

# Evaluation of a prototype vaccine against enterotoxigenic Escherichia coli diarrhoea

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		<input type="checkbox"/> Protocol
<b>Registration date</b> 18/03/2011	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan
		<input type="checkbox"/> Results
<b>Last Edited</b> 18/03/2011	<b>Condition category</b> Infections and Infestations	<input type="checkbox"/> Individual participant data
		<input type="checkbox"/> Record updated in last year

**Plain English summary of protocol**  
Not provided at time of registration

## Contact information

**Type(s)**  
Scientific

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## Additional identifiers

**EudraCT/CTIS number**  
2009-015741-23

**IRAS number**

**ClinicalTrials.gov number**

**Secondary identifying numbers**  
EudraCT number: 2009-015741-23, OEV-120

# Study information

## Scientific Title

Evaluation of the safety and immunogenicity of a prototype enterotoxigenic Escherichia coli (ETEC) vaccine: a three-armed, double-blinded, randomised, single-centre study

## Study objectives

Enterotoxigenic E. coli (ETEC) bacteria are known to be a primary cause of traveller's diarrhoea and diarrhoea in children in developing countries. ETEC bacteria produce heat-labile toxin (LT), heat stable toxin (ST) or both toxins and colonise the intestine by means of so called colonisation factors (CFs).

The aim of this study is to determine if a new potentially improved prototype ETEC vaccine, consisting of bacteria over-expressing the colonisation factor CFA/I and administered together with a hybrid of the binding subunits of LT and cholera toxin (LTB/CTB), is safe and gives rise to stronger immune responses than a previously tested ETEC vaccine, consisting of a natural CFA/I expressing ETEC strain + CTB.

## Ethics approval required

Old ethics approval format

## Ethics approval(s)

1. Independent Ethics Committee in the Gothenburg region (IECGR) in Sweden approved on 26 /10/2009, amendment approved 13/03/2010, ref no 570-09
2. Western Institutional Review Board (WIRB) Olympia, Washington, USA approved on 11/05 /2010, ref no 20100565

## Study design

Three-armed double-blinded randomised single-centre study

## Primary study design

Interventional

## Secondary study design

Randomised controlled trial

## Study setting(s)

Hospital

## Study type(s)

Treatment

## Participant information sheet

Not available in web format, please use the contact details below to request a patient information sheet

## Health condition(s) or problem(s) studied

Enterotoxigenic E. coli (ETEC) diarrhoea

## Interventions

Healthy adult volunteers will be immunised with two consecutive doses of two different ETEC vaccines (Vaccine A and Vaccine B) with 12-16 days interval. Vaccine A consists of ETEC bacteria that over-express the colonisation factor CFA/I + LTB/CTB hybrid protein. Vaccine B consists of a previously tested CFA/I expressing ETEC strain + CTB protein. The vaccines will be mixed with a bicarbonate buffer and administered orally.

The volunteers will be randomised into three different study arms:

First arm: Subjects immunised with 2 doses of Vaccine A

Second arm: Subject immunised with 2 doses of Vaccine B

Third arm: Subjects immunised with 2 doses of Vaccine B; each dose containing 4 times higher numbers of bacteria and 4 times more LTB/CTB protein compared to the second arm

## **Intervention Type**

Drug

## **Phase**

Not Applicable

## **Drug/device/biological/vaccine name(s)**

Enterotoxigenic E. coli (ETEC) vaccine

## **Primary outcome measure**

1. To evaluate the safety of a new prototype ETEC vaccine (Vaccine A) and to compare the immunogenicity, i.e. intestinal or intestine-derived IgA antibody responses, against CFA/I and LTB, of the new prototype ETEC vaccine with that of a previously tested ETEC strain in combination with CTB (Vaccine B)

1.1. The safety of the vaccines will be determined by evaluation of study diaries throughout the study period, by clinical chemistry and haematology tests (at screening and 7 days after each immunisation) and by physical examination (at screening and on day 42)

