SYNOPSIS

Name of Sponsor:

Solvay Biologicals B.V.

Individual Study Table: **(For National Authority Use only)**

Name of Finished Product:

Influvac® 2009/2010

Name of Active Ingredient:

A/Brisbane/59/2007 (H1N1)-like strain;
A/Brisbane/10/2007 (H3N2)-like strain;
B/Brisbane/60/2008-like strain.

Study Title:

Immunogenicity, Reactogenicity and Safety of the Trivalent Influenza Subunit Vaccine Influvac® for the Season 2009/2010. An Open-label, Baseline-controlled, Multi-center Study in Two Groups: Adult Subjects ≥ 18 and ≤ 60 Years and Elderly Subjects ≥ 61 Years of Age. Week 3 Results.

Investigator(s):

PPD

Study Center(s):

PPD Belgium
PPD
Germany.

Publication (Reference):

Not applicable.

Study Period:

11 JUN 2009 (first subject first visit) to
09 JUL 2009 (last subject last visit Week 3)

Phase of Development:

Phase IIIa

Objectives:

The primary objective of this study was to determine the immunogenicity of the trivalent influenza subunit vaccine Influvac® for the season 2009/2010, in two groups of 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-label, baseline-controlled study in two groups of subjects: adults aged ≥ 18 and ≤ 60 years PPD and elderly ≥ 61 years of age PPD Subjects were screened within 14 days prior to Visit 1 (Day 1) or at Visit 1 (Day 1). Eligible subjects were vaccinated at Visit 1 (Day 1) after blood sampling for baseline hemagglutination inhibition (HI) antibody titration. Subjects were asked to record local and systemic reactions daily on a questionnaire at home for 72 hours after vaccination. After 2 weeks (Visit 2, Day 15) and 3 weeks (Visit 3,

Day 22), the subjects returned to the study center for blood sampling and assessment of safety and tolerability. This report concerns the analysis of the Week 3 results. The Week 2 clinical study report (Day 15 results) was issued on 17 JUL 2009.

Number of Subjects (Planned, Consented, Randomized and Analyzed):
Planned 120 subjects, consented 120 subjects, vaccinated 120 subjects, analyzed safety 120 (60 adults aged ≥ 18 and ≤ 60 years and 60 elderly aged ≥ 61 years), analyzed efficacy 115 (57 adults aged ≥ 18 and ≤ 60 years and 58 elderly aged ≥ 61 years).

Diagnosis and Main Criteria for Inclusion:
Adults and elderly subjects in good health who had not been vaccinated against influenza in the 6 months previous to study entry.

Test Product, Dose and Mode of Administration, Batch Number:

A single 0.5 mL dose of trivalent influenza subunit vaccine Influvac® (season 2009/2010) given intramuscularly and containing approximately 15 mcg hemagglutinin for each strain:

- A/Brisbane/59/2007 (H1N1)-like strain;
- A/Brisbane/10/2007 (H3N2)-like strain;
- B/Brisbane/60/2008-like strain

Batch number: 1067456-610344.

Duration of Treatment:

Single dose on Day 1.

Reference Therapy, Dose and Mode of Administration, Batch Number:

Not applicable.

Criteria for Evaluation

Efficacy:

The following serological parameters were to be derived separately for each strain and for each vaccination group:

- the pre-and post-vaccination seroprotection rates
- the proportion of subjects with seroconversion or at least a four-fold increase in HI antibody titer
- the geometric mean fold increase.

Safety:

Spontaneously reported adverse events (AEs) 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 influenza vaccine immunogenicity results and the safety results up to Week 3 inclusive.

Adults aged ≥ 18 and ≤ 60 years

Sixty subjects were vaccinated, all of whom were included in the safety sample; 30 males and 30 females. Their mean age was 39.5 years (range 20-59 years).

Elderly aged ≥ 61 years

Sixty subjects were vaccinated and included in the safety sample; 28 males and 32 females. Their mean age was 69.1 years (range 60-84 years).

Efficacy Results:

The efficacy sample comprised 115 subjects: 57 adults aged ≥ 18 and ≤ 60 years and 58 elderly aged ≥ 61 years. Five subjects were excluded from the efficacy sample. Three subjects were excluded due to aspecific agglutination of the serum sample (two subjects had missing baseline and Day 22 HI titer data and one subject had missing Day 22 HI titer data). One subject was excluded due to no swab being taken after the subject experienced an IRI. One subject was excluded due to the administration of anticancer medication and radiotherapy within 36 months before the day of vaccination.

