Participant Information Sheet

Study Title:

First in human study of Sirona: A study to determine safety, feasibility and tolerability of an expanding hydrogel pill, designed to promote weight loss in adults with a body mass index of 30-40-SIRONA

Invitation to Participate

We would like to invite you to take part in our research study evaluating a potential slimming aid. Before you decide, we would like you to understand why the research is being done and what it would involve from you. Please talk to others about the study if you wish.

Part 1 tells you the purpose of this study and what will happen to you if you take part. Part 2 gives you more detailed information about how the study will be conducted.

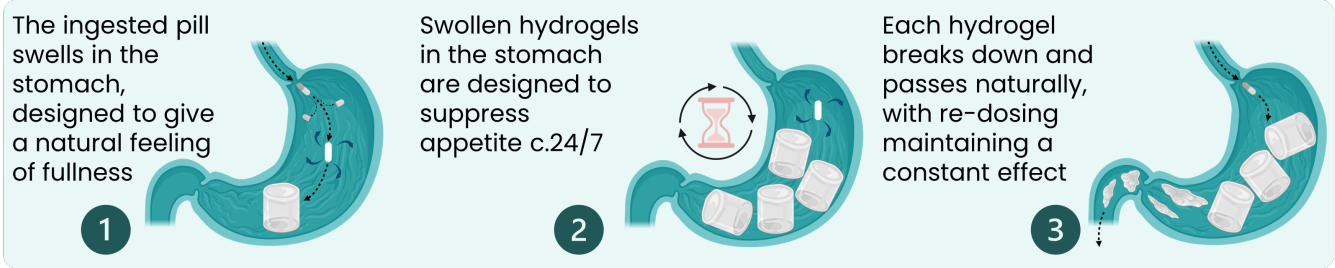
Please ask us if there is anything that is not clear. Take time to decide whether or not you wish to take part.

Part 1

1. What is the Purpose of the Study?

Obesity is the most serious public health problem in the UK and developed world reducing quality of life and life expectancy. There is an urgent need for new therapies to aid weight loss allowing healthcare workers to help people living with obesity to lose weight earlier, and to prevent progression to a higher class of obesity.

Oxford Medical Products (OMP), a slimming aid manufacturer, has developed Sirona. Sirona is a hydrogel, in pill form, that expands when it reaches the stomach, where it occupies space for a period of time. Sirona has been designed so that while it is in the stomach, it *may* lead to less hunger and eating, such that the person *may* lose weight over time. This study is the first step to finding out if Sirona will work as intended.



This study is a **First in Human** study. This means that this study will be the first time that Sirona will be taken by humans. Sirona has been through multiple studies in the laboratory and in animals showing no safety concerns. This part of the study will assess how safe, how well tolerated and how practical it is for healthy adults to take Sirona (hydrogel).

Through this study, we would also like to understand the possible effects of Sirona on feelings of fullness, eating and weight loss. To do this, the study will compare people who take Sirona with people who are taking placebo pills for 12 weeks. Participants will be randomly allocated to be part of the Sirona group or the placebo group – this is called 'randomisation' and will be done via a computer-generated system.

The placebo is a similar looking pill that has none of the planned effects but is safe for adults to take. The study visits and assessments during this period will be the same whether you are given placebo or Sirona. It is important that you and most the study team who are in contact with you at study visits *do not know* whether you are given Sirona or placebo to take during the first 12 weeks. This is called 'double-blinding' and is done so that we can ensure the study is fair and provides the most accurate information about the effects of Sirona. Only a certain few people will know what each participant is given.

After the first 12-week study period, all participants and the study team will find out whether they were taking Sirona or placebo. This is called 'unblinding'. Participants taking Sirona will then be asked to continue with Sirona for another 12 weeks. Participants who were taking placebo will then be given the opportunity to start Sirona pills and take these for the next 12 weeks. This will help to understand the effects over a longer period of time.

2. Why am I being asked to participate in the study?

We are inviting you to take part because you have indicated you might be interested to volunteer in this study and have a body mass index (BMI) of between 30 and 40, are between the ages of 18 and 65 years, and are prepared to travel to [site name: Southampton Hospital/Southmead Hospital] and Oxford Centre for Magnetic Resonance Imaging for study visits.

