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**A Proof-of-Concept Study for Vitamin A Nasal Drops in Post-Viral Olfactory**

**Loss (APOLLO)**

IRAS: 294741

Participant Information Form v1.3 02/Aug/21

**Project Sponsor:** University of East Anglia

**Chief Investigator:** ProfessorCarl Philpott

**Co-Investigators:** Sara Bengtsson, Saber Sami, Allan Clark, James Boardman, Thomas Hummel

**Introduction**

We would like to invite you to take part in medical research investigating the effects of vitamin A drops on the sense of smell. You have been invited because you have been identified as someone who has suffered a loss or distortion of their sense of smell caused by a viral infection.

**What do Vitamin A drops do?**

Vitamin A, when taken into the body, is converted to a substance called retinoic acid (RA). This is important in tissue development and regeneration including that of the smell receptors. By giving Vitamin A drop treatment direct to the area in the nose where the smell receptors are, it should help the specialised smell receptors damaged by the virus(es) to regenerate and help to restore the sense of smell.

**Why is this research taking place?**

There have already been some studies undertaken with vitamin A for people with smell disturbances, but the design of the studies means that more evidence for using it as a treatment for smell disturbance is needed. This study is called a “proof-of-concept” study as we will be aiming to show that the nerve/brain pathways respond to the treatment.

**What will happen to me if I take part?**

The study will take place at the University of East Anglia Brain Imaging Centre (UBIC). Following your consultation at the Norfolk Smell & Taste Clinic (located at the James Paget University Hospital), you will be invited to attend the UBIC which is located on the University of East Anglia (UEA) campus near the Norwich Medical School. As part of the study, you will be invited to make two visits, one at the beginning of the study and one at the end of the study after three months. If you have received this information sheet through Fifth Sense, we will invite you to a research clinic to check that you are able to participate in the study.

On your visits to the UBIC, you will undergo a scan using a technique known as functional Magnetic Resonance Imaging (fMRI). This does not involve any x-ray radiation but uses magnetic fields to generate pictures of your brain. While you are in the scanner, you will be asked to wear a mask over your nose, through which smells will be delivered in short bursts of up to 5 seconds. The scanner software will enable us to detect changes in brain activity due to smells being detected. We will also measure the size of relevant parts of the brain/nerve pathways so that we can compare them between the two visits. When there is an improvement in the sense of smell, these structures usually increase in size.

Each visit to UBIC will last about one and half hours in total. You will also be asked to complete a questionnaire about your sense of smell at both visits and at the second visit you will be asked to repeat the smell test that you received before entering the study.

To find out whether treatment results in trials are due to the medication being tested and not due to other factors we need to do what is called a randomised controlled trial. In such trials participants are allocated randomly into two groups, one of which receives the actual medication and the other an inactive but otherwise indistinguishable alternative, sometimes known as a placebo. Neither the participant nor the researchers know who is in which group until the end of the trial, when the results are compared. In this case, some people will receive Vitamin A drops and some will receive peanut oil drops – the inactive alternative. Neither you nor the researchers will know which drops you have received; this information will only be known the Clinical Trials Unit team. You will have a 2 to 1 chance of receiving the vitamin A drops. Between each visit to UBIC you will be asked to apply two drops to each nostril each day and you will be taught how to put them in the nose. At the second visit you will be asked to return the (empty) bottles of drops that you were given at the first visit.

**What happens if am allergic to peanuts?**

If you have a known or suspected allergy to peanuts, you will not be able to participate in the trial as the drops in both arms of the study contain peanut oil. There may also be other reasons that you might not be able to participate in the trial which the research team will check with you before you can enter the trial.

**What are the benefits of taking part?**

There is a possibility that your sense of smell may improve by participating in the study. Furthermore, this scientific research hopes to provide better treatment options in the future for those people with similar smell disturbances.

**What are the disadvantages?**

There is a possibility of minor side-effects from using the drops such as irritation of the nose. Some people may also feel claustrophobic inside the MRI scanner; if you suffer with claustrophobia, please discuss this with the research team. If you are female and pregnant or planning to become pregnant, you should not participate in the study, as there is a risk of the vitamin A causing harm to the unborn child.

