Participant Information Sheet (PIS)

EarMetrics®-Oximeter - a Targeted Oxygenation Observation Study

(EMO-TOS)

A Controlled Desaturation Study to establish the Safety and Performance of the EarMetrics®-Oximeter Validation Device

First in Human (FIH) – healthy adult volunteer study

*You have been invited to take part in research being undertaken at **University Hospitals Birmingham NHS Foundation Trust (UHB)** and sponsored by **EarSwitch Ltd.** Before you make a decision about taking part, we would like to explain to you why the study is being carried out, what it will involve and your role. Please take time to read the following information carefully and discuss it with others if you wish. If there are aspects of the information sheet that are not clear, then please contact the research team using the details provided.*

For the further information about the company EarSwitch Ltd and their technology: https://www.earswitch.co.uk

What is the purpose of the study?

We are undertaking a controlled desaturation study to investigate the safety and performance of the new medical device, EarMetrics® – Oximeter Validation Device, in measuring different blood oxygen levels within the body.

What is a Controlled Desaturation Study?

The term '***desaturation***' describes a reduction in the amount of oxygen in someone's blood.

The controlled desaturation study is designed to safely reduce the amount of oxygen breathed in by a healthy volunteering participant. Reduced oxygen in the air breathed in, results in reduced amount of oxygen in the volunteer's blood. The oxygen content in the volunteer's blood is then measured by taking repeated blood samples.

Controlled desaturation studies are performed in a highly controlled setting with nurses and doctors present throughout providing continuous monitoring of your welfare. Controlled desaturation studies follow the standard protocol in keeping with established internationally agreed standards. Controlled desaturation studies have been performed more than 10,000 times with no serious adverse events; so controlled desaturation studies are very safe. ***Your safety is paramount and prioritised throughout the study***.

What is the EarMetrics®-Oximeter validation device?

We are undertaking a study to investigate the safety and performance of the EarMetrics®-Oximeter Validation Device for the calculation of blood oxygen levels. This pulse oximeter is intended to be placed in the ear canal, to estimate blood oxygen levels.

As the skin inside the ear does not contain any pigmentation (skin colour), measuring blood oxygen levels from this part of the body is likely to provide more accurate measurements for people with darker skin, unlike finger pulse oximeters that are currently used in clinical care.

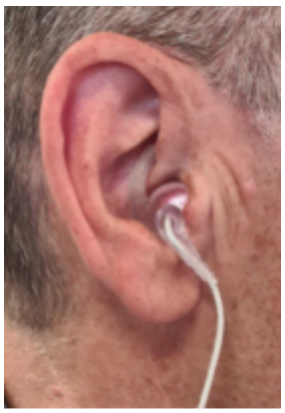

Figure 1) *Positioning of Earpiece within the ear*

Figure 2) *Silicone Eartip fitting on Earpiece Sensor Unit*

Figure SEQ Figure * ARABIC 3) *Photograph of the components of the EarMetrics® – Oximeter Validation Device*

How will we Perform the Controlled Desaturation Study with the EarMetrics®-Oximeter Validation Device?

The aim of the study is to show that the EarMetrics®-Oximeter Validation Device can safely measure blood oxygen levels in comparison to the "gold-standard" method of measuring blood oxygen levels (SaO2), with acceptable accuracy. We will do this by measuring blood oxygen levels whilst gradually reducing the oxygen breathed.

Healthy adults will start breathing oxygen at the same levels as in room air (21% oxygen) and this will be gradually reduced. The measurements from the EarMetrics®-Oximeter Validation Device will be compared to the known correct value in the blood (SaO2). The SaO2 is measured by obtaining multiple blood samples from an artery in the body.

Repeated arterial blood samples are obtained by inserting a small plastic tube into the artery, ***an arterial cannula***, so your blood vessel needs to be pierced only once (or twice). You will be closely and continuously monitored and kept safe by clinical staff throughout the study.

What will happen next?

After providing you with this Participant Information Sheet and the Health Assessment Form a member of the research team will contact you via phone after a minimum of 48 hours to see if you are still interested in participating in this study. This telephone call will also provide the opportunity to discuss the study in more detail and answer all your questions and concerns.