The following tables summarize the serology results.

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

Efficacy Sample

	A (H3N2) - like (N=57)	A (H1N1) - like (N=57)	B - like (N=57)
Seroprotection			
Percentage:	89.5% (78.5%~96.0%)	100.0% (93.7%~100.0%)	93.0% (83.0%~98.1%)
Proportion:	51/57	57/57	53/57
Seroconversion or 4-fold increase			
Percentage:	82.5% (70.1%~91.3%)	89.5% (78.5%~96.0%)	87.7% (76.3%~94.9%)
Proportion:	47/57	51/57	50/57
MFI			
Geometric mean:	33.3 (19.5~57.0)	39.8 (24.7~64.1)	22.8 (15.2~34.2)
n:	57	57	57

Note: 95% confidence limits are given between brackets

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

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

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

Efficacy Sample

	A (H3N2) - like (N=58)	A (H1N1) - like (N=58)	B - like (N=58)
Seroprotection			
Percentage:	87.9% (76.7%~95.0%)	81.0% (68.6%~90.1%)	53.4% (39.9%~66.7%)
Proportion:	51/58	47/58	31/58
Seroconversion or 4-fold increase			
Percentage:	44.8% (31.7%~58.5%)	39.7% (27.0%~53.4%)	32.8% (21.0%~46.3%)
Proportion:	26/58	23/58	19/58
MFI			
Geometric mean:	6.0 (3.6~10.0)	4.5 (3.1~6.6)	2.7 (2.0~3.8)
n:	58	58	58

Note: 95% confidence limits are given between brackets

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

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

Three weeks after vaccination, the three vaccine strains showed an adequate increase in antibody levels that met all three criteria for the specified serological parameters for influenza vaccines in adults aged ≥ 18 and ≤ 60 years (as described in the CHMP Note for Guidance on Harmonization of Requirements for Influenza Vaccines). For elderly aged ≥ 61 years, the two vaccine A strains met all three CHMP criteria and the vaccine B strain met two criteria three weeks after vaccination.

Safety Results:

There were no deaths during the study.

Adults aged ≥ 18 and ≤ 60 years

During the 72 hours after vaccination, 28 subjects (46.7%) reported any local reaction and 17 subjects (28.3%) reported any systemic reaction. Tenderness (pain or discomfort upon touch) was the most frequent local reaction (38.3%): headache (15.0%), malaise (11.7%) and shivering (11.7%) were the most frequent systemic reactions.

Fifty-three subjects (88.3%) reported no inconvenience after vaccination, seven subjects (11.7%) reported mild inconvenience and no subjects reported moderate or severe inconvenience.

Eleven subjects (18.3%) reported 22 treatment emergent AEs. One serious AE of type I diabetes mellitus was reported which was considered to be unrelated to the vaccination. No other serious AEs were reported. No severe AEs were observed. The following AEs were reported in more

than one subject: oropharyngeal pain (four subjects), nasopharyngitis (three subjects), nasal congestion, pain and headache (two subjects each). No other AE was reported in more than one subject.

Elderly aged ≥ 61 years

During the 72 hours after vaccination, 11 subjects (18.3%) reported any local reaction and 10 subjects (16.7%) reported any systemic reaction. Tenderness (pain or discomfort upon touch) was the most frequent local reaction (10.0%): fatigue (10.0%) was the most frequent systemic reaction.

Fifty-eight subjects (96.7%) reported no inconvenience after vaccination, one subject (1.7%) reported mild inconvenience and one subject (1.7%) reported moderate inconvenience. No subjects reported severe inconvenience.

Six subjects (10.0%) reported nine treatment emergent AEs. One subject was reported with one severe AE (cough). Cough was reported for two subjects. No other AE was reported in more than one subject.

Conclusion:

The Week 3 results of this study indicate that Influvac® 2009/2010 induced an adequate antibody response in the studied populations, fulfilling the CHMP requirement for influenza vaccine immunogenicity. This is consistent with observations in previous years. At least one CHMP criterion was met for all three strains in the Influvac® 2009/2010 vaccine, for both age groups.

Influvac® 2009/2010 was safe and well tolerated in this study.