***These results are supplied for informational purposes only.***
***Prescribing decisions should be made based on the approved package insert.***

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| **Sponsor/ Company:** | Sanofi Pasteur | **Study Code:** IPV17<br>**Study Identifier:** NCT00258843 |
| **Proprietary Vaccine Name:** | Inactivated Poliomyelitis vaccine (IMOVAX Polio™) | |

**Title of the Study:** Clinical Safety Evaluation Study of the sanofi pasteur's Inactivated Poliomyelitis Vaccine (IMOVAX Polio™) Administered as a Single Booster Dose at 18 Months of Age in Healthy Chinese Children, and as the First Dose of Primary Vaccination at 2 Months of Age in Healthy Chinese Infants

**Study centre:** 1 site in China

**Publications:** None at the time of report writing.

**Study period:** Date of First enrollment: 06 November 2005
Date of Last visit (contact): 10 January 2006

**Development phase:** Phase I like, pre-requisite for Phase III

**Methodology / Trial Design:**

Open, monocenter, trial. Children and infants were included and immunized in two steps such as:

Group 1: children of 18 months of age

Group 2: infants of 2 months of age

The study was first conducted among children (Group 1). It was planned in the Amended Protocol (version 3.0, dated 18 October 2005) that a brief summary of the safety data of children (Group 1) written by the Principal Investigator was to be submitted to IRB/EC for notification before the enrollment of Group 2 (infants). If no related SAE occurred in Group 1, the statistical analysis was to be performed after all subjects in Group 1 and Group 2 (infants) have completed the study and an interim analysis was not necessary. If at least one related SAE occurred in Group 1, an interim analysis of Group 1 data from Visit 01 to Visit 03 may be performed if requested by the IRB/EC and/or Chinese Health Authorities.

**Objectives:**

**Primary objective:**

To describe the tolerance in terms of occurrence of serious adverse reactions and severe adverse reactions (injection site and systemic) within 8 days after one dose of IMOVAX Polio™ administered in children and infants.

**Secondary objectives:**

- To describe the tolerance of IPV in terms of occurrence of solicited (terms pre-listed in the Case Report Form [CRF]) injection site and systemic reactions within 8 days after the injection.
- To describe the tolerance of IPV in terms of occurrence of unsolicited adverse events (AEs) within 28 days after the injection.
- To describe the tolerance of IPV in terms of occurrence of serious adverse events (SAEs) throughout the trial.

**Sample size** (Number of Subjects):

- Planned sample size: 40 subjects (20 children in Group 1 and 20 infants in Group 2)
- Number of subjects included: 40 subjects (20 in each group)
- Number of subjects completed: 40 subjects (20 in each group) (completed the vaccination regimen and/or some follow-up period, as defined in the protocol)
- Number of discontinued subjects: none
- Sample size for primary analysis: 40 subjects (20 in each group)

**Assessment Methods:**

- **30-Minute Observation Period** - Subjects were kept under observation for 30 minutes after the vaccination to ensure their safety. Any AE (either injection site reaction or systemic AEs) that occurred during this 30-minute period were recorded in either the solicited or unsolicited AE tables of the CRF.
- **Reactogenicity (Solicited Reactions from D0 to D7 after the Vaccination)** - All solicited injection site and systemic reactions that occurred on the day of vaccination and for the next seven days (i.e., Day 0 to Day 7) were recorded daily by the subject's parent(s)/guardian in the diary card.
- **AEs from D0 to D28 after the Vaccination** - The subject's parent(s)/guardian were instructed to record any other medical events that may occur between D0 and D28 after the vaccination with information on start and stop dates, severity (mild, moderate, and severe), and action taken for each event. The Investigator was to assess the causal relationship between each unsolicited adverse event and vaccination as either not related or related.
- **SAE** - Information on SAE was collected and assessed throughout the trial, from inclusion until the last study visit. For each solicited reaction and unsolicited AE reported, the Investigator was to indicate whether it was an SAE. Any SAE that occurred throughout the trial was also to be reported by the Investigator using SAE Alert and SAE Reporting forms. The Investigator was to assess the causal relationship between the SAE and vaccination as either not related or related.

**Schedules of Vaccination and Specimen Collection:**

One vaccination of IMOVAX Polio ™ (IPV) for both Groups 1 and 2. In Group 1, it was given as a booster dose at 18 to 20 months of age children. In Group 2, it was given as a first dose at 2 months of age infants.

No blood sample (BS) was drawn in both groups.

**Duration of Participation in the Trial:**

The total duration of follow-up (first visit to last visit) for a subject was four weeks.

**Product Under Investigation:**

IPV vaccine (IMOVAX POLIO ™) manufactured by Sanofi Pasteur SA

**Form/Dose/Route:**

Suspension of IPV/0.5mL/Intramuscular (I.M.) into the anterolateral area of the right thigh

**Batch number:** Y1140-1

**Control Product:** Not applicable

**Other Product(s):** Not applicable

**Endpoints:**

**Primary endpoints:**

- The occurrence, time to onset, duration, and severity of any serious adverse reactions between D0 and D7 after the dose.
- The occurrence, time to onset, and duration of any severe adverse reactions between D0 and D7 after the dose.

**Secondary endpoints:**

- The occurrence, time to onset, number of days of occurrence, severity, and seriousness of the solicited (terms pre-listed in the CRF) injection site reactions between D0 and D7 after the injection such as: injection site tenderness, erythema, and swelling.
- The occurrence, time to onset, number of days of occurrence, severity, and seriousness of the solicited systemic reactions between D0 and D7 after the injection such as: fever (axillary temperature ≥37.4°C), vomiting, abnormal crying, drowsiness, loss of appetite, and irritability.

