< *insert local letterhead* >

Participant Information Leaflet

The iHOLDS Trial: **H**igh **O**r **L**ow **D**ose **S**yntocinon for **i**nduction of labour

Version 1.0a dated 12th May 2021

We invite you to take part in a research study

Thank you for taking the time to read this Information Leaflet. We would like to invite you to take part in a research study (also known as a clinical trial) for women who are having their labour induced.

Joining the study is entirely up to you. If you choose not to take part, you will receive the normal standard of care which may include treatment with the standard dose of the study drug, artificial oxytocin (sometimes referred to as Syntocinon).

Before you decide we would like you to understand why the research is being done and what it will involve for you. Your Midwife or a member of the Research Team will go through this Information Leaflet with you to help you decide whether or not you would like to take part, and to answer any questions you may have.

Part One of this Information Leaflet tells you the reasons for doing this study, what will happen to you if you take part, and any potential risks or benefits that you should be aware of.

Part Two gives you more detailed information about how the study is being run and how your data will be used.

Contents

PART ONE

1. Background to the research

Induction of labour

About 34% of (or one in three) first time mothers have their labour induced. Labour induction is the process we use to start labour artificially. This may be required for a variety of reasons, most commonly because you have gone past your due date, or because your waters have broken but your labour contractions have not yet started.

Labour can be induced in different ways. Usually the cervix (neck of the womb) is softened using vaginal prostaglandins. This means a small 'tablet' or 'pessary' is inserted into the vagina where it slowly starts to soften and open the neck of the womb over several hours. Some women will go into labour at this point but many still require their waters to be broken artificially. If contractions still do not start, a drug is given using a drip in the arm to start them off. The drug used is artificial oxytocin and this is given to around 60% of women (six in ten) who have labour induced.

Artificial oxytocin/Syntocinon

Oxytocin is a natural hormone produced by the brain which plays a significant role in child birth as it helps to make the muscles in the womb contract during labour. There are man-made drugs almost identical to the natural hormone oxytocin which are widely used across UK Maternity Units and have been since the 1960s.

Syntocinon is one of these drugs, which helps the contractions build up to the best strength and speed to encourage vaginal birth. It is given by a drip into your arm. All over the country the same standard dose and speed is used to increase the contractions to the best strength and frequency. Once this happens the dose is not increased any further. The dose and speed of oxytocin are adjusted up or down depending on the number of contractions you are having whilst making sure your baby stays safe.

All women and their babies having oxytocin are monitored closely and you will be looked after by an identified Midwife on the Labour Ward who will also be monitoring the baby's heart rate continuously using Electronic Fetal Monitoring (EFM). If any concerning changes happen, the drug will be stopped or slowed down and this will usually settle the changes over a short period of time (i.e. over several minutes).

There are no known long term health problems associated with the use of oxytocin for either you or your baby. Breastfeeding will not be affected by the dose given.

The standard dose (i.e. the one we usually give) may make your womb contract too often (this happens to about 20% or one in five women). If that happens it may sometimes cause changes in your baby's heart rate which may indicate your baby is becoming 'tired' or distressed (this happens to about 10% or one in ten women and is called 'hyperstimulation'). Rarely oxytocin may also cause you to retain more fluid than normal. To reduce the chances of this happening, the dose and speed of the drip are carefully controlled and you and your baby will be closely monitored throughout.

The most common relatively minor side effects include:

- *Pain/discomfort:* Oxytocin will increase contractions, and is likely to make them more painful for you. Before the treatment starts your Midwife will discuss your options for pain relief, which may include an epidural. The dose is increased every 30 minutes and this allows time for your contractions to build up and for you to get used to them.
- *Headaches*: Your Midwife will be able to give you pain relief to help with these.
- *Nausea and vomiting*: These are quite common in labour even without oxytocin, and your Midwife will be able to give you anti-sickness drugs to help with this if needed.
- *Increased heart rate (tachycardia) or reduced heart rate (bradycardia) in women*: You will be closely monitored through treatment and your treatment will be slowed down or stopped if the changes in your heart rate become a cause for concern.

Your Midwife or Obstetrician can discuss further if you wish. You will be closely monitored throughout treatment and supported by the team caring for you whilst receiving the drug.

2. What is the iHOLDS Trial trying to find out?

Standard dose vs higher dose artificial oxytocin

Many mothers who undergo induction of labour (including those who receive oxytocin) require an unplanned caesarean section to safely deliver their baby. While necessary, caesarean sections (also known as c-sections) generally result in longer hospital stays. C-sections can increase the chance of complications for both mother and baby, and are major surgery that most women would rather avoid. Women whose first baby is delivered by caesarean section are also more likely to require caesarean sections for future babies.

We want to find out if increasing the dose of oxytocin will reduce the chances of requiring a caesarean section. This study will compare the standard dose used routinely in hospitals, with a higher dose. The aim is to achieve regular contractions more quickly, and also allows a higher maximum dose to be used if necessary. The higher dose is already used in some hospitals but we need to see how well it works in comparison with the standard dose.