You will not be able to take part if you:

- take oral medications of any kind (i.e. contraceptive pills, blood pressure medication etc.)
- have a history of mental health issues in the last two years
- have any surgery or history of health problems in your stomach or gut
- are pregnant, or intend to become pregnant during the period of the study (6 months)
- are participating in another study at the moment
- are taking part in weight loss or diet programmes.

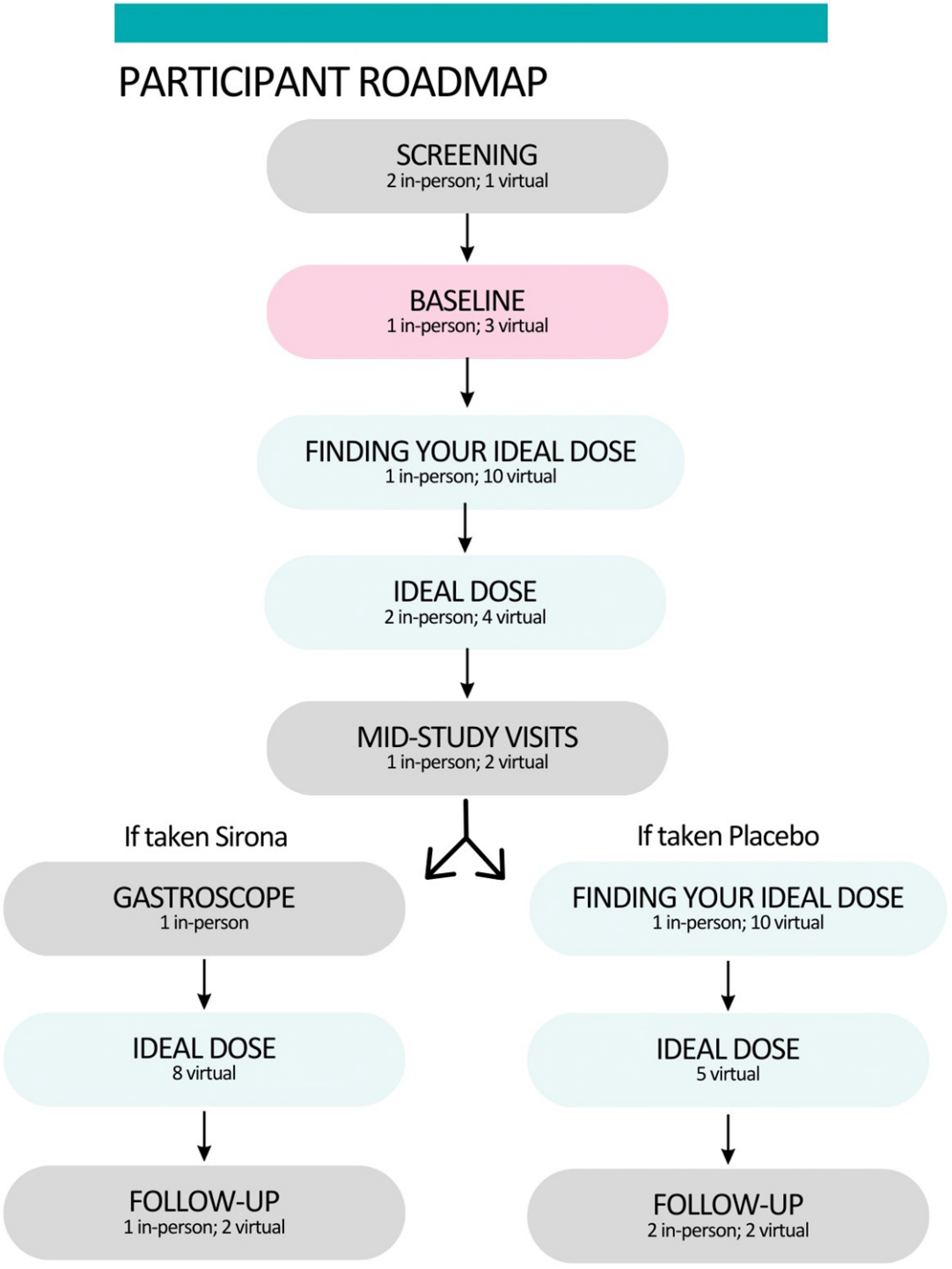
The study team will discuss your medical history with you and will run a series of screening tests to check if you are able to take part (see screening details below).

3. Do I have to take part?

No, it is up to you to decide to join the study. If you agree to take part, we will then ask you to sign a consent form (see Part 2). You are free to withdraw at any time without giving a reason. This would not affect the standard of care you receive.

