# A randomised, double-blind, placebo-controlled, single-centre phase IIb trial as part of the EU-funded UNISEC project to assess the immunogenicity and safety of different formulations and dosing regimens of FLU-v vaccine administered subcutaneously in healthy adults aged 18-60 years.

Published: 30-06-2016
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To investigate the safety of the vaccination and the immune responses generated by the different formulations and dosing regimens of FLU-v in healthy adults.

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|---|---|
| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Viral infectious disorders |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON43976

**Source**
ToetsingOnline

**Brief title**
FLU-v 003

### Condition

- Viral infectious disorders

**Synonym**

influenza flu

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** PepTcell Limited (trading as SEEK)
**Source(s) of monetary or material Support:** It is funded by an FP7 European grant and private funding

## Intervention

**Keyword:** FLU-v, immunogenicity, safety, vaccine

## Outcome measures

### Primary outcome

• to evaluate the safety of the vaccine (FLU-v or placebo)

• to evaluate the cellular immune response generated after vaccination with

FLU-v or placebo after 42 and 180 days compared to before v vaccination (day

0).

### Secondary outcome

• to compare the level of antibody responses specific to FLU-v at 42 and 180

days after FLU-v or placebo vaccination compared to prevaccination levels.

# Study description

### Background summary

Flu, caused by influenza virus, is one of the major respiratory infections in humans that it is passed from person to person. The influenza virus often mutates resulting in new variants of influenza, this is why new vaccines against flu are required every year. The annual vaccine protects against the latest predicted strains of influenza. This is not only very costly, but in occasions the prediction is not right offering poor protection.
In rare occasions, influenza can be passed from farmed animals to humans creating new variants that spread very quickly and are very infective. These

can result in pandemics. It is very difficult to predict these influenza strains and so is preparing a vaccine against it using traditional methods. There is a need for a universal influenza vaccine. This vaccine should target parts of the virus that remain unchanged so that it confers protection against all strains of the influenza virus.
FLU-v is a vaccine that covers four very conserved regions of proteins NP, M1 and M2 of the influenza virus. FLU-v is expected to achieve protection against a broad range of influenza strains. FLU-v generates an immune response that can detect and destroy cells infected with influenza minimising the severity of the symptoms and the number of hospitalisations associated with flu.

## Study objective

To investigate the safety of the vaccination and the immune responses generated by the different formulations and dosing regimens of FLU-v in healthy adults.

## Study design

A randomised, double-blind, parallel group, controlled single centre study, stratified by age group.

## Intervention

Randomized subjects will receive two subcutaneous vaccinations 21 days apart of Placebo or FLU-v with or without adjuvant. Adjuvant is a mineral oil that may enhance the effect of FLU-v. Blood samples will be taken before vaccination, 21 days after vaccination is completed and after 6 months to measure the intensity and duration of the immune responses generated by the vaccine.
In addition, in order to measure the efficacy of FLU-v in protecting against flu, subjects will be asked to fill in a daily questionnaire during the flu season to record any influenza-like symptoms. If infection is suspected, a swab will be taken to perform a laboratory test to confirm that it was caused by influenza

## Study burden and risks

FLU-v has undergone extensive safety research in animals and has been tested previously in humans. The results showed that there were no concerns on the safety and tolerability of FLU-v.
In this study some subjects will receive Placebo, FLU-v alone or adjuvanted, that is adding a mineral oil that may enhance the effect of FLU-v. The adjuvant used in this trial, Montanide ISA-51, has been safely used in many other human trials. The most common local reactions are local pain, tenderness, redness at the injection site. Less frequently, hardness and swelling of the area around the injection can be observed.

Possible known side effects associated with the FLU-v vaccine are redness, swelling, pain and / or itching at the site of injection, nausea and mild flu-like symptoms may occur. These side effects are usually more common at the start of the study and typically don*t last more than a few days. Subjects will complete a study diary card of all symptoms they may experience after vaccination (up to day 42) and inform the study centre about any other adverse event experienced during the study to get more information about the safety of FLU-v.