Randomisation

As we don't know which dose is best, the iHOLDS Trial will compare the standard dose with the higher dose. Women will be put into two different groups and this will be decided 'randomly' using a computer. This is a little like 'tossing a coin' to decide who gets which dose, and is a very standard way that research trials are run. This is really important so that the two groups for the iHOLDS Trial have a similar mix of women in them. Having a similar mix means that we know that if one group of women does better than the other, it is very likely to be because of the dose of the drug used and not because there are differences in women who happened to be in each group.

There is an equal chance of being given either the standard or the higher dose. The standard dose of oxytocin is what is usually used for women who have their labour induced, and is what you will be offered whether or not you agree to take part in this study. In the study, neither you nor your Midwife or Obstetrician will know which group you are in, so they will not know whether you are given the standard or higher dose (although if they need to find out they can do so). This is known as a randomised double-blind trial. If you decide to join the study, both you and your baby will be closely monitored throughout, in exactly the same way as you would if you were receiving standard of care oxytocin.

3. Why have I been asked to take part in the study?

To enable us to answer our research question, we plan to recruit 2,400 first time mothers such as yourself who require oxytocin during induction of labour. We are carrying out our research in approximately 30 hospitals throughout the UK, all of whom have been carefully selected based on their experience of running clinical trials. They all routinely use the standard dose of oxytocin during induction of labour.

4. What would taking part involve?

- If your Obstetrician and/or Midwife decide it is necessary to give oxytocin to induce your labour, and you are happy to join the study after reading this Information Leaflet and asking any questions you may have, you will be asked to sign a Consent Form.
- You can sign the Consent Form at any time before or during the induction of labour process. If you sign it before induction of labour begins, if and when a decision is made for you to receive oxytocin your consent will be verbally reconfirmed.
- Following consent, your Midwife will telephone some information through to our study randomisation line and you will be allocated either the standard or higher dose of the drug.
- You will be given either the standard or higher dose of the drug via a drip in your arm. Both you and your baby will be monitored closely whichever dose you receive.
- Information will be collected from your medical notes about your labour, birth and care, before you and your baby go home and this will be reported to the iHOLDS Trial Office.

- With your consent we will let your GP know you are participating in the study.
- While neither you nor your baby will need any extra tests or visits, we will be asking you to fill in a short multiple choice questionnaire about two weeks after your birth with some simple questions to find out how the birth experience was for you. You can choose whether you complete the Maternal Satisfaction Questionnaire on your smart phone, by email or we can send it in the post to you.

5. What are the possible benefits of taking part?

We cannot predict whether you or your baby will benefit directly from taking part in this trial, but the information we get from carrying out this study could potentially change the way oxytocin is administered to women in the future. Many of the tests and treatments used in hospitals today have been developed with the help of people who took part in research. You will not be paid for your participation in this trial, however all women who take part in the trial and return the Birth Satisfaction Questionnaire will be sent a £5 Amazon shopping voucher.

6. What are the possible disadvantages and risks of taking part?

There are a number of known risks associated with oxytocin when it is given which are outlined in question 1 of this Information Leaflet. We are finding out whether increasing the dose of oxytocin (both the strength and the speed it is given at) will reduce the chances of having a caesarean section, but it may increase your chances of experiencing side effects. The dose and speed of the drug is controlled by your Midwife and Obstetrician who will not know whether you have been given the standard dose or the higher one. They will look after based on the number of contractions you are having while monitoring closely how your baby is doing.

Information in **Part Two** of this Information Leaflet gives more details about how the study is being run and what to do if you have a problem to do with the study. If you are considering joining the study please read this information too.

PART TWO

7. Who is organising and funding the research?

The iHOLDS Trial is a national study run by the Birmingham Clinical Trials Unit (BCTU) at the University of Birmingham. Birmingham Women's and Children's NHS Foundation Trust is the Sponsor of the trial (the group legally responsible for its conduct) and the BCTU is responsible for the day to day running of the study. The trial is being funded by the Department of Health (NIHR Health Technology Assessment programme). The team looking after you will not receive payment for including you in this study.

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

Public members sit on the panel which reviewed and agreed to fund the trial. We have consulted a group of service users during the design of this study. We have dedicated patient and public (PPI) representatives on both our Trial Steering Committee and Co-Applicants Group who have helped to ensure all information provided to women is clear and understandable. PPI input will continue to be an integral part of the trial.

9. Who has reviewed the study?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee (REC), to protect your interests. This study has been reviewed and given favourable opinion by the West Midlands – Edgbaston Research Ethics Committee. This study has also undergone rigorous review by a multidisciplinary group on behalf of the trial funder as part of the funding review process.

10. Will my taking part in the study be kept confidential?

Yes. If you agree to take part in this trial, your details and any information collected about you for this research will be handled, stored and destroyed in accordance with the General Data Protection Regulation (GDPR) and the Data Protection Act 2018.

