

F.A.Q.: Human nasopharyngeal colonization using a genetically modified strain of the bacteria, *Neisseria lactamica*

This document contains information and common questions about the proposed study of introducing a genetically modified strain of the bacteria, *Neisseria lactamica*, into the nasal cavity of adult volunteers.

Glossary

Colonised: Someone that has the bacteria living within the back of their throat.

Colonisation: The process by which the bacteria comes to live within the back of the throat.

Genetic modification: The artificial transfer of DNA from one species into another.

Nasopharynx: The inside part of the throat that connects to the inside part of your nose.

Nasopharyngeal: Of or relating to the nasopharynx.

Strain: A single isolate, or type, of bacteria derived from the throat of an individual.

Information on *Neisseria* bacteria species

What is *Neisseria lactamica*?

It is a species of bacteria that lives in part of the throat known as the nasopharynx in young children and adults. It is part of the normal population of bacteria found in healthy people.

Does *Neisseria lactamica* cause disease?

No. It is part of the normal population found in healthy people.

What is *Neisseria meningitidis*?

It is a different species of bacteria that also lives in part of the throat known as the nasopharynx in children and adults. It is part of the normal bacterial population, but in very rare cases it causes invasive meningococcal disease in babies and adolescents.

Does *Neisseria meningitidis* cause disease?

Neisseria meningitidis is the cause of invasive meningococcal disease.

What is invasive meningococcal disease?

It is a rapidly developing, often lethal disease caused by *Neisseria meningitidis*. It is characterised by meningococcal meningitis (bacteria causing inflammation of the tissues surrounding the brain) and meningococcal septicaemia (bacteria in the blood). Survivors are often left with life-long health problems.

Is *Neisseria lactamica* safe to give to volunteers?

Yes. We have given it to over 300 adult volunteers with no ill effects.

Is there a benefit to being colonised by *Neisseria lactamica*?

Yes. People that are colonised by *Neisseria lactamica* are less likely to be colonised by *Neisseria meningitidis*. Without *Neisseria meningitidis* people cannot get invasive meningococcal disease.

What evidence is there that colonisation by *Neisseria lactamica* prevents colonisation by *Neisseria meningitidis*?

We have observed that the number of people colonised by *Neisseria meningitidis* in individuals colonised by *Neisseria lactamica* is reduced by half.

Will colonisation by *Neisseria lactamica* mean I become permanently protected against invasive meningococcal disease?

No. The protective effect is limited to the period of colonisation by *Neisseria lactamica*.

How long can *Neisseria lactamica* live within an individual?

It can live for at least 6 months in some people.

What are you trying to achieve in this study?

We have introduced a gene into *Neisseria lactamica* with a view to induce harmless colonisation in volunteers. For further information see below - 'What is the purpose of this genetic modification?'

How do you give the bacteria to volunteers?

We will place a small volume of liquid containing the bacteria into both nostrils of volunteers.

[Information on genetic modification](#)

What genetic modification has been made to *Neisseria lactamica*?

We have added a single gene from *Neisseria meningitidis* called *nadA*. It enables the *Neisseria lactamica* to make a protein called *Neisseria* adhesin A, also known as NadA.

What is NadA?

Neisseria adhesin A, also known as NadA, is a protein from *Neisseria meningitidis*. Bacteria that make NadA, stick to human body cells in larger numbers than bacteria that do not.

What effect does the genetic modification have on *Neisseria lactamica*?

The modified bacteria is more adherent to cells grown in the laboratory. We believe this may increase the number of people that become colonised by the bacteria.

What is the purpose of this genetic modification?

There are three reasons for conducting this study. Firstly, it is a way to study the induction of immunity when people become colonised in the nasopharynx. By measuring the response of the immune system to NadA we will learn more about the normal mechanism of protection against meningococcal disease. Secondly, it is a way to measure the effect of current vaccines on the ability of potentially harmful bacteria to colonise people. NadA is included in the new meningitis B vaccine, Bexsero. Thirdly, we expect genetically modified *Neisseria lactamica* to colonise more volunteers compared to the wild type organism we currently use. We anticipate this will reduce colonisation by *Neisseria meningitidis*. In the future we aim to explore the use of this to protect against invasive meningococcal disease.

Could the genetically modified *Neisseria lactamica* cause disease?

The inserted gene, NadA, has not been shown to be involved any disease symptoms, so we believe that *Neisseria lactamica*, modified to make NadA, is safe.

Why is the genetic modification necessary?

The wild type *Neisseria lactamica* only colonises a third of volunteers. We believe that the production of NadA by the bacterium will increase the proportion of volunteers that become colonised. As colonisation by *Neisseria lactamica* reduces colonisation by *Neisseria meningitidis*, we believe it will help prevent invasive meningococcal disease, both by facilitating more efficient colonisation but also by inducing strong immunity to *Neisseria meningitidis*.