1.2. Intestinal antibody responses are based on enzyme-linked immunosorbent assay (ELISA) measurements of specific antibodies in stool extracts (day 0, 7 and 21)

1.3. Intestine-derived antibody responses are based on ELISA measurements of specific antibodies secreted from cultured peripheral blood cells (using the ALS method) or on ELISPOT assay determinations of the numbers of specific antibody secreting cells (ASC) among peripheral blood mononuclear cells (day 0, 7 and 21)

## **Secondary outcome measures**

1. To evaluate IgA and IgG antibody responses against CFA/I, LTB and CTB in serum as well as specific IgA in those mucosal samples that are not used as primary endpoints

1.1. Serum and intestinal antibody responses are based on enzyme-linked immunosorbent assay (ELISA) measurements of specific antibodies in sera (day 0, 7, 14, 21 and 42) and stool (day 0, 7 and 21), respectively

1.2. Intestine-derived antibody responses are based on ELISA measurements of specific antibodies secreted from cultured peripheral blood cells (using the ALS method) or on enzyme-linked immunosorbent spot (ELISPOT) assay determinations of the numbers of specific antibody secreting cells (ASC) among peripheral blood mononuclear cells

## **Overall study start date**

12/05/2010

## **Completion date**

# Eligibility

## Key inclusion criteria

1. Males or females aged 18-55 years
2. Healthy constitution as established by medical history, medical examination and clinical chemistry and haematology testing
3. Give written informed consent to participate
4. Willing and able to communicate with the investigators and understand the requirements of the study
5. Sexually active females should unless being menopausal agree to use reliable contraception as assessed by the investigator, during 1 month prior to inclusion and one month after the last intake of study vaccine and should have a negative pregnancy test before each vaccination

## Participant type(s)

Patient

## Age group

Adult

## Lower age limit

18 Years

## Upper age limit

55 Years

## Sex

Both

## Target number of participants

60

## Key exclusion criteria

1. Has received the oral cholera vaccine Dukoral® in the last 5 years
2. Travelled to ETEC-endemic area within the last 2 years
3. Concomitant intake of immunomodulating drugs during the study period or less than four weeks prior to the first immunisation
4. Vaccination with some other vaccine during the study period or within two weeks prior to trial vaccination
5. Any condition which would limit the subjects ability to complete the study in the opinion of the investigator
6. History of drug or chemical abuse in the year before the study
7. Receipt of any other investigational product in the month before study entry
8. Concomitant participation in any other clinical study
9. Donation of blood 6 weeks before study entry or at any time during the study
10. Females who are pregnant
11. Females who are nursing
12. History of gastrointestinal or systemic inflammatory or autoimmune disease
13. Any known hypersensitivity to any ingredient in the vaccines

- 14. Gastroenteritis within two weeks prior to vaccination
- 15. Antibiotic therapy within six weeks prior to the vaccination

**Date of first enrolment**

12/05/2010

**Date of final enrolment**

01/06/2011

## **Locations**

**Countries of recruitment**

Sweden

**Study participating centre**

Dept. of microbiology and immunology

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## **Sponsor information**

**Organisation**

Gothenburg University Vaccine Research Institute (GUVAX) (Sweden)

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**Sponsor type**

University/education

**ROR**

<https://ror.org/01tm6cn81>

## **Funder(s)**

**Funder type**

Other

**Funder Name**

PATH (USA)

**Alternative Name(s)**

Program for Appropriate Technology in Health

**Funding Body Type**

Government organisation

**Funding Body Subtype**

Other non-profit organizations

**Location**

United States of America

**Funder Name**

Sahlgrenska University Hospital (Sweden) (ref: LUA/ALF)

**Funder Name**

Swedish Research Council (Sweden)

**Alternative Name(s)**

Swedish Research Council, VR

**Funding Body Type**

Government organisation

**Funding Body Subtype**

National government

**Location**

Sweden

## Results and Publications

**Publication and dissemination plan**

Not provided at time of registration

**Intention to publish date**

## **Individual participant data (IPD) sharing plan**

### **IPD sharing plan summary**

Not provided at time of registration