SYNOPSIS

Name of Sponsor/Company: Solvay Pharmaceuticals	**Individual Study Table**	**(For National Authority Use only)**
Name of Finished Product: Influvac® 2006/2007		
Name of Active Ingredient: A/Wisconsin/67/2005 (H_3N_2)-like strain; A/New Caledonia/20/99 (H_1N_1)-like strain; B/Malaysia/2506/2004-like strain.		
Title of Study: Immunogenicity and Reactogenicity of the Trivalent Influenza Subunit Vaccine Influvac® for the Season 2006/2007. An Open, Baseline-controlled Study in Two Groups of Healthy Subjects: Adult Subjects Aged ≥ 18 and ≤ 60 Years and Elderly Subjects ≥ 61 Years of Age. Week 3 Results.		
Investigator(s): PPD		
Study Center(s): PPD, Belgium.		
Publication (Reference): Not applicable		
Study Period: 13 JUL 2006 (First Subject First Visit) – 05 AUG 2006 (Last Subject Last Visit)	**Phase of Development:** IIIa	
Objectives: The primary objective of this study was to determine the immunogenicity of the influenza vaccine (surface antigen, inactivated), further referred to as trivalent influenza subunit vaccine Influvac®, for the season 2006/2007, in two groups of healthy subjects: adult subjects aged ≥ 18 and ≤ 60 years and elderly subjects ≥ 61 years of age. The safety objective was to collect data on the safety and tolerability (reactogenicity and overall inconvenience) of Influvac®.		
Methodology: This was an open, baseline controlled study in two groups of healthy subjects: adults and elderly. Subjects were screened within 14 days prior to Visit 1 (Day 1) or at Visit 1. Eligible subjects were vaccinated at Visit 1 after blood sampling for baseline hemagglutination inhibition (HI) antibody titration. A questionnaire to assess reactogenicity was handed out at Visit 1. After two weeks (Visit 2, Day 15) and three weeks (Visit 3, Day 22), the subjects returned to the study center for blood sampling and assessment of safety and tolerability.		
Number of Subjects (Planned, Consented, Randomized and Analyzed): Planned 120 subjects, consented 119, vaccinated 119, analyzed safety 119 (59 adults aged ≥ 18 and ≤ 60 years and 60 elderly aged ≥ 61 years), analyzed efficacy 118 (58 adults aged ≥ 18 and ≤ 60 years and 60 elderly aged ≥ 61 years).		
Diagnosis and Main Criteria for Inclusion: Healthy adult and elderly subjects who had not been vaccinated against influenza in the six months previous to study entry.		

Name of Sponsor/Company: Solvay Pharmaceuticals	**Individual Study Table**	**(For National Authority Use only)**
Name of Finished Product: Influvac® 2006/2007		
Name of Active Ingredient: A/Wisconsin/67/2005 (H_3N_2)-like strain; A/New Caledonia/20/99 (H_1N_1)-like strain; B/Malaysia/2506/2004-like strain.		

Test Product, Dose and Mode of Administration, Batch Number:
A single 0.5 mL dose of Influvac® 2006/2007 vaccine given intramuscularly and containing approximately 15 mcg hemagglutinin for each strain:
- A/Wisconsin/67/2005 (H_3N_2)-like strain
- A/New Caledonia/20/99 (H_1N_1)-like strain
- B/Malaysia/2506/2004-like strain

Batch number: K01B.

Duration of Treatment:
Single dose on Day 1.

Reference Therapy, Dose and Mode of Administration, Batch Number:
Not applicable.

Criteria for Evaluation:
Primary Efficacy:
Serological parameters according to the Committee for Medicinal Products for Human Use (CHMP) Note for Guidance on Harmonisation of Requirements for Influenza Vaccines (CPMP/BWP/214/96 1997), derived from the observed HI titers:
- The pre- and post-vaccination protection rates
- The proportion of subjects with seroconversion or at least a four-fold increase in HI titer
- The mean fold increase (MFI)

Safety and Tolerability:
Spontaneously reported adverse events were monitored throughout the study. Tolerability (reactogenicity and overall inconvenience), including local and systemic reactions, was recorded by the subjects on a questionnaire during the first 72 hours after vaccination.

Statistical Methods:
Serological results were evaluated according to the criteria specified in the CHMP Note for Guidance (CPMP/BWP/214/96 1997). All analyses were performed by age group. Safety and tolerability (reactogenicity and overall inconvenience) were summarized by means of absolute and relative frequencies and by the duration of the local and systemic reactions.

Summary – Conclusions
This report presents the Week 3 immunogenicity results and the safety results up to Week 3 inclusive.
Adults aged ≥ 18 and ≤ 60 years
Fifty-nine subjects were vaccinated, all of whom were included in the safety sample; 29 males and 30 females. Their mean age was 39.8 years (range 18-60 years).
Elderly aged ≥ 61 years
Sixty subjects were vaccinated and included in the safety sample; 32 males and 28 females. Their mean age was 70.6 years (range 61-86 years).

Name of Sponsor/Company: Solvay Pharmaceuticals	**Individual Study Table**	**(For National Authority Use only)**
Name of Finished Product: Influvac® 2006/2007		
Name of Active Ingredient: A/Wisconsin/67/2005 (H_3N_2)-like strain; A/New Caledonia/20/99 (H_1N_1)-like strain; B/Malaysia/2506/2004-like strain.		

