rotavirus infection [3,4]. The same cut off was used for RotaTeq by Libster et al. [1]. We stand by both the scientific design and immunogenicity data presented both of which have been placed in context in the paper with a clear presentation of the inherent limitations therein.

Conflict of interest

Dr. Prasad S. Kulkarni, Dr. Sajjad Desai, Dr. Bhagwat Gunale, and Mr. Abhijeet Dharmadhikari are employed by SIIPL, which manufactures the BRV-PV.

References:

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- [2] Dennehy PH, Bertrand HR, Silas PE, Damaso S, Friedland LR, Abu-Elyazeed R. Coadministration of RIX4414 oral human rotavirus vaccine does not impact the immune response to antigens contained in routine infant vaccines in the United States. *Pediatrics* 2008;122(5):e1062–6.
- [3] Ward RL, Bernstein DI, Shukla R, et al. Protection of adults rechallenged with a human rotavirus. *J Infect Dis*. 1990;161(3):440–5.
- [4] Moulton LH, Staat MA, Santosham M, Ward RL. The protective effectiveness of natural rotavirus infection in an American Indian population. *J Infect Dis* 1998;178:1562–6.

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