Participation is ***voluntary***, and you can decline your participation in the study at any point.

What will happen to me if I take part in the study?

If you agree to take part in the study, you will be invited to University Hospitals Birmingham's Clinical Research Facility (CRF) at the Queen Elizabeth Hospital, Birmingham. You will only need to attend the CRF once for a single study session. The duration of the study session is approximately 3-4 hours.

On the day of the study session, a member of the research team will speak to you to make sure you still want to take part in the study. They will answer any questions and confirm you are eligible to take part in the study. If you decide to take part in the study, you will be asked to sign a consent form. You will be offered a copy of the consent form to keep.

A research nurse will check you are able to take part by taking a number of measurements including your height, weight, ethnicity and skin tone. We will record your skin tone and ethnicity to ensure that we recruit a representative group of participants.

Before proceeding further, we need to perform a couple tests to confirm it is safe for you to participate.

1. If you are female, you will be required to take a pregnancy test (if you are pregnant or trying to become pregnant, you will not be able to take part). The pregnancy test will be performed on the urine sample collected on the day of the study session. The urine will be dipped with pregnancy test dipstick and destroyed immediately within the research facility as soon as the test result has been confirmed (in 10min of the test).
2. To ensure that your blood circulation is strong enough for you to participate in the study we will squeeze your wrist for approximately a minute (the Allen's test).

If it is safe for you to participate, you will become eligible to participate.

The research team (nurses and doctors) will then move through the following steps with you:

1. Routine non-invasive equipment to measure basic observations will be applied to your shoulders and arms. This includes a blood pressure cuff, 3-lead ECG (monitoring of the heart rhythm and rate with 3 dots/stickers placed on the shoulders) and a finger clip oximeter.
   The blood pressure cuff will repeatedly measure your blood pressure. The 3-lead ECG will continuously measure your heart rate, and the pulse oximeter will continuously measure the oxygen content in your blood. This equipment is important and will monitor your body's responses throughout the study and ensure your safety.

2. One EarMetrics®-Oximeter Validation Device Earpiece will be placed in your ear; this is like an earbud used for listening to music. The EarMetrics®-Oximeter Validation Device Earpiece includes a camera sensor so a member of the research team can look at high-resolution video and photo images of the ear canal to make sure the device is positioned correctly. As part of the study, there are two slightly different versions of the EarMetrics®-Oximeter Validation Device Earbuds: earbud A and earbud B and to help comfort and fit, as per figures 1 and 2. There are soft Silicone EarTips applied over the Earbud. The Silicone Eartips are available in "Wide" and "Narrow" sizes, as per figures 1and 2. If earbud A with the appropriate size eartip is not comfortable for you or provides a poor image or signal, we will try earbud B with the eartip. An

adequate image and signal will need to be obtained by the research team before progressing to the next steps of the study. The other ear will be checked if the first is unsuccessful.

3. A small amount of lidocaine (a commonly used local anaesthetic drug) will be injected into the skin over the artery in your wrist and then you will have a small plastic tube inserted into an artery (blood vessel) in your wrist, ***arterial cannula***. This small plastic tube (arterial cannula) will be used to take multiple arterial blood samples throughout the session. *(Please see Figure 4 and 5 below)*. Ultrasound may be used to facilitate insertion of the arterial cannula into the artery. Maximally 2 attempts will be made to insert the arterial cannula.

4. The position of the plastic tube within the artery will be confirmed before progressing to the next steps of the study.

5. A tight-fitting mask will be fitted over your mouth and nose and adjusted for your comfort and to minimize gaps between the mask and your face. *(Please see Figure 6 below).*

6. The mask will deliver different levels of oxygen to temporarily reduce your blood oxygen levels in a controlled and stepwise manner. The lowest blood oxygen level you will reach will be similar to being approximately 4200 to 5100 meters above the sea level. In comparison, Mount Kilimanjaro is 5895 meters high. Medical personnel will be with you throughout the study. Your oxygen levels will not be low for the entire duration of the session. Oxygen levels will be reduced to a specific target for a few minutes at a time.
   If you do not tolerate the reduced oxygen level, we will terminate the desaturation process, and your oxygen level will be restored by providing extra oxygen. With your permission we would have one more attempt to reduce your oxygen level, but no further attempts will be made.
   Throughout the controlled saturation procedure, you will be closely monitored by the trained clinical and nursing staff.

