SYNOPSIS

Name of Sponsor:
Abbott Biologicals B.V. (formerly Solvay Biologicals B.V.)

Individual Study Table:

(For National Authority Use only)

Name of Finished Product:
Influvac® 2010/2011

Name of Active Ingredient:
A/California/7/2009 (H1N1)-like strain;
A/Perth/16/2009 (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 2010/2011. 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

Investigators:
PPD

Study Centers:
PPD Belgium
PPD
Germany.

Publication (Reference):
Not applicable.

Study Period:
03 JUN 2010 (first subject first visit) to
01 JUL 2010 (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 2010/2011, in two groups of subjects: adults aged ≥ 18 and ≤ 60 years and elderly ≥ 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 diary at home for 72 hours after vaccination. 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. This report concerns the analysis of the Week 3 results. The Week 2 clinical study report (Day 15 results) was issued on 08 JUL 2010.

Number of Subjects (Planned, Consented, Randomized and Analyzed):
Planned 120 subjects, consented and vaccinated 121 subjects, analyzed safety 121 (60 adults aged ≥ 18 and ≤ 60 years and 61 elderly aged ≥ 61 years), analyzed efficacy 112 (52 adults aged ≥ 18 and ≤ 60 years and 60 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 six 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 2010/2011) given intramuscularly and containing approximately 15 mcg hemagglutinin for each strain:

- A/California/7/2009 (H1N1): derived strain used reass. virus NYMC X-181;
- A/Perth/16/2009 (H3N2): like strain used reass. virus NYMC X-187 derived from A/Victoria/210/2009;
- B/Brisbane/60/2008.

Batch number: 1071032-610464.

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 diary during the first 72 hours after vaccination.

Statistical Methods:

Serological results were evaluated according to the criteria specified in the Committee for Medicinal Products for Human Use (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 39.9 years (range 18-57 years).

Elderly aged ≥ 61 years

Sixty-one subjects were vaccinated and included in the safety sample; 30 males and 31 females. Their mean age was 72.0 years (range 61-87 years).

Efficacy Results:

The efficacy sample comprised 112 subjects: 52 adults aged ≥ 18 and ≤ 60 years and 60 elderly aged ≥ 61 years. For nine subjects (7.4%, eight adults and one elderly subject), Day 22 and/or Day 1 HI titers were missing. For one adult no Day 22 serum sample was available because the subject refused to have a blood sample taken at Visit 3, while the Day 1 HI titers could not be determined due to aspecific agglutination; for five adults and one elderly subject both Day 1 and Day 22 HI titers could not be determined due to aspecific agglutination; and for two adults Day 1 HI titers could not be determined due to aspecific agglutination. These nine subjects were therefore excluded from the efficacy sample.

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=53)	A (H1N1) - like (N=53)	B - like (N=53)
Seroprotection			
Percentage:	98.1% (89.7%~100%)	98.1% (89.7%~100%)	86.5% (74.2%~94.4%)
Proportion:	51/52	51/52	45/52
Seroconversion or 4-fold increase			
Percentage:	92.3% (81.5%~97.9%)	92.3% (81.5%~97.9%)	75.0% (61.1%~86.0%)
Proportion:	48/52	48/52	39/52
MFI			
Geometric mean:	55.1 (36.8~82.5)	46.7 (30.6~71.3)	16.6 (11.3~24.2)
n:	52	52	52

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=60)	A (H1N1) - like (N=60)	B - like (N=60)
Seroprotection			
Percentage:	96.7% (88.5%~99.6%)	86.7% (75.4%~94.1%)	65.0% (51.6%~76.9%)
Proportion:	58/60	52/60	39/60
Seroconversion or 4-fold increase			
Percentage:	41.7% (29.1%~55.1%)	45.0% (32.1%~58.4%)	6.7% (1.8%~16.2%)
Proportion:	25/60	27/60	4/60
MFI			
Geometric mean:	3.7 (2.7~5.0)	3.8 (2.7~5.3)	1.7 (1.4~2.0)
n:	60	60	60

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, Influvac® 2010/2011 induced an adequate antibody response in the studied populations, fulfilling the CHMP requirement for influenza vaccine immunogenicity.

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 the seroprotection criterion three weeks after vaccination.

Safety Results:

There were no deaths, no other serious AEs and no premature discontinuations due to AEs during the study.

Adults aged ≥ 18 and ≤ 60 years

During the 72 hours after vaccination, 16 subjects (26.7%) reported any local reaction and 16 subjects (26.7%) reported any systemic reaction. Tenderness (pain or discomfort upon touch) was the most frequent local reaction (16.7%); fatigue (16.7%) and headache (11.7%) were the most frequent systemic reactions.

Forty-eight subjects (80.0%) reported no inconvenience after vaccination, 12 subjects (20.0%)

reported mild inconvenience and no subjects reported moderate or severe inconvenience.

Eleven subjects (18.3%) reported 13 treatment-emergent AEs. No severe AEs were observed. No AE was reported in more than one subject. Four TEAEs in four subjects were assessed as related to the vaccination by the investigator.

Elderly aged ≥ 61 years

During the 72 hours after vaccination, eight subjects (13.1%) reported any local reaction and six subjects (9.8%) reported any systemic reaction. Tenderness (pain or discomfort upon touch) was the most frequent local reaction (9.8%); fatigue (3.3%) and increased sweating (3.3%) were the most frequent systemic reactions.

Fifty-three subjects (96.4%) reported no inconvenience after vaccination, two subjects (3.6%) reported mild inconvenience and no subjects reported moderate or severe inconvenience.

Three subjects (4.9%) reported four treatment-emergent AEs. No severe AEs were observed. No AE was reported in more than one subject. No TEAEs were assessed as related to the vaccination by the investigator.

Conclusion:

The Week 3 results of this study indicate that Influvac® 2010/2011 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® 2010/2011 vaccine, for both age groups.

Influvac® 2010/2011 was safe and well tolerated in this study.