Who will have access to my data?

The Birmingham Clinical Trials Unit at the University of Birmingham which is running the study (Data Processor), and the Birmingham Women's and Children's Hospital NHS Foundation Trust which is the legal Sponsor for the study (Data Controller). The University of Aberdeen is responsible for the computer system which will randomise you to standard or higher dose oxytocin, and will receive minimal information about you before you enter the study.

What information will be accessed about me and my baby?

We will be using information from your medical records regarding your labour and the birth of your baby as part of this study. If you or your baby are unwell before going home we would also like to have access to this information. You and your baby will not be identified by name and will be identified by a unique 'Participant Number' supplied by the University of Aberdeen during the randomisation process. The only identifiable information supplied to us by your hospital will be your date of birth and initials, which may be used in routine communication between us and your hospital, as well as during the randomisation process. We would also like to record your ethnicity (i.e. your racial background).

In addition we will keep a copy of your signed Informed Consent Form at the BCTU which will be stored separately to your research data and will include your name. The Consent Form will capture your preferred method of receiving the Maternal Satisfaction Questionnaire and you will be asked to provide either your email address, mobile number or postal address for this purpose. If you would like to receive the £5 Amazon shopping voucher as a thank you for completing the questionnaire, we will need to collect your postal address or email address to send this to you.

If you provide your consent to do so, we may contact you in the future to ask permission to collect additional information about you and your baby via NHS Registries. This additional consent is entirely optional and saying no will not affect your participation in this study.

How will my information be stored and used?

All information about you will be securely stored and only people working on the study, or working to ensure the study is running correctly, will have access to the data. We are responsible for looking after your information and using it properly. Information collected about you and your baby will be kept for at least 25 years after the study has finished. This allows the results to be verified if needed.

Occasionally, we may need to check your medical records to make sure that the information provided about you is accurate. This will be done either by clinical staff or by designated trial personnel. The data we collect from you and your baby will be analysed alongside data of other study participants to help us determine the best dose of oxytocin to use. We hope to confirm whether a higher dose helps to reduce the chance of a caesarean section. Under no circumstances will you be identified in any way in any report, presentation or publication arising from this or any other study. Any data stored long-term would not identify you as an individual.

Will anyone else have access to my data?

It may also be necessary to allow authorised personnel from Government regulatory agencies and/or NHS bodies to have access to information about you. This is for your protection, and is to ensure that the research trial is being conducted to the highest possible standards. In addition, we may share anonymised data collected through the iHOLDS Trial with other research collaborators; you and your baby would not be identified by name in any data shared outside of the trial.

11. Involvement of my General Practitioner (GP)

With your consent, we will also let your GP know that you and your baby have taken part in the iHOLDS Trial. Your GP will be provided with a summary of the study but will not be aware of which dose of the drug you are randomised to.

12. What if something goes wrong?

If you have a concern about any aspect of this study, you should 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 through your hospital's Patient Advice and Liaison Service (PALS) team or via the independent NHS Complaints Advocacy Service. In the unlikely event that you or your baby were harmed by taking part in this research trial, there are no special compensation arrangements, if the care offered was appropriate. However, as with standard healthcare, if you were harmed by care that was felt to be negligent, then you may have grounds to consider legal action. The normal National Health Service complaints mechanisms will be available to you in the same way as they are for standard clinical care.

13. What if I change my mind?

Your decision to take part in this research is entirely voluntary and you can change your mind at any stage without offering a reason. This will not affect the standard of care you or your baby receives. Should you decide to discontinue trial treatment and if oxytocin is still in the best interests of you and your baby, the team looking after you will recommence treatment at the standard dose using hospital stock. In this event, although you would no longer be formally in the trial, we would like to continue to collect routine clinical information about you and your baby relevant to the study, and to send you the Maternal Satisfaction Questionnaire for completion after birth, *unless you explicitly tell the staff looking after you that you do not wish for this to happen*. All information collected up until the point of withdrawal of consent will still be used in the study analysis to ensure the integrity of the research.

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

Once the research is complete we aim to publish the results in reputable medical literature. Confidentiality will be ensured at all times and you and your baby will not be identified in any publication. A link to the published results, together with a short lay summary of the study results will be provided on our website when available. It may take several years to complete recruitment and analyse the study results.

Thank you for taking the time to read this Information Sheet.

Contact Information

If you would like more information or have any questions about the iHOLDS Trial you can also talk to:

Your Research Midwife (telephone number: <number>, email: <email address>)
or <insert PI name> (telephone number: <number>)

You can also visit our website: www.birmingham.ac.uk/iHOLDS

Support can also be found through the NHS Patient Advisory and Liaison Service (PALS) (telephone number: <number>, email: <email address>)

Birmingham Women's and Children's NHS Foundation Trust

FUNDED BY NIHR | National Institute for Health Research

BCTU Birmingham Clinical Trials Unit

UNIVERSITY OF BIRMINGHAM