PARTICIPANT INFORMATION SHEET

Version 1.2 [21 OCT 2025]

Research Ethics Committee Ref: 25/LO/0701

Ultra-portable rapid-dispersal buccal lyophilised naloxone for constant carriage: testing in healthy volunteers

We would like to invite you to take part in a research study. Before you decide to take part, it is important for you to understand why the research is being done and what it will involve. It is important that you understand that you should only take part if you want to. Deciding not to take part will not disadvantage you in any way. Please take as much time as you need to decide whether or not to participate. Also, please take the time to carefully read this information sheet and discuss it with others if you wish. Ask me if there is anything that is not clear or if you would like more information.

What is the purpose of the study?

This study is investigating the pharmacokinetics (absorption, distribution, breakdown and elimination) of a rapid-dispersal ultra-portable formulation of naloxone. We are testing a new form of naloxone - a life-saving medication that reverses opioid overdoses. Current naloxone comes as injections or nasal sprays, which can be difficult to carry around. We've developed a new wafer form that dissolves in the cheek and may be easier to carry. This study will compare how quickly and effectively this new form is absorbed compared to existing naloxone formulations. We need to test this in healthy volunteers before it can be used in real-world overdose situations.

It is up to you to decide whether you want to take part. If you would like to enter the study, you will be asked to sign a consent form. If you change your mind later on, you can leave the study at any time and without giving a reason. We will ask you why you decided to withdraw as this may give us important information which may be useful for improving our research studies.

Who can take part?

We are recruiting 12 healthy volunteers for stage 1 of this study. Participants must have adequate venous access and willingness for a within-session in situ cannula during each visit.

To take part, you must:

- Be a healthy man or woman, aged 18-60 years
- Have a body mass index (BMI) 18 - 30.0kg/m2.
- Show proof of identity
- Use effective contraception for the duration of the study and for at least 2 weeks after
- Be available to attend the CRF for 6 visits, including the screening, and 5 experimental visits, as well as attend the final follow-up.

To take part, you must **not:**

- Have or use any prescribed medications (apart from contraception)
- Use recreational drugs – we'll test your urine for them during the study
- Use over-the-counter medications or health supplements.
- Intake more than 14 units of alcohol weekly.
- Test positive in an alcohol breath test, or positive in a urine drug screen
- Be pregnant or breastfeeding.
- Have had surgery or a medical condition that might affect the absorption of medicines.
- Have participated in other clinical trials in the past 3 months
- Have veins that aren't suitable for taking many blood samples
- Have any screening test results that show you're not suitable, even if you're healthy

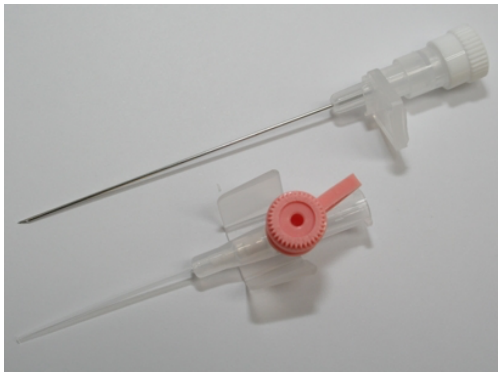
What will happen to me if I take part?

If you choose to take part in the project, you will be invited for a Baseline visit at the Clinical Research Facility (CRF) in King's College Hospital. This visit will start with an explanation of the study. You'll be given time to ask as many questions as you like and to read the information sheet again. Once you are sure that you want to participate in the study, you can read and sign a consent form.

To complete the baseline visit, you will provide a urine sample to test for drugs (and pregnancy in women of childbearing potential) and an alcohol breath test. We will also take a blood sample to test liver function, kidney function and your blood cells. A doctor will complete a brief medical assessment that will include a thorough clinical history, physical examination, height, weight, BMI, ECG, vital signs (including heart rate, respiratory rate, blood pressure and temperature) and laboratory tests of blood and urine to check that you're able to take part in the study. They will also ask questions about your physical and mental health as well as smoking, alcohol and drug use.