7. When the targeted blood oxygen level is stable, up to 5 separate blood samples will be taken. These blood samples are a small volume and will be painlessly taken through the arterial cannula (the small plastic tube in your artery).
   In total less than 170 ml of blood (less than 35 teaspoons) will be taken (in comparison 450 ml of blood is taken in a full UK blood donation). Due to the nature of the arterial cannula equipment, approximately 45 ml of your blood will

be used for analysis and then immediately destroyed; whilst the remaining 125ml of your blood will be immediately destroyed without analysis. This ensures accurate analysis of your blood's true oxygen levels.

8. The collected sample is placed on ice the result from the blood gas analyser is obtained. A standard hospital ID label will be attached to the sample tube as an identifier. All collected blood will be destroyed in the same facility at the time of the desaturation study and your blood will not undergo any further analysis.

9. When all the required blood samples are collected, the facemask will be removed.

10. Once all the required blood samples are taken, the arterial cannula in your wrist will be removed and a dressing will be applied over the artery. Pressure will also be applied over the affected wrist, by the research team for at least 15 minutes.

11. After the mask is removed and the arterial cannula is removed, the nurses and doctors will continue monitoring you for 5 - 15 minutes whilst breathing room air. The nurses and doctors will monitor you by checking your heart rate, blood pressure and oxygen levels. They will ensure your body has returned to your body's baseline and that you are feeling well before you leave the research facility.

The session should take approximately 3-4 hours in total. The study can be stopped at any time as per participant or clinical request.

You will be provided with a letter about your participation for you and your GP. Your GP can then log your participation in your medical records.

The following day a member of the research team will contact you via the phone to confirm that you are well.

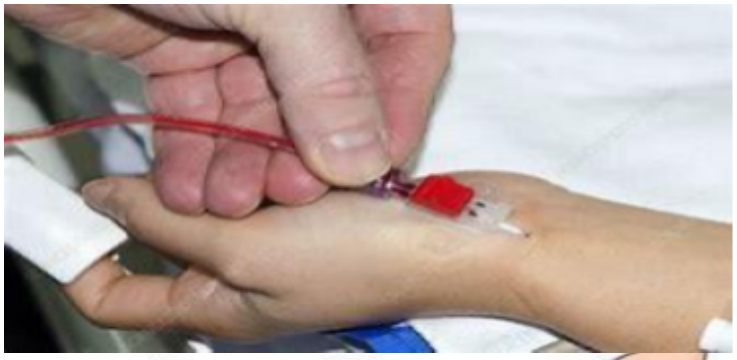

Figure 4) *Arterial cannulation Stock Image - C014/4772 - Science Photo Library - Arterial cannulation. Nurse connecting a line (tube) to a cannula inserted in a patient's radial artery. Cannulas in the radial artery are used to take repeated blood samples during (https://www.sciencephoto.com/media/479477/view/arterial-cannulation)*