As the vaccine is provided in a sealed single use vial, overdosing is unlikely.

FLU-v vaccine is still under research and we don*t know the effect to an unborn child if given to a pregnant woman. For this reason pregnant women are excluded from taking part in this study. Women who are at risk of becoming pregnant will be asked to have a pregnancy test before taking part to exclude the possibility of an unknown pregnancy. Effective contraception (combination of hormone and condom) must be used by women of childbearing potential from the start until 30 days after the last vaccination, and (condom) by men up to 90 days after the last vaccination. Women with young children will not be able to breastfeed either.

The entire study will not exceed 7 months. There will be a total of 5 planned visits during the study. On the first visit, subjects will be screened by medical research staff to decide if they are suitable and in good health to take part in the study. A small blood sample will be taken to assess overall health and exclude pregnancy. If suitable, the next four visits will be scheduled. On visit 2 (day 0), a blood sample will be taken to get a baseline of how the subject*s immune response was prior the vaccination and the first vaccination will be administered. On visit 3 (day 21) the subject will discuss any symptoms they may have experienced after the first vaccination and the second vaccination will be administered. On visit 4 (day 42) a blood sample will be taken to determine the immune responses to the vaccine, and any symptoms to the second vaccination will be discussed. On visit 5 (day 180) another blood sample will be taken to find if the responses to the vaccine are long lasting. Visits 2 and 3 will be at Isala, however visits 1, 4 and 5 can take place where the subject was recruited from (ie.place of work or education). Transport to Isala will be reimbursed to the subject.

During the study, subjects will not be able to use immunosuppressive or cytotoxic drugs, immunoglobulin or other blood products or any other experimental agent (vaccine, drug, biologic, device or medication) since those can affect the responses to FLU-v and compromise the results of the study.

In order to determine the efficacy of FLU-v to combat influenza infection, all subjects will be asked to fill in a diary recording any flu-like symptoms they may have during the influenza season, December to March. If the study personnel suspect they may have the flu, an additional visit will be set up to take a

nasal/throat swab. A laboratory test will determine if the symptoms are caused by influenza or not.

## Contacts

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## Trial sites

### Listed location countries

Netherlands

## Eligibility criteria

**Age**
Adults (18-64 years)
Elderly (65 years and older)

### Inclusion criteria

- Healthy males or healthy non-pregnant females (as indicated by a negative blood pregnancy test during the screening visit) between the ages of 18 and 60 years, inclusive;
- Women of childbearing potential (not surgically sterile or postmenopausal for greater than or equal to one year) and men must agree to practice appropriate contraception (a combination of barrier and hormonal methods for women and a condom for men) from screening and throughout the study treatment and for at least 30 days (up to Study Day 51 for females) and 90 days (up to Study Day 111 for males). After the last dose of the IMP);
- Is in good health, as determined by a comprehensive clinical assessment {vital signs (heart

rate, blood pressure, oral temperature), blood chemistry test (electrolytes, renal/kidney function, liver function, C-reactive protein, complete blood count), medical history, general physical examination, self-reported illness} and the clinical judgment of the investigator;
- Able to understand and comply with planned study procedures;
- Provides signed informed consent form.

