Title of Trial: A Phase II Randomized, Double-Blinded, Controlled Study in Healthy Adults to Assess the Safety, Reactogenicity, and Immunogenicity of a Monovalent Influenza A/H7N9 Virus Vaccine Administered at Different Dosages Given With and Without MF59 Adjuvant

Clinical Trial registration site if applicable (e.g. ClinicalTrials.gov): NCT01938742

Authors/sponsors: National Institute of Allergy and Infectious Diseases (NIAID)

Study Design: Randomized, Parallel Assignment, Double Blind

Vaccine: H7N9
Manufacturer: Sanofi Pasteur

Type (whole virus/subvirion/subunit/live/recombinant/DNA/vector):

Adjuvant: MF59

Delivery system/site: Intramuscular injection

Doses (antigen and adjuvant):
Experimental: Group 1
100 subjects receive 3.75mcg sanofi A/H7N9 antigen plus Novartis MF59 adjuvant on Day 0 and 21

Experimental: Group 2
100 subjects receive 7.5mcg sanofi A/H7N9 antigen plus Novartis MF59 adjuvant on Day 0 and 21

Experimental: Group 3
100 subjects receive 15mcg sanofi A/H7N9 antigen plus Novartis MF59 adjuvant on Day 0 and 21

Experimental: Group 4
100 subjects receive 15mcg sanofi A/H7N9 antigen plus Novartis MF59 adjuvant on Day 0 and 15mcg sanofi A/H7N9 antigen on Day 21

Experimental: Group 5
100 subjects receive 15mcg sanofi A/H7N9 antigen on Day 0 and 15mcg sanofi A/H7N9 antigen plus Novartis MF59 adjuvant on Day 21

Experimental: Group 6
100 subjects receive 15mcg sanofi A/H7N9 antigen on Day 0 and 21

Experimental: Group 7
100 subjects receive 45mcg sanofi A/H7N9 antigen on Day 0 and 21

Study population: 700 volunteers, 19-64 years

Health status: Healthy

Specific inclusion criteria:
• Provide written informed consent prior to initiation of any study procedures.
• Are able to understand and comply with planned study procedures and be available for all study visits.
• Are males or non-pregnant females, 19 to 64 years old, inclusive.
• Are in good health, as determined by vital signs (oral temperature, pulse, and blood pressure), medical history, and targeted physical examination based on medical history to ensure any existing medical diagnoses or conditions (except those in the Subject Exclusion Criteria) are stable. Subjects may be on chronic or as needed (prn) medications if, in the opinion of the site principal investigator or appropriate sub-investigator, they pose no additional risk to subject safety or assessment of reactogenicity and
immunogenicity. Note: Topical, nasal, and inhaled medications (with the exception of steroids as outlined in the Subject Exclusion Criteria (see section 5.2)), vitamins, and contraceptives are permitted.

- Oral temperature is less than 100.4 degrees F.
- Pulse is 50 to 115 bpm, inclusive.
- Systolic blood pressure is 85 to 150 mmHg, inclusive.
- Diastolic blood pressure is 55 to 95 mmHg, inclusive.
- Female subjects of childbearing potential who are not surgically sterile via tubal sterilization, bilateral oophorectomy, or hysterectomy or who are not postmenopausal for \( \geq 1 \) year must agree to practice highly effective contraception that may include, but is not limited to, abstinence from intercourse with a male partner, monogamous relationship with a vasectomized partner, male condoms with the use of applied spermicide, intrauterine devices, and licensed hormonal methods with use of a highly effective method of contraception for a minimum of 30 days prior to study product exposure and agree to practice highly effective contraception for the duration of study product exposure, including 2 months (defined as 60 days) after the last study vaccination. A highly effective method of contraception is defined as one which results in a low failure rate (i.e., less than 1 percent per year) when used consistently and correctly. Method of contraception will be captured on the appropriate data collection form.
- Female subjects of childbearing potential must have a negative urine or serum pregnancy test within 24 hours prior to study vaccination.

Clinical Endpoints Assessed:

Safety assessments:
- Occurrence of study vaccine-related serious adverse events from the time of the first study vaccination through approximately 13 months after the first study vaccination.
- Occurrence of solicited injection site and systemic reactogenicity on the day of each study vaccination through 7 days after each study vaccination.

Immunogenicity assessments:
- Percentage of subjects achieving a serum HAI antibody titer of 1:40 or greater against the A/H7N9 antigen contained in the study vaccine at approximately 21 days after the second study vaccination.
- Percentage of subjects achieving seroconversion (pre-vaccination HAI titer <1:10 and post-vaccination HAI titer \( \geq 1:40 \) or pre-vaccination HAI titer \( \geq 1:10 \), minimum four-fold rise in post-vaccination HAI antibody titer).

Results: Not yet available

Safety:

Immunogenicity

GMTs:

GMT Ratios (post:pre):

Per cent responding (4 fold or greater rise and definition for reporting):

Per cent responders at specified tite:

Others assays:

Status of trial (ongoing/completed): 2013-2014 (ongoing)