4. What will happen if I take part?

The study will take place over approximately seven months, split into several stages: screening, baseline tests, first 12-week stage, second 12-week stage and follow up appointments. First, you will have a series of screening assessments, to check you are eligible to take part.



Total visits: 39

Total visits: 47

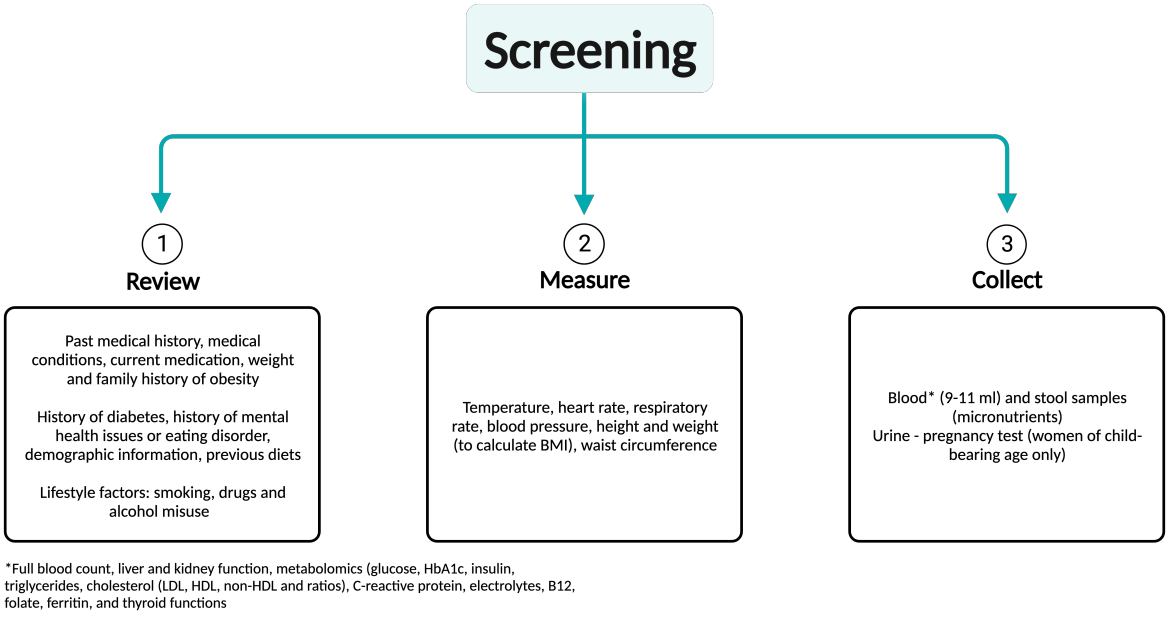
Visits for all trial participants unless specified. Virtual visits include online assessments of appetite, dietary intake, welfare calls, and online/telephone appointments with psychologist and dietitian.

Initial Screening (can take between 2-4 weeks)

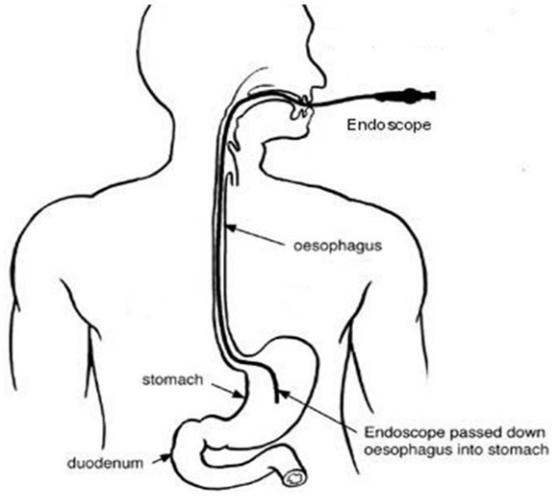
Once you are ready to proceed with the study screening (after having all your questions answered), you will be invited to the hospital to check your medical history and to sign a consent form to agree to participate.

You will then be asked to swallow a Sirona dummy pill. If after training and help, you are not able to swallow the dummy pill you will be excluded from further participation in the study and no further procedures will be undertaken.

If you can swallow the dummy pill, you will undergo the screening activities outlined below, including a psychological evaluation (performed by a weight-loss psychologist) to check you are ready and in the right frame of mind to lose weight.



