# Phase I clinical trial to assess safety and immunogenicity of an MVA-based influenza H5 vaccine in healthy adults

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Primary objectiveSafety assessment of the MVA-H5-sfMR vaccine in humans. Study subjects will undergo physical examinations performed before and on fixed time points during the study. Clinical chemistry is performed on the blood samples that are...

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

## Summary

### ID

NL-OMON38408

**Source**
ToetsingOnline

**Brief title**
Phase 1 study with an MVA-based influenza H5 vaccine

### Condition

- Viral infectious disorders

**Synonym**
flu, Influenza

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Erasmus MC, Universitair Medisch Centrum Rotterdam
**Source(s) of monetary or material Support:** European Research Council (ERC) grant - Fluplan

## Intervention

**Keyword:** influenza virus, Modified Vaccinia virus Ankara, vaccine, vector

## Outcome measures

### Primary outcome

Safety of the vaccine (registration of local and systemic reactions and

clinical chemistry analysis)

### Secondary outcome

Immune responses to influenza virus hemagglutinin and the vector (MVA) (both

cellular and humoral immune responses)

# Study description

### Background summary

Influenza viruses of the H5N1 subtype are transmitted from birds to humans on a regular basis since 2003, particularly in South-east Asia and Egypt, resulting in over 600 clinical infections and and a mortality rate of almost 60%. These viruses are highly pathogenic and are considered to be a serious threat for animal and human health. Therefore the development of H5N1 vaccines is considered a priority by the WHO.

To address the hurdles in pandemic influenza vaccine development new vaccine platforms are explored and under development. One of the promising platforms is Modified Vaccinia virus Ankara. This virus is replication deficient in mammalian cells (with a few exceptions) due to a block in morphogenesis which means no new infectious virus particles are formed. After immunization the vector virus can efficiently enter mammalian cells and induces in a single round of infection with expression of viral and recombinant genes that results in strong protein/antigen production. MVA has been developed as an alternative smallpox vaccine and has been administered to over 120,000 individuals and was shown to be safe and effective in these individuals and also proved to be safe in immunocompromised subjects.

MVA virus can be used to shuttle a foreign gene, e.g. hemagglutinin gene from influenza A/H5N1 virus. This way it can function as a viral vector that induces a neutralizing antibody response against this highly pathogenic avian influenza

virus. Therefore such a vaccine is considered a suitable candidate as pandemic influenza vaccine.

The preclinical evaluation of an MVA-based H5N1 vaccine candidate in mice and macaques demonstrated that the vaccine is safe and strongly immunogenic in these animals. All together this makes MVA a promising pandemic influenza vaccine platform for the future. Therefore a clinical trial is conducted with the MVA-H5 vaccine.

## Study objective

Primary objective

Safety assessment of the MVA-H5-sfMR vaccine in humans. Study subjects will undergo physical examinations performed before and on fixed time points during the study. Clinical chemistry is performed on the blood samples that are drawn throughout the study and local and systemic reactions are monitored with a daily dairy card during the first week after immunization.

Secondary objective

Assessment of the immunogenicity of the MVA-H5-sfMR vaccine in humans. The immunogenicity will be determined by measuring influenza-specific antibody titers in the hemagglutination inhibition assay and virus neutralization assay. Furthermore the induction of HA-specific cytotoxic T cells will be assessed.

## Study design

-Randomized double blind clinical trial
-Duration: 20 weeks (with 5 site visits: inclusion visit and 0, 4, 8 and 20 weeks after the first immunization)
-Setting: Erasmus MC, Rotterdam, The Netherlands

For further details please refer to the study protocol (document C1 of the CCMO application)

## Intervention

The study subjects will receive one or two intramuscular immunizations (four week interval) with the vaccine or the control vaccine in the upper arm.

## Study burden and risks

In a recent study with an MVA-based vaccin (the dose was comparable to the highest dose in the current study) most subjects experienced mild to moderate local reactions such as pain at the injection site. This lasted for

approximately two days together with light swelling and redness of the injection site. The majority of the subjects experienced no or mild to moderate systemic reactions (headache, fever, myalgia, nausea).

Next to the possible side-effects the burden associated with participation consists of: investment of time for the study-visits, filling out the dairy cards, the intramuscular injection(s) in the upper arm (immunizations) and the blood sampling (inside of the elbow).

## 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

• 18-35 years of age
• Female volunteers must acquire an acceptable form of contraception during the study

period and to have a negative pregnancy test on the days of immunization.
• Refrain from blood donation during the study period
• Written informed consent
• Able and willing to comply with all study requirements

### Exclusion criteria

• Pregnancy or lactation
• Acute or chronic illness
• Known allergy to eggs, egg products or chicken protein
• Previous immunization with a recombinant MVA
• Previous immunization with an influenza A/H5N1 vaccine

## Study design

### Design

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

### Recruitment

NL

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| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 17-12-2012 |
| Enrollment: | 80 |
| Type: | Actual |

### Medical products/devices used

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| Product type: | Medicine |
| Generic name: | Genetic modified organism |

## Ethics review

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| Approved WMO Date: | 13-11-2012 |
| Application type: | First submission |
| Review commission: | CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag) |
| Approved WMO Date: | 14-11-2012 |
| Application type: | First submission |
| Review commission: | CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag) |
| Approved WMO Date: | 07-01-2014 |
| Application type: | Amendment |
| Review commission: | CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag) |
| Approved WMO Date: | 08-01-2014 |
| Application type: | Amendment |
| 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 | EUCTR2011-003035-66-NL |
| CCMO | NL37002.000.12 |

## Study results

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| Date completed: | 04-07-2014 |
| Actual enrolment: | 27 |