Pandemic Influenza Vaccine Clinical Trial Abstract Minimum information:

**Title of Trial:** Post-licensure commitment study to compare the clinical efficacy of Fluzone High-Dose vaccine and Fluzone vaccine

**Clinical Trial registration site if applicable (e.g. ClinicalTrials.gov):** NCT01427309; FIM12 (Sanofi Pasteur registration)

**Authors/sponsors:** Dr Carlos Diaz Granados, Dr David Greenberg and others / Sanofi Pasteur

**Study Design:** Randomized and blinded trial.

**Objectives:**

- **Primary Objective:** To compare the clinical efficacy of Fluzone High-Dose vaccine to that of Fluzone vaccine in adults ≥ 65 years of age, with respect to laboratory-confirmed influenza (≥ 14 days post-vaccination), caused by any influenza viral type or subtype, associated with the occurrence of a protocol-defined influenza-like illness (PD-ILI)

- **Secondary Objectives**
  
  To assess the clinical efficacy of Fluzone High-Dose vaccine relative to that of Fluzone vaccine in adults ≥ 65 years of age based on various clinical illness definitions, methods of influenza confirmation, and similarity of the infecting strains to the vaccine strains

**Vaccine:**

- **Manufacturer:** Sanofi Pasteur

- **Type (whole virus/subvirion/subunit/live/recombinant/DNA/vector):** Seasonal trivalent inactivated split vaccine

- **Adjuvant:** None

- **Delivery system/site:** Intramuscular injection

**Doses (antigen and adjuvant):** 60µg pes strain in Fluzone High–Dose vaccine and 15µg pes strain in Fluzone vaccine

**Study population:** ~32,000 participants ≥ 65 years of age enrolled in 126 study sites in the US and Canada. Participants randomized 1:1 to receive 1 dose of Fluzone High-Dose vaccine or Fluzone vaccine and followed for illness until the end of each season

- **Age range:** Health status: adults 65 years of age and older without moderate or severe acute illnesses (the study allowed inclusion of individuals with high-risk chronic comorbid conditions)

**Specific inclusion/exclusion criteria:**

**Clinical Endpoints Assessed:**

- **Safety assessments:** Surveillance for Illnesses Compatible with Influenza Infection. Passive Surveillance: phone calls to report symptoms to the research site initiated by the subject. Active surveillance: subject contacted by call center querying about occurrence of reportable symptoms and followed by site contact, if appropriate. Influenza infection was confirmed by culture, PCR, or both
Immunogenicity assessments:

Results:

Safety: Entire Study Period

<table>
<thead>
<tr>
<th>Subjects experiencing at least one:</th>
<th>Fluzone High-Dose (N=15,992)</th>
<th>Fluzone (N=15,991)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAE</td>
<td>1323</td>
<td>1442</td>
</tr>
<tr>
<td>Related SAE</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>AE of Special Interest (AESI)</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>SAE leading to study</td>
<td>99</td>
<td>103</td>
</tr>
<tr>
<td>discontinuation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death (any cause)</td>
<td>83</td>
<td>84</td>
</tr>
</tbody>
</table>

Efficacy:

High-Dose vaccine efficacy:

Laboratory-confirmed influenza caused by any viral type or subtype (regardless of similarity), associated with a PD-ILI

<table>
<thead>
<tr>
<th>Associated with PD ILI</th>
<th>Fluzone High-Dose (1.43)</th>
<th>Fluzone Relative (1.89)</th>
<th>Efficacy % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Associated</td>
<td>227 (1.43)</td>
<td>300 (1.89)</td>
<td>24.2 (9.7; 36.5)</td>
</tr>
</tbody>
</table>

Status of trial (ongoing/completed): Completed on May 2013