You will also undergo two Gastroscopies during the study. During this procedure, you will be asked to swallow a thin, flexible tube called an endoscope. The endoscope has a camera on the end, which is used to look inside the oesophagus (gullet) and stomach. The gastroscopy is performed in order to make sure that it is completely safe for you to participate in this study. The procedure itself takes approximately 15 minutes and you will be in the endoscopy unit for approximately two hours (depending on if you have sedation). You will have the opportunity to discuss the procedure with the endoscopy team to decide if you would like to have sedation for this procedure. If you decided to have sedation, we will ask you to be collected from the appointment by a member of your family or friend. If any abnormality is found, both you and your GP will be informed, and you will be excluded from the study.



When all the data above has been collected and checked if it is safe for you to take part, your research doctor will then be able to confirm your eligibility and the research team will book your further study visits.

Following successful screening, your participation in this study will last approximately 6 months**.**

Study visits and assessments

Diet plan:

Before you are given any pills, you will meet with a qualified dietitian, who will give you diet and physical activity counselling. You will receive information on how to follow a 1500 calorie diet and guidance and ideas to increase your exercise.

You will be able to discuss how you get on with this plan with the dietitian throughout the study.

Baseline visit:

Before you take Sirona for the first time, you will be invited to a baseline study visit. You will be asked to complete appetite ratings and portion selection tasks. These measures will be taken every 30 minutes for 3 hours.

An example timeline is shown below:

- 9:00 - participants arrive
- 10:00 – appetite measurement 1
- 10:01 – consume 2 pills with warm water
- 10:30 – appetite measurement 2

- 11:00 – appetite measurement 3
- 11:30 – appetite measurement 4
- 12:00 – appetite measurement 5
- 12:01 – participants can eat drink/ eat

Each appetite measurement will take approximately five minutes and will include a combination of visual-analogue scales (VAS) (e.g., “How hungry do you feel right now?”, anchored: ‘not at all’/ ‘extremely’) and a virtual portion selection task where you will use a slider to select ‘ideal’ and ‘maximum’ portions of different foods.

You will be asked to repeat these assessments after your first dose of either Sirona or placebo, after 6 weeks, and again at the end of the study (see figure below for the timeline of visits).

At baseline, 12 weeks and at the end of the study, you will be asked to complete two questionnaires with questions about your quality of life (EUROQOL, 5D-3L) and eating behaviour (Three Factor Eating Questionnaire, TFEQ).

Taking Sirona or Placebo:

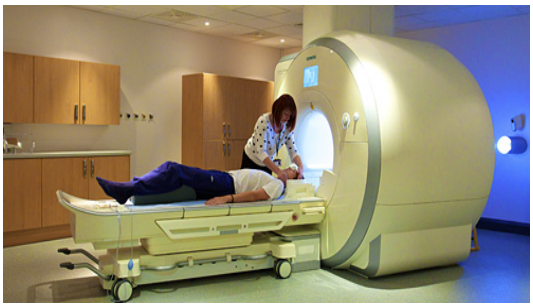
Your first treatment dose will happen at your next clinic visit, after the baseline assessments have been completed, and with the support of the study team. The study doctor will ensure that adequate medical supervision and care is available to you during the study. This includes the management of any side effects. Sirona or placebo pills should be swallowed with a glass of warm water (250ml). Please do not exceed the dosage of Sirona or placebo given to you by the study team. The treatments must not be taken by anyone else for health and safety reasons. If you believe someone other than yourself has taken one of the pills, you must report this to the team immediately. All remaining pills, packaging and paperwork (e.g. pill diary) should be retained and returned to the clinic at your next visit.

WP2 dose escalation and Week 5 dosing pattern

WEEK	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 7
1	1		1		1		1
2	1	1	1	1	1	1	1
3	2		2		2		2
4	2	1	2	1	2	1	2
5	2	2	2	2	2	2	2

Key
1 Sirona/placebo pill

You may experience temporary nausea in the first 24-48 hours after dosing. You will be asked to complete a nausea assessment scale (MSSS) once a day for the first 5 weeks, starting on the evening of your first dosing day. You will be asked to rate the severity of your nausea on a scale from 0-6. The clinical team will support you to try different ways managing the nausea according to how you feel on this scale. This will include drinking sips of water to stay hydrated. You will also be provided with a prescription of anti-sickness medications to take if feelings of nausea become too much to manage on your own. According to your experiences, your next dose may be adapted following discussion with one of the study doctors. This will ensure the dose (number of pills taken at one time) is appropriate and acceptable for you.



