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

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| **Sponsor:** Sanofi Pasteur<br>**Drug substance(s):**<br>Meningococcal (Groups A, C, Y and W-135) Polysaccharide Diphtheria Toxoid Conjugate Vaccine | **Study Identifiers:** U1111-1174-4339, NCT02699840<br>**Study code: MTA92** |
| **Title of the study:** Observational Safety Study of a Meningococcal (Groups A, C, Y and W-135) Polysaccharide Diphtheria Toxoid Conjugate Vaccine (Menactra®) administered in individuals 2 through 55 years old under Standard Health Care Practice in the Russian Federation | |
| **Study center(s):** Multi-center in Russian Federation | |
| **Study period:**<br>Date first subject enrolled: 27/Feb/2016<br>Date last subject completed: 25/Jul/2016 | |
| **Phase of development:** Not applicable (observational study) | |
| **Objectives:** To describe the safety profile after 1 dose of Menactra administered from 2 through 55 years of age under standard health care practice. | |
| **Methodology:**<br>Subjects and/or subjects' parent(s) recorded information for solicited reactions in a Diary Card (DC) from Day (D) 0 to D7 after vaccination, and for unsolicited non-serious adverse events (AEs) from D0 to D28 after vaccination.<br>Unsolicited AE was defined as an observed AE that did not fulfill the conditions prelisted in the case report form (CRF) in terms of diagnosis and / or onset post-vaccination, i.e., excluding solicited reactions, e.g., headache between D0 and D7 was considered a solicited reaction (i.e., prelisted in the CRF), a headache starting on D7 was considered a solicited reaction, whereas headache starting on D8 post-vaccination was considered to be unsolicited AE.<br>Unsolicited non-serious AE was defined as unsolicited AE which did not meet serious adverse events (SAE) criteria.<br>SAEs were to be reported throughout the study (Visit 1 through Visit 2).<br>Study staff reviewed safety data collected after vaccination with the subject and/or subject's parent(s) at Visit 2. All subjects and/or parent(s) were asked to notify the site immediately about any potential SAE at any time during the study.<br>SAEs and AEs related to vaccination:<br>At any time during the study, any subject, who experienced SAE or AE, was followed until either of the following was true:<br>- The SAE or AE was considered by the Investigator to be related to vaccination, and was not resolved by the end of the subject's participation in the study;<br>- The subject was discontinued from the trial due to SAE or AE;<br>Any such subject was followed until the condition resolved, became stable, or became chronic. | |

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| **Number of subjects:** | Planned: 100<br>Treated: 100 |
| **Evaluated:** | Safety: 100 |

**Diagnosis and criteria for inclusion:**

Inclusion criteria:

1) Aged 2 through 55 years on the day of enrollment

2) For adults (18-55 years old): Informed consent form has been signed and dated by the subject.

For minors: Informed consent form has been signed and dated by the parent. In addition, in accordance with the Institution Ethics Committee/Institution Review Board requirements and as appropriate for the age of the subject:

- subjects aged 14 to 17 years were required to sign and date the informed consent form,
- subjects aged 10 to 13 years were required to sign and date the assent form,
- for subjects under 10 years, consent was asked orally according to subject's age and ability for understanding.

3) Receipt of one dose of Menactra in routine practice according to the approved local product insert on the day of inclusion and prior to enrollment to the study.

Exclusion criterion:

1) Participation at the time of study enrollment (or in the 4 weeks preceding the enrollment) or planned participation during the present study period in a clinical study investigating a vaccine, drug, medical device, or medical procedure.

**Study treatments**

**Investigational medicinal product(s)**: Menactra

Formulation: Solution of Meningococcal (Groups A, C, Y and W-135) Polysaccharide Diphtheria Toxoid Conjugate Vaccine

Route(s) of administration: Intramuscular injection

Dose regimen: Single injection

**Administration Schedule:** 1 injection

**Duration of observation:** 28 days

**Criteria for evaluation:**

Safety:

- Occurrence of solicited (prelisted in the subject's DC and CRF) injection site and systemic reactions occurring up to 7 days after vaccination;
- Occurrence of unsolicited non-serious AEs up to 28 days after vaccination;
- Occurrence of SAEs throughout the study (from enrollment to visit 2);

**Statistical methods:**

All additional revisions were descriptive.