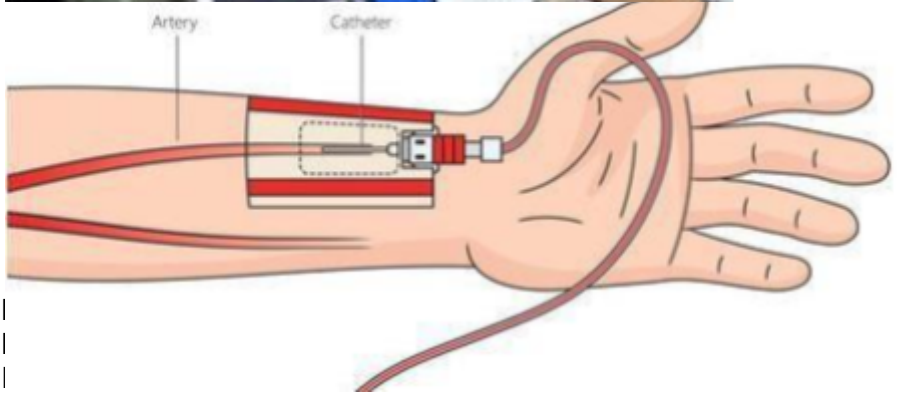

Figure 5) *Arterial line structure thin catheter inserted into an artery diagram hand drawn schematic vector illustration. Medical science educational illustration (https://stock.adobe.com/uk/search?k=%22arterial+line%22)*

Where will the Controlled Desaturation study take place?

Clinical Research Facility,
Heritage Building,
Queen Elizabeth Hospital Birmingham (UHB),
Mindelsohn Way Edgbaston,
Birmingham
B15 2TH

In addition to changing my mind, is there any reason I may not be able to continue in the study?

If we cannot obtain a good signal or image with either earbuds A or B in either of your ears, you will not be able to continue in the study.

If you cannot tolerate the tight-fitting face mask, you will not be able to continue in the study.

If you cannot tolerate the insertion of the arterial cannula, you will not be able to continue in the study.

If we cannot insert the arterial cannula into the artery after 2 attempts, you will not be able to continue in the study.

If we cannot safely achieve lower oxygen levels i.e. oxygen levels drop too low on more than 2 occasions, you will not be able to continue in the study.

What are the possible benefits of taking part in the study?

There will be no direct medical benefits to you at this stage in the development of the EarMetrics®-Oximeter Validation Device. In the future, the EarMetrics®-Oximeter Validation Device may improve the monitoring of oxygen levels of patients in health care settings.

If you are enrolled in the study, you will be given a £100 Love2Shop voucher to thank you for your time.

What are the possible disadvantages of taking part in the study?

There are potential risks to your participation, although you will always be under close and continuous medical supervision in a dedicated research facility. Overall, the risks are low.

Over the last 30 years public and private hypoxia laboratories have conducted more than 10,000 hypoxia studies with zero serious adverse events from either the hypoxia procedure or the arterial lines. Based on these data the risk of even minor adverse events is less than 0.03 %.

All the risks will be discussed with you before confirming that you would like to take part in the study.

What are the risks related to the insertion of the arterial cannula?

Before inserting the arterial cannula, the research team must ensure that your blood circulation is strong enough for you to participate in the study we will squeeze your wrist for approximately a minute (the Allen's test). This may cause minimal discomfort.

We will insert an arterial cannula. This is a thin tube which will be inserted into an artery in your wrist and be used to take multiple blood samples. Arterial cannulas are frequently inserted into very unwell patients or patients undergoing major surgery and requiring close monitoring and frequent blood samples. When inserting the needle there may be mild to moderate discomfort.

A small amount of local anaesthetic will be injected under the skin to reduce the associated discomfort of inserting the arterial cannula. The injection of local anaesthetic may cause short-term pain (burning or stinging) and short-term

numbness in your fingers. Rarely, a person may have an allergic reaction to the drug used in the injection.

When attempting to insert the arterial cannula we may use an ultrasound to help us insert the tube into your artery. If we are unable to insert the arterial cannula successfully you will be withdrawn from the study.

The cannula may give you the following symptoms, but the overall risk is believed to be low:

- Pain or pressure in your wrist
- Discomfort when saline is flushed through (cool, burning or tingling sensation)
- Bruising or a small scar

There is an exceptionally small risk that the plastic tube may break under the skin. If this happens you will need an additional procedure to remove this.

Whenever the skin is pierced, there is a risk of infection. The research team will reduce the risk of infection, by cleaning the skin, using gloves during insertion and use of dressings whilst the arterial cannula is in-situ and after the arterial cannula is removed.

Whenever the skin is pierced, there is a risk of bleeding and bruising. The research team will by applying sustained pressure after each attempted insertion of the arterial cannula and removal of the arterial cannula.

What are the risks related to the EarMetrics®-Oximeter device?