Body Imaging (MRI): You will be asked to have one MRI scan during the first 12 weeks of the study (approximately week 11-13), after fasting overnight. This is a type of scan that takes detailed pictures of inside your body, and takes between 20-60 minutes. These visits will be held at the Oxford Centre for Clinical Magnetic Resonance Research (OCMR) and will show if/where the Sirona or placebo pills are present in your gut. Travel expenses will be covered for these visits.

Virtual assessments:

Appetite assessment: Ecological Momentary Assessments (EMA) will be carried out via your mobile phone. At two-hourly intervals you will receive text-message prompts to complete online assessments of your appetite and dietary restriction. This will include a combination of VAS and a virtual portion size selection task. This will allow the study team to look at the sustained effect of Sirona and how you adapt to your change in diet. This 12-hour window will be individually tailored for you according to your personal sleep-wake routine. Each text message will contain a URL link to pavlovia.org, a secure website which will host the EMA and store these data.

EMA measures will be taken over 2 days during the baseline period before you take any pills. Thereafter, EMA measures will be taken once a fortnight until the end of the study.

Food intake: You will be asked to provide a record of your dietary intake (all foods and drinks consumed for 24 hours) using an online tool (INTAKE24 online dietary recall system) for three days at baseline (before you take any pills), then again after 12 and 24 weeks of dosing.

Feedback questionnaire: You will be asked to complete two participant experience questionnaires; one at the end of the first 12 weeks and a second one at the end of the study for you to share your experience of taking part. The questionnaire will be completed online.

5. What if I have questions or concerns during the study?

You can ask questions to the study doctor, nurse, dietitian, or any researchers you have contact with during the study about anything that you don't understand both now and later.

6. What are the disadvantages to taking part in the study?

You may experience some side effects after consuming Sirona/placebo. **At this stage we do not know the exact side effects of Sirona in humans. This study will be looking at this aspect.** Based on their clinical experience, the study team suggest that the side effects may be similar to having a gastric balloon (including nausea and occasional vomiting for a small number of people for the first 24-48 following dosing). It is important that you tell your doctor or nurse if you experience any effects whether you are taking Sirona or placebo. They will suggest ways to make you more comfortable. If these symptoms are particularly severe, there is a chance that you will need to be admitted to hospital for treatment. If this does happen then it is likely that the symptoms will settle within 24-48 hours. You will be fully supported and cared for by the study team.

- You will need to attend several clinic appointments in [insert trial site] and travel to Oxford for MRI appointments.
- You will need to have regular blood tests (may experience mild discomfort, such as bruising and tenderness) and a gastroscopy.
- Some people feel anxious inside an MRI scanner, and it can be noisy. We will provide ear plugs and make you as comfortable as possible.
- You will need to attend your hospital appointment fasted (no eating or drinking calorie-containing drinks from midnight the night before your appointments).
- Alcohol consumption should not affect the function of the Sirona/placebo pills, although it may cause heartburn and indigestion. We advise either abstinence from alcohol or moderate consumption during the study.
- It is important not to exceed the dosage of Sirona/placebo given to you by the study team. There is a potential risk with taking too many pills (e.g. uncomfortable swelling or rupture of your stomach).
- As this is a first-in-human study, you have to remain in the UK for the period of the study (for insurance reasons).

7. Expenses and Payments?

As the study requires many hospital visits at two different sites and also two gastroscopies, participating will require a significant time commitment from you. Therefore, you will be paid a total of £1200 for participating in the study. You will receive £100 after completion of the first dosing visit, £400 after completion of the week 13 visit and £700 after attending the final follow up visit.
You will also be able to claim back any expenses incurred during your hospital appointments to cover the cost of food purchased whilst in hospital (maximum £15/day).

We will need to note your bank details so that payments can be made directly into your bank account. If you do not have a bank, building society, credit union or Post office account we can provide shopping vouchers. Please note it may take approximately one to two weeks for the reimbursements for food purchased and study participation to be processed.

