SYNOPSIS

Name of Sponsor/Company	Daiichi Sankyo Co., Ltd.
Name of Finished Product	Adsorbed cell culture-derived H5N1 influenza virus vaccine 30μg/mL intramuscular injection "Kitasato Daiichi Sankyo" Adsorbed cell culture-derived H5N1 influenza virus vaccine 60μg/mL intramuscular injection "Kitasato Daiichi Sankyo"
Name of Active Ingredient	Inactivated influenza vaccine
Title of Study	A randomized, double-blind, controlled study of KIB-PCI in Japanese healthy adult volunteers
Investigators	―
Study Centre(s)	5 sites
Publication (reference)	None
Studied Period	―
Phase of Development	Phase 3
Objectives	To assess the non-inferiority of KIB-PCI to Egg-derived influenza A (H5N1) vaccine in immunogenicity in Japanese healthy adult volunteers
Methodology	A multicenter, randomized, double-blind, parallel-group, active-controlled study
Number of Patients (planned and analyzed)	Planned: 800 subjects KIB-PCI group: 400 subjects, Egg-derived influenza A (H5N1) vaccine group: 400 subjects Enrolled: 802 subjects KIB-PCI group: 401 subjects, Egg-derived influenza A (H5N1) vaccine group: 401 subjects Analyzed (Safety):800 subjects KIB-PCI group: 400 subjects, Egg-derived influenza A (H5N1) vaccine group: 400 subjects Analyzed (Immunogenicity): 794 subjects KIB-PCI group: 398 subjects, Egg-derived influenza A (H5N1) vaccine group: 396 subjects
Diagnosis and Main Criteria for Inclusion	Diagnosis: Healthy Japanese adult volunteers Inclusion: 1) An age range from 20 to 64 years old at the time of obtaining informed consents 2) A subject without any health problems to participate in the study, judged by investigators or sub investigators 3) Able to comply with all trial procedures, take examinations stipulated in the protocol, and report their symptoms
Test Product, Dose and Mode of Administration, Batch Number	Test product (batch number): KIB-PCI 15 μg/mL formulation (CR-PCI-012) Dosage and administration: Two-dose intramuscular administration of KIB-PCI (0.5 mL) at 15 μg (as HA content) Each vaccination was administered in the deltoid region on opposite sides of the body, 14-28 days apart.
Duration of Treatment	6 weeks
Reference Therapy, Dose and Mode of Administration,	Controlled product (batch number): Egg-derived influenza A (H5N1) vaccine 15 μg/mL formulation (CR-PIA-102)

Batch Number	Dosage and administration: Two-doses intramuscular administration of Egg-derived influenza A (H5N1) vaccine (0.5 mL) at 15 μg (as HA content) Each vaccination was administered in the deltoid region on opposite sides of the body, 14-28 days apart.
Criteria for Evaluation	Primary endpoint: The difference in seroconversion rates (SCR) of the SRH antibody against the H5 antigen The ratio of geometric means titer (GMTR) of the SRH antibody against the H5 antigen Secondary endpoint: SRH antibody titer against the H5 antigen HI antibody titer against the H5 antigen Neutralizing antibody titer against the H5N1 influenza virus
Statistical Method	The immunologic non-inferiority of KIB-PCI to the control vaccine (Egg-derived influenza A (H5N1) vaccine) was assessed. The non-inferiority was demonstrated if both of the following criteria were satisfied at approximately 3 weeks after the 2nd vaccination. 1) The upper limit of the 2-sided 95% CI for the difference in SCR (control vaccine minus KIB-PCI) did not exceed 10%. 2) The upper limit of the 2-sided 95% CI for the ratio of GMTR on the basis of GMT before the 1st vaccination (control vaccine divided by KIB-PCI) did not exceed 1.5.
Summary - Conclusion	Immunogenicity summary: SCR of SRH antibody measured by using homologous antigen approximately 3 weeks after the 2nd vaccination was 55.67% (95% CI: 50.57 to 60.68) in the KIB-PCI group and 95.54% (95% CI: 92.95 to 97.38) in the control vaccine group. The difference in SCR was 39.87% (95% CI: 34.37 to 45.11). The GMTR of the SRH antibody approximately 3 weeks after the 2nd vaccination calculated by using homologous antigen was 3.816 (95% CI: 3.432 to 4.242) in the KIB-PCI group, and 9.850 (95% CI: 9.136 to 10.621) in the control vaccine group. The GMTR ratio was 2.582 (95% CI: 2.281 to 2.922). Immunologic non-inferiority of KIB-PCI to the control vaccine was not declared by evaluating the difference in SCR and the ratio of GMTR of the SRH antibody. Additional analysis was conducted by using cell cultured antigen after unblinding of the randomization schedule. SCR of the SRH antibody approximately 3 weeks after the 2nd vaccination was 55.67% (95% CI: 50.57 to 60.68) in the KIB-PCI group and 50.92% (95% CI: 45.78 to 56.05) in the control vaccine group. The difference in SCR was －4.75% (95%CI: －11.73 to 2.29). The GMTR of the SRH antibody approximately 3 weeks after the 2nd vaccination was 3.898 (95% CI: 3.512 to 4.326) in the KIB-PCI group, and 4.622 (95% CI: 4.189 to 5.099) in the control vaccine group. The GMTR ratio was 1.186 (95%CI: 1.033 to 1.361). Immunologic non-inferiority of KIB-PCI to the control vaccine was shown by evaluating the difference in SCR and the ratio of GMTR of the SRH antibody. Safety summary: The incidence of adverse events was 79.5% (318/400) in the KIB-PCI group and 88.3% (353/400) in the control vaccine group. There were no major differences between the two groups in terms of the incidence of adverse events. 1 SAE was reported by 1

	subject in the KIB-PCI group (Seventh nerve palsy reported as right facial palsy) and 1 SAE reported by 1 subject in the control vaccine group (completed suicide). Although seventh nerve palsy was considered as a reactivation of the varicella-zoster virus by the investigator, it was considered vaccination-related because it occurred approximately 8 days post-vaccination with KIB-PCI. The subject recovered from this SAE. Completed suicide was considered by the investigator that it was unlikely related to the vaccination. Conclusion: Immunologic non-inferiority of KIB-PCI to the control vaccine was not declared by evaluating the difference in SCR and the ratio of GMTR of the SRH antibody. There were no major differences in the incidence of adverse events between the two groups. In conclusion, KIB-PCI had no significant safety concerns, compared with the control vaccine.
Date of Report	March 12, 2015