**Will this research affect my treatment?**

No. This research will have no impact on the treatment that you receive from the Norfolk Smell & Taste Clinic if you have been attending there as a patient, other than that we will not arrange to see you there as a patient during your 3-month period of participation in the study.

**What happens when the research study stops?**

Once you have completed the trial, you will return to normal NHS care for your smell disturbance. If at the end of the trial you have not had any improvement in your sense of smell, you can discuss with your doctor what course of treatment is best for you next. As we won’t know what treatment you received in the trial, you may want to consider taking the active treatment after the trial.

**What if something goes wrong?**

Nothing in this study is expected to cause you any harm. The study is covered by an indemnity insurance policy held by the University of East Anglia (U.M. Association Limited – ref UM014/13). If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions. If you remain unhappy and wish to complain formally, you can do this by contacting Professor Bill Fraser, Head of School, Norwich Medical School, University of East Anglia, Norwich Research Park, Norwich NR4 7TJ (w.fraser@uea.ac.uk). Or you can contact the Patient Advice and Liaison Services (PALS) department, James Paget University Hospitals NHS Foundation Trust, Lowestoft Road, Gorleston, Great Yarmouth, NR31 6LA Tel. 01493 453240 email : PALS@jpaget.nhs.uk

**What will happen if I don't want to carry on with the study?**

It is entirely your own decision whether to participate in this study. Participating or not participating in this study will have no impact on the treatment you receive. You can withdraw from the study at any time, without reason. Participation is voluntary, and no financial reward will be given to participants, other than reimbursement for any travel expenses. Details of how to claim travel expenses will be provided by the research team.

**How will my information be kept confidential?**

We will need to use information from you and from your medical records for this research project. This information, accessed by Professor Philpott and the research nurse assigned to the study, will include your initials, NHS number, name and contact details.  People will use this information to do the research or to check your records to make sure that the research is being done properly. Additional members of the research team who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead.  We will keep all information about you safe and secure. Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

**What are your choices about how your information is used?**

* You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have.
* We need to manage your records in specific ways for the research to be reliable. This means that we won’t be able to let you see or change the data we hold about you.

**Where can you find out more about how your information is used?**

You can find out more about how we use your information

* at [www.hra.nhs.uk/information-about-patients/](https://www.hra.nhs.uk/information-about-patients/)
* by asking one of the research team
* by sending an email to dataprotection@uea.ac.uk
* by ringing us on 07824527234

[www.hra.nhs.uk/patientdataandresearch](http://www.hra.nhs.uk/patientdataandresearch)

The information recorded will be pseudo-anonymised (so those analysing the data cannot identify you directly) and stored on password-secured hospital and university computers. Information will only be accessed by members of the research team. Anonymised information collected may be used for future research and anonymised data may be shared with future researchers. UEA will carry out this research under the provisions of the General Data Protection Regulation (EU) 2016/679 and will be using information from you and your medical records in order to undertake this study. UEA will act as the data controller for this study. This means that UEA, are responsible for looking after your information and using it properly.

The James Paget University Hospital will use your name, telephone number, email address and contact details to contact you about the research study, and make sure that relevant information about the study is recorded, and to oversee the quality of the study. UEA will enter these details onto a secure randomisation system when you enter the trial, and these details, along with the information collected from you and your medical records will be sent to and accessed by the team at the Norwich Clinical Trials Unit (NCTU). Your identifiable information will be held on an encrypted, password protected database at UEA, which is separate to the database where your pseudo-anonymised trial data are kept. This will ensure that all information about you to be kept confidential. The people who analyse the information will not be able to identify you and will not be able to find out your name or contact details.

**What is patient data?**

When you go to your GP or hospital, the doctors and others looking after you will record information about your health. This will include your health problems, and the tests and treatment you have had. They might want to know about family history, if you smoke or what work you do. All this information that is recorded about you is called patient data or patient information.