8. What are my responsibilities if taking part in this study?

- Be honest about your medical history and current conditions.
- Tell the study team about all drugs you are taking including vitamins, herbal medicines etc.
- Take Sirona/placebo as instructed by the study team.
- Complete all online appetite, food intake measurements, and questionnaires.
- Tell the study team about any problems you have during the study, including any discomfort or illness.
- Inform the study team if your address or phone number changes.
- Avoid excessive alcohol and any drugs not approved by the study doctor while taking part. If you are going to take any new medicine, you should call the study doctor or study team before taking it.
- Inform the study team if you become pregnant while in the study or within 30 days after your last dose of Sirona/placebo.
- Inform the study team if you have been in a study in the last 30 days or are in a study now.
- Follow all other instructions (dietary and medicine restrictions) given by the study team required for the study.

9. What are the benefits to taking part?

You may experience weight loss by taking part in this study. However, there is no guarantee that Sirona/placebo provided to you in this study will directly benefit you. Your participation may help others as information learned from this study will be used to plan future studies to benefit other people with obesity.

10. Are there any reasons why I might stop being in the study?

The study doctor has the right to stop your participation in the study at any time.

You may be taken out of the study without your agreement for any of the following reasons:

- if staying in the study poses a health risk to you, in case of serious complications after taking Sirona/placebo,
- if you need treatment that is not allowed in this study,
- if you become pregnant during the study,
- if it is felt by the Principal Investigator that it is not in your best interest to continue in the study,
- if the study is stopped by the Sponsor,
- if you have been found to have entered the study in violation of criteria explained at the start,
- if you do not follow the study instructions.

11. What are the alternatives for treatment?

People with excess weight currently have three options: diet and exercise, medical treatment, or surgery. Your clinical team will discuss all alternatives with you.

PART 2

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

You can stop taking part at any time. We will ask you to provide a reason, but you do not have to. There will be no change to your health care if you withdraw. No further procedures will be undertaken if you withdraw consent, but we may ask to follow you to ensure your safety is maintained. We will retain the data collected up to the point of your withdrawal of consent.

13. What if there is a problem?

If you participate in the study and are experience any symptoms or side effects, then please do call the emergency trial contact number provide on this sheet. In the case of life-threatening emergencies (e.g. choking) please do call the emergency services (999).

If you have a concern about any aspect of this study, you should ask to speak to the researcher team (via the above contact details) who will do their best to answer your questions and arrange for urgent clinical review, should this be needed. If you remain unhappy and wish to complain formally, you can do this through the NHS PALS [Patient Advisory and Liaison Services]. (available [insert site details]). Tel no. [insert site details]. Email: [insert site details]

Every care will be taken in the course of this study. However, in the unlikely event that you are injured by taking part, compensation may be available. If you suspect that the injury is the result of the Sponsor's (Oxford Medical Products) or the hospital's negligence, then you may be able to claim compensation. After discussing with your study doctor, please make the claim in writing to Mr James Byrne, who is the Chief Investigator for the study and based at Southampton General Hospital.

The Chief Investigator will then pass the claim to the Sponsor's Insurers, via the Sponsor's office. You may have to bear the costs of the legal action initially, and you should consult a lawyer about this.

Participants may also be able to claim compensation for injury caused by participation in this study without the need to prove negligence on the part of Trust or another party. You should discuss this possibility with your study doctor in the same way as above.

Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated by members of staff or about any side effects (adverse events) you may have experienced due to your participation in the study, the normal National Health Service complaints mechanisms are available to you. Please ask your study doctor if you would like more information on this.

14. How will we use information about you?

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 participant data must follow UK laws and rules.

The Sponsor will be using information about you, from your medical records to undertake this study, and will act as the 'Data Controller' for this study. This means that they are responsible for looking after your information and using it properly. Study data collected from your medical notes will be recorded in a secure electronic study database. This information will remain pseudoanonymised and will only be identifiable using your assigned study identifier (participant number). We will not collect any personally identifiable information such as your name, NHS number and contact details (mobile number and your email address). Your direct care team and other members of the research staff will only use this information to do the research or to check your records to make sure that the research is being done properly. Certain individuals from the Sponsor organisation and regulatory organisations may also look at your medical and research records to check accuracy of the research study.

The Emmes data management team is based in India and the study database is located on servers in the USA. Access to the study database (pseudoanonymised data) is limited to key staff and they must follow applicable data privacy rules about keeping your information safe.

Following the study, the researchers may publish or share anonymised results of the study with other researchers to aid shared understanding. Results may be used to guide research in the future. You will not be identified in any of the study results or published data. The Sponsor will retain identifiable study data for at 25 years after study conclusion.

15. 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.