After completing the baseline visit, each volunteer will be invited to complete **five experimental visits**. They will also be conducted at the King's CRF, each one taking place a minimum of 36 hours apart. On each experimental visit, you will stay at the CRF for approximately 4.5 hours. To ensure all naloxone has cleared from your system, experimental visits will be scheduled at least 36 hours apart. There is no strict maximum timeframe between visits; however, most participants are expected to complete the study within 6 weeks. The entire study is anticipated to be completed within 3–4 months.

You will be asked to abstain from alcohol and illicit drug use throughout the study. When you arrive, the researchers will ask you to provide a urine sample for drug testing and a breath test for alcohol. If you test positive on either of these, you will be asked to reschedule the appointment. The next step is inserting a cannula into your arm so that we can collect blood samples from you throughout the study. A cannula (picture on the right) uses a needle to place a small plastic tube into a vein. Inserting a cannula is similar to having a blood test. It can be slightly irritating, but most people don't notice it.



Once the first blood samples have been collected you will complete some scales measuring your mood and experiences. You will then be given either one of the three naloxone formulations, with four different administration methods. The order of administration will be randomized for each participant:

- **Buccal naloxone**: On two experimental visits, as a single 2mg dose and 4mg (as two units of 2mg).

- **Sublingual naloxone**: A single 2mg dose.
- **Intramuscular naloxone**: A 0.4mg dose (0.4mg/1ml dose of naloxone ampoule)
- **Intranasal naloxone**: A single 1.8mg dose (single spray)

After administration of naloxone, we will perform a visual analogue scale (VAS) assessment: this will assess participants taste and local tolerability to the form of naloxone.

After being given the naloxone, you will have time to relax in the department, watch television, listen to music or read a magazine. Please don't be afraid to ask for anything; you are our guest, and we want to make sure you have as pleasant a time as possible.

Following the fifth (and final) experimental visit, we will conduct a telephone/online follow-up, 7-14 days after your visit in the CRF. This will conclude your participation in the study.

Throughout the study, we will periodically check for any side effects or changes in your health. We ask that you also additionally inform the research team anytime during your participation if you experience any changes in your health or take any medication.

Procedure		**Experimental visits[1]**					**Follow-up**
	Screening ≤ 28 days prior to IMP administration/Visit 1	**Visit 1**	**Visit 2**	**Visit 3**	**Visit 4**	**Visit 5**	**7-14 days post-final visit (telephone/ online)**
Written informed consent	X						
Demographic information[2]	X						
Medical assessment[3]	X						
Eligibility assessment/review	X	X	X	X	X	X	
Urine pregnancy test	X	X	X	X	X	X	X[8]
Urine drug screen	X	X	X	X	X	X	
Alcohol breath test	X	X	X	X	X	X	
IV cannulation		X	X	X	X	X	
Blood sampling (FBC, LFTS, U&Es)[4]	X						
Urinalysis[4]	X						
Vital signs[5]	X	X	X	X	X	X	
ECG[5]	X						
Randomisation		X					
IMP administration[6]		X	X	X	X	X	
Administration site check		X	X	X	X	X	
PK Sampling[7]		X	X	X	X	X	
Buccal Wafer Disintegration time		X	X	X	X	X	
Visual Analogue Scale (VAS)		X	X	X	X	X	
AE Review[9]	◄	———	———	———	———	———	►
Conmed Review[9]	◄	———	———	———	———	———	►

Participants will be discharged on the same day as admission for each experimental visit.