When information about your health care joins together with information that can show who you are (like your name or NHS number) it is called identifiable patient information. It’s important to all of us that this identifiable patient information is kept confidential to the patient and the people who need to know relevant bits of that information to look after the patient. There are special rules to keep confidential patient information safe and secure.

**What sort of patient data does health and care research use?**

There are lots of different types of health and care research.

If you take part in a clinical trial, researchers will be testing a medicine or other treatment. Or you may take part in a research study where you have some health tests or answer some questions. When you have agreed to take part in the study, the research team may look at your medical history and ask you questions to see if you are suitable for the study. During the study you may have blood tests or other health checks, and you may complete questionnaires. The research team will record this data in special forms and combine it with the information from everyone else in the study. This recorded information is research data.

In other types of research, you won’t need to do anything different, but the research team will be looking at some of your health records. This sort of research may use some data from your GP, hospital or central NHS records. Some research will combine these records with information from other places, like schools or social care. The information that the researcher collects from the health records is research data.

**Why does health and care research use information from patients?**

In clinical trials, the researchers are collecting data that will tell them whether one treatment is better or worse than other. The information they collect will show how safe a treatment is, or whether it is making a difference to your health. Different people can respond differently to a treatment. By collecting information from lots of people, researchers can use statistics to work out what effect a treatment is having.

Other types of research will collect data from lots of health records to look for patterns. It might be looking to see if any problems happen more in patients taking a medicine. Or to see if people who have screening tests are more likely to stay healthier.

Some research will use blood tests or samples along with information about the patient’s health. Researchers may be looking at changes in cells or chemicals due to a disease.

All research should only use the patient data that it really needs to do the research. You can ask what parts of your health records will be looked at.

**How does research use patient data?**

If you take part in some types of research, like clinical trials, some of the research team will need to know your name and contact details so they can contact you about your research appointments, or to send you questionnaires. Researchers must always make sure that as few people as possible can see this sort of information that can show who you are.

In lots of research, most of the research team will not need to know your name. In these cases, someone will remove your name from the research data and replace it with a code number. This is called coded data, or the technical term is pseudonymised data. For example, your smell test might be labelled with your code number instead of your name. It can be matched up with the rest of the data relating to you by the code number.

In other research, only the doctor copying the data from your health records will know your name. They will replace your name with a code number. They will also make sure that any other information that could show who you are is removed. For example, instead of using your date of birth they will give the research team your age. When there is no information that could show who you are, this is called anonymous data.

**Where will my data go?**

Sometimes your own doctor or care team will be involved in doing a research study. Often, they will be part of a bigger research team. This may involve other hospitals, or universities or companies developing new treatments. Sometimes parts of the research team will be in other countries. You can ask about where your data will go. You can also check whether the data they get will include information that could show who you are. Research teams in other countries must stick to the rules that the UK uses.

The bigger research team may include people who check the quality of the research. Regulators may also need to check the research. They will compare the recorded research data with your health records. They might read your health records through a secure internet connection or at the hospital or clinic. All the computers storing patient data must meet special security arrangements.

If you want to find out more about how companies develop and sell new medicines, the Association of the British Pharmaceutical Industry has [information on its website.](https://www.abpi.org.uk/)

**What are my choices about my patient data?**

* You can stop being part of a research study at any time, without giving a reason, but the research team will keep the research data about you that they already have. You can find out what would happen with your data before you agree to take part in a study.
* In some studies, once you have finished treatment the research team will continue to collect some information from your doctor or from central NHS records over a few months or years so the research team can track your health. If you do not want this to happen, you can say you want to stop any more information being collected.
* Researchers need to manage your records in specific ways for the research to be reliable. This means that they won’t be able to let you see or change the data they hold about you. Research could go wrong if data is removed or changed.

**What happens to my research data after the study?**

Researchers must make sure they write the reports about the study in a way that no-one can work out that you took part in the study.

Once they have finished the study, the research team will keep the research data for several years, in case they need to check it. You can ask about who will keep it, whether it includes your name, and how long they will keep it.

Usually, your hospital or GP where you are taking part in the study will keep a copy of the research data along with your name. The organisation running the research will usually only keep a coded copy of your research data, without your name included. This is kept so the results can be checked.