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. These organisations may be universities, NHS organisations or companies involved in health and care research in this country or abroad. Your information will only be used by organisations and researchers to conduct research in accordance with the UK Policy Framework for Health and Social Care Research.

16. 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/
- our leaflet available from www.hra.nhs.uk/patientdataandresearch
- by asking one of the research team
- by sending an email to the Data Protection Office at [insert site data protection email address]
- by ringing the Health Research Authority on [insert number]

17. What will happen to any samples I give?

Study samples will be analysed for the purposes of the study. All blood samples for routine clinical monitoring will be tested and discarded as clinical waste, according to standard procedures.

18. What will happen to the results of the research study?

The results from the study will be written into a paper for other researchers and doctors to read. The results will also be made available to you via your study team and through accessing the ISRCTN (International Standard Randomised Controlled Trial Number).

19. Who is organising and funding the research?

Oxford Medical Products is organising the research and will be Sponsor, and they will also be funding this research. The doctor in charge of the study overall will be part of the study management board and will act as the safety reviewer Professor James Byrne is an experienced surgeon who works for Southampton NHS Trust and not for OMP. He will not be paid for including you in this study.

20. Who has reviewed the study?

All research in the NHS is looked at by an independent group of people called a Research Ethics committee to protect your safety, rights, well-being, and dignity. This study has been reviewed and given a favourable opinion by the South Central-Hampshire B Research Ethics Committee.

21. Further information and contact details

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 doctor, who will be able to provide you with up to date information about the treatment and procedures involved. If you require any further information or have any concerns while taking part in the study, please contact one of the following people:

Your Investigating Doctor or Nurse

Insert relevant study doctor/nurse contact details

Your Dietician

Insert relevant research team contact details

If you decide you would like to take part, then please read and sign the consent form. You will be given a copy of this information sheet and the consent form to keep. A copy of the consent form will be filed in your patient notes, one will be filed with the study records.

You can have more time to think this over if you are at all unsure. At the screening visit, you will be given the opportunity to talk to one of the study doctors about taking part and to ask any questions.

Thank you for taking the time to read this information sheet

Informed Consent Form

Safety and Feasibility study of an orally administered hydrogel as an intervention for weight loss in adults with a BMI of 30-40

Participant Study ID Number……

Sr. no.	**Your consent**	Please Initial each box
(1)	I confirm that I have read and understood the information sheet **version 2.0** dated **24Nov2023** for the above study and have had the opportunity to ask questions.	
(2)	I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.	
(3)	I understand that relevant sections of my medical notes and data collected during the study, may be looked at by individuals involved in the trial, from regulatory authorities, from the NHS Trust or from the Sponsor (Oxford Medical Products), where it is relevant to my taking part in this research and any further research that may be conducted in relation to it , even if I withdraw from the study. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or be published.	
(4)	I agree to the use of any data or results that arise from this study, provided that it is only for scientific purpose(s)	
(5)	I agree to my pseudoanonymised data on the study database being processed/stored on servers in the USA and accessed by the study data management team based in India, for the purposes of this study	
(6)	I agree for blood samples to be taken and to provide a stool sample for study purposes.	
(7)	I agree to being contacted on my personal mobile phone for the purpose of this study.	
(8)	I agree to the use of my bank details for study expense reimbursements and payments for study participation.	
(9)	I agree for my general practitioner (GP)/family doctor to be contacted regarding my participation in this study and/or to obtain medical history if	

	required.	
(10)	I agree that I will not leave the UK during taking part in the study.	
(11)	I understand that I will be allowed to talk to friends and family about the trial. I agree that I will not share texts or post photographs about taking part in the trial on public forums, such as social media. I understand that this is because Sirona is a new product, early in development and not yet publicly available.	
(12)	I agree to inform the hospital research team immediately if someone else takes one of my study pills.	
(13)	I agree to return all remaining study pills, packaging and paperwork to the research team at my follow up visits.	
(14)	I agree to comply with the instructions of study doctor and inform study staff immediately if any problems occur during the study.	
(15)	I agree to participate in the study*	

**Please ensure that your study doctor provides you with the copy of the signed and dated form after the complete documentation*

Investigator or designee: *Your signature below means that you have fully and carefully explained the study to the* ***Participant:*** *By signing this consent form, you indicate that you are voluntarily choosing to take part in this study.*

Name of Investigator or designee		Signature	Date	

When complete: one for participant; one for site file; one for medical notes