1. Minimum 36 hrs between experimental visits.
2. Demographic information obtained will include sex, age, BMI, weight/height.
3. Includes review of pre-existing conditions, physical examination, medical, smoking, drug and alcohol history, and a conmed review of all medical products (incl. over-the-counter and herbal)
4. List in full in section *'What will happen to me if I take part?'*
5. Heart Rate (during the V1 recorded via ECG), Respiratory Rate, Blood Pressure, Temperature, taken in supine position
6. Five-way crossover design, in a randomised order for each participant on each study visit.
7. PK Sampling times detailed in section '*How many blood samples will we take and why?'*
8. WOCBP will be asked to confirm the result of a urine pregnancy test completed on that day, previously provided by the research team on the last dosing visit
9. All AEs and Conmed medications will be captured starting from the moment informed consent is obtained until the completion of follow-up

How many blood samples will we take and why?

On the first visit, you will have roughly 14 blood samples taken using the cannula. Each test only takes a small volume of blood (<2mls), so they won't affect how you feel. Samples will be taken at the following timepoints: pre-dose, at 2, 4, 6, 8, 10, 12.5, 15, 30 and 45 minutes and 1, 1.5, 2, 4 hours post-dose. The last blood sample will be 4 hours after the first sample and at that point, the cannula will be removed. The same procedure will happen on each experimental visit (Visit 1 – 5).

We will collect blood samples so that we can measure levels of naloxone. The blood samples will be stored in freezers at the CRF in King's College Hospital until they are ready to be delivered and subsequently analysed at KCL Laboratories located in the Department of Nutritional Sciences, Franklin-Wilkins Building, 150 Stamford Street, London SE1 9NH.

The blood samples collected during the study will be used solely for the purpose of this study, pharmacokinetic analysis to measure naloxone levels, and will be destroyed after completing the analysis. Only plasma will be stored for analysis and no human tissue will be retained at the end of the research. All biological samples will be handled, transported, stored, accessed, and processed in accordance with the 2004 Human Tissue Act.

Do I have to take part?

Participation is completely voluntary. You should only take part if you want to and choosing not to take part will not disadvantage you in any way. Once you have read the information sheet, please contact us if you have any questions that will help you decide to take part. If you decide to take part, we will ask you to sign a consent form, and you will be given a copy of this consent form to keep. You can withdraw if you later change your mind, without giving a reason. If you are a member of KCL or SLaM, as with all participants, participation is voluntary, and participation or non-participation has no impact upon relationships/employment status in your workplace.

Will I be reimbursed for taking part?

Participants will be reimbursed for their time at a rate of £16.00 per hour, reflecting the total time commitment of 25 hours for the five experimental visits in stage 1, totalling £400, in addition to £20 for completion of the screening visit. Upon successful completion of stage 1 components, participants will receive an additional completion bonus payment of £100, resulting in a total compensation payment of £520.00 for each volunteer. This payment of £520.00 for successful completion of stage 1 components is inclusive of all travel expenses to and from the clinical trial facility (no additional travel reimbursement will be provided).

For Stage 2 participants, the payment will be proportional to the number of experimental visits required, which will be determined after analysis of Stage 1 results. Punctual attendance for all blood tests is crucial to the study, and payment is contingent on completing all required aspects.

Participants who complete the screening visit but are unable to begin experimental visits of stage 1 will receive £20 as partial compensation. In case of withdrawal, participants will be reimbursed for the proportion of study they have completed using a pro-rata payment.

We can send the money via bank transfer which may take up to 4 weeks.

What are the possible risks of taking part?

Naloxone is a very safe medication and is not known to have any serious side effects. If you feel unwell you will be able to stop at any time. The most common side effect is nausea, though other effects such as vomiting, dizziness, headache, tachycardia, and sweating may occur. These are typically mild and self-limiting.

During the study, you should report if you feel unwell or different in any way. After you leave the CRF, you still need to tell the study staff if you continue to experience any feelings of being unwell or different that you had during the study.

Are there any longer-term effects?

There are no known long-term adverse effects of naloxone. There is limited information on naloxone and pregnancy, you must therefore agree to use effective contraception during the study. If you do become pregnant during the study, we ask you to inform the study team immediately.

What are the possible benefits of taking part?

In addition to being paid for your time, you may enjoy the experience of taking part in research. Your participation in this trial will contribute to scientific progress and help improve overdose prevention strategies and access to life-saving medication.