Is the genetic modification stable?

Yes. A single copy of the gene has been permanently introduced into the DNA of the strain of the bacteria used in the study. The gene does not change over time.

Information on release and transmission of *Neisseria lactamica*

What do you mean by ‘deliberate release’?

This is a legal term stipulated by the Department for Environment, Food & Rural Affairs (DEFRA). It means that once volunteers have been colonised with the genetically modified *Neisseria lactamica*, it is deemed to have been ‘deliberately released’ from the laboratory into the environment.

How are you going to release the bacteria?

We will place a small volume of liquid containing the genetically modified bacteria into both nostrils of volunteers.

Does *Neisseria lactamica* spread between people?

Yes. We believe it is passed between close contacts such as family members in the household.

How is *Neisseria lactamica* spread between people?

The exact mechanism of spread is unknown, but requires close contact between people. It cannot be picked up from inanimate objects such as door handles.

How far is it like likely to spread through the population?

This is unknown, however we do not expect it to spread beyond close contacts.

Ecological impacts

Could the genetically modified strain of *Neisseria lactamica* completely replace the unmodified organism?

This is unlikely. In the laboratory, it grows in the same way and rate as the unmodified bacteria, and the presence of NadA is likely to induce immunity, which will lead to weaker colonisation.

How long does *Neisseria lactamica* survive outside of the human body?

It dies very quickly unless it is spread to another person, although exactly how long this takes is unknown.

Could *Neisseria lactamica* colonise animals, such as family pets?

No. It only colonises humans.

Experimental design

What strain of *Neisseria lactamica* will you be using in this study?

The parent strain is Y92-1009. It was originally isolated from the throat of a healthy individual in 1992.

What type of volunteers will be used?

Healthy consenting adults between the ages of 18 and 45.

Can I participate in this study?

Yes. You will be able to participate in this study, once it has been approved and opened for recruitment, via the NIHR Southampton Clinical Research Facility.

Where is this study going to be conducted?

The NIHR Southampton Clinical Research Facility at University Hospital Southampton.

Will the volunteers be kept isolated from the general public?

For the first 5 days after receiving the inoculation they will reside in the hospital's clinical research facility. After that they will be discharged home.

Health and safety questions

Is this a vaccine?

This genetically modified strain of *Neisseria lactamica* is not being used as a vaccine at the current time. However, if it is shown to induce an immune response in volunteers then it might be further developed for such a purpose in the future.

Does this replace the need to vaccinate against invasive meningococcal disease?

No. People should continue to receive currently licensed meningococcal vaccines offered within the UK immunisation schedule.

Can this be used to treat invasive meningococcal disease?

No. Genetically modified *Neisseria lactamica* would provide no benefit for the treatment of established invasive meningococcal disease.

As someone who is not participating in this study, could the genetically modified *Neisseria lactamica* spread to me?

Yes, there is a theoretical possibility that it could if you come into close contact with one of our volunteers. It is possible it will spread to close contacts of volunteers participating in this study, such as family members.

I am immunocompromised. Could genetically modified *Neisseria lactamica* make me ill?

We will exclude any volunteers that have contact with immunocompromised people. We do not know exactly what would happen if genetically modified *Neisseria lactamica* colonised an immunocompromised person, but anticipate that there will be no ill effects based on available evidence. There is no evidence to suggest that genetically modified *Neisseria lactamica* is any more likely to make you ill than unmodified strains.

I am pregnant. How could the genetically modified *Neisseria lactamica* affect my unborn child or me?

Colonisation by *Neisseria lactamica* is most common in nursing mums and their babies. There is no reason to believe that genetically modified *Neisseria lactamica* would be harmful, but it would have the same ability to colonise expectant mums and their babies.

I have young children. How will the genetically modified *Neisseria lactamica* affect them?

It is unlikely that they will come into contact with genetically modified *Neisseria lactamica*, but if they do, the likeliest outcome will be harmless colonisation.

How will genetically modified *Neisseria lactamica* affect the elderly?

It is unlikely to have any impact on the elderly.

Will participation in this study make me more susceptible to infections of the nose and throat?

No.

Are there any lasting effects of being colonised by *Neisseria lactamica*?

No. At the moment we believe *Neisseria lactamica* is only beneficial whilst present in the back of the throat.

What safeguards are in place?

Volunteers will be monitored as residents in the NIHR Southampton Clinical Research Facility for 5 days after receiving the bacteria and outpatient monitoring will be maintained with all volunteers throughout the duration of the study. Routine control procedures will prevent spreading of the bacteria within the research facility. Volunteers will be trained in behaviours that minimise spread to others. In the extremely unlikely event that any disease occurs after colonisation, infection with the genetically modified *Neisseria lactamica* is easily treated by the standard antibiotic ciprofloxacin.