If you agree to take part in a research study, you may get the choice to give your research data from this study for future research. Sometimes this future research may use research data that has had your name and NHS number removed. Or it may use research data that could show who you are. You will be told what options there are. You will get details if your research data will be joined up with other information about you or your health, such as from your GP or social services.

Once your details like your name or NHS number have been removed, other researchers won’t be able to contact you to ask you about future research. Any information that could show who you are will be held safely with strict limits on who can access it.

You may also have the choice for the hospital or researchers to keep your contact details and some of your health information, so they can invite you to take part in future clinical trials or other studies. Your data will not be used to sell you anything. It will not be given to other organisations or companies except for research. For further details on GDPR rules about data management, see appendix 1.

**How can you find out the results?**

Anonymised results will be posted on the UEA Rhinology website ([www.uea.ac.uk/rhinology-group/research](http://www.uea.ac.uk/rhinology-group/research)). We will also contact our patient charity Fifth Sense, so they can post the results on their website and Newsletters. No patient identifiable information will be used in the results. We will contact all participants to let them know when the study results are released.

**Who has reviewed the study?**

All research that involves NHS patients or staff, information from NHS medical records or uses NHS premises or facilities has to be approved by an NHS Research Ethics Committee before it goes ahead. This study has been reviewed by the **xxx Research Ethics Committee**. Approval does not guarantee that you will not come to any harm if you take part, however approval means that the Committee is satisfied that your rights will be respected; that any risks have been reduced to a minimum; have been balanced against possible benefits and that you have been given sufficient information on which to make an informed decision.

**Who is organising and funding this study?**

The APOLLO study is funded by the National Institute of Health Research (NIHR): Research for Patient Benefit funding stream. The University of East Anglia are sponsoring this trial. The ENT doctor at your hospital who has recruited you is not being paid for his/her part in the study beyond his/her normal salary and does not benefit personally from your taking part in this trial.

**How have patients and the public been involved in this study?**

A patient representative, on behalf of the charity Fifth Sense, is a member of the research team and has advised on the study details and the study information provided in this information sheet. He will continue to be involved throughout the study so that the study conduct and results remain focused on patient benefit.

**Will my GP be informed of my involvement?**

With your permission, your GP, and other doctors who may be treating you, will be notified that you are taking part in this study. We may also contact your GP to check your status, if we cannot reach you directly.

***Further Information***

You are encouraged to ask any questions you wish, before, during or after your treatment. If you have any questions about the study, please speak to your study nurse or ENT doctor, who will be able to provide you with up-to-date information about the study. If you wish to read the research on which this study is based, please ask your study nurse or ENT doctor. If you require any further information or have any concerns while taking part in the study, please use the contact details below. If you decide to enter the study, you will be asked to sign the consent form, a copy of which will be provided to you for your own records.

**Contact information**

This study is being undertaken by Professor Philpott, a consultant ENT surgeon. If you have any concerns or would like further like information regarding the study, please contact:

*Chief Investigator:*

Professor Carl Philpott

Professor of Rhinology & Olfactology

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Thank you for considering participating in this study.

**APPENDIX 1**

**Will the use of my data meet GDPR rules?**

GDPR stands for the General Data Protection Regulation. In the UK we follow the GDPR rules and have a law called the Data Protection Act. All research using patient data must follow UK laws and rules.

Universities, NHS organisations and companies may use patient data to do research to make health and care better.

When companies do research to develop new treatments, they need to be able to prove that they need to use patient data for the research, and that they need to do the research to develop new treatments. In legal terms this means that they have a ‘legitimate interest’ in using patient data.

Universities and the NHS are funded from taxes and they are expected to do research as part of their job. They still need to be able to prove that they need to use patient data for the research. In legal terms this means that they use patient data as part of ‘a task in the public interest’.

If they could do the research without using patient data they would not be allowed to get your data.

Researchers must show that their research takes account of the views of patients and ordinary members of the public. They must also show how they protect the privacy of the people who take part. An NHS research ethics committee checks this before the research starts.