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, initials, 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. People who do not need to know who you are will not be able to see your name or contact details. Similarly, your data will not be shared outside the UK. Your data will have a code number instead. KCL and SLaM are responsible for looking after your information. We will keep all information about you safe and secure by:

- Keeping all data pseudo-anonymised and stored on a password-protected computer.
- Data will be collected using source data worksheets (paper questionnaires).
- Each study participant will be given a study ID.
- The source documents will be kept in locked cabinets. Study data will be transcribed to the Elsevier MACRO EDC system and only members of the team will have access to it.

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.

Your GP will be notified that you are participating in the study so that it can be recorded in your medical records.

How will we use information about you after the study ends?

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. Any personal data collected, will be stored and accessible for over 3 years after the study has ended. Research data generated by the study will be stored for 25 years. The study data will then be fully pseudo-anonymised and securely archived or 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. We need to manage your records in specific ways for the research to be reliable. You have the right to ask us to access, remove, change or delete data we hold about you for the purpose of the study. You can also object to our processing of your data. 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.

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

You can find out more about how we use your information:

- At http://www.hra.nhs.uk/patientdataandresearch
- Our leaflet available from:
  - https://slam.nhs.uk/personal-information-gdpr (SLaM)
  - https://www.kcl.ac.uk/research/support/rgei/research-ethics/kings-college-london-statement-on-use-of-personal-data-in-research (KCL)
- By asking one of the research team
- By sending an email to the Data Protection Officer(s):
  - Claire Delaney-Pope, informationgovernance@slam.nhs.uk (SLaM)
  - Olenka Cogias, info-compliance@kcl.ac.uk (KCL)

What if I change my mind about taking part?

You are free to withdraw at any point of the project, without having to give a reason. Withdrawing from the project will not affect you in any way. You can withdraw your data from the project up until the final experimental visit. Your rights to access, change or move your information are limited in order for the research to be reliable and accurate. If you withdraw from the project, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally identifiable information possible.

How is the project being funded?

This study is being funded by the Chief Scientist Office (CSO), NHS Fife and Health Innovation South East Scotland (HISES). It is also supported by Catalent, from their Swindon UK facility, who will provide the study drug and formulation.

What will happen to the results of the study?

We will publish the results in peer-reviewed scientific journals, presentations at international research conferences, publications on website and submission to regulatory authorities. We also intend to send out a press release with the results of the study to major news outlets. We can send you a copy of the final study report if you would like one. If you would like a copy, we would retain your contact details so that we can send you a copy, this may be for 1-2 years after the study is completed.

Data arising from the trial will be owned by KCL. It is intended that the results of the study will be reported and disseminated at international conferences and in peer-reviewed scientific journals. Where appropriate, the results will be disseminated to the general public by means of press releases, posts on social media and at public engagement events. The Consort Guidelines and checklist will be reviewed prior to generating any publications for the trial. Individual participants will not be identifiable in publications.

Who has reviewed the study?

All clinical research is looked at by an independent group of people, called a Research Ethics Committee (REC), to protect participants' interests. This study has been reviewed and given favourable opinion by London Bridge REC.

Who should I contact for further information?

If you have any questions or require more information about this study, please contact the research team using the following contact details:

[Insert researchers name & contact details here]

What if there is a problem?

You should first contact the research team either via the email address and phone number provided.

If you wish to complain or have any concerns about any aspect of the way you have been approached or treated during this study, you should contact the investigators using the details provided.

If you're ill while you're on the ward, we'll give you any immediate treatment you need. If you're ill after leaving the ward, call us as soon as you can.

In the event that something does go wrong, and you are harmed during the research you may have grounds for legal action for compensation against King's College London and/or SLaM NHS Foundation Trust, but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you (if appropriate). King's College London has obtained insurance which provides no-fault compensation i.e. for non-negligent harm, you may be entitled to make a claim for this.

Thank you for reading this information sheet and for considering taking part in this research.