- The occurrence, nature (Medical Dictionary for Regulatory Activities [MedDRA preferred term]), time to onset, duration, severity, relationship to vaccination, and seriousness of unsolicited (spontaneously reported) AEs between D0 and D28 after the injection.
- The occurrence, nature, time to onset, duration, severity, and relationship to vaccination of any SAE that occurred throughout the trial.

**Statistical methods**

Analysis of safety:

Descriptive analysis - For each safety endpoint, the percentage of subjects with the endpoint (e.g. with a given symptom) was computed with its 95% Confidence Interval (CI).

Solicited adverse reactions that occurred between D0 and D7 after the injection were described by severity, time to onset, and number of days of occurrence.

Unsolicited events were analyzed by nature (primary System Organ Class and Preferred Term), severity, relationship to vaccination, time to onset, and duration.

MedDRA was used to classify unsolicited AEs and the percentage of subjects with a symptom pertaining to specific Preferred Terms was tabulated.

All SAEs and discontinuations due to AEs were to be described with details.

Sample size:

As per requirement of the Chinese Health Authorities for safety surveillance, the sample size was set to 20 evaluable subjects per group. A total of 40 subjects were enrolled.

**Results summary:**

**Disposition of subjects -** As planned in the protocol, 40 subjects were enrolled (20 subjects in each Group 1 and Group 2). The study was first conducted among 20 children (Group 1) and since there were no safety issues such as SAE found among the 20 children in Group 1, 20 infants (Group 2) were subsequently enrolled in the study and were vaccinated. The average follow-up duration for subjects in both Group 1 and Group 2 was 28 days. All 40 included subjects completed the study. No subject had early termination from the study for voluntary withdrawal due to an AE or for other reasons. There were no protocol deviations.

**Demographic Characteristics** - The mean age (± standard deviation) of subjects was 19.0 months (± 0.05) in Group 1 and 2.0 months (± 0.01) in Group 2. On average, subjects in Group 1 weighed 10.6 kg (± 1.2 kg) while subjects in Group 2 weighed 5.5 kg (± 0.07 kg). There were slightly more female than male subjects in both groups (60.0% and 55.0% for Groups 1 and 2, respectively).

**Safety:**

A total of 27 subjects (67.5%) had at least one solicited reaction (injection site or systemic) during the entire study period (28 days follow-up), 13 subjects (65.0%) in Group 1 and 14 subjects (70.0%) in Group 2.

Solicited injection site reactions within 8 days after vaccination were observed in five subjects (12.5%), three subjects (15.0%) in Group 1 and two subjects (10.0%) in Group 2.

Solicited systemic reactions within 8 days after vaccination were observed in 27 subjects (67.5%), 13 subjects (65.0%) in Group 1 and 14 subjects (70.0%) in Group 2.

Unsolicited events within 28 days after vaccination were reported in 11 subjects (27.5%), eight subjects (40.0%) in Group 1 and three subjects (15.0%) in Group 2. No AE had led to study discontinuation of any subject, no SAE was reported, and no death occurred during the study, whichever the group.

**Results on Primary Safety Endpoints**

No serious adverse reaction was reported within 8 days from vaccination, whichever the group.

Out of the 40 subjects, eight subjects (20.0%) had severe adverse reactions within 8 days after vaccination, two subjects (10.0%) in Group 1 and six subjects (30.0%) in Group 2. In Group 1, one subject had severe vomiting, crying, loss of appetite, and irritability and another subject had severe loss of appetite. While in Group 2, two subjects had severe irritability, two subjects had severe crying, one subject had severe somnolence, and one subject had severe injection site pain. All of the severe adverse reactions observed in the two groups did not last for more than 3 days after vaccination, none required any hospitalization, and none was considered as an SAE.

**Results on Secondary Safety Endpoints**

Solicited injection site reactions (defined in the protocol as tenderness, erythema, and swelling) were reported within 8 days after vaccination in five subjects (12.5%), three subjects (15.0%) in Group 1 and two subjects (10.0%) in Group 2. The most frequent was injection site tenderness. Except for one case of severe injection site tenderness, all of the reported solicited injection site reactions were of mild severity and all of which occurred within 3 days from vaccination. None of the subjects with solicited injection site reactions required any action for the treatment of the reaction, i.e. medication or hospitalization.

Solicited systemic reactions (defined in the protocol as loss of appetite, abnormal crying, drowsiness, fever, irritability, and vomiting) within 8 days after vaccination were observed in 27 subjects (67.5%), 13 subjects in Group 1 and 14 subjects in Group 2. Abnormal crying was the most frequent systemic reaction followed by irritability, loss of appetite, drowsiness, vomiting, and fever (in order of frequency). Most of the reported solicited systemic reactions were of mild severity that usually occurred within 3 days from vaccination. No severe fever was reported.

Unsolicited events within 28 days from vaccination were observed in 11 subjects (27.5%). Interestingly, infants had lower incidence of unsolicited events (n = 3) than children (n = 8). All of the reported unsolicited events were systemic events without any case of severe unsolicited event, and none was related to vaccination.

No SAE was reported, no AE had led to study discontinuation, and no death occurred during the study.

**Conclusions:**

- The study vaccine (IMOVAX Polio™) administered as a booster dose in children and as a first dose in infants was generally well tolerated. No serious adverse event was observed and the incidence of severe adverse reactions was low. No severe fever was reported.
- The solicited injection site and systemic reactions observed were the usual reactions expected from any pediatric vaccinations, generally of mild severity, transient (< 3 days duration), and none of which required any hospitalization.
- Infants appeared to have had a lower incidence of unsolicited events, but in general, unsolicited events were low in both groups. No severe unsolicited event was reported and none was related to vaccination.
- No SAE was reported throughout the trial.

**Date of Report:** 07 April 2006