Efficacy Results:

The efficacy sample comprised of 118 subjects: 58 adults aged ≥ 18 and ≤ 60 years and 60 elderly aged ≥ 61 years. One subject was lost to follow-up.

The following tables summarize the serology results.

Serology: Summary Results for All Strains, ≥ 18 and ≤ 60 Years of Age (Day 22 Results, Post-vaccination Data)

Efficacy Sample

	A (H3N2) - like (N= 58)	A (H1N1) - like (N= 58)	B - like (N= 58)
Seroprotection			
Percentage:	100% (94%~100%)	88% (77%~95%)	90% (79%~96%)
Proportion:	58/58	51/58	52/58
Seroconversion or 4-fold increase			
Percentage:	76% (63%~86%)	55% (42%~68%)	74% (61%~85%)
Proportion:	44/58	32/58	43/58
MFI			
Geometric mean:	11.0 (7.3~16.7)	8.1 (5.2~12.8)	10.2 (7.2~14.4)

95% confidence limits are given between brackets

CHMP Criteria for Healthy Subjects between 18 and 60 Years of Age:

Seroprotection:	> 70%
Seronconversion/4-fold Increase:	> 40%
MFI:	> 2.5

Name of Sponsor/Company: Solvay Pharmaceuticals	**Individual Study Table**	**(For National Authority Use only)**
Name of Finished Product: Influvac® 2006/2007		
Name of Active Ingredient: A/Wisconsin/67/2005 (H_3N_2)-like strain; A/New Caledonia/20/99 (H_1N_1)-like strain; B/Malaysia/2506/2004-like strain.		

Serology: Summary Results for All Strains, ≥ 61 Years of Age (Day 22 Results, Post-vaccination Data)

Efficacy Sample

	A (H3N2) - like (N= 60)	A (H1N1) - like (N= 60)	B - like (N= 60)
Seroprotection			
Percentage:	95% (86%~99%)	67% (53%~78%)	78% (66%~88%)
Proportion:	57/60	40/60	47/60
Seroconversion or 4-fold increase			
Percentage:	50% (37%~63%)	25% (15%~38%)	53% (40%~66%)
Proportion:	30/60	15/60	32/60
MFI			
Geometric mean:	3.5 (2.7~4.5)	2.5 (2.0~3.0)	4.3 (3.3~5.7)

95% confidence limits are given between brackets

CHMP Criteria for Healthy Subjects >= 61 Years of Age:

Seroprotection:	> 60%
Seronconversion/4-fold Increase:	> 30%
MFI:	> 2.0

Three weeks after vaccination the three vaccine strains showed an adequate increase in antibody levels. For both age groups the requirements as described in the CHMP Note for Guidance were met, which means that for each strain at least one out of three criteria are met. In adults aged ≥ 18 and ≤ 60 years all three CHMP criteria were met for all three strains. In elderly aged ≥ 61 years for two strains all three CHMP criteria were met while for the H_1N_1 strain two out of three criteria were met.

Safety Results:

(percentages mentioned are based on non-missing data)

Adults aged ≥ 18 and ≤ 60 years

During the 72 hours after vaccination, 13 subjects (22.4%) reported any local reaction and one subject (1.7%) reported any systemic reaction. The most prominent local reaction was impairment of the movement of the arm (10%); headache was the only systemic reaction (2%). Fifty-seven subjects (98.3%) reported no inconvenience after vaccination, one subject (1.7%) reported mild inconvenience, none of the subjects rated the inconvenience as moderate or severe.

Five subjects (8.5%) reported five treatment emergent adverse events. None of these events was serious. No severe adverse events were observed. The only adverse event reported in more

Name of Sponsor/Company: Solvay Pharmaceuticals	**Individual Study Table**	**(For National Authority Use only)**
Name of Finished Product: Influvac® 2006/2007		
Name of Active Ingredient: A/Wisconsin/67/2005 (H_3N_2)-like strain; A/New Caledonia/20/99 (H_1N_1)-like strain; B/Malaysia/2506/2004-like strain.		

than one subject was injection site movement impairment (n=2; 3.4%); the relationship to the vaccine of these events was considered probable.

Elderly aged ≥ 61 years

During the 72 hours after vaccination, seven subjects (11.9%) reported any local reaction and three subjects (5.1%) reported any systemic reaction. Pain at the slightest pressure was the only local reaction reported in more than two subjects (8%); increased sweating, headache, malaise and insomnia were the only reported systemic reactions (2% each).
Fifty-eight subjects (98.3%) reported no inconvenience after vaccination, one subject (1.7%) reported mild inconvenience and no subjects reported moderate or severe inconvenience.
Three subjects (5.0%) reported four treatment emergent adverse events. None of these events was serious. No severe adverse events were observed. No adverse event was reported in more than one subject.

Conclusion:

The Week 3 results of this study indicate that Influvac® 2006/2007 induced an adequate antibody response in the studied populations, fulfilling the CHMP requirement for immunogenicity. For all three strains in the Influvac® 2006/2007 vaccine all three CHMP criteria were fulfilled, for the adult group. In the elderly group, all three CHMP criteria were met for two strains in the vaccine, while for the third strain (H_1N_1) two of the criteria were met.

Influvac® 2006/2007 was safe and well tolerated in this study.