You will have the EarMetrics®-Oximeter Validation Device placed in your ear canal. This will transmit light into the tissues to measure your blood oxygen levels. Some light is absorbed by the blood depending on how much oxygen is present. The sensor detects how much light is reflected. This should provide no risks to your health or safety. The sensors may be warm to the touch. There are no expected risks directly from the EarMetrics®- Oximeter Validation Device.
Earbud materials contacting user's skin in normal use are:

- Cable to the device sensor: FEP - N3180 fluoropolymer
- Handle material: Formlabs BioMed Clear (cured)
- Earbud: Formlabs BioMed Flex80A (cured)
- Silicone Eartip materials: Otoform Ak X (cured)

If skin irritation occurs, the use of the EarMetrics® Oximeter Validation Device will be ceased.

What are the risks related to reducing my body's oxygen levels?

You will have your blood oxygen levels temporarily decreased in a stepwise and controlled manner. You will be asked at several points if you are comfortable and happy to continue. Most people do not notice when their oxygen levels are low but sometimes the following temporary symptoms can occur:

- Dizziness
- Quick breathing
- Noticeable change in the speed of your heart rate
- Anxiety
- Sweating
- Feeling hot
- Tingling in your hands
- Loss of consciousness

If you have any of these symptoms you will be given more oxygen. The symptoms will then go away within a couple of minutes.

What are the risks related to the equipment used during this study?

There may be a small risk of skin irritation from the following, although the risks are believed to be minimal:

- The mask material is soft and flexible to reduce discomfort as much as possible.
- Stickers placed on your upper arms/shoulders to measure your heart activity. This may cause skin irritation, including making your skin red, or an allergic reaction. When the stickers are removed there may be some pulling on your skin or hair.

Who is organising this study?

The study is being organised by EarSwitch Ltd. and the NIHR HealthTech Research Centre in Devices, digital and robotics (HRC DDR). The study protocol, this information sheet, and other study documents have been developed by the research team with support from the HRC DDR Patient and Public Involvement and Engagement Manager and HRC DDR Patient and Public Involvement and Engagement Group.

The study has been approved by Cambridge East Research Ethics Committee (REC) – Ref no 25/EE/0038.
The study has been approved by the MHRA (Medicines and Healthcare products Regulatory Agency).

Who can I contact for support?

You are welcome to contact the following researchers from the NIHR HealthTech Research Centre in Devices, Digital and Robotics for support or if you have any questions in relation to this study:

Chief Investigator Dr Dhruv Parekh
Dr Omolola Afelumo
Ms Kulli Kuningas.

Please see their contact details below:
Email: healthtechddr@uhb.nhs.uk
Telephone: 0121 371 8537 (Mon – Fri 8am – 4pm)
Address: NIHR HealthTech Research Centre in Devices, digital and robotics (HRC DDR), MD-TEC, 3rd Floor East, Heritage Building, Birmingham, B15 2TH

What if I have any concerns or if something goes wrong?

If you have a concern about any aspect of this study, you should first ask to speak to a member of the research team who will do their best to answer your questions. If you remain unhappy and wish to complain formally, you can do this by contacting UHB's Patient Advice and Liaison Service (PALS) via one of the following methods:

- E-mail at PALS@uhb.nhs.uk
- Call on 0121 371 3280

We will provide compensation for any injury caused by taking part in this study in accordance with the guidelines of the Association of British Healthcare Industry (ABHI)
We will pay compensation where the injury probably resulted from:

- A device being tested as part of the trial protocol.
- Any test or procedure you received as part of the trial.

Any payment would be without legal commitment. (Please ask if you want more information on this). We would not be bound by these guidelines to pay compensation where the injury resulted from a drug or procedure outside the trial protocol or where the protocol wasn't followed. The study is insured with Markel International Insurance Company Limited.

You do not have to take part. Your participation in this study is ***strictly voluntary.*** You can change your mind and withdraw from the study at any time, without giving us any reason. Your withdrawal from the study will not affect any future medical care.

How will we use information about you?

