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	Confirmatory clinical trial of KIB-PCI in healthy adult Japanese volunteers
Investigators	―
Study Centre(s)	3 sites
Publication (reference)	None
Studied Period	―
Phase of Development	Phase 2/3
Objectives	To assess the immunogenicity and safety of two different doses of KIB-PCI in healthy adult Japanese volunteers
Methodology	A double-blind, randomized, two-arm, dose-comparing multicenter study
Number of Patients (planned and analyzed)	Planned: 600 subjects (30 μg group: 300 subjects, 60 μg group: 300 subjects) Enrolled: 602 subjects (30 μg group: 300 subjects, 60 μg group: 302 subjects) Analyzed (Safety): 600 subjects (30 μg group: 298 subjects, 60 μg group: 302 subjects) Analyzed (Immunogenicity): 596 subjects (30 μg group: 297 subjects, 60 μg group: 299 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 30 μg/mL formulation (CR-PCI-012) KIB-PCI 60 μg/mL formulation (CR-PCI-015) Dosage and administration: Two-dose intramuscular administration of KIB-PCI (1 mL) at 30 or 60 μg (as HA content) Each vaccination (14-28 days apart) was administered in the deltoid region on opposite sides of the body.
Duration of Treatment	6 weeks
Reference Therapy, Dose and Mode of Administration, Batch Number	None
Criteria for Evaluation	Primary endpoint: SRH antibody titer against the H5 antigen Secondary endpoint:

	HI antibody titer against the H5 antigen Neutralizing antibody titer against the H5N1 influenza virus
Statistical Method	The following analyses were carried out in each group 1) Seroconversion rate For SRH antibody titer, the seroconversion rates with their 95% confidence intervals (95% CIs) were calculated at approximately 3 weeks after each vaccination. 2) Geometric Means Titer Ratio (GMTR) For SRH antibody titer, GMTRs with their 95% CIs on the basis of geometric mean titer (GMT) before the 1st vaccination were calculated at approximately 3 weeks after each vaccination. 3) Seroprotection rate For SRH antibody titer, the seroprotection rates with their 95% CIs were calculated at approximately 3 weeks after each vaccination.
Summary - Conclusion	Immunogenicity summary: The seroconversion rate (95% CI) in SRH antibody titer approximately 3 weeks after the 2nd vaccination was 65.97% (60.18 to71.43) in the 30 μg group and 78.13% (72.90 to 82.76) in the 60 μg group. The GMTR of SRH antibody titer (95% CI) approximately 3 weeks after the 2nd vaccination was 5.595 (5.028 to 6.226) in the 30 μg group and 7.014 (6.351 to 7.746) in the 60 μg group. The seroprotection rate (95% CI) in SRH antibody titer approximately 3 weeks after the 2nd vaccination was 65.97% (60.18 to 71.43) in the 30 μg group and 77.08% (71.79 to 81.81) in the 60 μg group. The increases in SRH antibody titer were observed in both groups. Safety summary: The incidence of adverse events was 84.9% (253/298) in the 30 μg group and 85.8% (259/302) in the 60 μg group. The most frequently reported adverse events were injection site pain, injection site erythema, and malaise in both groups and their incidences were similar in the 30 μg group and 60 μg group: 70.5% (210/298) *vs.* 74.8% (226/302) for injection site pain, 25.8% (77/298) *vs.* 25.8% (78/302) for injection site erythema, and 26.5% (79/298) *vs.* 29.1% (88/302) for malaise. Other than those above, the incidence of each adverse event was similar in the two groups. During the study, only one subject in the 30 μg group experienced SAE (Intestinal obstruction), which was assessed as not related to the study drug. The subject recovered from this SAE. Conclusion: From these results, it was suggested that two-dose intramuscular administration of KIB-PCI at 30 or 60 μg had sufficient immunogenicity. There were no major differences in the incidence of each type of adverse events between the 30 μg group and the 60 μg groups. In conclusion, both of these dosages had no significant safety concerns.
Date of Report	March 12, 2015