SYNOPSIS

Name of Sponsor/Company	Daiichi Sankyo Co., Ltd., Sanofi KK
Name of Finished Product	Squarekids Subcutaneous Injection Syringe
Name of Active Ingredient	Purified diphtheria toxoid, Purified tetanus toxoid, Purified *Bordetella pertussis* antigens, and inactivated polioviruses type 1, 2 and 3.
Title of Study	Immunogenicity and Safety of DD-687 given subcutaneously as a three-dose primary and booster vaccination versus commercially available DTaP and OPV in infants in Japan
Investigators	
Study Centre(s)	23 sites
Publication (reference)	The immunogenicity and Safety of a New Quadruple Combination Vaccine, Including Undiluted IPV (Salk vaccine) J Jpn Pediatr Soc. 2015;119(4):669~79
Studied Period	
Phase of Development	Phase 3
Objectives	To demonstrate that the seroprotection rates against polio viruses types 1, 2 and 3 are over 90% approximately 1 months following the primary vaccination series with DD-687
Methodology	Multi-center, two-arm, randomized, unbalanced, double-blind, clinical study
Number of Patients (planned and analyzed)	Planned: 374 subjects (test product 249 subjects, controlled product 125 subjects) Analyzed: Immunogenicity: 355 subjects for primary (test product 235, controlled product 120) 363 subjects for booster (test product 241, controlled product 122 subjects) Safety: 376 subjects (test product 248 subjects, controlled product 128 subjects)
Diagnosis and Main Criteria for Inclusion	Healthy Japanese infants who fulfill all of the following criteria: 1) Aged 3 months to 8 months inclusive on the day of inclusion 2) Informed consent form signed by the parent(s) or other legal representative 3) Able to attend all scheduled visits and to comply with all trial procedures

Test Product, Dose and Mode of Administration, Batch Number	Test product (Batch number) DD-687 (CR-NTV-003) Dosage and administration For subjects allocated into group A, 0.5 mL of DD-687 as a three-dose primary vaccination every 3-8 weeks, starting at 3-68 months of age, and followed by DD-687 booster dose 6-18 months after the three-dose primary vaccination
Duration of Treatment	Approximately 2 years
Reference Therapy, Dose and Mode of Administration, Batch Number	Control product (Batch number) DTaP (AM010A) OPV (COPV Lot1) OPV placebo (GOPV Lot1) Dosage and administration： For subjects allocated into group B, 0.5 mL of DTaP as a three-dose primary vaccination every 3-8 weeks, starting at 3-68 months of age, and followed by DTaP booster dose 6-18 months after the three-dose primary vaccination Between completion of three-dose primary vaccination and booster vaccination, 0.05 mL of OPV for group A or 0.05 mL of OPV placebo for group B was orally administered two times every 6-10 weeks.
Criteria for Evaluation	Seroprotection rate, seroconversion rate and GMT for anti-D, anti-T, anti-PT, anti-FHA, anti-polio 1, 2 and 3 antibodies after three-dose primary vaccination and booster vaccination
Statistical Method	Seroprotection and seroconversion rate with their 95% confidence intervals (CIs) for each antigen were calculated at post-injection3 and post-injection4. GMT with their 95% CIs for each antigen were calculated at pre-injection1, post-injection3, pre-injection4 and post-injection4. A 95% CI was constructed around the study-derived point estimate of the seroprotection rate against poliovirus 1, 2 and 3 approximately 1 month after the third dose of DD-687. The primary objective was achieved if the lower bound of each of the 95% CI was >90%. For each antigen, the non-inferiority of DD-687 versus DTaP and OPV was demonstrated if the 95% CI of the difference (test vaccine minus control vaccine) lay entirely above the clinically

	acceptable limit for non-inferiority (-10%) Reverse cumulative distribution curves were also presented.
Summary - Conclusion	Approximately 1 month after the three-dose primary vaccination with DD-687, all infants were seroprotected against polio virus types 1, 2 and 3. Also, after primary series, the non-inferiority of DD-687 versus DTaP and OPV was demonstrated for all antigens. Additionally, DD-687 was highly immunogenic for each antigen when administered as booster dose approximately 1 year after completion of primary series. DD-687 was well tolerated with similar safety profiles to DTaP +OPV.
Date of Report	24/June/2015