We will need to use information from you for this research project. This information will include your name, contact details, medical history, height, weight, date of birth, skin colour, ethnicity, emergency contact details and address. People will use this information to do the research or to check your records to make sure that the research is being done properly. Your data will not be shared outside the UK.

EarSwitch Ltd is the sponsor of this research and is responsible for looking after your information. The information about you will be kept safe and secure by:

- A high-resolution photo and video images of the ear canal will be taken during the study session to confirm the earpiece is in correct position. The photo and video images will be shared with the EarSwitch company. If the device is turned on and not positioned within the ear canal, it is possible that you could be identified from the photo and video images. When reviewing the images, the EarSwitch company will remove and destroy any images that can identify you.
- EarSwitch company and research team will use your blood results and images from the ear to assess the ability of the EarMetrics®-Oximeter in participants with a range of skin tones. These investigation results and your characteristics (age, skin tone, ethnicity and gender) will be reviewed and stored without your personal details (name, date of birth, address) using secure study specific database REDCap™ (Research Electronic Data Capture). Your data will have a code number instead.
- If necessary, personal data collected, processed, and stored within the context of the above-mentioned study will be made available to the competent supervisory authority or to certain agents of the EarSwitch company called monitors, qualified to ensure that the registry is being conducted properly and safely.

People who do not need to know who you are will not be able to see your name or contact details.

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.
We will keep your study data for a maximum of 25 years. The study data then will be securely destroyed.

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.

You have the right to ask us to remove, change or delete data we hold about you for the purposes of the study. We might not always be able to do this if it means we cannot use your data to do the research. If so, we will tell you why we cannot do this.

If you agree to take part in this study, you will have the option to take part in future research using your data saved from this study. The data saved from this study without any personal identifiable information will be kept by the EarSwitch Ltd.

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/ and www.hra.nhs.uk/patientdataandresearch

- **By asking the members of the research team:**
  Email: healthtechddr@uhb.nhs.uk
  Telephone: 0121 371 8537 (Mon – Fri 8am – 4pm)

- By contacting the Data Protection Officer at UHB Research & Development Department: Rachel Seabright Rachel.Seabright@uhb.nhs.uk

- By contacting the Data Protection Officer at EarSwitch Ltd: Charlie Ross charlie@earswitch.co.uk

What will happen to the results of the study?

The data and images (video and photo), which are not identifiable and have no personal details (e.g. name, date of birth and address) will be analysed by EarSwitch Ltd., and the results will be written into a report which will be included in an application for regulatory approval for the EarSwitch Ltd. EarMetrics®-Oximeter. This report will only include anonymised research data.

A summary will be written for participants to let them know the outcome of the study.

The research data may be shared with the wider international scientific community

via publications and conference presentations. Your personal and medical data will always remain fully anonymized

How do I take part?

If you would like to take part in this study, please contact us:

Email: healthtechddr@uhb.nhs.uk

Telephone: 0121 371 8537 (Mon – Fri 8am – 4pm)

We will then discuss eligibility and schedule your study visit. By emailing or phoning us to register your interest, you are consenting to having your name, email address and phone number stored by the NIHR HealthTech DDR for this research purpose only.

How do I prepare to attend?

- Please attend with a short-sleeve t-shirt under coats and jumpers etc
- Please remove any nail varnish.
- Please ensure you are well fed and well hydrated before attending.
- If you are running late, then please let us know. We may need to reschedule for another date and/or time.
- No further preparation is required to participate.

For more information

Some general information about research is available online.

For the further information about the company EarSwitch Ltd and their technology:
https://www.earswitch.co.uk/

For the further information about Clinical trials and medical research – getting involved:
Clinical trials - NHS

For further information about pulse oximetry:
https://www.england.nhs.uk/coronavirus/wp-content/uploads/sites/52/2022/02/pulse- oximeter-easy-read-2022-digital.pdf

For further information about the Clinical Research Facility at Queen Elizabeth Hospital, Birmingham:
https://www.research.uhb.nhs.uk/about-us/facilities-and-infrastructure/clinicalresearch-facility/

Thank you for considering taking part in this research study.