**Summary:**

**Population characteristics:** Among the 100 subject's distribution by gender was 47 males and 53 females. The median age of study cohort was 13.6 years old. All 100 enrolled subjects completed the study according to the protocol.

**Safety results:** The rate of solicited injection site and systemic reactions, occurred within 7 days after vaccination was 52.0% (95% Confidence interval [CI] = 41.8- 62.1%). The rate of solicited injection site reactions was 49.0% (95%CI = 38.9 - 59.2%), the rate of solicited systemic reactions was 20.0% (95%CI = 12.7 - 29.2%).

The total rate of unsolicited non-serious AE up to 28 (+7) days after vaccination was 9.0% (95%CI = 4.2 - 16.4%) and of unsolicited AR 0.0% (95%CI = 0.0 - 0.0%).
No cases of SAEs/deaths were reported throughout the study period.
Overview of safety data after vaccine injection is shown in the Table 1.

**Table 1. Safety overview after vaccine injection – Safety Analysis Set**

| | Total (N=100) | | |
|---|---|---|---|
| **Subjects experienced at least one:** | **n/M** | **%** | **95% CI** |
| **Solicited reaction** | 52/100 | 52.0 | (41.8; 62.2) |
| **Solicited injection site reaction** | 49/100 | 49.0 | (38.9; 59.2) |
| **Solicited systemic reaction** | 20/100 | 20.0 | (12.7; 29.2) |
| **Unsolicited AE** | 9/100 | 9.0 | (4.2; 16.4) |
| **Unsolicited AR** | 0/100 | 0.0 | (0.0; 3.6) |
| **Unsolicited non-serious AE** | 9/100 | 9.0 | (4.2; 16.4) |
| **Unsolicited non-serious AR** | 0/100 | 0.0 | (0.0; 3.6) |
| **Unsolicited non-serious injection site AR** | 0/100 | 0.0 | (0.0; 3.6) |
| **Unsolicited non-serious systemic AE** | 9/100 | 9.0 | (4.2; 16.4) |
| **Unsolicited non-serious systemic AR** | 0/100 | 0.0 | (0.0; 3.6) |
| **AE leading to study discontinuation** | 0/100 | 0.0 | (0.0; 3.6) |
| **SAE** | 0/100 | 0.0 | (0.0; 3.6) |
| **Death** | 0/100 | 0.0 | (0.0; 3.6) |
| **During the study** | | | |
| **SAE** | 0/100 | 0.0 | (0.0; 3.6) |
| **Death** | 0/100 | 0.0 | (0.0; 3.6) |

n: number of subjects experienced endpoint.
M: number of subjects with available data for the relevant endpoint.

The most commonly reported injection site reactions (of any grade) were injection site pain (43.0%), injection site erythema (21.0%) and injection site swelling (12.0%). Most of injection site reactions were of grade 1 or 2 intensity, with onset occurred within D0-D3 and resolved within 7 days after vaccination.

Frequency of grade 3 injection site reactions was the following: Injection site pain – 2% (2/100 cases), injection site erythema – 3% (3/100 cases) injection site swelling – 1% (1/100 cases).

Most cases of injection site pain were 1 to 3 days in duration (37.0%). Injection site erythema and injection site swelling persisted mainly for 4-7 days (15.0% and 7.0% respectively). There was no injection site reactions persisted for 8 or more days.
Solicited systemic reactions, occurred within 7 days after vaccine injection, were reported as follows:
Headache and malaise were the most commonly reported solicited systemic reaction (13.0% each), followed by myalgia (10.0%).
Fever was reported only for 1 subject (1%).
Few cases of Grade 3 systemic reactions were reported: 1 (1%) for fever; 1 (1%) for malaise and 1 (1%) for myalgia. No Grade 3 cases of headache were reported.

The majority of solicited systemic reactions were of grade 1 or 2 intensity, occurred within D0-D3 after vaccination, and resolved after 1-3 days. No solicited systemic reactions had 8 days of duration or more (0/100 cases).

During observation period after vaccination (28 (+7) days), 9 unsolicited AEs were reported in 7 subjects (2 subjects experienced 2 AEs each. The most commonly reported unsolicited AEs were viral respiratory tract infections of grade 2 (4.0%; 95%CI = (1.1 - 9.9%) and rhinitis of grade 1 (2%; 95%CI = (0.2 - 7.0%). There were no unsolicited adverse events related to Menactra.

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