

Review Regarding Concomitant Administration - Rotarix

MEMORANDUM

BLA/STN Number:

125265

BLA Sponsor:

GlaxoSmithKline Biologicals

BLA Product:

Human Rotavirus Vaccine Live, Oral

BLA Purpose:

To:

File

From:

Vladimir Chizhikov, DVP

Through:

K. Chumakov, DVP

Copy to:

Luba Vujcic, Regulatory Coordinator, DVRPA.

DATE:

November 1, 2007

Reviewed Documents:

125265/0.9 5.3.5.1.

Rota-033

125265/0.6 5.3.5.4.

Other Study Reports

125265/0.1 5.3.5.1

Study Report Rota-060

125265/0.0 5.3.5.4

Study Reports SOP RD-CIV-003

125265/0.0 5.3.5.4

Study Reports Val POPCO1SOP RD-CIV-003

125265/0.0 5.2

Tabular listing of all clinical studies

125265/0.0 5.3.5.1

Study report Rota-005, Rota-006, Rota-007, Rota-014, Rota-023, Rota-033, Rota-036, Rota-39

Background

GlaxoSmithKline (GSK) Biologicals' candidate oral live attenuated human rotavirus (HRV) vaccine, Rotarix®, is composed of a live, attenuated rotavirus derived from the human 89-12 strain which belongs to the G1 serotype and P[8] genotype. The proposed vaccination series consists of two doses administered orally. The first dose should be administered in infants 6 weeks through 14 weeks of age. There should be an interval of at least 4 weeks between the first and second dose. *Rotarix* is intended to be indicated for the prevention of rotavirus

gastroenteritis caused by G1 and non-G1 types (including G2, G3, G4, and G9) when administered as a 2-dose series to infants 6 to 24 weeks of age.

When incorporating a new vaccine into an existing routine immunization schedule, it will likely be administered concurrently with other routine childhood vaccines, according to local country schedules for routine infant immunization (such as 2, 4, 6 months of age in the US). Therefore, immunogenicity of co-administered routine childhood vaccinations (DTaP, DTwP, HepB, Hib, IPV, OPV, pneumococcal 7-valent conjugate vaccine and meningococcal group C conjugate vaccine) was evaluated during the course of the HRV vaccine development in studies Rota-005, Rota-006, Rota-007, Rota-014, Rota-023, Rota-033, Rota-036, and Rota-060. Clinical randomized, placebo-controlled study of the safety, reactogenicity and immunogenicity of two doses of GSK Biologicals' oral live attenuated human rotavirus (HRV) vaccine co-administered with either oral polio vaccine (OPV) or inactivated polio vaccine (IPV) in healthy infants showed that immune responses and the safety profiles of the administered vaccines were unaffected. To exclude potential effect of concomitant use of two live (HRV and OPV) vaccines on immune response to each vaccine, OPV vaccine was administered two weeks after HRV vaccination.

Review and Comments

The purpose of the current review was to assess the adequacy and performance of the serologic methods used by the sponsor to demonstrate that Rotarix vaccine did not interfere with poliovirus immune response in infants when HRV was concomitantly administered with combined vaccines containing Inactivated Poliovirus Vaccine (IPV) as one of vaccine components (e.g. Pediarix®, Infanrix hexaT, InfanrixT IPV Hib, Pentacel) as well as with Oral Poliovirus Vaccine (OPV) (administration two weeks apart.)

To assess the relative immunoresponse the sponsor measured the titers of poliovirus neutralizing antibodies in the blood of placebo and Rotarix vaccinated infant groups. The titers of poliovirus antibodies in both groups were determined by using -----

-----.

Comments: According to presented data, the determination of antibody titers during clinical studies of Rotarix vaccine was carried out using two different laboratories, the SmithKline Beecham Biologicals, Rixensart, Belgium and ----- in -----. The reviewer noted that the primary submission 125265/0 contained the SOP for ----- test procedure, used for assessment of the titer of antibodies against polio type 1, 2 and 3, as well as the results of its validation only from Belgian laboratory. The SOP and its validation results from -----
--- should additionally be requested. In addition, the SOP (SOP RD-CIV-003) of -----
test represents a ----- of the analytical protocol that has -----.
The description of the differences ----- of ----- test procedure
should be additionally requested to assess a potential impact of changes made on the test performance and comparability.

The following questions have been addressed to the sponsor in the Filing Notification (Deficiency Identified) submitted on August 02, 2007:

1. The titers of antibodies against poliovirus types 1, 2, and 3 during clinical studies of Rotarix vaccine were determined by using an ----- test adapted from the ----