## Exclusion criteria

- Has a known allergy to any of the components of the vaccine.
- Has a history of severe reaction following immunization.
- Persons with immune deficiency/disorder, whether due to genetic defect, immunodeficiency disease, or immunosuppressive therapy.
- Women who have a positive pregnancy test during the screening visit or who are breastfeeding.
- Has a history of any of the following (reported by subjects):
o Acute disseminated encephalomyelitis (ADEM);
o Neoplastic disease - current or previous;
o Asthma or severe allergic disease;
o Bleeding disorders
o Chronic Hepatitis B and/or C infection;
o Chronic liver disease;
o Diabetes mellitus;
o Guillain-Barré syndrome;
o HIV;
o Rheumatoid arthritis or other autoimmune diseases;
o Severe renal disease;
o Transplant recipients;
o Unstable or progressive neurological disorders.
- Receipt of medicines/treatments that may affect evaluation of immunogenicity such as:
o Oral or parenteral steroids, high-dose inhaled steroids (greater than 800 micrograms/day of beclomethasone dipropionate or equivalent) or other immunosuppressive or cytotoxic drugs (azathioprine (Imuran), cyclosporine (Neoral, Sandimmune, SangCya); monoclonal antibodies such as basiliximab (Simulect), daclizumab (Zinbryta), infliximab (Remicade), rituximab (MabThera), alemtuzumab (Campath and Lemtrada), omalizumab (Xolair), abatacept (Orencia), adalimumab (Humira and Exemptia) and etanercept (Enbrel)basiliximab (Simulect), daclizumab (Zenapax), and muromonab (Orthoclone OKT3); corticosteroids such as prednisone (Deltasone, Orasone); tacrolimus (Prograf, Advagraf, Protopic); Glatiramer acetate (Copaxone); Mycopehnolate (Cellcept); Sirolimus (Rapamune); (within 6 months of vaccination in this study)
o Immunoglobulin or other blood products (within 3 months of vaccination in this study);
o An experimental agent (vaccine, drug, biologic, device, blood product, or medication) within 1 month of vaccination in this study, or expects to receive an experimental agent (during the study period).
o Influenza antiviral medication (within 4 weeks of vaccination in this study).
- Has received any influenza vaccine within 6 months of vaccination in this study.

- Has influenza-like illness (a sudden onset of symptoms and at least one of the four systemic symptoms-fever or feverishness, malaise, headache, myalgia and at least one of the three respiratory symptoms-cough, sore throat, shortness of breath) or acute respiratory infection (a sudden onset of symptoms and at least one of the four respiratory symptoms-cough, sore throat, shortness of breath, coryza(Rhinitis) and a clinician*s judgement that the illness is due to an infection) within 6 months prior to vaccination in this study. These symptoms must have stopped you from carrying out your normal daily activities such as attending work or school for a period of at least 3 days.
- Has an acute illness, including an oral temperature greater than 38 degrees Celsius, within 1 week before vaccination.
- Has a history of alcohol or drug abuse within the last 2 years deemed unsuitable for inclusion by the investigator.
- Any abnormal haematology values and/or serum chemistries judged by the Investigator as clinically significant.
Being considered ineligible is based on the judgement of the investigator and in the event of uncertainty about the participant*s medical status regarding any of the exclusion criteria mentioned, the participant*s primary care physician will be consulted. Consultation of the primary care physician will only take place after having received written approval from the participant, and will concern medical information about exclusion criteria only.

# Study design

## Design

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| Study phase: | 2 |
| Study type: | Interventional |
| Intervention model: | Parallel |
| Allocation: | Randomized controlled trial |
| Masking: | Double blinded (masking used) |
| Control: | Placebo |
| Primary purpose: | Prevention |

## Recruitment

NL

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|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 22-08-2016 |
| Enrollment: | 222 |
| Type: | Actual |

### Medical products/devices used

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| Product type: | Medicine |
| Brand name: | FLU-v |

## Ethics review

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| Approved WMO Date: | 30-06-2016 |
| Application type: | First submission |
| Review commission: | CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag) |
| Approved WMO Date: | 22-07-2016 |
| Application type: | First submission |
| Review commission: | CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag) |

## Study registrations

### Followed up by the following (possibly more current) registration

No registrations found.

### Other (possibly less up-to-date) registrations in this register

No registrations found.

### In other registers

| Register | ID |
|---|---|
| EudraCT | EUCTR2015-001932-38-NL |
| CCMO | NL55061.000.15 |